Feline Husbandry

Diseases and Management in the Multiple-Cat Environment

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Dedication

This book is dedicated to all of the cat lovers (individuals and groups) who have supported me and my research during the past 18 years. I am particularly indebted to the members of Save Our Cats and Kittens, who were there when I needed help the most, and to the Robert H. Winn Foundation affiliated with The Cat Fanciers' Association. Finally, I am grateful to my own family, my wife Gerie and our children Stephanie, Holly, Collin and Megan, and to my mother Evelyn Pedersen. Though the word "husbandry" is often applied to the relationship of man and his animals, the term is firmly rooted in experiences of the ultimate living group, the human family.

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Preface

The domestic cat is one of the most difficult animal species to propagate under conditions of close confinement and intense breeding. This is due in part to their comparatively thin veneer of domestication and, in part, to their distinct constitutional nature. Unlike cattle, horses, sheep, goats and dogs, cats are solitary and territorial animals. Therefore, it is against their nature to be confined to limited space and with a large number of other cats. Overcrowding and poor husbandry lead to myriad infectious diseases and behavioral problems. The fact that cats are pure carnivores has also led to many nutritional problems. Though cats require large amounts of animal tissues for food, modern commercial cat foods are increasingly of nonanimal origin. This has led to an interesting array of nutritional disorders.

In spite of difficulties in rearing large numbers of cats in confined quarters, catteries and multiple-cat households are a permanent and increasingly common fixture of modern civilization. Therefore, we must learn how to raise cats in a manner conducive to their optimum health and reproduction. This can be approached in 2 ways: to further domesticate cats by careful selective breeding so they can better tolerate multiple-cat environments; or to optimize conditions within the multiple-cat environment in such a way as to ensure good health. Unfortunately, neither approach is widely practiced. Genetic selection is largely for body conformation and coat color, and often involves extensive inbreeding. Inbreeding, especially when done improperly, leads to more genetic defects and developmental anomalies, and less vigor. Unfavorable husbandry and breeding practices are not done intentionally. Rather, they result from a lack of knowledge of proper husbandry and breeding procedures. Hence, the impetus for this text.

This book was written for veterinarians, laboratory animal managers, veterinary students and cat breeders. This audience was targeted because the goal of raising healthy cats requires that both veterinarians and cat breeders work together. Unfortunately, both cat breeders and veterinarians tend to look only at the individual sick animal: What disease does it have? How do we treat it? The real questions should be: What disease does it have? Why did this disease occur? How can we prevent it from happening to others?

When dealing with confined cat populations, the individual animal is only an indicator of problems in the environment as a whole. Most disease, whether it is behavioral, reproductive, genetic, infectious or nutritional in nature, results mainly from inadequacies in management of the environment in which modern cats live. Therefore, control of disease in multiple-cat environments involves good husbandry practices. The word *husbandry* literally means "to manage carefully and economically." Though often applied to farmers caring for livestock, good husbandry is a moral obligation for everyone involved in the human-animal interaction.

Niels C. Pedersen, DVM, PhD

Contents

Chapter 1

History of Domestic Cats and Cat Breeds

J. Wastlhuber

Domestic cats have intrigued people throughout the world for centuries. Though in some cultures they have been treated as revered creatures, they have at times been considered objects of fear and superstition. Cats still remain mysterious animals, slightly beyond our total understanding. They live somewhat apart from people despite a long history of association and acceptance. Cats have been able to maintain their wild ancestral characteristics and dignity even though they comfortably adapt to the households and conditions of our modern life.

In an age when human individuality is consistently threatened, when the pressures of overcrowding, noise and visual uniformity have become inherent to our daily existence, people are almost envious of cats' autonomous spirit. Cats are used by the advertising industry as familiar symbols of independence, power, graceful elegance and soft luxury. The cat's admired self-sufficiency, combined with an ability to offer affectionate, playful companionship, allows many people to experience natural animal behavior within their own homes.

At one time in America and elsewhere, cats were mostly appreciated for their hunting ability on farms in rural areas. Now urban families show an interest in cats solely for their beauty and personality. Humane organizations and cat fanciers are increasingly successful in their efforts to educate people. Careless breeding of unwanted and stray cats may some day be eliminated, giving hope for a future in which all cats will be valued and protected.

Purposeful and responsible breeding of pedigreed cats has been a peripheral activity for some time in many parts of the world, and began in the late nineteenth century in England. A growing curiosity about the origins and characteristics of the various pedigreed cats is evidenced by the public's enthusiastic response to cat shows and the numerous books in recent years about the different breeds. Understanding the concept of selective breeding of cats begins with an exploration of their early domestication, and the origins and genetic development of the breeds we know today.

Domestication

Human culture evolved thousands of years ago from a nomadic hunter-gatherer type of existence into an agriculture-based civilization. This is when domestication of animals began. Ancient domesticated animals included cattle, dogs, goats, pigs and sheep. The earliest remains of these species are found in the Middle East, along the eastern shores of the Mediterranean and extending to the Caspian Sea and Persian Gulf. The most primitive motive for breeding animals was for provision of meat. Later many other uses for live animals were recognized, and deliberate animal breeding is said to have begun around 3000 BC.

The earliest reproductions of the cat have been found by archaeologists in ancient Egypt, on the island of Crete, in Cyprus, the Orient and among pre-Columbian cultures in the New World. Ancient art of India shows cats in sculptures. When farming and stock rearing began, granaries and barns most likely encouraged multiplication of mice, who were happily protected from their usual predators and provided with an abundance of easy food. Wild and, later, semi-wild cats were probably enthusiastically welcomed by early farmers as the great agricultural civilization of Egypt began to develop in the Nile Valley. The cat's introduction into Egypt is usually credited to the Ethiopians, who brought a few cats into Egypt after their conquest of Nubia.

The Egyptians were prolific artists and they depicted cats in unsurpassed statues, paintings, bas-reliefs, friezes and ornaments. They were sharp observers and skilled with detail, giving us an opportunity today to see these early cats. It is obvious that these people readily accepted cats and loved them with a passion for many of the same reasons as we do today. Through Egyptian art, we can understand their aesthetic appreciation for the beauty and grace of these animals, which go beyond their utilitarian purposes. Evidence that cats became part of Egyptian family life is apparent in paintings that show them to be as pampered as those of today. Cats were embellished with jewelry and often were mummified after death and buried in a special cat cemetary.

At what point the Egyptian cats could be considered domesticated, and how this came about, is not clear. One theory is that wild kittens may have been raised in captivity, with the tamer ones staying to catch mice and reproduce, while the more wild kittens left. Later, some attempt to breed cats, selecting those with rodent-hunting ability and a docile temperament, may have led to gradual domestication. Other speculation is that genetic mutation, abruptly or gradually, may have inhibited certain types of behavior. While wild cats remain essentially solitary except when mating, mothering and being part of a litter, domesticated cats accept people and usually other cats, as well as other animals, in a way that suggests a "litter-like" belonging. The domestic cat, therefore, never matures to a "normal" adult.[44]

Domestic cats as with other domesticated animal species, have a smaller brain than wild cats. This not only reduces aggressiveness but also impairs sensitivity to some degree. Domestic cats may also have a modified hormone balance, associated mainly with a smaller adrenal gland and reduced adrenal secretions.[28] Probably many factors, including genetics and selective breeding, played a part in creating the modern household cat. In any event, cats were semi-domesticated around 2000 BC and fully domesticated in Egypt by about 1000 BC, which is almost 3000 years ago.

Cult of the Cat

No one knows how the simple appreciation for a beautiful and useful animal gradually evolved into deification. The cult of the cat in Egypt eventually reached such an intensity that the penalty for taking a cat's life was death.

It may have originated from the Egyptian fear of darkness. It was noticed that cats had what Egyptians believed was a magical ability to see at night. The Egyptian word for "cat" is "mau," which means to see. The widening and narrowing of the pupils of their eyes showed a relationship between the cat and the sun and moon. Death was considered the ultimate darkness; therefore, cats were thought to have the power to overcome even death. Every year the Nile flooded, destroying crops of grain, but the sun brought new abundant crop growth. The power of the sun and worship of the sun god, Ra, became merged with the cat. The circular form of a sleeping cat became a symbol for the cycles of nature, eternity and many lives.

Another early association with cats was to motherhood and fertility. The cat thus came to represent Bastet, the goddess of sexuality and fertility. Worship of the cat finally peaked around 950 BC, with a yearly festival in honor of Bastet. More than 700,000 people travelled to Bubastis for each annual festival. Historians agree that there was a good deal more intoxication than religious zeal at these gatherings. Some describe the ceremonies as a giant

orgy of drinking, music and general frenzy. This was approved, as it seemed to increase fertility, not only for the crops but Egyptian women as well.[4]

The association of cats with pleasure, the fascination with their graceful body movement and eyes that seem to penetrate the soul and mind, and their self-sufficiency despite domestication are to a great extent the underlying reasons for many people's attraction to cats today.

Migration

Cats were jealously kept from outsiders by the Egyptians, but Phoenician traders eventually exported them to Europe, where they were needed to combat the increasing rat problem. Travelling monks took them east to the Orient and Roman armies smuggled them out of Egypt. Romans especially valued their cats, as they did everything Egyptian. Wherever their armies marched they took their animals, including cats. The Romans also probably took cats to England, though cats were first introduced to the British Isles by the Phoenicians in exchange for tin.

Once cats became common in other parts of the world and their role was diminished to primarily that of a working animal, the cat cult began to decline, beginning about 350-100 BC. Eventually, because the Hebrews associated cats with pagan idolatry and with the rise of Christianity, cats became creatures of the devil and were connected with witchcraft throughout medieval Europe.

Several centuries after Christ, some Asian countries began to import more cats. India was the first to introduce them into religion and Hindu rites, and for a long time obliged each of the faithful to feed at least one cat under his roof.[18] In China, cats were popular pets since the beginning of the Christian era and were considered bearers of good fortune.

In Japan, domestic cats were introduced probably in the 6th century AD, at the same time as Buddhism. Because it was the custom to keep 2 cats in each temple to protect the manuscripts against mice, the role of the earliest Japanese cats was that of guardian. Eventually replicas were placed at entrance doors to protect village homes and to repel disease-carrying rodents. Cats were cherished and kept indoors or on leashes until the Japanese government passed a law in 1602 that ordered all cats released so they would be free to catch the vermin destroying the silkworm industry of the country. The cats of Japan then fell from their aristocratic level to that of a working animal.

Two factors figured strongly in the worldwide migration of domestic cats. Barbarian invasions swept across Europe, bringing with them rats and the plague. The cat's value as a rat catcher brought cats to all corners of the world and helped counteract in Europe the backlash of the church. Second, from earliest times cats have always inspired symbolic connections and superstition. The tradition of bringing cats on board ships was, in addition to the need for combatting vermin, a result of the belief that they brought good luck and could foresee storms. Therefore, oceans did not hinder the spread of cats, as they did the migration of other land animals. Cats were able to enter the New World and Australia because of their compatibility with ships and human explorers. In every port, kittens born on the ships left to settle in new areas. The first cats in America were undoubtedly brought by the pilgrims and were European domestic cats.

Origins from Wild Cats

The exact origin of domestic cats from wild cats is another unanswered question. Cats are divided into 3 main genera: the great cats (lions, leopards, jaguars, tigers); the cheetah; and the small cats, consisting of over 30 varieties, all in the *Felis* genus. All housecats worldwide belong to this genus, known as *Felis catus*. The largest of the *Felis* genus are the puma (100-130 lb) and the caracal (30-50 lb). The smallest is the black-footed cat of southern Africa and the Kalahari Desert (2.5-4.5 lb).

Within the *Felis* genus are various species and subspecies. A fundamental criterion for determining the ancestors of *Felis catus* would be its ability to mate with one of the other *Felis* species and produce fertile offspring. Though domestic cats have successfully mated with many other small cats in the *Felis* genus, including the Geoffroy's

cat, which has a different number of chromosomes, the offspring are not fertile.

Domestic cats can produce fertile offspring after mating with several of the small wild cat species. The wild ancestor of the domestic cat originated in the Middle East, and authorities generally speculate that it is *Felis libyca*, called the African wild cat, of the *Felis sylvestris* species complex.[28] These moderate-sized cats (10-18 lb) are found in Africa and Asia, from the Middle East to India, and also on Corsica, Sardinia and Majorca. They have a lithe body and tawny brown coat, with light stripes on hare-like ticked fur. The legs and tail are ringed with stripes. Unfortunately, these wild cats are rare today and genetically pure examples are almost extinct. They can be interbred with housecats to produce fertile hybrids and they have an identical chromosome structure and number. Mummified Egyptian cats examined in the British Museum had a brain size identical to that of *Felis libyca*.[28]

At one time it was thought that domestic cats descended from the European wild cat, *Felis sylvestris*. This ferocious and intractable cat is found in many regions of Britain, France, Spain, Italy, Germany and central Europe, but is unknown in Scandinavia. It is massively built and muscular, and weighs 10-24 lb or more. The head is broad, with a wide skull and clearly convex profile. It has a heavy jowled appearance, thick fur and a short, thick, heavily ringed bushy tail. The coat is yellowish gray, with vertical mackerel-patterned stripes.

It is believed that *Felis libyca* and *Felis sylvestris* are varieties of the same species. They have identical karyotypes, and mate with each other as well as with domestic cats to produce fertile offspring. *Felis sylvestris* may have played a part in the domestic cat's evolution by interbreeding with domestic cats brought into Europe, possibly introducing the genes for a darker tabby pattern, stocky body type, and smaller, more rounded and wide-set ears. The European wild cat has the largest brain of the *Felis sylvestris* species, considerably larger than that of domestic cats, making it unlikely as a prime ancestor.

Other wild cat species have been suggested as contributing to the evolution of domestic cats. One often mentioned because of its similarity to the Abyssinian breed is *Felis chaus*. These cats are found in Egypt and throughout southern Asia. In the examination of mummified cats from 600-200 BC by Morrison-Scott of the British Museum, there was a small percentage of *Felis chaus* cats; however, these may have been wild rather than domestic cats, and probably were rare. Also the lack of the Abyssinian tabby gene in modern Egypt and Sudan, as reported by the Carnivore Genetics Center, indicates this was not the area of origin.

Evolution of Breeds

The original Egyptian cats were fairly uniform in appearance. Judging from artwork and examined mummified cats, their coat seems to have been short and reddish or yellowish, with only vestigial tabby-like markings or light spotting. These characteristics suited the cats for a desert environment. The body was lithe and muscular, with long elegant bones. The head was moderately large, with large jaws. This body type was adapted to hunting and travelling over large unprotected areas.

Environmental Adaptation

As these cats began to spread around the world, they gradually changed to adapt to their new environments. One of the earliest and most important changes in the cats of Europe was the development of a definite tabby pattern and different body and head type. These variations could be attributed to evolutionary adjustment to a cold environment, favoring a "cold climate compact conformation" as opposed to the "warm climate sinuous form," described by geneticist Roy Robinson as the 2 main domestic cat structural types.[28] However, the influence of possible matings with *Felis sylvestris*, the European wild cat, cannot be ruled out. These cats are sturdily built, with a broad head and blunt nose. They also have far more defined mackerel tabby markings than those seen on the Egyptian cats and may have introduced this important pattern to domestic cats, providing better camouflage in a wooded landscape.

Mutations

Once domestic cats acquired a mackerel tabby pattern and sandy gray color with

black markings, several "ancient mutations" occurred. Recessive mutation on the original or "wild" mackerel tabby allele, which created the classic tabby pattern; nonagouti (solid coat color), which does not allow the tabby pattern gene (carried by all cats) to be manifested; sex-linked orange color; dilution factor; piebald white spotting factor; dominant white; and long hair.

Though many main genes of domestic cats play a part in the genetic variation needed to create different breeds, there are fewer mutant genes in cats than in other animal species. All cats are black or sex-linked red or, in females, a combination of both colors. These colors are seen in various forms and patterns according to the influence of other genetic factors. The dilution factor, for example, acts on colors to produce a lighter tone, turning black to blue or red to cream. Red Abyssinians look red but are not. This is the result of a recessive gene in the black series, called the light brown or cinnamon gene. The concurrent actions of rufous polygenes, which intensify yellow ground color, result in a rich reddish tone. Other important later mutations were the Abyssinian ticked tabby pattern, the albino series (Siamese, Burmese, etc), inhibitor series (chinchilla, shaded and smokes), Manx, bobtail, Rex (Cornish, Devon), hairless Sphynx and, more recently, the wirehair and curled ear.[47]

Geneticists have shown with "cline maps" the probable origin of many of the original colors and patterns. For instance, it seems most likely that the mutation for the Abyssinian ticked tabby pattern originated where the highest concentrations of the gene may be found today. This is centered around Calcutta (37% of cats are ticked). The island of Ceylon has 30% of cats ticked. Other concentrations of the gene include Singapore (24%), Hong Kong (19%) and into Russia.

Though the original breed based on this gene was refined in England, its introduction to that country and others would probably have been the result of colonists and merchants stopping in Calcutta, the major port of disembarkment for the Indian Ocean. A 150-year-old stuffed Abyssinian of Indian origin, purchased and documented by the Leiden Museum, Holland, about 1834, is a unique early example of a modern breed and reinforces the Far East origin of the Abyssinian (T^a) gene.[33] The same gene is also responsible for another ticked breed found in southeast Asia, the Singapura.

A particularly interesting mutation occurred somewhere in the Far East, resulting in the temperature-sensitive albino series of alleles. This gave us the Siamese, Burmese (called Copper Cats in early times) and Tonkinese, a hybrid combining both varieties. These cats are described and pictured in manuscripts from the ancient Thai city of Ayudha (existing from 1350 to 1767). Blue-eyed solid whites and albino pink-eyed whites also were produced by this series.

Geographic Restriction

Another major reason for perpetuation of mutant genes, along with environmental adaptation, was geographic restriction. A mutant of ancient origin is the recessive longhair gene. This gene was probably of spontaneous origin and then became fixed through inbreeding in an isolated cold climate. Speculation is that this happened in Turkey, possibly in Iran and also in Russia.

A letter written in 1856 by M. Lottin de la Val refers to his encounter with a "beautiful species of cat on the great Armenian plateau at Erzeroum," and that these longhaired Angora cats were the dominant variety in Kurdistan. He described whites, grays (blues) and orange-spotted (Turkish Van) cats. Kurdistan is a mountaineous plateau in eastern Turkey, adjacent to Iran (Persia). It seems to be the logical place for development of the longhair gene, providing isolation and a cold climate. The early inhabitants were primitive, nomadic people, not likely to have valued unusual cats as trade items from elsewhere. Angora and Persian cats eventually reached Europe by caravans over the mountains by the late 16th century.[12] Longhaired cats were also imported directly from Russia into England. But instead of the solid colors found in Persia and Turkey, all of these were brown tabbies, with the exception of 2 that were black.

The British eventually began to make a distinction between the longer-bodied, large-eared and mostly blue-eyed white cats from Turkey and the more compact, large-boned, shorter-headed golden-eyed cats

from Iran. They preferred Persian-type cats, mainly because of the deafness in Turkish white cats, which decreased the popularity of what we now know as Turkish Angora cats. Had it not been for the Turkish Angora colony established at the zoo in Ankara, this beautiful breed might have become extinct. It is now accepted in many colors other than white, and deafness is no more of a problem than in any other white cat.

Another early longhaired cat was described in the book, *Histoire Generale des Voyages*, published in the early 18th century. The Sumxu was from the area around Peking in China and had pendulous ears, and black or yellow extremely glossy long fur. It is interesting to note that mutations in cats very often have repeated themselves. An American painting by Joseph Stock, a portrait of "Mary Jane" with her cat in 1838, shows a young girl with a folded-eared cat. This was 123 years before the discovery of the mutation in Scotland in 1961, which led to development of the Scottish Fold breed.

American domestic longhaired cats were most likely descendants of European shorthairs who arrived in this country with the early settlers of New England. Cats carrying the recessive longhair gene were better able to thrive in the harsh climate of northern New England. Through geographic isolation and survival of the fittest, they became the basis of the Maine Coon breed.

Other well-known breeds probably originated as a result of geographic restriction. The Manx is one of the oldest examples of a spontaneous mutation that existed in isolation on the Isle of Man in the Irish Sea off the west coast of England for many centuries. The Korat was believed to have originated in a high remote region in northeastern Thailand, known as the Korat Plateau.

Superstition

In addition to evolutionary adjustment and geographic restriction, a third factor in establishment of breeds is myth and superstition. Korats, like other Oriental cats, were considered to bring good luck by the Thai people and could only be obtained as a gift. A pair of Korats was a traditional wedding present, symbolizing a gift of silver, which would bring prosperity and ensure a long, happy marriage. The blue color, which is a result of recessive dilution of solid black, and silvery tipping were perpetuated for this reason.

Occasionally these cats were given as a token of great esteem. Cats in the Far East were sometimes kept as sacred animals in temples because of the belief that the soul of a very spiritually advanced person entered the body of a cat when that holy person died. Following the cat's death, the holy person's soul would finally reach Paradise. Oriental cats were therefore often confined and bred by monks in isolated monasteries keeping gene pools separated and helping to firmly establish breeds.

Human Preference

Another important factor, human preference, affected migration of cats with various patterns and colors. For example, the highest frequency of the sex-linked orange allele occurs in India, southeast Asia and Japan, and has diffused westward.[28] The bright color may have been appealing, causing people to import cats into Europe and England for their beauty as well as for their hunting ability.

Breeds and Cat Shows

Distinction between cats based on appearance began to interest some people by the 18th century, if not earlier. In 1756, cats were featured in *Histoire Naturelle* by Comte de Buffon, indicating recognition of breeds. By the mid-19th century, the concept of cat breeds was established in England. People began to take notice of some of the more exotic-looking cats, which the British took home from their trading and colonization travels. Cats imported from the Far East were startling in comparison to the more familiar stocky homegrown British shorthaired cats. The longhairs from Turkey and Persia were equally sensational, and the Russian Blues from the Archangel seaport area were also different.

With the work of Louis Pasteur in the mid-19th century, the cat's position in society changed drastically. Suddenly most ani-

mals were dreaded as potential disease carriers. But cats, known to be a model of cleanliness, were acceptable and once again were welcomed into European and British homes to be appreciated for their beauty and personality. Cat breeds became even more respectable because Queen Victoria owned 2 blue Persians.

Cat Shows

The first National Cat Show at the Crystal Palace in London in 1871 marked a revolution in attitude and the true beginning of cat breeding for exhibition. The show drew an entry of 170 cats and kittens, but not everyone approved of the unusual cats. A contemporary journal described one of the cats as "an unnatural, nightmare kind of cat." This was a sealpoint Siamese. The National Cat Club was founded in 1884, and the British began to refine and develop most of the breeds that eventually were exported to America. By 1889, the Crystal Palace show entry was 600 cats, and more than 20,000 people crowded in the huge hall to see the pedigreed cats.

The first cat in America to have pedigree records established was the homegrown Maine Coon. People in Maine were proud of their handsome longhaired cats and kept track of parentage long before official cat registries were begun. A black and white, known as Captain Jenks of the Horse Marines, was mentioned in cat literature as early as 1861. When the first large American cat show was held in New York in 1895, a Maine Coon was best cat. They declined in popularity as the more flamboyant Persians came into the country from England.

The Cat Fanciers' Association

The beginning of the American Shorthair breed started with a pedigreed red tabby British Shorthair imported in 1900 or 1901. This animal eventually was the first shorthaired cat registered by The Cat Fanciers' Association (CFA). Other British Shorthairs were later imported and bred to domestic shorthairs in America. These American cats still retained the powerful muscular body type of the cats brought over by early settlers because there had been no opportunity to crossbreed with the more slender Oriental cats. The breed was called Domestic Shorthair until 1966, when it was renamed the American Shorthair. Until recent years, this breed maintained an "open registry," allowing outcrossing to mixed-breed domestic cats to enlarge the gene pool and keep the breed healthy and vigorous.

In addition to natural breeds and established breeds, which have been continuously bred to maintain their original appearance or modified to the arbitrary preferences of breeders, certain breeds are considered hybrids. Some examples are the Oriental Shorthair, Colorpoint Shorthair, Bombay, Tonkinese and Ocicat. These cats have been created by mating 2 or more breeds to create a distinctive type of animal.

Other breeds have come about as the result of spontaneous mutation. A mutation, or hybrid, by CFA rules, may be bred back to the breed from which it originated for a specified length of time to ensure a large gene pool. CFA rules generally require 5 generations of CFA-registered cats behind any imports or cats from another association; however, there are many exceptions to this requirement.

With the organization of CFA in 1906, registration of cats and kittens, promotion of cat shows, and the goal of improving the general welfare of cats became firmly established in America. An orange and white male longhaired cat, named Peter, who was born May 2, 1906, was the first cat to be registered with CFA. Today this organization is the largest pedigreed cat registry in the world, and licenses over 350 shows each year in North America and Japan. History was made for the CFA in 1988 when the organization's constitution was modified to allow foreign club memberships. This is the beginning of CFA shows throughout the world.

Other registry groups include several smaller associations in America, the Governing Council of the Cat Fancy (GCCF) in England, the Canadian Cat Association; the Federation Internationale Feline (FIFe) in Europe and its affiliated clubs in various parts of the world, and independent cat-registering organizations in Europe and Australia. Each organization has its own rules for shows, breed recognition or acceptance, and written standards for breeds. There is increasing communication among breeders

throughout the world and exchange of cats for breeding purposes. In 1987, the first cat show ever held in Russia drew about 30,000 visitors to Moscow.

New breeds are occasionally introduced, through discovery in their native land or as a result of hybrid matings. The latest mutation to be recognized is the curled-back ear, which occurred in 1981, leading to the American Curl as a new breed. All of the registering associations have their own rules on accepting new breeds and colors. CFA is conservative and difficult concerning new varieties.

The purpose for rigid requirements is to allow time to fully evaluate whether a new addition will really enhance the cat fancy. A new breed should be distinctive and not infringe on the appearance of an existing breed. Rather than the whim of one individual, there should be sufficient breeders interested in a planned breeding program and reason to believe that the public will respond in a positive way to the new cats as desirable pets. Matings must demonstrate that the appearance of offspring is predictable, and a proposed standard must be developed once there is some experience with resulting offspring. Most of all, it is important to determine that the new bred is free from any harmful genetic traits and will be an asset to the world of pedigreed cats.

It takes a minimum of 10 breeders working with a new breed and documentation of at least 50 specimens to formally apply for CFA registration, which is the first step in recognition. Once registration is achieved, the cats may be presented at shows in the "Miscellaneous Class," which is noncompetitive, so that judges, other breeders and the public become familiar with the new cats' traits. A 5-year minimum is required before the breed may apply for the next step.

"Provisional breed" status requires 100 or more specimens and, among several other requirements, a breed standard proposal. The breed must then be extensively shown in all areas of the country, reports submitted by judges, and information presented to the CFA Board regarding every aspect of the breed. Finally, with proof that 25 different cats have been shown in all 7 American Regions, a standard agreed upon by the breeders, and an outline of all acceptable colors and patterns developed, the new breed may be presented to the CFA Board for "Championship" status, allowing full competition with the other breeds.

Acceptance at preliminary levels carries no guarantee for automatic eventual Championship approval. Often many years go by, along with a great deal of expense, hard work and devotion, to achieve full CFA acceptance of a breed. Recognition of new colors within existing breeds involves similar requirements and sometimes evokes strong resistance from established breeders.

The CFA presently recognizes 31 pedigreed breeds of cats (Table 1). Four additional breeds have been accepted by CFA for registration. Divisions have been created within 2 of the breeds, Persian and Burmese. Among the almost 60,000,000 cats in homes in the United States, it has been estimated that less than 10% are pedigreed. The popularity of the various breeds, as determined by breed registration figures, is given in Table 2. Almost two-thirds of pedigreed cats registered by CFA in 1988 and 1989 are of the Persian breed.

Philosophy of Breeding

One of the prime reasons for the continuing growth of the cat fancy is the competitive and social contact of a variety of different people bound together by their interest in cats. Cat shows are the focus of this contact, and allow breeders to assess their breeding programs and promote the various breeds to the public. Mixed-breed "household pets" are also included for competition in their own class. Cat shows serve as a major means to educate the public about cats in general and to elevate the status of cats in society.

Most people who breed cats are idealists who work hard to produce large litters of beautiful kittens, anticipating all to be excellent, desirable examples of their breed. Hardy, healthy kittens and cats with good maternal abilities are taken for granted by novices. Breeding cats is challenging, and those who stay involved over a long period find they need some knowledge of veterinary medicine and genetic principle; hence the need for books on feline husbandry.

People who breed cats believe they benefit society in several ways. There is great

Table 1. Breeds recognized by CFA for championship competition, 1990.

Abyssinian	Korat
American Shorthair	Maine Coon
American Wirehair	Manx
Balinese	Ocicat
Birman	Oriental Shorthair
Bombay	Persian
British Shorthair	Solid Division
Burmese	Shaded Division
Sable Division	Smoke Division
Dilute Division	Tabby Division
Chartreux	Parti-Color Division
Colorpoint Shorthair	Bi-Color Dvision
Cornish Rex	Himalayan Division
Cymric	Russian Blue
Devon Rex	Scottish Fold
Egyptian Mau	Siamese
Exotic Shorthair	Singapura
Havana Brown	Somali
Japanese Bobtail	Tonkinese
Javanese	Turkish Angora

Breeds Accepted for Registration

American Curl	Oriental Longhair
(Longhair and Shorthair)	Turkish Van
Norwegian Forest Cat	

historic value for all of those breeds, which would become extinct without the continuing interest of a relatively small number of people. Another factor is the tendency throughout history for the public to want both unusual as well as predictable appearance and personality in cats. The desire for something out of the ordinary is characteristic of every culture as it becomes more affluent. Some people are attracted to cats with the "wild cat" look of an Abyssinian, Somali, Ocicat or Egyptian Mau. Others like the exquisite, racy style of a Cornish Rex, the dependent and highly vocal Siamese, or the placid sophistication of a Persian. To emphasize and maintain the visual distinction among the various breeds, as well as the associated temperament, are constant goals of breeders.

Because the range in size among breeds is relatively slight, breeders have manipulated polygenes to emphasize subtle differences in coat texture, colors and patterns, as well as body and head type, always battling the temptation to push them to the extreme. The smallest of the breeds is the Singapura, which weighs 4-7 lb, and among the largest of breeds are the Maine Coons and Ocicats, with males at 15-18 lb.

The less than 10% of pedigreed cats estimated to be in American households compares to more than 50% of purebred dogs in pet-owning households. Interest in pedigreed cats as pets appears to be rapidly increasing throughout the world, and cat breeders want to respond to this growing demand without jeopardizing the vigor and quality of their breeds. Breeders do not believe that their activities worsen the mixed-breed cat overpopulation problem, because if all recognized breeds were to disappear, it would not only be a great loss but would not begin to affect the circumstances created by a lack of caring and knowledge on the part of those who don't place significant value on cats.

In understanding the philosophy of cat breeding, it is important to realize that breeding is not based solely on genetics. A cat is a combination of genes, but a breed is a combination of qualities as determined by breeders. Unlike the situation with animals bred for food production, speed or other performance, the whole purpose for maintaining cat breeds is to increase their appeal by enhancing distinction in appearance and personality. The science of genetics is used to help in breed classification and to ensure that cats will breed true to given expectation; however, many breeding decisions and classifications are arbitrary and inconsistent. If breeders were only concerned with producing strong, healthy, beautiful cats, then mixed-breeds would suffice. Without the desire and effort to achieve distinct breed identity, the cat fancy would not exist.

Producing homozygous animals of the most uniform appearance and personality should not be the goal of cat breeders, as this can reduce resistance to disease. Some variety within the scope of breed standards is necessary to keep the breeds healthy. Fortunately, in most breeds there is strong demand from the public for pet kittens that may vary somewhat from the ideal standard. Ethical breeders always sell these with written agreements stipulating that these pet quality animals will be altered and not used for breeding.

Table 2. Numbers of the various breeds registered with the Cat Fanciers' Association in the United States, 1988 and 1989.

Breed Name	Male	Female		1989 Total	1988 Total
Persian					
Traditional	9,485	14,148	23,633		
Pointed Pattern	8,885	12,636	21,521		
Colorpoint Carrier	4,659	7,034	11,693		
Total Persian				56,847	53,121
Siamese	1,544	2,199		3,743	3,710
Abyssinian	1,158	1,511		2,669	2,387
Maine Coon	1,144	1,305		2,449	2,001
Burmese	468	738		1,206	1,080
Oriental Shorthair	521	658		1,179	1,054
Exotic Shorthair	417	707		1,124	950
American Shorthair	492	612		1,104	1,002
Scottish Fold	421	562		983	844
Birman	372	546		918	731
Colorpoint Shorthair	318	465		783	715
Ocicat	321	401		722	519
Cornish Rex	316	390		706	660
Manx	220	332		552	569
Tonkinese	223	326		549	399
Balinese	211	286		497	484
Russian Blue	216	276		492	472
Somali	225	254		479	444
Devon Rex	137	173		310	239
British Shorthair	133	155		288	275
Japanese Bobtail	76	150		226	188
Javanese	70	121		191	191
Egyptian Mau	89	96		185	180
Norwegian Forest Cat	58	76		134	185
Chartreux	57	62		119	87
Bombay	52	62		114	83
Turkish Angora	49	55		104	151
Korat	47	51		98	124
Havana Brown	45	42		87	102
Singapura	28	36		64	59
American Curl	34	26		60	47
Cymric	23	34		57	39
Turkish Van	243	33		57	63
American Wirehair	24	33		57	63
Oriental Longhair	5	9		14	86
Total Cats Registered	32,558	46,587		79,145	73,254

In recent years breeders have become increasingly concerned about the detrimental effects of selective breeding on the health of pedigreed cats, as well as the difficulty in finding outcrosses within the breeds without common ancestry. Problems occasionally surface, and sometimes they are not recognized until they are widespread and it is almost impossible to rectify the situation.

When problems arise from intensively breeding certain bloodlines, breeders have several options. They may consider outcrossing to imported cats or cats from other

States, 1988 and

)88 Total
53,121
3,710
2,387
2,001
1,080
1,054
950
1,002
844
731
715
519
660
569
399
484
472
444
239
275
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86
73,254

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m intensively breeders have consider out- its from other

associations of the same breed, using another breed, or requesting that CFA allow use of cats of unknown parentage, either from the country of origin or through use of mixed-breed cats. In February, 1989, the CFA Board of Directors ruled to allow Japanese Bobtail breeders to register bobtailed cats of unknown parentage from Japan. Undoubtedly this will set a precedent.

In some instances, enlarging the gene pool helps solve problems of general health, and replaces cats lost to defects that cause death or have been culled from breeding because they carry defects. However, outcrossing, in itself, does not solve specific genetic health problems if they are caused by a recessive gene or by a dominant gene with incomplete penetrance or other complicating factors, such as polygenic heredity. Outcrossing can actually spread a lethal or harmful genetic factor that may remain undetected for several generations. With inevitable linebreeding to recapture the lost phenotype, the harmful genes eventually reappear. Outcrossing would have to be continuous to be effective. As soon as carrier cats appear on both sides of the pedigree, there is a chance of recurrence.

Some fanciers have begun to use test breedings to establish "clear" cats, which can then be used in outcross matings to bring new genes into the breed. Methods for test breeding have been established by Roy Robinson in the book, *Genetics for Cat Breeders*.[27] Test breeding, however, is often highly impractical for a breeder. Rigorous selection, requiring removal of not only affected cats but both parents producing a litter with one affected kitten, is still the most successful solution for breeding problems at this time.

Another alternative is being explored. Through the use of molecular biology in pilot studies funded by the Robert H. Winn Foundation (established by CFA to provide funds for feline health studies), scientists are using DNA hybridization patterns to identify undesirable genes in cats. In the future it may be possible to diagnose genetic weaknesses through a simple blood test before cats are bred. Kittens or cats appearing normal but carrying genes for health defects could be sold as pets and thus eliminated from breeding programs.

Chapter 2 contains a detailed discussion on feline genetics.

Cat Breeds

British Shorthair

The British attitude toward cats in the 1800s was that they were primarily skillful ratters. This view began to change around the time of the first important cat show, the Crystal Palace Exhibition of 1871 in London. The British Shorthair was prominently represented at this show, which was organized by Harrison Weir, a well-known painter and illustrator.

Weir was also the author of the first comprehensive book on cats, *Our Cats and All About Them*, published in Britain in 1889. The book included general information about cat care and breed standards, and the British Shorthair was prominently featured. At the same time, English children were being exposed to the delightful mischievous antics of the cats drawn by Louis Wain, who, for 60 years from 1880 to the beginning of World War II, illustrated domestic cats and rare breeds in hundreds of books, magazines and newspapers. Wain's cats were depicted fondly as close family companions that did much to popularize them as esteemed pets with unique beauty and character. By the end of the 19th century in England, cats had evolved into a highly fashionable status symbol, and British Shorthairs were very much respected.

The early British Shorthairs were the result of free breeding among feral stock and therefore varied in appearance. In the late 1800s, breeders gradually began selecting cats that most clearly displayed the type they most desired. The body of a fine British Shorthair reflects the hardiness and powerful build needed by a working cat that has survived through self- reliance. Today's standard describes a medium to large cat. The body is compact, with good depth and a full broad chest, short to medium strong legs, and rounded paws (Fig 1).

The British Shorthair head is the first noticeable difference between this and other breeds derived from domestic shorthairs. The head is round and massive, with very wide-set rounded ears and large round eyes. The profile has a gentle dip to the nose and

the muzzle is distinctive because of large round whisker pads, all giving a soft appealing expression to the face. Eye color is a stunning deep gold or copper, except in the whites, which may also have blue eyes or odd eyes (one blue and one gold).

After World War II, all of the breeds suffered and the British Shorthairs were almost extinct. The few left were bred to cats of more foreign type, and later breeders had to work hard to restore the breed. Persian outcrosses were used to recapture the massive bone and stocky body type. This however, produced a different coat texture, which was often soft, and fluffy and sometimes too long. The original British Shorthair coat was short, dense and resilient, with a "crisp" firmness rather than a soft feel. Because today a long or fluffy coat is cause for disqualification, much work has been concentrated on preserving the original coat. In the early days, the most popular colors were the solids, especially blue; however, today, cats of many colors and patterns are bred.

Interest in the breed grew slowly in America during the 1960s and 1970s. American associations resisted recognition of the British Shorthair because of the Persian blood in their background. It was thought that there was a genetic similarity to the American hybrid breed, the Exotic Shorthair, which is a cross between the American Shorthair and Persian. The British Shorthairs finally achieved CFA Championship status in 1980.

The temperament of these cats is often compared to that of their ancestral English owners: dignified and reserved. British Shorthairs are gentle and not disturbed by noisy household activity. They enjoy attention but are not pushy. In contrast to their imposing appearance, their tiny voices can hardly be heard. They are generally hardy and easy to groom.

Scottish Fold

The story of the Scottish Fold breed begins in the rugged Perthshire region of Scotland in 1961. William Ross, a shepherd, happened to notice an unusual pure white cat with forward-folded ears on a neighbor's farm. He and his wife, Mary, were intrigued and were told that the mother had normal ears and the father was unknown. They were promised a kitten from this cat, named Susie, if she ever produced another with folded ears. The following year Snooks, who was white like her mother, was born with folded ears, and the Rosses began to develop this unique breed that evolved from a spontaneous natural mutation. It was later discovered that the gene responsible is a simple dominant one, and all registered

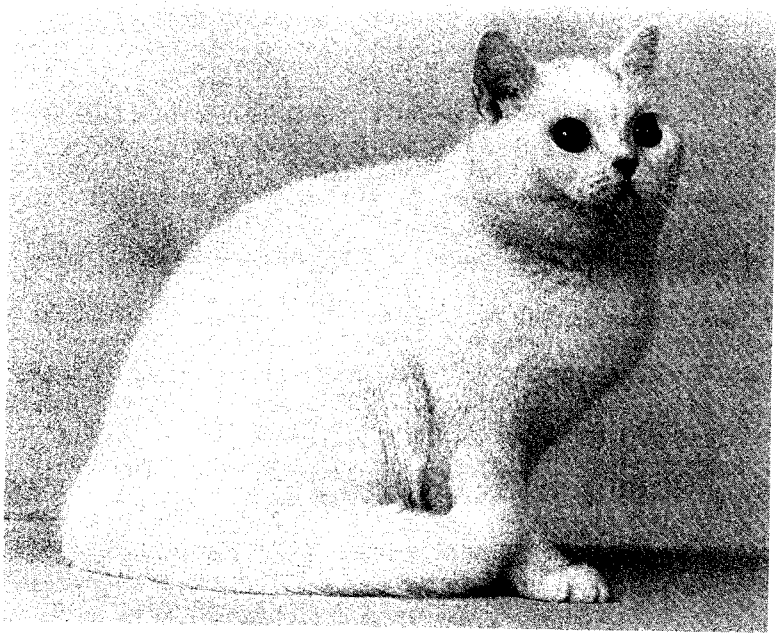


Figure 1. A female British Shorthair. (Photograph by Jane Howard)

Scottish Folds today trace their heritage to Susie and Snooks.

Snooks was bred to local farm cats and British Shorthairs in Scotland to produce the foundation stock. Photographs of these early cats indicate that the body, head and coat qualities, characteristics of modern Folds, were firmly established from the beginning. The sturdy, well-padded, moderate body, short neck, round and full-cheeked head, and extremely dense and resilient short coat all helped these cats withstand the harsh Scottish climate and the condition that were part of their lives as working farm cats.

By 1966 the Ross's cats were registered with the British GCCF (Governing Council of the Cat Fancy). Dr. Niel Todd, a New England geneticist and a founder of the Carnivore Genetics Research Center in Massachusetts, became interested in the breed and brought 3 Folds to America in 1970. Though several litters were born through Dr. Todd's efforts, it was not until Salle Wolf Peters acquired Hester, one of the original 3 imports, as well as a daughter of Snooks, that the first Scottish Fold was registered in America in 1972. By 1973 Folds were accepted for experimental registration by all of the American associations. CFA Championship status followed in 1978.

The early breedings of Folds in America were to the various breeds then available: American Shorthairs, Persians, Exotic Shorthairs and mixed-breeds. This outcrossing created hybrid vigor and helped maintain the breed's sweet easy-going temperament. Outcrossing to American Shorthairs and British Shorthairs is still allowed by CFA. Despite the efforts to maintain a large gene pool, for many years, the breed has been besieged with denouncements of defects related to the folded-ear mutation.

In 1974 the breed was banned in England by the GCCF. The official reason given was that there were problems of ear mite infestation and that many Folds were born deaf. Americans rejected this decision, arguing that cattery conditions were responsible for ear mites and not folded ears. Because most of the Ross's early stock was white, the Americans believed the incidences of deafness were connected to the genetics of blue-eyed whites, which sometimes cause kittens to be born deaf in both pedigreed and mixed-breed litters. As Americans continued to breed Folds in many other colors, the "deafness problem" was greatly reduced.

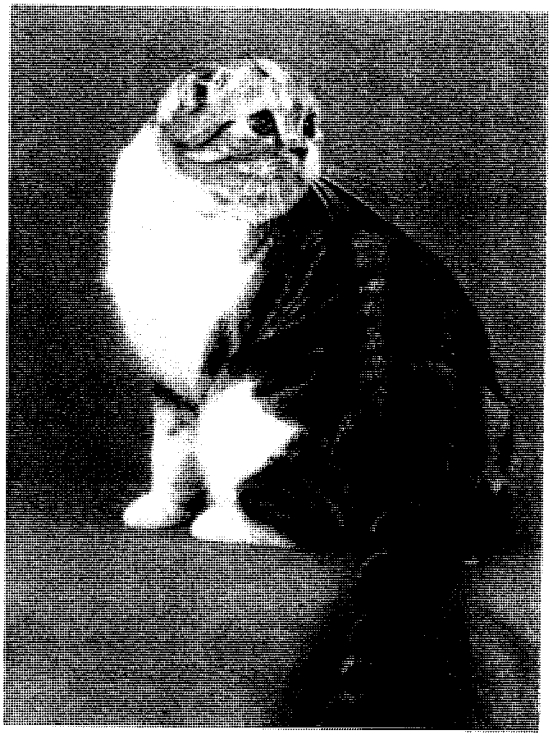
The most serious problem seemingly inherent in the breed actually was that of skeletal abnormalities. To increase the percentage of folded-eared kittens, breeders often crossed folded-eared cats. The resultant skeletal abnormalities were described as osteodystrophy by Dr. Oliphant F. Jackson, a British geneticist. When in the later 1960s the Rosses presented several of their cats to Dr. Jackson at the Royal Free Hospital Medical School in London, he began breeding Folds. His studies led to isolation of the mutated gene responsible for folded ears and a great deal of information about the effects of this condition. He wrote, "The skeletally affected cats have not only short, thick inflexible tails but gross deformity of the limb extremities." When he bred Fold to Fold, 1 of 3 folded-eared kittens developed lesions, even if neither parent showed evidence of the deformity. When a folded-eared cat with lesions was bred to a straight-eared cat, none of the folded-eared kittens had lesions.

Dr. Jackson's report was published in the *Bulletin of the Feline Advisory Bureau* in 1975. Though his work demonstrated that osteodystrophy could be avoided by not breeding Fold to Fold, breeding stopped in England. Breeders in America tested Jackson's findings and discovered the same results. The first sign of the problem in a Fold is a tail that is overly thick at its base, foreshortened and inflexible due to abnormally thick coccygeal vertebrae. This is cause for disqualification in the show ring by a CFA judge. Though some kittens show no radiographic (x-ray) signs of defects when they are young, problems become evident with age. Some breeders still question whether Jackson's findings may have been the result of early close inbreeding and hope that in the future, after years of constant outcrossing, it may be eventually possible to safely breed folded ear to folded-ear cats.

Currently, conscientious breeding practice requires keeping straight-eared Folds as well as several cats of the allowable outcross breeds to produce cats free of os-

teodystrophy. Though the breed is most distinguished by their tightly folded ears, other characteristics add to their special look. Large round eyes, a gentle nose curve, prominent cheeks and whisker pads all contribute to the sweet expression of surprise that is typical of the Scottish Fold face. Medium sized with a well-padded, rounded body, these cats give the impression of softness and cuddly appeal (Fig 2). With a sweet natured, quiet and friendly personality, they are as "laid back" as their early British domestic ancestors.

Figure 2. The Scottish Fold. (Photograph by Jane Howard)



Manx

The origin of the Manx is surrounded by legend and mystery. Tailless ancestors lived on the Isle of Man in the Irish Sea off the west coast of England for many centuries. The best-known legend dates back to 1588, when one of the ships in the Spanish Armada was wrecked near the Isle of Man, and several tailless cats are said to have swum ashore and lived to perpetuate the breed. It was also speculated for many years that Manx cats evolved from the short-tailed and tailless cats taken from Japan to England by Phoenician traders in ancient times. Now it is known that, genetically, the bobtailed cats from the Orient and the Manx cats were entirely different.

Genetics experts today believe that the Manx is a result of a spontaneous mutation and that a dominant gene, along with modifying polygenes, is responsible for variable tail length. Records on the Isle of Man describe the cat as a mutation originating from resident domestic cats.

The various tail types are generally classified in 4 groups. The show-quality Manx is "rumpy," with no complete sacral vertebrae. The rump is completely rounded and there is a hollow at the base of the spine. Some associations, including CFA, allow the "rumpy-riser" without penalty as long as only a few flexible sacral vertebrae are present and the rump appears rounded. A "riser" with fixed vertebrae fused in a vertical position, so "it stops the judge's hand," as described in the CFA standard, is penalized.

A "stumpy" has a short tail, sometimes with curved or kinked coccygeal vertebrae. A "longy" is a tailed Manx with a normal-appearing tail. The stumpy and longy Manx, along with the genetically normal-tailed offspring, are valuable as breeding cats. Many Manx breeders think it is desirable to dock the tails of "longy" kittens shortly after birth to increase their acceptability as Manx pets to be altered and not shown.

It is surprising that the Manx, though one of the oldest known breeds, is still considered among the most difficult to breed. The primary characteristic, taillessness, has long been thought to be the result of the genetic defect that can cause associated weaknesses affecting the whole spinal column. This notion has been challenged in the last few years by American breeders who have greatly decreased incidences of weakness through careful use of sound cats.

Another factor in the breed is the lethal nature of the Manx gene. Homozygous kittens, inheriting the gene from both parents, die in the womb, thus reducing the breed's average litter size. However, because the Manx breed has few reproductive problems, the average litter size, according to CFA lit-

ter application birth statistics for 1989, is higher than that of 6 other breeds and has increased since 1979.

Despite some drawbacks, the Manx has continued to thrive as a favored pet throughout the world since the earliest days of the cat fancy. A Manx club existed in England in 1901, and Manx were among the first cats registered in Europe. They arrived in America during the 1930s. A loyal group of followers and dedicated breeders remains determined to overcome any problems that may be inherent to the breed.

Taillessness is by no means the only quality to distinguish the Manx. The Manx is stout, of medium size and solidly muscled, with sturdy bone structure (Fig 3). Rounded shoulders, hindquarters and head describe the overall impression of these cats. Prominent cheeks and jowls, a well-developed muzzle with large round whisker pads, full round eyes and widely spaced medium-sized ears characterize the head, which is slightly longer than broad and sits on a short thick neck. The line from shoulders to rump should be a short smooth continuous arch. Broad chest development causes the forelegs to be set well apart.

Because the hind legs are relatively long, the rump is considerably higher than the shoulders. Muscular thighs and a deeper flank than that of any other breed add to the impression of great substance. The short dense coat also has a unique double texture, with a noticeable cottony undercoat and hard, glossy, open guard hairs. Almost all coat colors and patterns are allowed in the Manx except for those showing hybridization with the Siamese gene.

The Manx breed has maintained its popularity not only through its appearance but also because of a lively owner-oriented personality. Their reputation for being intelligent, clownish, affectionate and devoted companions helps ensure the strong, loyal following enjoyed by this breed.

Cymric

At one time, Manx were bred with British Shorthairs and American Shorthairs, when the stock from the Isle of Man became scarce; outcrossing is still practiced in England. In the late 1960s in North America, long-haired kittens began to appear, reflecting the recessive gene inherited from the tailed outcrosses. Longhaired and shorthaired cats were commingled on the Isle of Man and by the Isle of Man government cattery. A group of enthusiasts began to develop this variety and the long-haired Manx is now called a Cymric. These cats attained their "provisional" status as a separate breed in CFA and are also recognized by several other associations. Full Champion-

Figure 3. The Manx. (Photograph by Jane Howard

ship status was approved for the Cymric in 1989.

The standard is almost identical to that of the Manx, except for the coat, which is of medium length. The distinguishing look of the Cymric is accentuated by a coat gradually lengthening from the shoulders to the rump, with hair on the breeches, abdomen and neck ruff longer than on the trunk (Fig 4). The neck ruff is bib-like around the chest, and toe tufts and ear tufts are desirable. Cymrics appear to be Manx in full costume.

American Shorthair

The first domestic cats in North America arrived with the pilgrims from Europe. Domestic shorthairs are said to have been on board the Mayflower in 1620. It may be assumed that these ship cats would have been chosen for their skill in hunting as well as their hardiness and easy-going temperament. These cats intermated for generations in the New World, and their progeny gradually moved across the country with the pioneers, being used to control the rodent population in colonial settlements and as companions. The harsh weather, particularly in northern New England, favored strong healthy animals able to survive in the most severe conditions.

American domestic cats were free roaming and free breeding but remained of consistent appearance until the late 19th century, when the more exotic imports began to come into the country. Originally the breed was known as the "Shorthair." The first shorthaired cat to be registered by CFA was actually an imported British Shorthair, a red tabby male sent in 1900 to Mrs. Jane Cathcart. Mrs. Cathcart was a cat lover who promoted the Shorthair breed in the early 20th century. Later a silver tabby male was imported from England. In 1904 Mrs. Cathcart registered the first American-born Shorthair, "Buster Brown," a male smoke of unknown domestic parentage.

Though for many years domestic shorthaired cats were taken for granted and neglected in the show ring, several dedicated breeders worked to develop a variety of colors and perfect the tabby patterns while maintaining the hardy, muscular structure of the early "native" cats. By the late 1950s there were 50 Domestic Shorthairs, as they were then called, in the CFA Stud Book. Gradually breeders became anxious to distinguish their pedigreed cats from mixed-breed cats, who generally no longer displayed the original large-boned body conformation. The breed was renamed the American Shorthair in 1966.

The CFA show standard strongly emphasizes the character of the early true "working cat," with "no part of the anatomy so exaggerated as to foster weakness" and "conformation indicating power, endurance and agility." The coat should be thick, even and of hard texture, "dense enough to pro-

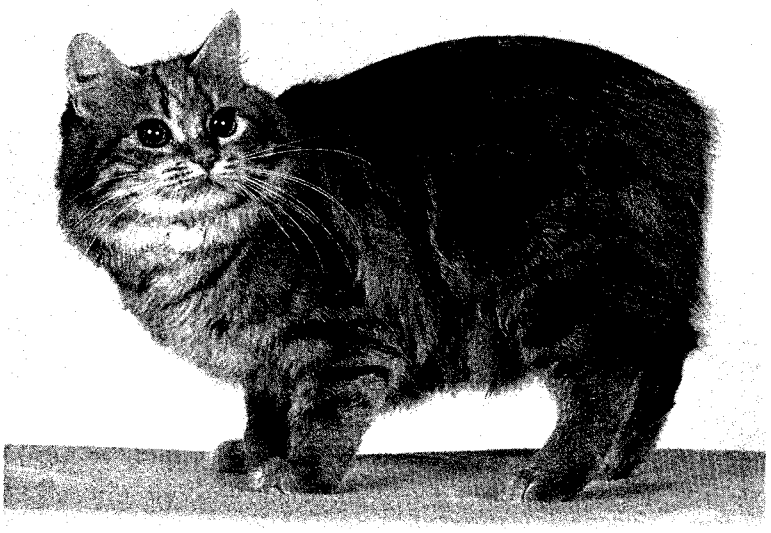


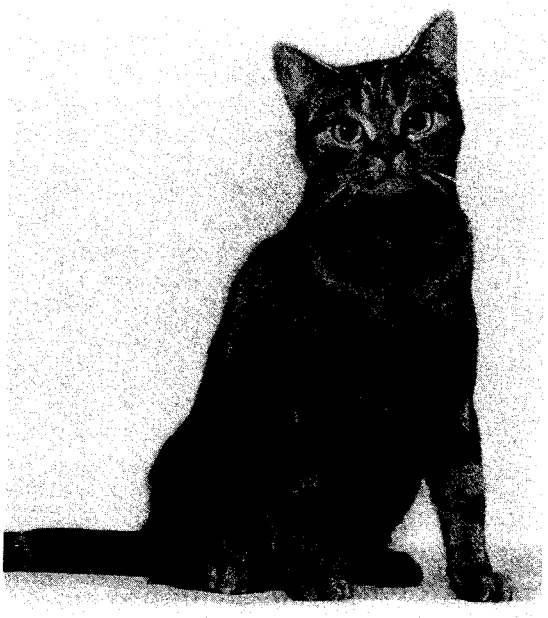
Figure 4. The Cymric. (Photograph by Richard Katris)

tect from moisture, cold and superficial skin injuries." The American Shorthair head is large, with jaws "strong and long enough to successfully grasp prey."

Today's American Shorthairs have achieved the highest national awards in show competition. They reflect the athletic power, good health, intelligence and disposition of their ancestors, while displaying the rich color and refined pattern derived from selective breeding. The high contrast of dense black classic tabby markings on pale silver or the deep red tone of a red tabby American Shorthair coat is unknown in mixed-breed cats. Brilliant gold eye color and coppery brown ground color with striking black markings give the brown classic tabby American Shorthair a special dramatic presence (Fig 5). Over 30 solid colors and patterns, including shaded, smoke, calico and tortoiseshell, are recognized in this breed, which continues to gain popularity with exhibitors and the public.

The personality of an American Shorthair is best described as "laid back." These cats are usually not demanding, have soft voices and tolerate handling from gentle youngsters. They get along with other animals as long as the number is small, and fit comfortably and quietly into a busy household. An American Shorthair tends to be suspicious of the unknown, careful before jumping, and testing before trying, characteristics that probably originated from their need to survive.

Figure 5. The American Shorthair. (Photograph by Jane Howard)



Maine Coon Cat

Along with the American Shorthair, the Maine Coon Cat is one of the oldest breeds of North America, and was also considered a "working cat." These semi-long-haired cats were first recognized in the American state of Maine and were referred to as "shag cats." Many charming tales relate the origin of Maine Coons. The best known claims they resulted from the matings of the semi-wild cats to raccoons. The appearance of the earliest cats, dark gray-brown tabby with long bushy tails, led to this belief and the breed's name.

Some breeders today believe that the breed originated from crosses of early long-haired Angoras, brought to America by English seamen. These cats are said to have mated with short-haired domestic cats already in New England. Considering how unlikely it would be for long-haired cats, which require periodic grooming, to be selected for sea journeys, the recessive long-hair gene more likely was carried by some of the original short-haired cats accompanying European settlers to America. The few long-haired cats resulting from matings of these cats may have had the best chance for survival in the harsh winter climate of Maine and eastern Canada. With nature selecting the strongest, the cats eventually evolved into an exclusively long-haired breed. These hardy, handsome and large cats were undoubtedly adept at controlling mouse populations on farms and valued for their amiable disposition, which remains today.

Natives of Maine were proud of their big, beautiful cats and kept records and pedigree information for many years. The first Maine Coon mentioned in cat literature, in 1861, was known as Captain Jenks of the Horse Marines.

Maine Coons were often exhibited at early cat shows; a neutered brown tabby

male named "Gosie" won Best Cat at the 1895 Madison Square Garden show. Their popularity as show cats declined, however, by the end of the 19th century, when the fashionable Persians were introduced to North America from England.

Nevertheless, Maine Coon cats remained highly regarded as household pets. Because of the persistent dedication of a few cat fanciers, the breed once again achieved show recognition and appreciation in the late 1960s. With Championship status finally allowed by CFA in 1976, their admirers greatly increased throughout America and have now extended to Europe. Today Maine Coon classes in shows are large, and these cats once again place high in the finals.

The show standard reflects the breed's early background, and calls for a solid, rugged cat of medium to large size and a distinctly characteristic shaggy long coat (Fig 6). Though there is a myth depicting 37-lb Maine Coons, males are usually not more than 15 lb and females 12 lb. They tend to appear larger than other breeds because of their heavy coat texture and prominent long bushy tail.

Their body is long, muscular, broad chested and substantially boned. A fine Maine Coon head is medium long, with a squareness to the muzzle and high cheek bones emphasizing huge expressive eyes, along with large high-set, well-tufted pointed ears. Though tabby patterns are most common, Maine Coons come in a great variety of colors and patterns acceptable for show, including bi-color, smoke, shaded, tortoiseshell and solid.

Maine Coon cats are confident and easy going, and adapt equally well to a family environment or showhall situation. Often said to be "dog like," Maine Coons are outgoing and sociable companions.

Figure 6. The Maine Coon Cat. (Photograph by Jane Howard)

American Wirehair

Another breed considered of "Yankee" origin is the American Wirehair. The first known mutation in the United States was recognized in 1966 when a litter of kittens was born on a farm in Vernon, New York. One kitten in the litter was a wiry-coated orange and white male. The owner contacted a local cat breeder, who acquired this kitten, later named Council Rock Farm Adam of Hi-Fi, and a normal-coated female littermate.

In conjunction with other breeders, a program was established to determine the pattern of inheritance for this unusual coat. Hair samples were sent to A.G. Searle and Roy Robinson in England, who confirmed that not only were the guard hairs bent in a hook-like way, but that the thickness of the hair shafts differed from that of all other cats.[23] It was determined that there was no connection with Rex cat coat mutations and that the coat contained all 3 hair types of normal cats (down hairs, awn hairs, guard hairs). The oddity represented a true spontaneous mutation.

Adam was first bred to his littermate sister, producing 2 Wirehair females and 2 normal-coated kittens. When one of the Wirehair females, "Hi-Fi Amy of Katzenreich," was mated to her father (Adam), they produced the first homozygous Wirehair cat in 1969. Adam was also mated to an unrelated white domestic shorthair, producing 3 Wirehair kittens and one normal-coated kitten. This indicated that the gene

responsible was autosomal dominant rather than recessive.

With more breedings, the pattern of dominance continued; however, a great deal of variance became apparent in coat texture and length. Some coats were sparse, hard and tightly crimped. Others were thick and more protective, while retaining the wiriness. Breeders are still working today on standardizing the coat, which, according to the CFA standard, should be "very dense, resilient, crimped, and coarse." The effect is bouncy and delightful to touch. Even the whiskers and eyebrows are crimped. Long or fluffy fur is penalized.

The breed was granted Championship status by CFA in 1978 and is still rare in the United States. The unusual appearance of these cats has begun to attract attention from cat lovers throughout the world; examples are now found in Canada and Europe. Though Adam and Amy were of slim, agile conformation, with very tall ears, long legs and a long tail,[22] the CFA standard calls for a body type closer to that of the American Shorthair.

The body structure should be of medium proportion, with a well-rounded torso and legs of medium bone and length (Fig 7). The head shape, however, with prominent cheek bones and a slight whisker break, is closer to the original mutated cats. Wirehairs may be of almost any color or pattern, except Siamese pattern and coloring. The American Shorthair may be used as an outcross.

The American Wirehair's personality is similar to that of the American Shorthair, but owners believe Wirehairs are a little more welcoming toward strangers. They are happy, gentle and loving.

American Curl Longhair, American Curl Shorthair

The most recent spontaneous mutation to be recognized in domestic cats is the curled ear. Grace and Joe Ruga, living in southern California, noticed the ears curving up and backward on a cat that arrived at their home in 1981. This black longhaired female, named "Shulamith," became the founding cat of the American Curl breed when, in her first litter and others to follow, she produced kittens with the same curved ears. Shulamith and her curl-eared offspring were mated to both long-haired and short-haired cats, and it was soon confirmed that the mutant was the result of a simple dominant gene. Crossing homozygous curled-eared cats, produced all curled-eared kittens.

Dedicated breeders have been working to develop a consistent appearance for both the American Curl Longhair and American Curl Shorthair. A written standard has de-

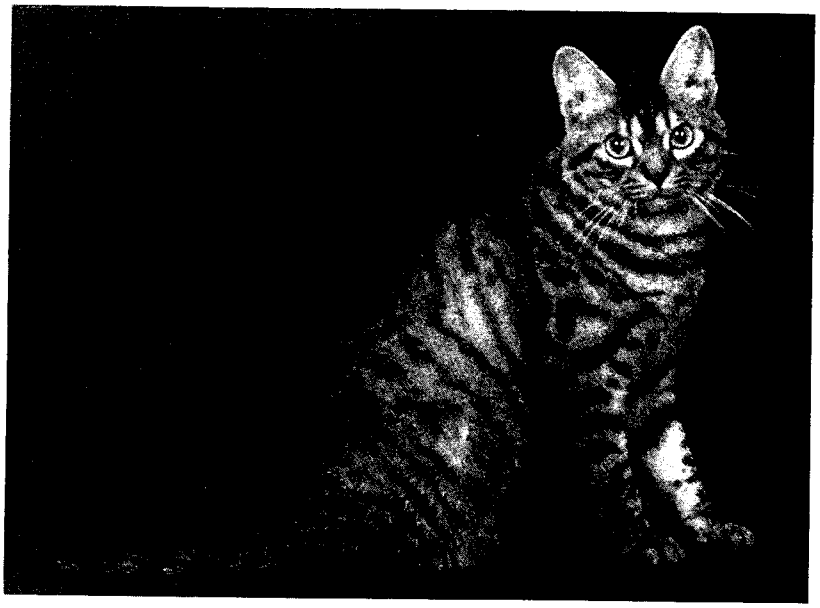


Figure 7. The American Wirehair. (Photograph by Jane Howard)

fined the cat as well balanced and medium sized, with a body slightly heavier than that of the foreign or Oriental breeds. The long-haired version should have a moderately long coat of silky texture, with a minimal undercoat, so it lays flat on the body. The tail fur is full and plumed. Shorthaired Curls have a short soft coat that lies flat but is not tight and close to the body (Fig 8). All colors and patterns are allowed, including the Siamese pointed pattern.

Critical factors in achieving distinguishing character for the breed relate to the facial expression and unique ear formation. Much of the point allotment in the proposed standard (52 pts), therefore, has been devoted to the head, ears and eyes.

The ears have firm cartilage from the base to about one-third of the height. There is a smooth curving arc toward the center of the back of the skull. Breeders believe it is important that the ears are wide at the base and flexible for easy cleaning. An extreme curl that causes the ear tip to touch the back of the ear or head, giving the appearance of no ear at all, is cause for disqualification.

The head is a modified wedge, with gentle contours and large expressive eyes. Any nonpedigreed domestic cat conforming to the standard description may be bred to a cat tracing its pedigree to Shulamith to be registered as an American Curl.

The breed has been accepted by several American associations and may be exhibited for Championship competition in The International Cat Association (TICA). CFA allowed registration of Curls in 1986 and the breed is evaluated in the noncompetitive Miscellaneous class. A wide genetic base has provided a healthy foundation, with no skeletal defects connected to the ear formation reported so far. Response from the general public has been very favorable.

Cornish Rex

Though genetic mutations given the term "rex" had occurred in other mammals, the first such mutation was noticed in cats on July 21, 1950. A tortoiseshell and white domestic shorthair, named "Serena," delivered 5 kittens on a farm in Bodmin Moor, Cornwall, England. One cream male kitten had a peculiar curly coat. "Kallibunker," as he was named by Mrs. Nina Ennismore, Serena's owner, became the foundation cat of the Cornish Rex breed. Mrs. Ennismore contacted the reknown British geneticist, A.C. Jude, who advised her on how best to attempt to develop these cats. Because of a strong resemblance to a mutant breed of rabbits commonly known as Astrex, the name "rex" was decided upon.

In 1957, a Rex female, pregnant by her Rex sire (out of Kallibunker and Serena), was exported to California. Two rex-coated

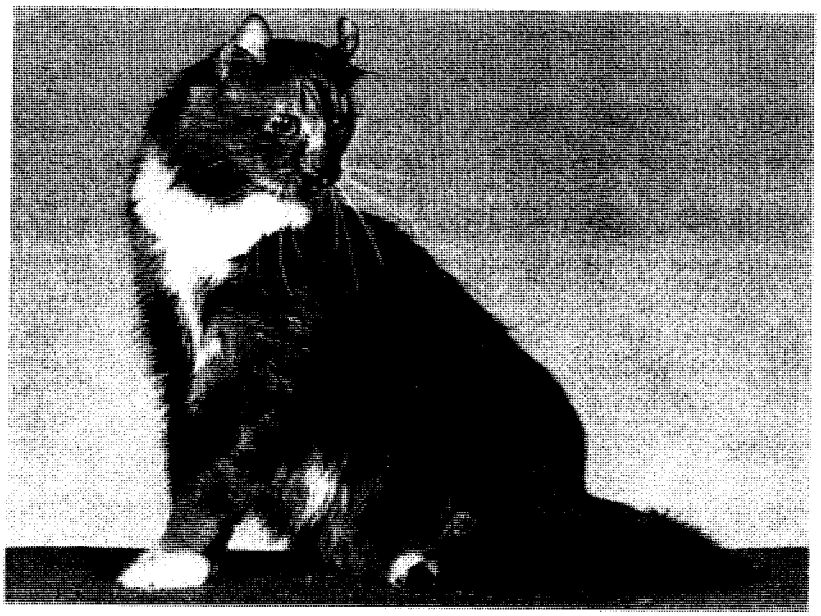


Figure 8. The American Curl. (Photograph by Richard Katris)

kittens out of this litter established the breed in America. The male, "Marmaduke," was the first Cornish Rex registered in the CFA. Because he was the only fertile Rex male in America, he was bred first to a Siamese and later to American Shorthair stock, thus creating the large variety of colors in the breed as it exists today.

At about the time the rex mutation occurred in England, another rex-coated cat was discovered by Dr. Rose Scheuer-Karpin in Germany in August, 1951.[29] A black adult female with short wavy hair was seen among the many feral cats of the Hufeland Hospital grounds at Berlin-Buch. The ancestry of the cat, "Laemmchen," was not known; however, several nurses believed she had been seen as early as 1947.

When Laemmchen was successfully mated to one of her sons in 1957, she produced a litter with one normal-coated and 3 wavy-coated kittens. One was sent to Mr. Jude in England, but unfortunately died while in quarantine. The German cat fancy showed no interest in the Rex kittens Laemmchen continued to produce. In America, however, several breeders were anxious to obtain these curly cats after press reports carried the news around the world of the first Rex shown in public at the Paris Cat Club exhibition in 1960. Two independent breeding experiments in America, mating Cornish Rex cats to German Rex cats, eventually proved that the varieties were the same mutation. Because of their genetic compatibility, CFA recognizes both strains as the same breed. The Cornish Rex received CFA Championship status in 1964.

The normal feline coat consists of 3 types of hair. Guard hairs, or the outercoat, provide a protective barrier to the elements. The undercoat consists of awn hairs, which are variable but thinner, as well as the down or wool hairs, which are near the skin, providing insulation. Coats of Cornish Rex cats appear to be lacking all guard hairs.[27] Any present are modified so as to be identical with the awn hairs. The soft undercoat texture with its wavy growth pattern produces a distinct appearance and unique feel. Any obvious guard hairs on a Cornish Rex disqualify it in the show ring.

The marcel waved coat is not the only unusual quality of the Cornish Rex breed. These cats are the most gazelle-like of domestic cats, being described as of "racy" body type by the CFA standard and often compared to Whippet dogs. Cornish Rex are small to medium sized, and all contours are curved and slender (Fig 9). Their bones are fine and delicate, but the cats feel suprisingly heavy and muscular. When standing, a Cornish Rex's back is naturally arched, exaggerating the very long slim legs. The Cornish Rex head type is narrow, with a double-curved profile consisting of a rounded forehead and a Roman nose. Oval eyes and large high-set ears add to the alert and highly stylized appearance.

It is interesting that the autosomal recessive mutation that created the coat changes seems to have affected the body and head type as well. Breeders have noticed that in hybrid litters, rex-coated kittens look entirely different from their domestic-looking littermates. This was evident even with Kallibunker, who was unlike his mother.[11] Though it is often said that the body temperature of a Cornish Rex is normally higher than that of other cats, this is not the case. Nevertheless, these cats do feel very warm to the touch. They tend to seek out cozy places and are especially good lap cats. Because they lack guard hairs, shedding and dander are minimized, making the breed sometimes acceptable to certain people with allergic reactions to cats.

The temperament of the Cornish Rex is active, talkative, inquisitive and highly affectionate. They are social with people and other animals, and considered by their devoted owners to have a keen sense of humor.

Devon Rex

After the discovery of the Cornish Rex, a number of other rex mutations were reported in America. These were incorporated into the Cornish breed, if compatible, or not pursued. A completely different rex mutant, however, was discovered in the county of Devon, England, in 1960. Miss Beryl Cox provided a home for a pregnant stray cat, who presented her with a litter of kittens containing one black kitten covered with curls. The sire was assumed to be a curly-

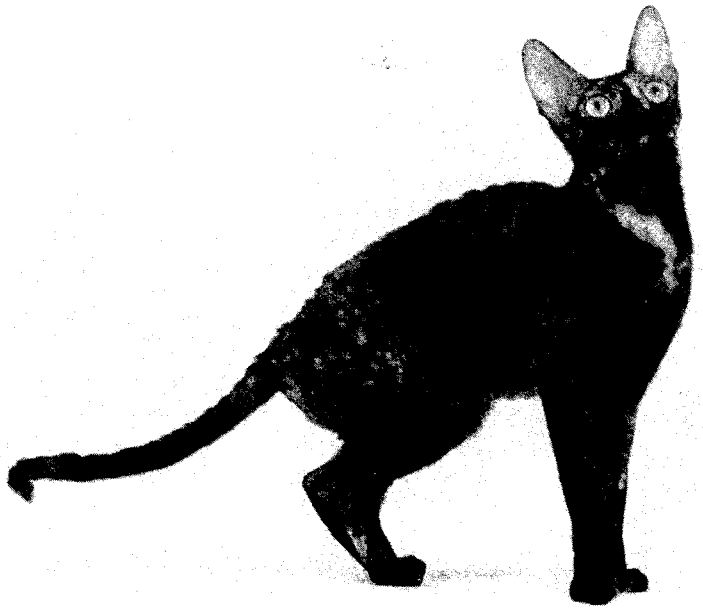


Figure 9. The Cornish Rex. (Photograph by Jane Howard)

coated feral cat who was observed living in a nearby abandoned tin mine.

Miss Cox read in the newspaper about the Cornish Rex cats and eventually allowed "Kirlee" to go to a breeder, Brian Stirling-Webb. Everyone assumed this cat would add a needed outcross to the breed. However, after Kirlee was mated to 9 Cornish Rex queens and produced 29 kittens, all normal coated, it was acknowledged that a new mutated gene had been discovered. Rex gene II, as it was named, proved to be autosomal recessive, and further interbreeding with the Cornish gene I was discontinued.[11]

The Devon Rex was officially recognized as a separate breed by the Governing Council of the Cat Fancy in England in 1967. Shortly after this time they were exported to the United States and were soon accepted by several associations for registration and showing. CFA, however, remained insistent that all wavy-coated cats were to be considered Rex and would not distinguish between the 2 types. After years of considerable pressure from dedicated Devon Rex breeders, the breed was finally given separate registration in 1979 and Championship status in 1983.

Unlike the Cornish Rex, the coat of the Devon Rex has all 3 types of hair: guard, awn and down. The guard hairs are modified and reduced, and the awn hairs are irregular in thickness, all resulting in a soft, fine and densely rippled coat texture. The coat is not as close lying and uniform in wave as that of the Cornish Rex. The reduced keratin (protein) in the hair, combined with environmental, hormonal and other factors, contributes to hair breakage and bare patches, which are a problem in establishing coat reliability in the breed.[11]

The body and head of today's Devon Rex cats worldwide are remarkably close to those of Kirlee, who had a distinct appearance aside from his coat mutation. The Devon head is described in the CFA standard as having an "elfin look" created by large eyes, a short muzzle, prominent cheekbones and huge low-set ears (Fig 10). These striking ears are often accentuated by ear-tip tufts and "earmuff" fur at the base. The Devon body is moderate and muscular, with medium-fine, long sturdy legs and a long tapered tail.

This breed is one of the most charming, with its irresistible impish face matched by an alert devilish personality. They are somewhat talkative but have quiet voices and are very responsive to people. They need a maximum of freedom within a home to express their playfulness and love of heights. They appeal to those who like an avant garde appearance combined with outgoing friendliness.

Egyptian Mau

"Mau" is the Egyptian word for cat. The Egyptian Mau is not only one of the oldest known breeds, but also is considered to be the only naturally spotted breed. The spotted pattern of the Egyptian Mau is genetically a version of tabby marking and is the breed's most distinguishing feature. Some geneticists believe that domestic cats that appear spotted are in fact mackerel tabbies with broken, rather than continuous, vertical lines. A mackerel tabby carrying the allele for the recessive classic tabby pattern may show a modified mackerel striping, which is irregular and broken, sometimes to such an extent that the cat becomes a "spotted" tabby, such as those reported in England in the early 1900s.

If this were the mechanism responsible for the Egyptian Mau spotting, then breeders would expect to see a predictable 25% ratio of both mackerel- and classic tabby-patterned offspring. Because this is not the case, breeders believe it is more likely that the Egyptian Mau spotting is a separate mutated tabby pattern.

Though some Maus show the broken mackerel type of spotting, the proper pattern is randomly arranged spots of varying size and shape. The spots, whether small or large, must be distinct. If they are aligned at all, they tend to follow horizontal rows running the length of the body. It is very rare for Egyptian Maus to produce other than spotted offspring, adding strong evidence to the probability that Mau spotting is recessive to the other tabby alleles.[31]

The ancient forerunner of this breed is thought to be a domesticated spotted subspecies of the African wild cat, *Felis libyca* (*ocreata*), which was taken to Egypt from the Ethiopian highlands. This was the conclusion of Morrison Scott of the British Museum after examination of mummified cats from 600 BC to 200 BC.[17] Numerous symbolic depictions of these cats clearly record their ancient background and importance in Egyptian mythology. One of the best known, in the Papyrus by Hu-Nefer (1100 BC), is the spotted cat Ra, beheading the serpent Apep, a symbol of the defeat of evil by the forces of good. Maus are often shown as working cats killing rats, mice and snakes, as well as valued household pets. A tomb painting found in Thebes, dating around 1400 BC, shows a spotted cat acting as a duck retriever for an Egyptian hunter.

From about 1580 BC, cats in Egypt became firmly identified with the goddess Bast. Their revered status as the focus of a religious cult ensured their protection and led to the practice of mummification after death. As a result, scholars have been able

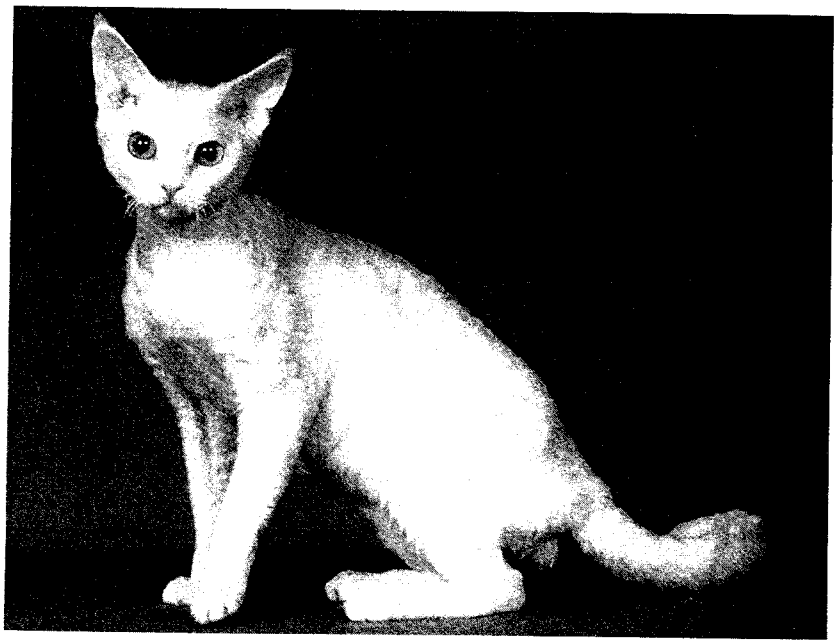


Figure 10. The Devon Rex. (Photograph by Jane Howard)

to compare the modern Egyptian Mau with the spotted cats of ancient Egypt.

Cats derived from breeding Siamese to British Shorthairs in the late 1960s were called Egyptian Maus in England; however, these are now more correctly known as Oriental Spotted Tabbies. In America, hybridization has not been considered an acceptable practice. The breed was established from 3 cats brought to the United States from Italy by the Russian princess, Nathalie Troubetskoy, in 1953.

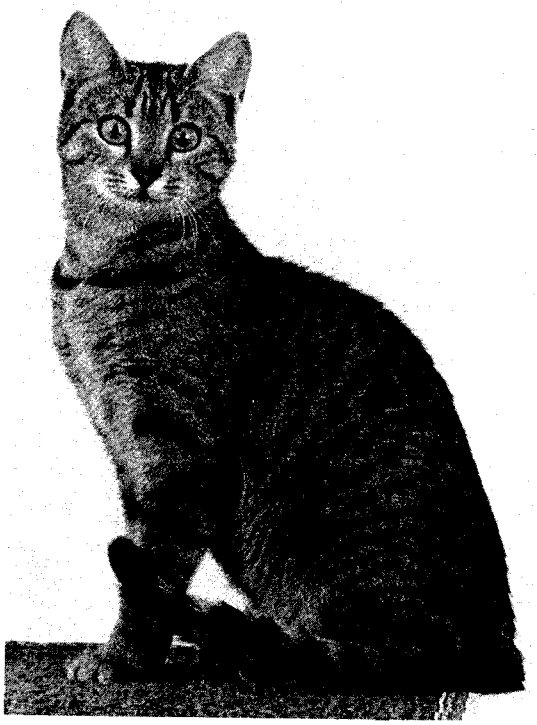
Described in Marcel Reney's *Mes Amis Les Chats* (1940), Egyptian Maus had been bred and shown before World War II by Europeans who imported them from the Middle East. After the war, the exiled Princess Troubetskoy rescued some of the remaining Maus in Italy. Through her contacts among the foreign ambassadors to Italy, she was able to import several Egyptian Maus via the Syrian Embassy so that she could reduce the amount of inbreeding necessary to keep the breed pure. These Maus were registered with the Federation Feline Italienne and were exhibited before her move to the United States.[17] One of the cats acquired through the Syrian Embassy was named "Baba of Fatima." This silver female later became the first American Champion of the breed.

CFA Championship status was achieved by the breed in 1977. There are 3 recognized colors: silver, bronze and smoke. Contrast between the lighter ground color and deeper markings is important to the dramatic effect. The eye color is a light "gooseberry" green, and the coat is medium short, with a silky, fine texture. The head and muzzle are moderately long and the profile gently contoured (Fig 11). The medium to large ears are erect, and the large, almond-shaped eyes are slanted slightly toward the ears.

The Egyptian Mau body is medium sized and graceful, with well-developed muscles. The hind legs are proportionately longer and there is a loose flap of skin extending from the flank to the hind leg knee. This is also a characteristic of wild cats and allows for long strides when running.

Maus are reported to be especially loyal and devoted to their owners, and adjust well to other pets and children. They are considered moderately active, alert, friendly and playful, with a quiet melodious voice.

Figure 11. The Egyptian Mau. (Photograph by Jane Howard)

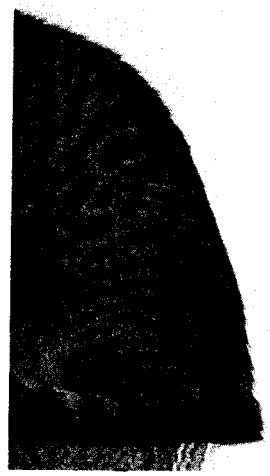


Abyssinian

Though the Abyssinian is another of the oldest known breeds, there continues to be controversy concerning its history. Abyssinians resemble the ancient Egyptian cats, portrayed in paintings and sculptures as elegant animals with muscular bodies, beautiful arched necks, large ears and almond-shaped eyes. Abyssinians today still retain a "jungle look" similar to that of *Felis libyca*, the African wild cat ancestor of all domestic cats.

The source of the name "Abyssinian" is not because Ethiopia, formerly Abyssinia, is thought to be the original home of the these cats, but rather because the first "Abyssinian" exhibited at a show in England was said to have been imported from that country. The British book *Cats, Their Points, Etc*, by Gordon Staples, published in 1874, contains the first mention of an Abyssinian. The book shows a colored lithograph of a cat with a ticked coat and no tabby mark-

Mau. (Photograph by Jane



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ings on the paws, face or neck. The description reads, "Zula, the property of Mrs. Captain Barrett-Lennard. This cat was brought from Abyssinia at the conclusion of the war. . . ." British troops left Abyssinia in May, 1868, so this may be the time when foreign cats with ticked coats first entered England.

Unfortunately there are no written records tracing the early Abyssinians to these imported cats, and many British breeders believe the breed was actually created through crossing of the various existing silver and brown tabbies with English ticked cats called "bunny" cats.[8]

Recent studies by geneticists show that the most convincing origins of the mutated Abyssinian ticked tabby gene are along the coasts bordering the Indian Ocean and parts of southeast Asia. In fact, the earliest identifiable Abyssinian is a taxidermy exhibit in the Leiden Zoological Museum in Holland. This ruddy ticked cat was purchased around 1834-1836 from a supplier of small wild cat exhibits and labeled by the museum founder as "Patrie, domestica India." In addition to the color details, the graceful body, slim leg bones and head type are close to those of a modern Abyssinian. Though the breed was refined in England, its introduction to that country and others may have been the result of colonists and merchants stopping in Calcutta, the major port for the Indian Ocean.[33]

Abyssinians were shown in early British cat shows held at the Crystal Palace. The first written standard appeared in 1889, describing the cats as "deep brown, ticked with black, somewhat resembling the back of a wild (only not so grey) rabbit." The current CFA standard calls for a deep orange brown undercoat ticked with black, which gives a burnt sienna overall coat color.

In the late 1880s, cross-breeding experimentation by the British produced some silver or perhaps blue Abyssinians, judging by such names as "Aluminum II" and "Salt," the first 2 exports to America in the early 1900s. One prominent breeder, H.C. Brooke, was strongly opposed to the silver coloring and used a deep red-brown cat named Ras Brooke, hoping to bring back the once preferred rufus tone. This cat may have been responsible for introducing the mutated light brown (b^l) or cinnamon gene into the breed. The gene is carried as a recessive to the original ruddy color and produces the "red" Abyssinian, called "sorrel" by some associations and "cinnamon" by others. Red Abyssinians have chocolate brown ticking and overall rich coppery-red radiance.

World War I halted cat breeding in England and it was not until the late 1930s that several top-quality ruddy Abyssinians were exported to form the foundation of today's American breeding stock. At the end of World War II there were only 12-15 Abyssinians left in England, and breeders struggled to revive the breed. Since then the popularity of Abyssinians throughout the world has grown steadily. The first American-bred red Abyssinian kitten was born in 1952 out of 2 imported British ruddies. This color was recognized by GCCF in England in 1963. After a battle for acceptance, reds received CFA Championship status in 1964.[9]

During the 1950s several breeders began to register blue-ticked kittens occasionally born in their Abyssinian litters. These reflected the genetic "dilute" factor that had evidently been present in some bloodlines, causing the black ticking of ruddy cats to become slate blue on a warm beige ground color. The same factor acting on the reds produces the "fawn" Abyssinians with their light cocoa brown ticking. By the late 1970s these dilute-colored Abyssinians began to capture the attention of breeders and the public. In 1984 the blues achieved CFA Championship status, and the fawns followed with full show status in 1990. In England, Europe, Australia and New Zealand, other colors are accepted.

An important factor in defining the Abyssinian breed is a short, fine, silky, dense and resilient coat showing even and distinct ticking. Each hair shaft on the back and sides is banded with alternating light and dark color, creating an overall "wild rabbit" effect. Though the ticked tabby pattern normally includes striping and markings on the legs, tail and chest, these have been eliminated on the Abyssinian breed through many years of selective breeding. Facial markings, however, are considered desirable. The body is lithe and graceful, with firm muscles (Fig 12). Abyssinians

stand high on slim legs and display a characteristic eagerness. The head is a modified wedge, with gentle contours. Large brilliant almond-shaped eyes and large alert ears give the face a lively expressive look.

These cats are well known for their fast graceful movement and playful intelligent personalities. They are usually bold, sociable with other animals and intensely curious. Responsive and sensitive to people's moods, Abyssinians stay close to their owners and want to be part of all household activity. Their desire to participate and interact with people allows many of them to accept training, learn to walk on a leash, and enjoy travel and other adventures. Though highly demonstrative in showing affection and wanting attention, they are freedom loving individuals and generally prefer not to be overly restrained.

Somali

All Abyssinian pedigrees may be traced back to cats of unknown ancestry in Britain. Considering the need to outcross after the World Wars, it is not surprising that when the cats imported to North America were linebred, the recessive gene for long hair was expressed in some lines. "Raby Chuffa of Selene," a male who was sent to the United States in 1953 and appears in the pedigrees of many Abyssinians, is thought to be an early important carrier of the long hair gene.[42]

Figure 12. The Abyssinian. (Photograph by Jane Howard)

For years, long-haired kittens that occasionally cropped up in litters were quietly sold or kept as pets, never to be used for breeding. The first to be recorded and bred was owned by a Canadian. This male, "May-Ling Tutseita of Dunedin," in the 1960s began the oldest Canadian Somali line. About the same time in the United States, an Abyssinian breeder, Evelyn Mague, using her cats carrying the long hair gene, began serious work to develop these cats as a separate breed. She also established the name "Somali" for the breed, associating the Somalia area of Ethiopia, which was formerly called Abyssinia. The name emphasizes the breed's derivation from the established Abyssinian gene pool rather than from purposeful hybridization with another breed. In 1972 Mrs. Mague founded the Somali Cat Club of America with Canadian and American membership, and the breed received CFA Championship status in 1979.

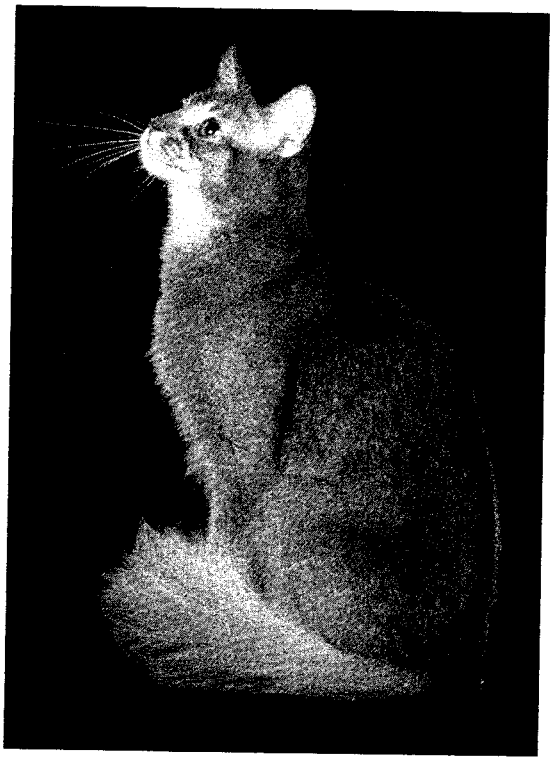
Early British Abyssinians exported to Europe, Australia and New Zealand also produced occasional long-haired offspring. Small groups of breeders in these areas began to develop their own breeding programs. Despite the great distance separating the cats, their pedigrees may be traced to the same English ancestors.

The CFA Somali standard is almost the same as that of the Abyssinian, with the exception of the coat. However, several subtle differences distinguish the breed. Whereas the Abyssinian is a medium-sized cat, the Somali is medium sized to large. With its full-coated body and long brush-like tail, Somalis generally appear more substantial (Fig 13). The medium-long coat feels extremely soft due to a fine double-coat texture. Often there are multiple broad bands of ticking, giving a rich intensified color tone. Such details as tufts on the ears, dark color up the rear legs to the hock, and strong facial markings add to the dramatic

"wild" appearance of the breed. The coat colors accepted for CFA Championship competition are the same as in the Abyssinian: ruddy, red, blue and fawn.

Like Abyssinians, Somalis have quiet voices and lively, companionable personalities. CFA allows breeding to Abyssinians though the resulting short-haired kittens, which look exactly like Abyssinians, must be registered as Somalis. These "variants" are often valuable in Somali breeding programs and make beautiful pets. FIFe, in Europe and elsewhere, allows the shorthaired variants to be shown as Abyssinians.

Figure 13. The Somali. (Photograph by Jane Howard)



Singapura

The ticked tabby gene (T^a) is dominant to all other feline tabby patterns and is prominent in feral and street cats throughout southeast Asia. On the 225-square-mile island of Singapore at the southern tip of the Malay Peninsula, small cats with a brown-ticked coat pattern and delicate coloring have been noticed since at least 1965. These cats, with their large almond-shaped eyes and distinct head and body type, are unlike the typical deeper-colored ticked street cats of the area, which often have short twisted "bob" tails and usually display the white spotting factor.

The characteristic dark brown ticking on a warm old-ivory ground color of the Singapura is thought to occur from the combination of 2 major genes native to southeast Asia. The Abyssinian ticked tabby gene (T^a) is modified by the Burmese gene (c^b), which changes black ticking to deep brown and results in the soft warm coat coloring.

Tommy and Hal Meadow, breeders who became interested in the cats while living in Singapore, used 3 brown-ticked cats in 1975 to establish the breed. A fourth, obtained from the Singapore SPCA, was imported in 1980 by another cat breeder and is in the background of many American Singapuras. The Meadows presented the Singapuras at several cat shows and concentrated on a breeding program to produce consistency in color, pattern, health and disposition.

CFA accepted the Singapuras for registration in 1982. Though these cats are still relatively rare, many breeders throughout America are now devoted to their advancement. Full Championship status was granted to the breed by CFA in 1988.

Fully grown Singapuras are the smallest of the pedigreed breeds. Females weigh about 4 lb and males about 6 lb. Their body is moderately stocky and muscular, with the space outlined by the underside of the trunk, legs and floor forming a square. Heavily muscled legs taper to small short oval paws. The head is rounded, with a definite whisker break and medium-short broad muzzle. Large medium-set ears and brilliant wide-set large eyes, with unusual cheetah-like markings at the inner corners, give a special facial expression to these cats (Fig 14). Because the Singapura coat is very short and close lying, the ticking effect resembles fine-grained sand. The cats show some barring on the inner front legs and back knee but should not display chest markings.

Singapuras are curious, friendly, playful and relatively quiet. Females usually have small litters of 3 kittens. There is far

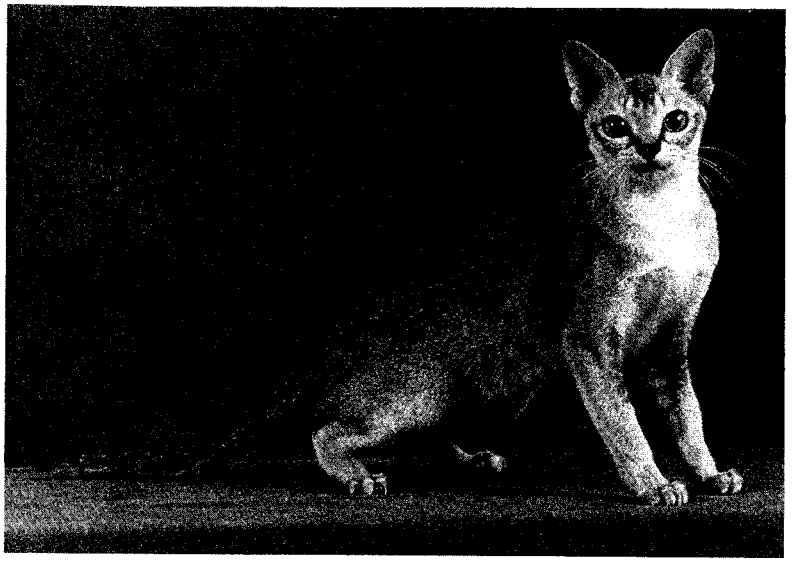


Figure 14. The Singapura. (Photograph by Jane Howard)

greater demand for these cats and kittens than those available.

Ocicat

The epitome of a wild cat for most people would be a large, muscular, boldly spotted cat. The Ocicat is a spotted beauty that retains the gentle temperament of a domestic cat.

"Tonga," the first Ocicat born, was a surprise to Virginia Daly, a well-known breeder from Michigan. Through cross-breeding of Abyssinians to Siamese, she had been attempting to achieve a ticked tabby-pointed Siamese. In 1964 a lovely male kitten was born with golden spots on an ivory body. Though Tonga was sold as a pet, subsequent breedings of the same parents produced other spotted cats that became a new hybrid breed.

In 1966 the Ocicat was accepted for registration by CFA. In addition to Siamese and Abyssinians as the foundation cats, Ameican Shorthairs were added to achieve color genes. It took 20 years to fully develop the breed and to finally achieve CFA Championship status in 1987. The breed has now become popular with both cat fancy exhibitors and the general public. Abyssinians are acceptable for outcross breedings until 1995.

Ocicat males weigh 12-15 lb and females 7-10 lb. Their "jungle cat" appearance bears no resemblance to any of the foundation breeds. An athletic and powerful yet graceful body with well-muscled legs, gives this cat a commanding presence (Fig 15). The coat is short, close lying and sleek, emphasizing the large, scattered, thumbprint-shaped spots. The head is carried gracefully on an arching neck and is a modified, slightly curving wedge with a broad muzzle and firm jaw. Ocicat eyes are large and almond shaped, angling slightly upward toward the ears, which are moderately large and set neither too high nor too low.

In the preferred pattern, the spots suggest the classic tabby pattern. The genetics underlying this spotting remain a controversial subject among experts. Based on breeding experience, some breeders suspect that a separate gene for spotting modifies a pattern created by one mackerel tabby gene and one classic tabby gene.[35]

Twelve colors are accepted in Ocicats: tawny (or brown spotted), blue, chocolate, cinnamon, fawn, lavender and the silver versions of each of these. The sex-linked orange gene is not allowed in the breed, as the resulting tortoiseshell pattern would interfere with the spotting pattern.

Ocicats are hardy, vigorous cats, full of vitality and fun. They are highly sociable with people, dogs and other cats. They are nondemanding, adaptable, easy going and confident, making them excellent family companions.

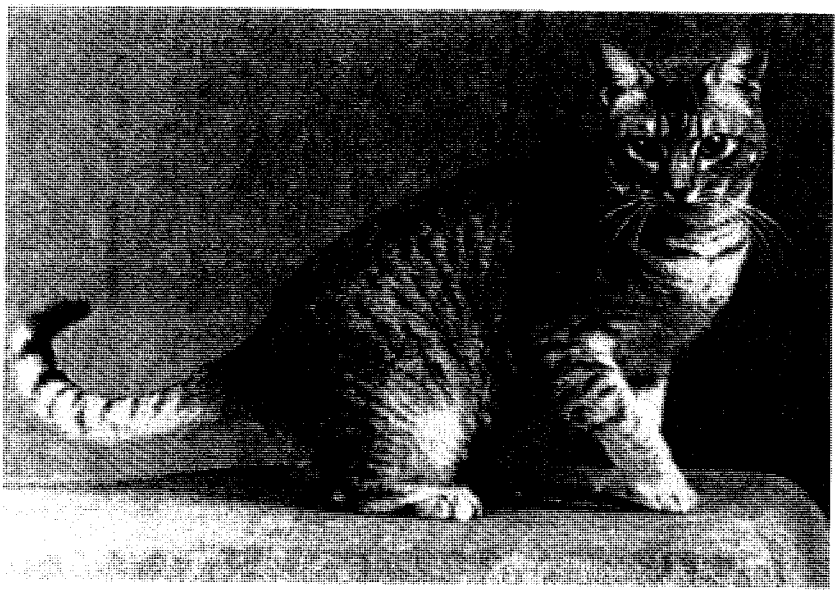


Figure 15. The Ocicat. (Photograph by Jane Howard)

Russian Blue

Solid-blue short-haired cats with a "foreign" slender body type were present at British cat shows as early as 1875. They were said to have been taken to England by sailors from the White Sea port of Archangel in northern Russia, and were therefore called Archangel cats.

In the well-known *The Book of the Cat*, by Miss Frances Simpson (1903), the Russian cats at the turn of the century were described by one of the earliest breeders, Mrs. C. Carew Cox. She states that many of the blue short-haired cats were actually of Russian origin. However, it is clear that the cats featured in early breedings were nondescript and lacked a common standard for body and head type. Though many were fairly long and elegant, others had a round face and compact body.

Much attention was given to the coat, which Mrs. Carew Cox said was to be "short and close, glossy and silvery" but sometimes is "rather wooly and furry." From the few photographs available, it is apparent that these early cats had thick, dense fur similar to the best of our modern Russian Blues. An even shade of light silver-blue was also appreciated then as it is today. The Russians competed with the British cats in one class at the shows, but reports indicate that the more cobby British type usually won.[39]

World War II brought an end to the original breeding stock, and in 1945 efforts to reestablish the breed necessitated crossbreeding with Siamese. The 1952 standard called for an "elongated, elegant body, graceful lines, delicate bones and light type. . . . The skull is flat and narrow, the forehead sloping. . . ." The thick double coat seemed to have totally disappeared in the 1950s. Eventually in the late 1960s there were serious efforts to breed away from the Siamese type. According to reports in British publications, efforts were made to bring back the thick plush coat.

Work to restore the idea of the original Russian Blue cat was also underway in Scandinavia in the late 1940s. Breeding stock based on Russian Blues from Finland and Denmark imported to Sweden was combined with Siamese outcrosses. Russian Blue breeding in America started with imported British cats in 1947 and later cats from Scandinavia. Many Russian Blue breeders currently believe the British lines are responsible for the beautiful light plush coats of the Russians today, and that the Scandinavian cats have contributed the brilliant green eye color. Over the last 20 years, using occasional British and Scandinavian imports, the body and head types have finally been stabilized in America. Because of variations in the standards, however, Russians still deviate in appearance

around the world, including the allowance of colors other than blue in Australia, New Zealand and England.

CFA states that the head should be a smooth, medium wedge, with a distinctive flat-topped skull and straight nose profile defined by a downward angle (Fig 16). The body is lithe, graceful, firm and muscular without being tubular in appearance. There are many points in the standard for coat and color, describing a fine, soft, plush and dense double texture, with an even bright blue color throughout. Lighter shades are preferred and the guard hairs are silver tipped, giving the cat a lustrous silvery sheen.

Russians are gentle and slightly reserved cats with a dignified manner. They have a very quiet voice, are very affectionate with their owners, and live happily with children and other pets. They are moderately active, well behaved and playful all of their lives.

Chartreux

For many years, little had been written in the English language about the historic blue short-haired cats that were common in France and described in French literature in the late 1500s. The name "Chat des Chartreux" first appeared in the Dutch *Universal Dictionary of Commerce, Natural History and the Arts and Trades*, by Savarry des Bruslon, 1723. Though their origin was attributed to the Chartreux monks, who were said to have had the first of the breed, no records have survived the natural calamities and political upheavals to positively confirm the breed's ancestry.[13] It is assumed that the cats were kept and bred by the monks (best known for their potent green liqueur) to keep their monastery, La Grande Chartreuse, located high in the mountains near Grenoble, free of rats and mice. John Jennings, in his book, *Domestic or Fancy Cats* (1893), writes that the original blue cats bred by the Chartreux monks were longhaired.

The Chartreux cat has throughout history been admired by the French for its sturdy and large structure and its powerful hunting ability. The Dutch trade manual also referred to the Chartreux cat's use in the fur industry. Chartreux pelts were prized for their thick wooly texture similar to that of an otter.[14]

By 1756 the Chartreux was listed among the 4 recognized cat breeds in *Natural History*, by Comte de Buffon, along with the Domestic, Spanish and Angora. There is no doubt that this ancient breed was distinctly removed from the European Domestic cat; however, the first recorded selective breeding of Chartreux began around 1930 on the small island of Belle-Ill-sur-Mer in the Atlantic off the northwestern coast of France, where free-roaming ancestors of the Chartreux were found on the grounds of the Le Palais Hospital. Colonies of Chartreux still exist in France today, where pure Chartreux are differentiated from the hybrid mixtures of blue British Shorthairs and Chartreux.

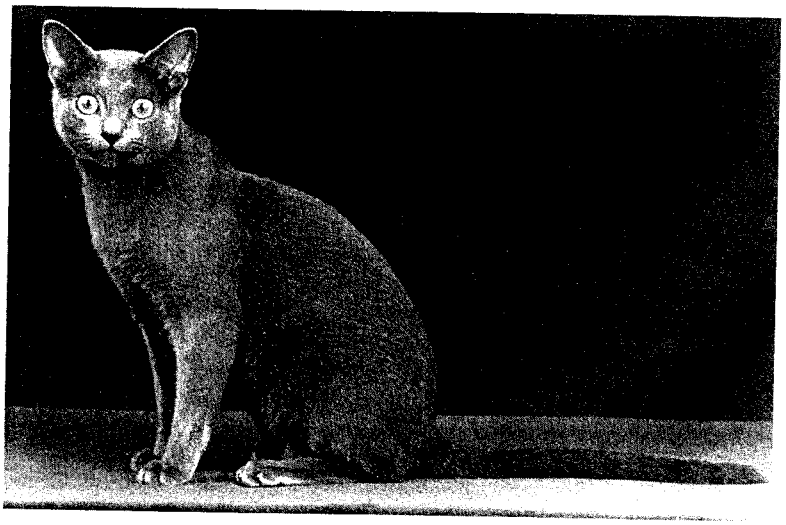


Figure 16. The Russian Blue. (Photograph by Jane Howard)

Helen and John Gamon of La Jolla, California, were intrigued by the description of the Chartreux in Fernand Mery's book, *The Life, History and Magic of the Cat*, published in 1966. They went to France in 1970 to find cats of pure lines to import. These formed most of the foundation breeding stock for the American and Canadian Chartreux we know today. Other imports broadened the gene pool during the 1970s, and CFA accepted the breed for registration in 1979. Championship status was achieved in 1987.

Breeders are dedicated to preserving the Chartreux in its pure form, and the standard therefore emphasizes the historic qualities of these unique cats. Accepted in the blue color only, clarity and iridescent brilliance are important. The coat is dense and water repellent, with a slightly wooly texture that allows it to "break" like sheepskin. Because the degree of wooliness depends on age, sex and habitat, this is difficult to achieve and is usually best exhibited by mature males.

The Chartreux body and head types ensure that these cats will not be confused with other blue cats. The breed's husky, robust structure is referred to as "primitive." While the large male example is sometimes described as a "walking fortress," with broad shoulders, deep chest, strong bones and solid muscle mass, the female is expected to be of medium size. The breed is slow to reach full maturity. All Chartreux are extremely supple and agile, rather than coarse or clumsy. Their legs are relatively fine boned and appear almost dainty in comparison to their body mass.

The head is noted for its round broad shape, powerful jaw and full cheeks (Fig 17). The muzzle is comparatively more narrow than that of other breeds and is tapered, with slight whisker pads. The eyes are round and range in color from copper to gold. The medium-sized ears are set fairly high and erect. Chartreux have an exceptionally alert, sweet and "smiling" expression.

Often described as a "dog-like" cat, the Chartreux has a loyal attitude toward its owner and a nonaggressive, cautious demeanor with strangers. They give the impression of great dignity and stability, and

Figure 17. The Chartreux. (Photograph by Jane Howard)

are well behaved and extremely quiet. In fact, In fact, Chartreux are sometimes said to have no voice at all. A legend explains that they took vows of silence with the monks, causing them to become mute. Their faint chirping sounds are unlike that of any other breed. Chartreux cats play with seriousness, wanting to "kill" their toys, and are considered to be comedians by their owners. They maintain a "joie de vivre" well into old age.

Turkish Angora

The recessive long hair gene is considered to be one of the 7 "ancient mutations" in cats. Authorities agree that this most likely took place in the Middle East. For centuries Europeans referred to long-haired cats as Angoras or Persians. There have been suggestions that the Pallas' cat, *Felis manul*, a wild cat with a heavy body and a thick long-haired coat, may have been the ancestor of domestic long-haired cats. Most zoologists, however, have rejected this theory because of fundamental differences, and consider mutation to be more likely.

The precise era and location within the Middle East for the origin of the long hair

gene are open to speculation. Long-haired cats, however, from both Turkey and Persia were first introduced to Europe by the end of the 16th century and early 17th century. Other early long-haired cats were imported from Russia and Afghanistan. A print identifying an "Angora" cat was included in Buffon's *Histoire Naturell*, published in 1756, and illustrates a long-bodied graceful cat with a full coat and long ruff around the shoulders. By the late 1700s, sea traders began bringing Turkish Angoras to America from Europe and the Orient.

A letter written in May, 1856, by Lottin de la Val, which is quoted in Fernand Mery's book, *The Cat*, reports his finding a "beautiful feline species (the Angora) on the great Armenian plateau at Erzerum." He noted that the Angora was the dominant variety among the cats of Kurdistan, where he had seen whites, grays and orange-spotted cats. This isolated mountain region in the eastern part of Turkey would have been a logical place for these cats to multiply and thrive because of the cold environment.

Differences in the Angora and Persian long-haired varieties were gradually noticed by the British at the time of the first Crystal Palace Cat Show in 1871. The Persian, as well as the Afghanistan longhairs, had coats described as wooly, a larger head and stronger body than the more rangy Angoras. The Angora coat texture was desribed by an English writer in 1868 as "of fine texture, generally longest on the neck but also on the tail." Though all of the longhairs were bred together, gradually the Persian became the preferred variety in England. By the turn of the century, through cross-breeding in England and Europe, the Turkish Angora breed had become virtually extinct except in its homeland.

Early in the 20th century the Turkish government established a breeding program at the Ankara Zoo to preserve the pure white Angora cats with blue eyes, amber eyes and odd eyes (one blue and one amber). Though the other colors inherent to the breed occasionally occurred in litters, white was the only color officially preserved by the Zoo. In 1962 and 1966, Colonel and Mrs. Walter Grant, followed by other American breeders, began to import several Angoras directly from the Zoo with certificates of ancestry. Virginia and Thomas Torio travelled to Ankara in August, 1966, to purchase a male and female, and discovered the Zoo had at that time less than 30 cats.[38]

"The Original Turkish Angora Society" was founded in the late 1960s to promote the white Turkish Angora cats in America with ancestry traceable to the Ankara Zoo.[25] The breed was recognized by CFA in 1970 and achieved Championship status in 1973. The only coat color accepted was white, though other recessive colors continued to appear in some lines. Many breeders believed these cats would help increase the limited gene pool and gradually promoted colors other than white. These were finally acknowledged by CFA in 1978.

A breed known as the "Angora" was given preliminary recognition in Britain and is similar to the Angora cats of Turkey and North America, except that is based on a genetic program using Siamese and short-haired cats carrying the long hair gene rather than cats imported from Turkey. The "Turkish" cat, as recognized in England and elsewhere, is known in America as the Turkish Van.

Turkish Angoras are medium sized and extremely graceful, with refined boning. The hind legs are longer than the front, and the paws are small and dainty (Fig 18). The head is wedge shaped, with a definite taper toward the chin. Long, pointed erect ears are tufted and set high on the head. The long, full tail is often carried horizontally over the body as the cat is moving. Angoras have a silky, medium-long coat with a wavy tendency and should carry a long, full neck ruff. Any color or pattern is accepted today except those showing Siamese hybridization.

Angoras are said to have a humorous, polite, sweet nature. They are playful and mischievous, and stay affectionately close to their owners. As in any breed or in mixed-breed cats, some of the pure white cats are born partially or totally deaf; however, Turkish Angora breeders do not believe this is a detriment, as these cats seem to enjoy their lives as pets and get along as well as their hearing littermates.[25] Those cats which are hearing impaired must be placed

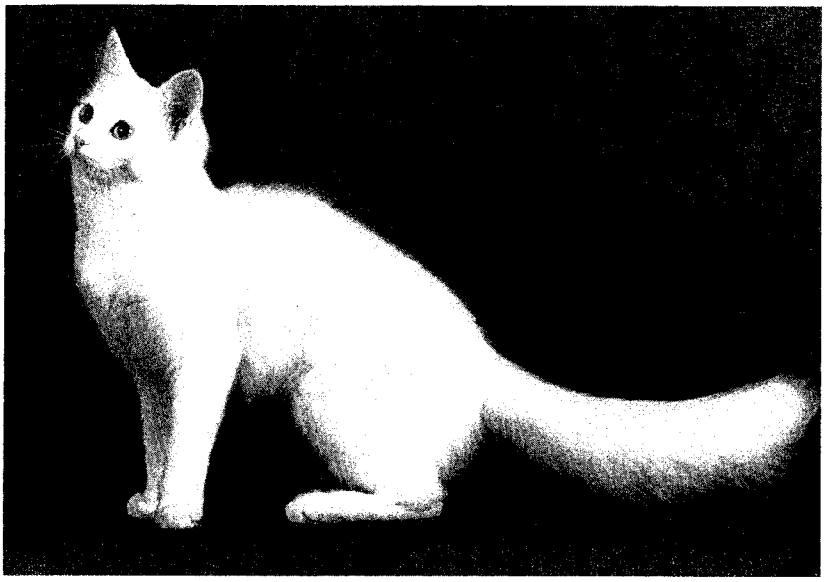


Figure 18. The Turkish Angora. (Photograph by Jane Howard)

in homes assuring absolute protection from outside dangers.

Turkish Van

Along with the other longhairs known by the late 19th century in England, and Europe, cats with a medium-long coat and colored markings on the head and tail came from the Lake Van region of eastern Turkey. In 1955, 2 Britons touring the area were intrigued to see cats still resembling the original longhairs described centuries ago when they were first taken to Europe. Aside from their special piebald pattern, limiting color to the head and tail, the cats were well known in the area for their love of water and swimming. The Britons imported a pair of Van kittens and started a breeding program in England. After several more trips by breeders to eastern Turkey and mating efforts with the additional stock, the "Turkish" was recognized in 1969 in Britain by the GCCF. It also now has full acceptance in FIFe and other European registries, as well as in The International Cat Association (TICA) and the American Cat Fanciers' Association (ACFA) in America.

The first Van cats imported to England were auburn and white. The genetics of the auburn color are the same as for the sex-linked orange color, but the deeper tone is probably a result of many years of breeding in a limited area. Though auburn and white was the color originally preferred, black and white is more usual in the Lake Van area. The cats also carry the dilute factor, allowing cream/white and blue/white. Calicos, as well as tortoiseshells, may also be produced.

In 1982 a British breeder brought some of her Turkish cats to America, where they were shown. In a few years interest in this natural breed has grown and more cats have been imported to North America. In 1988 the bred was recognized by CFA for registration with the name Turkish Van.

Bea van der Lende and Leen Kort, in search of Turkish Van cats, travelled in 1987 from The Netherlands to Van, a province of East Anatolia, of which the capital and largest city is Van (located on the shores of Lake Van). They reported that to the Turkish people of the area, a Van cat is an odd-eyed white cat with one blue and one yellow eye. Though they were able to take 2 black and white cats with them, it is now difficult to fine the original bi-colored Van cats.[40] The Ankara Zoo has recently started a breeding program for the Van cats of eastern Turkey under the protection of the Turkish College of Agriculture. The cats are maintained in natural circumstances within the Van region, and kittens are not allowed

out of the area until their numbers increase.[41]

The Turkish Van is considered one of the largest domestic cats. Males weigh 12-18 lb or more at full maturity and the females 7-12 lb. They have broad hips and massive shoulders, with long legs set wide apart. The head is a wide, moderately short wedge, substantially broad to harmonize with the large body (Fig 19). Vans have expressive tails, always in motion, with fox-like fullness.

Their soft coats feel like cashmere with no trace of undercoat. The length varies according to the time of year and maturity of the cat but should be semi-long.

Because of their size and unusually active nature, these cats need space and a great deal of understanding to help them adapt to household living. Not all of them like to swim, but owners say they do seem fascinated with water and are more apt to take a dip in sinks and tubs than most cats.

Norwegian Forest Cat

A large semi-long-haired cat, known as the "Skogkatt" (Forest Cat) in Norway, has been a familiar animal on Norwegian farms for centuries. Even today they may be seen in the woods of central Norway and near the Swedish border. Natives speculate that this may have been the cat mentioned in Norse mythology that Thor, the Thunder God, could not lift because of its huge size. The Vikings may have taken the original cats back with them from their sea journeys, or the cats may have entered Norway with the crusaders returning from wars in the Holy Land.[10] In fairy tales of the mid-19th century, the Forest Cat is referred to as a "fairy cat."

The first efforts in Norway to have the "Wegies," as they are often called, recognized as a distinct breed began in the 1930s. In 1938 the first Norwegian Forest Cat was exhibited at a show in Oslo, Norway. Following World War II the cats were threatened with extinction. Breeders worked to preserve the original characteristics and form of these beautiful cats. A serious breeding program was started in the early 1970s and in 1976 the Federation Feline Internationale (FIFe) accepted the breed, which attained full Championship status the following year. Today classes of Norwegian Forest Cats in European cat shows are among the largest of any breed. In Norway there are 50-180 at each show.

Americans began to take notice of this breed in the late 1970s. The first breeding pair was imported in 1979. A Norwegian Forest Cat Fancier's Association was established in the early 1980s and the breed was presented to the various American registering associations. CFA approved the Wegies for registration in 1987. They are currently evaluated in the noncompetitive Miscellaneous class.

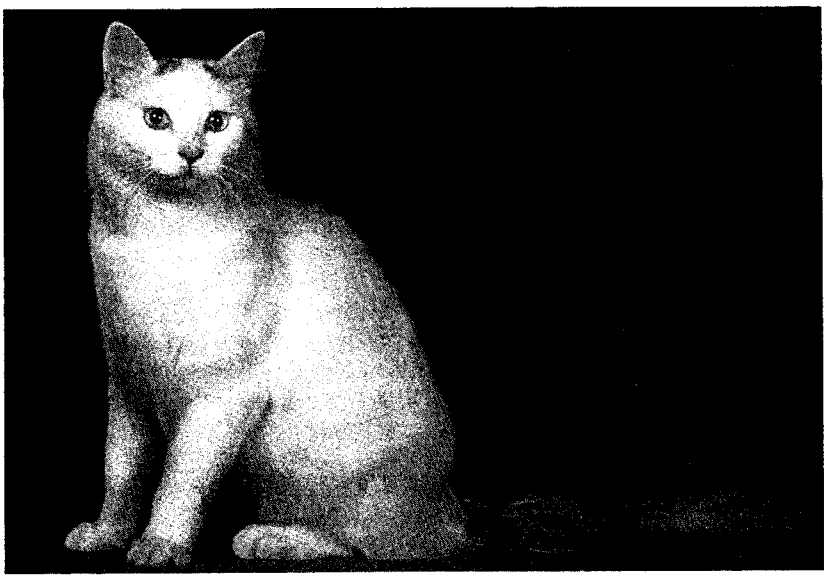


Figure 19. The Turkish Van. (Photograph by Jane Howard)

The most distinguishing feature of this natural breed is the quality of the coat. A Wegie is in full coat during the winter months, with a long, thick double texture and huge ruff, a flowing tail and furry britches on the hind legs (Fig 20). The wooly undercoat insulates against the coldest weather, while an oily guard hair outercoat repels rain and snow. The coat does not tangle or mat and requires minimal grooming. In summer, following natural molting of the undercoat, only the shaggy outercoat remains, along with a full tail and tufts in the ears and on the toes.

The Norwegian Forest Cat is medium sized to large, powerful and moderately long, with muscular hind legs slightly longer for jumping and climbing. The head is an equilateral triangle, with the ears forming the outer edges. Brown tabbies and black and white were said to have been the original colors and are still very popular; however, all colors except the pointed pattern or Burmese brown are accepted. Wegies are friendly, loving and hardy.

Persian

To many cat fanciers, Persians represent the most glorious of pedigreed cats. Their long flowing silky coats suggest opulence and luxury. Huge round eyes and a massive body structure give these cats a striking appearance. Their quiet, gentle temperament lends an aura of serenity and dignity to their surroundings. The Persian breed, which is divided by CFA into 7 divisions for competition, is the most popular of all the breeds at shows. Persian registration accounts for more than two-thirds of the total pedigreed cats registered with CFA.[5]

The earliest long-haired cats seen in Europe were introduced by the caravans traveling from Persia and Turkey during the late 16th century. In the most comprehensive 18th century book on natural history by Comte de Buffon (1756), an excerpt from *Voyages de Pietro della Valle* (1586-1652) refers to these long-haired cats. The Italian traveller mentions not only Angora cats but also a different species from the province of Khorazan in Persia, which he describes as gray, with very long, fine, glossy and silky coats.[12]

Angora and Persian longhairs were much admired in France and England, and were commonly crossed. Solid white fur was the favorite, and the blue-eyed white cats first appearing in England were generally Angoras, while the whites with yellow eyes were of the larger, more stocky Persian type. Eventually the British preferred the longhairs with Persian background, partially to avoid the tendency for deafness seen in the blue-eyed white Angoras.[32] Because the dominant white gene can suppress the expression of any other color gene, it is "masking." Many other colors were carried as recessives by these early cats. Long-

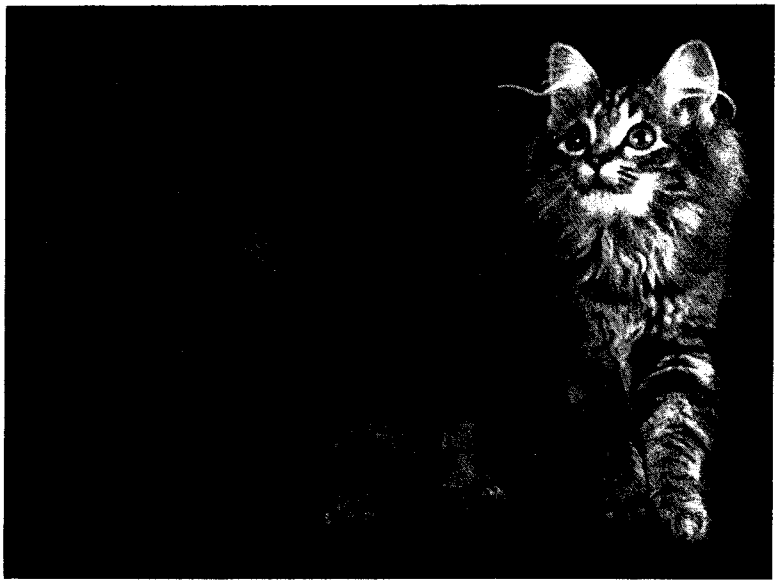


Figure 20. A Norwegian Forest Cat kitten. (Photograph by Jane Howard)

haired cats also were imported into England from Russia. These were said to have been blacks and tabby patterned.

By 1901 the stud books in England showed Persians in black, white, blue, orange, cream, sable, smoke, tabby, spotted, chinchilla, tortoiseshell, bi-color and tricolor. Though blacks were the first to be registered, blue Persians soon became the most popular, probably because Queen Victoria owned 2.[45] Persians were exported to North America from Europe at the end of the 19th century. American breeders accepted them with great enthusiasm and used the British standards as a starting point. Eventually the breed was developed to the massive cobby body type and immense coats seen in showhalls today.

Persians may be large or medium sized, with considerable variation. Overall quality and balance are determining elements. The Persian body appears rounded and should be equally massive across the shoulders and rump. Boning is thick and strong, and the legs short. Though Persian coats vary somewhat, depending on color, the ideal is a fine, glossy hair texture standing well off the body, with a huge ruff and full tail.

The CFA Persian standard calls for a round head with a very wide skull and powerful jaws. The nose is to be "short, snub and broad" with a "break." In recent years breeders have given much attention to the shortness of nose and degree and placement of the break, which is the stop at the nose transition from the forehead. Some prefer this to be a deep indentation, while others believe the break should not be overly severe. Silver Persians, for example, usually have less extreme nose breaks. Judges have latitude in interpretation, in that the standard wording is not specific concerning the degree of this feature, except for the "Pekeface" Reds.

Several other aspects of the head structure have great effect on the overall look. Small ears set low on the head and tilted forward, along with full, large, round, brilliant eyes set far apart, are important characteristics that contribute to a desired sweet expression. The standard calls for Persians to have a "proper bite." Cats are disqualified if they display any "deformity of the skull resulting in an asymmetric face and/or head." Conscientious breeders take special care to select breeding cats that maintain the Persian head appearance without displaying the problems often associated with a brachycephalic (overly shortened) head type.

The 7 Persian divisions have been established on the basis of color and pattern. The various colors in the *solid division* are to be even in tone, sound to the roots and without markings (Fig 21). All have copper eye color, with whites also competing in separate classes for blue-eyed cats and odd-eyed cats (one blue and one copper eye).

Figure 21. A solid-colored Persian. (Photograph by Jane Howard)

The *shaded division* is for silver cats with white undercoats tipped with black, the "cameos" (red tipped with white undercoat), tortoiseshell cats with white undercoat, and golden cats, which have warm cream undercoats tipped with black (Fig 22). The goldens, though tipped, are the result of a separate gene recessive to the shaded inhibitor gene. "Chinchilla" or "shell" tipping is very slight and gives a sparkling appearance to the coat, while "shaded" tipping is darker. Silver and golden cats have green or blue-green eyes distinctly outlined with black. Cameos and tortoiseshells have brilliant copper eyes.

Cats in the *smoke division* are genetically similar to shaded cats, except the tipping is so deep that the cat appears solid, blue-cream or tortoiseshell colored on the surface, but has a white undercoat evident when the coat is parted (Fig 23).

Tabby division cats come in 3 patterns: classic, mackerel and patched. They are seen in many colors, and the rich contrast of today's Persian tabby markings is truly

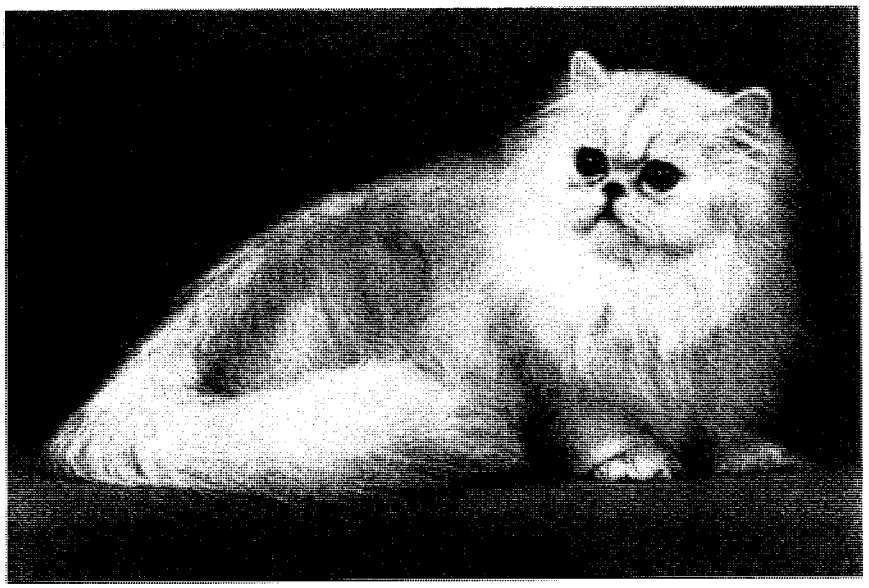


Figure 22. A shaded Persian. (Photograph by Jane Howard)

Figure 23. A smoke Persian. (Photograph by Jane Howard)

dramatic (Fig 24). The patched tabby is a classic or mackerel pattern with the addition of red and/or cream patches. The color and pattern is a result of the sex-linked red gene. "Peke-face" red tabby Persians conform in color to the standard for red tabbies; however, these cats have differing underlying bone structure in the head.

The *parti-color division* is for tortoiseshell and blue-cream cats (Fig 25). As of 1990, a separate *bi-color division* was established by CFA for cats of accepted colors combined with piebald white spotting (formerly in the parti-color division) (Fig 26). Van bi-color cats are white with colored patches confined to the extremities (head, ears, legs and tail). Calicos, Van calicos and tabby and white cats are also included in this division.

Cats in the *Himalayan division* were at one time considered a separate breed. Crosses between Siamese and long-haired cats were tried in the 1920s and 1930s. After years of work the goal of producing a cat with Persian type, also displaying the Himalayan or Siamese point-restricted pattern, became a reality (Fig 27). By 1961 all of the American associations had recognized the Himalayan as a breed. Gradually the Himalayans became indistinguishable in type from the Persian breed. Finally in 1984 CFA declared the Himalayan cats with colorpoint pattern a Persian division, making offspring of crossbreeding eligible for championship competition in the appropriate Persian color class. Many point colors are accepted in this division, including solid colorpoints, lynx (tabby) points, tortie and blue-cream points. All cats in the Himalayan division must have deep vivid blue eyes. Solid color chocolate and lilac cats resulting from Himalayan/Persian crosses are shown in the Solid Division in CFA.

Persian breeders often believe certain personality traits go with various colors or patterns. Tabby Persians seem to be especially active and outgoing. Tortoiseshells are often mischievous. Himalayans tend to be entertaining and playful. Generally, however, Persian cats are universally known for their sweet, gentle, affectionate and soothing temperaments. They are passive and adaptable to any living arrangement. Though they do have short bursts of playful energy, Persians are rarely destructive and generally remain content as quiet observers. Daily grooming and combing are necessary to keep their long soft coats free from tangles and mats. Occasional bathing is also needed to keep their coats shiny and free of excessive oil. Most Persians become accustomed to this care, which should be started when they are kittens. They grow to welcome the daily attention. Their owners also tend to be people who look upon the grooming routine as a pleasant experience and part of the enjoyment of living with a Persian cat.

Figure 24. A tabby Persian. (Photograph by Jane Howard)

Figure 25. A tortoiseshell Persian. (Photograph by Jane Howard)

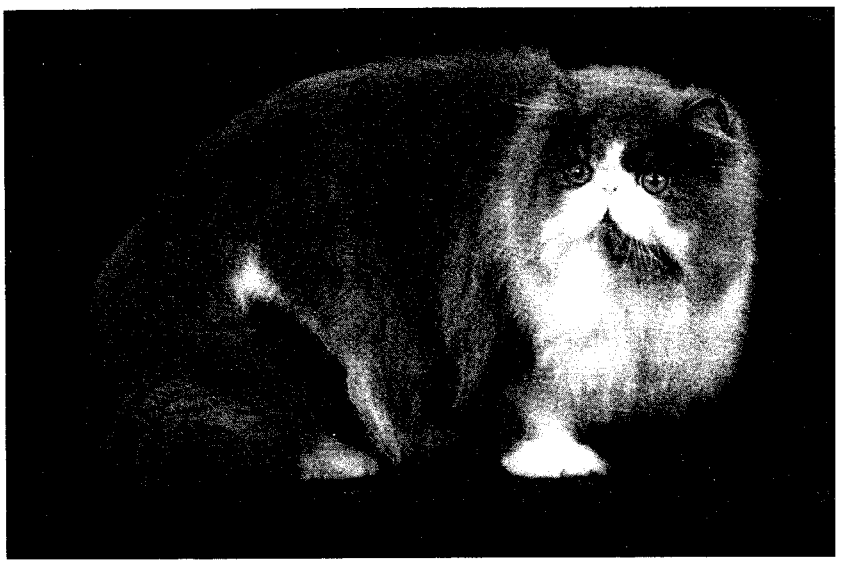


Figure 26. A bi-colored Persian. (Photograph by Jane Howard)

Exotic Shorthair

For many years British breeders have experimented with crossbreeding Persian and Russian Blue lines into the British Shorthair breed. In the 1950s and 1960s in America some breeders began using Persians in their American Shorthair breeding programs, as at that time there was an open registration policy. The purpose was to add colors not available in the American Shorthair gene pool, such as chinchilla and shaded silver, which existed only in the Persian breed. As a result of this hybridization, the American Shorthairs began to acquire some undesirable characteristics, including round heads and soft, overly long coats. Most breeders then discontinued the outcrossing.

These hybrid cats, however, were appreciated by some breeders for their own exceptional and unique beauty. In 1966, through the initiative of a prominent CFA judge, Jane Martinke, who suggested a program for recognizing the hybrids, CFA decided to designate the new breed as Exotic Shorthair. The ideal was to be a shorthaired Persian, and all breeders of the hybrid American Shorthairs were given the opportunity to transfer registration of their

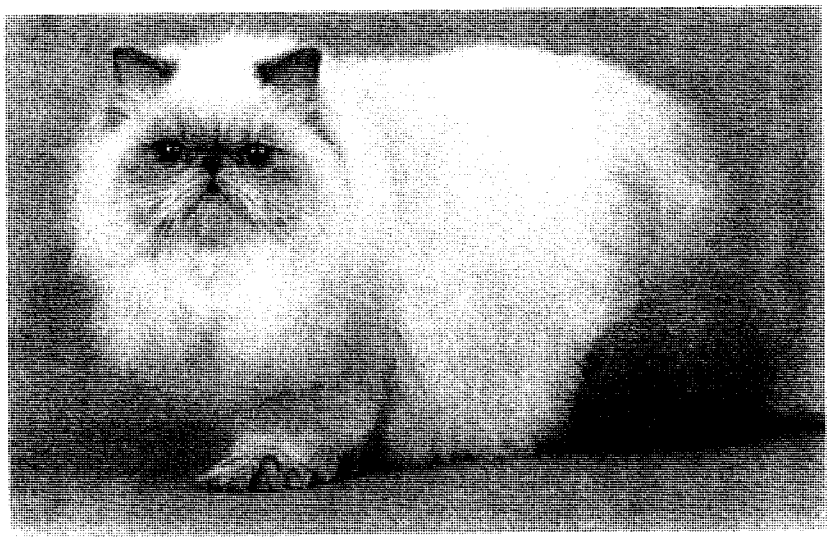


Figure 27. A Himalayan Persian. (Photograph by Jane Howard)

cats to the new breed. By 1967 the Exotic Shorthairs were accepted for Championship status. Burmese and Russian Blues were also used in the early years of this breed, because at that time any shorthair was allowed. Today only Persians are accepted as outcrosses.[24]

The standard for Exotic Shorthairs is identical to that for Persians except for the coat, which should be of medium length, soft and plush, standing out from the body (Fig 28). The length is slightly longer than that of other short-haired cats but should not be long enough to "flow," as does the Persian coat. Exotics are accepted in all of the colors described in the Persian breed. Because of its close association with the Persian, this breed has been judged with the long-haired breed group at CFA shows since 1983.

After many years of dedicated work, breeders have produced Exotic Shorthairs equal in body and head type to the Persian. Despite this, the breed has its own distinct appearance, which some call the "teddy bear look." The stocky body is boldly apparent, and their short legs and neck are more easily seen without the long coat to hide the conformation (Fig 28).

Many owners say their Exotics have livelier personalities than Persians. The easy coat maintenance holds great appeal to pet owners who like the massive, round-faced Persian look but do not want to comb a cat daily. Because of the Exotic's dense, soft coat, an occasional bath and regular light combing are desirable to avoid excessive shedding.

Siamese

The most familiar short-haired breed throughout the world is the Siamese. These cats are easily recognized by their distinct color pattern, the result of a genetic mutation causing pale body hair and dark extremities (muzzle, ears, legs and tail). The Siamese gene is temperature sensitive, creating darker extremities, and is part of the "albino" series of alleles, which progressively diminishes the amount of pigment in the hair. Also included in this series are the Burmese, "light-phase Burmese (Tonkinese), blue-eyed albino and pink-eyed albino cats.

The Siamese gene and pattern is well known to breeders of other animal species and referred to as the "Himalayan" pattern. In cats it is also known as the "colorpoint" or "point-restricted" pattern. Because the first cats to be recognized with this coloring came from Siam, now Thailand, the color mutation has long been associated with the Siamese breed, even though the true origin of the gene is not known. Blue eye color, also characteristic of Siamese, is linked to this major color gene and may be intensified through selective breed-

ing to the deep vivid brilliance seen in show-quality Siamese cats.

The cats known today as "Siamese" represent only one of several early varieties of cats native to Thailand that have been well documented in the oldest known book devoted to cats. The manuscripts called *The Cat-Book Poems* are housed in the Thai National Library in Bangkok and were saved from the ancient Siamese city of Ayudha, founded in 1350 and burned by invaders in 1767. This remarkable graphic record of early cats was brought to the attention of the western world in the 1970s by Daphne Negus. Descriptions and illustrations clearly depict pointed cats with very pale coats and minimal dark coloring on the extremities. It is interesting to note the slim body and legs, along with large ears and a sharply tapered muzzle. There is evidence that the pointed cats were especially valued and kept by royalty, ensuring their good care and perpetuation.[46] Seal-pointed cats living within the high walls of the Royal Palace were protected from crossmating and remained genetically fairly pure.

Another mention of the Siamese pattern in early literature, by naturalist Simon Pallas, described 3 cats in central Russia in 1793 with a light chestnut brown body and black ears, paws and tail. Because the Siamese pattern depends on temperature, point development and color shading vary with the climate, as well as the cat's age. The cooler the environment, the darker the color. The Russian cats may have represented a separate mutation or may be related to the cats of Siam. Pallas described their head as "longer toward the nose than in the common cat," which seems similar to the head on those from ancient Siam.

The earliest known Siamese cats imported to the western world were a pair of seal points from Bangkok in 1884 presented to the sister of the British consul general in Thailand. She exhibited "Pho" and "Mia" in 1885 at the annual Crystal Palace Cat Show.[37] Siamese were reported to be in England at least 14 years earlier, however, as they were evidently present at the first Crystal Palace Cat Show of 1871. Described then as "an unnatural, nightmare kind of cat," they caused a sensation. Much controversial comment accompanied the cats brought from Siam because of their body and head type, kinked tails and crossed eyes.

The first British show standard, which originated in 1892, and rewritten in 1902 on formation of the Siamese Cat Club, called for a "striking-looking cat of medium size, if weighty, not showing bulk, as this would detract from the admired svelte appearance. In type, in every particular the reverse of the ideal short-haired domestic cat . . . also distinguished by a kink in the tail." It was not until many years later that the kink was to be considered a fault, along

Figure 28. An Exotic Shorthair. (Photograph by Jane Howard)

with crossed eyes. Generally the features considered desirable in show-quality Siamese in 1902 have been achieved in today's cats.

In the early 1900s the breed in England consisted of not only the "royal" or seal-point color, but included some other cats from Siam described as "chocolates." The latter consisted of several distinct genetic types: solid brown cats (known today as Havana Browns, as well as the Burmese cats), and warm brown cats with dark points, most likely the Tonkinese of today. Reports from early shows indicate that chocolate-point Siamese also existed and were bred soon after the first cats from Siam were imported and that at least one blue point was registered before 1900. In that solid blue cats were illustrated in *The Cat-Book Poems* manuscripts, it is not surprising that some seal-point Siamese entering England carried the recessive gene for the dilute factor, which changes seal to blue and chocolate to lilac. In the book, *The Siamese Cat*, published in 1908, author Henry Milner Rideout wrote that "the King (of Siam) has officially declared that the Blue Cats are royal."[34]

The first known American cat fancier to import and breed Siamese, Mrs. Clinton Locke, obtained a pair from Lady Marcus Beresford in England, whose original cats were brought from the Royal Palace in Siam. This pair, a seal-point male and chocolate-point female, produced 2 cats that were big winners at the 1902 show in Chicago.[34,37] Blue points were recognized by CFA in 1932, but chocolate points did not receive full recognition until 1950 in England and 1951 in America. Though lilac points are inevitable when the dilute factor is combined with the chocolate color, it was not until the mid 1950s in America and 1960 in England that this dilute color was accepted.[46]

Many more point colors have been introduced through crossbreeding with Siamese; however, CFA and determined traditional breeders consider only the classic 4 colors originating from ancient Siam to be true Siamese. Pointed cats of other colors are classified by CFA as the Colorpoint Shorthair breed. Most CFA breeders are of the opinion that restricting hybridization in Siamese is necessary to maintain the excellent unblemished body color and even point color. They believe that certain tabby patterns in the cat's genotype tend to be reflected in ghost markings on the body.

Since the first British show standard of 1902 described a "marten" face and a head rather long and pointed," the tapering wedge-shaped head form has been the goal of Siamese breeders. Eyes are almond shaped and slanted toward the nose. The profile is a long straight line from the top of the head to the tip of the nose. The ears are strikingly large, continuing the lines of the wedge. The body is medium sized and a combination of firm muscularity and fine boning, resulting in a substantial yet very lithe, svelte cat (Fig 29). The torso is tubular, with the shoulders and hips continuing the sleek graceful lines emphasized by the close-lying coat. Long slim legs and a long thin tail complement the overall elegant yet strong appearance.

One of the best-known and most endearing personality traits of Siamese is their distinct noisy voice and ability to communi-

Figure 29. The Siamese. (Photograph by Jane Howard)

cate. Siamese are intelligent, precocious and highly social with people and other animals. They love to play with toys and leap to high surfaces, making ideal pets for people who appreciate their special devotion and active companionship. Siamese females have large litters and few reproductive problems. They are the most popular short-haired breed, based on CFA registration numbers (Table 2), and often live to a very old age.

Oriental Shorthair

Most of the cats in southeast Asia today are not pointed cats. *The Cat-Book Poems* manuscripts, dating from 1350 to 1767, in Siam, described and illustrated a variety of cats, including some with coats of jet black, black and white bi-color, solid brown, blue/gray and shaded silver, as well as point-restricted coloring. The original cats imported to England from Thailand were often of solid color. It was not until the Siamese Cat Club in the late 1920s issued a statement excluding all but blue-eyed pointed cats from breeding and showing that other Thai cats began to decline in favor.[46]

After World War II Baroness von Ulman, working with 2 other British breeders, began efforts to breed a solid brown cat with the chocolate brown gene carried by the Siamese, rather than the sable of the Burmese. The resulting cats of Siamese type and solid chestnut color were recognized in 1958 as a breed called the Chestnut Brown Foreign Shorthair. Around 1962 the British geneticist, Patricia Turner, began her long-term breeding program to produce blue-eyed solid white cats of Siamese type. These cats were eventually accepted in England in 1977 as a separate breed, known as "Foreign Whites." The solid white color produced by the dominant white gene "masks" the underlying genetic color of cats. Therefore, in the course of Ms. Turner's breeding program, which used Siamese cats as well as non-Siamese cats, there were many kittens born of solid or patterned color all over.

The first British tabbies of foreign type to attract attention were spotted and received acceptance as the Oriental Tabby breed in 1978. Numerous solid and patterned colors have since been produced over the years, some with brilliant contrast and others of pastel subtlety. The sleek tight coat of the Oriental Shorthair seems to accentuate the detail of pattern and beauty of every color tone (Fig 30).

American cat fanciers were captivated by the first Oriental Shorthairs in England and began importing them in the early 1970s. Several breeding programs also were underway in America and Europe during the early 1960s and 1970s. CFA Championship status was granted to the Oriental Shorthair in 1977, dividing the breed into 5 color groups: solid, shaded, smoke, tabby and parti-color. All have green eyes, except the whites, which may have blue or green

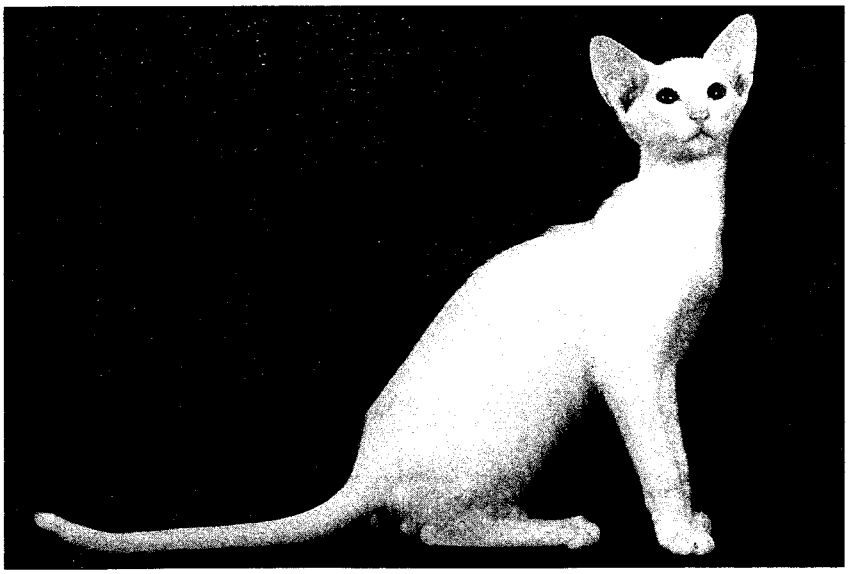


Figure 30. The Oriental Shorthair. (Photograph by Jane Howard)

eyes. Because Siamese and Colorpoint Shorthairs may be used as outcrosses, the health and vigor of the breed reflects its huge hybrid gene pool.

The Siamese or colorpoint gene is recessive to the full color gene, making it inevitable that Oriental Shorthairs will produce pointed cats. CFA rules state that those meeting the Colorpoint standard may be shown in Colorpoint Shorthair classes; however, the Siamese breed does not allow these "variants." In other associations and in Europe, the pointed variants are considered Siamese. The Oriental Shorthair standard is almost identical to that of the Siamese, except for color.

Like their Siamese relatives, Oriental Shorthairs are active and extremely outgoing toward people and other animals. Some owners believe they are generally a little less talkative than Siamese and are more inclined to use body language.

Colorpoint Shorthair

The Colorpoint Shorthair breed looks identical to the Siamese, except for color. The breed was the result of the early hybrid experiments by cat fanciers in Britain, who crossed Siamese with red domestic shorthairs and Abyssinians in an effort to develop more than the 4 traditional Siamese colors. Two red points were shown at the Siamese Cat Club show in England in 1934; however, the first red points (then called "orange points") and seal tortie points had poor Siamese body and head type. Breeding programs for red points were established in America in 1947 and again in England in 1948, but again the cats lacked the desired refined body type, which might have been achieved had there been more intense linebreeding to Siamese. Siamese breeders were biased against them for many years, and it was not until 1966 that they were finally accepted (as Siamese) by the British GCCF (Governing Council of the Cat Fancy).[46]

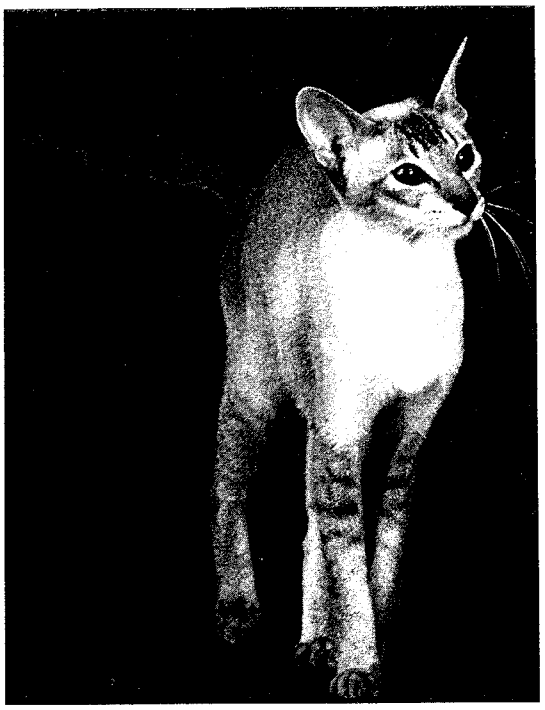
CFA has continued to refuse acceptance to these hybrids as Siamese but did recognize the Colorpoint Shorthair as a separate breed in 1964. Since then, many other colors have been developed and accepted, including blue-cream points, chocolate-tortie points and lilac-cream points. Most other North American associations, as well as FIFe in Europe, consider these cats as Siamese.

The 10 "lynx point" colors now included by CFA were created by introduction of Tabby Shorthair outcrosses in the early 1900s in England and in the 1960s in America and England. These cats with tabby markings restricted to the point areas are called "tabby-point Siamese" in England and in other associations.

The CFA standard for Colorpoints is almost the same as that for Siamese, except for the color descriptions. Siamese may be used for outcross breedings. It has taken a great deal of time and hard work, but the cat fancy finally has taken note of the exceptional quality and beauty in these cats. A seal lynx-point Colorpoint Shorthair achieved a top CFA National Award in 1982, marking modern history for this breed (Fig 31).

Acceptance by the general public was immediate, as the personality of Colorpoints includes the vocal audacity and demanding, intelligent nature of Siamese cats, along with a great variety of striking point colors.

Figure 31. A lynx-point Colorpoint Shorthair. (Photograph by Jane Howard)



The gene pool is huge and the breed is hardy.

Balinese, Javanese, Oriental Longhairs

Over the years long-haired kittens appeared occasionally in Siamese litters. Though the most likely reason for the occurrence of this recessive gene would be a throwback to non-Siamese cats somewhere in the ancestry, many breeders preferred to believe that long-haired Siamese were the result of a spontaneous mutation. In 1940, 2 breeders recognized the special beauty in a silken coat added to the elegant grace of the Siamese cat and began to purposely breed these long-haired cats. They chose the name "Balinese" because the flowing movement of these cats seemed similar to that of the dancers of Bali.

In the face of strong opposition and reluctance on the part of Siamese breeders to allow matings to top-quality cats, the early Balinese began with a heavier body type than that of the Siamese, and acceptance was difficult. Breeders continued to work for finer boning by breeding back to Siamese, while at the same time being careful to not sacrifice the long silky coat. In 1970 CFA granted Championship status to the breed, recognizing only the 4 colors accepted in the Siamese breed: seal point, chocolate point, blue point and lilac point. The breed standard is almost the same as that of the Siamese; however, Balinese appear to have softer lines and a less extreme body type because of the long coat. One of the distinct features of these cats is their plume-like tail (Fig 32).

Almost at the same time as the Balinese cats were becoming known, breeders were already working to develop other point colors through breedings to American Shorthairs. Long-haired kittens also were cropping up in matings of Colorpoint Shorthairs that had been developed through hybrid breeding with cats carrying the recessive gene for long hair. In 1986 CFA granted Championship status to these cats as the Javanese breed (Fig 33). In several other associations, however, they are considered Balinese.

It was inevitable that one day breeders would want Oriental Shorthairs in long coats to complete the series of Siamese-type breeds. In the late 1970s and 1980s breeders began crossing Balinese to Oriental Shorthairs, and the second generation produced long-haired Orientals (Fig 34). It is not easy to maintain good coat quality and yet keep the refined body type; however, with the cooperative attitude of today's Siamese and Oriental Shorthair breeders, matings to top-quality cats are helping this breed advance. These cats were accepted by CFA for registration as the Oriental Longhair breed in 1988 and are evaluated in the noncompetitive Miscellaneous class.

Havana Brown

All-brown cats were among the earliest cats to come into England from Siam (Thai-

Figure 32. The Balinese. (Photograph by Jane Howard)

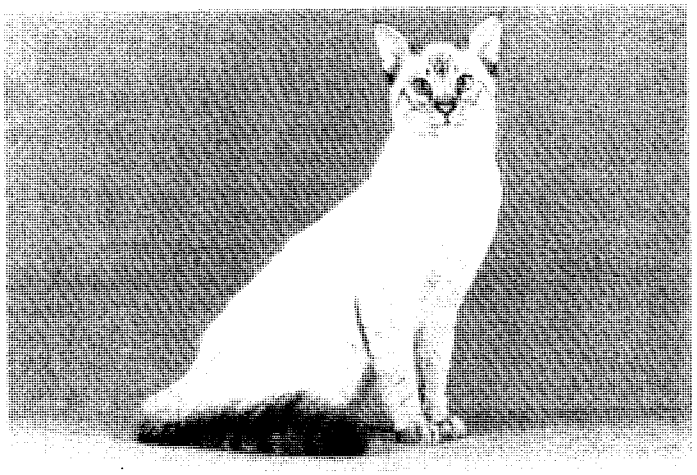


Figure 33. The Javanese. (Photograph by Jane Howard)

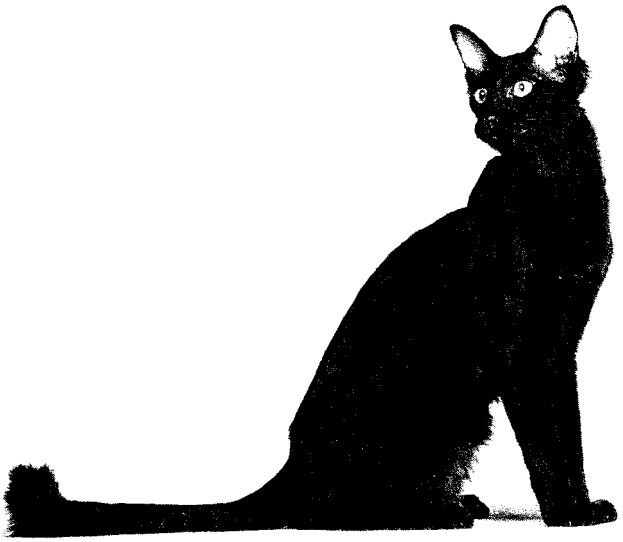


Figure 34. The Oriental Longhair. (Photograph by Richard Katris)

land) in the late 1800s. It is now assumed that the genetics of these cats were not all the same. Some would today be called Burmese, while others carried the brown gene of the Siamese chocolate-pointed cats. After the Siamese Cat Club ruled that only blue-eyed pointed cats should be bred and shown, all of the self-brown cats disappeared from the cat fancy.

Around the early 1950s breeders working independently and later together began a breeding program designed to recreate the self-chocolate brown short-haired cat. In 1954 the first kitten of the new color to be registered was born.[2] "Bronze Idol" resulted from a mating of a seal-point Siamese, carrying chocolate, to a solid black cat, also carrying chocolate. (The black cat had been from a seal-point Siamese bred to a black.) This kitten became the foundation of the new Chestnut Brown Foreign breed in England, which was later renamed "Havana" after a rabbit breed of the same color. The breed as it exists today in England would be considered a Chestnut Oriental Shorthair by CFA classification, in that the head and body type are the same as in the Siamese.

The first Havanas in America were imported from England in the late 1950s. Breed recognition was given in 1959, with the word "Brown" added to the name. American breeders preferred to maintain the early moderate body and head type, rather than strive for a Siamese-like cat.

The breed gradually evolved in America into a form totally distinct from that of any other breed. In 1964 full CFA Championship status was achieved by the Havana Brown.

The North American Havana Brown head is particularly unique in the world of cats. The muzzle has been described by breeders as resembling a protrusion on the face rather than an extension of the head. There is a pronounced break on both sides behind the whisker pads. When viewed in profile, there is a distinct stop at the eyes, and the end of the muzzle appears almost square (Fig 35). Large ears are round tipped and tilted forward. Brilliant green oval eyes add to the penetrating alertness of the Havana Brown. Graceful and moderately lithe in body type, Havanas are firm and muscular, and substantial in every way but never coarse or cobby. They stand high on long, straight legs and have a medium-long slender tail. Females have slim, dainty legs. The rich warm mahogany brown color and smooth, lustrous coat give this cat its true glory.

The Havana Brown temperament is even, quiet and gentle. They are demanding of attention from people, and have a soft voice and loud purr. Havanas are adaptable and able to play and amuse themselves, but they are happiest with feline companionship and love to curl up with several cats to enjoy mutual grooming. They are a hardy breed with no known genetic defects. Often called a feline connoisseur's cat, Havana Browns are still surprisingly rare and undiscovered by the general public.

Figure 35. The Havana Brown. (Photograph by Jane Howard)

Birman

The "Sacred Cat of Burma," as the Birman is often called, is a long-haired stocky cat with seal, chocolate, blue or lilac point-restricted color. Over the body there is a faint golden beige cast (the "golden mist") in all 4 colors. Distinctive pure white feet are important to the breed. Though the Birman's true origins are uncertain, the cats are forever linked to southeast Asia because of a famous legend that explains their coloring.

In the time of Buddha the ultimate goal of followers was to pray, work and be selfless in an effort to reach the state of being beyond self and senses, that of Nirvana. If an individual failed in this striving, his soul would be reincarnated in that of a lower being. Many believed human souls were residing in the bodies of cats, which led to a great love and care of cats throughout ancient Asia and the keeping of cats by Buddhist monks.

The legend of Birman cats evolved before the birth of Christ. One hundred pure white cats with yellow eyes lived with monks as guardians of the Temple, Lao-Tsun, built in Burma to honor the goddess Tsun-Kyan-Kse who ruled over the transmutation of souls. One day raiders attacked this temple and the head monk, Mun-Ha, was killed. His loyal cat, Sinh, placed his paws on his master's body and turned to face the golden image of the goddess. Instantly the cat's coat turned from white to golden and his eyes became sapphire blue like hers. Only his paws remained pure white where they touched the priest as a symbol of purity. All of the other temple cats developed the same coloring. After 7 days of mourning Sinh died, taking the soul of his master to Paradise. Since that time all of the remaining golden cats with white paws were considered sacred and custodians of the souls of

the monks. Only a few very worthy people were permitted to possess one of them.[26]

The Birman was first recognized as a natural breed by the French in 1925. Their modern history started when a pair was sent or smuggled to 2 men living in France from the High Priest of the Lao-Tsun Temple. The 2 men had travelled to Burma and helped protect the Buddhist monks from Brahmin aggression. They reported seeing the Birman cats and learning of the legend. The 2 cats were sent in 1919 as a gesture of gratitude, but on the sea journey the male died. The female fortunately was pregnant and founded the breed in France, which later flourished throughout Europe.

After the devastation of World War II only 2 Birmans were known to have survived in Europe, "Orloff" and "Xenia de Kaabaa," and work to reestablish the breed had to begin again.[26] The first cats to enter North America came from France in 1959. Many more were imported from France and England, including 2 kittens born to a pair directly obtained from a temple in Cambodia.[6] Through collaboration with French breeders, Birmans became well established in America and were registered with CFA by 1966. Championship status in CFA was granted in 1967.

The coat of the Birman is very different from that of other long-haired cats. It is silky and medium long, with a texture that does not mat. The coat is wavy on the belly. Birmans are strongly built, elongated and stocky, with heavy legs. The head is of medium length and the nose has a Roman down-turned shape in profile. The ears are of medium size and set as much on the side of the head as on top (Fig 36). The eyes are placed wide apart, and almost rounded and deep blue.

Only the 4 point colors (seal, chocolate, blue and lilac) are accepted by CFA; however, in some associations additional colors are allowed. The body should have the "golden mist" beige cast; much attention is given to the 4 white "gloves." The front paws are white, ending in an even line across the paw at the second or third joints. Back paws have white "gloves" and "laces" extending up the back of the hock, ideally ending in an inverted V. Faultlessly gloved cats are the exception, and the Birman

Figure 36. The Birman. (Photograph by Jane Howard)

standard emphasizes that the cat is to be judged as a whole. Nevertheless, lack of white on any paw or white in the point areas is cause for disqualification. The white spotting gene responsible for the very restricted degree of white on Birmans is generally thought to be a recessive gene and not part of the more common dominant piebald spotting gene.[16]

Birmans are gentle, well-mannered cats, yet they have boundless energy and like to seek attention by using their quiet voices. They blend easily into an active household, adjust well to cats of other breeds and enjoy endless lap sitting.

Burmese

The story of the Burmese breed begins with one female cat, "Wong Mau," who was imported to America from Burma in 1930. Dr. Joseph C. Thompson, a psychiatrist from San Francisco, served as ship's doctor in the US Navy and developed a keen interest in the Far East. He had spent time as a Buddhist monk in a monastery in Tibet and

had become familiar with the self-brown short-haired cats seen throughout southeast Asia for centuries. These cats, known as "copper" cats, were described and illustrated in the ancient Thai manuscripts. *The Cat-Book Poems*, preserved from the city of Ayudha (1350-1767). Dr. Thompson, who also bred Siamese cats, acquired Wong Mau and began a breeding program to determine her genetic makeup with the intention of establishing a new breed in America resembling the Asian copper cats.[30,43]

The initial matings of Wong Mau, which produced the foundation pedigree for the breed and determined the genetic principle of the Burmese cat, were outlined in an article published in the April, 1943, issue of the *Journal of Heredity*. The article confirmed Dr. Thompson's belief that Wong Mau represented a hybrid cat containing one gene for Burmese (solid brown) and one gene for Siamese (point restricted). This he believed gave her what he called the lighter shade of Burmese. The article reported that, by mating Wong Mau to a seal-point Siamese, "Tai Mau," and inbreeding with the hybrid offspring, it had been possible to produce 3 generations of true-breeding "purebred" Burmese with a "dark color phase."[36] These and other later breeding experiments proved the existence of the Burmese gene (c^b) and established that all Burmese cats are homozygous for a color gene, which is a member of the albino series of alleles and causes solid black to appear dark sable brown. Today Wong Mau as a Burmese-Siamese hybrid with intermediate color would be considered a Tonkinese.

CFA accepted the Burmese for registration in 1936 with a Siamese body and head conformation. During the 1930s and 1940s other American breeders working with Dr. Thompson imported a few more cats from Burma to enlarge the gene pool, but outcrossing to Siamese continued. The dark-phase true-breeding and the light-phase intermediate brown-pointed cats (Tonkinese) were considered Burmese, causing a great deal of confusion. In addition, the brilliant gold eye color of the early imports was quickly diminished to a chartreuse green. CFA finally decided to suspend registration of the breed altogether in 1947.

Around this time the first Burmese were exported from America to Europe and the breed was recognized by the GCCF in Britian in 1952. They are now popular in all parts of Europe, Scandinavia, Australia and New Zealand. In addition to the original sable brown, other colors have been introduced. The Burmese conformation in countries to which they were exported remains moderately "foreign" or slim; however, this is no longer the case in America.

Dr. Rosemonde Peltz, a breeder of Burmese and authority on many cat breeds, described in the 1978 CFA Yearbook the tremendous blow American Burmese breeders suffered when the breed was suspended by CFA. In her comprehensive history of the breed, she said, "The most striking aspect of the whole disheartening situation is that they continued to breed. . . to present an excellent Burmese of the best type possible."

After a determined effort, CFA registration was reinstated in 1953, based on a new color standard allowing only a "solid coat without markings." The body type was described as "medium, dainty, long." By 1957 the CFA standard was again changed, calling for a body "midway between Domestic Shorthair and Siamese." The key words, "somewhat compact," entered the standard in 1959, and there has been no major change in wording since then. The concept of the American Burmese gradually became that of the medium-sized cat with "substantial bone structure, good muscular development and surprising weight for its size." Later the word "somewhat" was dropped to further emphasize a compact body type.

The head is rounded, with a broad, short muzzle showing a nose break. Large rounded expressive eyes should be brilliant gold. A special sweet expression gives the Burmese a distinctive appearance (Fig 37). The early Burmese cats of the 1930s had heads described as "appleheads," which were "dome shaped" when seen from the front, between the ears. These cats were also considered "chunky" in body type. During the late 1950s breeders started to bring this stocky image back and to avoid the dainty or svelte Siamese appearance.[7]

By the mid-1970s some breeders began selecting for a more extreme shortening of the nose to emphasize the round head called for in the standard. The resulting skull changes eventually lead to a head type that

is believed to be associated with cranial facial lethal deformities in newborn kittens.[21] In an effort to eliminate defects in the breed, the concept of the desired Burmese look is again being challenged as breeders work on solutions. One important aspect of the breed, which was never changed, is its gleaming, very close-lying coat with a fine, glossy, satin-like texture.

As a result of the early years of Siamese hybridization, 2 recessive genetic factors remained in some Burmese lines. The mutant *chocolate gene* produces, in the Burmese breed, "champagne" coloring, while the *dilute factor* affects the sable and champagne colors to create blue and platinum, respectively. Though these colors began to attract interest from some breeders, they were strongly opposed by others who had worked for years to identify the Burmese breed solely with the solid dark sable brown coloring of the Asian copper cats. In 1980 CFA decided to identify a separate breed, called the Malayan, to accommodate the 3 additional colors. Finally, in keeping with the changing history of this breed, Malayan cats were incorporated into the Burmese breed in 1984, and are currently judged in a separate Dilute division.

It has been said that Burmese remain kittens all their lives. They are notoriously intelligent and fun loving, often surprising people with inventive games. A characteristic movement associated with the breed is a dance with the hind legs called the "Burmese shuffle." Though their voice is relatively quiet, they use a variety of noises to communicate. These cats have a strong need to be close to their owners and are cuddly lap sitters. Burmese females tend to be especially clever and bossy, and often take the lead in a household with other breeds. Altered males are usually mellow and loving.

Figure 37. The Burmese. (Photograph by Jane Howard)

Tonkinese

Hybrid offspring from Siamese cats bred to Burmese are the basis of the Tonkinese breed. The Burmese (c^b) gene is only partially dominant to the Siamese (c^s) gene. Combining the 2 results in an intermediate blend of coloring in the heterozygous cats, who have a dark-pointed pattern but deeper body color than Siamese. Matings of these Tonkinese cats produce a predictable average of 50% with hybrid Tonkinese coloring, 25% with homozygous Burmese coloring and 25% with homozygous Siamese point-restricted coloring. The solid-colored and pointed offspring are called "variants" and can never be eliminated in this breed. Though today no further outcrossing is allowed to Siamese and Burmese, variant cats are valuable in breeding programs and make highly desirable pets.

The well-known foundation cat for the Burmese breed, "Wong Mau," would today be considered the first recognized Tonkinese to be imported to America. Most likely some of the brown cats described in England in the late 1800s as "chocolate Siamese" were also early Tonkinese. It can easily be presumed that Tonkinese hybrids lived in ancient southeast Asia as long ago as Siamese and Burmese "copper" cats existed, as they undoubtedly interbred. The brown hybrids quickly lost favor in England during the early 1900s when only the "Royal" seal-point cats with light body color and blue eyes could be shown.

Modern experiments in breeding Tonkinese began on the east coast in America and in Canada during the 1960s. Originally called "Golden Siamese," "Honey Siamese" and "Chocolate Siamese," by 1967 they were finally referred to as "Tonkanese" and had achieved acceptance by the Canadian

Cat Association (CCA). In 1971 North American breeders voted to call the breed "Tonkinese" and worked for acceptance by American registering associations. CFA finally allowed registration in 1978 and full Championship status in 1984.

In addition to the blended coloring from the 2 ancestor breeds, the Tonkinese breed presents an intermediate body and head type. These cats are neither long and lithe like the Siamese, nor compact and round like the Burmese. Medium conformation, as described throughout the Tonkinese breed standard, is not as easily defined and understood as extreme type. Achieving a consistent head and body type from such opposites has been very difficult for breeders. Muscular and surprisingly heavy, the Tonkinese is a moderately proportioned and balanced cat. The head is a modified wedge, with gently curved contours and a blunt muzzle. The ears are medium sized and set as much on the sides of the head as on top (Fig 38). The eyes are almond shaped, slanted along the cheekbones and set wide apart. The unusual aqua color is a definitive characteristic of the breed. The Tonkinese coat has a quality completely unlike the extremely sleek and satin-like textures of its ancestors. Described as "mink," it is medium short, close lying, fine, soft and silky, with a lustrous sheen, but it does not lie tightly against the body. There are 5 accepted coat colors: natural mink with dark brown points and medium brown body; champagne mink with medium brown points; blue mink; platinum mink; and honey mink (derived from the light brown or cinnamon gene).

The Tonkinese personality seems to be a "happy medium," according to the enthusiastic cat fanciers who enjoy these cats in their homes. Tonkinese are active cats, outgoing with people and other animals, even tempered and only slightly vocal. They are charming and fun, yet gentle and affectionate, easy to groom and hardy.

Bombay

The challenge of creating a new breed is the ultimate dream of some cat fanciers. Nikki Horner, from Louisville, Kentucky, started breeding cats at the age of 16. After winning top national awards with several breeds and producing numerous grand champions, she became one of the rare individuals who actually achieved this aspiration. The Bombay breed represents her desire to produce a copper-eyed black short-haired cat with Burmese conformation. The image of a domestic cat with the exotic appearance of a "mini-panther" led to her choice of the breed's name, inspired by the black leopard of India.

Her first attempts with crossbreedings of black domestic shorthairs to Burmese in 1958 were unsuccessful, producing offspring that were, in her words, "big and horsey." The coats were too long and the

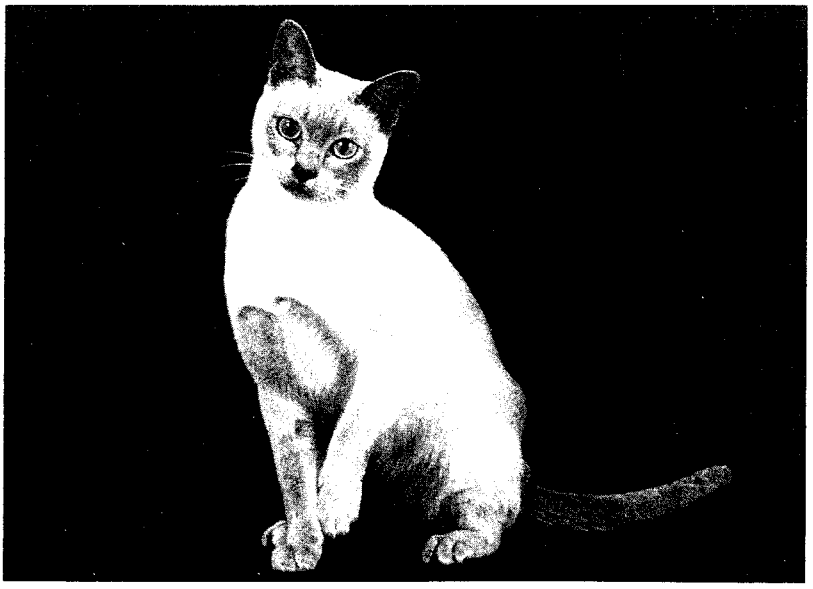


Figure 38. The Tonkinese. (Photograph by Jane Howard)

eye color poor. Eventually she found the right combination of cats, starting with a black American Shorthair male with deep copper eye color and a Grand Champion sable Burmese female. Through a long process of inbreeding and outcrossing and careful selection, she was able to consistently produce a black cat unlike any other. Eighteen years after the original attempted breeding and following a great deal of effort to promote acceptance of the breed, the Bombay achieved CFA Championship status in 1976. Outcrossing to Black American Shorthairs and sable Burmese is still allowed.

The Bombay and Burmese standards are almost identical, except for color. Because of a few subtle variations, however, many judges and breeders interpret the description of type to be different. Whereas the Burmese body is "presenting a compact appearance," the Bombay body is to be "of medium length," "neither compact nor rangy." Generally, Bombays are a little higher on their legs and have slightly longer body and tail proportions. The head is rounded with a short muzzle, but there should not be a "pugged" or "snubbed" look. A coat that is black to the roots is extremely important, along with black nose leather and paw pads (Fig 39). Deep gold to copper eye color is imperative for a top example of the breed.

Bombays are bold and outgoing, and make intelligent, affectionate companions. They generally combine the easy-going temperament of the American Shorthair and the inventive, more talkative character of the Burmese.

Figure 39. The Bombay. (Photograph by Jane Howard)

Korat

As one of the earliest known breeds in the world, the Korat is also probably the purest. Even today the breed is very similar in appearance to its native ancestors which were known to have lived wild in the jungles of the Malay Peninsula. All Korats trace their pedigrees to Thailand. These silver-blue short-haired cats with luminous green eyes have been cherished and rare in their native land for centuries, where they are known as the "Si-Sawat." ("Si" is the word for color and "sawat" is a wild fruit plant with a silver blue seed.)

Korats were described and pictured in *The Cat-Book Poems* from the ancient city of Ayudha (1350-1767), and have been the subject of many delightful stories and myths. Their shimmering silver color signifies wealth to the Thais and for hundreds of years Korats have been considered the symbol of good fortune. The Thai people describe Korat eyes as the color of young rice, associating the cats with good crops. The gift of a pair of Si-Sawat to a new bride is said to ensure a happy marriage and home. In early Thailand they were never sold but instead were offered as special expressions of honor or esteem.

Mrs. Jean Johnson of Oregon, who had lived with her husband in Bangkok for 6 years, travelled extensively in Thailand searching for the silver blue cats in the late 1950s and reported seeing only 5 or 6. They were not to be found on the streets and none were for sale. All those who possessed these cats were members of the Thai government, the Thai nobility or representatives of foreign governments. In June, 1959, a pair of Korats was sent to her as a gift from Thailand. "Nara" and "Darra," littermates, were the first Korats in America. To avoid close inbreeding, Mrs. Johnson

crossbred these cats for one generation to Siamese she had brought back from Thailand, carefully eliminating any progeny with Siamese characteristics from future breedings.[19]

Throughout the 1960s more cats were acquired from Thailand by the growing circle of Korat fanciers. Daphne Negus, an important pioneer in the breed, journeyed to Thailand to import 9 Korats as this number is believed by the Thai people to bring good luck. In 1965 the Korat Cat Fanciers' Association was established to protect and develop the breed, as well as to preserve its heritage. A standard was written based on the appearance of the original native cats, and the Korats were accepted by CFA for Championship status in 1966. Except for the early outcross matings, this breed has been as carefully guarded and exclusive as any in the cat fancy. Importing from Thailand is still allowed and Korats are now accepted by registering associations all over the world.

Like the ancient Korats, the breed today is muscular and semi-cobby with a body that has the "feeling of hard-coiled spring power" and a back carried in a curve. The head is unique, with the curving lines of the eyebrow ridges and the sides of the face forming a heart shape. The Korat's well-rounded eyes are large and brilliant, seeming oversized for the face (Fig 40). The ears are large and set high, giving an alert expression. The glossy, close-lying coat is heavily tipped with silver, resulting in an intense sheen often described as a halo effect and best appreciated in the sunlight.

Korats have a sweet, gentle disposition and are said to be highly protective of their owners and children. They communicate with people using their quiet voices, and do not like loud noises. Korats move with cautious dignity and prefer to remain close to their owners and familiar places.

Japanese Bobtail

Through close examination of many examples of early Japanese artwork, it is apparent that cats with short pom-pom tails must have been held in high esteem for centuries in the Far East. Domestic cats were introduced to Japan from China and Korea in the early 6th century. It was customary for every Buddhist temple to keep at least one pair of cats to protect the sacred documents from rodents. Numerous woodcut prints and painted screens picture cats with ladies of luxury and include them in Imperial family settings. In Japan, cats were obviously considered creatures of great beauty, elegant grace and delight. By contrast, early Chinese art emphasizes almost exclusively the hunting ability, agility and strength of the cat.[20]

Japanese folklore is rich with tales in which cats are often associated with good fortune or are transformed from women. The name for the cat, "neko," is sometimes given to geisha girls because of their ability

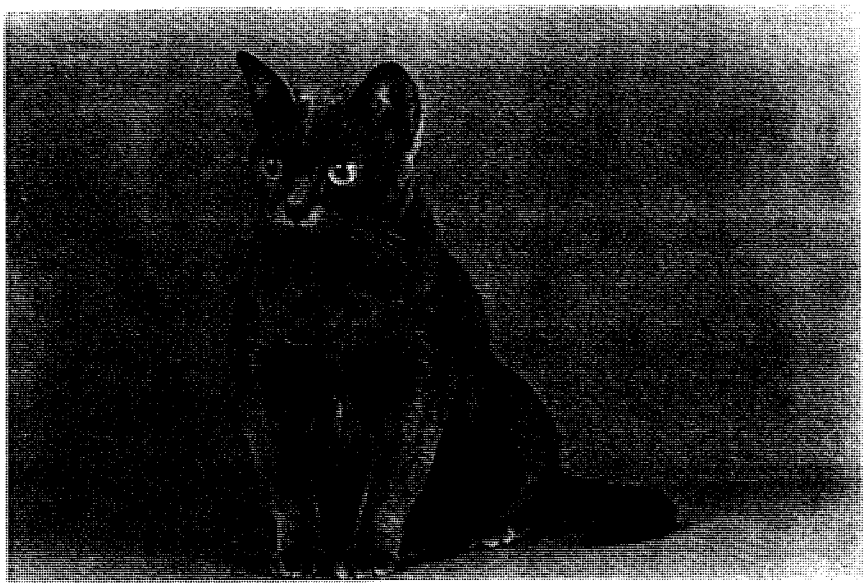


Figure 40. The Korat. (Photograph by Jane Howard)

to charm. A popular story includes the saying that cats with long tails take human form and bewitch people. This is one possible accounting for the presence of so many cats with the unique short kinked tail seen for centuries throughout Japan and other parts of the Orient. Another famous legend explaining why the cats of Japan so often have bobbed tails tells of a cat resting near the hearth whose tail was set afire by a spark. As the frightened cat ran through the streets of the Imperial City, all the houses turned to flames. By morning the city was destroyed, with only ashes remaining. The Emperor was so angry he decreed that the tails of all cats be cut short to avoid a similar disaster in the future.[15]

Perhaps the best-known of all legendary Japanese cats is "Maneki-Neko," a small attractive calico female, who was said to have beckoned and lured passersby and was associated with good fortune. She is represented with her paw raised in a welcoming way and was painted on the facade of the famous Gotokuji Temple near Tokyo, where hundreds of replicas remain. Maneki-Neko figurines, both antique and modern, may be seen in many Japanese stores and restaurants as a symbolic attraction to customers. The pom-pom tail is evident on the back of the statue.

The original cats entering Japan from China and Korea were solid black, pure white, black and white bi-colors, and occasionally black, red and white tri-colors. Tricolored calico cats, called "mi-ke," were considered a symbol of good luck, especially by Japanese sailors who believed these cats could foresee storms. Because of superstition and the Japanese belief in the connection between men and all living things, cats were ensured a reverent position for many years. Finally, between the 13th and 15th centuries, the Japanese silk industry grew in importance. When it became threatened by the mice attracted to the silkworms, the government decided that cats could no longer be pampered house pets. They were ordered to be set free to save the silk industry and grain harvests.

Appreciation for the beauty and personality of cats has never faded in Japan, and in modern times many of the pedigreed breeds have been imported. Among the common street cats seen today in Japan, most have bob tails. The tail structure is unique to each cat, with the bone often twisted like an "S" or even a corkscrew.

Extensive studies by geneticist Dr. Neil Todd proved that the gene responsible is recessive and completely different from the dominant Manx tailless gene. It is not a lethal factor and causes no deformities. Though occasionally there are bob tails with short straight tails, there are never full-length tails.

An American cat fancier living in Japan for almost 20 years admired the special beauty and charm of the Japanese Bobtails, and developed them as a breed. Judy Crawford began breeding cats of the colors that would produce the mi-ke tri-colored offspring shortly after World War II. One day in 1967, Elizabeth Freret, a cat breeder in America, was shown a Japanese Bobtail being boarded at a Maryland pet store for a family who had recently returned from Japan. She was fascinated to hear of the many street cats in Japan with short tails just like the one she had seen. A year later she was in contact with Miss Crawford and by August, 1968, 3 Bobtails arrived in America. After a standard was developed, the cats were presented to the CFA Board, which accepted them for registration in 1969. Championship status followed in 1976 and there has since been a continuous flow of Bobtail imports from Japan into North America.

The body standard for Bobtails is in keeping with the cat's original background as an elegant aristocratic housepet. Though they are muscular, the impression of the Japanese Bobtail is one of lean refined style, rather than massive structure. The American-bred Japanese Bobtails have developed away from the body type seen on the streets of Japan today. The hind legs are longer than the forelegs, but angled so that the back remains level when the cat is relaxed (Fig 41). The tail must be clearly visible and should not extend more than 3 inches. It may be rigid or flexible; however, because of the curves, a characteristic fluffy pom-pom effect is apparent.

The head shape forms an almost perfect equilateral triangle, with gentle curving lines, high cheekbones and a fairly broad muzzle. Large oval eyes are set at a pro-

nounced slant when viewed in profile. The large ears are upright, set wide apart on the head and tilted forward.

Bi-colors and tri-colors, along with solid blacks, reds, whites and tortoiseshells, are the most predominant colors. Other Japanese Bobtail colors include "patterned" categories denoting any variety of tabby striping or spotting with or without white. The dilute blues and creams are allowed in solid color or in the patterned categories. Preference is given to bold, dramatic markings and rich vivid color. The Bobtail coat is medium short, soft and silky, lying comfortably on the body without a noticeable undercoat.

Japanese Bobtails are ideal family pets with an alert, endearing personality. They are active in a gentle way and not overly demanding of attention. Their curiosity, ability to adjust to other animals and children, and quiet chirping voices contribute to the distinct Bobtail character.

New Breeds

Thirty-one breeds are currently recognized by the Cat Fanciers' Association for full Championship status. The Burmese breed is subdivided into 2 divisions, and the Persian breed is subdivided into 7 divisions. The breeds now accepted for registration only are the American Curl, Norwegian Forest Cat, Oriental Longhair and Turkish Van. These cats may be exhibited in the noncompetitive Miscellaneous classes. According to the CFA "Rules Governing Acceptance and Advancement of New Breeds and Colors: 1979," at least 5 years are needed after registration is established, along with other requirements that include a proposed standard, to be approved for recognition as a Provisional breed. Finally, after further evaluation and show requirements have been met, and with agreement among the breeders on the standard and acceptable colors, the breed may be presented to the CFA Board of Directors for Championship status consideration.

CFA is acknowledged to be one of the most rigorous and careful of all cat registry organizations in the world regarding approval of new breeds. CFA breeders and the elected members of the Board of Directors generally believe it is important to the future integrity of the cat fancy to determine whether a new breed will truly be an asset both in health and beauty before registration is allowed. Once development of a breed has commenced and many people have invested time and money, rejection becomes more difficult. It takes some preliminary work to present and evaluate the potential of a new breed before registration. Several factors are considered by CFA

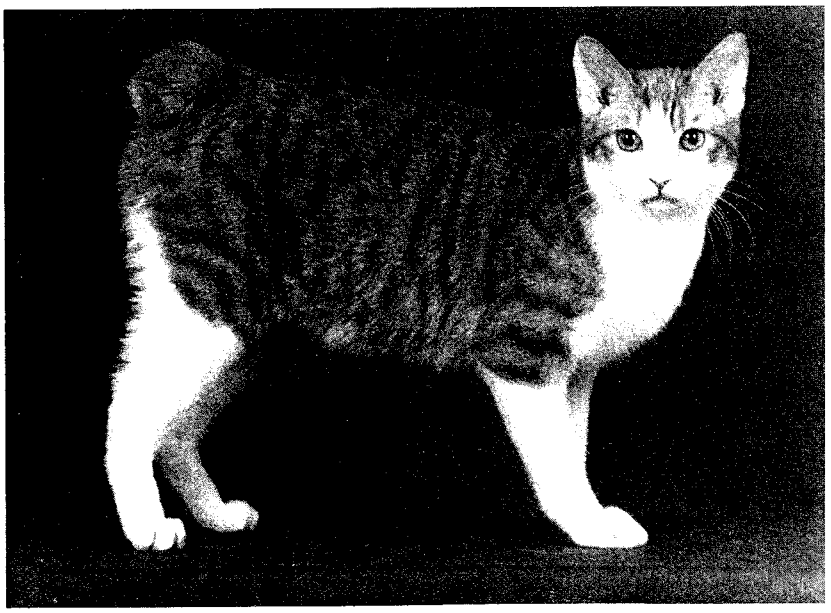


Figure 41. The Japanese Bobtail. (Photograph by Jane Howard)

Board Members before recognition of a new breed. These include:

- *Information on genetic makeup*, number of breeds or characteristics combined in the development of hybrids and predictable consistency in offspring produced.
- *History and background of the cats in their country of origin*, and/or genetic information regarding a spontaneous mutation.
- *Possible overlap in characteristics* that might threaten the distinctive qualities already associated with existing breeds.
- *Health status and potential for inherited genetic abnormalities*, temperament and general acceptability to the public as desirable pets.

With the increasing popularity of cats as pets in recent years, many new breeds have been developed. Some remain the whim of an individual and have not been able to meet CFA requirements of 10 breeders working with the breed for registration application. Some have not attempted CFA approval, while others have applied and were rejected. Following is a list of some breeds accepted by at least one association other than CFA:

American Bobtail: Originated from an initial mating of a mixed-breed short-tailed male to a Siamese female about 20 years ago. Subsequent matings indicate the dominant Manx gene is responsible for tails of various lengths. Introduction of the longhair gene with Himalayan breedings, and more recently with Maine Coons, has been allowed.

Burmilla: This breed is the result of a planned mating of a British Chinchilla Longhair (Persian) male to a Burmese female in 1982, producing shaded silver shorthairs of Burmese type (British standard). The Burmilla has been accepted as a provisional breed by the Cat Association of Britain.

Bengal: This breed is a hybridization of domestic cats with the native Asian Leopard Cat (a small spotted wild cat of high pattern contrast) to produce a spotted cat with wild appearance and domestic cat temperament.

California Spangled Cat: This breed has short hair, with a spotted pattern and "wild look." It was created by one man over a period of 15 years, using a variety of American domestic cat breeds and 2 imported cats from northern Africa and southeast Asia.

Longhair Scottish Fold: This breed evolved because of the recessive longhair gene in pedigreed Scottish Fold litters through use of approved outcross breeding. The pedigrees and appearance are the same as the parent breed, but the look is soft and round. The cats appear to have no ears at all, as they are folded down and covered with fur.

Nebelung: These blue semi-long-haired cats resulted from a chance mixed-breed cat mating. One breeder decided to replicate the appearance by introducing Russian Blue cats and breeding with mixed-breed long-haired cats of a type similar to that of the Russians.

Ragdoll: This breed was founded 25 years ago with the breeding of a long-haired mixed-breed female to a Birman male. They are very gentle and said to be limp when held. The cats are large and long-haired, with point-restricted color. Some are mitted and others have a bi-color pattern. The appearance is similar to that of Birmans. Controversy surrounds their origin.

Siberia: This is a long-haired cat originating in Russia. Some were imported to western Europe from Leningrad and also from Czechoslovakia. Following more than a year of complex arrangements, the first 3 Siberia kittens directly imported from Russia to America arrived on June 28, 1990. Another cat fancier travelled to Russia to bring back adult breeding Siberia cats from Leningrad and Moscow in July, 1990. Siberias are massive cats (males 17-26 lb), with a long mane, lustrous straight single coat without undercoat, and thick curls on the belly and breeches. Tabby colors are preferred.

Snowshoe: This short-haired cat was developed in the 1960s as a hybrid between the Siamese and American Shorthair bicolor (Fig 42). Breeders have experienced difficulty producing the desired white pattern with reasonable consistency.

Sphynx: This hairless cat resulted from a spontaneous mutation that has occurred

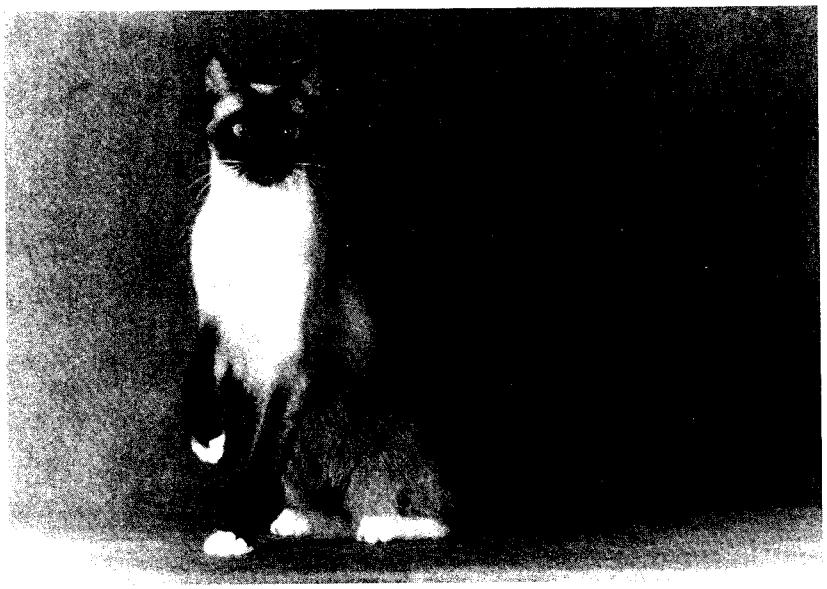
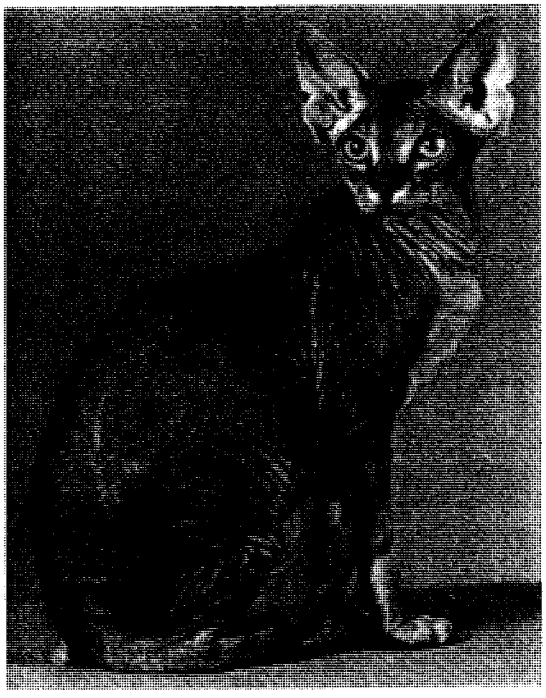


Figure 42. The Snowshoe. (Photograph by Jane Howard)

several times (Mexican hairless cats were pictured in Miss Simpson's 1903 *Book of the Cat*. The hairless gene is recessive to that for a normal coat but is dominant to that for the Devon Rex wavy coat. These cats have short down fuzz on some parts of the body. Their body conformation is striking, with wrinkled skin (Fig 43). Immune system and fertility problems were reported in the past, but in recent years the breeders have been able to produce robust cats.

Figure 43. The Sphynx. (Photograph by Jane Howard)



Selkirk: The most recent and unconfirmed mutation in domestic cats was seen in 1987 in a litter of housecats in Wyoming. One of the kittens was brought to a Persian breeder from the local humane society. This female had an unusual curly coat, evidently the result of a dominant gene, unlike the recessive Cornish and Devon rex genes. When bred to a Black Persian Champion, she produced 6 kittens, 3 of whom were curly. The coats are thick, plush and soft, falling in loose curls, rather than waves. Because the wirehair gene is also dominant, more work is needed to determine if the genetics of these cats are the same and if the kittens perhaps represent a semi-long-haired version. The proposed name for the new breed is "Selkirk."

Household Pet Cats

A true cat fancier has a love and appreciation for all cats, whether or not they are pedigreed. Many people involved in breeding pedigreed cats also include mixed-breed cats as part of their households, and help local humane societies or shelters in efforts to decrease pet overpopulation. Registering associations, such as CFA, include competition for nonpedigreed cats in their licensed cat shows as part of their interest in pro-

moting the welfare of all cats. The Household Pet Class at shows often serves as an introduction to people interested in joining the cat fancy and participating in cat club activities. Many go on to breed championship cats or to exhibit altered pedigreed cats in the Premiership competition.

Household pet cats are judged on their beauty, according to the subjective opinion of the judges, and on condition. CFA has no written standards for household pet cats, preferring each to be valued for its own uniqueness. Unlike pedigreed cats, which are compared to the ideal guidelines described in the various breed standards, household pets may be of any color, pattern, coat texture, or body and head type.

Condition requirements are the same for household pet cats as for pedigreed show cats. General good health and vigor must be reflected in the cat's overall appearance, as well as alertness, movement and coat quality. The cat must be in prime physical condition, with good muscle tone, sound bone structure and healthy weight. It is important for all show cats to be faultlessly clean and well groomed. Condition also includes a well-balanced temperament and receptiveness to the handling and judging procedure. Because the noise and activity of the showhall environment can intimidate some cats, judges disregard normal timid behavior. It is nevertheless surprising that most household pet cats seem to easily adapt to the show procedure and display delightful responsiveness to the attention they receive from judges and the public.

Household Pet Classes give judges an opportunity to educate visitors about the general characteristics of cats and the importance of altering cats not used for pedigreed breeding programs. All CFA Household Pet adult entries (over 8 months of age) must be castrated or spayed, and may not be declawed. Presentations of fine examples of household pet cats help increase people's awareness of the natural beauty and charm of all cats, and how they are enhanced by good care, diet and grooming.

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Chapter 2

Normal Genetics, Genetic Disorders, Developmental Anomalies and Breeding Programs

Roy Robinson and N.C. Pedersen

NORMAL GENETICS

Basic Principles of Genetics

It is convenient in zoologic research to have a standard against which deviating forms can be compared. In genetics, it is the phenotype of the normal animal; the "wild type," as it is formally termed. For the domestic cat, this is the smooth-coated mackerel-striped tabby African wild cat, *Felis libyca*. *Felis libyca* is one of a group of small cats inhabiting much of Asia and North Africa. The European wild cat, *Felis silvestris*, is akin to the African wild cat and the 2 species are regarded by some authorities to be geographic forms of a species complex.[31] The domestic cat (*Felis catus*) is almost certainly a domesticate of *F libyca*.

The early association between cats and people was probably a checkered affair because cats have a weak bonding instinct in comparison to dogs. The true domestication of cats was credited to the Ancient Egyptians about 4000 years ago. Domestication may have begun slowly, with cats living close to granaries and their inherent rodent population. The Egyptians revered many animals, and cats featured prominently in both life and death.[1,18] The cat slowly became a religious symbol, to be cherished and protected.

Subjugation of the Egyptians by the Romans secularized the cat, and the animal began to travel beyond the borders as a fascinating household companion. The Romans were primarily responsible for the spread of cats across Europe. There may have been other centers of origin of domestication of cats in the Middle East and India, but these are poorly documented. Other sources contain more detailed discussion on the origin of domesticated cats.[4,19,33]

Feline Karyotype

Karyotype refers to the number and structure of chromosomes within the cell nucleus (karyon = nucleus). Domestic cats have a karyotype consisting of 19 pairs of chromosomes (Fig 1).[2,22] These 19 pairs of chromosomes consist of 5 metacentrics (2 large, 3 small), 11 submetacentrics (7 large, 4 small), and 2 acrocentrics (both small). The remaining pair of chromosomes comprise the sex chromosomes. The X is a medium-sized metacentric, while Y is a small metacentric. Females have 2 X sex chromosomes (Fig 1), while males have an X and Y. Individual chromosomes have characteristic internal banding patterns as prepared with the classic trypsin-Giemsa technique (G-banding) (Fig 1) or the Ronne method (R-banding).[22] The wild species *Felis silvestris* and *F libyca* have karyotypes that are identical to that of domestic cats.

Basic Laws of Heredity

Chromosomes are made of building blocks called genes. Genes are the basic de-

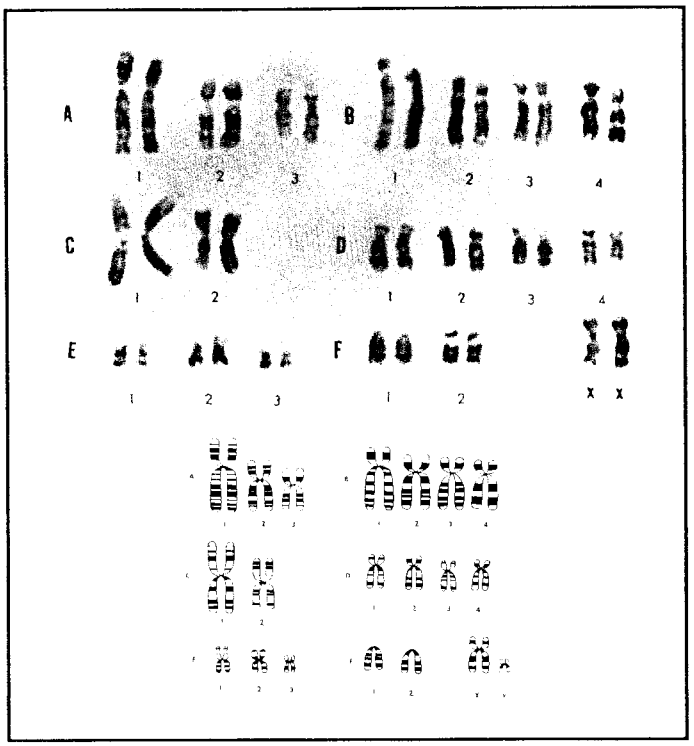


Figure 1. Top: The normal karyotype (19 pairs) of a normal female domestic cat by the G-banding (trypsin-Giemsa) technique.[2] Feline chromosomes are divided into 6 different groups (A-F) according to size and position of the centromeres. Bottom: A drawing of the normal karyotype of a male cat provides a better illustration of the position of the centromeres and the characteristic banding patterns on each pair of chromosomes. The bands correspond to regions within the chromosome that have distinctly different DNA structure, and hence staining affinity. Differences in DNA structure are due to differences in the structure of various genes found in each region. Because analogous genes are always found in the same locations (loci) and have the same basic DNA structure, the banding pattern is virtually identical from one cat to another. (Courtesy of Dr. K. Benirschke and *American Journal of Veterinary Research*)

terminants of heritable structure and function. Each gene provides the genetic code necessary for the cell to produce a single protein. Each protein product has a direct influence on the structure, function, metabolism and embryonic differentiation of cells.

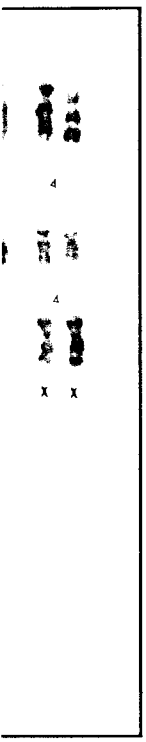
Chromosomes exist as pairs in all body (somatic) cells (Fig 1). Each chromosome reproduces itself during somatic cell division, forming 2, rather than 1, pair of chromosomes. Two of the chromosomes go to 1 daughter cell and 2 to the other, thus restoring the original chromosome number. Body cells containing 1 pair of each of the 19 types of chromosomes are called diploid (di = 2).

Figure 2. Checkerboard or Punnett square for deriving the expectations in matings of Aa x Aa. The gametes A and a from each parent are written across the top and down the left side of the diagram. The expectations are found by writing within each square the genotype of the sperm at the head of the column and the genotype of the ovum at the side of each row, continuing until each square is filled. The result is the genotypes to be expected for the mating.

		Genotype of Sperm	
		A	**a**
Genotype of Ovum	**A**	**AA**	**Aa**
	a	**Aa**	**aa**

During sexual division in the ovaries or testes, however, the numbers of chromosomes are reduced. As the germ cell divides to produce either sperm or ovum, each pair of chromosomes is not duplicated. Rather, 1 chromosome of the pair goes into 1 of the daughter cells and 1 goes into the other. Sperm and ovum contain 19 single, or unpaired, chromosomes. Cells containing only 1 chromosome of each pair are called haploid (haplo = 1). The normal complement of 19 pairs of chromosomes is restored when sperm and ovum fuse.

Reduction of the number of chromosomes in sex cells, and its restoration by fertilization, is a key factor in genetic diversity. Genes on corresponding chromosome pairs are hardly ever identical to each other. Segregation of chromosome pairs during formation of sperm or ova allows for genes on 1 chromosome to dissociate themselves from genes on the corresponding chromosome. Fertilization not only restores the normal complement of chromosomes, but



allows a chromosome to pair with a new chromosome that will likely carry many different mutant genes.

Each chromosome is made up of several thousand individual genes. These genes are always found at specific sites along the chromosome. Sites where specific genes are found are called loci (Fig 1). Though genes have a high degree of constancy, they are subject to change or mutation. These changes cannot be so great, however, that the gene no longer codes for a functional protein. If the gene mutates too much, its product will be defective and may have a lethal or deleterious effect on the organism (see section on Genetic Defects).

Changes in the structure (genetic code) of a gene will give rise to mutant genes. A mutant gene at the same locus as the original or wild-type gene is called an allele. Allelic genes are somewhat different from the parent wild-type genes; thus the proteins they induce in the cell may be slightly altered as well. If these alterations are not deleterious, they are reflected in slight alterations in the gene protein product, and the structure and function of the cell. These alterations lead to the phenotypic differences among all individuals. Heredity involves transmission of mutant or allelic genes in relation to original or wild-type genes.

Monogenic Inheritance

The fact that chromosomes exist as pairs in body cells, and singlets in reproductive cells, greatly affects the way genes are distributed from parent to offspring. For convenience, genes are symbolized by letters of the alphabet. An underlined capital letter (A) is used for the normal gene, and an underlined lower-case letter (a) for the corresponding mutant allelic gene. If gene A has only 1 mutation, that is, a, these individuals will be genetically characterized as AA, aa or Aa in regard to this gene. AA, aa or Aa is the genetic constitution or genotype of the individual from the time of fertilization until death. Individuals with the same gene on each pair of chromosomes (AA or aa) are called homozygotes (homo = same). Individuals with different genes at the same locus on each pair of chromosomes (Aa) are called heterozygotes (hetero = different). Gametes (sperm or ova) produced by AA individuals are 100% A, while aa individuals produce gametes that are 100% a. The heterozygote (Aa), in contrast, has 50% of its gametes A and 50% a.

Transmission of the hypothetical A and a genes is shown in Table 1. Six different matings are possible and the genetic distribution of offspring is dictated by the random union of germ cells. For instance, the mating AA x Aa gives AA, Aa and aa progeny in the proportion of 25%, 50% and 25%, respectively. These proportions are more often expressed as ratios, such as 1:2:1, than percentages. The random nature of the union of A and a is shown by the checkerboard diagram of Figure 2. The checkerboard derives the expectation for the mating of Aa x Aa. A mating of homozygotes, such as AA x aa, is referred to as the parental (P_1 x P_2) or first-cross, and the offspring as the first filial generation (abbreviated F_1). Such a mating would produce 100% heterozygotes of the genotype Aa. The mating of Aa x Aa could be expressed as F_1 x F_1. This cross would yield the second filial (F_2) generation. These 2 fundamental crosses are employed in experimental genetics to determine the mode of inheritance (dominant, recessive) of a new mutant or allelic gene.

Table 1 shows the progeny of a mating based on the known genotype of the parents. The genotype, in turn, determines the outward appearance of the progeny. The outward or physical expression of the genotype is referred to as the phenotype. The phenotype results from the anatomic and biochemical effects that gene A or a has on development of the organism, beginning at the time the ovum is fertilized by the sperm. The genetic expression of the A gene can follow 1 of 3 patterns: dominant, co-dominant or recessive. Given allelic genes, such as wild-type A and mutant a, it is common for the wild-type gene to be dominant over the mutant gene. The dominant gene is usually written as a capital letter and the recessive gene as a lower-case letter. In the example of the A gene, A is dominant over a and gene a is recessive to A. In a simple dominance/recessive relationship, the dominant gene A "switches off" or represses the recessive gene a when both are present in the same cell. The repressed a gene cannot

produce its protein product. As such, it cannot have any influence on the anatomic or biochemical makeup (phenotype) of the individual. If the a gene were codominant, both the A and a gene products would be produced and both would affect the phenotype.

The effects of dominance are such that the genotypes AA and Aa are outwardly indistinguishable from each other, thus modifying the expectations of Table 1. The mating of 2 parents having genotypes AA and Aa produces offspring with 100% wild-type phenotype of genotype A-. The dash after A indicates that the identity of the second gene is unknown (it could be A or a, and the animal would have the same phenotype). With an Aa x Aa breeding, the offspring are phenotypically 75% A- and 25% aa. This last mating illustrates the well-known phenotypic ratio of 3:1 that results from the matings of 2 heterozygotes.

Multiple Alleles

If a gene can mutate once, it can do so again. An allelic series at the same gene locus could come into being by repeated mutations. Regardless of how many alleles occur, only 2 can be present in the individual, and each of these is transmitted to a different gamete. This rule is shown by the tabulation of matings listed in Table 2. The example presented is 3 alleles for tabby pattern (see later discussion for description of the alleles and phenotypes). With 3 alleles there are 21 possible matings. This results in the progeny expectations shown in Table 2.

Table 1. The descent of a pair of allelic genes for 6 possible matings. The expected frequencies for progeny are shown as percentages. When there is more than 1 type, these are frequently expressed as ratios of 1:1 or 1:2:1, as the case may be. These are known as Mendelian ratios for the assortment of a mutant gene.

	PROGENY (%)		
Mating	**AA**	**Aa**	**aa**
AA x AA	100	–	–
AA x Aa	50	50	–
AA x aa	–	100	–
Aa x Aa	25	50	25
Aa x aa	–	50	50
aa x aa	–	–	100

To demonstrate the descent of the alleles from parent to progeny, the genotypes are tabulated as if no dominance exists between alleles. If the alleles are dominant to each other, for example, T^a to T and t^b, and T to t^b, this aspect must be taken into account in deriving the phenotype. The genotypes are grouped as appropriate. The 1:1 and 3:1 ratios recur as shown for 2 allelic genes.

Note the symbolism for multiple alleles. It is conventional to denote the wild-type gene by a capital letter (here, T), and a recessive gene by a lower-case letter. If there are more than 1 recessive mutant alleles, the lower-case letter is augmented by superscripts (for example, t^b). If the mutant allele is dominant to the wild type, the allele is denoted by a capital letter with a superscript (for example, T^a). In this manner, gene symbols are not merely a convenient shorthand but also convey information.

Sex Linkage

Most gene loci are borne by the ordinary chromosomes or autosomes; hence, heredity is said to be autosomal. In addition to autosomal chromosomes, there is a pair of sex chromosomes denoted as X and Y. Chromosomally, the female is XX and the male is XY (Fig 1). Consequently, the X is sometimes referred to as the "female" and the Y as the "male" chromosome. The X is a large chromosome and probably contains as many gene loci as an autosome of comparable size. Genes carried by the X are known as sex-linked. The mode of inheritance of sex-linked traits is more complex than that for ordinary or autosomal genes.

A well-known example is sex linkage of hemophilia A, which occurs in people, dogs, horses and cats. The responsible gene is carried on the X chromosome and is recessive. It is lethal in males because males do not have a second X chromosome and, therefore, lack a normal compensating dominant allele. Hemophilia A is perpetuated by female heterozygotes. Representing the normal gene as X^H and the hemophiliac gene as X^h, the typical mating that produces a hemophiliac is X^HY x X^HX^h. The genotypic expectations are X^HX^H, X^HX^h, X^HY and X^hY in the ratio of 1:1:1:1. The phenotypic expectation is 2 normal females, 1 normal male and 1 hemophiliac male. One of the fe-

males is a carrier of the hemophiliac gene (X^HX^h).

In contrast to the X chromosome, the Y chromosome is small and carries few genes. Denoting the Y as the "male" chromosome is probably appropriate, because its primary function appears to be converting undifferentiated embryonic gonad tissue into testes. In anomalous XO individuals, where the Y has been lost, the gonads develop into ovaries. Phenotypically, XO individuals are female, even though their ovaries function less efficiently than those of normal XX females. Such individuals are usually sterile.

Bigenic Inheritance

Each chromosome of a pair is transmitted independently of other members of the pair. Genes on one of the chromosomes are inherited independently of genes on the other. It is necessary, therefore, to understand not only how single pairs of genes (A versus a) are inherited, but how many pairs of genes interact in the same mating.

The interaction of pairs of genes can be illustrated by 2 of the basic color mutants of cats. One is a gene for chocolate-brown pigment (b), a mutant allele of the black pigment (B) gene. The second is a mutant gene for slate-blue or dilute color (d), a mutant allele of dark or dense color (D). Allele b and d are inherited as recessive to B and D, respectively. When a brown (bbDD) is mated to a blue (BBdd), the progeny (BbDd) are black because of the dominance relationships of the 2 pairs of genes. When black F_1 offspring are mated together, the F_2 progeny assort into 9 black, 3 brown, 3 blue and 1 lilac.

The derivation of the above 9:3:3:1 ratio is shown by Figure 3. The checkerboard is merely an extension of that shown in Figure 2. This is the case for all checkerboards once the principle of their construction is understood. The above ratio is found by

Table 2. The descent of 3 allelic genes for 21 possible matings. The expectations may be shown alternatively as ratios. For example, the 25:50:25 percentages may be expressed as 1:2:1.

	PROGENY (%)					
Mating Type	T^aT^a	T^aT	T^at^b	TT	Tt^b	t^bt^b
$T^aT^a \times T^aT^a$	100	–	–	–	–	–
$T^aT^a \times T^aT$	50	50	–	–	–	–
$T^aT^a \times T^at^b$	50	–	50	–	–	–
$T^aT^a \times TT$	–	100	–	–	–	–
$T^aT^a \times Tt^b$	–	50	50	–	–	–
$T^aT^a \times t^bt^b$	–	–	100	–	–	–
$T^aT \times T^aT$	25	50	–	25	–	–
$T^aT \times T^at^b$	25	25	25	–	25	–
$T^aT \times TT$	–	50	–	50	–	–
$T^aT \times Tt^b$	–	25	25	25	25	–
$T^aT \times t^bt^b$	–	–	50	–	50	–
$T^at^b \times T^at^b$	25	–	50	–	–	25
$T^at^b \times TT$	–	50	50	–	–	–
$T^at^b \times Tt^b$	–	25	25	–	25	25
$T^at^b \times t^bt^b$	–	–	50	–	–	50
$TT \times TT$	–	–	–	100	–	–
$TT \times Tt^b$	–	–	–	50	50	–
$TT \times t^bt^b$	–	–	–	–	100	–
$Tt^b \times Tt^b$	–	–	–	25	50	25
$Tt^b \times t^bt^b$	–	–	–	–	50	50
$t^bt^b \times t^bt^b$	–	–	–	–	–	100

counting the numbers of each color as determined by the genotypes and remembering that B and D are dominant to b and d, respectively. The 2 pairs of genes have combined at random in the F_2 to reproduce the original brown and blue and a new color, the lilac. This is a recombinant color, produced by the 2 genes b and d in individuals, with the genotype bbdd.

The variation produced by recombination of genes between disparate individuals is fundamental to both pure and applied genetics. The principle may be extended to 3, 4 or many pairs of genes. Such recombination has created the many breeds and varieties of cats existing today. The prime source of variation is gene mutation, but this can be greatly extended by recombination and selective breeding. The section on normal feline genetics describes the known mutant alleles of cats and how these have been used to diversify modern breeds.

Epistasis and Hypostasis

The above pairs of genes had phenotypic effects that were independently expressed, resulting in 4 distinct phenotypes by recombination. Pairs of genes frequently interact at a phenotypic level to interfere or prevent expression of one or the other, however. Black cats are a common example of this phenomenon. Tabby cats may be striped or blotched, due to the genes T and t^b, respectively. The tabby pattern occurs in conjunction with the agouti gene A, responsible for the grayish background coloration. The A gene has a mutant allele a, which produces a solid-black cat. The tabby pattern is not manifested upon a totally black background; hence, the a gene obscures or masks expression of the T and t^b genes. This phenomenon is termed epistasis. Gene a is said to be epistatic to T and t^b. Conversely, genes T and t^b are said to be hypostatic to a. Other cases of epistasis/hypostasis are described in later sections.

Figure 3. Checkerboard for deriving the expectations for the simultaneous inheritance of 2 pairs of genes (B versus b, and D versus d). The procedure is the same as that for the simpler checkerboard of Figure 2. The genotypes of the gametes (sperm or ovum) are formed by combining the 2 pairs of genes at random. These are entered within each of the 16 squares to give the genotypes to be expected for the mating. Phenotypes produced by the various genotypes depend upon the degree of dominance of members of gene pairs and interaction of expression between the 2 genes.

		Genotype of Sperm			
		BD	bD	Bd	bd
Genotype of Ovum	BD	BBDD Black	BbDD Black	BBDd Black	BbDd Black
	bD	BbDD Black	bbDD Brown	BbDd Black	bbDd Brown
	Bd	BBDd Black	BbDd Black	BBdd Blue	Bbdd Blue
	bd	BbDd Black	bbDd Brown	Bbdd Blue	bbdd Lilac

Linkage

Genes are not inherited independently if the 2 gene loci are on the same chromosome. Genes on the same chromosome tend to stay together during the splitting, randomization and recombining of chromosomes during gamete formation and fertilization. This phenomenon is known as linkage. Though one might assume that genes on the same chromosome maintain their relative positions indefinitely, this is not the case. Homologous chromosomes can exchange segments with each other at the time of cell division. The extent to which genes recombine in this manner depends upon their relative positions on the chromosomes. If 2 genes are situated close together, the likelihood that the chromosome will split between them is very small. If the 2 genes are situated some distance apart, the likelihood of such a split is much greater.

Polygenic Inheritance

Genetic variation is either qualitative or quantitative. Qualitative variation is produced by genes that have major effects upon the phenotype. Coat colors produced by the B, b, D and d genes are fitting examples. Allowing for dominance, each gene introduces a major qualitative change to the phenotype. Further, the change is consistent and the genes can be followed from generation to generation by phenotype. Such genes are

termed major genes, with reference to their major effects upon the phenotype.

Quantitative variation, on the other hand, varies from one extreme to the other, and no discontinuity is introduced by a single major gene. The classic example is body size, a characteristic that is easily determined by measurement or weight. The genetic component of body size is due to many different genes that have small effects singly, but large effects cumulatively. The combined effects of these genes produce increasing differences of size, depending upon their numbers and the direction in which they are acting. Such genes are termed minor genes, with reference to their minor individual effects upon phenotype. They are also called polygenes, referring to the number of genes required for the phenotypic expression of a single characteristic.

It is possible to conceive of groups of polygenes: positive polygenes when the effect of each polygene is to enhance the expression of a characteristic, and negative polygenes when the effect is to decrease the expression. Polygenes do not differ biochemically from major genes. The difference is only in the magnitude of their phenotypic effects. Though polygenes are not individually identifiable or easily manipulated, they are the basis of most selective breeding.

Polygenes are ubiquitous and there is no phenotypic characteristic they do not affect to some extent. The extent that polygenes affect the phenotype can be estimated by a factor known as heritability (symbol h^2). Information on the extent to which phenotypic variation may be genetically determined is useful, though interpretation can be tricky. In general, the higher the heritability of a polygenic characteristic, the greater the potential for selective breeding. Conversely, the lower the heritability, the greater the influence of the environment as compared to heredity. If the environment is standardized, and the heritability remains low and the variation large, either an unknown environmental factor has been overlooked or the specific heritability of the characteristic is not understood.

Polygenic inheritance can be manifested in 3 forms. First, it may appear as a "pure" polygenic character that varies continuously from one extreme to the other. Body size is an obvious example. Second, the polygenic variation may interact with a major gene. Such an example is hair length. Long hair is produced by a recessive gene (l); however, the hair length of long-haired (ll) cats is variable, and this is due to polygenes. The same polygenes induce variation in hair length in normal short-coated cats, but their effects are magnified in the presence of the l gene. Polygenes can affect the expression of a mutant gene. Such polygenes are frequently referred to as modifiers and are usually specific for the character they are affecting. Third, the mode of inheritance of a character may be polygenic, yet the expression differs sharply from what is expected. Examples are umbilical or inguinal hernias and cryptorchidism. Animals with one of these defects lack the requisite number of polygenes for normal development.

The distinction between normal and defective is abrupt but the underlying heredity is polygenic, not monogenic as might be anticipated. Such anomalies are known as threshold characters, the allusion being that the defect develops as a result of failure to attain a critical threshold of normal development. Characteristics that develop in this manner can be detected because their prevalence differs from the Mendelian expectation. The frequency of hernias or retained testicles may differ among strains or families of cats, reflecting differences in basic polygenic inheritance.

Color Variation

Free-living domestic cat populations are heterogeneous for coat color and hair quality; this situation has persisted for hundreds of years.[27] The numbers of mutant genes responsible for this variation are few, and their mode of inheritance and phenotype interactions have been largely elucidated.[10] Phenotypic variation was seized upon by cat fanciers (notably in Britain) in the latter half of the 19th century as the basis of breeds.[18,19] Names and exhibition standards of excellence were drafted for breeds with one or more different phenotypes.

Since these early days, additional mutant genes have been discovered that gave rise to further color varieties and styles of coat ac-

ceptable to cat fanciers. Today there is an impressive range of breeds of exhibition cats. A general discussion of the effects of mutant genes upon the phenotype and of the genotypes of breeds may be found in other sources.[16,20]

Table 3 lists the mutant genes found in various cat breeds.

Tabby Alleles

The wild-type tabby is the mackerel pattern of narrow vertical, slightly curving black stripes upon a yellowish-gray background (Fig 4). The stripes may be unbroken or broken into short bars or spots, particularly low on the sides and stomach. The tabby coat color is composed of 2 components: the agouti background and the tabby pattern.

The grayish background is known as agouti. Agouti is the universal camouflaging color of most mammals. It is especially common in rodents such as mice or rats. The coat is composed of black hairs subterminally banded with yellow; the tip is black, followed by a band of yellow and then black, which pales quickly to slate blue as the pigment granules become sparse toward the root. The "brightness" or yellowness of the coat usually depends upon the width of the yellow or agouti band. The tabby pattern is superimposed upon the agouti as a disruptive pattern. It tends to "break up" the outline of the animal, and is a supplementary form of camouflage. The pattern is created by the displacement of agouti-banded hairs with all-black hairs.

Figure 4. The mackerel or striped tabby pattern is found on many wild cat species. The mackerel pattern consists of black stripes with an intervening agouti ticking.

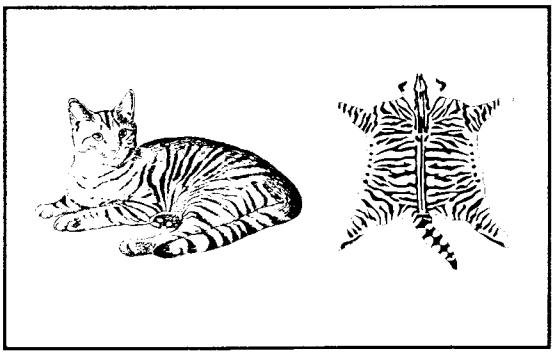


Table 3. Symbols and designations of mutant genes in cat breeds.

Symbol	Designation	Characteristic
a	Nonagouti	Self-color
b	Brown	Chocolate brown
b^1	Light brown	Cinnamon brown
c^b	Burmese	Dark sepia (sable)
c^s	Siamese	Light sepia (sealpoint)
c^a	Blue-eyed albino	White coat
c	Pink-eyed albino	White coat
Cu	Curl	Ear carriage
d	Blue dilution	Slate blue
Dm	Dilute modifier	Lighter blue
Fd	Folded ears	Ear shape
g	Gloving	White nose/paws
hr	Hairless	Absence of hair
I	Inhibitor	Pigment suppression
l	Long hair	Coat length
M	Manx	Taillessness
O	Orange	Red/cream color
p	Pink-eyed dilution	Tan color
Pd	Polydactyly	Extra toes
r	Cornish rex	Short coat
Rd	Dutch rex	Short coat
re	Devon rex	Short coat
ro	Oregon rex	Short coat
S	Piebald	White spotting
T^a	Abyssinian	Tabby pattern
t^b	Blotched tabby	Tabby pattern
W	Dominant white	White coat
Wh	Wire hair	Rough coat

The classic or "blotched" tabby pattern is distinctly different from the striped or mackerel tabby (Fig 5). The name is derived from the irregular spiral and whorls of tabby pattern on the sides of the animal. These may coalesce to form bars and blotches of color. The head markings are unchanged but the bars on the legs and rings of dark pigments on the tail are more pronounced. The overall effect is of a darker tabby. The blotched tabby is inherited as an autosomal recessive to the striped wild type and is symbolized by t^b.

The Abyssinian has a very different form of tabby markings. The amount of tabby markings is sharply reduced, with vestigial markings evident only on the face, lower parts of the legs, tail and flanks (Fig 6). This tabby is the basis of the Abyssinian breed and is inherited as an incomplete dominant to the striped tabby. It is symbolized by T^a.

The locus for the tabby alleles is symbolized as T and the blotched and Abyssinian

Figure 5. The blotched or classic tabby pattern is recessive to the striped tabby pattern. The colored stripes are arranged as irregular whorls and spirals. The ideal shoulder pattern resembles a "butterfly," while the flank should have a solid blotch of color encircled by one or more rings.

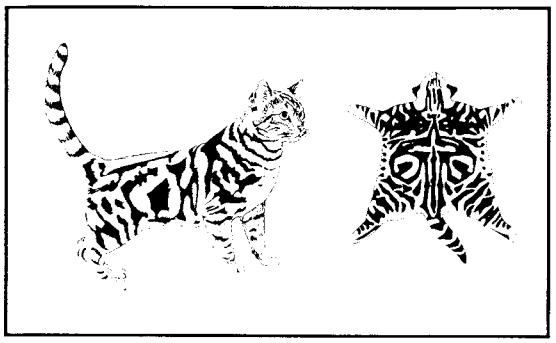


Figure 6. The Abyssinian tabby pattern is dominant to the mackerel or striped tabby patterns. Faint tabby markings remain on the face, and sometimes on the tail and lower legs.

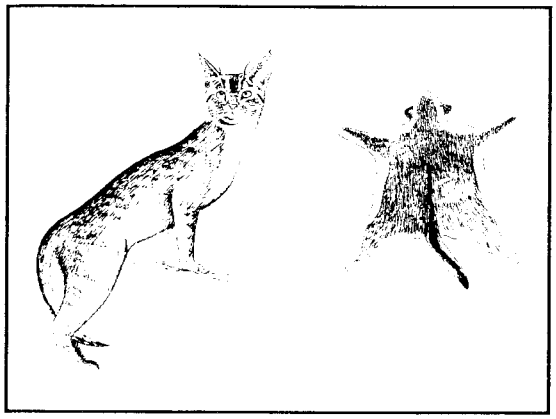
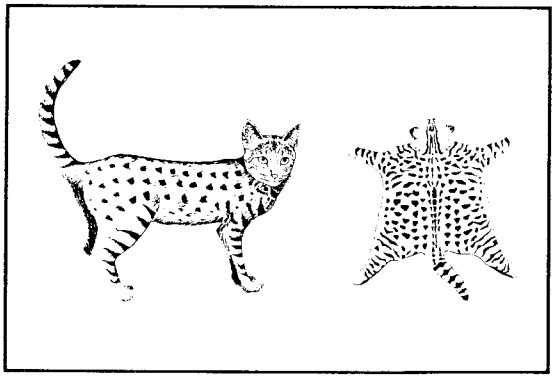


Figure 7. The genetics of the spotted tabby are uncertain. Some people say it is a distinct type of tabby, while others claim it is a "broken-lined" striped or blotched tabby. The broken-line effect would be due to the action of a modifying gene or genes.



patterns are mutant alleles of the locus, as indicated by their respective symbols t^b and T^a. The dominance relationships between the wild-type gene T and the 2 mutant alleles is of interest. The T^a is not fully dominant to T, so that the homozygote T^aT^a shows little or no tabby stripes on the legs, while the heterozygote T^aT shows greater amount of leg striping. The 2 Abyssinians are known as ticked and lined, respectively. The 3 tabby alleles show a steady progression from light to dark tabby pattern.

A fourth type of tabby recognized by cat fanciers is the spotted tabby. In these cats, the striped pattern is not uniform but appears as short bars or spots (Fig 7). There is a tendency for the vertical or classic stripes of ordinary tabbies to be interrupted, and this tendency is enhanced in some cat breeds. One theory is that a gene (or genes) is present that interrupts formation of the solid stripes at intervals along their course. The suggestion has been also made that the spotted tabby is due to a third mutant allele of the T locus. This is speculation, however, because no breeding data have been published to support this.

Nonagouti

The agouti gene A induces the characteristic band of yellow upon the hairs. The locus has produced a mutant a, which produces a phenotype lacking the characteristic. The hairs are consequently unbanded or black tipped, fading to blue toward the roots. This results in the well-known black cat. The allele, designated as nonagouti, is inherited as an autosomal recessive to normal agouti. Note that it is the agouti background coloration that has changed and not the tabby pattern. The tabby markings cannot be observed because of the uniformly black coat, but their presence can often be discerned as a darker "ghost" pattern in the coats of kittens. Tilting the animal from side to side usually reveals the nature of the pattern by reflective light.

Brown Pigmentation

The coat is normally colored by black pigment granules, produced by a gene symbolized as B. The B locus has given rise to 2 mutant alleles, designated as brown (b) and light brown (b^l). The order of dominance is

B over b over b^l. The b allele produces a dark-brown or chocolate color, while the brown of b^l is distinctly lighter. The difference in intensity is most apparent when b or b^l is combined with nonagouti a. The genotype aabb produces the Havana brown, and the aab^lb^l produces the cinnamon brown.

Albino Alleles

The C locus for full production of pigment in the coat has 4 mutant alleles. The C locus determines the quantity of pigment in the pigment granules. Only the wild-type gene C (full color) permits the maximum amount. All of the mutant alleles decrease the amount of pigment in successive steps. The cat is devoid of pigment in the final step. The resultant phenotype is the pink-eyed white cat, or albino. For this reason, the alleles of C are known as the albino series.

Each of the C-alleles progressively reduces the amount of pigment in the coat. The fully colored CC cat is an intense black in combination with nonagouti (aaCC). The Burmese allele c^b produces a dark sepia-brown phenotype that is slightly but perceptively darker on the extremities (head, feet, tail) when substituted for C in the aaCC genotype (aac^bc^b). The iris may be pale yellow or greenish. The Siamese allele c^s produces a light sepia-shaded body with dark extremities (aac^sc^s). The irides are clear blue. The blue-eyed albino (allele c^a) has a white coat, dull-red pupils and light-blue irides.[30] Finally, the pink-eyed albino allele c has a white coat, red pupils and translucent irides.

The order of dominance for the alleles is conventionally taken to be $C > c^b > c^s > c^a > c$. The C gene is fully dominant to all of the mutant alleles, but the alleles are incompletely dominant to each other. For example, the phenotype of c^bc^s is intermediate to c^bc^b and c^sc^s. The extremities of c^bc^s individuals remain dark sepia but the body fur is appreciably lighter than that shown by c^bc^b, The result is the so-called Tonkinese cat. However, there is variation of expression, and some c^bc^s individuals may be so dark as to be difficult to distinguish from c^bc^b. Incomplete dominance between alleles of the albino series is common, for the cat as well as for other species.

The c^b and c^s alleles are thermosensitive, that is, the biosynthesis of melanin pigment is responsive to skin temperature. The lower the temperature, the more pigment is produced. This is the reason for the darker extremities of phenotypes induced by these alleles; the temperature of the extremities is slightly lower than that of the trunk. If a Siamese (aac^sc^s) is kept in a cool environment during the molting period, the new coat will be appreciably darker than the old. Conversely, if a bandage is applied to a small area of shaven skin, the new growth of hair under the bandage is white.[5]

There is a quantitative reduction in the eye pigmentation in Siamese cats.[25] The layers of pigmented cells are fewer than normal and the pigment granules are less densely packed. All parts of the eye are affected, especially the iris and choroid tissues. The different albino alleles have similar but graded effects upon eye pigmentation. There is an increasing interference with pigmentation until full albinism is reached.

Blue Dilution

The intensely colored hairs of black or chocolate cats are due to the regular and dense packing of myriad pigment granules in the cells of the hair shaft. The number of granules decreases toward the base of the hair, causing the hairs to be black or chocolate at the tip and bluish at the base. The slate-blue color of blue cats is due to interspersing of hairs with more-pigmented hairs containing less pigment.[8,9,21] The color clumping results from the faulty disposition of pigment granules during hair growth. The pigment granules of the eye tissues are not affected.[9] The locus responsible for the regular disposition of granules is designated as D (dense) and the mutated allele that induces irregular disposition as d (dilute). The d allele is inherited as an autosomal recessive to D.

Dilute Modifier

The dilute modifier (Dm) gene is only expressed in conjunction with the dilution gene d. The effect of Dm is to lighten the color of dd, and to produce a brownish cast to the coat.[28]

Inhibitor

The inhibitor gene I partially suppresses pigment production in the coat. The gene is inherited as an autosomal dominant to wild type.[29] The hairs are colored at the tips and become colorless toward their base. The I gene disrupts normal biosynthesis of pigment granules by melanocytes in the hair follicles.[8] Suppression is greater for the lighter agouti areas of the coat than for the darker tabby markings. Hence, the phenotype is a whitish cat with a dark tabby pattern (silver). Eye color is unaffected.

Pink-Eyed Dilution

As the designation of this mutant allele implies, the coat is diluted to a light tan and the eyes are pinkish (depigmented). The mutant allele was discovered but could not be perpetuated.[26] The allele may recur in the future. It would be a desirable addition to the known mutant alleles of the cat. Pigment granules in hairs of pink-eyed dilute cats were very small and yellowish brown, in contrast to the normal dark-brown or black coloration.[8]

Sex-Linked Orange

The ginger, marmalade, red or yellow coat color is due to a mutant gene O (orange). The O gene gives rise to some unusual phenotypes. These are derived from the fact that the gene is sex-linked, the O locus being on the X chromosome. While the female may have 1 of 3 genotypes on the X chromosomes, OO, Oo or oo, the male can have only 2, OY or oY, where Y is the male chromosome. The mode of inheritance of O is shown in Table 4.

The phenotype produced by the O gene is a Tabby pattern with a yellow ground color and Tabby markings accentuated by orange or red. The action of the gene is to convert biosynthesis of eumelanin (a black-brown pigment) to phaeomelanin (a yellow-orange pigment). The Tabby pattern remains because of a greater concentration of pigment granules in the markings than in the background. The nature of the Tabby is determined by the Tabby alleles, exactly as for the ordinary gray Tabby. Therefore, the genotypes of the striped, classic and Abyssinian Tabby are OOTT, OO$t^{b}t^{b}$ and OO$T^{a}T^{a}$, respectively.

Only the female can be heterozygous for O and the wild-type gene o. The phenotype of Oo cats is not orange, but a mosaic of orange and wild type (usually, orange and Tabby or orange and black) known as Tortoiseshell. Tortoiseshelling occurs because of variable inactivation of one or the other of the 2 X chromosomes in cells of the developing female egg. Areas of skin resulting from inactivation of the X chromosome carrying an O gene are normally colored; areas of skin arising from cells where the X chromosome carries the O gene is active are orange. The heterozygous Oo female cat is

Table 4. Inheritance of the sex-linked gene orange (O). The chromosome constitution is shown for each individual, where X^{o} represents the O-bearing X chromosome.

Mating			Offspring	
Dam		Sire	Males	Females
Orange $X^{o}X^{o}$	x	Orange $X^{o}Y$	Orange $X^{o}Y$	Orange $X^{o}X^{o}$
Black XX	x	Orange $X^{o}Y$	Black XY	Tortoiseshell $X^{o}X$
Tortoiseshell $X^{o}X$	x	Orange $X^{o}Y$	Orange $X^{o}Y$	Orange $X^{o}X^{o}$
			Black XY	Tortoiseshell $X^{o}X$
Tortoiseshell $X^{o}X$	x	Black XY	Orange $X^{o}Y$	Tortoiseshell $X^{o}X$
			Black XY	Black XX
Orange $X^{o}X^{o}$	x	Black XY	Orange $X^{o}X^{o}$	Tortoiseshell $X^{o}X$
Black XX	x	Black XY	Black XX	Black XX

Black = nonorange (black, tabby, blue, chocolate, etc)

in effect composed of 2 types of cells in respect to functioning genes on the X chromosome.

When a mutant gene on the X chromosome has obvious phenotype expression, the heterozygote would be expected to show the simultaneous effects of each. Therefore, the heterozygote Oo would be expected to have a coat displaying both orange (O chromosome functional) and wild-type (o chromosome functional). The coat displays a mosaic of orange/tabby or orange/black due to the competitive spread of melanoblasts as these populate the skin to ultimately become melanocytes responsible for coloring the hairs. Those melanocytes with the functioning O gene produce orange hairs, while those with a functioning o gene produce Tabby or black hairs. The expression may vary from mosaics with little expression of orange to others with extensive areas, reflecting the irregular migration of embryonic melanoblasts.

The conversion of eumelanin to phaeomelanin makes the O gene epistatic to alleles at the agouti (A and a) and black gene loci (B and b). Cats of genotypes AABBOO, aaBBOO, AAbbOO and aabbOO are of indistinguishable orange phenotype. This may be seen by examining the corresponding tortoiseshells of genotype AABBOo, aaBBOo, AAbbOo and aabbOo. In each case, the orange areas of the mosaic are indistinguishable orange, while the nonorange areas are Tabby, black, chocolate Tabby and chocolate, respectively. The last 2 tortoiseshells are uncommon and the first 2 types common. The black Tortoiseshell is the conventional "tortie," while the Tabby Tortoiseshell has been called a "torbie" or "patched tabby."

Piebald Spotting

Cats with splotchy white markings are known as piebald. Piebald spotting is due to the autosomal dominant gene S. Expression of the S gene varies widely. Some cats have small spots or streaks of white on the chest and ventral midline of the abdomen. Others are extensively white, with remnants of pigmentation confined to the head and base of the tail. In spite of this variation, there is regularity in the progressive increase of white coloring. As the amount increases, the ventrum (abdomen, chest, throat) becomes white. With more white, a white "blaze" extends from the nose to between the eyes, and white creeps up the sides of the animal. A "collar" of white often forms around the shoulders. With the greatest amount, most of the trunk becomes white and the colored areas occur as patches or spots of decreasing size.

A depiction of the progression of white spotting is shown by Figure 8. The depiction should be regarded as merely a guide since there is considerable variation. When cats are graded by the amount of white in the coat, the frequency distribution strongly suggests that the S gene is incompletely dominant. The heterozygous expression ranges over grades 3 to 6, and the homozygous expression over grades 5 to 9. There is overlapping of phenotype for the 2 genotypes.

The wide variation of white spotting may be due to 2 alleles: restricted spotting and piebald spotting.[32] These data can also be explained in terms of single incomplete dominant gene. Other investigators explained their observations as the inheritance of spotting by a single incomplete dominant gene with genotypes of SS and Ss.[7]

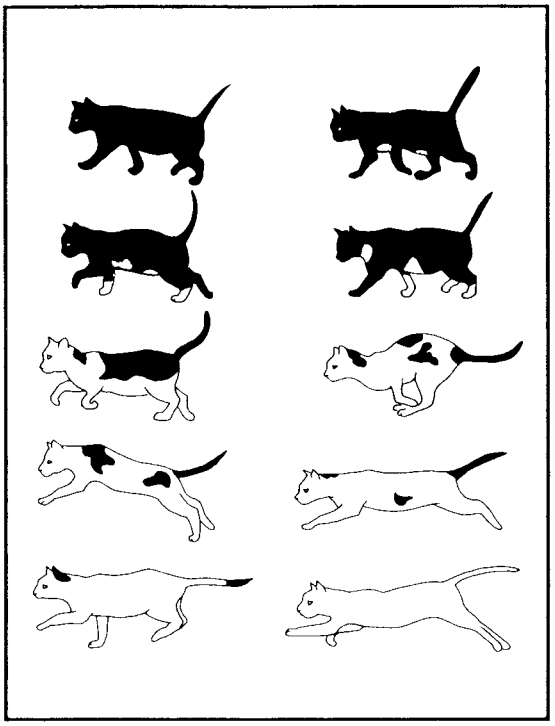
Gloving

Gloving is a form of restricted spotting, with the white confined to the paws and occasionally on the nose, chest and abdomen. Gloving has been ascribed to an autosomal recessive gene g, though the supporting evidence is not extensive. In a minority of heterozygotes Gg, the dominance of G is incomplete. It is unknown if g is independent of S or is an allele of the locus.

Dominant White

The dominant white gene W produces a completely white coat in most cats. Some kittens with this gene have small spots of colored fur on their heads that disappear with age. The iris may be yellow, blue or heterochromatic. It is common for one iris to be yellow and the other blue; such animals are called "odd-eyed." Deafness, unilateral or bilateral, is common in dominant-white cats. It has been suggested that W is an allele of S.[32] Though there is evidence to support this, it is not wholly convincing. For

Figure 8. Piebald spotting is due to an autosomal dominant gene that varies greatly in the degree to which it is expressed. Coat colors under the genetic influence of the piebald spotting gene can range from all white to all black, with any gradation in between.



practical purposes, W assorts independently of S.

The W gene interferes with migration of cells from the neural crest of the early embryo, probably by reducing their numbers. Neural crest cells are responsible for development of several tissues and organs. Included among these cells are the melanoblasts that populate the skin to form melanocytes for hair pigmentation. The absence of melanocytes produces the white coat that is a consistent feature of the W gene. Studies revealed that the eyes of yellow-eyed white cats were normally pigmented, while those of blue-eyed white cats were markedly pigment deficient.[25] In particular, the tapetum was completely absent. Depigmentation of the eye was due to an absence of stromal pigment cells.

A deficiency of eye pigmentation (blue irides) coupled with defective hearing, is a less consistent manifestation of W. Among a sample of 185 white cats, 68% had blue eyes and 44% displayed signs of deafness. Among the 60 cats with yellow eyes, 22% were deaf, while among the 125 cats with blue eyes, 55% were deaf.[3] The cause of deafness in W cats has been the subject of intensive investigation.

Whiteness is not inevitably associated with deafness. White cats with the underlying c^s Siamese gene have deep blue eye color and are not deaf.

Variations in Coat Hair

In addition to providing camouflage for stalking prey, the coat of cats protects the skin from abrasion and insulates against sunburn and heat loss. These properties result from the composition of coat hairs. There are 2 primary types of coats: the top coat and undercoat. The top coat affords a protective covering for the softer undercoat and has tactile properties. The vibrissae and stout facial hairs have a sensory function. The undercoat provides the main insulation from fluctuating temperature.

The coat is composed of 3 types of hair: guard hair, awn hair and down hair. Guard hairs are the least numerous. They are stout and straight, tapering to a fine point. Awn hairs are more numerous and thinner than guard hairs, and have a characteristic subapical thickening before tapering to a fine point. These 2 hair types constitute the top coat. Down hairs are the thinnest and by far the most numerous. They have a similar diameter throughout their length. Their main function seems to be as insulation. All awn hairs have a subapical swelling, but some are straight like guard hairs and others are undulated. The 2 forms are distinguishable, but there tends to be a gradual rather than distinct transition from one to the other.

Long Hair

The extra-long coat of the long-haired or Persian breeds is due to an autosomal recessive gene l. The coat is composed of the same types of hairs as present in the short-haired coat but they are greatly elongated. Two possibilities exist to explain the longer hair: the hairs grow more rapidly before the growth phase terminates, or the period of growth is extended. Long-haired cats have not been examined in respect to these 2 possibilities. If studies on long-haired Angora

rabbits (a comparable genetic hair type) can be extrapolated, an extension of the growth period is the more likely explanation.

Rex Mutants

The rex coat is shorter than normal, while the vibrissae are excessively curved, bent, broken or less numerous, depending on the particular rex mutant. There is a tendency for the coat to have marcel waving, but this is not a universal feature. Rex cats have received considerable publicity, and as a consequence, a number of rex mutants have been reported. Only a few of these have been genetically investigated. Rex mutants from different areas have similar phenotypes but there may be subtle differences. Most are inherited as autosomal recessives, but a recent rex mutant appears to be an incomplete dominant.

The Cornish rex mutant (r) displays recessive inheritance. The coat is short and plush, with a tendency toward marcel waving. The whiskers are shorter and more curved than normal. The density of the coat is reduced, varying from a sparse covering to a thick pelage. Guard hairs appear to be lacking or closely resemble the thinner awn hairs. The subapical swelling of the awn hairs is less obvious than normal or may be absent.[13,21]

The German rex mutant resembles the Cornish rex phenotypically.[11] The mutant gene is recessive to the normal coat gene. Though there is good evidence that the German rex is also a spontaneous mutant, breeding experiments prove that the Cornish and German mutants are identical.[13]

The Devon rex (re) superficially resembles the Cornish rex. The coat is shorter than normal and inclined to be sparse. There is a frequent loss of hair from the abdomen, chest and shoulders. In extreme cases, the whole trunk is naked. Transient growth of hair is often apparent. All 3 types of hair are present, but they are of irregular diameter. The hairs are frequently broken, which is unusual for such a resilient substance as keratin. The vibrissae are reduced in number and easily bent or broken, and may appear as stubble. Cornish and Devon rexes are caused by different mutant genes at independent loci.[12]

The Oregon rex (ro) gene is inherited as a recessive.[14] Superficially, the Oregon rex resembles the Cornish rex. The guard hairs are absent, and the awn and down hairs appear to be thinner than normal. On the other hand, the subapical swelling of the awn hairs is more pronounced and straighter than awn hairs of the Cornish rex. The awn hairs project above the down hairs, as normally expected. Though the data are not conclusive, the Cornish and Oregon rex genes appear to be different.[14]

Unlike the above rex mutants, the Dutch rex gene (Rd) is inherited as an autosomal dominant.[17] The coat is short and has a bristly feel. Guard hairs are absent or reduced in size and appear like awn hairs. They are tortuously wavy and protrude in random directions above the down hairs, giving the cat a bristly texture. The down hairs are excessively wavy. The vibrissae are of normal number but they are crinkled and bent. The coat thins with age and may be lost from some regions of the body. Preliminary breeding data suggest that the coat of the homozygote RdRd is more abnormal than the heterozygote Rdrd. The coat of the former is sparser and more prone to loss.

There are additional reports of rex-type mutants from the US (2 additional cases), England (1 additional case), Australia, Italy and Sweden.[16] Breeding data on these rexes are meager, but the mutants appear to be recessive in nature. It is impossible to tell at this time whether these represent mutants at loci different from those listed above. Repeat mutations at the same gene loci are known to recur at a low rate, as indicated by the same rex mutants occurring in England and Germany.

Wire Hair

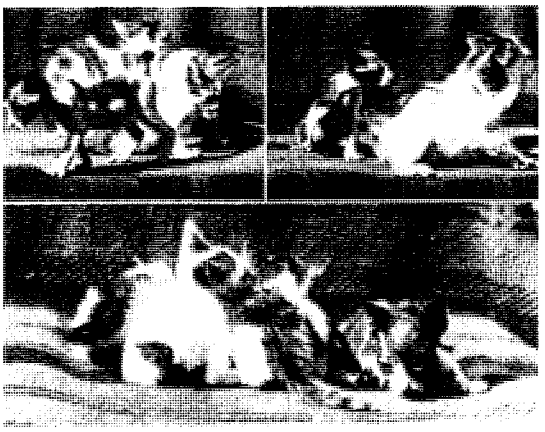
The wire-haired coat appears unkempt, wavy and coarsely textured when stroked. All 3 hair types are present but they are thinner than normal and show exaggerated curvature. Some may be coiled like springs, while others display a "shepherd's crook" configuration at the distal end. A dominant mode of inheritance is indicated by fanciers' breeding records. The mutant allele is symbolized by Wh.[16]

Sphynx

The Sphynx or hairless cat is not totally hairless. Most have a fuzzy growth on parts of the body such as the shoulders. Others may show a seasonal transitory weak growth of hair. The hairlessness is inherited as an autosomal recessive (symbol hr).[15]

Hairless cats have appeared spontaneously for eons, and some have been called "dog-cats."[23,24] Such cats have evoked a great deal of notoriety for the discoverers (Fig 9).

Figure 9. Hairlessness is inherited as an autosomal recessive defect.[23] The appearance of such mutants has created a great deal of notoriety in the past. Such hairless mutants have often been referred to as "cat-dogs," probably due to their resemblance to several thinly haired breeds of toy dogs. Lately, such a defect has been used as the basis of a new breed of cats typified by the Sphynx. (Courtesy of Dr. H. Sternberger and *Journal of Heredity*)



Physical Variation

In addition to mutant genes that affect color and coat, a number of genes modifying physical attributes have been recognized. Because none of these genes is linked to color and coat genes, they are found in many breeds. Unfortunately, some of these mutant genes are associated with undesirable anomalies.

Manx

The most well-known gene is for taillessness in the Manx or tailless cat. The tailless condition is due to a dominant gene M, which is a prenatal lethal when homozygous (MM). Though heterozygotes (Mm) are viable, they are subject to a number of life-threatening anomalies of the lower vertebral column and intestinal tract. A sufficient number of heterozygotes survive, however, thus allowing the Manx to persist.

Four grades of Manx are recognized: the true Manx or "rumpy", which lack tail vertebrae; "rumpy-riser", in which a small number of vertebrae can either be seen or felt; "stumpy," in which where sufficient vertebrae are present to form a short tail, often movable but usually knobby or kinked; and "longie," in which the tail is almost as long as normal (Fig 12). Normal cats (mm) bred from heterozygotes are known as "tailed Manx." Normal females, while not strictly "Manx," are useful in perpetuating the Manx breed through matings with Manx males.

Japanese Bobtail

These cats have a short tail about 2-3 inches long and characterized by curves and angles. Little is known of the inheritance of the truncated tail, though the condition is thought to be inherited as a recessive. The Bobtail has extensive white areas with patches of black (aaSS), orange (aaOOSS) or black and orange mosaic (aaOsSS).

Scottish Fold

The pinnae of the adult Scottish Fold are folded forward, giving the cat a somewhat dejected look. The ear fold is not present at birth but becomes evident at about 4 weeks of age. The ears become more rigid with age. The condition is due to an autosomal dominant gene Fd. The heterozygote Fdfd is normal except for the folded ears. The homozygote FdFd is subject to a crippling thickening of joints of the limbs and tail, however (Fig 10).[6] Some heterozygotes Fdfd also develop similar joint anomalies, though much milder than those of homozygotes. Affected animals eventually are unable to walk. Fold-to-Fold matings should be avoided. Folds should only be mated to normal-eared animals (bred from similar matings).

American Curl

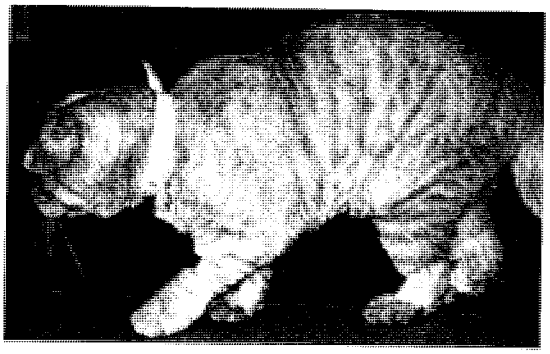
The American Curl has the distal portion of the ear pinnae slightly curled backward.

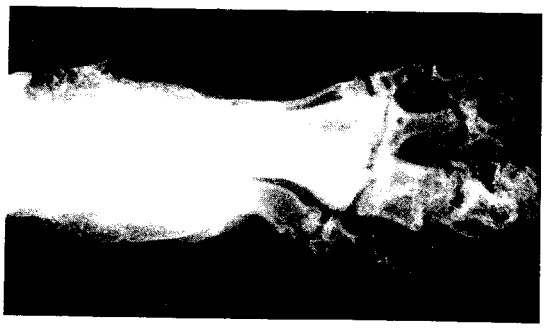
This gives an alert appearance to the animal. The Curl condition is due to an autosomal dominant gene Cu. Preliminary observations indicate that the homozygote CuCu is devoid of other anomalies, but this requires confirmation. The heterozygote Cucu suffers from no apparent problems in other organs.

Polydactyly

These cats have extra toes on the feet. Both front and back paws are affected, but the back feet are never affected unless the front feet also have extra digits. There is variation in both the numbers of supernumerary toes and the degree of development of the extra toes. The maximum for the front legs is 7 toes. The condition is due to an autosomal dominant gene Pd.

Figure 10. Top: A cat that is homozygous for the Scottish Fold gene. The cat has severe skeletal disease resulting from overexpression of the basic cartilage anomaly caused by the gene. Heterozygotes have abnormalities mainly of the ear cartilage, but some may also have skeletal anomalies that are generally minor compared to those manifested by homozygotes. Bottom: A radiograph of the distal hind limb of this cat shows severe bone and joint changes characterized by compression and thickening of the long bones, collapse of joint spaces, destruction of joint surfaces and underlying subchondral bone, and extensive periarticular new bone formation.





Genetics of Breeds

The primary determinants of cat breeds are color, coat quality and conformity (body shape and stance). It is difficult to say which is the most important. Coat color and quality are determined by major genes and combinations thereof. These features are monogenic, therefore. In contrast, conformation is determined mainly by polygenes.

Two broad categories of conformation have been recognized: a stocky, powerfully built animal; and a more gracile, sinuous animal. The first category usually embraces "homegrown" breeds, that is, breeds that are "native" to the western hemisphere and classified as American, British or European. The second category embraces "foreign" or "oriental" breeds. The last category must not be taken too literally. It came into being due to the importance of the uniquely colored Siamese during the latter part of the 19th century. These cats had a graceful body conformation as compared with British breeds. Henceforth, any cat originating from the Far East or of slender build was regarded as having foreign conformation. A number of breeds that have been created in countries far removed from southeast Asia are regarded as "foreign," however. Differences of head shape and body build exist between breeds of both "western" or "foreign" categories, but these are minor and usually subtle except to the astute cat fancier.

In discussing the genotypes of breeds, varieties or colors of cats, it is conventional to list only mutant genes. This focuses attention on the relevant genes and avoids unnecessary repetition. Exceptions occur when the full genotype is not known. A general exposition of genotypes of breeds has been published.[16]

Short-Haired Breeds

Tabbies: The common gray-brown domestic Tabby is usually striped or blotched. Both forms are due to a single gene difference. The spotted Tabby may differ by a major gene, but this is debatable (as explained earlier). Many spotted forms are

striped cats in which the stripes are interrupted to produce short bars or spots. These can be bred by selection, which implies that at least part of the breakup of the striping is inherited. Conversely, those who desire well-defined, unbroken, stripes must select for the feature.

The exhibition brown Tabby differs from the domestic Tabby; it has a definite body conformation, brighter agouti color, and a prominent tabby pattern. The tabby pattern can be bred in many colors by combining the alleles with other mutants (Table 5). Some of these mutants are common and may be observed in domestic cat populations. The less common mutants are becoming increasingly popular among the more modern oriental category of breeds. Note that the brown Tabby is the fancy name for the black Tabby; the genetic brown Tabby is the chocolate Tabby (chestnut tabby in the US).

Abyssinian: The Abyssinian is a distinctive form of tabby. The tabby pattern is virtually absent from the body, but a limited amount of striping may sometimes occur on the flanks and lower part of the forelegs. This has been eliminated by selective breeding in exhibition strains. Obvious striping occurs in first-cross Abyssinians because the allele $\underline{T}^a$ is incompletely dominant to other Tabby alleles. Some typical tabby markings remain on the head and distal portion of the tail. The Abyssinian allele has been systematically combined with other genes to engender an impressive range of varieties (Table 6). The basis for the Abyssinian breed is the unique phenotype produced by the $\underline{T}^a$ allele. Some varieties have been selected for a richly colored rufescent phenotype.

Table 5. Genotypes of striped and blotched (classic) Tabbies.

Name	Striped	Blotched (classic)
Brown	TT	t^bt^b
Chocolate	bbTT	bbt^bt^b
Blue	ddTT	ddt^bt^b
Lilac	bbddTT	$bbddt^{bb}$
Cinnamon	b^1b^1TT	$b^1b^1t^bt^b$
Fawn	b^1b^1ddTT	$b^1b^1ddt^bt^b$
Silver	IITT	IIt^bt^b
Red	OOTT	OOt^bt^b
Cream	OOddTT	$OOddt^bt^b$
Torbie	OoTT	Oot^bt^b

Singapura: This breed has the Abyssinian allele $\underline{T}^a$ combined with the Burmese allele $\underline{c}^b$. It differs from the Abyssinian breed in not having the rufescent polygenes and in displaying dark brown ticking on a pale ivory background color. The breed also differs in conformation.

Self-Colors: The nonagouti allele $\underline{a}$ is responsible for the self-colors. Alone, the allele produces the solid black. In combination with the $\underline{b}$ and $\underline{d}$ mutants it produces 3 additional colors: chocolate ($\underline{aabb}$), blue ($\underline{aadd}$) and lilac ($\underline{aabbdd}$). These 4 phenotypes may be viewed as the basic colors of cats, since they recur regularly within breeds. No matter how breeds may differ for coat texture and body conformation, color is inherited independently. This permits development of distinctive breeds with identical color genotypes (Table 7). The outstanding example of this process is the self-blue. Several well-established breeds are of this color. These breeds differ not only in conformation, but also in the intensity of the shades of blue.

Red Tabby and Tortoiseshell: The ginger or marmalade exhibition version of the domestic cat is known as the red Tabby. The intensity of color is greatly enhanced, especially the darker tabby markings. In this respect, the blotched (classic) is preferred because the patterned area is greater than that normally shown by the striped Tabby. The richness of color is due to rufescent polygenes that determine the intensity of red/yellow pigmentation.

The red Tabby is produced by the sex-linked gene $\underline{O}$. Since the $\underline{O}$ gene is borne on the $\underline{X}$ chromosome, the male genotype is $\underline{O}Y$, where $\underline{Y}$ represents the male chromosome. The female genotype is $\underline{OO}$, homozygous for the $\underline{O}$ gene. The heterozygote $\underline{Oo}$ is the Tortoiseshell, a mosaic phenotype of orange and nonorange colors, where $\underline{o}$ is the nonorange wild-type gene. Only the female genotype of $\underline{OO}$ will be discussed in this section, the male genotype $\underline{O}Y$ being taken for granted. This is to distinguish between the orange ($\underline{OO}$) and tortoiseshell ($\underline{Oo}$) for expository purposes. When the Tortoiseshell is

Table 6. Genotypes of British Abyssinian varieties.

Name	Genotype
Black* (Ruddy)	T^aT^a
Chocolate	bbT^aT^a
Blue*	ddT^aT^a
Lilac	$bbddT^aT^a$
Sorrel* (Red)	$b^1b^1T^aT^a$
Fawn*	$b^1b^1ddT^aT^a$
Red	OOT^aT^a
Cream	$ddOOT^aT^a$
Black Tortoiseshell	OoT^aT^a
Chocolate Tortoiseshell	$bbOoT^aT^a$
Blue Tortoiseshell	$ddOoT^aT^a$
Lilac Tortoiseshell	$bbddOoT^aT^a$
Sorrel Tortoiseshell	$b^1b^1OoT^aT^a$
Fawn Tortoiseshell	$b^1b^1ddOoT^aT^a$
Black Silver	IIT^aT^a
Chocolate Silver	$bbIIT^aT^a$
Blue Silver	$ddIIT^aT^a$
Lilac Silver	$bbddIIT^aT^a$
Sorrel Silver	$b^1b^1IIT^aT^a$
Fawn Silver	$b^1b^1ddIIT^aT^a$
Red Silver	$IIOOT^aT^a$
Cream Silver	$ddIIOOT^aT^a$
Black Silver Tortoiseshell	$IIOoT^aT^a$
Chocolate Silver Tortoiseshell	$bbIIOoT^aT^a$
Blue Silver Tortoiseshell	$ddIIOoT^aT^a$
Lilac Silver Tortoiseshell	$bbddIIOoT^aT^a$
Sorrel Silver Tortoiseshell	$b^1b^1IIOoT^aT^a$
Fawn Silver Tortoiseshell	$b^1b^1ddIIOoT^aT^a$

* Four colors recognized by CFA in the US.

combined with piebald spotting (QoSS), the color is known as tortoiseshell and white or calico.

The O gene is epistatic to alleles A, a, B and b. All OO cats that are homozygous or heterozygous for any of the alleles are indistinguishably red Tabby. The situation is different for the Tortoiseshell. Though the orange areas of the mosaicism are red Tabby, nonorange areas show the effects of the above alleles. The "standard" Tortoiseshell is the black of genotype aaOo. The Tabby Tortoiseshell ("torbie" or "patched tabby") of genotype AAOo is common among domestics. The other tortoiseshell colors, such as chocolate (aabbOo), chocolate Tabby (bbOo), cinnamon (aab^1b^1Oo) and cinnamon Tabby (b^1b^1Oo), are appearing in some foreign and oriental breeds.

Cream and Blue-Cream: The Cream is a red Tabby degraded in intensity of pigmentation by the dilution gene d; the genotype is ddOO. Cream is an apt description of the color. The markings of the blotched Tabby appear as dark cream against a pale-cream background. The pattern of the striped tabby is not so obvious, however, with some individuals appearing almost as a self-color.

The exhibition blue Tortoiseshell, known as the blue-cream, has the genotype aaddOo. Phenotypically, the cat is a mosaic of cream and blue pigmentation. The blue Tabby Tortoiseshell ("blue torbie" or "blue patched tabby") (ddOo) is not easily distinguishable from the blue Tabby (dd), especially if the cream areas are small or diffuse. Other light-colored Tortoiseshells are being bred in some foreign and oriental breeds, such as the lilac Tortoiseshell (aabbddOo) and Fawn (aab^1b^1ddOo).

Silver, Tipped and Smoke: In the Silver, the yellow-gray agouti component of the Tabby is absent, creating the superficial illusion of an off-white cat with black Tabby markings. These cats may have any of the 3 tabby patterns, of which the blotch or classic is probably the most outstanding. Breeders have selected for a clear white background color and solid Tabby markings to realize maximum contrast. The Silver phenotype is produced by the I allele, and the genotypes are IITT (striped or "mackerel"), IIt^bt^b (blotched "classic") and IITaTa (Abyssinian).

Table 7. The names and genotypes of self-colors in the US and UK.

UK	US	Genotype
	American SH black	aa
British Black	British SH black	aa
Foreign Black	Oriental SH black	aa
Bombay	Bombay	aa
British Blue	British SH blue	aadd
Foreign Blue	Oriental SH blue	aadd
Russian Blue	Russian Blue	aadd
Chartreux	Chartreux	aadd
Korat	Korat	aadd
	Havana Brown	aabb
Havana	Oriental SH chestnut	aabb
Foreign Lilac	Oriental SH lilac	aabbdd
Cinnamon	Oriental SH cinnamon	aab^1b^1
Caramel		aaddDm-

The Cream is a
sity of pigmen-
l; the genotype
scription of the
olotched Tabby
st a pale-cream
of the striped
ver, with some
as a self-color.
iseshell, known
the genotype
cat is a mosaic
ition. The blue
orbie" or "blue
ot easily distin-
bby (dd), espe-
e small or dif-
rtoiseshells are
n and oriental
Tortoiseshell
ddOo).
In the Silver,
ponent of the
the superficial
th black Tabby
ve any of the 3
blotch or clas-
anding. Breed-
ir white back-
y markings to
he Silver phe-
allele, and the
r "mackerel"),
and IITaTa

of self-colors in the

Genotype
aa
aa
aa
aa
aadd
aadd
aadd
aadd
aadd
aabb
aabb
aabbdd
aab^{1}b^1
aaddDm-

The I gene inhibits pigment in the hair to a variable degree. The silver may be regarded as the minimum degree of inhibition. The inhibition may be more pronounced, giving rise to the shaded silver. Such cats have obvious white undercoats and rarely discernible tabby markings. The most extreme expression is the tipped or "chinchilla". In these animals, only the tip of the hair is pigmented and the tabby markings are not discernible.

The effectiveness of the I gene in eliminating pigment is due in part to the fact that the silver and tipped breeds are agouti. When the I gene is combined with nonagouti, the reduction is significantly less. In fact, all of the hairs are now distally pigmented and not merely the tabby pattern hairs, as in the silver tabby. These aaII individuals are known as Smoke. The expression of light undercolor varies from indistinguishable, or barely distinguishable, from the slate blue of the normal nonagouti (aa), to light blue and finally white. There are several cases on record of black cats breeding as Smokes. These are almost certainly instances of very dark Smokes.

The Silver tabby, shaded Silver, Tipped (chinchilla) and Smoke phenotypes may be combined with b, d and O alleles to produce the usual range of colors (Table 8). These have been exploited in the oriental group of breeds to establish phenotypes not recognized by the traditional breeds. The Silver tabby, shaded Silver and Tipped varieties have identical genotypes, differing only in the expression of I. The expression of the I gene is probably governed in part by modifying polygenes.

Siamese: The Siamese is probably the best known of the exotic breeds. Siamese have a light-colored body, dark extremities and blue eyes. The amount of pigment in the extremities is sufficient to be modified by other mutant genes. It is possible, therefore, to have many varieties of Siamese, while retaining the characteristic coloration and pattern.

The original Siamese is the Seal Point, with the simple genotypes of aac^sc^s. Other varieties have been developed by combining various color genes (Table 9). The Lilac Point variety is also known as Frost Point. The Tabby varieties are sometimes designated as Lynx Points.

The 2 phenotypically identical red and red Tabby Point Siamese are worth noting. They owe their existence to the objection of breeders that the agouti allele could be inadvertently introduced into their stock by indiscriminate mating of the 2 genetically different Red-Point Siamese. This problem was overcome, or at least contained, by ensuring that each type of Red Point is mated only within its respective series.

Tonkinese: The Tonkinese is a name given to the heterozygote aac^bc^s. Typically the coloration is midway between Burmese (aac^bc^b) and Siamese (aac^sc^s). The coat is a dark to medium sepia brown, being closer in appearance to the Burmese than to the Siamese. However, the body fur is lighter, contrasting with the dark sepia-colored extremities. The usual color is the seal (aac^bc^s), but any of the nonagouti Burmese or Siamese varieties may occur as Tonkinese.

Burmese: The Burmese is a nonagouti that, when combined with the c^b allele, produces a blend of sepia browns. They are shaded dark dorsally and light ventrally, with rich dark extremities. The basic genotype of aac^bc^b has been combined with other color genes to create the varieties listed in Table 10. The action of the c^b allele is to lighten the color. As a consequence, the genotypes listed in Table 10 have the usual

Table 8. Genotypes of Silver and Smoke varieties of Orientals and other breeds.

Name	Silver	Smoke
Black	II	aaII
Chocolate	bbII	aabbII
Blue	ddII	aaddII
Lilac	bbddII	aabbddII
Cinnamon	b^{1}b^{1}II	aab^{1}b^{1}II
Red	OOII	OOII
Cream	ddOOII	ddOOII
Black Tortie	IIOo	aaIIOo
Chocolate Tortie	bbIIOo	aabbIIOo
Blue Tortie	ddIIOo	aaddIIOo
Lilac Tortie	bbddIIOo	aabbddIIOo

Table 9. Genotypes of British Siamese varieties.

Name	Genotype
Seal*	aac^{s}c^s
Chocolate*	aabbc^{s}c^s
Blue*	aac^{s}c^{s}dd
Lilac*	aabbc^{s}c^{s}dd
Red	aac^{s}c^{s}OO
Cream	aaddc^{s}c^{s}ddOO
Seal Tortie	aac^{s}c^{s}Oo
Chocolate Tortie	aabbc^{s}c^{s}Oo
Blue Tortie (Blue Cream)	aac^{s}c^{s}ddOo
Lilac Tortie (Lilac Cream)	aabbc^{s}c^{s}ddOo
Seal Tabby (Lynx)	c^{s}c^s
Chocolate Tabby (Lynx)	bbc^{s}c^s
Blue Tabby (Lynx)	c^{s}c^{s}dd
Lilac Tabby (Lynx)	bbc^{s}c^{s}dd
Red Tabby (Lynx)	c^{s}c^{s}OO
Cream Tabby (Lynx)	c^{s}c^{s}ddOO
Seal Tortie Tabby (Lynx)	c^{s}c^{s}Oo
Chocolate Tortie Tabby (Lynx)	bbc^{s}c^{s}Oo
Blue Tortie Tabby (Blue Cream, Lynx)	c^{s}c^{s}ddOo
Lilac Tortie Tabby (Lilac Cream, Lynx)	bbc^{s}c^{s}ddOo

* Recognized by CFA in the US. Other colors recognized as colorpoint shorthaired breed.

phenotypes but are perceptibly paler in tone.

Burmilla: The Burmilla was developed by crossing the Burmese and Chinchilla, engendering a unique phenotype that has been exploited by breeders. The undercolor is white, overlaid with colored ticking and Tabby barring on the legs and rings in the distal tail. The basic genotype is IIt^{b}t^b. The color of the ticking depends upon the presence of other genes, such as the chocolate bbIIt^{b}t^b or blue ddIIt^{b}t^b. Other Tabby alleles may replace t^b.

White Coat with Orange, Blue or Odd-Colored Eyes: The coat is completely white due to the presence of the W gene. The iris may be orange or blue, depending on whether or not the W gene can change the normal orange color to blue. In a small proportion of cats, the iris may be partially orange and blue, commonly affecting one eye more than the other. Such cats are known as odd-eyed. The variation of iris color results from the erratic influence of W upon eye pigmentation. A deficiency of pigment produces a wholly or partially blue eye.

Foreign White: This cat is a true-breeding blue-eyed white of genotype c^{s}c^{s}WW. The W gene produces the completely white coat but the iris is not invariably blue. However, the irides can be made consistently blue by combining W with the c^s gene.

Bicolors: These cats have large white areas due to the piebald gene S. The amount of white should not be too extensive because this would upset the "balance" of colored and white markings. The colored areas may be any one of the usual known colors, tabby or black being the most common.

Snowshoe: The Snowshoe is a cat of Siamese coloration, with the addition of restricted white spotting. The lower portion of the front and rear legs is white, often accompanied by an inverted V wedge of white extending between the eyes to the nose, and small areas of white on the stomach. The g or a similar gene is probably involved. Varieties of Snowshoes include the Seal, Chocolate, Blue and Lilac, with identical genotypes for the comparable nonagouti series of Siamese.

Long-Haired Breeds

The major difference between the short- and long-haired or Persian breeds is the coat length. There are additional differences in head and body conformation, but less emphasis is placed upon these. The difference in coat length is due to the gene l

Table 10. Genotypes of Burmese varieties.

Name	Genotype
Brown* (sable)	aac^{b}c^b
Chocolate* (champagne)	aabbc^{b}c^b
Blue*	aac^{b}c^{b}dd
Lilac* (platinum)	aabbc^{b}c^{b}dd
Red	aac^{b}c^{b}OO
Cream	aac^{b}c^{b}ddOo
Brown Tortie	aac^{b}c^{b}Oo
Chocolate Tortie	aabbc^{b}c^{b}Oo
Blue Tortie	aac^{b}c^{b}Oo
Lilac Tortie	aabbc^{b}c^{b}Oo

* Recognized by CFA in the US.

for long hair. However, the luxurious coat of the exhibition long hairs differs appreciably from the Domestic Long Hair. The coat is longer, softer and more dense. These differences are due to modifying polygenes that enhance the effect of the primary l gene.

The color genes are inherited independently of the long-hair gene, and almost all of the phenotypes of short-haired cats are also found with long hair. These breeds often have comparable names, which aids identification. Exceptions will be discussed in this section.

Cameo: The Cameo is an orange cat with a light or white undercolor, due to the joint effects of the Q and I alleles. The amount of undercolor, or conversely the amount of distal pigmentation varies. Consequently, 3 varieties of Cameo are recognized: Shell, the lightest, in which only the tips of the hairs are orange; Shaded, in which the amount of orange is greater; and Smoke, the darkest, in which the hairs are most heavily pigmented. The cream Cameo, produced by addition of d to the genotype, also occurs in 3 varieties that parallel those for the red (Table 11). The Tortoiseshell and blue-cream Cameo are mosaics of red Cameo and nonagouti Smoke, and cream Cameo and blue nonagouti Smoke, respectively.

Himalayan and Kashmir: The Himalayan varieties are long-haired Siamese differing in both hair length and conformation. They have the sturdy build of the traditional long-haired breeds. The 10 varieties of the nonagouti Siamese series are recognized for exhibition purposes. The genotypes are identical to the first 4 of column 2 of Table 9, with the addition of the ll gene. In Great Britain, the Himalayan is known as the Colorpoint. Varieties that have colored points other than self-color are known as Kashmir. Because of extensive cross-breeding to Persians, the Himalayan is now a variety of the Persian in the United States.

Birman: The Birman is similar to the Himalayan, but with the addition of low-grade white spotting. The spotting is ideally confined to the feet. They are "gloves" for the forefeet and short "stockings" for the hind legs. The spotting is probably due to the g gene. Accordingly, the genotypes of the various colors are identical to those of the Himalayan, with the addition of gg.

Table 11. Genotypes of British longhair Cameo varieties.

Name	Genotype
Red Shell* (chinchilla)	aaIIIIOO
Red Shaded*	aaIIIIOO
Red Smoke*	aaIIIIOO
Tortoiseshell* (shell, shaded, smoke)	aaIIIIOo
Cream Shell	aaddIIIIOO
Cream-Shaded	aaddIIIIOO
Cream Smoke	aaddIIIIOO
Blue Cream* (smoke)	aaddIIIIOo

*Recognized by CFA in the US.

Balinese and Javanese: The Balinese and Javanese are basically long-haired Siamese. Both the coloration and conformation are typically Siamese, the latter differentiating the Balinese from the more sturdily built Colorpoint. Balinese is the name given to the 4 nonagouti varieties (Seal, Chocolate, Blue and Lilac Points), while Javanese is the name given to all of the other varieties. Their genotypes are identical to those of the Siamese varieties, with the addition of ll.

Tiffanies: Tiffanies are long-haired Burmese that occur in the usual Burmese colors. The genotypes of Tiffanies are identical to those of the Burmese, with the addition of ll.

Silver, Chinchilla and Smoke: The long-haired Silver is identical in structure to the short-haired Silver. The genotype is identical, with the addition of ll. The Chinchilla represents the extreme expression of the inhibitor gene I. The coat is white except for pigment at the extreme tip of the hair. The long hair effectively obscures the pigmented hair tips, but their presence is apparent on the coat of young kittens. When the hair is very short, a tabby pattern similar to that of the Silver Tabby may be observed. As the hair continues to lengthen, however, the pattern gradually diffuses. The Smoke is a combination of nonagouti and inhibitor (aaIIII), being blackish with a light or white undercolor.

Golden Chinchilla: The Golden is a segregant of Chinchilla parents that are heterozygous for I. The Golden has a Tabby pattern more dispersed than that found in the ordinary brown Tabby. The effect is to produce a brighter-yellow cat; hence the name Golden. The dispersion of the Tabby pattern is probably a means of creating the light color of the Chinchilla. The action of the I gene is strongest when the amount of pigment is already reduced by other genes. Dispersion of the Tabby would facilitate creation of the Chinchilla phenotype. Exactly how the Golden differs from a brown Tabby is unclear.

Turkish Van: This breed displays the extreme expression of piebald spotting combined with orange. The coat is completely white except for small patches of orange on the head or shoulders and an orange tail. The genotype is llOOSS. The cream Turkish is phenotypically identical except that the patches and tail are cream; the genotype is ddllOOSS.

Ragdoll: This breed displays combinations of genes not found in older breeds. Ragdolls may be likened to colorpoints, with the addition of the spotting gene S. Indeed, when the S gene is absent, the variety is called "Colorpoint." When a small amount of white is present (probably the heterozygote Ss), the variety is called "Mitted." When the white areas are extensive (probably Ss or SS), the variety is called "Bicolor." Four colors are recognized: Seal, Chocolate, Blue and Lilac. The genotypes are identical to those for the comparable Colorpoint, with the addition of Ss or SS as described above.

Angora: The Turkish Angora is a long-haired breed with a sinuous body conformation, as opposed to the more stocky conformation of most other long-haired breeds. In this respect, the Angora resembles foreign-type breeds with long hair. It differs by having no short-haired counterpart. The cat may be bred in all of the usual colors.

Somali: The Somali is a long-haired Abyssinian, having the same range of varieties and identical genotype, with the addition of ll.

Maine Coon: This breed originally was bred in the northern United States as a domestic for catching vermin. Recently, it has been adopted as a breed for exhibition purposes. The coat is long, due to the l gene, but more heavy and shaggy than the other long-haired breeds. The Maine Coon is bred in the usual range of colors.

Norwegian Forest Cat: This is another breed developed from long-haired domestics originally bred to reduce rodent populations. Now recognized for exhibition purposes, these cats have a coat that is dense and shaggy, differing from the fuller and softer coat of the traditional Long Hair. Most of the usual colors occur in the breed.

Cymric: The Cymric is a long-haired Manx of genotype llMm. Most colors are recognized.

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GENETIC DISORDERS

Surveys of genetic disorders in cats are few. One extensive compendium covers primarily congenital (developmental) diseases, but includes many traits that are probably not genetic.[143] Other authors are careful to distinguish between "probable" and "possible" genetic disorders.[48] Some are written mainly for laymen.[135] Some reviews deal only with metabolic diseases of genetic origin.[38,107,119] Included as disorders are genetic deviations from the norm that may not necesarily be harmful to the cat.

Genetic Disorders of the Skin

The haircoat of cats is composed of 3 distinct types of hairs, each having different functions. The stouter primary guard hairs are the longest and taper to a fine point. The secondary guard or awn hairs are slightly thinner than the primary guard hairs and are more numerous. They have a subapical swelling and taper to a fine point. Some awn hairs are straight but most show some degree of undulation. The wool or down hairs are the most numerous. They are very fine, flexible and of even diameter. The primary and secondary guard hairs make up the topcoat, and the wool hairs the undercoat. One of the functions of the haircoat, particularly the wool hairs, is to insulate the skin against excessive heat loss. The guard hairs act as a protective covering for the softer wool hairs. The primary guard hairs also have a sensory function. The vibrissae and other facial whiskers are extra stout hairs and presumably serve a tactile purpose.

Long Hair

Long hair (l) is not usually viewed as an anomaly.[135] However, the long coat is due to exceptional growth of the hair fibers. No studies have been made of the growth of individual hairs in cats. Measurements of growth of hairs in long-haired Angora rabbits (due to a recessive mutant gene comparable to that of cats) revealed that the rate of growth per day is normal but the growth or anlagen phase was of longer duration.[49] Exhibition long-haired cats have a longer and fuller coat than ordinary domestic cats because modifying polygenes increase the length of the hairs, especially the wool hairs.

Rex Coat

Four distinct rex-type coat mutant genes are known and others may also occur. The 4 genetically independent mutants are: Cornish rex (r), Devon rex (re), Oregon rex (ro), and Dutch rex (Rd).[129,132,137,145] A fifth rex (German rex) is inherited as a recessive to normal coat.[130] This gene mutated independently of the others, but it is either a repeat of the Cornish rex or is a similar allele at the same locus.[131] The coat type is easily recognizable and rex cats have originated from many parts of the world. Additional cases have been described in the United States, Italy, Australia and Sweden.[135] In each case, monogenic recessive inheritance is indicated. It is not known if these are distinct from the 4 known rex genes.

The coat of the rex breeds is abnormally short, waved or curled. All of the hair types are reduced in length, especially the guard

hairs, which are usually grossly abnormal or even absent. The vibrissae are short, typically bent, twisted or wriggly, depending upon the severity of affliction. No studies have been published on the growth of the rex coat in cats. An analysis of growth of the rex coat in rabbits, which is due to a recessive gene comparable to that of cats, showed that the growth phase was of normal length but the rate of incremental growth per day was less.[49]

The coat of the Cornish rex feels thinner than normal due to an absence of primary but not secondary guard hairs. Some coat may be lost, leaving bare areas. This is relatively uncommon. On the other hand, the Devon rex is very prone to coat loss, especially over the shoulders, chest and abdomen. All 3 hair types are present but grossly abnormal in comparison with those of the Cornish rex. The hairs show marked constriction of diameter along their length and break easily. It is characteristic of Devon rex for the vibrissae to appear stubby due to breakage.[129] The dominant gene for Dutch rex produces a rex type of coat in the heterozygote Rdrd and a very thin coat in the homozygote RdRd.[137,139]

Wire Hair

The wire-hair (Wh) coat appears unruly in contrast to the smooth coat of normal cats.[135] All 3 hair types are thinner in diameter than normal, and the primary guard hairs are curved instead of straight. The awn hairs are very undulated and may even be coiled. A "shepherd's crook" type of configuration may be present in the region of the subapical swelling. The wool hairs display exaggerated undulations. The coat may be slightly springy to the touch.

Sparse Fur

Sparse fur (sf) individuals exhibit partial alopecia, resulting in a thin coat that is rough to the touch. All of the hairs are short and deformed, while the vibrissae are bent or curled. A reddish or reddish-brown encrustation forms about the eyes, nose and mouth, and frequently affect the fur of the chest and abdomen. The eyelids become thickened and the globe shows signs of septic deterioration if left untreated.[139]

Hairless

Hypotrichosis has a long history of recurrence among cats. Cases have been described in Europe, North Africa and North America over the last 50 years (Fig 9). At least 3 distinct mutant genes (h, hd, hr) have been implicated. Cats with the 3 mutant genes have not been interbred; hence, it is unknown if 2 or more are alleles at the same locus or if all 3 represent independent loci.

Hairless cats are not completely devoid of hair, at least not until they are fully adult. Sparse down may be evident in kittens, but it is subsequently lost. Some hair growth occurs with each successive molt cycle as the individual matures. This is transitory, however, and the adult may be virtually hairless. The French hairless (h) may be temporarily covered by hair and the vibrissae are normal.[89] On the other hand, the Canadian hairless (hr) never has much hair and the vibrissae are short and curly.[133] Microscopic studies revealed that 2 types of hair fibers are present. One is distinctly thicker than the other, possibly representing vestigial guard and wool hairs, respectively. All of the fibers lack well-formed hair bulbs. The skin is thicker than usual and a number of hairless kittens display retarded growth.

The Redcar hairless (hd) manifests the most extreme expression of hypotrichosis.[65,136] Affected kittens never have more than a fine coating of down. The skin is soft at birth but steadily became thickened and wrinkled. The vibrissae are short, thin and crinkled. A brownish secretion can be seen about the nostrils and eyes, and under the chin. Few Redcar hairless kittens live beyond 2 weeks of age. One male that survived to about 3 months had defective, easily split claws. This tendency toward early death differentiates the Redcar hairless from the other 2 hairless mutants, both of which are viable and relatively hardy.

Cutaneous Asthenia

Scattered reports of cutaneous asthenia (cut) are found in the literature. It was not until 1977 that the genetic basis of the disorder in cats was elucidated, in spite of the fact that a similar malady was known to be a heritable trait in dogs, mink, cattle and

sheep. The condition arises from a severe deficiency of connective tissue, involving packing defects of the collagen fibrils and fibers in the reticular layer of the dermis. The skin is extremely hyperextensible and fragile (Fig 11). It is easily lacerated, even by normal scratching or play, and healing leaves white paper-chain scars. The skin often feels velvety to the touch. The anomaly is due to a dominant gene.[120]

A similar anomaly has been designated as dermatosparaxis.[23,29,70] No genetic studies were made with the affected cat, but reports described defective structure of the collagen fibrils, fibers and bundles. Conversion of precursor proteins to mature collagen is due to amino acid deficiencies in the NH_2-terminal procollagen peptidase.

Genetic Disorders of Sensory Organs

Progressive Retinal Atrophy

Progressive retinal atrophy (PRA) is an insidious malady. Retinal degeneration can be well-advanced before outward signs are obvious. In the late-developing type, this may even be after the cat has reproduced. This increases the difficulties of elimination by selective breeding. At least 3 different forms of PRA are known (rt, Rdy, rdy). They are differentiated from each other by age of onset and mode of inheritance. The PRA syndrome of cats is similar to retinitis pigmentosa in people and could serve as a useful animal model for the human disease.[112]

Figure 11. A cat with cutaneous asthenia. The skin is hyperelastic and easily stretched. (Courtesy of Dr. D. Patterson and *Journal of Laboratory Investigation*)

The clinical signs of PRA are bilateral dilation of the pupils (mydriasis), some nystagmus, hyperreflectivity of the tapetum lucidum, and progressive diminution of the retinal blood vessels. The photoreceptor layer of the retina, containing the rods and cones, undergoes progressive degeneration, with consequent steady deterioration of electroretinogram readings. Defective vision is manifested by cautious behavior and stumbling into objects that are normally avoided. The uniform descriptions of PRA in cats do not indicate that they are necessarily identical, either genetically or in their pathogenesis. When the onset of the rod-cone degeneration occurs at an early age, the process could be described as dysplasia rather than atrophy.

Scarcely any of the early reports on PRA showed that the condition was inherited. One exception hinted that some Siamese cats displayed a familial tendency for the malady.[15] Other data suggest a dominant mode of inheritance.[164] Signs of PRA were seen in kittens as early as 3 weeks of age, followed by rapid and progressive degeneration of the photoreceptor cells within a few months. Since retinal development is not completed until about 6 weeks of age, degeneration was thought to be rod-cone dysplasia.[42]

Another type of PRA described in Persian cats was clearly inherited.[141] The quantity of breeding data was limited but sufficient to indicate monogenic recessive inheritance (proposed gene symbol rt). The condition was apparent by 12-15 weeks of age, as evidenced by mydriasis. Histologic examination revealed only remnants of rods and cones and thinning of the outer layers of the retina.

The retinopathy in Abyssinians that occurs at an early age, is midway between the types of PRA described above.[4] The first signs were observed in 4- to 5-week-old kittens, and degeneration was well advanced by about 12 weeks. The anomaly was due to a dominant gene designated Rdy. A search for a homozygous individual among 4 affected kittens from heterozygous parents failed, however. Another group described a

stock of affected Abyssinian cats descended from a single male.[160] The investigators noted the resemblance of the disorder to taurine deficiency but were unable to document a defect in taurine homeostasis.

A third type of retinal degeneration, in Abyssinians, was found to be due to a recessive gene rdg.[110,111] This form differs from the preceding ones by a later age of onset and slower progression. The condition is diagnosed in most affected individuals between 18-24 months of age; the advanced stages of the disease are not reached until about 3 1/2-4 years. The initial signs of degeneration are in the peripheral and central regions of the photoreceptor layer of the retina. The central area is not involved until the final stages, and then less severely than that of the periphery. The inner retinal layers and the pigment epithelium appear to be unaffected.[112,113] Analysis of DC-recorded electroretinograms indicated that the rods are affected earlier than the cones.[114] The late onset of retinal degeneration indicates atrophy of the rod-cone layer, rather than dysplasia.

Central Progressive Retinal Atrophy

A form of PRA commencing in the area centralis of the retina was thought to be heritable.[6,63] The pathologic condition can be induced, however, by a dietary deficiency of the amino acid taurine.[3,64]

Cataract

Extensive bilateral cataracts by 12 weeks of age have been reported in Himalayan cats.[140] The cataracts were sufficiently dense to interfere with normal tapetal reflection in one case. In another case, the cataracts were extensive but insufficiently dense to be visible without ophthalmic examination. The amount of breeding data was limited but adequate to establish a monogenetic recessive heritability of the malady.

Epibulbar Dermoids

A unilateral epibulbar dermoid, attached by a broad pedicle to the conjunctiva inside the lateral canthus of either eye is familial in cats.[66] The pigmented dermoids have hairs that cause irritation of the cornea and keratitis if not removed. Dermoids may be due to an autosomal gene with incomplete penetrance or they may have a polygenic threshold inheritance.

Corneal Mummification

The occurrence of corneal mummification in semi-inbred strains of the colorpoint breed in Britain prompted the suggestion that the condition is caused by a recessive gene.[158] Mummification occurred in cats from 10 months to 8 years of age.

Corneal Edema

Corneal dystrophy is probably inherited, but the mode of inheritance has not been determined.[9] The anomaly was manifested at about 4 months of age as progressive edema of the anterior corneal stroma. The edema increases as the condition worsens, the corneal stroma thickens, and bulbous lesions appear in the corneal epithelium. This is followed by breakdown of the corneal stroma and epithelium and secondary bacterial infection.

"Cherry Eye"

Prolapse of the gland of the third eyelid (nicitating membrane) has been seen most often in Burmese cats, in which it is thought to be a heritable condition. The problem is thought to be due to weakness in the cartilage or fibrous tissue that supports the gland. The prolapsed gland becomes very edematous, enlarged and hyperemic, resembling a small cherry attached to the third eyelid.

The treatment has been excision of the prolapsed gland, though this can lead to complications of inadequate tear production. Newer reconstructive surgeries are therefore recommended.

Abnormal Visual Pathways

Albino mammals completely lack melanin pigment; hence, their eyes are pink or red and the coat white. They also have a misrouting of the visual pathway from the retina to the brain. The anomaly has been detected in albinos of all species so far examined, including Syrian hamsters, guinea pigs, rabbits, mice, rats, ferrets, mink and

one species of monkey. The visual pathway is affected in cats carrying either the albino (c) or Siamese (c^s) allele, but not the Burmese (c^b) allele.

The ganglion axons from the retinal cells of the eye normally travel to the lateral geniculate nucleus of the thalamus. This nucleus is sited in each side of the brain. Each eye contributes fibers to defined layers of the lateral geniculate nuclei. A disproportionate number of fibers in Siamese cat (c^sc^s) crosses to the lateral geniculate nucleus on the side opposite to the eye. The lateral geniculate nuclei are incorrectly innervated in reverse order. The cat's brain probably does not receive a distorted picture, however.

Elegant experiments suggest that the visual field is compensated by either of 2 methods.[57,72,82] The most direct is apparent suppression of the abnormal information when it reaches the visual cortex (the "midwestern pattern"). The other compensation method involves rearrangement of information inputs to recreate a normal visual field (the "Boston pattern"). The 2 methods of compensation may not be absolute, but rather part of a continuum.[24,25] The method of compensation may depend upon the extent of the erroneous crossover of ganglions. Misrouting is present from the earliest prenatal stages of development of the ganglion pathway and arises at the optic chiasm.[147] Misrouting may interfere with normal binocular depth perception and is responsible for the convergent squint to which Siamese are particularly prone.[83]

The Siamese allele (c^s) falls short of complete albinism, but the complete albino allele (c) has recently been recognized. Examination of the visual pathway in albinos reveals misrouting to be much greater than in Siamese. A much higher proportion of the ganglion axons crosses over to the opposite lateral geniculate nucleus. As a consequence, organization of the visual field in the cortex differs from that observed for Siamese.[31,90] The albino allele is completely recessive to full color (C) as regards eye and coat color, but not for misrouting of ganglion axons. Heterozygous Cc albinos or Siamese have similar misrouting, but less extreme.[91]

Deafness in Mixed-Breed White Cats

White coat color is due to a dominant gene W.[156] These cats may have yellow or blue irides (or heterochromatic for yellow/blue), unilaterally or bilaterally. They may also be unilaterally or bilaterally deaf. Blue irides, though indicative of partial depigmentation, are not considered to be anomalous. Deafness, on the other hand, is considered to be detrimental. The W gene has a slight but significant effect on postnatal viability.[8]

Blue color of the iris and deafness are correlated, as may be seen from the following observations extracted from the literature.[8,99] Among a group of 240 mixed-breed white cats, 68% had blue eyes and 45% were deaf. However, when the 2 traits are considered together, 39% were blue-eyed and deaf, 29% were blue-eyed but were not deaf, 7% had yellow eyes and were deaf, and 25% had yellow eyes but were not deaf. The correlation coefficient between the 2 traits is 0.34 (1.0 being total correlation). The association is increased when considering the relationship between color of the eye and deafness on the same side of the head. Among a sample of 748 eye and ear combinations, 49% were blue and deaf, 18% were blue and were not deaf, 8% were yellow and deaf, and 25% were yellow and were not deaf. The correlation between ipsilateral blue eyes and deafness is $r = 0.46$.

The simplest explanation of these observations is that the W gene has a syndrome of effects.[135] The gene is completely penetrant regarding coat depigmentation but is only partially penetrant for blue iris color and deafness. Arguments supporting independent genes for blue irides and deafness are not convincing. The penetrance of these 2 traits probably depends upon the genetic background against which the W gene is assorting; thus, the incidence of either trait varies among strains of cats. In this connection, long-haired animals displayed a higher incidence of blue irides and deafness than short-haired cats.[99] The chromosome carrying the long-haired gene may also carry genes enhancing penetrance of blue eye color and deafness.

The incidence of blue irides and deafness is higher among mixed-breed white kittens

when both parents are white than when one parent is white, suggesting that penetrance of both traits is greater in homozygous WW individuals. This implies that W is incompletely dominant in its primary effect. This would not be apparent if coat color alone is considered, because the presence of a single W gene would suffice to remove all pigment from the hair. In support of this hypothesis, the small spots of colored fur seen in a minority of white kittens, but not apparent at adulthood, are more frequent in heterozygotes than in homozygotes.[8]

Pigmentation of the eye in yellow-eyed white cats is essentially normal. On the other hand, the eyes of blue-eyed white cats are partially depigmented. The iris and retina epithelia are normally pigmented but pigment is absent, wholly or in part, from the iris, choroid stromata and tapetum. The partial depletion of pigment is comparable to the macroscopically observable heterochromia of the iris.[151] The absence of tapetum usually results in marginal or obvious dilation of the pupil.[8] Tissues affected by the W gene originate from the neural crest, while those derived from the embryonic optic cup (iris and retinal epithelium) are not affected.[151]

Loss of hearing is due to degenerative processes in the inner ear, unilaterally or bilaterally. Histologically, these degenerative changes have been traced back as far as the fourth and sixth days postpartum.[11,12] The extent of the cochlear anomaly is variable and may affect each ear differently. The changes appear to begin with collapse of Reissner's or tectorial membranes and atrophy of the stria vascularis. Eventually, all or part of the organ of Corti and spiral ganglion neurons are involved. Variability is such that some organs may appear superficially normal (tunnel of Corti and hair cells), while others are wholly abnormal.[100,126] Hearing loss may progress rapidly over several weeks, or slowly, extending for months. Degenerative changes may slow down or halt with time.[127] Degenerative changes of the cochlear structures are associated with progressive deterioration of the primary ganglion neurons. The deterioration was initially considered to be a secondary change. However, it seems that the neural elements may be subtly affected from the onset. An unusually high proportion of unmyelinated fibers can be seen in the lamina spiralis, as well as in neurons with clear and empty cytoplasm and minute nuclei. The nonmyelination could be noted in 2- and 4-day-old kittens, earlier than the first appearance of histologic lesions.[100] The age of onset of spiral ganglion degeneration may be variable. In some strains of W individuals it may be delayed for several months. Whatever the time course, the malady appears to be progressive.[44,163]

Investigation of the retinogeniculate ganglion pathways in W cats revealed no signs of abnormality.[56,92] A few blue-eyed white animals were clearly abnormal, but breeding experiments showed that their genotypes were $c^s c^s Ww$. The W gene is epistatic to c^s in regard to coat color. On the other hand, eye color is invariably blue due to the degrading action of the c^s gene on production of melanin pigment. It is evident, therefore, that the c^s gene can disrupt normal decussation of the visual pathways independently.

Preliminary analysis of the distribution of 16 amino acids and sugar content among perilymph, cerebrospinal fluid and serum revealed both qualitative and quantitative differences. Notable differences were not observed, however, among fluids from white cats with normal hearing or deafness.[45]

The W syndrome of white coat, blue or heterochromatic iris, and deafness has been compared with Waadenburg's syndrome in people. Defects in the embryonic neural crest are common to both syndromes, but they have a different genetic basis. The effect on hair pigmentation in people is confined to a white forelock, a far less drastic suppression of pigment than found in cats. The facial abnormalities observed in people are absent in the feline syndrome.

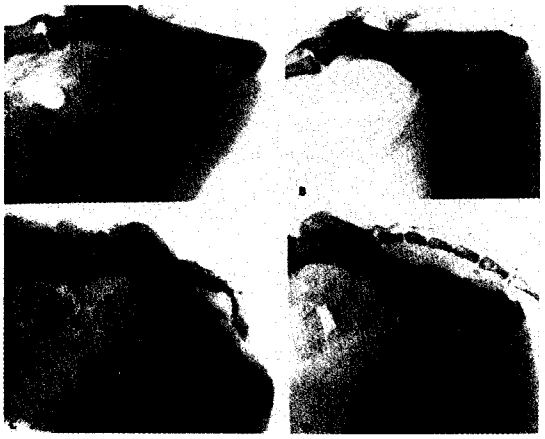
Deafness may be avoided in white cats by using underlying c^s genes. This is why purebred white cats are usually not deaf.

Malformations

Manx Taillessness

Manx taillessness is due to a dominant gene M, which is a prenatal lethal when homozygous MM.[150,154] Manx cats with no or abbreviated tails are heterozygotes. Since the Manx gene varies in expression, most

Figure 12. The 4 tail types in Manx cats are: rumpy, the absence of coccygeal vertebrae (top left); rumpy-riser, reduced number of rigid vertical coccygeal vertebrae (top right); stumpy, reduced number of coccygeal vertebrae in a ventral position (bottom left); and normal-tailed Manx (bottom right). (Courtesy of Dr. J. Howell and *Journal of Heredity*)



Manx cats are not totally tailless. Four categories of taillessness are recognized: rumpy, in which no coccygeal vertebrae are apparent; rumpy-riser, in which 1-7 vertebrae can be felt, usually immovable; stumpy, in which 2-14 vertebrae are present, usually movable but often knobby or bent; and longie, in which the tail is shorter but superficially normal (Fig 12). The rumpy is held as the ideal of the breed.

Some heterozygotes, though born alive, have anomalies of sufficient severity to affect them as kittens or later in life. The proportion of such overly anomalous heterozygotes may be linked to additional genetic selection for short body conformation. Manx cats bred for short body conformation produce more diseased heterozygotes than Manx with longer bodies.

Some heterozygous Manx cats may exhibit abnormalities in addition to the obvious tail defects. In the mildest cases, the gait in the hind limbs is often affected. A peculiar stilted walk or hopping movement is due to maldevelopment of the caudal vertebral column. The whole spine is probably affected to some degree, but the major changes occur in the caudal part. The thoracic, lumbar, sacral and coccygeal vertebrae are small, deformed, occasionally fused and reduced in number.[71] In Manx with more severe caudal spinal deformities, both fecal and urinary incontinence are frequent occurrences, apparently due to denervation insensitivity of the anal and perineal area.[36,74,88,101] The perineal fur of such kittens is often stained and matted. Both the colon and bladder may be greatly enlarged. Some heterozygotes may develop megacolon, constipation and obstipation later in life. Such cats probably have partial denervation of the colon at birth. The colon tends to become larger, more sacculated and more atonic over time. Spina bifida and related gross anomalies are seen in a smaller proportion of heterozygotes.

The Manx syndrome is caused by abnormal development of the caudal region of the embryonic neural tube. This leads to defects of the caudal vertebral column, especially spina bifida, and the spinal cord. The spinal cord may terminate abruptly due to an absent sacral cord segment, which normally would innervate the colon, bladder, hind leg muscles and perineum. Vertebral anomalies are derived from the same neural tube disorder.[36,88]

Manx cats have been associated with the Isle of Man, situated off the west coast of England; hence the name Manx. The Manx cat has been said to originate on the island, but this is doubtful. The belief is encouraged for commercial and social reasons. Cats with the Manx gene have appeared in small numbers in many parts of the world. The gene even occurs in "pockets" of unusually high frequency, which is unusual considering its highly deleterious nature. Human preference for novelty is probably responsible for such pockets. However, the M gene may have a selective advantage that would enhance its frequency.[1] The hypothesis is based upon breeding data that show that M is assorted from the normal allele at a significantly higher proportion than could be accounted for by random assortment.[150,154] A model was proposed to reflect this selective advantage and applied to the unusually high frequency data for M in the Isle of Man cat population. The model could not explain all the observed high frequency in the population, and the author concluded that both human preference and selective advantages were maintaining the high frequency.[1]

A sample of 314 progeny from Manx x Manx matings drawn from the records of a prominent English breeder consisted of 201 Manx and 113 tailed kittens. This closely fits to the expected 2:1 ratio of Manx:tailed.[139]

Brachyury

An inherited shortening of the tail has been described in the Siamese cat.[109] The tail was consistently shorter than normal, though with some variation. Breeding data were consistent with a monogenic recessive inheritance (br).

Polydactyly

Polydactylous cats have extra or partly formed digits on the feet. This is especially noticeable in the front feet. Polydactyly is induced by the action of a dominant gene Pd, possibly by enhancing the growth potential of the preaxial region of the embryonic limb bud.[17,33,34,144] Expression of polydactyly is variable. One investigation listed as many as 8 recurring types of anomalies, 3 for the fore and 5 for the hind feet. Once the gene has affected a certain developmental path, the outcome is more or less prescribed. Variation in expression extends from enlargement of a single digit to the presence of 3 quasi-normal extra digits. Difference of expression is frequent between right and left feet and front and rear feet. The hind feet are very rarely affected in the absence of front feet anomalies. Breeding data are inadequate to establish whether any of the various types are genetically controlled by modifying polygenes.

Split-Hand

An extrosyndactyly designated as split-hand is due to a dominant gene Sh. It is usually expressed by a central cleft of the forefeet with some syndactyly (fusion of digits). The anomaly varies from reduction in the number of phalanges to disorganization of the metacarpal and carpal bones. Syndactyly is evident as double claws and fused paw-pads. Even the most severely affected cats can run and jump normally, though climbing is somewhat impeded.

Folded Ears

The pinnae of normal cats are carried in an upright, "pricked-eared" position. The pinnae of fold-eared cats, however, are bent forward at the apex. The ears appear normal for the first 4 weeks of life, but then begin to bend forward. The fold is permanent by about 3 months of age. The condition is inherited as an autosomal dominant (Fd).[135]

Fold-eared cats are usually heterozygotes Fdfd without other abnormalities. The homozygote FdFd not only has folded pinnae but sometimes gross anomalies of the coccygeal vertebrae and distal bones of the limbs. Clinically, the tail is inflexible, stubby and thick, and the feet are swollen and arthritic (Fig 10). The activity of such animals is curtailed. The toenails grow in a curve to penetrate the pads. The coccygeal vertebrae and smaller bones of the distal limbs are shorter than normal and the deformed vertebrae have wide epiphyseal plates. The primary cartilage anomaly results in disturbed epiphyseal growth. Ossification is deficient and irregular.[73]

Early observations of fold-eared cats indicated that the skeletal anomalies were confined to homozygotes. It has been subsequently found that some heterozygotes could also be grossly affected, with thick short tails, swollen feet, and impaired activity.[139]

American Curl

The American curl (Cu) is a recently discovered mutant gene. It is outwardly expressed by backward curving of the pinnae. The degree to which the ears curve backward is variable, though the abnormal gene appears to be fully penetrant. Most affected cats examined have been heterozygotes resulting from numerous outcrosses to unrelated stock. About 50% of the resultant kittens had curled ears, indicating a dominant mode of inheritance. A homozygous curl-eared male has not revealed any other anomalies by 2 years of age, thus differentiating the condition from the folded ear trait.[139] Early breeding reports have indicated a potential problem in some cats with hard cartilage. There is a tendency toward narrowness at the base of the ear, making it difficult to clean the ears. Breeders are beginning to select for a broad ear base to avoid this problem.

Meningoencephalocele

This malformation is due to herniation of meninges and brain tissue through a fissure in the skull. It is perinatally lethal. A pedunculated mass of skin filled with brain tissue and fluid may be seen arising from the top of the head. The mandible is normal but the tongue is large and often split. The maxilla is shorter than normal, with a cleft replacing the nostrils and sometimes extending into the palate. Dentition is abnormal, and the eyes and sometimes eye sockets are missing. The top of the skull may be depressed. The dorsal cerebrum is herniated and the parts of the brain remaining in the skull are compressed. There is extensive hemorrhaging. Primitive eye tissue may be present in the skull, consisting of groups of retinal cells, pigmented epithelium and portions of optic nerves and lens.[168]

The frequency of affected kittens corresponds with the assortment of an autosomal recessive gene mc. The gene may have variable heterozygous expression, but the evidence is ambiguous.[149]

An inherited midfacial malformation has also been described in Burmese cats.[149] The genetic basis of this disorder was the same as meningoencephalocele but the description of the anomaly was somewhat different.

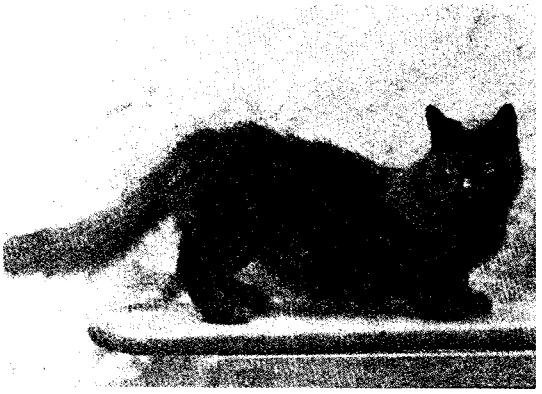
Four Ears

The name is prompted by a small extra pinna on each side of the head. This is probably only one superficial expression of a more fundamental affliction. Affected cats are microphthalmic, with slightly undershot jaws. Body size seems to be unaltered and the animals are often lethargic.[93] The anomaly has also been called "duplicated pinnae" (gene symbol dp).

Osteogenesis Imperfecta

Osteogenesis is an inheritable disorder of bone that leads to excessive bone fragility and pathologic fractures. It is a heterogeneous syndrome in people, with each type having its own peculiar pattern of inheritance, clinical symptomatology and biochemical defects. A 12-week-old domestic kitten with severe bone fragility and multiple pathologic fractures has been described.[171] The kitten may have resulted from a mother-to-son mating. This condition is not to be confused with secondary nutritional hyperparathyroidism, an acquired bone disorder of kittens that is caused by feeding excessive amounts of organ meat.

Figure 13. Cat with foreleg micromelia.[165] Such animals are often called "kangaroo cats" by laypeople. The hind limbs are of normal size but the long bones of the forelimbs are shorter than normal. (Courtesy of Dr. H. Williams-Jones and *Veterinary Record*)



Patellar Luxation

Luxation of the patellae is becoming more common in cats. The Devon rex was one of the first breeds recognized to have this condition. No obvious defects of bone structure appear to be responsible for the luxation. Occasional luxation may not lead to lameness, but recurrent luxation can cause lameness. The breed incidence suggests a genetic influence but the mode of inheritance is unknown.[35,47] The proportion of affected animals is less than 25% on the basis of assortment of a recessive gene. Either a proportion of affected individuals have escaped detection or the anomaly has a polygenic threshold character.

Medial patellar luxation has also been seen in the Chartreux, an old and rare breed of French short-haired cats. The luxation is particularly severe by 1-2 years of age. The trait is definitely genetic in this breed, but the precise mode of inheritance is unknown. The defect is probably polygenic. An increasing incidence of medial patellar

Figure 14. Severe cleft palate in a newborn Siamese kitten.[97] (Courtesy of Dr. H. Loevy and *Cleft Palate Journal*)

luxation has recently been recognized in Abyssinian cats.

Foreleg Micromelia

An apparent case of foreleg micromelia has been described.[165] The affected cat had unusually short long bones in the forelegs (Fig 13). It was healthy but measured merely 6.75 inches from shoulder to ground and 9.25 inches from croup to ground. The animal could move quickly in spite of the abbreviated forelimbs. Similarly affected kittens occurred in at least 4 other litters. The dam, a great dam and some of the animal's progeny also had the deformity. These details suggest that micromelia is inherited but do not establish the mode of inheritance.

Protruding Sternum

Protrusion of the cranial sternum is commonly seen in Siamese cats, and in breeds derived from Siamese. The defect is less common in Abyssinian cats and mixed-breeds. The defect does not appear to be associated with any health problems. The qualification status of purebreds with this defect is unresolved. The defect is heritable, but the mode of inheritance is unknown.

Cleft Palate

The condition is often genetic. The first sign is usually inability of affected kittens to suckle properly. The extent of the cleft is variable. In mild cases only the soft palate is involved, while in severe cases there may be clefting of the hard palate and a harelip (Fig 14). In studies of the defect in families of Siamese, the anomaly was clearly familial yet the precise mode of inheritance was unclear.[96,97] The frequency of anomalous kittens among 10 litters of 43 kittens was 30.2%, a close approximation to the expected 34.9% of an autosomal recessive gene. An alternative possibility is that cleft palate is a polygenic threshold character. Cleft palate can also have nongenetic causes, often from medicating pregnant queens with such drugs as griseofulvin during pregnancy.

Craniofacial Anomaly of Burmese

The condition is caused by an autosomal dominant gene with variable expression depending on modifying genes.[115,168] It is manifested by exencephaly, lack of eyes or a nose, mild to severe hydrocephalus, and a severely protruding jaw. Some affected individuals may also exhibit a double set of whisker pads, cleft palate and rotated ear flaps. The defect has been linked to a change of the head shape in the breed. In fact, it is thought that Burmese cats with exceptionally rounded heads and short faces are heterozygous for the gene. A few cats with normal heads have produced abnormal kittens, and some Burmese cats with extreme head structure consistently produce normal kittens.

Neuromuscular Disorders Due to Heritable Errors of Metabolism

An increasing number of inherited neuromuscular defects has been recognized in cats. They share features of abnormal behavior, such as tremor or ataxia, and generalized weakness. The degenerative changes in the neuronal pathways may be similar for several of the maladies even though they are caused by deficiencies of different enzymes. Some of the anomalies may serve as models for comparable human diseases.

GM1 Gangliosidosis

Kittens with this neuronal degenerative syndrome are normal until 2-3 months of

age, when a fine tremor of the head and hind legs becomes apparent. The tremor becomes more pronounced in the ensuing months, lead to generalized dysmetria. Affected cats show spastic quadriplegia by 7-8 months, and grand mal seizures by one year of age. There is steady deterioration of vision in the final stages.

Histologic examination of the spinal cord and brain reveal extensive neuron ganglia degeneration, as indicated by swelling and cytoplasmic vacuolation.[2] Total ganglioside N-acetyl-neuraminic acid content in the cerebral cortex is about 2 1/2 times normal. A pronounced deficiency in beta-galactosidase activity is present in affected homozygotes. The deleterious gene (ga-1) behaves as a codominant at the biochemical level. Phenotypically, GM1 gangliosidosis is expressed as a recessive trait. The disease is remarkably similar to juvenile GM1 gangliosidosis in people.[3,46]

GM2 Gangliosidosis

The signs of this disease are similar to those of GM1 gangliosidosis but are caused by a different enzyme deficiency. Affected kittens are normal until 6-10 weeks of age when a fine head tremor appears. The tremor increases in severity and is followed by ataxia that progresses to paresis and paraplegia. The head has an unusual rounded appearance and the corneas are diffusely opaque. Affected kittens have difficulty eating because of the head tremor and occasional dysphagia.

Neuron cell bodies throughout the nervous system, including the autonomic ganglia and retina, are distended and almost devoid of Nisi substance, and have foamy cytoplasm. The total ganglioside content is 2-3 times greater than normal, especially for the GM2 ganglioside component. Beta-galactosidase activity is at normal levels, but levels of beta-hexosaminidase are only a fraction of normal. The activity of the latter enzyme in heterozygotes is intermediate to those of homozygous affected and normal cats. Though phenotypically the anomaly may be regarded as a complete recessive, the ga-2 gene behaves as a codominant at the biochemical level. The associated histopathologic lesions are remarkably similar to those of GM2 gangliosidosis type II (Sandhoff disease) in people.[26,27]

Mannosidosis

Glycoproteins containing branched alpha-mannosyl residues are constituents of cell membranes and are found in many body fluids. A deficiency of alpha-mannosidase causes abnormal metabolism of alpha-mannosides and excessive accumulation of mannose-rich oligosaccharides in body fluids and within cell lysosomes. A genetic deficiency of alpha-mannosidase has been reported in domestic and Persian cats.[14,75,157] It appears to be an autosomal recessive trait by pedigree analysis (Fig 15).

Figure 15. Top: Pedigree analysis of a group of Persian cats with mannosidosis. Bottom: Typical affected kitten. Kittens with mannosidosis are apathetic in appearance, demented and generally weak. They rapidly develop tremors, ataxia and impaired righting reflexes. (Courtesy of Dr. M. Haskins, University of Pennsylvania)

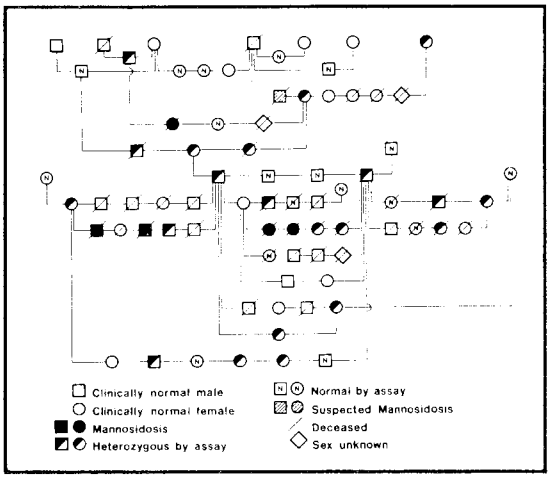
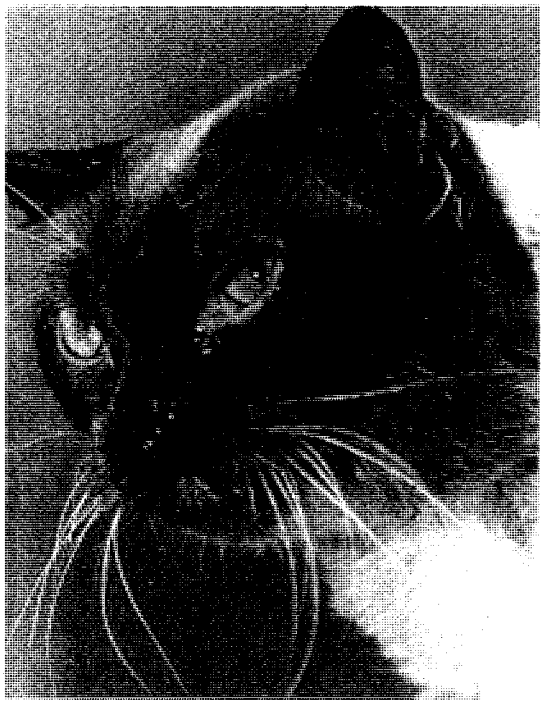


Figure 16. Siamese cat with mucopolysaccharidosis I. Affected cats have broad faces with shortened noses, frontal bossing, depressed nasal bridge, small ears, thickened skin over the neck and corneal opacities. (Courtesy of Dr. M. Haskins, University of Pennsylvania)



Clinical signs of mannosidosis appear during the first days or weeks of life and include generalized weakness, apathy and diarrhea, followed by progressive tremor, ataxia and impaired ability to recover a normal posture (Fig 15). The voice steadily weakens and the abdomen becomes swollen due to hepatomegaly. The most obvious histologic findings are vacuolation of neurons and glial cells of the central nervous system and hepatocytes. Vacuolation is minimal in kittens at 7 days of age but extensive from 12 days of age on. Vacuoles in cells appear "empty," but they are filled with mannosides. Analyses of lysosomal enzyme activity reveals a dramatic reduction in levels of alpha-mannosidase and increased levels of 7 other associated enzymes.[157]

Most affected kittens show none of the above clinical signs but are born dead or die in the neonatal period. It is uncertain if this early death is related to mannosidosis or to acute infections possibly associated with immunologic incompetence. Several affected kittens lacked thymic tissue; thymic atrophy may be due to disease in general and not specifically to mannosidosis, however. The inheritance pattern of the feline disease is consistent with an autosomal recessive gene (man).[75]

Mucopolysaccharidosis I

The primary features of mucopolysaccharidosis I in adult cats are a broad, short nose, frontal bossing, depressed nasal bridge, small ears, corneal opacity and thickened skin over the dorsal aspect of the neck (Fig 16). Affected animals adopt a crouched position, with forelegs spread. Pain can be elicited by manipulation of the head, neck and hips. The skeleton is defective; cervical vertebrae are wide, asymmetric and frequently fused, and the sternum is unusually concave. Bilateral coxofemoral subluxation, associated with shallow acetabula and abnormally shaped femoral heads, is also common.

Postmortem examination reveals hepatosplenomegaly; both the liver and spleen are difficult to section. The left atrioventricular heart valves are thick and white. Cerebral

Figure 17. Cat with mucopolysaccharidosis VI. The head is smaller than normal, the face flattened and the muzzle short and broad, with a depressed nasal bridge. The upper eyelids are swollen and drooping. (Courtesy of Dr. M. Haskins, University of Pennsylvania)

ventricles appear abnormally large. Neurons in the cranial nerve nuclei, reticular formation, hypothalamus, hippocampus and middle layers of the cerebral cortex, and of the dorsal horn of the spinal cord, are grossly swollen with vacuolated cytoplasm. Electron microscopic studies demonstrate mucopolysaccharide-filled lysosomes in neurons of the spinal cord, left atrioventricular valve, neutrophils, hepatocytes and fibroblasts of the eye and spleen.[60,61]

Assay of enzymatic activity in peripheral leukocytes and cultured fibroblasts reveals a marked deficiency in alpha-L-iduronidase, but not of other lysosomal enzymes. Cells from the mother of one affected cat, and 1/3 half-siblings, revealed alpha-L-iduronidase activity of about half normal. This observation is consistent with the assortment of an autosomal semidominant or codominant gene (Mps-1). Histopathologic lesions closely resemble those of Hurler's syndrome in people.[61,62]

Mucopolysaccharidosis VI

Signs of this disease appear at 3-6 weeks of age. Body size and tail length are reduced, the head is smaller than normal, and the face is flattened, with a short, broad muzzle and depressed nasal bridge (Fig 17). The upper eyelids also appear to be swollen and drooping, with the palpebral opening narrower than normal. The corneas have a ground-glass opacity with prominent Descemet's membranes. Retinal atrophy is observed in some animals, while the pupils of other animals respond only to very bright light. Affected animals adopt a crouched posture, with abducted stifles, cervical inflexibility, and a gait that becomes increasingly clumsy. Posterior paresis occurs at about 7 months of age in some individuals. Spot tests of urine are positive for glycosaminoglycans, in contrast to normal animals in which none are found. The primary glycosaminoglycan is dermatan sulfate.[59,63,76,104]

Many parts of the skeleton are severely anomalous, particularly in older cats. The spinal column is severely affected, with fusion and proliferative lesions of the cervical, thoracic and lumbar vertebrae. Fusion is evidenced by bony ridges and disruption of the intervertebral disks. The pelvis has shallow acetabula, and the femoral heads are flattened and sometimes subluxated. All of the long and many of the short bones exhibit epiphyseal dysplasia. Some osseous changes are progressive.

Histologic examination reveals vacuolation of the cytoplasm in fibroblasts of the atrioventricular valves, eyes, skin, aorta and spleen, bone marrow granulocytes, keratoblasts and pigment epithelium. Affected cells are packed with small inclusions when viewed by electron microscopy. These are not readily observable at the light microscopic level. The inclusions have a clear, granular or lamellar appearance.

Fibroblasts from homozygous affected individuals are deficient in arylsulfatase B lysosomal enzyme. Levels of 5 other lysosomal enzymes are significantly elevated.[63] Heterozygotes may have lower arylsulfatase B activity than normal, but the range of variation overlaps that of homozygous normals. Heterozygotes are usually detectable by assaying both arylsulfatase B and arylsulfatase A activities, and calculating the ratio of the former to the latter.[105,106,159]

The first arylsulfatase B-deficient cat was discovered in 1976 and was used to develop an inbred strain of affected animals. Subsequently, a second cat with the defect was discovered and it was also established as a strain. Both cats were Siamese but unrelated. Crosses between heterozygotes of the 2 strains produced affected individuals identical in every clinical respect to those of the 2 strains, suggesting that the 2 deleterious genes are identical alleles. A thorough analysis of partially purified arylsulfatase B from the 2 types of affected cats revealed 2 different variants with different and distinctive physical and chemical properties, however.[104] The gene products of each allele could be separated by gel electrophoresis. It is apparent that the alleles behave as codominants to the normal gene and to each other. The allele carried by the first strain is designated Mps-6^a and the allele carried by the second strain as Mps-6^b.

Successful alleviation of mucopolysaccharidosis has been accomplished by bone marrow transplants. After a male cat with advanced disease received whole-body irradiation to destroy its own bone marrow cells, it then was infused with bone marrow

cells from a histocompatible female sibling.[51] The transplantation was successful and subsequent karyotyping revealed a stable chimeric situation of 73% recipient cells and 27% host bone marrow cells. This corneal opacity completely disappeared and the face became more normal in appearance. There was an improvement in movement of the head and neck, and in ability to walk.

This anomaly is being extensively researched. The information obtained from this work is of considerable interest to researchers in feline medicine but also holds considerable promise for those studying human medicine. Feline mucopolysaccharidosis VI is similar but not exactly identical to the Maroteaux-Lamy syndrome of people. Other than hepatosplenomegaly, which is absent in affected cats but present in affected people, the similarities are striking.

Glycogen-Storage Disease

Various metabolic defects in the enzymatic processing of stored glycogen to glucose have been observed in people and dogs. Three related Norwegian Forest Cats have been found to have an inherited deficiency of alpha-1, 4 glucan:alpha-1, 4 glucan 6-glucotranserase (branching enzyme).[169] Two of the cats developed generalized muscle tremors, weakness and fever beginning at 5 months of age. These signs progressed to tetraplegia with severe muscle atrophy and limb contractures by 8 months of age. Serum creatine phosphokinase activity was greatly increased. One of the 2 severely affected cats died of heart failure at 13 mnths of age. The third cat died before clinical signs developed. Histologic examination of all 3 cats demonstrated intracytoplasmic storage of PAS-positive material in skeletal and cardiac muscles and the nervous tissues. Family studies suggest a simple autosomal recessive inheritance.[169] The condition is analagous to type-IV glycogen-storage disease of people.

Glycogenesis is thought to be a heritable disease of cats.[142] No genetic studies have been made, however. The initial affected individual was described as "a young, apparently healthy cat." The absence of clinical signs was thought to be due to accumulation of glycogen that had not yet reached a critical level. The glycogen-glucose content of the gray matter of the brain and spinal cord of the affected cat was about 6 times greater than normal. The cytoplasm of both nerve and glial cells contained large numbers of spherical glycogen-loaded bodies. The overall clinical appearance closely resembles Pompe's disease, which is a recessive inherited glycogen storage anomaly of people.

Neuroaxonal Dystrophy

Neuroaxonal dystrophy is a progressive axon dystrophy mediated by a recessive gene nd. The disease is likened to infantile neuroaxonal dystrophy in human infants and may be a useful animal model.[166] Affected cats have a light grayish coat color similar to that of the lilac phenotype. Defective kittens behave normally for the first few weeks of life but then develop progressive ataxia. Nodding of the head progresses to shaking by 5-6 weeks of age. The gait becomes uncoordinated several weeks later. Ataxic individuals overreach with their paws and have poor or no placing ability. A slow pupillary reflex indicates impaired vision. The inner ear shows marked depletion and abnormal neurons in the spiral ganglia.

The most prominent lesion in the brain is ballooning of the nerve cell processes in the superior lamina of the inferior olivary and lateral cuneate nuclei. The nucleus ventralis lateralis and ventralis anterioralis of the thalamus and cerebellar vermis are affected to a lesser extent. The swollen axons have a fine granular quality, with an occasional dark center. There is neural loss and increased glialization. Loss of Purkinje cells and depopulation of the granular cell layer occur in the cerebellar vermis.

Spheroid Lysosomal Disease

Kittens with spheroid lysosomal disease are normal until about 8-12 weeks of age, when a tremor develops and progresses to head nodding and body swaying.[86] Locomotion is slow, with ataxia, dysmetria and falling. The sense of direction also is disturbed. Handling precipitates seizures of short duration. The appetite is normal but feeding habits are clumsy. The anomaly is due to an autosomal recessive gene (sl).[10]

Neuronal lesions are present throughout the brain, particularly in the frontal cortex,

medial geniculate body, superior colliculi, caudate, dentate, cuneate and ambiguous nuclei, and cerebellum. The cervical spinal cord is less severely affected. The most striking lesion is numerous spheroid bodies. These are inapparent in the frontal cortex but prominent in the corpus callosum, brainstem and cerebellar white matter. The spheroid bodies are presumed to be swollen myelin sheaths. The lymph nodes and spleen contain large vacuolated macrophages. This may be a lysosomal storage disease, though the accumulated substance has not been identified.[86]

Sphingomyelinosis

Three cases of sphingomyelinosis have been described.[162] Affected cats developed tremor, ataxia, posterior dysmetria, anorexia and loss of interest in surroundings beginning at 4-5 months of age. A higher-than-normal amount of GM2 and GM3 gangliosides were found in the brain, and a 9- to 10-fold increase of cholesterol and sphingomyelin in the liver of affected individuals. Tissue assays failed to detect sphingomyelinase activity. A study of 8 suspected heterozygotes revealed 5 with one-half normal levels of sphingomyelinase activity. Though the deleterious gene (sp) could be regarded as a recessive based upon clinical phenotype, it behaves as a semi-dominant or codominant at the biochemical level. The anomaly is very similar to Niemann-Pick's disease in people.

Tremor

This nervous disorder is manifested as a continuous whole-body tremor in kittens 2-4 weeks of age.[117] The trunk and head roll and bob in an undulating manner, while the tail weaves in circles. Shaking abates when the animal is at rest or when it is held very firmly. Affected kittens continue to tremble even when suspended by the neck. The gait is normal except for some stumbling on rough surfaces. Swimming ability is slightly impaired. Electroencephalograms of one kitten revealed significant seizure-like activity. Affected individuals grow less quickly than normal and may be less viable. No gross histologic changes in the cerebellum can be detected.

Hydrocephalus

Most cases of hydrocephalus arise as isolated events and probably constitute mishaps of embryonic development. Nevertheless, a series of affected animals in a partially inbred strain of Siamese cats indicated a simple monogenic recessive inheritance (hy) of the trait.[148] Affected kittens were stillborn, hydrocephalic and often bloated, with edema of the limbs.

Globoid Leukodystrophy

Early signs of this disease are weakness and incoordination of the hind limbs beginning at 5-6 weeks of age.[77] The condition becomes steadily worse and the dysmetria may spread to the forelimbs. A tremor is present. Affected kittens are usually euthanized at an early age before the disease has run its full course. The cerebellum is apparently normal, but the white matter of the brain has a dull color with extensive loss of axons and myelin. Globoid cells are distributed throughout the more severely affected areas. Evidence favoring a genetic basis for the anomaly is weak. A similar disease is inherited as a recessive trait in dogs and people.[77]

Hyperchylomicronemia

Kittens with hyperchylomicronemia (hce) exhibit normal growth but have persistent lipemia.[5,79-81] At about 8-9 months of age, the animal develops signs of peripheral nerve paralysis. Both the cranial and cervical nerves are affected. There may be absence of the corneal reflex, inability to chew food, absence of the patellar reflex and inability to extend the digits. The major clinical feature of the anomaly is disseminated, often multiple nodular granulomas and hematomas in many tissues. These lesions appear to compress the peripheral nerves, especially at sites where the nerves are subject to injury. There is some evidence of axonal degeneration and loss of myelinated fibers. Individuals fed a high-fat diet had more pronounced lipemia and more severe neuronal signs. A low-fat diet diminishes the level of lipemia and reverses clinical signs. The condition is inherited as a recessive, with the proposed symbol hce for the causative gene.

Thiamin Deficiency

A group of enzyme deficiencies in people causes a relative or absolute deficiency of thiamin (vitamin B_1). The Wernicke-Korsakoff syndrome is a neurologic disorder seen mainly in alcoholics and other people on vitamin-deficient diets. People with the defect (abnormal transketolase enzyme) have a relative deficiency and are clinically normal when eating diets containing recommended levels of thiamin but show clinical signs when eating diets containing inadequate amounts of the vitamin.

A thiamin-responsive neurologic disorder has been recognized as an autosomal recessive defect in Burmese kittens.[102] The kittens were normal until 4-10 months of age, when they developed episodes of hind limb ataxia, forelimb rigidity, hopping gait, hypermetria, protrusion of the claws, pupillary dilation, muscle tremors, head-nodding, weakness and convulsions. Attacks appeared to be precipitated by fish diets or stress. A poor to good response, depending on the individual, was seen after thiamin supplementation (100-500 mg/day). An autosomal recessive disorder of domestic short-haired kittens was clinically and histopathologically similar to Leigh's disease (subacute sclerosing encephalomyelopathy) in people.[68] Affected kittens developed progressively worsening intention tremors and undulating body movements when they began to walk and died at 10-12 weeks of age of convulsions. The kittens had elevated serum pyruvate and lactate levels, indicating a pyruvate carboxylase or thiamin triphosphate catalyzing enzyme deficiency.

Hematologic Disorders of Genetic Origin

Chediak-Higashi Syndrome

There is a remarkable transspecies similarity of Chediak-Higashi syndrome (CHS) for various species in which the anomaly has been described (cattle, mice, mink, people).[22] In all of these species and in cats, the anomaly is caused by a recessive gene ch.

The Chediak-Higashi syndrome is characterized by a varied spectrum of signs. The coat color is lighter than normal due to massive coalescence of the pigment granules in both the medulla and cortex of the hair. The color has been termed "blue-smoke," which is said to be lighter than the normal blue-smoke. The pigmentation of the eye is reduced. The iris is paler than normal, being light yellow, yellow-green or greenish. A reddish fundic reflection is apparent, instead of the usual bright yellowish-green. The tapetum is mostly depigmented or absent. Consequently, affected cats are photophobic. Fine nystagmus is evident. Most affected animals have cataracts of varying severity.[122,123]

Affected cats have large intracytoplasmic abnormal granules of different sizes in the WBC of bone marrow and blood. The bleeding time is prolonged after minor surgery and small hematomas frequently form at the site of venipuncture. This may be due to a defect of platelet function. Affected cats may be more susceptible to infectious disease (as in other species with CHS), but this has yet to be demonstrated.[85]

Cats with CHS have misrouting of the optic fibers similar to that observed in Siamese and albino cats. The anomalous condition is less severe than that observed in albino animals, though this could have been due to the fact that the CHS cats examined were more pigmented specimens.[30]

Pelger-Huët Anomaly

This anomaly is manifested as hyposegmentation of nuclei of circulating granulocytes.[87,161] Erythrocytes, lymphocytes and platelets appear normal. There is a small decrease in lobation of nuclei of megakaryocytes of bone marrow. The Pelger-Huët anomaly probably arises from a defect in nuclear segmentation or lobation of hematopoietic stem cells.[87] Breeding data are consistent with monogenic dominant inheritance (Ph). The condition is often benign, though chemotactic function of neutrophils and *in-vitro* immunologic responsiveness is depressed.

Neutrophil Granulation

The cytoplasm of normal feline neutrophils has a pale, indistinct granular appearance after staining with eosin dye. However, individuals have been observed in which the cytoplasm contained fine eosino-

philic granules. This granulation could have resulted from a qualitative difference in the enzyme content of normal granules or the presence of abnormal granules (probably lysosomal). Cats with these unusual neutrophils are not clinically sick. The condition is inherited as a recessive trait (ng) to normal cytoplasm.[69]

Hageman Factor Deficiency

A deficiency of blood clotting factor XII (Hageman Factor) results in a prolonged thromoboplastin time. Cats homozygous for factor XII deficiency have only 1-2% of normal factor XII activity in their plasma, while heterozygotes had an average of 64%. The disease is caused by an incompletely dominant gene (hag). The trait is usually regarded as recessive, however, because heterozygotes are not clinically normal.[55,84]

Hemophilia A

Hemophilia is characterized by hematoma formation and prolonged bleeding following injury or surgery. Bleeding results from failure of one of the steps in the complex process of blood clotting. A common form of hemophilia is designated as hemophilia A. The condition is monogenically inherited and sex-linked; the locus for the responsible gene is carried by the X chromosome. Typically, only males are affected. If the deficiency is pronounced, males may not survive to breeding age.

Cats with a marked deficiency of clotting factor VIII, indicative of hemophilia A, have been described.[28] No breeding results were given, but all 3 affected cats were males. The manifested signs are typical of the disease in people. Hemorrhaging is less severe following minor trauma in comparison with that shown by affected dogs, however.

Hemophilia B

A family of cats deficient in blood clotting factor IX has been described.[40,41] The deficiency gives rise to hemophilia B, which is characterized by spontaneous and protracted bleeding following injury or surgery. Clinical signs are milder than those of hemophilia A.

von Willebrand's Disease

A bleeding disorder compatible with von Willebrand's disease in people and other animals was identified in a 9-year-old Himalayan.[50] The cat did not manifest bleeding problems earlier in life and related cats had no history of similar problems. The condition in people and other animals is inherited as an autosomal recessive or dominant trait associated with decreases in factor VIII-von Willebrand's protein and problems with platelet aggregates.

Porphyria

Hemoglobin, the principal oxygen-carrying protein in RBC, is synthesized from heme and globin. Defects in heme synthesis or degradation result in accumulation of precursor molecules, mainly uroporphyrin I and coproporphyrin I. These precursor molecules are deposited in large amounts in various tissues and secreted in great amounts in the urine. Uroporphyrin and coproporphyrin are colored compounds that impart a brownish discoloration to the teeth and bones of affected individuals and a brown to red discoloration of urine. Urine, bone and teeth fluoresce red under ultraviolet light (Fig 18).

At least 2 different genetic defects in heme biosynthesis have been recognized in cats.[37,52-54,153] The disease in domestic cats is associated with teeth and urine discoloration, mild anemia and increased numbers of refractile bodies in RBC. Otherwise, the animals are not clinically ill. This type of porphyria is inherited as an autosomal re-

Figure 18. Siamese cat with the dominant form of porphyria. When illuminated with a Wood's lamp, the teeth glow intensely under fluorescent lighting because of porphyrin pigment. (Courtesy of Dr. M. Haskins, University of Pennsylvania)

cessive trait (po). There is a reduction of porphobilinogen deaminase activity to about half of normal in RBC and liver.[37] This type of enzyme deficiency is similar to that described for hepatic porphyria in people.

Porphyria of a different type has been described in Siamese cats.[37] Affected animals had a similar discoloration of teeth, bones and urine but were ill with depression, listlessness and severe hypochromic anemia, with abnormally shaped RBC (anisocytosis, poikilocytosis, target cells, nucleated RBC). Pedigree analysis of this trait was consistent with an autosomal dominant or recessive inheritance. More thorough biochemical and genetic analyses are required to define the differences in these 2 types of porphyria in cats.

Aplastic Anemia

A delayed-onset form of aplastic anemia has been observed in some bloodlines of Japanese Bobtail cats. Affected kittens are normal until 6 months of age or so, and then develop progressive myelofibrosis and pancytopenia over the next few months. The genetic basis for the disorder has not yet been determined.

Genetic Disorders of Miscellaneous Organs

Patent Ductus Arteriosus

A higher incidence of patent ductus arteriosus in the Siamese breed suggests a genetic basis.[146] Patent ductus arteriosus results from failed closure of the fetal vascular bypass between the aorta and pulmonary artery. It can lead to heart failure later in life.

Primary Endocardial Fibroelastosis

Endocardial fibroelastosis is an anomaly observed in Siamese and Burmese cats.[58,117] The disease appears to be heritable in the Burmese but its genetic basis in Siamese is not known.[118,167] Abnormal lymphatic drainage from the heart is thought to cause chronic endocardial edema.[167] The inheritance pattern suggests a dominant trait, though further research on the exact genetic basis is needed.[167] It appears to be almost identical to a similar genetic disease of human infants.[167]

Clinical signs attributable to cardiac failure are seen at 3-16 weeks of age. Sudden death with few preceding signs is the most common presentation. Difficult respiration, open-mouth breathing and cyanosis may be noticed near the time of death in some animals. The left side of the heart, including the atrium and ventricle, are greatly enlarged. Fluid may accumulate in the thoracic cavity as the heart begins to fail. Marked heart enlargement is seen on radiographs and at necropsy. The endocardium is gray to white because of increased amounts of elastic tissue. Similar lesions occur with viral myocarditis, fetal anoxia, nutritional cardiomyopathy (taurine deficiency) and congenital vascular defects of the heart, so a thorough clinical workup is always in order before diagnosing the primary or heritable form of the disease.

Esophageal Achalasia

The muscles of the esophagus normally propel food to the stomach. If the cardiac sphincter fails to relax, food cannot pass easily into the stomach and the esophagus becomes dilated with ingesta. This leads to regurgitation of food. At other times there is unproductive retching. Achalasia has been observed in a group of cats with common ancestry, at the typical ratio for assortment of a recessive gene. Unfortunately, the data are insufficient to firmly establish the mode of inheritance.[21]

Polycystic Kidneys

Polycystic kidney disease (PKD) is manifested as multiple cysts in the renal cortex and/or medulla. Cysts may range from microscopic size to several centimeters in diameter. PKD in man can be acquired, developmental or heritable; this seems to be also true for cats.

A heritable form of PKD has been described in both mixed-breed and purebred cats.[32,170] The Persian breed is particularly affected. The mode of inheritance in people is autosomal recessive or autosomal dominant. Clinical features of PKD in cats resemble those of the autosomal dominant form of PKD in people.[170]

PKD may be asymptomatic for life, or may manifest itself as chronic renal failure. Most clinically affected cats show anorexia, weight loss, depression, vomiting, polyuria and polydipsia at 3-10 years of age. In addition to signs of renal failure, affected cats often have enlarged kidneys, with cystic structures apparent upon ultrasonography.

Pyloric Stenosis

Persistent and sometimes violent vomiting can be a sign of pyloric stenosis.[121] The condition can be relieved by pyloroplasty or pyloromyotomy. Seven of the affected cats described belonged to a related family of Siamese cats, which suggests a genetic propensity. The pedigree data were inadequate to establish the mode of inheritance.[121]

Renal Amyloidosis

This disease is particularly prevalent in Abyssinian cats and the closely related Somali. It has also been recognized in several other breeds. Affected animals are often young adults <6 years of age. A few cats ≥10 years have also died from the disease, however. They display chronic weight loss, dehydration, gingivitis and a rough coat. The kidneys are firm but smaller and paler than normal. There is a slight to severe pitting of the renal capsule and linear banding of fibrosis extending into the minor medulla. The renal lesions are characterized histologically by amyloid deposition, papillary necrosis and interstitial fibrosis. The amyloid deposits may be overlooked because of their weak staining properties. The familial incidence of the disease suggests genetic involvement, but breeding data are too fragmented to define the mode of inheritance. The genetic basis of the defect appears to be complex.

Umbilical Hernia

Umbilical hernia has a low but persistent incidence in kittens and adolescent cats. There is good evidence of a genetic basis for the anomaly.[134] This was first shown in a strain of Abyssinian cats.[67] The incidence among offspring rises sharply when one parent is herniated. The most compelling evidence was obtained from a partially inbred strain of Cornish Rex, in which the incidence approximated monogenic proportions. Unfortunately, breeding data were inadequate for genetic characterization. The most likely explanation is that the defect has a polygenic threshold character.[139]

Urolithiasis

A familial tendency toward urolithiasis has been interpreted as a genetic liability for the disease.[95] Such observations are of interest in alerting a keen observer to the possibility. Details given in reports are inadequate to establish the mode of inheritance, however.

Sex Chromosome Aberrations

Tortoiseshell Males

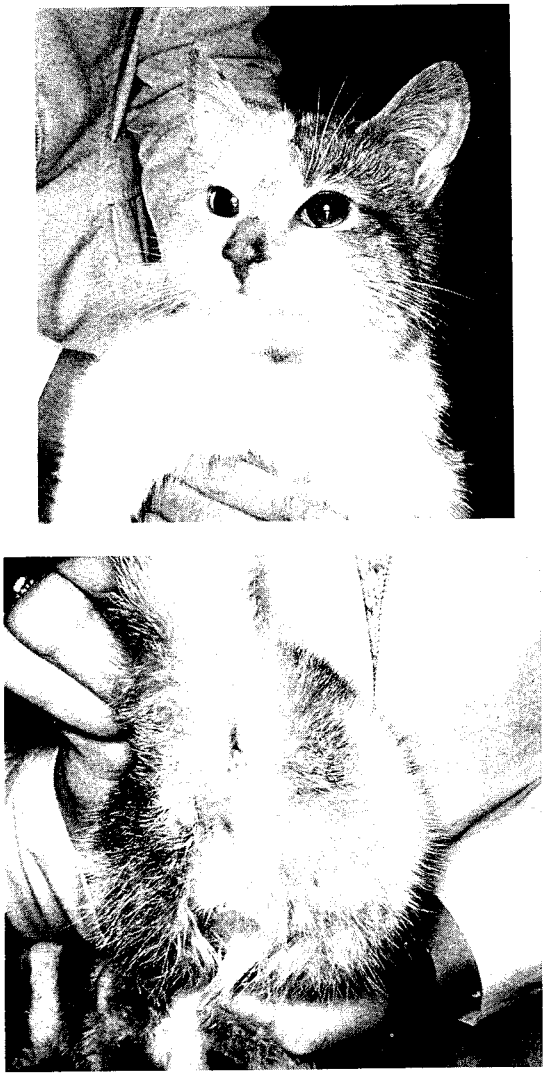
The black and yellow brindle or patchwork pattern of the tortoiseshell should only occur in female cats. Tortoiseshell male cats occur at a low frequency (1 in 3000), however (Fig 19). In most cases, tortoiseshell males have an anomalous chromosome constitution.[16,108,138] Most are sterile. A type of tortoiseshell male is fertile, however.

The O gene is carried by the X chromosome and the tortoiseshell pattern is produced by the heterozygote $\underline{O}o$. In the somatic tissues of the female cat, one of the X chromosomes becomes inactivated or nonfunctional. In fetal development, some somatic cells have one X chromosome inactivated and other cells have the other X chromosome inactivated. Descendants of these 2 different types of cells always have the same X chromosome inactivated as their ancestors. The effect of this differential inactivation would not normally be observed, but it is manifested in the tortoiseshell because of O and o genes on different X chromosomes. Those dermic cells in which the X chromosome carrying the O gene is functional produce red or orange hair, while dermic cells in which the X chromosome carrying the o gene is functional produce black hairs. The mechanics of embryonic cell growth, as well as its vicissitudes, result in the mosaic pattern of the tortoiseshell.

Therefore, the basic requirement for tortoiseshell pattern is the presence of 2 X

chromosomes in somatic tissue, one carrying the Q gene and the other the q; differential inactivation of the X gives rise to the pattern. It is possible to have anomalous sex chromosome constitutions and a male phenotype as a result of nondisjunction of chromosomes, fusion of polar bodies or double fertilization. One fairly common type is the 39,XXY ("Klinefelter"), in which an extra X has been gained.[125] The normal male cat has a 38,XY karyotype. The male-inducing influence of the Y produces a male and the 2 Xs are differentially inactivated. If one of the Xs carries gene Q and the other gene q, the phenotype is a male tortoiseshell.

Figure 19. A male tortoiseshell cat. The cat had the appearance of a female (top), but had typical (though atrophic) male genitalia (bottom).



The more common 39,XXY genotype above does not exhaust the possibilities for tortoiseshell males. These males have also been found with the following combinations of sex chromosomes in their cells: 38,XX/38,XY; 38XY/38,XY; 38,XY/39,XXY; 38,XX/39,XXY; 38,XX/57XXY; 38XY/57,XXY; 38XY/39XXY/40,XXY; 38,XX/38,XY/39XXY/40XXY and other more complex consitutions.[18,20,98,103] Such animals exhibit genetic mosaicism. Some of their cells carry the XX genes, while others have the XY or XXY genes with normal or excessive numbers of somatic chromosomes. These individuals are male but are usually sterile. Their testes are small and flaccid, and spermatogenesis is arrested at an early stage.

Fertile male tortoiseshell cats can sometimes arise from XX, XY mosaicism. If the cells forming the testes are derived from the normal XY karyotype, normal spermatozoa containing the haploid X or Y chromosomes can be formed. The situation would be analogous to the X chromosome mosaicism discussed next. Fertile tortoiseshell males can also be engendered by somatic mutation (occurring after fertilization in the early embryo) of q to Q or Q to q. Some of the cells would contain the X^{o} and others the X^{Q} chromosome; X^{Q}-bearing cells would express the orange color, while X^{q} cells would not. There is *prima facie* evidence for the occurrence of such individuals.[138] Significantly, these tortoiseshell males are fertile because chromosomally they have a "normal" XY karyotype.

The tortoiseshell male is of more than genetic interest in the United States. Like the elusive "pot of gold at the end of the rainbow," rumors have persisted that a tortoiseshell male cat is of great value to the finder. Veterinarians in private practice and in academic institutions are frequently contacted by owners of such cats attempting to "collect their reward." Such people should be gently advised of the rarity of their find but not of its value, which is no greater than for a normal cat.

XO Sterility

The normal female cat has 2 X chromosomes (38,XX). It is possible for one of the

parent cats to lose one of the X chromosomes during development of the gametes. Fertilization of a normal sex cell by an X-deficient gamete would result in an XO genotype. These cats are rare and only a few cases have been reported.[78,116] The XO cat is typically female but may be undersized and sterile. Such animals are likely to come to the attention of veterinarians because of persistent anestrus. Hormone treatment to induce estrus is likely to be unsuccessful. The XO condition can only be determined by examination of the chromosome complement of suspected XO females.

In the normal female cat of constitution XX, one of the X chromosomes becomes inactivated or does not function in the somatic cells shortly after birth. The reason probably resides in the necessity to "equalize" the influence of the X in relation to the autosomes between the sexes. Both the female and male cats have the same number of autosomes but the male has only one X. Hence, to produce the same "balance" between the X chromosome and the autosomes in the female, one of the 2 X chromosomes is inactivated.

An identical result would be achieved if one of the X chromosomes were lost during embryonic development. In other words, the XO female can survive even if the normal growth rate and viability are reduced, as shown by XO females of other species. On the other hand, the XX constitution is essential for maintaining normal ovarian development and function. The ovary of a 3-day-old XO kitten was histologically normal, whereas the ovary of an adult was small and lacked Graafian follicles and primordial germ cells.[78]

X-Chromosome Mosaicism

Two pregnant cats with unilateral ovarian dysgenesis (at ovariohysterectomy) had an X-chromosome mosaicism.[152] Both cats had 3 populations of cells, one containing only 37 chromosomes (missing one X chromosome) (37,X), one containing 38 chromosomes (both X chromosomes present) (38,XX) and one containing 39 chromosomes (3 X chromosomes) (39,XXX). The abnormal ovaries were apparently derived from cells with 37 (X) or 39 (XXX) chromosomes, while the normal ovary was derived from cells with the normal 38 (XX) karyotype. The fetuses had normal sex chromosome complements, apparently because they were derived from ova produced by the normal ovary.

Polyploidy of Autosomal Chromosomes

An obviously stunted and macerated feline fetus removed from a late gestation queen had 39 chromosomes.[7] The extra chromosome was due to trisomy of autosome D_2.

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DEVELOPMENTAL ANOMALIES

Normal Development

Developmental anomalies are caused by abnormalities in maturation of the embryo or any time from the one-cell stage to the full-term fetus. They can have a genetic or nongenetic basis. This section is concerned mainly with developmental anomalies that are either nongenetic in origin or of undetermined etiology.

To understand developmental anomalies, it is important to have basic knowledge of embryogenesis. Embryogenesis in domestic cats begins with the fertilized egg, a single cell about 0.1 mm (4/1000 inch) in diameter and ends 9-10 weeks later with birth of a kitten. After the egg is fertilized in the fallopian tubes, it migrates slowly to the uterus, where it attaches 0-12 days later. The fetus is composed of 250 cells at this point in development and is called a blastocyst. The blastocyst is a hollow ball, with the cells that will form the embryo clustered at one end of the ball. The remaining cells contact the wall of the uterus and form the placenta. The placenta serves both as a source of anchorage and nutrition. Nutrients and oxygen are transported from the maternal blood, across the wall of the uterus, and through the placenta to the developing embryo. Nutrition of the embryo during the early stages is mainly by diffusion, but as the embryo and placenta grow, a network of blood vessels develops both in the placenta and fetus.

Embryogenesis occurs from the 12th through 24th day of gestation. It is during this stage of life that the primitive organs begin to form. Gastrulation is the first event that occurs in embryogenesis. The group of cells that will become the embryo form a structure (gastrula) that resembles a deflated ball collapsed into itself. The wall of the gastrula is made up of 3 concentric layers of cells. The outermost layer is the ectoderm, the middle layer the mesoderm, and the inner layer the entoderm. The ectoderm will become the skin and epidermal tissues (nails, hair, glands of skin), nervous system, organs of sense, and lining membranes of the mouth and anus. The mesoderm eventually forms bone, cartilage, muscles, connective tissues, blood and blood vessels, lymphatic vessels and lymphoid organs (immune system), lining of the thoracic cavity (pleura), heart sac (pericardium), and abdomen (peritoneum), and the epithelial cells of the kidney and sex organs. The entoderm forms the linings of the pharynx, respiratory tract (except for the nose), digestive tract, and urinary bladder and urethra.

The neurula stage follows gastrulation. The neurula resembles a tube that is open along its long axis. The site where the 2 sides of the tube join will become the primitive nervous system and vertebral column. The heart begins to form during this stage, as do blood vessels within the embryo and placenta.

Neurulation is rapidly followed by a period when the primitive organs are formed. The primitive organs are well defined by 24 days of gestation in the cat. The fetus is about 1/2 inch long at this stage and is readily palpable (within its amniotic sac) in the abdomen of the dam.

Fetal growth continues from day 24 of gestation to term at 9-10 weeks. The various organs continue to develop during this period. This development occurs within the framework of the relatively primitive organ anlagen (organ precursors) delineated earlier during neurulation and organogenesis. For example, the renal glomeruli, tubules

and renal pelvis must develop within the anlagen of the kidney. This development must coincide with formation of adjacent blood vessels and lymphatics. The glomeruli must come into a proper relationship with the renal tubules, the renal tubules with the larger urine collecting ducts, and the collecting ducts with the renal pelvis. Various regions of the renal tubules must differentiate from other regions; some for control of electrolyte (salt) excretion and resorption, others for control of water retention and loss, and some for transport of filtered urine out of the kidney. Eventually the renal pelvis must be connected to the bladder by the urethra, and the bladder to the outside of the body by the urethra. Similar types of differentiation occur in all of the organs.

The formation of an individual organ or appendage involves 4 basic steps: growth, morphogenesis, cytodifferentiation and patterning. Growth involves cell replication and a commitment of a group of progeny cells to proceed along a certain course, such as formation of a limb, eye, ear, etc. Morphogenesis is creation of a rudimentary organ or appendage at the proper place within the developing fetus and at the proper time. Cytodifferentiation involves stepwise differentiation of the cells within the organ or appendage primordia. In the case of a developing limb, some groups of cells form bone or muscle, and others, tendons, nerves, skin, etc. Patterning refers to the ultimate end product. If it is a limb, it must mirror the opposite limb in size, position and growth rate. Not only is the limb patterned after its opposite, it is a limb patterned after every cat limb ever formed.

The fetal period ends with birth, but development continues for some time afterward. The fetus must be prepared for birth and an existence physiologically independent of its dam. For this purpose, the cardiovascular, respiratory, digestive and renal systems must become fully functional at the moment of birth or within minutes thereafter. The nervous, immune and reproductive systems, however, are still developing at birth. This development is not complete for weeks or months.

The preceding description of development of a feline fetus does not reflect the complexities of embryogenesis. Embryogenesis involves 2 basic processes: congregation of the cells that will eventually form a particular tissue or organ; and a stepwise differentiation of those cells from a primitive form to a highly specific functional state. Groups of cells are brought together by: evagination (infolding) or exvagination (folding outward) of the primitive blastocyst, gastrula or neurula; in-pouching or out-pouching of groups of cells within the tubular structure of the embryo; and migration of cells or groups of cells from one position in the embryo to another. Cell differentiation occurs through activation and deactivation of various genes and their protein products. These proteins serve as chemical signals. Adjacent cells and tissues interact with each other through chemical signals carried between cells. For instance, one group of cells may be altered in their differentiation when another group of cells contacts them. The interchange of chemical signals between the 2 groups of cells causes old chemical signals to be suppressed and new ones activated. The new concert of chemical signals causes the cells to embark upon new pathways of differentiation.

Given the complexity of embryogenesis, it is understandable that errors occur from time to time. Errors occurring very early in embryogenesis usually lead to fetal death, and abortion or resorption of the embryo. Such errors are seldom witnessed, therefore. Most fetal anomalies resulting in death of the embryo occur during gastrulation. Anomalies observed in full-term fetuses occur later in embryonic development. If the malformations are too great, the fetus cannot make the transition from a dependent to independent existence and dies within minutes or hours of birth. For instance, if the heart is malformed but the effects of the malformation can be circumvented by maternal attachments, the fetus survives in the womb but dies after birth. Malformations that lead to death at or near the time of birth are of limited importance. Malformations that are not immediately life threatening are far more important. Such malformations may be manifested weeks, months or years after birth. At this point, the kitten has established its own identity. Because this identity is often intermeshed with its human benefactor, the malformation is of medical importance. The nature of the malformation must be determined, and

a correction instigated by medical or surgical means, if possible.

Factors that lead to abnormalities in fetal development can be either intrinsic or extrinsic to the fetus. Intrinsic factors are usually of genetic origin; abnormal genes coding for abnormal types or amounts of proteins. If these proteins are important for cell differentiation, genetic defects result. Extrinsic factors usually affect the fetus through the dam. Drugs taken during pregnancy may cross the placenta and reach the fetus. If the drugs disrupt normal fetal development, anomalies may be induced. Such drugs are called teratogens. Radiation can also cause congenital anomalies, usually through chromosomal breakage that leads to gene anomalies. Cats, like all other life forms on earth, are exposed continually to small doses of radiation. Diagnostic radiation (radiographs) should be avoided during pregnancy. Infectious agents, particularly viruses, can also act as teratogens.

The effects of teratogenic drugs are often highly selective, both on the types of embryonic structures they affect and in the period during which they act. For instance, griseofulvin, a common drug used to treat ringworm, causes cleft palates if administered during pregnancy.[119] For such malformations to occur, the drug or its residue must be present in the fetal tissues during the crucial period when the palate is forming. Hydroxyurea, diphenylhydantoin, amaranth and mercury compounds have also been studied as teratogens in cats.[65-67] Their effect is usually seen 24-32 days after conception. Panleukopenia virus can infect the fetus via the placenta. It can cause an almost selective destruction of the Purkinje cell layer of the cerebellum during the last trimester of pregnancy. Affected kittens appear grossly normal at birth but have a peculiar gait (exaggerated or jerking movement of limbs, head, and body) when they begin to walk.

Many developmental anomalies have no demonstrable cause, some have specific causes, and others can be caused by several different factors. For instance, cleft palate can have a genetic basis or can be induced by drugs. Cerebellar hypoplasia in kittens is almost always caused by *in-utero* feline panleukopenia virus infection.[68-70] Several forms of cerebellar hypoplasia in people and other animals, however, are genetic. Though a few developmental anomalies have predictable causes, most occur for no apparent reasons (idiopathic). A few developmental anomalies are linked to certain breed or coat color characteristics. Breeds with greatly foreshortened faces may have a higher incidence of palate and skull anomalies than breeds with normal faces.[94] The foreshortened facial structure of certain cat breeds is influenced by the activities of many genes (polygenic traits). Because of the large numbers of genes involved in some traits, it may be very difficult to determine whether a given anomaly is genetic or nongenetic in origin.

Abnormal Development

About 5% of the patients seen by veterinarians in North America have various congenital defects.[103] The highest incidence was reported in swine and the lowest in cats. Multiple anomalies are seen in 1 in 20 of animals with developmental defects.[103]

Musculoskeletal Anomalies

Musculoskeletal deformities are by far the most common developmental problems in cats and other species. They often occur because of failures in closure of primitive tube-like structures in the embryo.

Schistosoma is a lethal developmental anomaly characterized by fissure of the abdomen and a lack, or rudimentary development, of the posterior extremities. Two kittens with such a defect had severe visceral herniation through an abdominal fissure and malformed posterior extremities.[114] One also had an associated cleft palate.

Failure of proper closure of the primitive neural tube can lead to a number of different defects at any point from the head to the tail. A *meningocele* is herniation of the meninges through a defect in the skull or vertebral column. A kitten with a cerebral meningocele has been described.[42] If it is relatively minor, and no other developmental anomalies are present in the brain, it can be potentially corrected. The one reported case, however, also had agenesis of the corpus callosum, septum pellucidum and hippocampal commissure.

Exencephaly is one of the most common congenital deformities observed among stillborn kittens.[33,138] It is a combination of defects about the face and head, including a dorsal opening of the skull with protruding meninges or brain, bulging eyes, and often a cleft palate. Exencephaly has also been associated with other embryonic tubular defects, such as *craniorachischisis, scoliosis* of the spine and *schistosomia reflexus*.[123,138]

Spinal dysraphism involves failure of closure of the part of the neural tube that forms the vertebral canal. A kitten with thoracolumbar spinal dysraphism was born alive but had no control over its deformed hind limbs.[114] A milder form of abnormal closure of the bony spinal canal, called *spina bifida*, has been described in a large number of kittens (Fig 20).[35,36,59,73,78,91] The disorder is most common in the lumbar spine. The closure defect is sometimes associated with protrusion of the spinal cord or meninges, and/or spinal cord dysplasia. The anomaly is most common in Manx cats, which have a genetic anomaly of the spinal cord. Affected kittens may be clinically normal, or have various degrees of posterior ataxia and gait anomalies. Fecal and urinary incontinence may also be a problem due to dysplasia of the lumbosacral spine.

Vertebral body anomalies are common in cats and usually of no clinical significance.[81] Most are detected on routine radiography. The most common vertebral body anomaly involves the presence of a fourteenth thoracic, or transition, vertebra. Incomplete or fused vertebrae can also be found throughout the spine, but most are concentrated in the thoracic and coccygeal spine. Vertebral anomalies of the coccygeal spine often lead to a *kinked tail*.[19] The kinked tail anomaly may have a genetic basis. A cat with no tail, sacral vertebral anomalies, and spina bifida has been reported.[35]

A 3-year-old cat with multiple skeletal defects of the skull bones, vertebral column and scapula has been described.[136] The cat had foreshortened temporal occipital and parietal bones, fused cervical vertebrae, a malformed thoracolumbar intermediate vertebra, a fused lumbosacral transitional vertebra, and an abnormal scapula.

Anomalies of the limbs are also common in domestic cats. *Amelia* is the complete lack of limbs. This rare defect has been described only once in cats.[19] An anomaly characterized by arrested development of the bones of the forelimbs has been described.[134] These so-called "*kangaroo cats*" have a characteristic appearance (Fig 13). The defect usually appears in females and may be genetic (see section on genetic disorders). *Peromelus ascelus* is an anomaly caused by agenesis of the hind limbs (Fig 21). The one case reported in the cat was nonlethal.[117] *Ectrodactyly*, an improper formation of all or part of a digit, has been described as a possibly heritable defect of the forepaw of the domestic cat.[117] *Syndactyly* is fusion of the digits. The defect is rare but has been reported in a cat.[50] *Polydactyly* is the presence of extra digits, most frequently on the forepaw. It is one of the most common genetic defects of cats (see section on genetic disorders). *Radial hemimelia*, caused by agenesis of the radius, has been described in a cat.[79] *Arthrogryposis* is a congenital fibrous ankylosis (fusion) of the

Figure 21. Peromelus ascelus (lack of hind legs) in a neonatal kitten.[117] (Courtesy of Dr. G. Schneck and Veterinary Medicine Publishing)

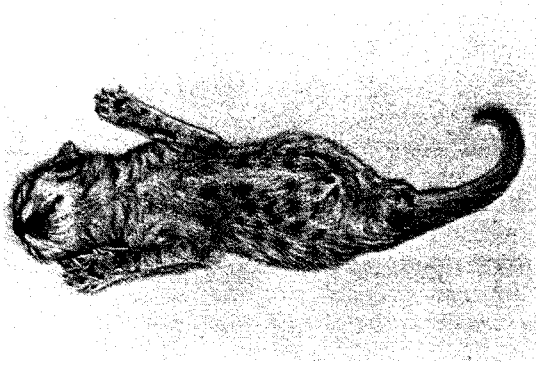
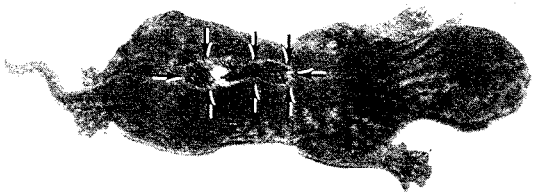


Figure 20. Kitten with spina bifida and rachischisis.[36] The hind legs are contracted. The area of spina bifida is outlined by arrows. (Courtesy of Dr. F. Frye and *Journal of the American Veterinary Medical Association*)



points of the extremities. This condition affected all 4 legs of a 2-month-old kitten.[114]

Harelip results from failed closure of the embryonic tube that forms the midline of the skull, in particular the upper lip. The defect can also involve a cleft between the nasal and oral cavities (involving the upper lip in the process), or a cleft between the upper lip and hard palate.

Cleft palate, sometimes with clefting into the nasal or oral cavity, is one of the most common defects of cats (Fig 14).[19,84,85] The incidence of the disorder increases with inbreeding, suggesting a strong genetic influence. A genetic form of the disease has been described in Siamese.[84,85] Some drugs, such as griseofulvin, have also been incriminated in the disorder.[119] Severely affected kittens have problems nursing, and commonly aspirate milk into the lungs. Surgical correction is difficult in animals this small.

Cleft soft palate is rare in cats. The throat of affected cats has a bird-like or gullet appearance (birds have a naturally cleft soft palate). The problem usually goes unnoticed for the first few months of life. The usual presenting complaint is a chronic nasal infection, due mainly to reflux of food from the oral to nasal cavity. Owners may notice the cat sneezing after eating or drinking. Food may sometimes be observed in the nasal discharge during such bouts.

Pectus excavatum is one of the more common and manageable musculoskeletal anomalies of cats.[8,41,121] Affected kittens are born with a flattened chest and pelvis. Their legs are held to the side rather than beneath the trunk, and they often move by "swimming motions" of their limbs; hence the nickname "swimmer kittens." The developmental basis for swimmer kittens is unknown. It appears to increase in frequency with inbreeding, and some queens may produce several kittens with the disorder. There is other circumstantial evidence, however, that the condition might also result from extrinsic factors, such as drugs or diet. Compression of the heart can be life-threatening in severely affected kittens. Kittens with severe chest compression can be treated with traction sutures and casts, but older cats may need surgical reconstruction.[8,121] Mildly affected kittens often grow out of the condition. As they begin to use their legs more, they learn to adjust and to keep their legs under their trunk. Though they may retain a degree of chest flattening when they are older, they function otherwise in a normal manner.

Excessive *dishing of the face*, referred to as "peke face" because of its similarity to the Pekingese dog, has been described in some long-haired Persian cats.[19] It is probably an exaggerated genetic expression of the polygenes and their modifiers that are normally associated with face structure in the breed. The "Peke face" has been bred into some American Persians and is considered normal.

Aplasia of the ramus of the mandible, associated with an anomalous ossification center, has been described in a cat with micrognathia (undershot lower jaw).[57]

Anomalies of the teeth are common in cats. In addition to developmental anomalies of the jaw that lead to overbite or underbite, several distinct anomalies have been observed. *Malpositioned canine teeth* is one such problem. The lower canines strike against the upper gum as they become full grown. This causes pain on eating and sores in the upper gums where the tips of the canines penetrate the flesh. The canines must be filed down or removed. *Adontia*, the complete absence of teeth, has been reported in one cat.[32] *Enamel hypoplasia*, either partial or complete, has been recognized in a number of cats. The underlying dentine is exposed, resulting in rough, brown, teeth. Dental caries are a problem in such animals. The affected teeth may be covered by reddened inflammatory tissue extending from the gingiva. Enamel hypoplasia does not begin in the fetus because formation of enamel occurs after birth. High fevers, drugs and unknown factors in some way affect formation of enamel in the developing tooth bud.

Some defects are associated with abnormal twinning. *Diprosopus*, the presence of 2 faces, has been described in cats (Fig 22).[2,11,23] The defect is usually lethal within a day or so. *Posterior twinning* due to fusion of the hindquarters of one twin to the body of the other, has been described in cats (Fig 23).[2,98,106,131] A *small extra pair of ears* on each side of the head has been reported in one cat, where it was thought to be a ge-

netic recessive defect. A "*reversed cat*" has been described at necropsy.[135] All internal organs that were normally on the right were on the left, and vice versa. The animal may have been one of a pair of identical twins.

Hernias of soft tissue structures may be either developmental or acquired. *Umbilical hernias* involve a defect in the body wall where the umbilical vessels enter the fetus.[43,51,54] If the defect is large enough, portions of the omentum and omental fat protrude to form a characteristic dome-shaped enlargement beneath the skin surrounding the umbilical vessels. In some cases, herniation may be into a remnant of the allantoic sac. If the defect is larger, viscera may also enter the hernial sac. The condition may have a genetic basis in some animals.[51] It is also a common acquired anomaly. If the queen fails to sever the umbilical cord, the newborn may drag the attached placenta and tear the body wall.[54] The problem is particularly acute when the queen fails to cut the umbilical cords of all of the kittens in a litter. The kittens become intertwined by their umbilical cords. As they become more and more entwined, they end up attached together by the base of their umbilical cords. Herniations of the viscera, strangulation of limbs and umbilical hernias are common in such situations. Though this is an acquired condition, it has been mistakingly described as a developmental *anomaly of the umbilical cord* in at least one report.[88]

Figure 22. Kitten with diprosopus (double face) as a result of abnormal twinning.[11] (Courtesy of Dr. T. Bissonette and *Journal of Heredity*)

Figure 23. Posterior twinning in a feline fetus.[106] (Courtesy of Dr. A. Reese and *Anatomy Record*)

A congenital abdominal fissure with partial evisceration has been described in a kitten.[114] A littermate with the same defect also had a thoracic fissure, schistosomus reflexus and cleft palate.

Inguinal hernias involve weakness in the development of the inguinal canal, through which blood vessels, nerves, lymphatics and the descending testes pass. It has been reported as a developmental anomaly in cats.[49] These hernias are usually quite small and involve mainly serosa, serosal fat and rarely abdominal viscera.

Diaphragmatic hernias are also developmental or acquired. A genetic form involving simple recessive inheritance has been proposed. It has been reported in as many as 1 in 500 births. Acquired diaphragmatic hernias usually involve trauma, though predisposing developmental weakness might exist in many cases.[3,4,17,19,37,58,64,77] Some involve communications between the abdominal and pleural cavities, usually involving the pericardial sac (pericardial-diaphragmatic hernias) (Fig 24).[104] The liver and intestines are often present in the chest or pericardial sac. These cats usually have

problems breathing or may suffer from cardiac tamponade and heart failure or vague gastrointestinal signs. *Hiatal hernias,* involving weakness in the diaphragm where the esophagus enters the stomach, have also been recognized in cats. If the hiatal hernia is large enough, it causes sliding of the gastric cardia into the thoracic cavity. The problem is clinically significant when gastric juices reflux into the esophagus. Reflux of stomach contents leads to esophagitis and persistent vomiting or regurgitation.

Neural and Ocular Anomalies

Congenital defects of the central nervous system and eyes are second in frequency only to those of the musculoskeletal system. *Cerebellar hypoplasia* is probably the most common developmental problem of the central nervous system of cats.[18,26,74,115,118] It is caused in most cases by fetal infection with feline panleukopenia virus.[68-70,75] Queens subclinically infected with the virus during the last trimester of gestation are most apt to produce kittens with this disorder. The virus selectively destroys the Purkinje cell layer of the cerebellum. Affected kittens are born with a small atrophic cerebellum (Fig 25). They appear normal until they begin to walk. Since the cerebellum is important for proprioception (spatial movements), these kittens appear uncoordinated when they begin to walk. They often have a characteristic hypermetria (exaggerated flexion and extension) of the limbs and head while moving. The kittens are otherwise normal, and make good pets. As they get older, they learn to function with their deficiencies but never achieve any degree of normal gait and proprioception.

Hydrocephalus, or "water on the brain," is caused by dilation of the ventricles of the brain with cerebrospinal fluid. The basic defect is inability to transport cerebrospinal fluid from the ventricles to the meningeal spaces and bloodstream. Kittens with hydrocephalus are born with larger-than-normal skulls and open fontanelles (soft spot on the head where the bones of the skull come together). Progressive digitation of the ventricles leads to pressure atrophy of the overlying cerebral cortex. Mildly af-

Figure 24. Lateral radiograph of a cat with a peritoneopericardial diaphragmatic hernia.[3] Barium is seen within intestinal loops in the pericardial sac. (Courtesy of Dr. C. Atkins and *Journal of the American Veterinary Medical Association*)

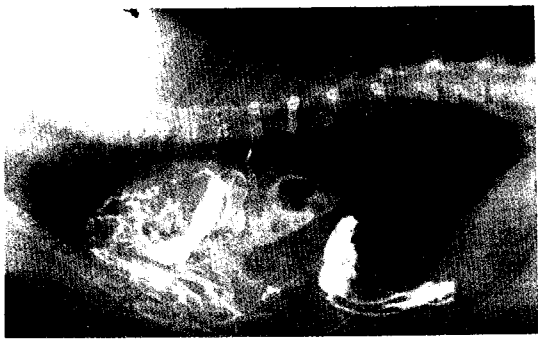
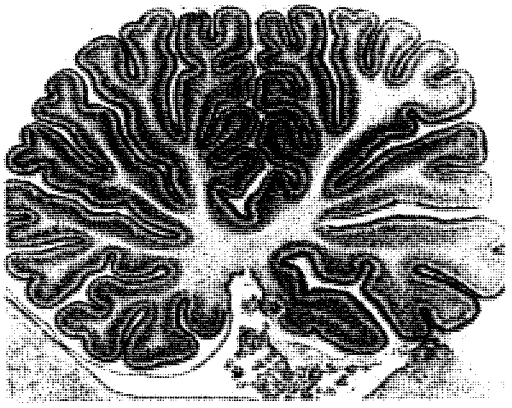


Figure 25. Top: Cross section of the cerebellum of a 14-day-old ferret that was inoculated on the first day of life with inactivated panleukopenia virus.[69] The cerebellum appears grossly and histologically normal. This is in contrast to the cerebellum of a 14-day-old ferret inoculated on the first day of life with virulent feline panleukopenia virus (bottom). The cerebellum of the affected ferret is extremely atrophic, the external germinal layer has been effaced, and the definitive granular layer has not developed. (Courtesy of Dr. L. Killam and *Journal of the American Veterinary Medical Association*))



fected kittens lack normal intelligence, manifested by a decreased response to external stimuli. More often than not, however, the condition is lethal within the first few weeks of life. The condition is possibly heritable in Siamese cats. It has been also associated with other defects, such as cleft palate, harelip, talipes (foot deformity) or generalized edema.[19,58,122]

Aplasia of the corpus callosum, leading to chronic epileptic-type seizures, has been described in a cat.[52]

Cyclopia is associated with midline fusion of developing eyes. Cyclopian kittens, therefore, have one large deformed centrally positioned eye. It is often associated with other defects of the skull and adjacent skin.[29,31] The condition is inevitably fatal.

Microphthalmia is a condition in which the eyes are inordinately small. It has been reported once in a cat but is not an uncommon defect.[19] It is often associated with enophthalmia, cataracts or other ocular anomalies.[99]

Cataracts are opacities of the lens. They are often associated with other ocular anomalies in kittens, such as microphthalmia, persistent pupillary membranes, and persistent hyaloid blood vessels.[99]

Ectopic lenses are rare in kittens.[1,19] They usually result from posterior or anterior luxation of the lens associated with incomplete development of the suspensory ligaments or zonular fibers. They can be associated with *microphakia* (small lens). The luxated lens often becomes cataractous and causes glaucoma if not removed.

Dermoids are vestigial growths of epithelium (containing hair, sebaceous glands and pigment) that are often found on the sclera next to the limbus. They sometimes extend out onto the cornea. If they do not cause corneal irritation and infection, they can be left alone. Excision is necessary when they cause problems.

Glaucoma is an enlargement of the globe due to excessive accumulations of aqueous humor and consequent increased intraocular pressure. It is usually associated with defects in the specialized structures in the base of the iris that drain the aqueous humor produced by the ciliary body. The defect is relatively rare in kittens.[19,102]

Keratoconus refers to a cone-like enlargement of the cornea when viewed from the side. The central cornea is often thin and opaque.[21] *Microcornea* occurs when the anterior cornea is too small. *Megalocornea* is a wide, flattened cornea.[19]

In *lagophthalmia*, the eyelids do not quite meet. This leads to dryness of the central cornea. Since tears are essential for maintenance of corneal hydration and defense against infections, the condition often leads to keratitis and central corneal ulcers that are difficult to treat. The condition is especially common in breeds with foreshortened faces.

Corneal opacities or *dystrophies* are not uncommon in kittens. They often result from bands of persistent pupillary membrane that adhere to the inner surfaces of the cornea, or to stromal edema of unknown etiology.[19,96]

Persistent tearing associated with abnormal nasolacrimal drainage is usually caused by anomalies of the lacrimal lake or nasolacrimal duct between the eye and nose. A defect in the lacrimal lake (pouch formed by the lids, adjacent to the nasolacrimal punctum) is a problem in breeds with foreshortened faces and lagophthalmia. Tears do not normally pool over the nasolacrimal puncta, thus impeding their flow into the nasolacrimal ducts. Rather the tears spill over the lower eyelids. Excessive tearing can also be caused by *atresia of the nasolacrimal puncta* (openings into the nasolacrimal ducts). The puncta are present on the medial surfaces of both the upper and lower lids. In all of these conditions, affected kittens show persistent tearing, discoloration of the hairs around the eyes, and sometimes secondary infectious conjunctivitis.

Colobomas are circular developmental anomalies in the eyelid, iris, choroid or optic nerve. These developmental anomalies often occur together to varying degrees. Colobomatous defects of the eyelids are often associated with iridal anomalies, while choroidal defects are often associated with retinal, scleral and optic nerve anomalies.

Anomalies of the eyelids, though common in puppies, are rare in kittens. Agenesis of the outer half of one or both upper eyelids has been described.[7,111] Most of these cats had strands of persistent pupillary mem-

brane extending from the iris to the posterior surface of the cornea. Notching defects of the iris, enlargement of the optic discs, scleral ectasia and choroidal hypoplasia are colobomatous defects of the posterior aspect of the eye.[7] *Entropion* is abnormal infolding of the upper or lower eyelids, while *ectropion* refers to outfolding. Both of these anomalies are rare in cats, though entropion may be common in some Persians..

Retinal degenerations can be heritable or acquired. The most common degeneration of the latter type is associated with diets low in taurine. Kittens born to taurine-deficient queens have cardiomyopathy and degeneration of the retina. Retinal lesions are characterized ophthalmoscopically by central areas of hyperlucidity and hyperreflexia (increased reflection of light).

Thoracic Organ Anomalies

The heart is formed early in embryogenesis by a complex series of events. It is not surprising, therefore, that there should be a number of developmental anomalies of the cardiovascular system. *Ventricular septal defects* are particulary common in cats.[80,90,120] The resultant hole between the 2 major chambers of the heart is usually quite large and most affected kittens die of heart failure before weaning. *Atrial septal defects* are uncommon in cats.[80,120] If large enough, they also can lead to heart failure early in life.

Neonatal endocardial fibroelastosis is a common anomaly of young purebred kittens.[14,30] Affected animals have cardiac dilation, with endocardial thickening and fibrosis. They usually die of heart failure within the first few weeks or months of life. There is good evidence that the disease is the same as dilative cardiomyopathy in older cats, and that it occurs when queens and kittens are fed a diet deficient in the amino acid taurine.[111]

Patent ductus arteriosus results from failure of the ductus arteriosus to close at birth. The ductus arteriosus is an embryonic communication that shunts blood from the pulmonary artery to the aorta, thus bypassing the uninflated, nonfunctional embryonic lungs. The shunt normally closes at birth when the lungs expand with air. Failure of the ductus arteriosus to close leads to excessive shunting of blood from the high-pressure aortic side to the lower-pressure pulmonary artery side (left-to-right shunt). Cats with patent ductus arteriosus are relatively common. The condition has a possible genetic basis.[24,80,120] Affected animals usually reach adulthood, and some may live long lives. Others, however, eventually develop heart failure.

Aortic stenosis is a relatively common anomaly of cats.[82,120,130] It consists of narrowing of the aortic valve or aortic outflow tract. The stenosis can be either supravalvular or subvalvular. Most affected cats survive to adolescence or into adulthood. If the stenosis is severe, however, heart failure ultimately develops.

Pulmonic stenosis is much less common in cats than aortic stenosis.[120,127,133] It involves narrowing of the pulmonary artery at the level of the pulmonary valve or a subvalvular narrowing. It has also been described in combination with an *aorticopulmonary septal defect.*[133] It may lead to heart failure later in life.

Tricuspid stenosis with an associated atrial septal defect and right ventricular hypoplasia has been described in a young cat.[86] The kitten was in heart failure, and the disorder was confirmed by angiocardiography.

Transposition of the great arteries has been observed in a healthy 4-month-old kitten with a heart murmur.[126] In this condition, the aorta originates dorsal to the right ventricle and the pulmonary artery dorsal to the left ventricle on the opposite side of the ventricular septum. This leads to a patent ductus arteriosus and a ventricular septal defect.

Dextroposition of the aorta (displacement of the aorta to the right) so that it overlies the right ventricle is a rare defect of unknown developmental etiology.[80] The only recorded feline case was detected at necropsy. The animal also had deformities in the ventricular septa and malformed atria. A *common truncus arteriosus* has been described in cats.[16,80] Cats with this anomaly have a common trunk for the aorta, coronary arteries and pulmonary artery that arises from a defect in the ventricular septum. Like dextroposition of the aorta, the condition is rapidly fatal.

A *persistent common atrioventricular canal* has been described in cats.[83] This involves a defect in the atrial and ventricular septa, with anomalous atrioventricular valves. Affected cats die at a relatively young age from heart failure. A multiple anomaly analogous to the *Taussig-Bing complex* in people has been described in a cat.[46] The animal had a ventricular septal defect, dextroposition of the aorta, an overriding pulmonary artery with left displacement, and pulmonic stenosis. The condition was rapidly fatal. A developmental anomaly analogous to the *tetralogy of Fallot* in people has also been described in several cats.[15,17,72] The defect consists of ventricular septal defect, pulmonary stenosis, dextroposition of the aorta, and right ventricular hypertrophy. Affected animals survive for some weeks or months in a state of ill health and ultimately succumb of heart failure. Similar *multiple heart defects* have been described.[27,100] These are basically combinations of the various defects discussed above. Affected kittens are stunted in growth and succumb to heart failure within several weeks or months.

Hypoplasia of the pulmonary trunk has been described.[80] In extreme cases, the animals are dyspneic almost from birth, and die at a young age. Some animals may survive into adolescence or adulthood.

Congenital unilateral *absence of a right pulmonary artery* was observed in a 2-year-old Siamese cat with acute dyspnea and edema of the left lung lobes.[48] At necropsy, the right lung lobes were one-fourth normal size and the right pulmonary artery was absent. Two small anomalous arteries passed from the aorta to the parenchyma of the right caudal lung lobes. The left ventricle was thickened.

Arteriovenous fistulas occur when large arteries connect directly to veins without an intervening capillary bed. If they are large, oxygenated blood is shunted away from the tissues and a larger workload is placed on the heart. A 5-month-old Persian kitten with respiratory difficulty and swelling in the neck had an anomalous internal brachial arteriovenous intercommunication.[92]

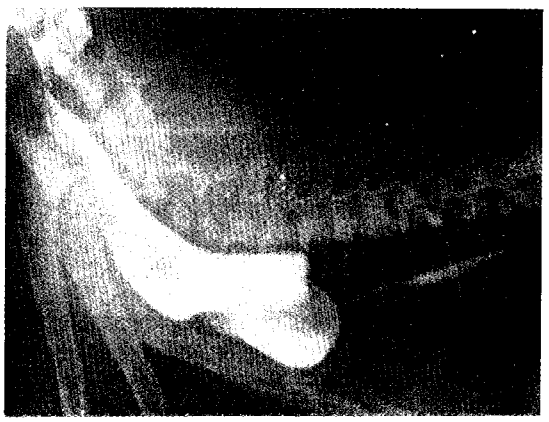
Persistence of the embryonic right aortic arch has been described in cats.[29,47,60,105,110,129] The condition does not involve the circulatory system *per se*. The persistent embryonic right aortic arch encircles the esophagus as it passes over the heart. Clinical signs result from stricture of the esophagus and dilation proximal to the stricture (Fig 26). It usually causes regurgitation of food soon after eating. The defect is visible upon barium administration. The dilated proximal portion of the esophagus often contains a hairball.

Cor triatriatum has been described in a 6-month-old female kitten that died of congestive heart failure.[38] In cor triatriatum, the pulmonary veins enter an accessory left atrium. The true left atrium and the accessory atrium connect through a narrow opening, thus obstructing pulmonary venous return.

Esophageal achalasia or megaesophagus is caused by failure of the esophageal-cardiac sphincter to relax upon presentation of a bolus of food (Fig 27). It is an uncommon defect in cats and thought to have a possible genetic basis.[20-23] The main clinical sign is regurgitation shortly after eating. Numbers of esophageal myenteric ganglia are similar in affected and unaffected cats, suggesting that the defect is different from esophageal achalasia of puppies.[21]

Aneurysm of the septum membranaceum has been recognized in a young cat at necropsy.[80] The aneurysm extended under the cusps of the tricuspid valve.

Figure 26. Persistent right aortic arch in a kitten causes accumulation of barium in the cranial esophagus.[47] Abrupt termination of the enlarged esophagus at the base of the heart is typical of persistent right aortic arch. (Courtesy of Dr. J. Hathaway and *Journal of the American Veterinary Medical Association*)



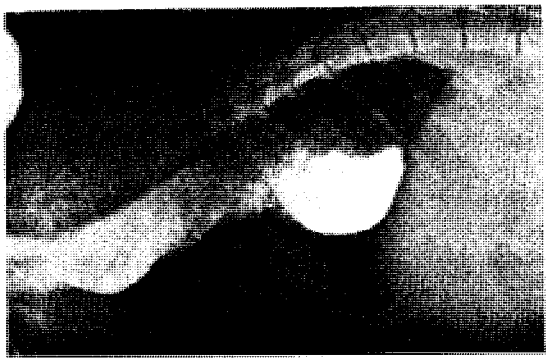
Anomalies of the lung are relatively rare. *Agenesis* of the *right or left lung lobes* has been recognized in cats.[114] The condition is usually asymptomatic and recognized at radiography for other conditions. The heart is characteristically shifted to the side of the missing lung lobes.

Abdominal Organ Anomalies

There are several specific developmental anomalies of the kidneys of cats. The presence of a *single kidney*, usually the left, is a common developmental anomaly in cats, with an incidence at necropsy of 2 in 1000 animals.[12,56,87,89,93,108] The single left kidney is usually larger than normal because of compensatory hypertrophy. The condition is usually asymptomatic and detected upon routine abdominal palpation for other conditions.[87,109] The right kidney is either missing entirely or small and misshapen.[12,87,107] Absence of the uterus and fallopian tube may be seen in female cats with agenic right kidneys.[53,89,108,112]

Renal ectopia is the congenital malposition of one or both kidneys; it is often associated with fusion of the developing kidneys.[56,61,87] The incidence in cats is about 5 in 1000 animals.[62] It occurs more often in male cats than females, and is usually an incidental finding at necropsy or upon clinical workup for renal disease.[87] Kidneys can sometimes be displaced to the pelvic region.[12,62] In one cat, an ectopic kidney was found embedded in the liver.[87] The displaced kidney is often subject to hydronephrosis, pyelonephritis and calculus formation.

Figure 27. Lateral radiograph of a cat with esophageal dilation caused by congenital esophageal achalasia.[23] Unlike the cat in Figure 26, the esophageal dilation extended from the thoracic inlet to the stomach. (Courtesy of Dr. D. Clifford and *JAVMA*)



Fusion of the 2 kidneys, usually at their caudal poles (*horseshoe kidneys*), is commonly recognized in cats.[12,62,87,125] The kidneys are often joined by a thin fibrous cord or a narrow band of renal tissue, giving the kidneys a horseshoe appearance. In some cases, the bridging tissue is much more substantial, forming a *unilateral fused kidney*.[12]

Polycystic kidney anomalies are common in cats.[5,12,25,95] Such kidneys contain a few, or many, small pea-sized cysts. The condition involves malformation of the tubules and can lead to renal failure from progressive fibrosis. The condition may be heritable.[25,87] It has been associated with cystic changes in the liver and pancreas.

Perirenal hygroma, or *perinephric pseudocyst*, is a common developmental anomaly of cats. It is usually clinically silent, and is incidentally detected either through palpation or radiography of the abdomen.[71] In this condition, there is marked accumulation of lymph-like material beneath the renal capsule, leading to renomegaly. The anomaly probably involves intercommunication of abnormal lymphatics with the pericapsular space. Excision of the pseudocapsule has been attempted. This should be avoided if possible, however, because it can lead to ascites in some cases.

Ureteral anomalies of cats resemble those described for people and other animals.[6,10,34,39,87,107,113,124] *Ureteral ectopia* is a condition in which one or both ureters do not enter the urinary bladder at the normal place. Unilateral and bilateral ureteral ectopia occurs at about equal frequency in cats. Females are more commonly affected than males, and most cases are diagnosed before the cats reach 6 months of age.[87] The most common place of termination is into the urethra; vaginal termination is much less frequent. Urinary incontinence, usually evident at 2-6 months of age, is the most frequent presenting complaint.[87] Perineal urine scalding and dermatitis are also prominent. In some cats, urinary incontinence is not the presenting sign. Urine chronically pools in the vagina or urethra

and leads to bacterial cystitis. The major presenting signs in such cats are dysuria, pollakiuria and hematuria. Cats with ectopic ureters and presented only for signs of urinary tract infection tend to be older (6-72 months) at the time of presentation than cats with urinary incontinence.[87] Hydroureter and hydronephrosis are frequent complications of ectopic ureters.[87] Unilateral renal hypoplasia and vulvar anomalies can accompany the ureteral defects in a small proportion of affected animals. Treatment for ectopic ureters is surgical. The abnormal ureters are transposed into the bladder or, in the case of unilateral ectopia, the affected kidney and ureter are removed. Surgical correction usually resolves the incontinence or infection.[87]

Anomalies of the bladder result from abnormal differentiation of the embryonic cloaca, usually resulting in connections between the bladder and colon, bladder and uterus, or *patent urachus*.[63,76,87] Connections between the colon and bladder, or uterus and bladder, usually result in urinary tract infections and associated signs. The urachus, an embryonic connection between the bladder and umbilical vessels, is used by the fetus to eliminate waste. The urachus closes at birth and atrophies. Kittens with a grossly patent urachus drip urine from the umbilical area.[44,116] In less severe cases, the intrabdominal urachus remains open but the umbilical connection closes. This leads to an intra-abdominal *diverticulum* off of the cranioventral pole of the bladder. If the diverticulum is sufficiently large and thin-walled, it can cause urine pooling in the bladder, increased incidence of urinary tract infections, and possibly enhanced incidence of struvite lithiasis.[40,97] Rupture of a diverticulum in a cat led to abdominal urine pooling and peritonitis.[44]

Urethral anomalies are rare in cats. An *ectopic urethra* opening entirely into the rectum has been described in one kitten.[87] The anomaly was also associated with atresia coli. A small *urethrorectal fistula* has been seen in an older cat.[132] The cat had pollakiuria, dysuria and hematuria resulting from a chronic urinary tract infection. *Urethral paralysis or malformation*, leading to urine incontinence, is frequently associated with severe caudal spinal deformities, especially in Manx kittens (see section on Manx defect).[55,87]

Developmental anomalies of the pancreas, liver, gallbladder and common bile ducts are relatively uncommon in cats. *Hepatic cysts* have been recognized in the liver, sometimes associated with polycystic renal disease or persistent urachus.[5] *Pancreatic cysts*, some >1 cm in diameter, have been observed incidentally at necropsy of older cats. It is uncertain whether they are present at birth or develop later. *Biliary atresia* has been recognized in several young cats manifesting poor growth and severe icterus. It involves the smaller intrahepatic biliary system and is usually fatal. *Persistent ductus venosus* is not uncommon.[9] The ductus venosus is a fetal shunt for portomesenteric blood to bypass the hepatic portal system. Failure of this shunt to close diverts venous blood from the intestine directly to the vena cava. This impairs liver development and greatly inhibits the ability to detoxify and process nutrients from the bowel. Affected cats usually have a single shunt between the liver, spleen or small intestine and the caudal vena cava, and manifest signs of periodic dementia, stupor, ataxia, excessive salivation, behavioral changes (hiding, aggression, crying, increased appetite, tail thumping) malaise and lethargy.[9] The shunt can be surgically closed.[9]

Congenital *agenesis of the small and large intestines* is a frequent finding in kittens dying during the first few days of life.[138] *Atresia ani* is a congenital stricture or absence of the anus.[138] Affected kittens may live for days to several weeks, though their growth is impaired and their abdomen is distended with feces-filled viscera.

Acute gastric rupture has been reported as a common cause of death in Abyssinian and Somali kittens. The kittens die within the first week or so of life, after a brief period of weakness and depression. At necropsy, the stomach is ruptured and the abdominal cavity filled with ingesta. The disorder may have a genetic basis.

Pyloric stenosis has been observed in a 6-day-old Persian kitten.[13] The kitten faded over a 4-day period and regurgitated milk from its nose as it nursed. At necropsy, the stomach was greatly dilated with ingesta and the pylorus was stenotic. The condition

may be heritable in some cats (see section on genetic disorders).

Megacolon in the cat is usually acquired (tail-pull injuries, aging) but also may be developmental. Most cats with the developmental form are Manx. Foreshortening of the caudal spine, even though it is not clinically manifested at birth or early adulthood, may be associated with progressive dilation of the colon later in life. This is due to a relative lack of colonic innervation at birth and eventual exhaustion of remaining nerves and plexi. Some non-Manx kittens may be born with *agenesis of the myenteric plexus* of the colon.[28,137] They suffer from malaise, chronic constipation and abdominal distension with hard feces. The condition can be corrected by surgical removal of the colon.

Persistent cloaca is a rare problem in kittens. In this condition, there is a common excretory orifice for both urine and feces. It usually involves atresia ani, with termination of the colon into the urethra. Because of the narrowness of the urethral opening, affected cats are usually severely constipated and clinically resemble cats with megacolon. Kittens with this defect have palpable masses of hard stool in the abdomen and grow more slowly than normal. If the musculature of the anal sphincter is still intact and can be identified, the colon can be transplanted to its normal site.

Reproductive System Anomalies

Cryptorchidism is the retention of one or both testicles at some point along their embryonic and postnatal migration from near the kidneys into the scrotum. Because it is probably genetic in origin, affected animals should not be used as breeders. Most retained testicles can be found in the inguinal canal, and this is the first place that should be surgically explored. If they are not found in this position, the abdominal cavity should be explored. The retained testicle is usually atrophic and does not produce normal sperm. It can produce male hormones, however, and cryptorchid cats can act like intact males. Cryptorchidism can be either genetic or nongenetic in etiology. In some cases, migration of the testicle may be delayed and the testicle will not reach the scrotum until the cat is 4-8 months of age. This can lead to problems between veterinarians and cat owners. If the veterinarian removes only the scrotal testicle, the cat may be presented again several months later for removal of a second testicle. *Monorchidism* refers to failure of one testicle to develop. *Microrchidism* refers to small testicles.

Ovarian hypoplasia is bilaterally small ovaries with incompletely formed follicles.[12] Unilateral ovarian hypoplasia is often associated with X-chromosome abnormalities and mosaicism (see section on genetic disorders). Several anomalies of the uterus of cats have been described. One or both uterine horns may be connected to the uterine body by a small band of connective tissue. The isolated uterine horn often becomes distended.[93] The uterine horns may be fused along part of their course or be unequal in length.[12,19] One uterine horn can be completely absent or present as only a thin fibrous cord, a condition called *uterus unicornis*.[12,19,108] Absence of a uterine horn can be associated with agenesis of the kidney on the same side.[89,108]

Hermaphroditism refers to the presence of both male and female gonadal tissue in the same animal. A cat with an internal ovary/testis and an external testis has been described.[45] *Pseudohermaphrodites* have gonads of one sex but external genitalia that call the actual sex into question. Such disorders are rare in cats.[12]

Developmental anomalies of the mammary glands are relatively uncommon in cats. *Polymastia*, the presence of extra mammary glands that are completely functional, has been described.[12] *Polythelia* refers to more than one teat on a gland; it is often associated with polymastia.[12] Abnormalities of the streak canals and cisterns have been described for cats.[12] These anomalies were associated with sebaceous-gland ducts opening into the streak canal, blind-ending of streak canals near the base of the teat, hairs associated with sebaceous glands that enter the lumen of the streak canal, and a common origin of 2 streak canals.

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BREEDING PROGRAMS

Creating a Breed

The objective of breeding purebred cats is to produce kittens that are vigorous, that consistently reproduce the characteristics of the breed from one generation to another, and that have all of the desirable traits put forward in the breed standard. Most purebred cats are based on combinations of certain coat characteristics, different coat colors and patterns, and various body conformations. These basic features are carefully molded together over many generations.

Many of the basic coat and body traits that constitute a breed started as mutations from the basic domestic cats. Since many of these mutations are rare, the first step in forming a breed usually involves breeding the offspring back to the mutant animal, or by mating the offspring to each other. To avoid concentrating undesirable homozygous alleles, these first breedings should involve as many animals as possible.

For instance, a rare mutation in the type and character of coat (*eg*, Rex) suddenly appears in a male kitten in one area of the world. This mutation is particularly appealing to people and an attempt is made to create a breed of cats based on this anomaly. The mutant male cat would usually be bred to a large number of normal-appearing female cats that are as genetically diverse as possible. If the desired genetic trait is recessive in nature, all of the offspring would carry the desired gene. The offspring would then be bred to each other. A certain percentage (1/4) of the offspring would be homozygous for the recessive gene and have the desired mutant phenotype. These second-generation offspring will breed true if

bred to other homozygous recessive animals. If there is a large pool of homozygotes to choose from, further inbreeding can be kept to a minimum. If the initial pool of homozygotes is small, and if continuous backcrossing to the original mutant is carried out, the number of different alleles at gene loci other than the mutant loci will be very small. Breeds started from a narrow genetic base may be inbred from the beginning and subsequent genetic manipulations will be extremely difficult. This difficulty arises from the limited assortment of alleles at all gene loci from which the breeder selects.

Assuming that the initial gene pool is as heterozygous as possible for all genes other than the ones required to give the breed its identity, the next step in breed evolution is creation of bloodlines. Bloodlines seldom arise from a joint consensus among all of the foundation breeders. If all of the breeders were in complete agreement as to how the breed should develop, the result would be one bloodline rather than many. Differences in perspective allow for many different bloodlines. Different perspectives are more apt to occur when various breeders are geographically or ethnically separated. A comparison between the same breed of cats in various countries of Europe, or between Europe and North America, yields more differences than a comparison of cats from the eastern and western United States. One breeder may favor a certain body conformation over another, while a second breeder might be more interested in certain coat characteristics or patterns. Bloodlines should evolve from the initial group of animals as early in breed creation as possible. The more phenotypic differences that eventually develop between bloodlines, the more genetic differences there will be between them. These phenotypic and genotypic differences allow for a tremendous amount of latitude in future breedings. Crosses between distantly related bloodlines will be more apt to result in offspring with extra vigor.

The success of a breed is determined by genetic manipulations done at its inception. Purebreds should begin from as wide a genetic base as possible. Diversity of opinions as to what the breed should look like are healthy and should be encouraged rather that suppressed. Show judges should also be allowed to develop some degree of differing opinions on what is an acceptable interpretation of written breed standards. A consensus among judges usually results in one thing; breeders select their stock for the same characteristics, resulting in extensive inbreeding and the discarding of phenotypically distinct bloodlines.

Breeding Practices

Four major breeding practices are used to develop and refine a pure breed of cats: close inbreeding, moderate inbreeding or linebreeding, linecrossing and crossbreeding.

Close Inbreeding

Close inbreeding involves mating individuals that are closely related to each other, such as matings of first cousin, mother to son, father to daughter, brother to sister, and offspring to grandparents.

Inbreeding is common, especially in the initial stages of breed development. Such inbreeding fixes the desired trait and increases the number of individuals that are phenotypically desirable. Inbreeding, however, leads to homozygosity. If inbreeding is done improperly, the resultant homozygosity also brings out deleterious traits, as well as desirable traits. To avoid buildup of deleterious genes, breeders must start with the widest possible genetic base and moderately inbreed as much as possible.

Linebreeding or Moderate Inbreeding

Linebreeding is breeding individuals within the same bloodline. A bloodline is a genetically and sometimes phenotypically distinct group of cats within a breed. Individuals within a bloodline differ from each other in most generations; common ancestors are only found far back in the early stages of the breed's formation.

Moderate inbreeding entails matings to more distant relatives than sons, daughters, mothers, fathers, cousins or grandparents.

The pedigree of a linebred kitten oftens show the same outstanding individuals on both maternal and paternal sides. Therefore, the percentage of kittens with allelic genes from those outstanding parents is high. If the bloodline is large and genetically diverse, this degree of inbreeding usually is

not deleterious. If the line is genetically close, however, linebreeding is equivalent to close inbreeding. That is to say, if the third cousins and great grandparents are as genetically homogenous as the individual's parents and first cousins, then it is somewhat presumptuous to believe that close inbreeding and linebreeding are any different. As it happens, linebreeding is popular among breeders of purebred cats. When linebred animals begin to lose vigor and reproductive capacity, the genetic diversity of the line has been essentially lost.

Linecrossing or Outcrossing Within a Breed

Linecrossing involves mating good breed examples of one bloodline with good breed examples from other more distantly related lines. It is the basis for creation of new bloodlines and should be the most widely conducted breeding practice. Ideal linecrossing involves selection of bloodlines that each have different strengths and weaknesses. The greater the phenotypic differences, the more genetically diverse are the blood lines. By mating individuals of 2 different bloodlines with complementing traits, a small proportion of their offspring have the good characteristics of each of the 2 lines without any of the bad. For instance, animals of one bloodline are known for their beautiful eyes, but have poor coats. Cats of another bloodline have good coat characteristics but poor eyes. When cats of the bloodlines are crossed, a small percentage of the offspring will have the desirable traits of both. Such individuals have a minimal genetic homozygosity for traits other than the ones being selected.

Good linecrossing requires thought and planning. It is also time consuming. Many breeders are unwilling or incapable of conducting sound programs that emphasize linecrossing. It is much easier, quicker, and ultimately cheaper to use inbreeding and linebreeding to obtain cats with the desired traits. Unfortunately, deleterious as well as desired genes are concentrated in the offspring, and the bloodline loses vigor.

Crossbreeding or Outcrossing To Another Breed

Crossbreeding is mating individuals from different breeds. Crossbreeding can be the basis of new breeds and is allowed in several established breeds. Animals with one or more desired traits are mated with animals having other desired traits. Crossbred animals are often more robust than either parent, a phenomenon known as hybrid vigor. The more phenotypically different the 2 breeds are, the more genotypically different they will be, and the more likely that hybrid vigor will be obtained. If the parental breeds are similar in many ways, as in conformation, head shape and coat color, both breeds are more genotypically similar and hybrid vigor in their offspring will be less noticeable.

Outcrossing To Nonpedigreed Cats

Outcrossing is sometimes used to increase the vigor of a breed. Nonpedigreed Japanese Bobtail cats have been imported to interbreed with pedigreed Japanese Bobtails in the United States. The British outcross their Cornish rex cats to domestic cats every third generation. This practice has assured the vigor of the breed.

Loss of Vigor

Intensive inbreeding within genetically homogenous blood lines ultimately leads to loss of vigor. This loss of vigor is usually manifested by decreased size at maturity, slowed growth, increased severity and duration of common infectious diseases, smaller litter sizes, increased neonatal deaths, and more developmental anomalies. The increased incidence of disease and lowered fecundity then impacts negatively on the breed's or bloodline's popularity.

Loss of genetic vigor within a breed or bloodline is often caused when breeders try to accentuate normal breed characteristics to the extremes of the breed standard. As an example, the face structure of some cats is abnormally flattened. Further attempts to shorten or widen the face beyond the current norms may increase developmental anomalies of the face, increase susceptibility to eye infections and decrease size. Some of these side effects occur because of anatomic factors (lagophthalmos, impaired tear drainage). Others arise from accumulation of associated deleterious modifier genes. Some flattening of the face can be brought about by minor genetic changes. Moderate

flattening of the face requires substantially more inbreeding, while severe flattening requires the activity of numerous genes. Accumulating enough modifying genes to bring about severe facial shortening requires a great amount of selection. If animals are selected and inbred to achieve one characteristic, it is almost certain that genetic diversity will be limited for other traits as well.

Genetic Anomalies

Progressive inbreeding could lead to a gradual decline in breed vigor. Before there is a total loss of vigor, however, the incidence of genetic anomalies may be a problem. Purebreeding, by its very nature, limits the number of possible alleles at each gene loci. The more homogenous the genetics of a bloodline or breed, the likelier it is to mate 2 individuals with similar deleterious genes. Genetic anomalies are generally of 4 types: simple autosomal recessive, simple autosomal dominant, polygenic, or sex-linked recessive. Examples of genetic defects that fit each of these categories have already been given.

Genetic anomalies are usually well established in a bloodline or breed by the time they are noticed. The mobility of people and their cats, and the notion that everyone must breed cats with the currently popular look, assures that the defects will be far flung. Genetic defects are more likely to be spread by males than females. Stud cats can sire hundreds of kittens within a year or less, while females can only produce a handful. It is not surprising, therefore, that many genetic defects can be traced ultimately to a male that was a great show winner several years before the appearance of the defect in the breed.

Eliminating Genetic Defects

What can a breeder do once a defect appears? The first, and most difficult step, is to get other breeders to recognize the existence of the defect and to work cooperatively to eliminate it. Second, the nature of the defect must be determined. Is it genetic, environmental or both? For example, cardiomyopathy occurs in both dietary and genetic forms. Before the importance of adequate levels of dietary taurine was understood, many catteries had tremendous losses from this disease. It was almost impossible, however, to get breeders to recognize the severity of the problem and to help in its elimination. Fortunately, the true cause of most cases of cardiomyopathy was discovered. The discovery did not come from any effort on the part of breeders, but rather from a serendipitous observation made by a cardiologist who noticed a relationship between cardiomyopathy and retinal lesions of the type previously described for cats fed taurine-deficient diets.

Nutritionally induced cardiomyopathy is not just a nutritional problem, however. Genetics may also play a role; most cats fed older taurine-deficient diets do not develop cardiomyopathy. This suggests that some cats differ in their dietary taurine requirements, or in the effects that low taurine levels have on the heart. It is not surprising, therefore, that cardiomyopathy was believed at one time to be largely a genetic disorder. Some breeds and bloodlines of cats develop feline infectious peritonitis (FIP) at a higher rate than others. Does this mean that FIP is a genetic disorder? No, FIP is caused by a virus. Genetic resistance factors play an important role in the disease, however. It is not always easy to determine whether any particular disorder is genetic or environmental.

Once a disorder is found to be of genetic origin, an effort must be mounted to eliminate it from the breed. The approach taken depends on what type of genetics are involved, that is, simple recessive, dominant, polygenic or sex-linked.

Theoretically, genetic defects caused by dominant genes should be the easiest to eliminate. Only affected individuals carry the genes, and these should be easy to recognize and remove from breeding. This is seldom the case, however. Most dominant genetic anomalies are caused by genes that are greatly influenced by modifier genes. Individuals with the abnormal gene are normal as long as certain modifier genes are not present. An example of such a situation is seen in the Burmese breed.[3] Massive lethal facial anomalies are thought to be caused by an autosomal dominant gene that is modified by a number of other genes. These modifying genes may be the same genes that were concentrated in the breed when the face structure was changed.[3]

Dominant traits of this type must be treated more as recessives.

Genetic anomalies associated with autosomal recessive genes will not be eliminated from a bloodline or breed merely by not breeding affected individuals. For every affected (homozygous recessive) individual, there are 2 heterozygous recessive cats. Because affected animals are usually not bred, the source of most affected cats is breedings between apparently healthy cats that carry one of the abnormal genes. Outbreeding also does not eliminate the problem. When a heterozygous carrier cat is bred to a distantly related animal (almost certainly a homozygous normal), half of their kittens will be carriers. This will not be the same carrier incidence obtained upon breeding 2 heterozygous affected animals, but the basic problem will not be resolved. Outbreeding yields no affected animals in the first generation, but thereafter the incidence is the same as before outbreeding.

There are only 2 proven means to eliminate a recessive gene from a breed or bloodline of cats. The first is to find a way to identify the apparently healthy carrier cats and eliminate them from breeding, and the second is test breeding. Rigorous selection of breeding cats is in some cases a more practical alternative and may gradually eliminate a genetic defect.

Identify Carriers: Identification of carriers is obviously the quickest, most effective and ultimately the cheapest means. Healthy heterozygous carrier cats, regardless of the trait, usually have some biologic abnormality. Female cats carrying the hemophilia gene have levels of factor VIII protein in their blood that are intermediate between those of homozygous normal and homozygous affected animals. The same is true for cats with the various storage diseases (mucopolysaccharidosis, lipid storage diseases). However, there are many recessive traits for which the genetic heterozygotic defect is unknown. If the precise defect is not known, there is currenty no way to devise tests for the detection of heterozygous carriers. Scientists have started to use DNA diagnostic technology to identify inherited diseases in cats. In the future this may allow screening of breeding cats with a blood test before mating.

Test Matings: Test matings involve breeding individuals with unknown genotypes with individuals of known genotype. The true genotype of the unknown individual is reflected by the phenotypes of the offspring. The fastest way to prove an animal is to breed it to an individual that is homozygous for the deleterious trait. If the healthy individual of the pair has one abnormal gene, half of their offspring are phenotypically abnormal. It does not take many kittens to determine whether an individual is free of the deleterious gene with such breedings. Unfortunately, homozygous affected individuals are often not healthy enough to breed. Most test matings involve, therefore, breeding healthy animals of unknown genotype to apparently healthy animals known to be heterozygous carriers of the deleterious gene in question.

Test matings are usually directed toward exonerating stud cats rather than queens. The reason for this is obvious. First, a stud cat is far more valuable and has a greater cumulative effect on good or bad traits in the breed or bloodline than a female. This is because the male can produce many more offspring. Second, it is easier and faster to prove a male because he can produce many more offspring in a brief time. Finally, if all affected animals are not bred and all stud cats are free of the abnormal gene, all kittens will be phenotypically normal regardless of the phenotype of the queens. For instance, given an anomaly of the normal X gene (x), all males will be XX and some females will be Xx and some XX. Regardless of which female the XX male is bred to, all of the kittens will be phenotypically normal (XX or Xx). None will be xx. Theoretically, a simple recessive genetic anomaly can be phenotypically eliminated from the breed by just making sure that all male cats are homozygous normal.

How many normal kittens must a male cat produce before it can be certified free of a simple recessive genetic defect? The answer depends on what type of female he is bred to and what degree of confidence (probability of error) is desired. It is preferable to breed the male to females known to carry the abnormal gene (homozygous or heterozygous). When such animals cannot be identified, the accepted practice is to breed the male to his daughters or siblings.

The daughters do not need to be from the same mothers. It is implicit that the male not be repeatedly bred to the same female. The progeny must be from as many different females as possible. The accepted level of confidence is 95%, that is, enough kittens are produced to lower the probability of the male's being a carrier to 5% or less. The minimum numbers of consecutively normal progeny required to certify a male free at the 5% level, using different types of matings, are listed in Table 1.

Some geneticists do not believe that a 5% possibility of error is acceptable, and advocate an error rate as low as 1%. To reduce the error to such a level, the number of consecutive normal kittens in an unknown male x heterozygous female mating would be 17 rather than 11.

The same type of test mating program must be carried out for sex-linked traits. Because most sex-linked traits are carried by the female, apparently normal females must be bred to apparently normal males. Apparently normal males are always homozygous normal in the case of sex-linked characteristics. Using the hemophilia gene (h) as an example, an X^HY male is bred to a carrier female X^HX^h. Half of the female offspring are homozygous normal and half are heterozygous carriers. Half of the males are normal and half are hemophiliacs. In such a breeding, the chances that the first male will be hemophiliac are 1 in 2 (1/2 or 50%) the chances that the next male will also be a hemophiliac are 1/2 x 1/2 (1/4 or 25%), the chances that the third male also will be hemophiliac are 1/2 x 1/2 x 1/2 = 1/8 (13%), the fourth 1/2 x 1/2 x 1/2 x 1/2 = 1/16 (6%), and the fifth 1/2 x 1/2 x 1/2 x 1/2 x 1/2 = 1/32 (3%). The chances that 5 consecutive males will be normal are, therefore, less than 5%.

Table 1. The number of consecutive normal offspring that must be produced by a normal-appearing male cat to certify him free of a given recessive genetic trait varies greatly with the genetic makeup of the females to which he was bred.

Matings	Number of Consecutively Normal Offspring
Male x homozygous affected female	5
Male x known heterozygous female	11
Male x apparently normal daughters	23
Male x full siblings (if one parent heterozygous)	23
Male x full siblings (if both parents heterozygous)	17
Male x full siblings (only if a common ancestor is heterozygous)	23

Test mating requires production of many kittens, most of which will be affected or carry the deleterious trait. It is necessary for breeders who undertake this method to ensure that all kittens produced are placed as pets to be altered. Moderate selection (eliminating affected cats from breeding) is rarely effective in ridding a breed of a genetic defect. However, rigorous selection (eliminating affected cats and the sire and dam) will in time be successful. In this case the gene pool of a breed may be seriously diminished, and expansion will be necessary through some type of outcrossing.

Elimination of polygenic traits is the most difficult. Test matings are impossible in such a situation due to the large number of genes involved and the infinite number of variables. A vigorous program of testing and elimination of affected individuals is the only course of action. Only the most severely affected are eliminated from breeding at the start. The phenotypic expression of the abnormality will become less severe and less frequent with time. If further reduction in the incidence of the anomaly is required, the emphasis of culling should be progressively changed to include fewer and fewer affected animals. The process of eliminating polygenic abnormalities can take many years or even decades. The trait will disappear from the breed or bloodline as slowly as it appeared.

The most difficult situation is eliminating polygenic anomalies that have a threshold effect. There are few gradations of the phenotypes; the offspring are normal or abnormal. In this situation, many of the apparently normal animals also carry the abnormal genes, and matings between normals may produce almost as many abnormal animals as matings between affected individuals. The only way to handle such a

situation is to vigorously cull all cats that have ever produced abnormal individuals.

Some genetic anomalies persist even in the face of control measures. The most common reason is relaxation of culling by breeders. This may be especially true when the incidence of certain anomalies begins to decrease and the problem is no longer perceived as serious. Emergence of a new champion male carrying the abnormal gene can trigger a new epidemic of mutants.

A second possible explanation for persistence of a defect is genetic linkage. The defect may be genetically linked to some breed characteristic, or paradoxically, some trait that is beneficial to health. The best examples of the former are found within such breeds as the Manx and Scottish Fold. Genes for these traits are lethal or sublethal but also are responsible for the desired phenotypic traits of taillessness and folded ears. Other deleterious genetic traits have been linked to coat color or skull conformation. Examples of the latter usually involve highly inbred lines of cats. Inbreeding usually leads to loss of vigor. In such a situation, the more homozygous (less vigorous) animals are culled and the heterozygous (more vigorous) animals are saved for breeding. Without doing anything about eliminating heterozygous animals that carry the deleterious genes, nothing much can be accomplished by culling. Offspring of heterozygous individuals tend to be healthy or sickly; the sickly ones are continuously culled and the healthy ones bred. This becomes a never-ending cycle.

Recommended Breeding Practices

A few general rules brought out in this discussion must be reemphasized:

Close inbreeding should only be reserved for creation of new breeds and fixing of certain genetic traits.

Linecrossing should be the basis of most matings. Linebreeding should only be done when the desired bloodline is large and genetically diverse. Optimal linecrossing or linebreeding should involve careful planning. This can usually be accomplished by selecting individuals with complementing weaknesses and strengths. A few offspring will have the complementary traits of both parents; these should be selected for show. If the mating involves individuals with all of the same phenotypic strengths, the likelihood that the parents are genotypically homogenous is high.

Breeders should become aware of what constitutes a different bloodline. Many breeders have no concept of what makes a bloodline. They believe that because Mrs. Jones has been breeding cats in California for many years, her cats are a different bloodline from Mrs. Smith's cats that have been bred for many years in New York. If 2 bloodlines are phenotypically similar, and have many of the same individuals in their pedigrees, they are not different bloodlines. Breeding Mrs. Smith's cats with Mrs. Jones' cats under this circumstance is not linecrossing, it is moderate inbreeding. If the lines are genetically very close, it can even be close inbreeding.

Breeders should work carefully to prevent emergence of genetic traits. Animals should be bred along correct genetic principles. Defects should be rapidly identified and eliminated. This may require a concerted effort among breeders. Overbreeding of certain toms should be discouraged. Toms that become very popular on the show circuit can be responsible for hundreds of kittens in a very short time. Given the fecundity of cats, thousands of cats directly related to certain toms can be produced within several years.

Do not breed for extremes in show standards. Fixing of extreme traits requires a great deal of inbreeding. Phenotypic selection of this magnitude can seldom be achieved without inbreeding at other genetic loci.

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Chapter 3

Reproduction and Reproductive Disorders

G.H. Stabenfeldt and N.C. Pedersen

NORMAL REPRODUCTION

Female Reproductive Physiology

Sexual Development

The onset of puberty in female domestic cats occurs at an average of 8-10 months.[50,79] However, it can occur as early as 4 months and as late as one year or more, depending on many different factors. The onset of puberty is most closely linked to growth rate and rarely occurs before the female cat reaches 5-6 lb. Cats that are well fed and fast growing reach maturity sooner than slower-growing animals. Growth rates are influenced by genetics, nutrition, intercurrent illnesses and social stresses. The onset of puberty may also be influenced by day length. Young female cats may be physically ready to enter estrus, but estrus is delayed several months because of the season of the year (short photoperiod) when adequate physical growth has been finally achieved. There also appears to be a great variation in the onset of puberty depending on breed. The consensus is that certain breeds, such as Persians and Abysinians, may come into estrus later (after 11-12 months of age) than such breeds as the Burmese (before 9 months).

Estrous Cycle

An estrous cycle consists of proestrus (1 day), estrus (5-6 days), and interestrus (8-9 days).[92] *Proestrus* is the period during which the queen shows sexual activity without allowing penile insertion by the male, though mounting may be allowed. Signs of proestrus usually occur in conjunction with the first day of the follicle growth phase.

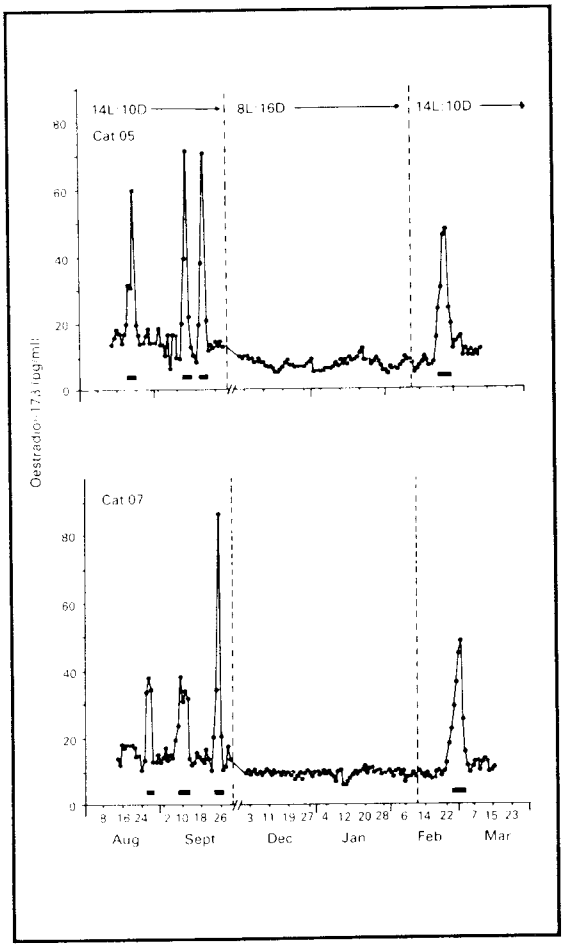
Estrus is the period in which the queen is sexually receptive and allows the male to copulate. Estrus usually begins on the second or third day of follicle growth, continues during the mature follicular phase, and then through regression of the follicles and a day thereafter.[92] Behavioral signs that characterize estrus include crawling with the pelvic region elevated, rolling and increased vocalization. The behavioral aspects of both estrus and proestrus arise from the effects of estrogen (produced by ovarian follicles) on the sexual centers located within the hypothalamus.

The term *interestrus* is used to describe the period of ovarian (and sexual) inactivity that occurs between ovarian follicle growth waves. While the minimal interestrous interval is 8-9 days, the onset of a new follicle growth wave can be delayed for various reasons, including illness and social stress. Therefore, the interestrus interval can be considerably longer than 8-9 days. If cats

are well nourished and socially comfortable, it is not unusual for queens to have 2 estrous cycles per month, with each cycle about 15-16 days long.

The domestic cat is seasonally polyestrous, with a series of estrous cycles occurring within a defined season.[92] Under natural photoperiod at Davis, California (latitude 38 degrees N), the breeding season begins as early as January 15th and extends to October. The months of November-January in the northern hemisphere are usually a time of sexual inactivity (anestrus). The onset of ovarian activity is caused by the effect of increased light stimulation of the hypothalamus which, in turn, influences production of gonadotropins from the anterior pituitary gland. If cats are exposed daily to at least 12 hours of light, ovarian activity (and estrus) occurs on a nonseasonal basis (Fig 1).[24,49,87,92] The reproductive seasons for cats in the southern hemisphere are reversed as compared to those for cats in the northern hemisphere.

Figure 1. Ovarian follicle activity varies with photoperiod.[63] During an initial 50-day period, cats were exposed to 14 hours of light and 10 hours of darkness daily (14L:10D). During the last 70 days of a subsequent 90-day period, cats were exposed to 8 hours of light and 16 hours of darkness daily (8L:16D). Cats were then exposed to the initial photoperiod of 14L:10D. Note the early return of ovarian activity (at 12 days for cat 05 and at 15 days for cat 07) upon return to a favorable photoperiod of 14 hours of light. The horizontal bars indicate periods of sexual receptivity.



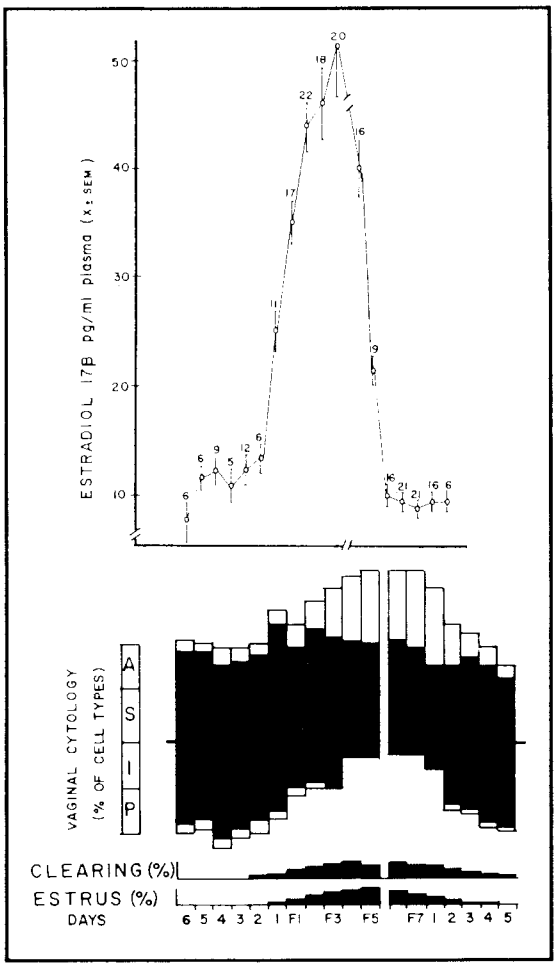
Cats have cyclic ovarian patterns in which groups of follicles grow and regress as often as twice a month.[92] Follicles grow for 3-4 days and mature for 2 days before regressing. Based on the ability of follicles to secrete estrogen, the total follicle wave (including regression) lasts 6-7 days (Fig 2). The minimal period between development of follicles (time between follicle regression and onset of a new follicle wave) is 8-9 days. As in other animals, gonadotropins are secreted in pulses.[53]

The cat is an induced ovulator in that copulation is required for ovulation.[21,32,54,93,113,114] Copulation elicits a surge of luteinizing hormone (LH) released from the anterior pituitary. This LH release is triggered by nerve impulses carried from the vagina to the hypothalamus via the spinal cord. The site in the brain that controls LH release lies in the medial basal hypothalamus and the medial preoptic region.[81,93,94] The brain center controlling sexual receptivity is different from the center controlling LH and resides in the anterior hypothalamus.[81]

The ovulatory surge of LH begins within minutes following copulation, peaks by 2 hours, and returns to baseline within about 8 hours (Fig 3). Though queens are often sexually receptive by the second or third day of ovarian follicle growth, the amount of LH released in response to copulation is often limited until the animal reaches the fourth or fifth day of follicle growth (third or fourth day of estrus).[4] Therefore, cats require several days of estrogen priming before copulation induces a surge of LH sufficient to cause ovulation. This delay in the response to copulation coincides with the time required for follicles to mature.

Ovulation usually occurs 24-30 hours after copulation and the initial release of

Figure 2. The occurrence of events during the follicular phase of the estrous cycle of the cat are based on plasma estradiol concentrations.[92] All data have been arranged according to the first day of the follicular phase (F1, first-day estradiol >20 pg/ml) and the last day of the follicular phase (F7, last-day estradiol >20 pg/ml). The histograms represent percent change in vaginal cytology, clearing of the vaginal smear and manifestation of sexual receptivity. Relative amounts of superficial (S) and intermediate (I) cells are shaded, and anuclear (A) and parabasal (P) cells are not. Note the shift to cornified epithelial cells (superficial and anuclear) during the follicular phase. Also note the progressive increase in animals coming into estrus as the follicular phase develops, and the tendency of animals to be in estrus after the last day of the follicular phase.



LH.[93] Ruptured (ovulated) follicles develop into corpora lutea that secrete progesterone within 24-48 hours after ovulation.[75]

The reader is also referred to other reviews on normal reproductive physiology of the cat.[3,18,20,29,36,43,61,62,65,89]

Mating Behavior

During mating, the male cat grasps the neck of the female with his teeth and rides forward on her back (Fig 4). The hind limbs of the male paddle against the sides of the female, causing the female's back to sag. This results in orientation of the female's external genitalia in a more horizontal position. This position is required for copulation because the penis of the male tends to be directed caudally, rather than cranially, as for other domestic species. Lateral deviation of the female's tail, an important sign of sexual receptivity, helps the male insert his penis.

The copulatory cry of the female can be used as an indication of successful mating. Females tend to growl during copulation, with the intensity increasing from a relatively low-pitched vocalization at the beginning, to a scream at the time the penis is inserted and ejaculation occurs. Because the scream can be heard at some distance, mating pairs do not have to be observed to know if copulation has occurred. Within seconds after ejaculation, the female rejects the male aggressively if he does not dis-

Figure 3. Patterns of luteinizing hormone (LH) concentrations in queens following copulation.[93] Animals that released LH in response to copulation tended to fall into 2 categories: LH release over a 4-hour period (dashed line, n = 6), or over a 16-hour period (solid line, n = 11); all animals ovulated in these 2 groups. Some animals failed to release LH in response to copulation (dotted line, n = 5) and, as a result, did not ovulate. Zero time represents the first copulation, with most animals having 2-3 additional copulations within the first hour.

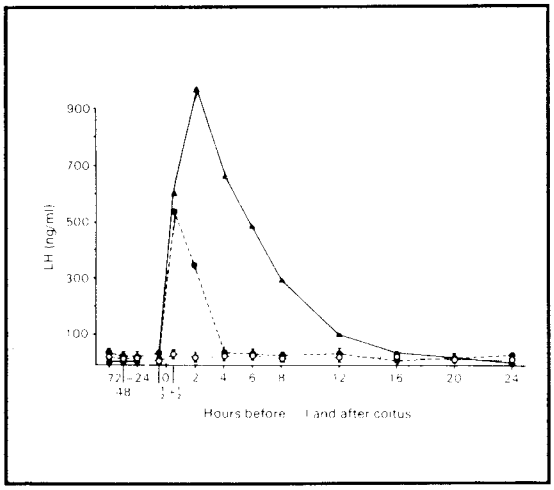
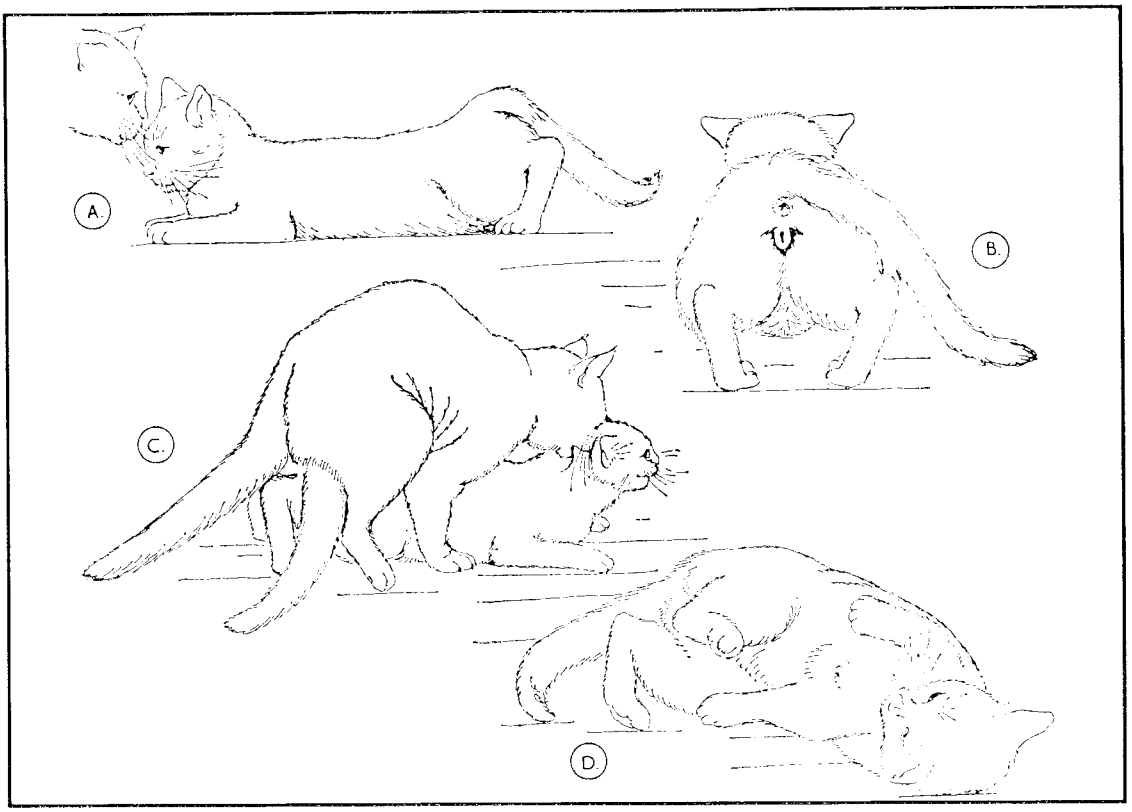


Figure 4. Behavior in sexually receptive queens.[85] A. Lordotic response to the male. B. Lateral deviation of the tail. C. Neck grip by the tom during intromission. D. Postcopulatory rolling.



mount immediately. In the period immediately following copulation, the female usually rolls in an agitated manner and licks her external genitalia. This relaxive activity can also be used to verify breeding. The queen usually repeats her sexual ritual of crawling and vocalization within a few minutes and breeding occurs again.

The reader is referred to other sources for additional information on sexual behavior of the cat.[50,68,98,103,104,106]

Vaginal Cytology During the Estrous Cycle

Hormonal changes during the estrous cycle of the cat are reflected by changes in the epithelial lining of the vagina (Fig 2).[43,62,69,71,92] The microscopic appearance of cells in smears made from vaginal swabs or flushings can be used as an indicator of the stage of the estrous cycle at the time of sampling. After collection, vaginal swabs or flushes are smeared onto a glass microscopic slide, fixed, stained and examined with a standard light microscope.

Anestrous and prepubertal vaginal smears contain numerous small, nucleated epithelial cells with distinct nuclear and cytoplasmic definition. Estrous smears contain numerous cornified epithelial cells, with curled edges and shrunken or absent nuclei (Fig 5).

Following ovulation (early metestrus), the borders of the cornified epithelial cells become ragged and hazy in appearance. Numerous polymorphonuclear neutrophils are present at this time. Later in metestrus, cornified epithelial cells are replaced by normal, noncornified epithelial cells, while neutrophil numbers progressively decrease.

Cytologic changes in vaginal cells in the cat during follicle growth are not as definitive as those in the dog because changes in noncornified and cornified cells are not as extreme. For example, it is common to find equal numbers of nucleated and anucleated

cornified cells, interspersed with a few noncornified epithelial cells, in the vaginal smear of the estrous cat. In contrast, smears from estrous dogs contain almost all anuclear cornified epithelial cells. As a result, vaginal smears are less helpful in cats, as compared to dogs, for defining the stage of the estrous cycle. Nevertheless, one can determine that a cat has ovarian follicle activity on the basis of a vaginal smear with a predominance of cornified epithelial cells.

Collection of vaginal cells in a cat may induce ovulation and interfere with breeding. Limiting penetration of the vaginal swab to 2 cm avoids LH release. Moreover, if one does not elicit the copulatory cry of the female (see above), it is unlikely that LH release leading to ovulation will occur (presuming the animal has mature ovarian follicles present). Also, flushing the vagina with saline for cell collection can be used if there is concern about inducing ovulation with the swab technique.

Breeding Queens

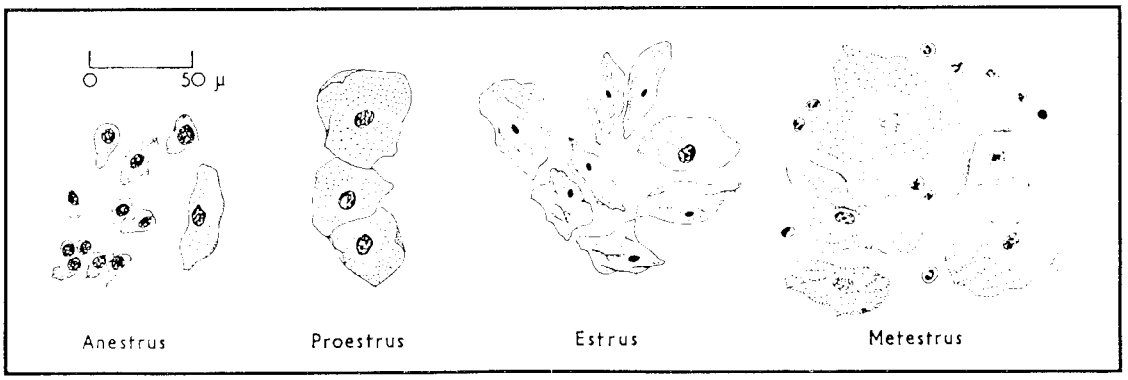
Under optimum conditions of light and temperature, queens can produce an average of 2.1 litters/year. The average interval between litters in one study was 22.5 weeks for the spring and summer, and 28.8 weeks for the fall and winter periods.[81] Litters were born at all months of the year when queens were exposed to 14 hours of light.[81] Under this photoperiod regimen, cats can have estrous cycles throughout the year, with litters born at all times of the year. In an Australian study of animals under natural photoperiod, Siamese and Persian litters were delivered throughout the year, though more litters tended to be born in the spring months.[80]

While queens can produce litters on a regular basis until 8-10 years of age, the prime breeding time for queens is 2-5 years. Litters are produced less frequently, and more erratically, with increasing age. The size of the litter, however, tends to be maintained through as many as 17 consecutive pregnancies.[81]

Queens should be fully mature before they are first bred. Though first-time matings usually occur without difficulty, if one of the pair is not sexually experienced, the breeding may not be consummated. Inexperienced queens may not allow mounting even though they show typical signs of estrus, while inexperienced males may ignore estrous queens. Some queens, regardless of past experience, reject all but a few select males. Experienced males may overcome sexual reluctance of the female by forcing copulation or patiently teasing the queen until she becomes receptive. Though not as common, sexually active males may also choose to ignore certain estrous queens.

It is not unusual for cats to copulate 4 times within an hour of introducing the male. In one study, copulation first occurred at an average of 4 minutes following introduction of the male, with the second and third copulations occurring at subsequent 5- and 6-minute intervals.[64] In general, the longer the animals are allowed to copulate, the longer the intervals between successive

Figure 5. Cytologic characteristics of vaginal epithelium during the estrous cycle.[85] In anestrus, exfoliated cells are mostly parabasal, with some intermediates. In proestrus, cells are mainly intermediate and superficial. During estrus, exfoliated cells are mostly superficial and anuclear (the latter are not illustrated here). In metestrus, leukocytes are present together with cornified epithelial cells that are beginning to degenerate.



copulations. In another study, 24 sexual contacts were noted in queens with unlimited access to males over a 36-hour period.[21]

If physiologic conditions are appropriate for ovulation (ovarian follicles are mature, estrogen priming for several days), it is unlikely that copulations beyond the first 2 or 3 will have any additional effect on induction of ovulation. In fact, females with mature ovarian follicles often ovulate after only 1 copulation. One study found no difference in litter size whether cats were mated on 1 or more (up to 5) days.[80] Limiting the male to a few ejaculations per breeding allows for more frequent use of the male.

Most breeders place the tom and queen together for at least 2 hours. As indicated above, the time that animals are left together is not a critical aspect of fertility. If several matings occur over a 30-minute period following introduction of the breeding pair, this is sufficient to cause ovulation if the female has mature ovarian follicles and the male is fertile. If breeding does not take place, the animals should be separated and brought together again several hours later. Alternatively, estrous queens can be left with toms until pregnancy is confirmed.

As indicated previously, queens can be sexually receptive during the early stages of follicle growth, but before they are sufficiently primed with estrogen to respond to copulation by releasing a preovulatory surge of LH.[4] Therefore, breeding queens beginning on the third day of estrus is the most efficient way to use males. The alternative is to allow breeding contact for 1 hour daily during the entire time the female is in estrus.

A queen can bear young in the same litter from several different sires. This situation can occur because of the 24- to 32-hour interval between the initial copulation-induced release of LH and ovulation.[93] A female can have the sexual drive to copulate 10-20 times during this 24- to 32-hour interval. If in an unrestricted environment, a queen could copulate with a number of males before the time of ovulation.[21] Sperm inseminated up to several hours before ovulation from any male would be equally capable of fertilizing the oocytes.

It is desirable to rebreed queens soon after the weaning of kittens, rather than to allow prolonged periods of cyclic ovarian activity. This recommendation is based on the increased incidence of uterine disease that occurs with age due to repeated exposure of the uterus to estrogens produced by ovarian follicles (see Infertility).[27,92] Pregnancy protects the endometrium against cystic endometrial hyperplasia and chronic inflammatory change. Early rebreeding of queens presumes that they are in a state of good nutrition and health.

Males can be used for breeding 3 times weekly, or for 3 consecutive days, without affecting sperm numbers.[96] Controlled breeding, in which copulatory contacts are limited, should sustain fertility of the male.

The reader is referred to other sources for further information on breeding management.[2,58,83]

Fertilization and Implantation

Feline spermatozoa must be activated (capacitated) before they can fertilize oocytes.[39] The process of capacitation, which occurs in the reproductive tract of the female following insemination, requires about 3 hours.[35] Penetration of the oocyte by the spermatozoan occurs within 20 minutes of contact with the oocyte.[73] While the life span of spermatozoa in the genital tract is not known, it is at least 32 hours, as this represents the copulation-to-ovulation interval in the queen. Fertilization occurs in the upper (ampullar) region of the oviduct.

Reduction of chromosome numbers from a diploid to a haploid state is an essential prerequisite for fertilization. This process begins before ovulation in the cat, with meiosis I completed (first polar body shed) before ovulation. Formation of the first polar body is necessary before fertilization can occur. Therefore, the oocytes of cats are ready for fertilization immediately upon ovulation and movement into the oviducts. Fertilization initiates the second phase of meiosis (meiosis II), or shedding of the second polar body.

Oocytes have been fertilized *in vitro* using spermatozoa obtained from the ductus deferens.[7] Oocytes obtained from ovarian follicles and fertilized *in vitro* have

produced embryos capable of full-term development.[33]

Newly formed embryos move from the oviducts into the uterus at about 5-6 days of age.[45] This interval allows the uterus (endometrium) to remove remnants of spermatozoa and to respond to the effects of progesterone produced by the newly developing corpora lutea. Progesterone influences the endometrium to produce secretions that are important for nurturing of embryos before implantation. Progesterone also causes increased vascularization of the endometrium in preparation for implantation of the embryos.

The free-living state of the embryos ends with implantation at 12-13 days after conception.[25] Before implantation, the embryos migrate within the uterus to equalize the number and spacing of fetuses within the 2 uterine horns.[100] This process of spacing of embryos optimizes the opportunity for fetal development, but it also results in some fetal loss. The average litter size in cats is 4-4.5 kittens.[50,81,100] One group of investigators found that implantation rates were 90% or greater for animals with 5 ovulations, 82% for those with 6-8 ovulations, and 50% for animals with 9-11 ovulations.[100] The largest litters came from animals with 8 ovulations, averaging 6.6 kittens per litter.

Once implantation occurs, formation of the placenta allows for exchange of nutrients between maternal and fetal vascular systems. Placentation in the cat is described as endotheliochorial, meaning that there are 4 layers of tissue between the fetal and maternal blood systems. Epithelial and connective tissue layers are absent on the uterine side. Grossly, the placenta interacts with the endometrium in a defined band that tends to surround the mid-portion of the fetus in the form of a zonary placenta.

Pregnancy Diagnosis

Careful records should be kept of breeding dates. Accurate information on gestation length is important during evaluations of potential reproductive problems. Pregnancy in the cat can usually be confirmed by abdominal palpation of the queen as early as day 15, when fetuses are evident as discrete, round, evenly spaced structures (Fig 6). In some animals, palpation can effectively detect individual fetuses as late as day 35. Individual fetuses become difficult to delineate by abdominal palpation after day 35 because the fetuses and placentas tend to merge with each other within the uterus. Fetal heads are palpable during the later stages of pregnancy, though palpation becomes more difficult in the last several weeks because of increased abdominal tension.

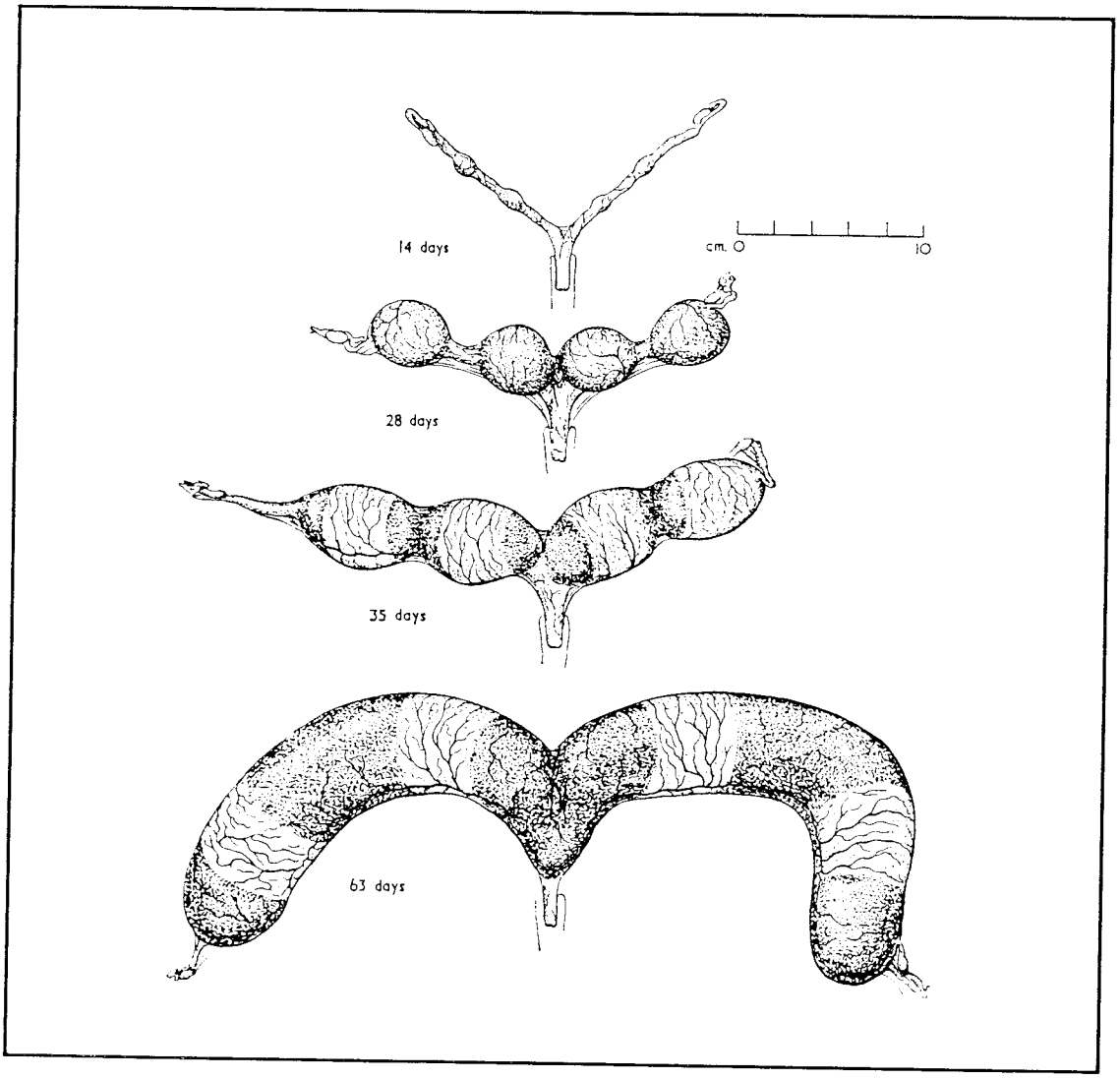
Ultrasonographic examination of the abdomen can be used to detect fetal masses as early as 14-15 days of gestation, and heartbeats can be visualized by ultrasonography by day 24.[23,29] Unless the queen is difficult to palpate because of obesity or abdominal rigidity, ultrasonography is no more reliable than abdominal palpation for pregnancy diagnosis. Radiographs are useful for pregnancy diagnosis only when fetal bones begin to calcify at about day 43 of gestation.[8]

Hormonal Changes During Pregnancy

Following ovulation, cells that originally lined the follicles are converted into progesterone secreting cells of the corpora lutea. Corpora lutea secrete increasing amounts of progesterone beginning 1-2 days after ovulation (2-3 days after breeding).[75] If implantation occurs, progesterone concentrations continue to increase through days 25-30, then slowly decline throughout the rest of pregnancy.[5,102] Maintenance of pregnancy depends upon the presence of corpora lutea through about day 40. At this time, an enzyme that is important for progesterone synthesis (3-beta-hydroxysteroid dehydrogenase), appears in the placenta.[66] Placental production of progesterone in cats is sufficient for maintaining pregnancy after day 40 through term in the absence of ovaries.

Other hormones associated with pregnancy include relaxin, $PGF_{2\alpha}$ and prolactin. Relaxin is produced by the fetoplacental unit beginning at about day 20 of gestation and continuing throughout the rest of pregnancy (Fig 7).[1,97] Relaxin is important for softening the connective tissues that surround the pelvis. This action allows for maximal expansion of the birth canal as the fetuses are delivered. Relaxin may also act in concert with progesterone in maintaining the uterus in a quiescent state during pregnancy.

Figure 6. Extrauterine view of fetuses developing within the gravid uterus.[85] Individual fetuses are evident as discrete masses through 28 days, and tend to merge by day 35. Zonary placentas are depicted by the lighter band-like areas.



Prostaglandin $F_{2\alpha}$ is produced by the fetoplacental unit and endometrium beginning at about day 30 of gestation and reaching peak values at day 45. A large increase in prostaglandin secretion occurs just before delivery. This increase in prostaglandin synthesis at the end of gestation plays a pivotal role in initiating parturition (see Parturition).

Levels of prolactin, another important hormone, increase significantly beginning at about day 35 (Fig 8).[5] Like $PGF_{2\alpha}$, prolactin concentrations plateau at about day 50 and increase suddenly just before delivery. Prolactin is important for development of mammary glands (mammogenesis) during pregnancy and initiation and maintenance of lactation. In contrast to relaxin and prostaglandin, prolactin source is the anterior pituitary. Estrogen and relaxin appear to influence secretion of prolactin through an effect on lactotrops in the anterior pituitary.

Gestation

The minimum gestation length in cats that is consistently compatible with delivery of viable fetuses is about 63 days. A com-

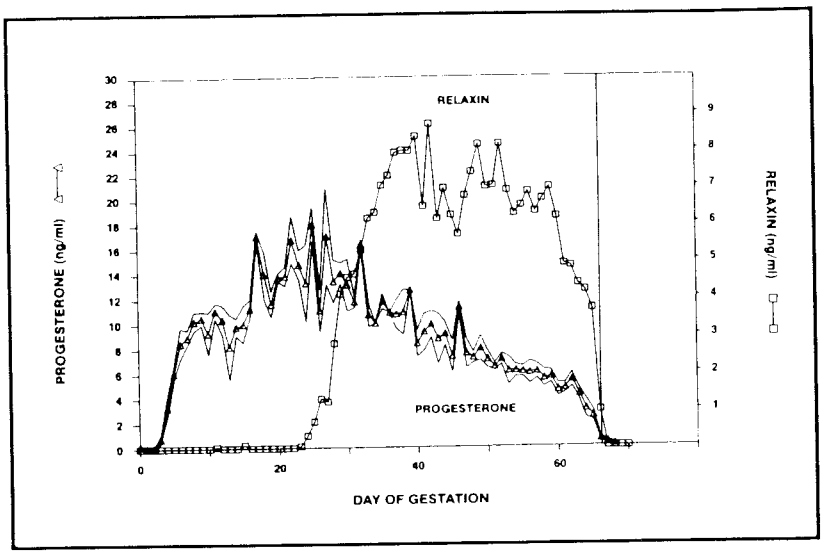


Figure 7. Patterns of progesterone and relaxin plasma concentrations in queens during gestation.[97] The vertical bar toward the right indicates the day of parturition.

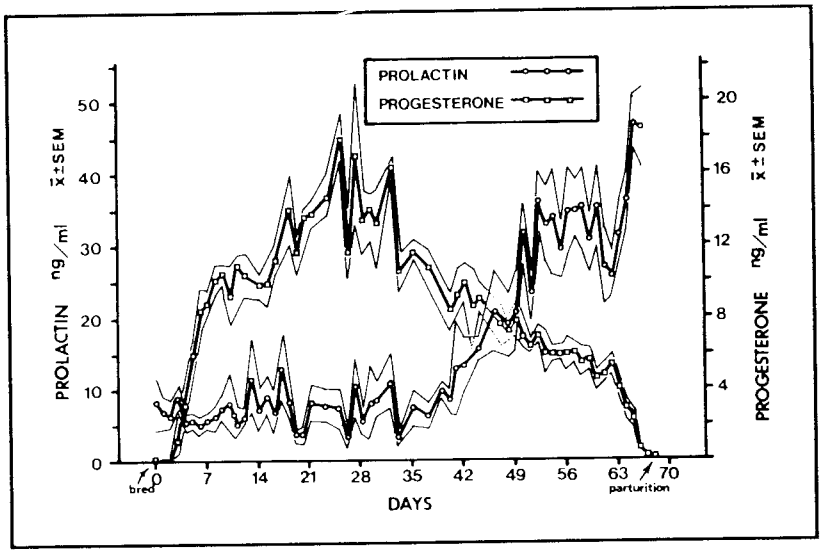


Figure 8. Patterns of prolactin and progesterone plasma concentrations in queens during gestation.[5] The lines bracketing the average concentrations indicate ranges of variations.

mon gestational interval in cats is 63-66 days.[80] Litters can be delivered at 61-62 days and survive, but fetal viability is reduced. Queens delivering at 60 days or before, usually lose their kittens through stillbirth or death after delivery. The loss that occurs with early delivery emphasizes that fetal growth and development compatible with survival require at least 63 days. Gestation lengths can be a few days longer than 66 days and still produce viable litters.

Parturition

Signs of impending parturition include rapid enlargement of the mammary glands during the last week of gestation. Milk can usually be expressed from the mammary glands 24-48 hours before delivery. As gestation ends, the queen spends more time in the nesting box and, within a day of delivery, the queen often shreds materials that line the box. The body temperature of the queen decreases before delivery, with rectal temperatures often declining to 99 F or lower by 12-36 hours before parturition.[62] Also, the queen may be restless, anxious, and more vocal than usual immediately before parturition.

Parturition is triggered by increased secretion of $PGF_{2\alpha}$, which begins several days before delivery. Increased secretion of $PGF_{2\alpha}$ results in regression of the corpora

lutea and a consequent precipitous decline in progesterone during the 24 hours preceding parturition. It is likely that prepartum prostaglandin secretion is driven by increased placental estrogen synthesis. This increased estrogen secretion is likely influenced by an increase in cortisol synthesis by the fetal adrenal glands.

The slow, rhythmic uterine contractions that initiate parturition (stage-I labor) are caused by prostaglandin secretion. This type of contraction is essential for increasing the total muscular tone of the uterus and presenting the fetus to the internal opening of the cervix. Both prostaglandins and relaxin are important for the softening and opening of the cervix that occur during stage I of labor.

When the fetus enters the birth canal, sensory impulses transmitted from the cervix to the hypothalamus result in oxytocin release from the posterior pituitary gland (Ferguson reflex). Oxytocin is transported by the vascular system to the uterus, where it acts with prostaglandins in promoting forceful contractions of uterine smooth muscle to propel the fetus through the birth canal (stage-II labor).[57]

Parturition occurs as a series of labors, one for each kitten. Hard labor involving pronounced straining and discomfort usually lasts only 5-10 minutes. This labor may be preceded by less intense straining and discomfort for 30-60 minutes. Following the birth of each kitten, the queen may show no obvious signs of labor for periods of 30-120 minutes or more. During interludes between deliveries, she may clean and nurse the kittens, or she may quickly clean the kittens and leave the nesting box until onset of the next delivery. As delivery of the next kitten begins, the cat returns to the box and the process is repeated. Owners should not attempt to put the queen back into her box during the resting interludes. In fact, exercise is helpful for subsequent deliveries. The entire litter is usually born in 2-6 hours. The entire delivery can last from 24-36 hours, though this is unusual. On rare instances, an entire litter may be born over a period of as long as 3 days.

As soon as each kitten is born, the queen usually bites off the umbilical cord, often before the placenta is passed. The placenta may be passed with each kitten, or in conjunction with a subsequent delivery. The queen usually eats the fetal membranes as soon as they are passed, a process that is neither deleterious nor beneficial to the dam. Some owners remove the kittens as soon as they are born so as to remove the fetal membranes, trim and/or tie the umbilical cord, and clean and dry the kitten. Such intervention should be done only if the queen neglects the kitten for the first 10 minutes following delivery. All of these activities are better done by the queen than the human observer. In fact, overly attentive owners often disturb the delivery process. It is best to leave the queen alone unless obvious problems arise.

Stage III of parturition involves involution of the uterus and restoration of the epithelium and submucosal (glandular) tissues to their normal nongravid state. Involution of the uterus is usually complete within 4-6 weeks postpartum. This relatively rapid process contrasts with involution in the dog, which takes 8-12 weeks.

Lactation

Mammary gland enlargement is noticeable beginning at about day 18 of gestation. Mammary development reaches its peak at the time of parturition. Milk is present in the glands 1-2 days before delivery. Prolactin is important for development of the mammary gland (mammogenesis) and secretion of milk (lactogenesis). Factors that cause increased prolactin secretion by the anterior pituitary during pregnancy are not fully known. Nevertheless, both estrogen and relaxin (produced by the fetoplacental unit) are probably important stimulators of prolactin secretion.

Prolactin secretion during lactation is maintained by suckling. Sensory input from the mammary glands to the hypothalamus blocks inhibitors of prolactin secretion, such as dopamine. The effect of suckling on prolactin secretion decreases as lactation proceeds, leading to a decrease in prolactin values over time.[5] Prolactin levels decline to basal concentrations within 2 weeks after weaning.

Lactational Anestrus

Lactation inhibits ovarian activity. The sensory input caused by suckling inhibits

synthesis of gonadotropin-releasing hormone in the hypothalamus, which is necessary for ovarian activity. Though some queens may show signs of estrus 7-10 days following parturition, most do not come into estrus until at least the third or fourth week of lactation, and often not until after the kittens are weaned.

Pseudopregnancy

Pseudopregnancy (pseudocyesis) is a syndrome that results from ovulation and formation of corpora lutea in the absence of pregnancy. This situation may result from fertilization failure or early embryonic death.[31] The corpora lutea formed following ovulation have a life span of 35-40 days in the absence of pregnancy.[75,90]

Progesterone concentrations in the pseudopregnant cat increase until about day 25 and then decrease (as the corpora lutea regress) to basal values by about day 40 after ovulation (Fig 9). Length of the luteal phase in the pseudopregnant cat is not influenced by the presence of the uterus because hysterectomy during the luteal phase does not prolong the life span of the corpora lutea.[107] This finding indicates that the uterus does not secrete $PGF_{2\alpha}$ in conjunction with regression of corpora lutea in the cat, as occurs in large domestic animals. This observation correlates with the finding that administration of $PGF_{2\alpha}$ (220-440 μg/kg) to pseudopregnant cats suppresses but does not terminate the activity of corpora lutea.[90,111]

Queens begin ovarian and estrous activity as early as 7-10 days following regression of the corpora lutea in pseudopregnant cats.[90,91] The minimal interval between estrous periods for a pseudopregnant cat is 6-8 weeks. This includes a 5- to 6-week luteal phase and 1-2 weeks for subsequent follicle development. The interval can be longer if the onset of ovarian follicle growth is delayed. The length of the pseudopregnant luteal phase in cats is shorter than that in dogs and other carnivores, which have pseudopregnancy periods similar to their gestation periods.[62]

The pseudopregnant cat seldom shows signs of pregnancy even though she is ex-

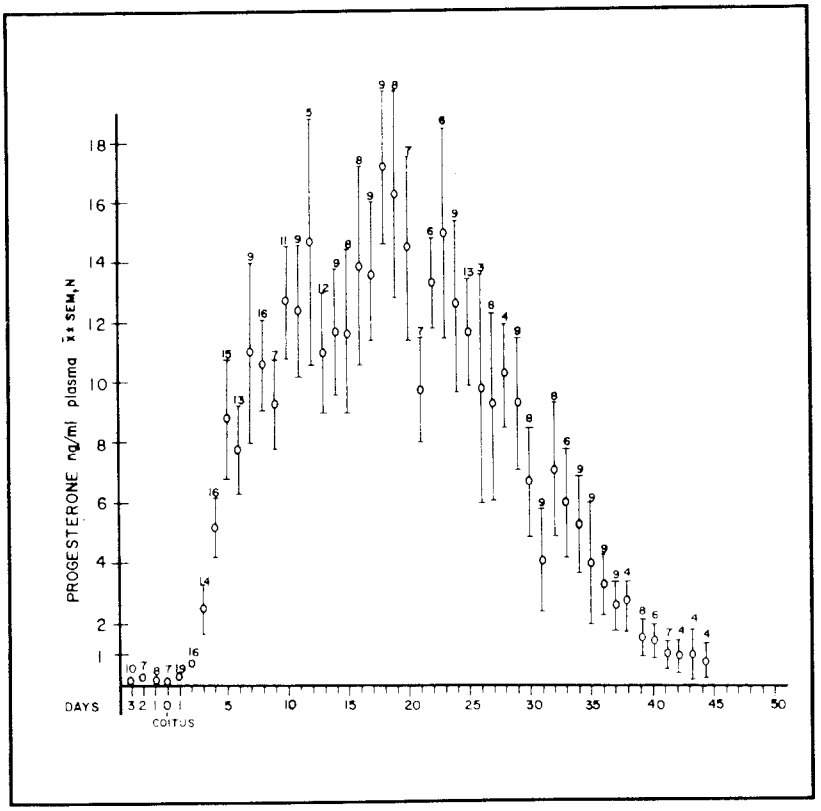


Figure 9. The pseudopregnancy phase of the estrous cycle of the queen as depicted by plasma progesterone concentrations.[90] Day 0 is the day of copulation. Note that the luteal phase terminates at about day 40 postovulation. The vertical lines intersecting the open circles (average values) indicate the range of values. The numbers indicate the number of observations.

posed to the effects of progesterone for up to 35 days following ovulation. If necessary, the signs of pseudopregnancy in the cat can be alleviated by treatment with estrogens or androgens. A better approach is to let the signs resolve with "tincture of time."

Male Reproductive Physiology

Male cats reach puberty at 6-9 months of age.[86] The reproductive life of a tom is about 14 years. During this time, toms do not have cycles of reproductive activity that are comparable to females in that production of germ cells and hormones by the testis tends to be continuous. Sexual activity is also continuous in that toms respond to estrous females at any time. Males exposed to natural changes in photoperiod, however, tend to have reduced spermatogenesis and testosterone production during shorter photoperiods (winter).

The volume of semen released at each ejaculation ranges from 0.03-0.3 ml. Each ejaculate contains 6 x 10^7 to 1.5 x 10^9 sperm/ml.[61] About 90% of the sperm in normal semen are motile. Abnormal forms constitute 10% or less of the total number.

Manipulation of Reproduction

Induction of Ovulation

Cat breeders often want to bring cats out of estrus without actual breeding. This is done by inducing the cat to ovulate. Ovulation can be induced in several ways. The most physiologic way is to use vasectomized or testosterone-treated castrated toms. Males selected for such use should have been active and competent breeders before vasectomy or castration. An advantage of using males for estrus detection is that the male can determine when a queen is in heat better than the owner can. This is an advantage when breeding types of cats that do not manifest outward signs of heat in a flamboyant manner. Use of altered males has several disadvantages. An extra cat must be kept in the cattery, and sexually active males may pose problems in terms of spraying and other obnoxious behavior.

Ovulation can also be induced by inserting a presterilized smooth glass or metal probe, or a moistened cotton swab into the vagina (Fig 10).[37,91] Eliciting the coital cry and postmating roll indicates successful stimulation. If unsuccessful, the process is repeated every 10-15 minutes for 1 hour, then again 12 hours later. Though this technique is widely employed, many breeders are worried about causing trauma to the vagina and introducing infections. These have not been problems in our experience.

Ovulation can also be induced efficiently with injections of luteotropins, such as human chorionic gonadotropin (250 IU given IM).[109] Synthetic gonadotropin-releasing hormone (25 μg given IM) also induces LH release and ovulation.[3,91] Cats only ovulate in response to gonadotropin treatment if they have large, mature ovarian follicles present, as evidenced by signs of estrus. Gonadotropins only work if the follicle is fully mature. It can be difficult to know when to treat cats with silent or vague signs of estrus.

A technique called "acupressure" has been recently developed by cat breeders.[118] It is claimed to be both safe and effective in inducing ovulation. Though this technique is new and has yet to be scientifically verified, it may work. The procedure consists of 3 sequential parts: foreplay, external vaginal stimulation and acupressure. The estrous queen is first patted for several seconds over the rear to mimic the paddling motions of the tomcat as he positions himself and the queen for copulation (Fig 11). Immediately afterward, the queen is lightly rubbed under the vulva with the middle finger of the hand (Fig 12). After vulvar stimulation, acupressure is immediately applied on the hollow between the tailhead and pelvis (Fig 13). The hollow is formed when the queen deviates the tail to the side, a normal mating position. Some queens have a definite right or left hand preference, depending on the position of the tail. The index finger is pressed into the space in a downward and inward direction. When it is properly done, one can purportedly feel a "vaginal pulsation." Successful stimulation is manifested by typical postcoital behavior (vocalization, rolling). The procedure is repeated every 10-15 minutes for one hour, and then again 12 hours later.

Regardless of the techniques used to induce ovulation, allowing persistent estrous activity without pregnancy can lead to uter-

ine changes in cats and make it more difficult for them to conceive at a later date. It may also increase the likelihood of pyometra.

Increased Ovarian Follicle Production

Exposure of cats to continuous light has been studied in relation to ovarian follicle activity.[63] Queens continuously exposed to light had more large antral follicles than queens exposed to 14 hours of light and 10 hours of dark (9 vs 4.5 follicles) (Fig 14). Estrogen production was also increased, suggesting that the follicles are normal from a physiologic view. Interestingly, estrous cycles occurred only once a month under continuous light, vs twice a month with 14 hours of light daily.

An important question is whether continuous exposure to light can significantly increase litter size in cats. As indicated previously, the number of fetuses implanted was related to the number of follicles ovulated, through about 8 ovulations (6.6 fetuses, 83% implantation rate).[100] When the ovulatory rate was greater than 8, the implantation rate (49%) and litter size (4.4 fetuses) were adversely affected. The number of follicles (9) produced in the continuous-light study described above is at the break-even point for efficient implantation.

Artificial Insemination

Semen can be collected from males by use of an artificial vagina.[96] Most males can be trained to use an artificial vagina within 3 weeks or less. An intact female in estrus, or a spayed female that has been treated with estrogen, is used as a "teaser." The penis is diverted into the artificial vagina as the male mounts the female.

Semen can also be collected by electroejaculation performed while the cat is anesthetized.[76,77] Electroejaculation requires construction of an electrical probe that fits into the rectum of the tom. No difference has been found in the number and quality of spermatozoa collected by electroejaculation or artificial vagina.[61]

Once semen is collected, it is usually diluted with sterile saline and deposited di-

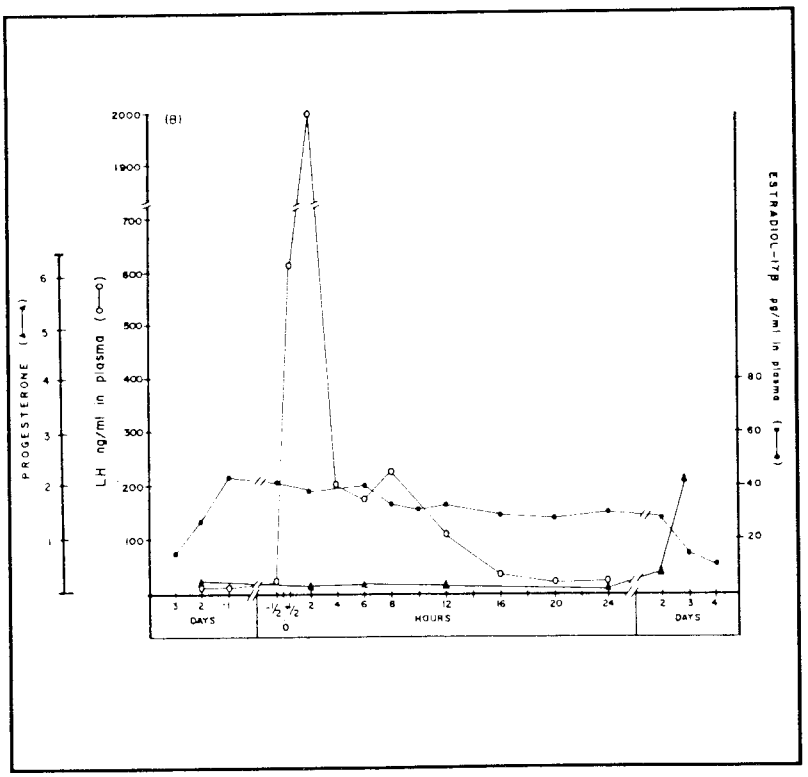


Figure 10. Release of luteinizing hormone (LH) caused by deep insertion of a vaginal swab in an estrous cat.[91] The animal ovulated in response to insertion of the swab as evidenced by the rise in progesterone concentrations on day 3. Zero time represents the time of insertion of the swab.

Figure 11. Foreplay stage of acupressure technique for induction of ovulation. The cat is being patted with the hand in such a way as to mimic the footwork of the male during the initial stages of breeding. (Courtesy of Cathy Galfo and Cherylee DeYoung).

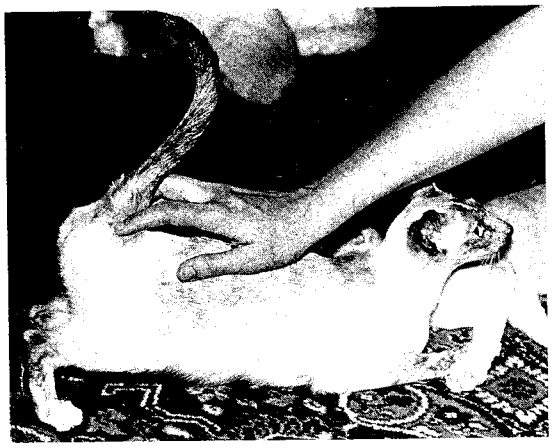
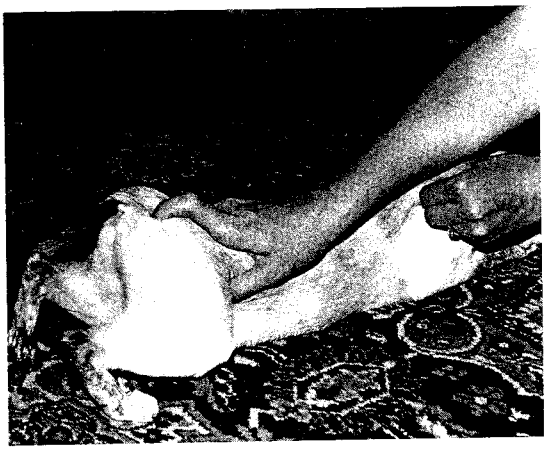
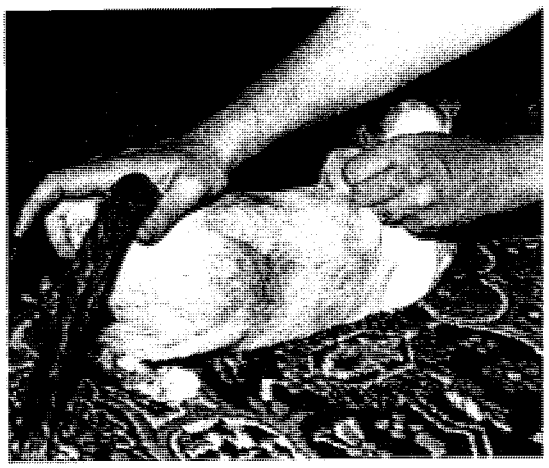


Figure 13. Acupressure step. The index finger is thrust into the hollow between the tailhead and pelvis (opposite the side of the deviated tail). Sudden downward and inward pressure over the area of the vagina triggers a typical postcoital response if the procedure is successful. (Courtesy of Cathy Galfo and Cherylee DeYoung).



rectly into the vagina of the female with a blunt cannula and syringe. The female must be treated with a hormone (LH, HCG, GnRH) to cause ovulation in conjunction with the insemination. A 75% conception rate has been achieved by artificial breeding.[96] Also, pregnancies have been produced in cats that have been inseminated with semen that was previously frozen for extended periods.[78] Therefore, there are no technical reasons why artificial insemination cannot be used in cats as it is used in other species.

Figure 12. Teasing or vulvar stimulation stage of the acupressure technique. The area under the vulva is being stroked with the middle finger. (Courtesy of Cathy Galfo and Cherylee DeYoung).



Embryo Transfer

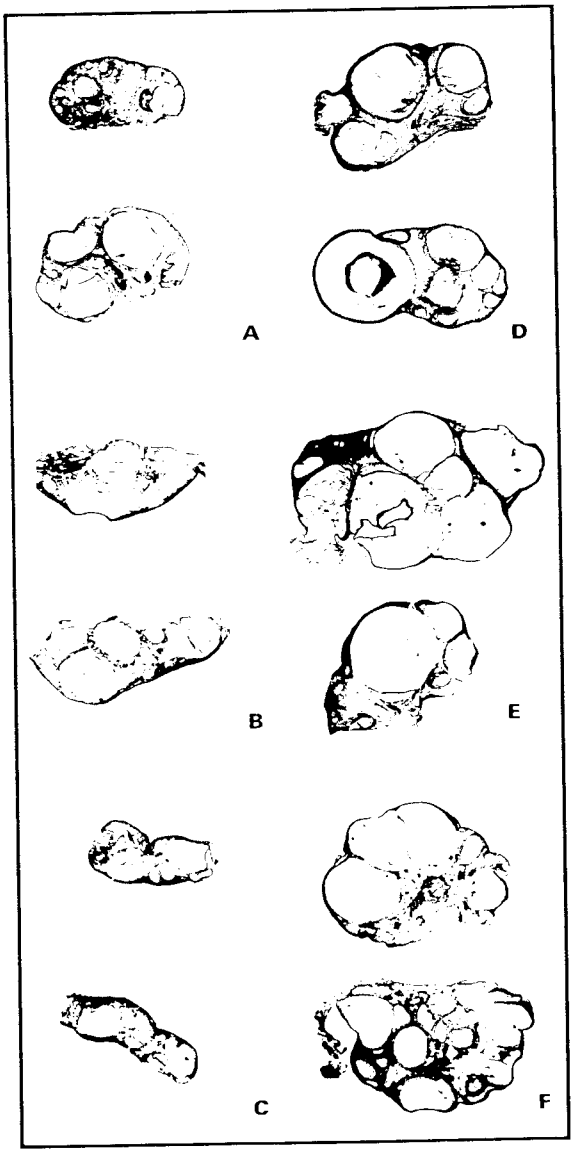
The feasibility of transferring embryos from one queen to another has been studied.[34,56,101] In general, the success rate of embryo transfer has been low. Most pregnancies ended through abortion or absorption of the fetuses. Fetal loss occurred in 1 of 3, 2 of 4 and 5 of 6 pregnancies established by embryo transfer.[34,56,101] Losses occurred at days 22, 25, 34, 35 or 39 of gestation in the latter study.[100,101] Oocytes collected from unovulated follicles induced by pregnant mare serum gonadotropin can be fertilized *in vitro*, leading to eventual development of term fetuses when transferred to recipient animals.[33] This finding suggests that failure of embryo transfer is not due to abnormal follicle development when hormone treatment is used to induce follicles.

Prevention of Estrus

Estrous cycles can be inhibited by use of progestational compounds. Megestrol acetate, a long-acting progestin, is particularly effective in preventing estrus.[48,74,108] Estrus prevention requires a megestrol acetate dosage of 2.5 mg/day for 8 weeks, or 2.5

mg/week for up to 18 months. At the end of 18 months, a rest period of 2-3 months is recommended. If the queen is to be bred following megestrol use, she should be bred on the second estrus following discontinuation of treatment.[15] Other long-acting progestational compounds, such as medroxyprogesterone acetate are also effective in preventing estrus, but are probably not as safe as megestrol acetate.

Figure 14. Cross sections of ovaries from cats exposed to various photoperiods.[63] The ovaries at A, B and C are from cats exposed to 14 hours of light daily. The ovaries at D, E and F are from cats exposed to 24 hours of light daily for at least 60 days. Ovaries were obtained on the third day of estrus. Note the greater number of large antral follicles in the ovaries of cats exposed to continuous light (D, E, F).



Long-term use of progestins in cats can lead to various complications, including pyometra, mammary gland hyperplasia and neoplasia, and diabetes mellitus.[29] Megestrol acetate also suppresses adrenocortical activity in cats.[14]

Androgens can also be used to inhibit estrus in cats. Mibolerone, an androgenic steroid, prevents estrus in queens when used at 50 μg/day beginning at least 30 days before the anticipated start of ovarian activity.[9] Mibolerone can be given as long as estrus inhibition is desired without interfering with subsequent reproductive performance.[15] Long-term use of androgenic compounds may cause some masculinization, including enlargement of the clitoris.

Termination of Estrus

Megestrol acetate can be used to suppress estrus in queens that are beginning to show estrual signs.[19] The recommended dosage is 5 mg/day for 3 days, followed by 2.5-5 mg/week for 10 weeks.[48] Most cats are out of estrus by the end of the first week of treatment.

Prevention of Pregnancy

Pregnancy can be prevented with estrogens in cases of unwanted matings. Estradiol cypionate (0.25 mg IM) given within 40 hours of mating retards movement of the ova through the oviduct and causes oocyte degeneration.[45] Side effects of estrogen treatment include prolongation of estrus, increased incidence of uterine disease, and the possibility of bone marrow suppression with overdosing or continued treatment.

A safer approach to mismating in cats is to induce abortion with $PGF_{2\alpha}$, given at 500 μg/kg daily for 2 days between 20 and 30 days of gestation.[72] While this procedure may require hospitalization, there is less danger of uterine disease than with estrogen treatment.

ABNORMAL REPRODUCTION

Nonparturient Infertility

Infertility is a relatively common problem in queens and toms. Infertility is usu-

ally considered to mean a failure to conceive. It may have multiple causes that are often difficult to determine. Aberrant sexual behavior of the queen and progressive uterine disease in the unmated female are important causes of infertility. In a following section, reproductive failure of animals that conceive but fail to deliver viable young will be discussed.

Persistent Seasonal Estrus

Queens occasionally remain sexually receptive for periods that are longer than the usual 5-6 days.[91] Persistent estrus can occur because of an aberration in sexual behavior, unusual ovarian follicle growth patterns, or abnormalities in ovarian activity.

Animals with behavioral problems can have normal cyclic ovarian follicle activity but remain sexually receptive during the period of follicle growth, as well as during periods of no ovarian follicle activity (interestrus) (Fig 15). The sexual centers in the hypothalamus of these animals appear sensitive to the low concentrations of estrogen present during interestrus. Conception is possible in such cats if the time of mating corresponds with an ovarian follicle wave. Cessation of estrus following mating indicates ovulation.

Another cause for continuous sexual receptivity involves ovarian follicle growth patterns in which follicular waves overlap (Fig 16).[91] In this situation, estrogen concentrations are elevated continuously above baseline values because of the continual presence of follicles. This is an unusual type of ovarian follicle growth pattern in the cat. Follicle waves in cats, as indicated previously, are usually separated by a minimum of 8-9 days. Conception is possible in cats with this type of ovarian follicle activity. Again, cessation of estrus suggests ovulation in the mated animal.

Sexual receptivity has been observed in pregnant animals even though they have plasma progesterone concentrations that normally suppress estrous activity. Estrogen secretion is normal in these animals and the cause is unknown. Sexually receptivity can also occur during the luteal phase of the pseudopregnant cat.[92] For example, estrus occurred in a queen about 17 days after copulation-induced ovulation that resulted in formation of corpora lutea (Fig 17). With a relatively short interval between estrous periods and in the absence of endocrine data, one might suspect ovulatory failure during the first estrus period. These examples emphasize that sexual behavior does not always occur as expected in relationship to changes in hormone secretion.

Persistent Nonseasonal Estrus

Persistent estrus that has no seasonal basis is usually caused by cystic follicular degeneration of the ovaries.[44,60] The affected ovaries are often enlarged and covered with numerous follicles in various stages of development. The condition is thought to occur more frequently in older nulliparous (never pregnant) queens, though it has been occasionally observed in multiparous (multiple pregnancies) queens as well. Queens with this disorder may mate continuously, though conception does not occur because of the absence of normal follicles. Affected queens usually lose weight and have a rough, thin haircoat.

Figure 15. Continuous estrous behavior in a queen with regular ovarian follicle activity.[92] Follicle activity is depicted by plasma estradiol concentrations. The animal was (inappropriately) sexually receptive between 2 follicle waves on about March 12 and again between 2 follicle waves on about April 10. The solid horizontal bars indicate sexual acceptance; the partially solid area in the bar indicates proestrus-like activity.

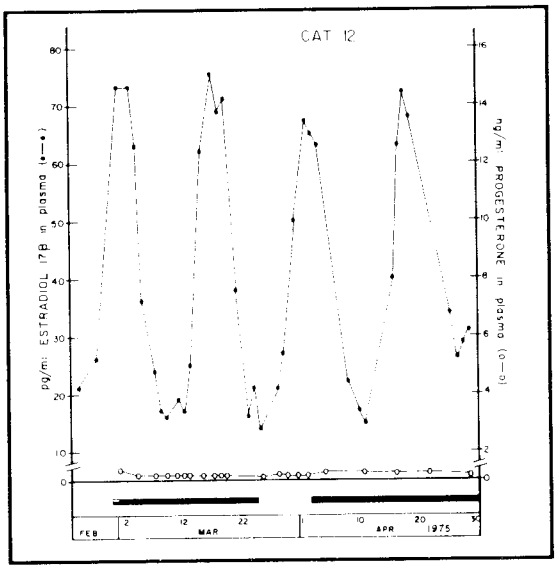
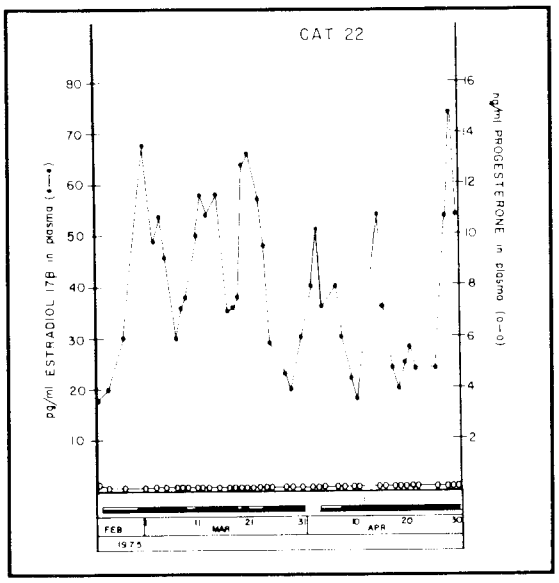


Figure 16. Continuous estrous behavior in a queen with ovarian follicle waves that overlap.[92] Follicle activity is depicted by plasma estradiol concentrations. The overlap was accentuated during the middle of March. Copulation was allowed only once, on April 12. Ovulation did not follow this mating because copulation occurred between 2 follicle waves. The solid horizontal bars indicate sexual acceptance. The partially solid bars indicate proestrus-like activity.



Persistent nonseasonal estrus has also been observed in older female cats with granulosa-cell tumors of the ovary.[62] The opposite condition, masculinization, has been described in older cats with luteomas, thecomas and dysgerminomas, which are rare.[11]

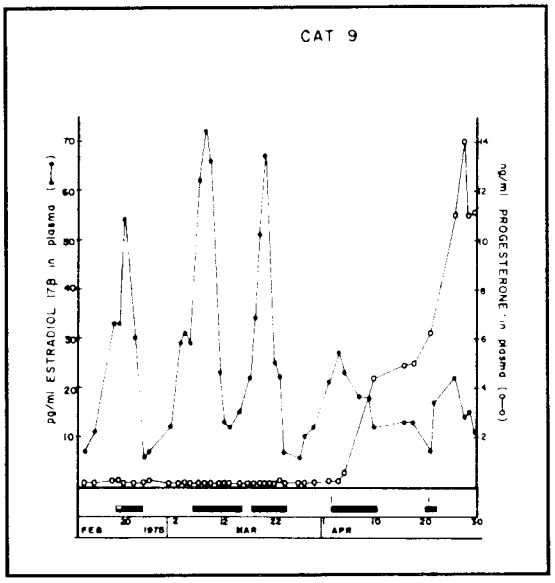
Estrogen analysis of plasma is helpful for diagnosis of persistent estrus involving sexual aberrations, ovarian disease or unusual ovarian follicle growth patterns.[92] For best results, blood samples must be obtained daily for up to 2 weeks. If cost is prohibitive, even a single estrogen analysis can be informative, especially if the sample is obtained at a time the animal is showing sexual activity. A single elevated value indicates functional ovarian follicles or an estrogen-secreting tumor. A low value, obtained in conjunction with sexual activity, indicates the animal has unusual sexual responses, a situation that could call for an extended sampling period to establish a precise diagnosis.

Estrogen values in animals with cystic follicular hyperplasia have not been defined. Cystic follicular hyperplasia is best diagnosed by ultrasonography or exploratory laparotomy. While progestin therapy can limit the clinical signs associated with cystic follicular hyperplasia in cats, the treatment of choice is ovariohysterectomy.

Silent Heat

Queens may fail to show outward signs of estrus even though they have normal cyclic ovarian activity, as evidenced by estrogen analysis.[91,92] One affected queen did not permit intromission by a male for 2 months even though several cohorts of follicles developed and regressed during this period; the queen did show signs of proestrus (Fig 18). Silent heat is often observed in colonies where females are housed together and in animals that are low in the social order of the group. These animals do not respond to introduction of a male, especially in the presence of people.

Figure 17. Sexual receptivity in a queen after breeding and during the luteal phase of pregnancy.[92] This animal had 3 distinct follicular waves before copulation was allowed (once) on April 1. Ovulation and formation of corpora lutea occurred as a result of breeding, as indicated by the subsequent increase in progesterone concentrations. This queen was sexually receptive again (April 20) 9 days after the end of the estrus associated with breeding. Most queens are not sexually receptive in the presence of high progesterone values. The solid horizontal bars indicate sexual acceptance. The partially solid area of a bar indicates proestrus-like activity.



The intensity of heat signs also may vary with breed and activity. Overweight and/or sedate cats tend to show fewer heat signs than thin athletic animals. Oriental breeds may show more intense estrus than Persians.

If silent estrus is suspected or diagnosed, alleviation of social stress and habituation of the queen with a gentle male may allow the queen to become sexually receptive. Estrous behavior may be enhanced by placing the female with queens that are sexually receptive. The condition can be diagnosed by analyzing serial blood samples for estradiol values, or examinating vaginal smears for cytologic changes.

Ovulatory Failure

Animals may fail to ovulate despite normal ovarian and estrous activity involving copulatory contact with a male (Fig 19).[91] One reason for failure is breeding too late in estrus. For example, if a female with normal ovarian and estrous activity, is bred late in the follicle wave, there are 2 possible reasons for ovulatory failure. One (unlikely) possibility is that the queen was unable to release an ovulatory surge of LH in response to copulation. The other (likely) possibility is that the follicles were regressing at the time of copulation and, therefore, were unable to respond to the LH surge by rupture (ovulation) and subsequent formation of corpora lutea. Queens remain sexually receptive until after regression of follicles. Thus, they can be bred at a time when mature, normal follicles are no longer present. As a general rule, queens should be bred (for the first time) no later than the middle of estrus, that is, by day 4.

Estrous Behavior in Spayed Queens

Ovariectomized cats occasionally may show signs of estrus. Owners become upset because they assumed all ovarian tissue was removed at surgery. The most common hormone finding in these cats is low plasma estrogen concentrations in conjunction with estrous behavior. This observation means that the behavior has no hormonal basis. These females may allow mounting, but do not allow intromission by the male. It is less common to find elevated estrogen values, which would indicate thal all ovarian tissue was not removed at surgery.

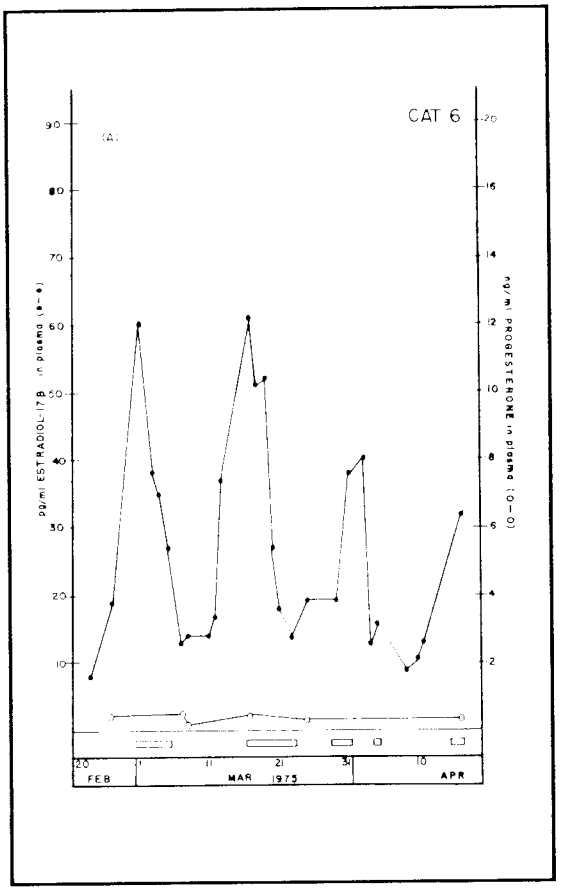
It is important to determine, if possible, that the signs reported by the owner are truly the signs of estrus, or if they are just proestrous signs in which the female allows mounting but not copulation. If the female allows intromission, this strongly suggests the presence of ovarian tissue.

Another approach to this problem is to use laparoscopy in an attempt to find ovarian tissue.[114]

Anestrus

Queens may have long periods of no sexual activity. True anestrus, defined as a state of no ovarian activity, can occur be-

Figure 18. Failure of a queen with ovarian follicle waves to express estrus.[91] The queen avoided the male at all times, though she would assume a lordotic position after manual stimulation (open bars), especially during periods of follicle activity (as indicated by plasma estradiol concentrations).

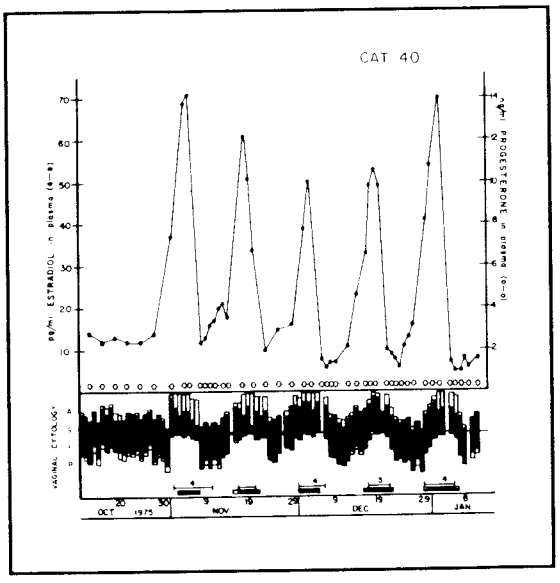


cause of insufficient photoperiod exposure, that is, exposure to less than 10 hours of light per day. True anestrus also occurs during the physiologic breeding season. Affected queens are often timid and adversely affected by social pressure, whether it occurs in conjunction with group housing or contact with other breeding queens. Such social stress can inhibit normal ovarian activity, as well as the expression of estrus in cats with normal cyclic ovarian activity.

Increasing age can be associated with longer interestrus intervals, or cessation of ovarian activity altogether. Cats that are chronically diseased, malnourished or genetically stunted may not have normal ovarian activity. Also, cats may not come into heat because of developmental abnormalities, such as gonadal hypoplasia, gonadal agenesis or hermaphrodism.[55]

Attempts have been made to induce estrus in otherwise normal anestrous females by hormone treatment.[16,17,111] Administration of follicle-stimulating hormone of pituitary origin (FSH-P, 2 mg IM daily for 5 days) can induce estrus by the fourth or fifth day of treatment. Human chorionic gonadotropin (250 IU IM) enhances ovulation when given on days 1 and 2 of the induced estrus. If the induced ovarian follicle development is normal, however, HCG administration is not necessary. The HCG should not be given too soon during folliculogenesis because it can cause premature luteinization of follicles. Queens should be bred at least twice daily during the induced estrus.[78,111] This allows the female to release an ovulatory surge of LH once the animal has been sufficiently primed by exposure to estrogen from the developing follicles.

Figure 19. Ovulatory failure in a queen.[92] The animal was bred on one day of 4 of the 5 follicle waves as shown by estradiol concentrations. The number of copulations and the day they occurred are indicated above each bar. Ovulatory failure may have resulted from breeding late in estrus and, thus, late in the follicle wave. Estrus is indicated by solid bars, proestrus by half-filled bars. Cyclic cornification of the vaginal epithelium (vertical bars) is indicated by the relative proportion of anuclear (A), and parabasal (P) (unshaded) as well as superficial (S) and intermediate (I) cells (shaded). Clearing of the vaginal smear is shown by the horizontal line.



Cystic Endometrial Hyperplasia

Cystic endometrial hyperplasia usually is associated with chronic hyperplasia and cystic glandular development of the endometrium (Fig 20).[7,29,51,59] These changes may stem from prolonged exposure to stimulatory effects of progesterone.[27] This hypothesis, however, arises from experience with dogs, in which progesterone has a long-term deleterious effect on the endometrium. As discussed previously, intact nonpregnant females can have repeated ovarian follicle waves. In this situation, estrogen is the dominant hormone and there is little or no progesterone in the absence of copulation. Therefore, in cats, pathologic changes observed in the endometrium are more likely caused by estrogens.

Cystic endometrial hyperplasia also is associated with infertility or early embryonic death. In one study, the disease was more prevalent in intact, aged nulliparous females than in multiparous females.[27] The incidence of lesions increased at about 10 years of age, though others have found severe lesions of the endometrium by 5 or 6 years of age. While uterine changes with age may not be as severe in cats as in dogs, uterine lesions are a greater problem in cats than previously perceived.

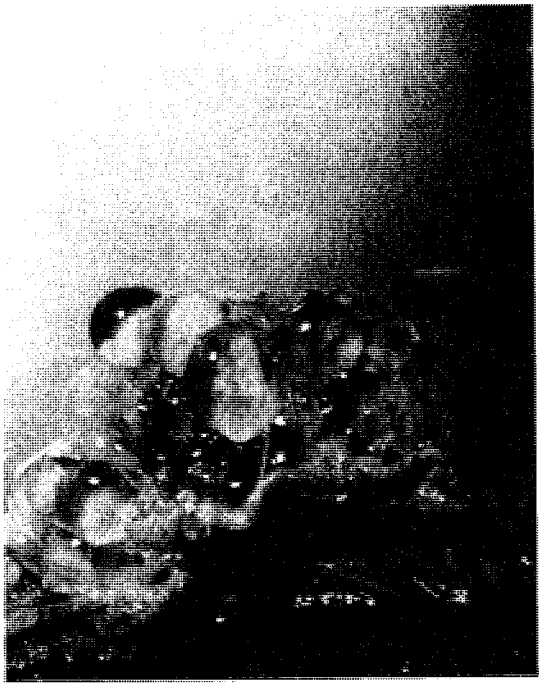
As indicated in an earlier section (Breeding of Queens), pregnancy protects the queen against pathologic changes in the uterus that inhibit fertility. Breeders are faced with a dilemma when they want to discontinue breeding a particular queen for

a time because this can contribute to future breeding problems. Nonpregnant queens can be protected against pathologic uterine changes by blocking cyclic ovarian activity. This can be done by maintaining animals in a photoperiod that suppresses ovarian activity (less than 10 hours of light) or using compounds, such as mibolerone, that block cyclic ovarian activity in cats without apparent uterine change.[9] Our experience is that interrupting the breeding of queens results in reduced fertility when the animals are returned to the breeding schedule, even in an interval as short as 12-18 months.

Nonparturient Endometritis

This disorder is usually a sequela of low-grade cystic endometrial hyperplasia and a complicating bacterial infection. Affected queens have varying degrees of systemic illness including depression, anorexia, fever and a purulent vulvar discharge. Leukocytosis is often evident in the hemogram. Severe uterine infections may be life-threatening. Treatment is with antibiotics selected on the basis of culture of the vulvar exudate. Bacteria commonly involved include *E coli*, especially hemolytic strains, beta-hemolytic streptococci, staphylococci, *Pasteurella* spp and various species of anaerobic bacteria. Ancillary use of $PGF_{2\alpha}$ for treatment of the condition should be explored, particularly for its ability to cause smooth muscle contraction and evacuation of the uterus.

Figure 20. Large cysts in the endometrium of a cat with cystic endometrial hyperplasia.



Pyometra

Pyometra (pus-filled uterus) is a relatively common reproductive disorder of cats.[30,51,59] Older nulliparous queens are more likely to be affected than younger or multiparous queens. Pyometra may also be associated with progestin treatment for estrus control, certain skin disorders or behavioral problems. Pyometra also has been observed following use of estrogens for mismating.

Like nonparturient endometritis, pyometra probably evolves from an underlying cystic endometrial hyperplasia that is complicated by bacterial infections of the types seen in endometritis. Pyometra differs from endometritis in that the degree of inflammation of the uterine wall is less and the amount of purulent exudate is much greater. Pyometra is usually manifested clinically within 4-6 weeks following an estrous period. The fact that queens tend to stop ovarian activity when they have pyometra is likely a reflection of the systemic effect of the disease.

Two types of pyometra occur: open and closed. In open pyometra, the cervix is partially or completely open and there is considerable drainage of pus from the vulva. In closed pyometra, the cervix is tightly closed and pus accumulates within the uterus, with no vulvar discharge. Clinical signs of pyometra include a variable purulent vulvar discharge, lethargy, anorexia, weight loss, polyuria and polydipsia. Leukocytosis is usually observed in the hemogram. The enlarged uterus can usually be detected by abdominal palpation, ultrasonography or radiography of the abdomen (Figs 21, 22). Pyometra usually affects both horns of the uterus, though cats with unilateral pyometra have been observed.

If queens with pyometra are not required for breeding, ovariohysterectomy is the treatment of choice (Fig 23). Medical treatment with $PGF_{2\alpha}$ has proven highly effec-

tive for breeding queens with open pyometra.[30,52,105] Medical treatment consists of $PGF_{2\alpha}$ (200 μg/kg/day IM for 2 days and 500 μg/kg/day for 5 days) combined with systemic broad-spectrum antibiotic treatment for 3-4 weeks.[52] Some cats become nauseated and vomit, and may shown signs of shock for a few minutes after prostaglandin administration.

Prostaglandin treatment causes immediate contraction of the uterus and gradual relaxation of the cervix. Drainage of pus from the uterus does not begin until the cervix is open. In open pyometra, the volume of vulvar discharge increases rapidly following prostaglandin treatment. The safety of prostaglandin treatment in closed pyometra remains to be established in cats. If prostaglandin treatment of closed pyometra is attempted, the animal must be closely monitored for any adverse effects. While it is not likely that prostaglandin administration will result in passage of pus into the abdomen (via the oviducts) or rupture of the uterus, constant monitoring with this therapy is imperative.

Pyometra in queens can also be treated by uterine drainage and flushing.[117] The affected uterine horn is externalized through a laparotomy incision. A stab wound is placed in the caudal portion of the uterus and a flexible catheter inserted. The pus is aspirated through the catheter. Aspiration is facilitated by periodically instilling warm saline into the uterus and manual massage. The cycle of aspiration, saline instillation and massage is continued several times until the affected uterine horn(s) are clean of exudate. Uterine evacuation and cleansing are sometimes facilitated by placing a second stab wound in the cranial part of the uterus. Saline can then be instilled in the cranial wound while aspiration is carried out through the caudal wound. Following cleansing, saline containing a broad-spectrum antibiotic or antibiotic combination is instilled into the uterus and the stab wounds closed with sutures. The queen is then treated with systemic antibiotics for several weeks. Selection of antibiotics should be based on results of culture and sensitivity testing of uterine exudate. This procedure should be used in animals that fail to respond to prostaglandin therapy.

Hydrometra

This condition involves accumulation of a large amount of watery noninflammatory fluid in the uterus. The condition is relatively uncommon compared to pyometra. Because there are no complicating secondary bacterial infections, clinical signs other than anestrus are usually absent. The mucinous exudate comes from glands that develop as part of the hyperplastic endometrium syndrome. Prostaglandins or ovariohysterectomy can be used to treat the condition.

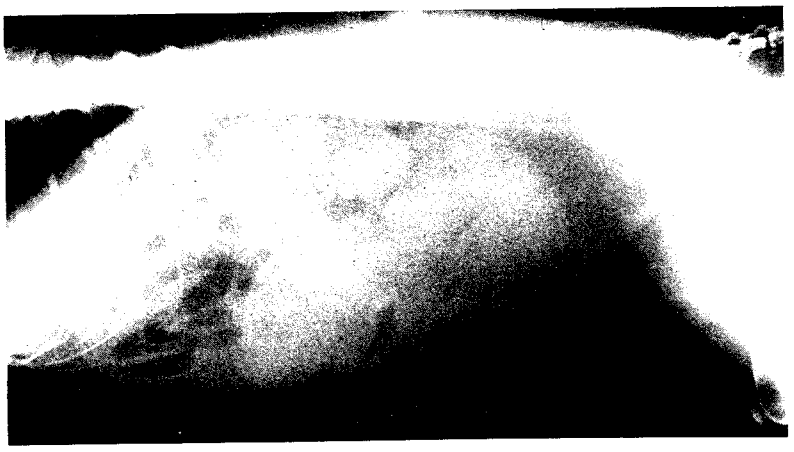


Figure 21. Cranial displacement of other abdominal viscera and uterine distention in a lateral radiograph of a queen with pyometra.

Extrauterine Reproductive Infections

Infections of the ovaries, oviducts, cervix and vagina are extremely uncommon in cats, as compared to other species.

Neoplasia

Tumors of the reproductive organs of cats are uncommon, other than of the mammary glands of older females.[11] This is because few cats are kept intact beyond 1-2 years of age and tumors of the reproductive organs occur predominantly in aged animals.

Because mammary gland tumors are relatively common and often malignant, they deserve special mention.[11,26,41,42] Most cats that develop mammary carcinomas are 10 years of age or older. Mammary tumors are 7 times more common in intact females than in neutered ones. This has led to the suggestion that cats should be ovariohysterectomized before onset of ovarian activity to avoid exposure of mammary ductal tissue to ovarian hormones. Mammary tumors have been induced or potentiated in male and female cats by chronic megestrol acetate therapy.[47] Mammary tumors are rare in male cats.

Most mammary tumors in cats are malignant and spread via the blood and lymphatic systems. The tumors often metastasize both locally and distantly while they are relatively small; therefore, metastases can appear within 1-36 months following removal of the primary tumor. The tumor

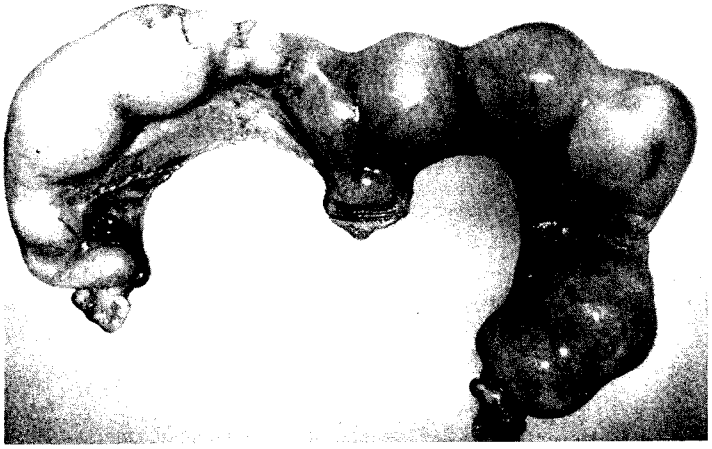


Figure 22. Uterine dilatations in pyometra may be mistaken for fetuses on abdominal palpation.

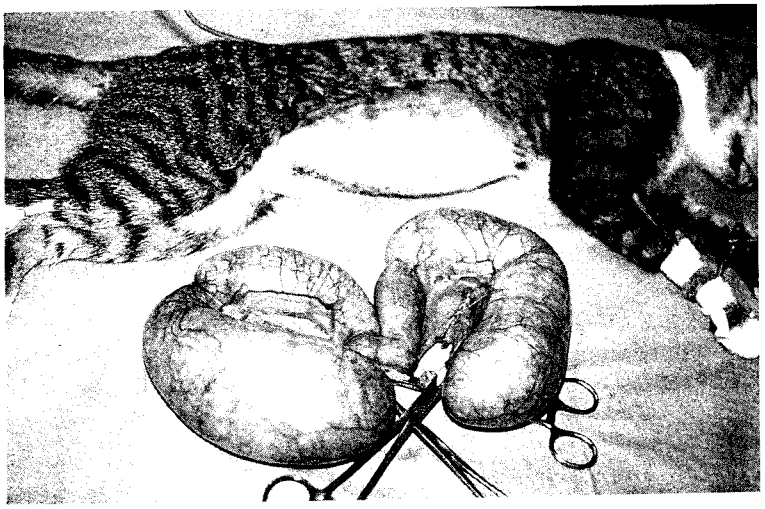


Figure 23. Grossly distended uterus removed from a queen with pyometra.

spreads progressively to the local skin and subcutis, lungs and chest wall (Figs 24, 25).

Lack of Libido in Toms

Lack of libido is relatively common in toms. Males should be given a general physical examination to detect conditions that may decrease libido, such as chronic illness and arthritis.

Normal libido may be reduced by inability to achieve intromission upon mating. In some cases, the penis may not extend normally from the sheath due to adhesions or other anomalies. Intromission can be inhibited by the accumulation of a ring of hair at the base of the penis (Fig 26). Inability to achieve intromission also can occur with disproportionate body length between the male and female. Because the male requires a neck hold for balance during mating, and therefore rides forward on the queen, a female with a long body may prevent intromission. Inability of the male to grasp the neck of the female due to inflammation of the mouth or loss of teeth also can affect the male's ability to copulate.

Decreased libido also may be due to lack of attraction between the male and a particular female, though the male may have normal libido with other females. Some cases of decreased libido may be due to behavioral factors unrelated to testicular activity. Toms with reduced libido often have normal testicular activity as judged by testosterone analysis and semen evaluation. While 1000 pg/ml is a low-normal serum level of testosterone, males can have normal libido with serum testosterone values considerably below 1000 pg/ml. Therefore, the importance of testosterone as a cause of reduced libido in male cats is questionable. If serum testosterone levels are reduced to the point of affecting libido, other reproductive functions including reduced spermatogenesis, also are likely to be affected.

Chromosomal anomalies (extra X chromosome) or male hermaphroditism (ovarian tissue present in testicles) usually result in reduced libido in affected males.[55]

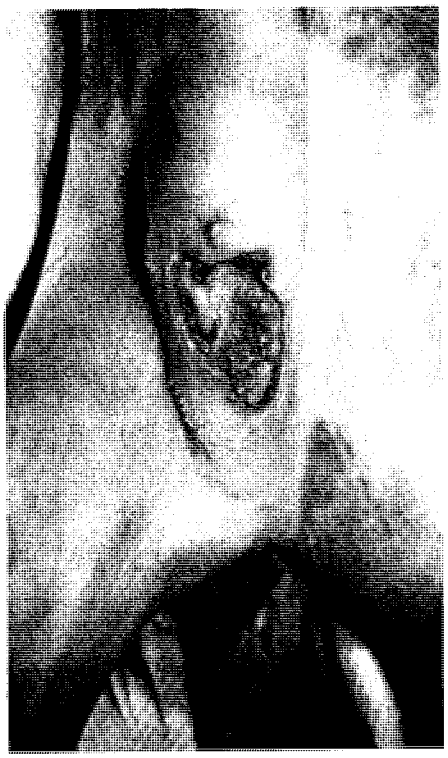
Libido may be increased by keeping the male from females, and then exposing the male to different estrous females for short periods. Use of testosterone to increase libido is not advised because testosterone deficiency is usually not the cause of decreased libido. Exogenous testosterone also inhibits normal production of endogenous testosterone by the male through the inhibition of luteinizing hormone secretion.

Poor Semen Quality

Males that copulate and ejaculate normally, but fail to impregnate queens, should have plasma testosterone concentrations and semen quality analyzed. Testicular biopsy can be performed in infertile toms, though hormone and semen analyses usually allow better evaluation of testicular function. Semen analysis allows assessment of sperm numbers and motility as well as morphology. Though semen can be collected with an artificial vagina, the problems associated with training the male to use the device make electroejaculation with the cat under anesthesia a better choice.[76,77,88,95]

If spermatozoan motility or morphology is abnormal, the reason for infertility is easily confirmed. It is more difficult, however, to find the reason(s) for sperm abnormalities, and more difficult yet to treat the con-

Figure 24. Ulceration with mammary carcinoma.



dition. If large numbers of white blood cells are present in the semen, especially if they are accompanied by bacteria, antibiotic treatment may improve sperm count and quality. Fortunately, infection of the male reproductive tract is uncommon.

Testosterone deficiency is usually not the cause of decreased spermatogenesis; therefore, testosterone treatment is unlikely to correct the problem.

Male Reproductive Infections

Microbial infections of the prostate gland, bulbourethral gland, testicles, epididymis and vas deferens are uncommon in male cats.[116] This might be anticipated, given the surprisingly low incidence of kidney, bladder and lower reproductive tract infections in cats as compared to such species as dogs.

Chronic low-grade bacterial infection of the spermatic cord can be a sequela of improper castration techniques. Leaving too much tunic after castration can create a nidus for bacterial infection. Suture materials used to tie off the spermatic cord may also cause irritation or encourage infection.

Figure 25. Pulmonary metastases from mammary carcinoma.

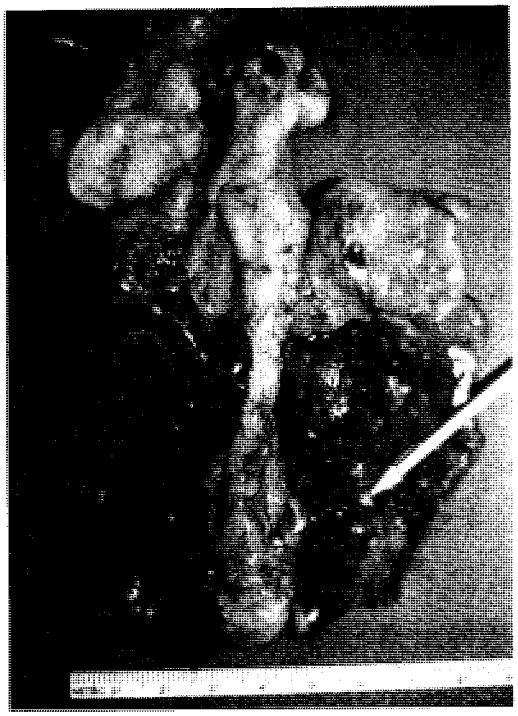
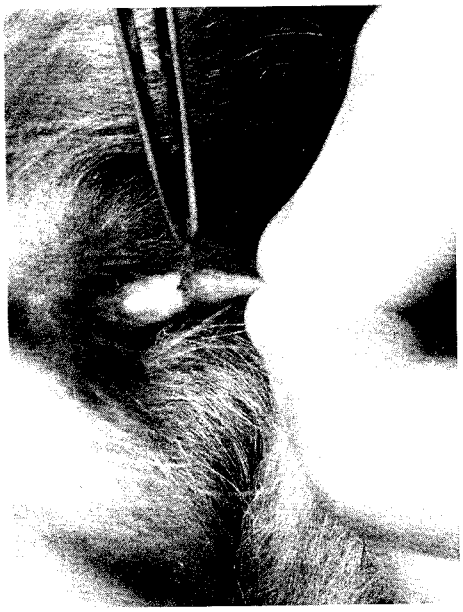


Figure 26. Hair ring encircling the glans penis. (Courtesy of Dr. B.L. Hart and *Laboratory Animal Science*)



In such cases, scrotal swelling and scirrhous enlargement of the spermatic cord stump may occur days or months after castration. The infection may eventually break through the overlying skin and form a chronic fistulous tract. Treatment consists of surgical removal of the infected tissues, including the involved remnant of the spermatic cord and any associated sutures.

A condition similar to scirrhous cord has rarely been observed in queens following ovariohysterectomy. Infection occurs in the uterine stump or the ovarian pedicle. Uterine stump infections may eventually drain into the vagina and cause chronic vaginitis. Infections of the ovarian pedicle may fistulate through the flank or cause localized granulomatous reactions in the abdomen. Peritonitis can be a sequela of either ovarian pedicle or uterine stump infections.

Periorchitis, manifested as testicular and scrotal enlargement, is a well-recognized complication of the effusive form of feline infectious peritonitis (see chapter on Infectious Diseases).

Cryptorchidism (Retained Testicles)

The testicles develop embryologically next to the kidneys and then migrate grad-

ually during fetal maturation through the abdomen, femoral (inguinal) canal, and finally into the scrotum. The testicles of cats are usually in the scrotum at birth or shortly thereafter. In cryptorchoridism, one (unilateral cryptorchidism) or both (bilateral cryptorchidism) testicles do not enter the scrotum. Unilateral cryptorchidism is far more common than bilateral cryptorchidism. Though the testicle(s) can be retained at any site along the normal migration path, usually they are retained within the femoral canal.

The cause of cryptorchidism most likely involves a defect in the structure or function of the gubernaculum. The gubernaculum is a cord that runs from the embryonic testicle to the scrotum. The testicle is pulled into the scrotum by progressive shortening of the gubernaculum. The retained testicle(s) does not develop normally because of the higher internal body temperature as compared to the temperature within the scrotum. The retained testicle produces male hormones but not viable spermatozoa. Therefore, if the scrotal testicle of a unilateral cryptorchid tomcat is removed and the retained testicle is left in place, the cat retains all of the physical and behavioral attributes of an intact male but is not fertile.

Cryptorchidism is a congenital and usually heritable trait in all species in which it has been studied. The precise genetics of the trait in cats are not known. It is apparently not a simple genetic trait, being polygenic in nature and possibly dominant. The trait is apparently carried by the queen that produces affected kittens. Therefore, queens that produce male kittens with cryptorchidism should be culled, along with affected males. Culling only affected males does not control the problem.

Human chorionic gonadotropin is used to treat cryptorchidism in men, but this practice has not been evaluated in tomcats. Surgical correction is usually not possible in cats because the retained testicle is usually too far from the scrotum.

Cryptorchidism in male cats can be diagnosed through determination of serum testosterone concentrations. Cats with a single retained testicle have serum testosterone values (200-1000 pg/ml) that are usually lower than the values for tomcats with scrotal testicles (1000 pg/ml or greater), but higher than values obtained from completely castrated tomcats (25 pg/ml).

The only treatment recommended for cryptorchid animals is castration. This involves removal of the scrotal testicle (if unilaterally cryptorchid) and the cryptorchid testicle(s) by surgical exploration of the abdomen or femoral canal. Some cryptorchid testicles move into the scrotum months after the normal time, so waitng until a cryptorchid animal is at least 1 year of age before castration is recommended. This is for the obvious reason that surgical removal of a scrotal testicle is easier and less expensive than removal of an abdominal testicle. Male cats with delayed testicular migration should be viewed in the same light as cats with permanently retained testicles. They are probably forms of the same heritable condition.

Gestational Reproductive Disorders

Ectopic Pregnancy

Pregnancies that occur outside of the uterus in the abdominal cavity are uncommon.[6,67] They usually occur when oocytes are fertilized outside of the fallopian tubes, or from retropulsion of fertilized oocytes as a result of abdominal trauma sustained shortly after mating. Acute signs of the disease are vague and include lethargy, abdominal tenderness and distention, with or without ascites. In some cases, however, a deformed, often mummified, fetus may be observed in the abdomen as an incidental radiographic finding, or at necropsy, with no history of acute clinical signs. Ectopic pregnancies must be differentiated from inapparent uterine ruptures, with expulsion of a fetus into the abdomen at the time of parturition.

Fibroadenomatous Mammary Hyperplasia

This condition is seen mainly in young queens at the time of puberty and in association with their first pregnancy or during pseudopregnancy.[12,40] Instead of normal mammary enlargement, the mammary glands become greatly enlarged (Fig 27).

The affected glands are hard and fibrous, with clearly delineated borders. Rapid growth of the affected tissue is sometimes associated with secondary bacterial infection and pressure necrosis of portions of the glands. Affected animals may show signs of illness including fever and depression. In most cases, however, affected queens are not ill and mammary enlargement is the main reason for presentation.

Fibroadenomatous hyperplasia of the mammary gland is treated by surgery (ovariohysterectomy) or hormone therapy. Spontaneous remission has been observed following pregnancy and lactation.[12]

Fetal Loss During Pregnancy

A general discussion of infectious, traumatic, genetic and nutritional causes of these disorders is provided in the chapter on Infectious Diseases.

Failure of corpora lutea to secrete adequate amounts of progesterone during pregnancy has been suggested as a cause of habitual abortion.[62] It is unlikely, however, that progesterone deficiency is a significant primary cause of abortion in the cat. Abortion is much more likely to be caused by abnormalities involving the endometrium or the fetuses. Nevertheless, queens that habitually abort are often treated empirically with progesterone.[62] Progesterone (in oil) can be given IM at 1-2 mg/kg body weight once weekly, beginning 1 week or more before the anticipated time of abortion and ending 7 days before parturition.

Dietary deficiencies can be a potential cause of abortion in cats. A deficiency of the amino acid, taurine, can result in abortion or birth of small kittens.[98]

Preparturient Vulvar Discharge

A bloody or purulent vulvar discharge at any time during gestation indicates impending abortion. Such signs are often an outward manifestation of abortion or fetal death and resorption.

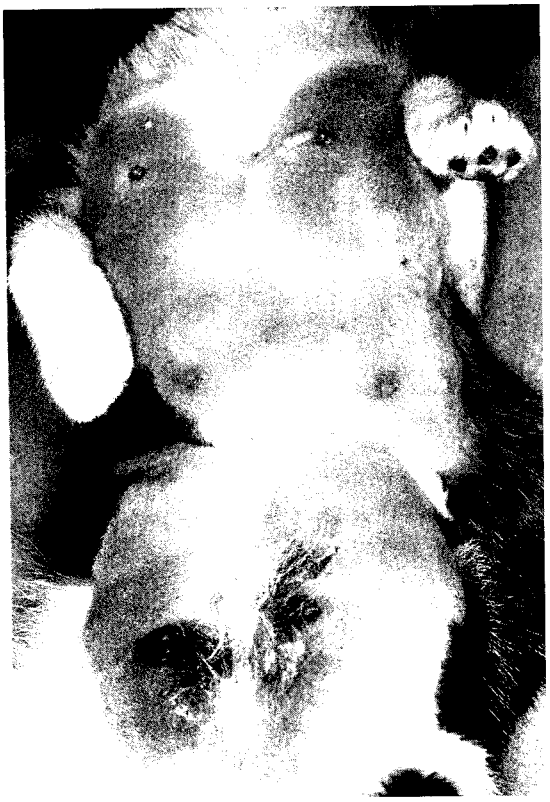
Parturient Disorders

Dystocia

Dystocia, or difficult birth, can occur in conjunction with the birth of any or all kittens in a litter. Dystocia is more likely, however, at onset of parturition during delivery of the first kitten. If the first kitten is born without difficulty, delivery of subsequent kittens usually is normal. It is important to recognize that the entire delivery process can be extended, sometimes occurring over 24 hours.

Dystocia is usually caused by lodging of a fetus within the uterus or pelvic canal. Kittens may not be able to pass through the pelvis because they are deformed or abnormally large. The pelvis may be too small for passage of normal-sized kittens or the kitten may be presented in an abnormal position. Kittens presented sideways, especially if they are doubled back on themselves, will almost always cause dystocia. Because the limbs of cats are relatively short as compared to the body, deliveries can occur whether the fetus is presented head or tail first.

Figure 27. Severe fibroadenomatous hyperplasia in a 9-month-old cat about 40 days pregnant. Note the pressure necrosis in the caudal glands. The mammary glands rapidly decreased in size after ovariohysterectomy.



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If any of the following signs are observed in the queen, dystocia should be suspected: straining for up to an hour that does not result in the delivery of a fetus; straining for at least 20 minutes, with a fetus obviously present in the birth canal; sudden depression with elevated (above 104 F) or subnormal (less than 97 F) rectal temperature; or sudden discharge from the vulva of large amounts (several teaspoons or more) of bright red blood and blood clots immediately before or after delivery, continuing for more than 10 minutes.

With any of these conditions, the queen should be examined and the position of the fetus determined. A kitten lodged in the birth canal is often found protruding (usually head first) from the vulva or positioned farther cranially in the pelvic canal. If the pelvic canal is empty, the abdomen should be carefully palpated to determine the fetus's position in the cranial pelvic inlet or the abdomen.

The position of the fetus is important for determining the best treatment of dystocia. If the head protrudes from the vulva, the fetus can be well lubricated with a lubricating jelly (Vasoline, K-Y Jelly) and gentle traction applied to the fetus. This traction should coincide with uterine and abdominal contractions by the queen. If the fetus cannot be delivered in 15 minutes of such effort, veterinary assistance should be sought.

If the fetus is within the pelvic canal but cannot be grasped with the fingers (obstetrical instruments should not be used by anyone other than a veterinarian), the pelvic canal should be lubricated and the cat allowed to continue in labor for an additional hour. If no kitten has been presented after this time, veterinary assistance should be sought.

If the fetus is at the cranial pelvic inlet but has not yet entered the pelvic canal, labor should be allowed to continue for 2 hours. If hard labor has not produced a kitten by this time, veterinary assistance should be sought.

Uterine Inertia

Uterine inertia is a failure of uterine musculature to contract in response to stimuli normally associated with parturition. Uterine inertia can be primary (uterine contractions are weak from the onset of parturition) or secondary (uterine contractions become progressively weaker as the birth process continues).

Primary uterine inertia results from inability of the uterus to contract effectively in response to hormones that cause uterine contractions ($PGF_{2\alpha}$ and oxytocin), or from failure of these hormones to be released in sufficient quantities at parturition. Primary uterine inertia is more likely to occur in overweight, sedentary queens.

Secondary uterine inertia, which is more common than primary uterine inertia, is due to exhaustion of the uterine musculature, usually from prolonged uterine activity. Exhaustion of the uterine musculature likely results from relative depletion of substrates in the myometrium necessary for proper contraction, or insensitivity of myometrial receptors to hormones that cause uterine contraction. Secondary uterine inertia is more common in queens that have very large litters.

Uterine inertia is difficult to diagnose in cats because they normally have prolonged periods of uterine inactivity between deliveries that last from minutes to hours. True uterine inertia requires veterinary assistance, while the uterine inertia that occurs normally between deliveries of individual kittens is not cause for concern.

Before treatment of uterine inertia, the animal must be checked carefully for fetal obstruction or uterine tears and ruptures. If a fetus is lodged in the birth canal or the uterus is damaged, use of substances that evoke strong uterine contractions is contraindicated. If there is no fetal obstruction or uterine damage, uterine contractions can often be stimulated by IV administration of oxytocin (single dose or continuous infusion). Before administration of oxytocin, it is important to determine serum calcium concentrations and correct any calcium deficit. If strong uterine contractions do not occur following combined calcium and oxytocin therapy, the kittens should be removed by cesarean section.

Uterine Torsion

Torsion of an entire gravid uterine horn, or part of a uterine horn is uncommon in cats. Uterine torsion tends to occur near or

at the time of parturition, though it has been observed at earlier stages of gestation (Fig 28). Torsion sufficient to obstruct the lumen of the uterus results in dystocia. Uterine torsion may cause a rupture, with release of fetuses into the abdominal cavity (see next section).

Clinical signs of uterine torsion often include acute abdominal pain, followed by depression and peritonitis. In some cases, however, the involved horn and associated fetal tissues undergo dry gangrenous necrosis without clinical signs. Uterine torsion may also spontaneously resolve following birth of the kitten(s), or following rupture and delivery of the kitten(s) into the peritoneal cavity.

Uterine Tear or Rupture

Uterine tears involve the mucosal surface (endometrium) and, at times, part of the underlying muscle layer (myometrium). They usually do not extend through the outer (serosal) membrane of the uterus. In contrast, uterine rupture involves all layers of the uterus. Uterine tears and ruptures often occur without obvious trauma. The gravid uterine wall can be very friable at term; contraction of the uterine musculature, coupled with pressure from fetal appendages, can be sufficient to tear or rupture the uterus.

A uterine tear may go unnoticed if it is shallow and no underlying blood vessels are severed. If a uterine artery is severed, however, profuse bleeding may result in death within 5-60 minutes. Rupture of an artery can be ascertained by the color of the blood (bright red because of its high oxygen content), the amount of blood (copious) and the form of the blood (presence of large clots) discharged from the vulva. Such bleeding represents a medical emergency, and the cat must receive veterinary attention immediately.

Uterine rupture may involve passage of the fetus and/or the placenta into the abdominal cavity. Some uterine ruptures cause an acute shock-like syndrome, with depression and abdominal pain early in the course of the syndrome. The condition may then spontaneously resolve with birth of the kitten(s), or may culminate with passage of the kitten(s) into the abdominal cavity with or without development of peritonitis. In cats with peritonitis, the abdomen has a doughy feeling on palpation and the animal shows signs of shock before death.

Uterine Prolapse

Prolapse of one or both horns of the uterus has been described.[28] The prolapse usually occurs during parturition or within 48 hours of delivery (Fig 29). The uterus is cleaned and replaced manually while the cat is heavily sedated or anesthestized. Ovariohysterectomy is indicated if the uterus is swollen, traumatized or necrotic.

Postparturient Vulvar Discharge

It is not uncommon for queens to have a reddish- to greenish-black vulvar discharge for several days to 3 weeks after parturition. The discharge consists mainly of degenerated blood and phagocytic cells. Such a discharge results from normal postpartum involution of the uterus. The duration and amount of discharge are proportional to the size of the gravid uterus, number of kittens, amount of hemorrhage during parturition, and rate of involution of placental attachment sites. If the discharge is not malodorous and does not contain large numbers of pus cells (neutrophils) or bacteria, and if the queen appears healthy, the discharge is of little concern. Veterinary attention is required if the discharge persists for longer than 3 weeks, or if it becomes copious or purulent, and the queen becomes depressed, febrile or anemic.

Retained Placenta

Each placenta is usually passed with the kitten or in conjunction with a subsequent kitten. In some cases, all or part of a placenta is retained in the uterus. The retained placenta undergoes necrosis and degeneration, and is often passed several days later. In some cases, the placenta slowly degenerates in the uterus and is absorbed. With placental retention, the amount and duration of postparturient vulvar discharge are often increased.

Retention of a placenta is usually not a medical emergency, providing that the retained material does not become infected. With secondary bacterial infection, vulvar

discharge becomes more copious, malodorous and purulent, and the queen may show depression, anorexia and fever. With secondary infection, the queen should be treated with antibiotics until the infection is resolved and the remaining placental tissue eliminated by resorption or vulvar discharge. In severe and life-threatening infections, the uterus and ovaries must be removed surgically (ovariohysterectomy).

Postparturient Endometritis

Postparturient bacterial infections of the uterus, while uncommon, are often severe when they occur. Postparturient uterine infections are more likely following first or second pregnancies, and are more likely to be a sequela of a difficult, rather than an uncomplicated delivery. Animals with retained placentas, fetal infections or uterine tears, are also more prone to postparturient uterine infections.

Clinical signs of postparturient endometritis often appear 2-10 days after parturition and are associated with a purulent, sometimes blood-tinged vulvar discharge. The queen may be depressed, inattentive to her kittens, anorectic, febrile and resentful of palpation of the abdomen. The uterus may be normal in size and consistency for the stage of involution, or enlarged and turgid. Kittens often become ill and may develop septicemia from contact with the vulvar discharge.

Figure 29. Postparturient uterine prolapse.

The vulvar discharge should be cultured to identify the most effective antibiotic therapy. Broad-spectrum antibiotic therapy (usually an aminoglycoside in combination with penicillins) should be initiated immediately. Once the organism is identified and its antibiotic sensitivity determined, the antibiotic regimen can be altered, if necessary. Bacteria commonly isolated from postparturient infections include *E coli*, *Pasteurella* spp, streptococci and staphylococci.

Figure 28. Torsion of one uterine horn (arrow) involved 2 of the 6 fetuses.

Anaerobic bacteria also can be primary or secondary pathogens in endometritis.

Postparturient Peritonitis

Severe bacterial peritonitis may occur postpartum as a result of uterine rupture, with or without fetal tissues present in the abdomen. The abdomen is often tender to palpation early in the course of disease, but becomes doughy, painless and distended on palpation after 1 or 2 days. Affected cats are often septic, depressed, anorectic and febrile. If the condition is not treated, shock rapidly ensues, leading to death.

Mastitis

Bacterial infection of lactating mammary glands (mastitis) is uncommon in cats.[38,83] Mastitis usually occurs within the first 2 weeks of lactation and tends to involve one or both caudal glands. Bacteria typically involved in mastitis are streptococci, staphylococci and *E coli*. Clinical signs include depression, anorexia and fever, coupled with reluctance of the queen to allow suckling. Bacterial septicemia in the queen may occur as a sequel in severe cases. The affected mammary glands are often swollen, hot and reddened. Infected glands may abscess or become gangrenous.[83] Sometimes the first evidence of mastitis in the queen is illness and death of the kittens from septicemia.

Treatment of uncomplicated mastitis involves culture of the milk to identify the offending bacteria and their antibiotic sensitivity. The queen should immediately be given aminoglycoside and penicillin antibiotics, with appropriate adjustments in therapy made when laboratory results are available. It is important to maintain adequate hydration in the queen.

Early weaning of the kittens is not necessary and, in fact, may complicate the problem due to retention of milk. If the kittens are depressed, blood cultures should be obtained and the kittens immediately given combined aminoglycoside-penicillin treatment pending culture and sensitivity results. If the kittens are not suckling, they should be hand fed. Failure to start immediate treatment of the kittens greatly increases mortality.

Queens with gangrenous or abscessed mammary glands should be treated both topically and systemically. Abscesses are lanced and drained, and gangrenous tissue debrided. Open wounds are then periodically cleaned, debrided and packed with topical antibiotic ointment or powder. It is not necessary to surgically remove the infected gland(s), as healing is usually rapid and complete once the lesion is opened and cleaned.

Postparturient Septicemia

Postparturient septicemia is a widely recognized but poorly described condition of queens that usually appears 2-10 days after parturition. It is usually associated with acute depression, anorexia, fever, agalactia, dehydration, shock and, in severe cases, death. Blood tests show evidence of hemoconcentration and an elevated white blood cell count associated with absolute neutrophilia and cellular toxicity. Blood cultures may yield aerobic bacteria, such as *E coli, Staphylococcus aureus, Streptococcus canis, Pasteurella multocida* and, in rare cases, highly pathogenic anaerobic bacteria, such as *Clostridium*.

The origin of the sepsis is often undetected but probably arises most commonly from the reproductive tract of the queen (see preceding sections on Postparturient Endometritis and Peritonitis). The mammary glands should also be carefully checked for evidence of mastitis (see preceding section on Mastitis). Treatment should be started promptly to avoid mortality. Shock, electrolyte and pH imbalance, and dehydration are usually treated by continuous intravenous administration of a balanced salty solution. Specific antibiotic treatment should be adjusted according to the antibiotic sensitivity of the bacterial isolate; however, affected animals should be treated with broad-spectrum antibiotics, such as a combination of penicillin and aminoglycosides, pending sensitivity test results.

Eclampsia

(Puerperal Tetany)

This condition, uncommon in queens, usually occurs during early lactation due to

reduced serum calcium concentrations resulting from milk production. Hypocalcemia results in tetany. Early signs include restlessness, muscle spasms and tremors, stiff gait, ataxia and increased salivation. Eclampsia may progress to lateral recumbency, with extreme clonic spasms of all skeletal muscles. Death may ensue from hyperthermia and respiratory muscle spasm.

Eclampsia is treated by IV administration of calcium gluconate or calcium chloride. In severe cases, lactation should be terminated and the kittens fostered onto other lactating queens. Once clinical signs subside, oral calcium gluconate supplementation should be provided for several weeks.

Preweaning Weight Loss and Diarrhea

Queens that have large litters and are lactating heavily often lose weight, and their haircoats become roughened in appearance. If this condition is allowed to continue too long, the queen frequently develops severe diarrhea. Once diarrhea occurs, the queen often loses additional weight, serum electrolyte levels are altered and dehydration results.

The cause of preweaning diarrhea of queens is unknown but is probably related to the chronic stress and malnutrition of chronic heavy lactation. In turn, stress and malnutrition may lead to decreased resistance to common bacterial infections of the bowel. Treatment consists of immediate weaning of the kittens, fluid therapy to correct fluid and electrolyte losses, and antibiotics to counteract potential bowel infections. With such treatment, recovery is usually rapid and uneventful.

The reader is referred to other sources for further information about problems associated with parturition and the perinatal period.[29,51,57,70] Other books contain further information on reproduction in cats.[10,15,22,29,115]

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Chapter 4

Common Infectious Diseases of Multiple-Cat Environments

N.C. Pedersen

Domestic cats seem to suffer inordinately from a variety of infectious diseases. Cats are not immunologic cripples, however. They belong to one of the most successful families of carnivores ever evolved on earth. Cats and their wild relatives are found on many continents and in varied climates. In their own environment, and under usual conditions of population density and pressure, cats handle infectious diseases very well.

Cats are not intrinsically sensitive to infectious disease, but seem so as a reflection of their modern environments. These environments are often totally different from the environments in which cats evolved. The concept that environment is one of the most important factors in determining the incidence and severity of disease is one of the pillars of our knowledge of infectious diseases. Infectious agents usually do not kill or incapacitate a significant number of their hosts. To do so would deprive them of the environment essential to their own survival. Therefore, when disease occurs, it must be the exception rather than the rule.

The term "infection" is not synonymous with the term "disease." Infection occurs when the microbe invades the body. Disease is caused by tissue damage from the invading microbe or the host's own attempts to contain or destroy the infectious agent. Many infectious agents cause mild or inapparent disease. For instance, most cats infected with coronaviruses, caliciviruses, parvoviruses, herpesviruses, feline leukemia viruses or feline immunodeficiency viruses do not demonstrate disease following infection. However, if factors are favorable, these same agents can cause severe and often fatal disease. Therefore, control and prevention of infectious "disease" depends on understanding factors that enhance the disease-causing potential of a microbe.

Factors Influencing Disease

We are frequently confronted with infectious diseases manifested in many different forms. Unfortunately, we are usually only aware of the most severe form. This form is often described in textbooks as being the "classic" or "typical" presentation. In truth, the proportion of animals developing this form of disease is usually small. When a cat is exposed to a disease agent under normal conditions, mild self-limiting or clinically inapparent disease usually occurs. When host and environmental factors are unfavorable, primary illness is more apt to be severe, persistent infections are more common, aberrant or chronic forms of the disease are more prevalent, and the overall death rate is higher.

Consider the following situation in which a young kitten is born to a household pet. As in most households, the queen is the sole cat and only about one-third of the households in the neighborhood have cats and very few of them produce kittens. There are very few kittens in the neighborhood, therefore, at any time. When the kittens are 6-9 weeks of age, they are weaned and adopted by a neighbor, friend or relative. The kittens are given only a panleukopenia vacci-

nation and dewormed. They live in their new homes for years without any apparent illness. Yet, when blood samples are taken years later, they contain antibodies to a number of different pathogenic microbes.

Contrast this to kittens born in a large cattery, where 25 adult breeding cats and numerous kittens of varying ages are raised together in several rooms. These kittens typically develop a series of clinical illnesses, starting as early as 2 weeks of age. Some of the kittens die before they reach 16 weeks of age, and a proportion of the survivors manifest signs of chronic disease. The death rate also is much higher than for kittens raised in a single-cat household. What so drastically altered the course of disease in the cattery-reared kittens? This question can only be answered through an understanding of factors that influence the course of infection (Table 1).

Heritable or developmental anomalies of the immune system can greatly influence the course of infection. Certain types of anomalies cause the host to be deficient in cell-mediated immunity, deficient in the ability to make all or certain antibodies, deficient in specific complement components, or deficient in the normal function of phagocytic cells. Some of these deficiencies may lead to a greater incidence and severity of infections, but may still allow the animal to live an otherwise normal life. Some anomalies may be so severe that the animal dies of overwhelming infections while still a kitten. Fortunately, heritable anomalies of the immune system are relatively rare in cats (see chapter on genetic disorders).

Table 1. Factors that influence the outcome of infection.

Host Factors
• Developmental and heritable anomalies of the immune system
• Undefined heritable resistance factors
• Maternal immunity (passive systemic and passive local)
• Age at time of exposure
• Multiple illnesses
• Nutritional state
Environmental Factors
• Population density
• Sanitation
• Ventilation
• Interchange of animals from one population to another
Agent Factors
• Virulence of the pathogenic microbe
• Strain differences
• Dose of the pathogenic microbe
• Route of infection

Undefined heritable resistance factors are far more important causes of immunodeficiency in cats than defined genetic abnormalities. Undefined resistance factors, as the name implies, are difficult to pinpoint to a specific defect. In this situation, a group of cats is born with an immune system that seems intact, and the animals are normal by every conceivable test of immune function. In spite of this apparent normalcy, one member of the group may react far differently from another when exposed to a certain infectious agent. This increased susceptibility to certain diseases may extend beyond individuals to bloodlines within breeds or to entire breeds themselves. For instance, breeds of Siamese origin seem to suffer inordinately from chronic nasal infections. Abyssinian cats appear to have more problems with gum disease than other breeds. Persians suffer inordinately from clinically apparent dermatophyte infections, and comprise an inordinate proportion of purebred kittens that succumb to feline infectious peritonitis.

As important as these undefined genetic factors are to disease, most breeders totally ignore disease resistance when selecting breeding stocks and developing bloodlines. They are often more interested in esoteric traits such as coat color, body conformation and size. Unfortunately, the fixing of many of these traits involves inbreeding. Inbreeding, if done properly, has a limited deleterious effect on the host, as witnessed in the many inbred strains of mice. More often, however, inbreeding is not done with care, and lethal or sublethal genes accumulate in increasingly greater numbers. The net effect of inbreeding is often a decline in vigor. This decline in vigor is hardly ever due to specific defects in immunity, but rather to accumulation of more subtle and multiple genetic defects that are impossible to define.

Maternal immunity is an important factor in infectious diseases occurring in kittens between 4 and 16 weeks of age. Maternal immunity provides protection for the

kitten from infectious diseases that may occur during the critical period when the kitten's own immune system is developing. Maternal immunity is of 2 types: passive systemic immunity and passive local immunity.[2]

Passive systemic immunity is derived from antibodies given to the kitten by its mother in the first milk (colostrum) during the first day of life.[2] Antibodies are concentrated in the colostrum in the mammary glands of the queen and are given to the kitten during nursing. The intestinal tract of the kitten is permeable to antibody globulins for the first day of life; after this time they are no longer absorbed but rather are digested in the same manner as other dietary proteins. A kitten ingesting colostrum attains levels of antibodies in its blood equal to those of the mother. Because these absorbed antibodies only have a finite lifespan in the body of the kitten, they eventually disappear. One-half of the total remaining amount is metabolized during each subsequent 7-day period.

Maternally derived antibody levels in blood are usually very low by 6-8 weeks of age, and negligible by 12-16 weeks. Fortunately, by about 4 weeks of age, the kitten's immune system begins to function and antibodies produced by the kitten's immune system appear in the blood at progressively higher levels. The period between 4 and 16 weeks of age is a time when relatively more and more of the antibodies are of kitten origin and less and less of maternal origin. Passive systemic immunity is present, therefore, when the kitten needs it the most and is gradually replaced as it is no longer needed. Passive systemic immunity is active in killing microbes that enter the bloodstream via local sites of infection in the skin or mucous membranes of the respiratory, gastrointestinal or urogenital tracts.

Situations that prevent adequate transfer of antibodies from the mother to the young cause the newborn animal to be susceptible to infection. Because the bulk of passive systemic immunity is derived from colostrum during the first day of life, adequate nursing of kittens at birth is essential. Failure of kittens to receive sufficient colostrum leads to severe and often fatal systemic infections in the neonatal period (first 2 weeks of life).

Passive local immunity is provided continually by the queen for as long as the kitten nurses. After the colostral phase of lactation ends (by 72 hours after birth), the kitten receives what is known as "milk."[2] Milk, like colostrum, also contains antibodies, but at much lower levels. These antibodies are of 2 types, IgG and IgA.[2] IgG antibodies are degraded by stomach acids, while IgA resists digestion and appears unaltered in the stool. Antibodies in the milk protect against infections that begin on the surfaces of the oral and intestinal mucous membranes. Pathogenic organisms ingested with the food are immediately destroyed by the milk antibodies; IgG works preferentially in the mouth, oropharynx and esophagus, and IgA works preferentially in the stomach and intestines.

Because the vast majority of common kittenhood infections begin in the oropharynx, passive local immunity is very important in preventing disease. Passive local immunity works in concert, therefore, with passive systemic immunity; one prevents infections locally, while the other works within the bloodstream. Passive local immunity, like passive systemic immunity, is slowly replaced by active local immunity. As the kittens reach 2-6 weeks of age, increasingly more antibody is produced by the tonsils and gut-associated lymphoid tissues and is transported into the saliva and mucus by cells lining the gastrointestinal, respiratory and urogenital tracts.[2]

For passive local immunity to be protective, the milk must contain the required complement of specific antibodies, the antibodies must be present in the milk in adequate amounts, and the milk must be ingested in sufficient quantities by the kitten. As an example, if the queen's milk does not have antibodies to rotaviruses, then the kittens will not be protected against rotavirus infection. Likewise, even if antibody is present in the milk, it is of no protective benefit if it is not ingested in sufficient quantity. Passive local immunity is lost when the kitten is weaned. In catteries, weaning is usually sudden. In nature, however, weaning is a slow affair. After 4-6 weeks of age, the kittens receive progressively less milk from their mothers (and less immunity) and the milk that is ingested contains progressively fewer antibodies. In this way, there is a slow

and progressive exchange of passive local immunity for active local immunity.

Age resistance is also very important. The immune system of the newborn kitten is very immature. By 2-4 weeks of age, the kitten's immune system begins a stage of rapid maturation. The immune system is well developed by 14-16 weeks of age. Continued development, albeit at a slower pace than in kittenhood, continues well into late adolescence.

If a kitten is infected at a young age, it does not respond as well to the infection and the resulting disease is much more severe. A number of factors allow microbes to overcome maternal immunity in young kittens. One of these factors is failure of the queen to pass on specific maternal immunity to the kitten. Even if the kitten is provided with maternal immunity to a specific pathogenic microbe, maternal immunity can be overcome if the exposure is severe enough. The maternal immunity may be sufficient to prevent infection with small numbers of the microbe, but not sufficient to prevent infection with exposure to large numbers of the microbe.

One of the best examples of age resistance has been demonstrated for feline leukemia virus (FeLV) infection (see section on FeLV infection). Almost all kittens infected in the neonatal period of life (first 2 weeks) become persistently infected and die within a few months to a year or so. In contrast, only about 50% of 12- to 16-week-old kittens become persistently infected following exposure; the rest recover and are immune for the rest of their lives. Even among those that become persistently infected, the disease course is longer. Adult cats are even more resistant to infection, with 70-95% recovering following initial exposure.

Multiple illnesses present in a cat at one time often make the cat more susceptible to coincidental infection with other disease agents. Disease can sap the body of necessary nutrients, or directly suppress the immune system and increase disease susceptibility. For instance, feline herpesvirus infection can damage the mucous membranes of the nasal passages, upper and lower respiratory tract, and conjunctiva of the eyes, and allow secondary invasion by resident bacteria. This is evidenced by a change in the character of the inflammatory secretions from clear (serous) to cloudy (purulent). Feline leukemia virus infection can increase the severity of many other diseases, including feline infectious peritonitis, hemobartonellosis, toxoplasmosis, cryptococcosis, feline immunodeficiency virus infection, feline herpesvirus infection, and a number of bacterial infections (see section on FeLV). Feline panleukopenia virus infection is immunosuppressive (see section on panleukopenia). Feline calicivirus infection is rarely fatal by itself, while feline panleukopenia has moderate mortality. If cats are infected with both calicivirus and panleukopenia virus at the same time, however, mortality is very high.[1] Flea infestations frequently increase dramatically in sick cats (see section on fleas). The reason for this is not completely understood, but may be due to decreased grooming.

Nutritional status is very important in determining a cat's resistance to infection.[4] Products of the immune response are proteins derived from body stores or directly from food that is consumed. Nutritional problems are usually manifested in kittens, pregnant and lactating queens, feral cats living in overpopulated or low-nutrient environments, and cats living in large multiple-cat households. Kittens are affected particularly severely. Caloric requirements per unit of weight in young animals are several times greater than requirements of adults. Specific nutrients, such as protein, vitamins and minerals, are also much different for young animals. Relative or absolute malnutrition is common in enterprises where large numbers of young animals are reared. Kittens are at the lowest end of the social order and must compete more for food, and are often further drained of energy and nutrients by kittenhood diseases.

Population density is one of the most important factors in determining the severity of disease within a population and in individuals within the group. The greatest single source (reservoir) for pathogens of cats is other cats. Many diseases of cats are carried and shed by a proportion of asymptomatic or partially symptomatic cats. A high population density favors spread of such infections because it increases the number of potential carriers in the environment, brings carrier and susceptible cats into closer proximity to each other, increases the

degree of environmental contamination of food, water, air and soil, and increases the dose or amount of infectious agent passed from contagious to susceptible animals. Equally important, overcrowding of cats increases socially induced stresses and increases competition for food. The former leads to increased adrenal gland secretions, immunosuppression and decreased resistance, while the latter increases the likelihood for relative or absolute malnutrition.

The effects of increased population density can be counteracted in part by enhancing ventilation (to dilute air-borne contamination) and excrement removal, and designing barriers to reduce social stresses. Unfortunately, these steps become more time-consuming and expensive as the population density increases. Most catteries and other large multiple-cat households do not make the necessary adjustments to the environments, and disease problems increase progressively as the population density rises.

Increased population density has an interesting interrelationship with other factors. For instance, in a normal urban situation, only every third or fourth household owns a cat and very few of these cats produce kittens. Kittens born in such households usually have no contact with cats other than the queen until they are 3-4 months of age. Then they begin to socialize with cats out of their immediate environment. Exposure to other cats is usually fleeting and the chance for infection low. In contrast, kittens born in a cattery or other large multiple-cat households are exposed to other animals immediately and become infected as soon as their maternal immunity is overcome (usually 4-12 weeks of age). In addition to exposure at a relatively young age, cattery kittens are apt to be exposed to much greater amounts of pathogenic microbes.

Interchange of animals between populations is important in disseminating disease. Each population has its own viral, bacterial, parasitic and protozoal flora. Because of the severity of disease in such environments, older animals are often carriers of the very disease agents that they suffered so much from as kittens. Cats within a given cattery or area are most resistant to the pathogens to which they are continuously exposed. However, they may have very little exposure to strains of organisms found in other isolated populations of cats. Animals transported from one population to another are likely to spread new strains and types of infectious agents into their new homes. In turn, they are also exposed to myriad unfamiliar microorganisms. Once a new type of infection is introduced into such a population, unfavorable environmental and host factors ensure rapid spread.

The spread of infection between relatively isolated populations involves both the group of animals into which the new animal is placed and the new animal itself. The newly introduced animal is often under heavy stress as a result of being uprooted from its familiar surroundings, transportation to the new surroundings, and disruption of social orders. Upon arrival in the new cattery, the cat is immediately bombarded with a number of pathogenic strains of microorganisms that it has never previously contacted. This exposure, coupled with stress, often leads to a series of infections occurring at one time or in rapid sequence. If the diseases are severe, the animal might require extensive treatment or even die. With time, however, the newcomer also becomes resistant to the resident organisms.

Introduction of new types of microbes into a group of susceptible cats by a newcomer has more serious consequences than the opposite situation described above. In the previous situation, only the cat that was introduced is affected. In this situation, a larger number of resident animals is involved. Pathogenic microbes spread very rapidly in a closed group of animals, especially when they have no resistance to them. An explosive outbreak of disease often follows. The outbreak may involve most of the population, and cats of all ages. As the new microbe establishes itself in the environment, disease becomes less frequent and occurs mainly in kittens. This is because the older cats become immune. This protective immunity is passed on to the kittens by their mothers, but only lasts until 6-12 weeks of age. At this time, the kittens are the only susceptible animals in the premises.

Interchange of kittens is most apt to cause problems, followed by interchange of

adolescents, then adults <4 years of age, and least likely, aged cats. Kittens are most susceptible to disease, and are the worst carriers and shedders of pathogenic microbes. With time, their immunity becomes progressively stronger, and fewer remain carriers; those that remain carriers also shed fewer organisms. Therefore, if new cats are to be introduced into a cattery, the emphasis should be on adult cats, followed by adolescents, and then kittens that are at least 16 weeks of age. Kittens younger than 16 weeks of age are most likely to cause problems. When purchased, they should be isolated and slowly introduced into the cattery.

Environmental temperature and humidity are significant factors in infection. Certain species of animals have optimum temperature and humidity requirements for good health. Cats do best when the humidity is low and the temperatures relatively high. Cold, wet climates are the worst. The exact temperature and humidity are often less important than fluctuations of temperature and humidity. If temperature and humidity fluctuate wildly from week to week, disease may be more of a problem even though the minimums and maximums are within the suggested levels.

Temperature extremes may influence disease by inducing stress. This has been one explanation for outbreaks of the common cold in people following extremely cold bouts of weather. More often, however, extreme weather changes cause animals to congregate together. For instance, animals and people are often brought together in cramped, poorly ventilated quarters during inclement weather. Certain ranges of temperature and humidity may also favor persistence of microbes in the environment. Heat and dryness have a destructive effect, while cold and dampness have a protective effect on microbes. Certain temperatures and humidities may even favor certain stages of the microbe. Warm, damp weather favors survival of many nematode ova and larvae. The life cycle of the flea from egg, larva, pupa to adult is very temperature and humidity dependent.

Stress is a nebulous term and difficult to measure. It can result from infectious diseases, noninfectious diseases, sudden and severe changes in the weather, nutritional inadequacies, and emotional instability. Stress is mediated through the endocrine (in particular the adrenal glands) and autonomic nervous systems. The endocrine and autonomic nervous systems interact closely with each other, so that effects on one are manifested on the other. Ultimately, stress has a negative effect on the sense of well-being of the cat and its ability to fight disease.

Stress is usually not outwardly apparent. Stress has its effect in subtle ways and over long periods. A cattery may appear well kept and the cats outwardly happy. But beneath this veneer there may be an increased incidence of behavioral problems (see chapter on behavior) and infectious diseases. Just as it is frequently impossible for one person to evaluate the level of stress that another person is undergoing, it is also often impossible for a cattery owner to appreciate the stress levels among individual cats or in the cattery as a whole.

Virulence of the organism is the propensity for a given dose of microbes to cause disease. Organisms that do not cause disease, regardless of the infecting dose, are considered avirulent. An organism that causes minimal disease, even when given in large numbers, is considered of low virulence. Pathogenic microorganisms that cause severe disease, even when given in small numbers, are considered highly virulent.

If the host is heavily stressed or immunocompromised by other diseases, an organism that is usually of low virulence may cause severe disease. Some species, breeds or bloodlines of animals are more susceptible to a given dose of a particular strain of pathogen than others. An organism of low virulence to one cat may be highly virulent to another, therefore. Some microorganisms are more virulent for reasons intrinsic to the organism itself. Disease-causing agents contain genetic material that determines their structure. The genetic structure of the organism, may greatly influence the ability of the organism to cause disease. For instance, some strains of *E coli* bacteria have surface proteins that allow for attachment to intestinal cells and also produce certain types of enterotoxins. They are the strains that are invariably associated with diarrhea. Other strains lack these proteins and

are not pathogenic. Some strains of feline leukemia virus are of low disease-causing potential, while others almost selectively cause anemia or lymph node cancers after a short period of infection. Caliciviruses exist in dozens, and perhaps hundreds, of serotypes or strains. The various serotypes can cause different severities of disease and even different disease signs. Feline infectious peritonitis virus also exists in numerous strains; some are very virulent, while others are minimally pathogenic.

Differences of strains of pathogens play a role in infection. Strains are genetically distinguishable members of the same species of organism. Strictly speaking, one organism differs in strain from another if the host's immune system perceives them in a different manner. For example, a particular *E coli* infection of the intestine elicits antibodies against the infecting organisms. If these antibodies fail to prevent infection with another isolate of *E coli,* then the second strain of *E coli* is a different strain. Strains may also be defined by the type of disease they cause; an *E coli* that causes enteritis is sometimes referred to as an "enteropathic strain," while an *E coli* that does not cause enteritis is termed "non-enteropathic."

The occurrence of different strains of microorganisms poses a threat to the host. Not only must the host generate immunity to each type of organism, but it must respond to several different strains of the organism. Many cattery owners and veterinarians believe that if a cat is given a vaccination for calicivirus that it will be immune to all calicivirus infections. However, caliciviruses exist in many strains and a cat immunized with a calicivirus vaccine is only immune to those strains in the vaccine. If the vaccine protects against almost all strains, or against the most important or common strains will it be effective. If the vaccine protects only against a few strains or against strains that are not commonly seen in the vaccinated population, it will not be effective. If only one strain exists for a particular pathogen, immunity to one isolate protects against all other isolates.

In regard to dose, generally, the more of an agent that is taken into the body at the time of initial exposure, the more severe the resulting disease. In the case of some pathogens, there is even a threshold dose for disease. For instance, many pathogenic intestinal bacteria do not cause infection if they are ingested at low levels. However, as the level of ingestion rises, a point is reached where disease occurs. The most important way to decrease disease is to limit the dose of the organism. Optimally, the dose should be reduced to zero, or to a level below the infection threshold.

Route of infection is also important. Infectious agents may enter the body by several routes, such as by mouth (oral), inhalation into the upper and lower respiratory tracts, up the urogenital tract, or inoculation through the skin. Most pathogenic microbes enter the body by the route that is most conducive to causing disease. This is called the "natural route of infection." Even if the organism were to enter the body by another route, the infection is often the same. In some cases, however, the route may greatly influence the disease course. Feline herpesvirus does not produce disease when inoculated into the muscles or subcutaneous tissues. However, if it is placed on the mucous membranes of the nose or eyes, it causes disease. This is because herpesvirus does not replicate very well at the slightly higher temperatures in the core of the body. The mucous membranes, being slightly cooler because of exposure to the outside air, favor virus replication. This phenomenon was used to produce some of the early feline herpesvirus vaccines. If the vaccine was given by injection into the tissues, it did not need to be altered so much in virulence. If the same vaccine were put on membranes of the nose or eyes, it would cause disease, however. It is not surprising, therefore, that many of the early live feline herpesvirus vaccines actually caused the very disease they were supposed to protect against; if vaccine virus contaminated the fur at the site of injection, it was rapidly groomed onto the tongue, paws and eyes, where it would cause disease.

Proper and Improper Immunization

Infectious diseases are more common and severe in young animals, so this is the obvious age group requiring immunization. Unfortunately, vaccines are only available for a handful of infectious diseases. However, these diseases are among the most im-

portant. It is important to understand why vaccines are given in a certain way so that their effect can be maximized. The most important questions are the timing and number of vaccinations.

Most kittens begin their vaccinations at 6 weeks of age. This age was not picked for arbitrary reasons. Maternal immunity (in particular, passive systemic immunity) interferes with vaccination for the first 4-6 weeks of life. This inhibitory effect disappears between 6 and 16 weeks of age as maternally derived antibodies disappear from the blood. The immune system has no need to respond to a vaccine before this time, because maternal antibodies are already present. Even if maternal immunity were not present, kittens <4 weeks of age have poorly developed immune systems and are not capable of responding well to vaccines. For both reasons, vaccinations should not be started earlier than 6 weeks of age.

Maternal immunity is also why vaccines are given as a series of injections, starting at 6 and ending at 12-16 weeks of age. The last immunization is given at a time when virtually all maternal immunity has disappeared and the kitten is fully immunizable. For some kittens this is as early as 6 weeks of age, while for others it is up to 12-16 weeks of age (depending on the level of antibodies obtained from the queen). If it were easy and inexpensive to determine the time when maternal antibodies to a particular vaccine disappear, then it would be possible to immunize the kitten with one dose of vaccine. So what, you might ask! Just give the immunization at 12-16 weeks of age when it is certain that virtually any kitten will respond. If only one dose is given at 12-16 weeks of age, however, some kittens might go unprotected for many weeks (those that lost their maternal immunity early). As a logical solution, why not give a dose of vaccine at intervals throughout this 6- to 16-week age period? If a kitten loses its maternal immunity at 6 weeks of age, the first immunization will provide protection. If it loses its maternal immunity at 9 weeks of age, the first dose will not be effective, but the second will provide protection, etc. By giving a series of immunizations at 3-week intervals, each kitten is unprotected for a minimum of time.

What determines the interval between kittenhood vaccinations? Three weeks is usually the minimum period between immunizations. The reason is because of what is called the "booster effect." Once maternal immunity is gone, the next dose of vaccine evokes an immune response and antibody production. This initial response may be low, however. Following a second immunization several weeks later, the immune response may be greatly amplified or "boosted." This booster effect is not as apparent if the vaccinations are given too closely together. An interval of 2 weeks does not give the immune system enough time to become adequately prepared for a second stimulus. Three-week or longer intervals provide more time for such stimulation. If 4-, 5- or 6-week intervals give a better booster effect than 3 weeks, why not use these intervals instead? The 3-week interval between vaccinations is a reasonable compromise. Two weeks is too short, and if you wait much longer than 3 weeks, the kitten may go unprotected for too long.

Terminology

Before studying infectious diseases, it is important to understand a few useful terms. An *epizootic* refers to a sudden or explosive outbreak of disease within a group of susceptible animals. The equivalent used term for human disease is *epidemic*. The spread of the disease is rapid, the *morbidity* (disease incidence) and *mortality* (death rate) may be high, and animals of all ages are often affected. Epizootics usually follow introduction of a disease agent into a population that has had no previous exposure to the microbe. As the population adjusts to the new infection by genetic selection (survival of the fittest) and immunity is acquired, a high degree of resistance develops in the survivors. This resistance is passed genetically to the offspring and from queen to kitten in the form of passive systemic and local immunity.

Development of genetic resistance and acquired immunity to a particular pathogen does not necessarily translate to disappearance of the organism from the environment. Many agents persist very well in resistant populations without causing serious illness. In fact, they have reached the ideal host-parasite relationship. The parasite and

host live together, sometimes for months, years or even lifetimes. Animals that harbor pathogenic microorganisms are called *carriers*. Some carriers shed the organisms continuously from their bodies; such animals are called *active carriers*. Calicivirus and feline leukemia virus carriers actively shed these organisms and are therefore active carriers. In other instances, the organism remains in a dormant or inactive form in the host and is only shed under certain circumstances. Such animals are called *latent carriers*. Feline herpesvirus carriers are latent carriers most of their lives, but under conditions of stress or other types of immunosuppression, they may temporarily become active carriers and shed the organism.

Disease that persists within resistant populations of cats is usually of an *enzootic* nature. The human equivalent of this term is *endemic*. Enzootic disease occurs mainly in young animals that have not yet acquired active immunity. Enzootic disease does not usually occur in older cats because older animals are usually infected when young and are immune. Enzootic disease is associated with much less morbidity and mortality than epizootic disease. It is more sporadic in its occurrence. Many cattery owners with enzootic herpesvirus, chlamydial, mycoplasmal and coronavirus infections underestimate the magnitude of their disease problems because the disease incidence and severity are not sudden and dramatic. Over a long period, however, more death and suffering can result from enzootic disease than from epizootic disease.

Sporadic disease refers to clinical infections that occur in a small proportion of animals at indefinite and often long intervals. Enzootic feline infectious peritonitis is often a sporadic type of disease. *Incidental, accidental* or *spurious diseases* usually involve individual animals and occur when the animal accidentally contacts a reservoir of the agent. A cat that contracts salmonellosis while feeding on an infected bird is spuriously or accidentally infected. *Nosocomial* infections result from exposure to pathogens that usually reside in a clinic or hospital. Nosocomial agents are often highly drug resistant, because they often originate from animals that are being treated heavily with antimicrobial drugs. Since most animals are hospitalized because of illness, and ill animals are more susceptible to infection, nosocomial infections are most likely to be seen in a hospital setting.

Environmental or *occupational diseases* occur when susceptible animals contact pathogenic microorganisms within their environment. The infectious agents have free-living niches in nature and do not require infection of cats for their survival. Cryptococcosis, a yeast infection transmitted in pigeon or dove feces, occurs mainly in cats from cities where pigeons abound or in homes where pigeon or dove cotes are maintained. Cat-bite abscesses, which occur almost exclusively in cats allowed to roam free, are occupational in origin, in that biting is a behavior that is occupational among free-roaming cats.

Opportunistic infections are due to microbes that are minimally pathogenic under normal circumstances but cause disease in immunocompromised hosts. Opportunistic organisms may be part of the normal flora of the cat or residents of the environment. Periodontal disease caused by normal oral bacteria in cats with feline immunodeficiency virus or FeLV infections is opportunistic.

Vectors are species of lower animals that transmit pathogens to susceptible hosts. Vectors may be inanimate, such as a grass awns or splinters, or animate, such as fleas or ticks. Many animate vectors are efficient transmitters of infectious diseases because they are natural prey species of the cat and important for the life cycle of the disease agent. Tapeworm infections (*Dipylidium canis*) are transmitted by fleas; one part of the life cycle of the tapeworm is in the flea, and the other in the intestine of the cat. Small birds, lizards, amphibians and rodents may be reservoirs for certain stages in the life cycle of *Toxoplasma*.

THE ENVIRONMENT AND DISEASE

Several hundred different bacterial, fungal, rickettsial, chlamydial, mycoplasmal, L-form, viral, protozoal and parasitic diseases affect cats.[3] Cats are exposed to these diseases in 8 general ways: 1) spread from the queen to the kittens *in utero* (congenital infections) or during the first 2 weeks of life (neonatal infections); 2) fleeting oral, mucous membrane or skin contact with excre-

tions (feces, urine), secretions (saliva, nasal mucus, tears, sexual fluids, pus), or exfoliations (dander, hair) from other cats; 3) bites, from which infectious material in the saliva of one cat is inoculated directly into the tissues; 4) inanimate fomites in the environment, such as vegetation, soil and water, that are contaminated with microorganisms; 5) contact with animals upon which the cat preys or *vice versa* (other mammals, reptiles, amphibians, insects); 6) mutation of one pathogenic agent to another within the body of the cat; 7) as opportunistic infections due to normal host or environmental microorganisms that take advantage of an immunocompromised host; and 8) as hospital-acquired infections (nosocomial infections), usually as a result of some medical procedure and involving antibiotic-resistant organisms.

Table 2 lists many of the common infectious diseases found in cats in various parts of the world and their major mode of infection. After reviewing Table 2, it should become obvious that certain diseases of cats may be more concentrated in one environment than another. For instance, free-roaming cats are at risk for diseases transmitted by inanimate fomites, such as vegetation, soil and water, or by animate fomites or vectors (prey animals of the cat, animals that may feed on the cat, or animals the cat may contact in its wanderings). Cats kept strictly indoors would not be exposed to such diseases. Biting, a behavior almost exclusively of outdoor cats, is not apt to be an important factor in disease transmission in cats kept indoors in stable groups. Diseases like FIV infection and cat bite abscesses are likely to be uncommon, therefore, in indoor cats but prevalent among outdoor animals.

By and large, only those diseases listed in Table 2 with a mode of transmission of congenital or neonatal, direct cat-to-cat contact, pathogenic mutants of common infectious agents, or opportunistic infections are likely to be important in catteries or cattery-like environments (pounds, shelters, multiple-cat households). It is also important to note that vaccines are available for many of the common diseases seen in cattery environments, and that use of such vaccines may modify the severity of disease in the environment. The degree of modification depends, however, on how routinely they are used and how good the vaccines are in preventing infection. For instance, panleukopenia vaccine is considered highly effective and has virtually controlled the disease in catteries. Feline calicivirus, herpesvirus and chlamydial vaccines are much less effective in controlling their respective diseases in high-density, high-stress environments. Feline leukemia vaccines, as presently formulated, are only partially effective in preventing infection.

In addition to whether cats are kept mainly indoors or allowed to run free, other factors play a role in the type of diseases that tend to be found within certain environments. The presence of breeding animals also in an important factor, as breeding allows for diseases that transmit from queens to their kittens, and adds kittens to the disease equation. Kittens are especially important because they represent a highly susceptible population. Kittens are more easily infected and are more likely to show disease signs. Because kittens often become sicker than older animals, they shed much more of the pathogen and are a greater source of infectious agents for other cats, especially for other kittens. Such environments as purebred catteries and pounds are much more likely to have serious infectious disease problems than multiple-cat households that keep only neutered animals, therefore. Pounds and shelters that accept large numbers of kittens also suffer more disease problems than similar institutions that accept mainly older cats.

The multiple-cat household with the lowest level of disease is one in which cats are purchased from a relatively disease-free source and maintained strictly indoors for the rest of their lives. The worst environment is an overpopulated, improperly constructed, purebred cattery. Though the range of diseases that occur in catteries is relatively smaller, the severity of disease can be worse than in free-roaming cats.

Though the worst environment in terms of severity of disease is a purebred cattery, the worst environment in terms of both severity and diversity of infections is a large, multiple-cat household of dozens of neutered and intact cats acquired as strays or from the feral pool of animals. These households often collect 20-60 or more adults as well as kittens, and cats are kept both in-

Table 2. Infectious diseases of cats and their common mode of transmission.

Disease	Causative Agent	Mode(s) of Transmission
	Viruses	
Pox	Rodent poxvirus	O,P
Panleukopenia	Parvovirus	C,D
Rhinotracheitis	Feline herpesvirus, type 1	C,D,O
Pseudorabies	Pseudorabies virus	P
Rabies	Field strains of rabies virus	D,P
	Vaccine strains of rabies virus	F,O
Enteritis	Coronavirus, rotavirus, astrovirus	D
Calicivirus infection	Feline calicivirus	C(?),D
FIP	Feline infectious peritonitis virus	C,D,M,O
FeSFV infection	Feline syncytium-forming virus	B,C
FeLV infection	Feline leukemia virus	B,C,D,M
Viral sarcomas	Feline sarcoma virus	M
Feline AIDS	Feline immunodeficiency virus	B,D(?)
	Bacteria	
Pseudomonas infection	*Pseudomonas*	O
Enteritis	*Campylobacter*	D,O
	E coli	D
Salmonellosis	*Salmonella*	D,P,O
Staph infections	*Staphylococcus*	B,C,D,O
Strep infections	*Streptococcus*	B,C,D
Pasteurellosis	*Pasteurella multocida*	B,C
Bordetellosis	*Bordetella bronchiseptica*	D,O
Tularemia	*Francisella tularensis*	P
Tetanus	*Clostridium tetani*	F
Anthrax	*Clostridium anthracis*	F
Tyzzer's disease	*Clostridium piliformis*	P,O
Plague	*Yersinia pestis*	P
Abscesses	Anaerobic and aerobic bacteria	B
Listeriosis	*Listeria monocytogenes*	P
Leptospirosis	*Leptospira*	P
Nocardiosis	*Nocardia*	F
Dermatophilosis	*Dermatophilus*	F
Mycobacteriosis	*Mycobacterium*	F,P,O
Actinomycosis	*Actinomyces*	B,F
Serratia infection	*Serratia marcescens*	N
EF-4 pneumonia	Eugonic fermenter-4	O
	L-Forms	
Abscesses, arthritis	Unknown species	B(?),D,P(?)
	Mycoplasmas	
Conjunctivitis	*Mycoplasma felis*	C,D
Fetal death(?)	*Mycoplasma, Ureaplasma*	C
Arthritis	*Mycoplasma*	D,O
	Chlamydia	
Conjunctivitis	*Chlamydia psittaci* var *felis*	C,D
Infertility(?)	*Chlamydia*	C
	Rickettsiae	
Hemobartonellosis	*Hemobartonella felis*	B(?),C(?),O
Q-fever	*Coxiella burnetii*	C,P

B = bites
C = congenital or neonatal infection
D = direct contact
F = fomites
M = mutation of agent
N = nosocomial infection
O = opportunistic infection
P = prey animals

(Table 2 continued)

Disease	Causative Agent	Mode(s) of Transmission
	Fungi	
Coccidioidomycosis	*Coccidioides immitis*	F
Histoplasmosis	*Histoplasma capsulatum*	F
Blastomycosis	*Blastomyces dermatitidis*	F
Cryptococcosis	*Cryptococcus neoformans*	F,O
Dermatomycosis	*Microsporum, Trichophyton*	D,F
Sporotrichosis	*Sporothrix schenckii*	F
Aspergillosis, mucormycosis, candidiasis	*Aspergillus, Mucor, Candida*	F,O
Protothecosis	*Prototheca*	F
	Internal Parasites	
Toxocariasis	*Toxocara cati*	C,D,P
Heartworm infection	*Dirofilaria immitis*	P,O(?)
Lungworm infection	*Aelurostrongylus*	P,O(?)
Nasal worm infection	*Mammomonogamus ierei*	P
Trichuriasis	Trichurid worms	D,P
Trichinellosis	*Trichinella spiralis*	P
Hookworm infection	*Ancylostoma, Uncinaria*	D,P
Stomach worm infection	Trichostrongyloid worms	D
	Spiruroid worms	P
	Physalopterid worms	P
Strongyloidosis	*Strongyloides*	D,F
Fluke infection	Lung flukes	P
	Liver and biliary flukes	P
	Pancreatic flukes	P
Tapeworm infection	*Dipylidium, Joyeuxiella, Taenia, Diphyllobothrium, Spirometra*	P
Thorny-headed worm infection	Acanthocephalan worms	P
	External Parasites	
Ear mite infestation	*Otodectes cynotis*	D
Mange mite infestation	*Cheyletiella*	D
	Chigger mites	F
	Demodex	C,D,O
	Notoedres	D,O
	Sarcoptes	P,O
	Lynxacarus	D,O(?)
Lice	*Felicola subrostratus, Trichodectes*	D,P,O(?)
Flea infestation	*Ctenocephalides felis*	D
	C canis, Pulex irritans	P
	Echidnophaga	P
	Protozoa	
Coccidiosis	*Isospora*	D,P
	Besnoitia, Hammondia, Sarcocystis	P
Toxoplasmosis	*Toxoplasma gondii*	D,P,O
Cryptosporidiosis	*Cryptosporidium*	D,P(?),O
Babesiosis	*Babesia, Nuttallia*	P
Cytauxzoonosis	*Cytauxzoon felis*	P
Giardiasis	*Giardia*	D,P,O(?)
Trypanosomiasis	*Trypanosoma*	P
Leishmaniasis	*Leishmania*	P
Encephalitozoonosis	*Encephalitozoon*	C,D
Hepatozoonosis	*Hepatozoon*	P

B = bites
C = congenital or neonatal infection
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doors and outdoors. A certain subpopulation moves freely between the 2 environments. Cats in such households suffer both from the common enzootic types of diseases that are the bane of purebred catteries, as well as from the more exotic diseases transmitted among outdoor cats.

Certain diseases may be greatly amplified by the type of environment. For instance, feline leukemia virus infection is enzootic among free-roaming cats, and 1-7% of such animals are persistently infected at any given time (see section on FeLV infection). In the decades before the discovery of FeLV detection tests, FeLV was rampant among both purebred catteries and multiple-cat households. The ultimate source of the virus for these catteries and households was cats that were infected in nature, but the subsequent rapid spread and severity of the disease were a direct result of the husbandry practices employed. In the outdoor environment, the virus is transmitted both by direct contact with secretions and by biting. Because outdoor cats are at some distance from each other and intimate contact is therefore limited, contact transmission involves a relatively small amount of virus. Because the cats are usually older when they contact infected cats, and exposure is apt to be slight, most infected cats recover and only a small percentage remain persistently infected and capable of transmitting the infection. If a FeLV carrier cat is brought into an indoor or indoor/outdoor environment with a high density of cats, close contact between animals, a high level of stress, and shared use of food and litter containers, contact transmission is much more efficient and the exposure dose is much greater. Many of the cats are also younger, and therefore more susceptible to infection. As a result of these unfavorable environmental factors, FeLV infection is much more severe; instead of about 5% of cats becoming persistently infected as in the outdoors, 30% or more of infected cats remain infected for life.

Feline immunodeficiency virus (FIV), another retrovirus, is a problem in outdoor cat populations but not in catteries and multiple-cat households (see section on FIV infection). FIV is spread almost exclusively by bites, while FeLV is transmitted efficiently both by bites and close contact. Once an FIV-infected cat is brought into the home or cattery, biting behavior is suppressed and so transmission of FIV decreases. FIV infection is only a serious problem, therefore, in multiple-cat households that adopt stray cats or those from the feral outdoor population and that allow their cats to run more or less free after they are tamed.

Pounds tend to have disease problems similar to those in catteries because they both deal with a mixture of older cats and kittens, and their housing and husbandry are similar. Therefore, pound cats suffer mainly from diseases that are spread by cat-to-cat contact. Further, the diseases seen in pounds are more apt to be of an acute nature, rather than a chronic one. Panleukopenia, herpesvirus infections, and various enteric and upper respiratory diseases are the most important infections seen in pounds. Such chronic diseases as FIV and FeLV infections and FIP are not apt to be a problem because the cats are not kept long enough for these diseases to develop.

Shelters, on the other hand, tend to have much less turnover of animals. Cats brought to the shelter are often older animals from owners that are no longer able to care from them, or strays and feral cats brought to the shelter by well-meaning cat lovers. Because shelter cats are kept for longer periods, sometimes for a lifetime, chronic infectious diseases are likely to be as important as acute ones.

Another group of cats worth mentioning is farm cats. If farms provide food for wild and semi-wild cats, farm-cat populations can sometimes become very large. As the populations grow larger, a greater proportion of the animals is comprised of kittens and adolescents. When the kitten and adolescent populations become large enough to sustain an epizootic, outbreaks of disease tend to occur. Vaccination is usually not carried out, and there is very little protection against common diseases. Panleukopenia is a particularly severe disease in such environments, and outbreaks are often associated with considerable mortality in younger animals. A farm may have 60 or more cats one year, and only a dozen the next year. The population slowly increases again, awaiting the next major outbreak of disease. This phenomenon has actually been used to limit a feral-cat population on an isolated island and bird sanctuary in Africa.

The cat population decreased from 3409 cats in 1977 to 615 in 1982 after introduction of panleukopenia virus.[5]

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DISEASE-CAUSING MICROBES

Several different types of pathogenic microbes are involved in infectious diseases of cats.[1] These include viruses, bacteria, mycoplasmas, chlamydiae, rickettsiae and rickettsial-like organisms, fungi, protozoa and ecto- and endoparasites. Before discussing diseases caused by specific agents belonging to each group, it is appropriate to know something in general about each of these types of agents.

Viruses are small particles that contain a single type of nucleic acid, RNA or DNA, and lack the essential enzyme systems required for independent survival. Therefore, they are parasites of living cells. The nucleic acid of viruses is surrounded by a protein coat. The DNA or RNA and its surrounding protein are known collectively as the nucleocapsid. Some viruses contain an additional outer carbohydrate-protein coat known as an envelope. Panleukopenia and caliciviruses are nonenveloped viruses containing either DNA or RNA, respectively. Feline herpesvirus and feline leukemia virus are enveloped viruses containing DNA or RNA, respectively. Viral particles attach to susceptible cells, and the viral DNA or RNA is released. The viral nucleic acid commandeers the synthetic machinery of the cell to produce its own proteins and nucleic acids. These are assembled into intact virus particles that are released from the cells by cell rupture or by budding from the cell surfaces. Viruses cause disease in several ways: by destroying the cells they infect; by interfering with normal cell metabolic functions; by interfering with cellular nucleic acids; or by focusing the host's immune response on the infected cell.

Unlike viruses, most bacteria are visible with conventional light microscopes. Bacterium have a rigid outer cell wall, lack a distinct nucleus and contain a single strand of circular DNA. Bacteria divide by a process of binary fission, where a single bacteria splits into 2 equal daughter cells. Bacteria are not obligate parasites of living cells; they can live freely on simple nutrients found in their environments. Bacteria may live in soil, water or plants, or in more complex animals. Many bacteria live on normal body secretions in the orifices of the GI, respiratory and urogenital tracts, as well as on the skin and its appendages.

Mycoplasmal, rickettsial and chlamydial organisms are more similar to bacteria than to viruses. However, they tend to be smaller than bacteria and are often the same size as very large viruses. *Rickettsia* species and *Chlamydia* species have both RNA and DNA, while *Mycoplasma* contain circularized DNA like bacteria. *Chlamydia* and *Rickettsia* have fairly rigid cell walls, while *Mycoplasma* has a cell wall that is thin and nonrigid. All of these organisms are obligate parasites of living animal cells; *Chlamydia* and *Mycoplasma* live in higher animals and *Rickettsia* live in lower animals. The animal cells provide the essential nutrients and metabolites that they cannot provide for themselves.

Fungi are true cells containing a membrane-bound nucleus with several chromosomes. They are somewhat larger than bacteria, and contain a complex rigid cell wall. Some fungi are free-living in the environment and feed off of nonanimal products. Others, such as the dermatophytes, live on the skin and in the hair follicles of higher animals. Fungi are highly pleomorphic in shape, depending on the environment in which they are found. Under certain growth conditions, fungi form complex thread-like structures called mycelia or hyphae. Under certain conditions, often in animal tissues, they exist as yeast-like bodies. Fungi are different from lower organisms in that they have both sexual and asexual developmental stages. The resting, and often infectious, stage of fungal organisms is called the spore. Spores are compact and well-pro-

tected from environmental degradation by a thick outer protective cell wall.

Protozoa are unicellular organisms that are structurally similar to animal rather than plant cells. Protozoa that are pathogenic to animals receive most of their nutrition from metabolic products of host cells. The exception is the intestinal protozoal parasites that can feed on products of digestion. Protozoa receive their nutrition by pinocytosis (ingestion of nutrients through evaginations of the cell wall) or through mouth-like openings. Intracellular protozoan parasites receive their nutrition by diffusion. Protozoa have many structural adaptations that facilitate their survival. Some can change their plasma membranes into a thick, protective cyst wall. Many have acquired means to travel through their environment, which is usually fluid. Pseudopods are temporary extensions of the cell wall through which cytoplasm streams, thus propelling the organism slowly forward. Flagella and cilia are microtubular structures rooted in a basal body at one end of the organism and may be free or attached to the body wall, forming veil-like undulating membranes. Movement by use of flagella and cilia is very rapid.

A parasite is any organism that requires another animal or plant for all or part of its life cycle. However, the term has been applied mainly to large complex multicellular microbes, most of which are visible to the naked eye. Parasites belong mainly to the animal phyla Nemathelminthes (roundworms), Platyhelminthes (flatworms and tapeworms), Acanthocephala (spiny-headed worms) and Arthropoda. The last group contains 6-legged arthropods (insects) and 8-legged arthropods (arachnids).

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DISEASES OF THE MULTIPLE-CAT ENVIRONMENT

Cats are infected by a large number of different microbes (Table 2), but only relatively few account for most disease problems. This is especially true for cats kept mainly indoors. Infectious diseases that are important for environments like catteries are generally those whose transmission involves 4 of the 8 mechanisms listed in Table 1. These include such mechanisms as: mother-to-fetus transmission; fleeting oral, mucous membrane or skin contact with contaminated excretions, secretions or exfoliations; mutation of one pathogenic agent to another within the host's body; and organisms normally within the environment that take advantage of an immunocompromised host.

Common infectious diseases in these categories include those caused by feline panleukopenia virus, feline herpesvirus, feline calicivirus, feline coronaviruses (enteric coronavirus and FIP virus), feline rotavirus (and miscellaneous enteric viruses), feline leukemia virus, several bacteria (*E coli, Salmonella, Pasteurella, Bordetella, Campylobacter,* streptococci, anaerobic bacteria), *Chlamydia, Mycoplasma,* dermatophytes, several protozoa (coccidia, *Giardia,* cryptosporidia) and parasites (ascarids, tapeworms, fleas, ear mites). Several additional diseases should be familiar to cattery owners, not because they are problems in catteries, but because of public health or differential diagnostic considerations. These include feline immunodeficiency virus infection, cat scratch disease, and toxoplasmosis.

Kitten mortality is a final topic of importance to cattery owners. Kitten mortality does not have a single cause, and is not always due to infectious agents. The reminder of the chapter will consist of specific discussions of each of the aforementioned diseases.

Kitten Mortality

Kitten mortality is relatively high among purebred or domestic (laboratory) catteries, especially when compared with other species of animals bred in captivity. This fact has led many managers of laboratory animal facilities to conclude that cats are among the most difficult species to breed in captivity.[3,15]

Kitten mortality tends to occur during 4 periods: *in utero* (abortions, fetal resorptions); at the time of birth (stillbirths); in the neonatal period (0-14 days of age); or in the immediate postweaning period (6-12

weeks of age). Mortality after this period is relatively low.

Kitten mortality figures vary greatly from cattery to cattery, depending on various causative factors. Mortality figures also depend on whether the cattery is conventional (infectious disease agents present) or specific pathogen free (SPF) (infectious disease agents not present). Kitten mortality (0-1 year of age) among conventional purebred catteries in the United States for the years 1975-76 averaged 34.5%, with about one-third being stillborn.[13] One-half of the mortality among live-born purebred kittens occurred during the first 7 days of life and over three-fourths before 6 weeks of age. In a study of kitten mortality in a Persian/Himalayan cattery from 1972-1977, yearly kitten mortality varied from a low of 24% to a high of 63%.[9] Mortality in 2 conventional domestic cat colonies maintained for laboratory purposes was similar to that in conventional purebred catteries, approaching 40%.[11] Following application of increased disease preventive measures, kittenhood mortality decreased to 35% for 2 years, then increased to over 60% following a particularly severe winter.[12] An outdoor/indoor conventional cattery lost 21.6% of live-born kittens before weaning and had 7.9% stillbirths.[15]

Kitten mortality among SPF catteries is lower than in conventional catteries, largely because of decreased deaths from infectious diseases after 2 weeks of age. One SPF cattery had a 14.8% preweaning mortality, including stillbirths;[16] another had 8.9% total kitten mortality.[3] Almost all of the deaths occurred before 7 days of age. Kitten mortality in another SPF cattery ranged from 12.6% to 29.4%, depending on the number of litters previously produced by the queens.[4]

Fetal deaths are extremely difficult to measure, especially if they occur early in gestation and the fetuses are resorbed. Many abortions also go unnoticed because of the propensity of the queen to eat the products of conception. Moreover, if accurate pregnancy examinations are not done at various times after conception, it is impossible to even determine if resorption or abortion occurred. In one large survey of purebred catteries, 2.1% of all feline pregnancies reportedly ended with abortion, and 0.7% in resorptions.[13] These figures, especially for fetal resorptions, are undoubtedly low. Such figures refer to total death of all of the fetuses in a litter, and do not take into account death of a portion of a litter. The mean litter size for a primiparous cat is around 2.8 kittens/litter, while for multiparous queens it is 3.3-4.5 kittens per litter.[2-4,14,15] If a cattery is averaging far below these levels, conception is abnormally low or fetal loss high.

Stillbirths are surprisingly common in both conventional and SPF catteries. Stillbirths in 3 different conventional catteries varied from 7.0% to 10.2%.[9,13,15] Reported stillbirths in SPF catteries have ranged from around 3% to 10% of total kitten births.[3,7,16] Stillbirths have multiple causes, including dystocia and resulting hypoxia, congenital defects incompatible with extrauterine existence, nutritional disorders and congenital infections.

More than one-half of kitten deaths occur in the neonatal period of life. Most deaths in this period are listed along with "fading kittens" by cattery owners. The neonatal period includes the first 10-14 days of life. Deaths occurring during this period result from disorders acquired *in utero*, during the birth process or within the first few days of life. Death losses during the neonatal period are highest in the first 3 days of life and taper off rapidly thereafter. Only one-fourth of kitten mortality occurs between 2 and 6 weeks of age.

The next peak in kitten mortality occurs in the postweaning period, from 6 to 12 weeks of age. Deaths in this period contribute less than one-fourth of the total kitten mortality in conventional catteries. Mortality during this stage is mainly due to infectious diseases potentiated by weaning stress, exposure to pathogenic microbes in the immediate environment, and loss of passive local (lactogenic) and passive systemic (maternal) immunity. Mortality varies greatly with environmental and genetic factors. Mortality during this period is very low in SPF catteries, due mainly to the absence of pathogenic microbes.

Causes

Kitten mortality occurs for the following reasons: congenital anomalies; nutritional diseases resulting from improper diets fed

to the queens; abnormally low birth weight; trauma during or after birth (dystocia, cannibalism, maternal neglect); neonatal isoerythrolysis; infectious diseases; and miscellaneous factors.

Gross congenital anatomic abnormalities have been observed in 6.8-20% of live-born and stillborn kitten fatalities.[3,7,8,10,13,16] Anatomic anomalies often involve cleft palates, cranial deformities (some with cleft palate), agenesis of the small and large intestines, cardiac anomalies, massive umbilical or diaphragmatic hernias, anomalies of the kidneys and lower urinary tract and skeletal anomalies. Congenital defects of a microanatomic or biochemical type probably account for an equal number of kitten deaths. Such defects usually go unreported and are usually included under the headings of stillbirths, fading kittens or undetermined deaths.

Queens fed inadequate diets during pregnancy may produce diseased and weak kittens. The most serious dietary problem of the last decade has been taurine deficiency. Commercial and prescription diets deficient in taurine were inadvertently fed to millions of cats. Deficiencies in dietary taurine led to an increased incidence of fetal resorptions, abortions, stillbirths and kittenhood deaths.[18] The main manifestation of the deficiency was a disease of the heart known as congestive cardiomyopathy. The so-called "kitten mortality complex," mistakenly ascribed to feline infectious peritonitis virus, was probably due to taurine-deficient diets.[14] Taurine deficiency may also have explained the seemingly high kitten mortalities described in purebred catteries in the United States in 1975-76.[13] Taurine is an amino acid that is abundant in animal meat. Therefore, foods made from vegetable proteins must be heavily supplemented with the substance. Fortunately, modern cat diets have been heavily supplemented with taurine, thus minimizing the problem.

Below-normal birth weight has been associated with higher kittenhood mortality. The normal birth weight (taken during the first day of life) of conventional kittens in one study varied from 70 to 144 g, with a mean of 106.4 g.[5] Conventional newborn kittens in a second study had a mean birth weight of 113 g.[2] These were similar to figures for SPF kittens of 69-150 g with a mean of 109 g.[3] The birth weight of kittens is not affected by the sex of the kitten, litter size or weight of the mother.[3,7] Larger queens tend to have smaller kittens than smaller queens, but kitten sizes are still within the normal range.[7]

The causes of abnormally low birth weights have not been determined, but are probably multifactorial. Though often attributed to prematurity, most abnormally small kittens are born at term. Their small stature probably is due to genetic or congenital illness. As such, genetic, developmental, nutritional and infectious causes are probably associated with many abnormally small kittens. In one study, 60% of the kittens that died during the first 6 weeks of life were underweight at birth.[7] Not only is abnormally low birth weight associated with a higher likelihood of stillbirth and mortality during the first 6 weeks of life, but there is a tendency for a disproportionate number of underweight kittens to be chronic poor doers and to die at a younger age.[4]

Many kittens that succumb in the first few weeks of life are of normal size, but their growth lags and they are subnormal in weight at the time of death.[7] Therefore, it is important to not only weigh kittens at birth, but also to weigh them at frequent intervals up to at least 6 weeks of age.

Growth rates of conventional and SPF kittens are similar.[3,5,11] Growth rate is most rapid between birth and 15 days of life and then slows somewhat; growth is faster in males than females after 12-16 weeks of age and in kittens with lower normal birth weights, but is not appreciably affected by litter size or weight of the mothers.[5] By 6 weeks of age, most normal kittens should have mean body weights of around 600 gm. The mean body weights of male domestic cats at 40 weeks of age is around 4000 g (4 kg) and that of females 2800 g (2.8 kg).[11] Since growth over this entire period is relatively steady, female cats are expected to grow at the average rate of 10 g/day and males at a rate of 14 g/day. The weights of individual cats may vary by 10% or more from the mean, and some purebreds may be substantially lower, though the normalcy of such poor growth may be questioned.

Deaths due to trauma during birth or the first 3 days of life accounted for 5-10% of total kitten losses in 2 colonies.[3,16] Trauma

also accounted for 19% of total kitten mortality among 0- to 8-week-old kittens presented to Angell Memorial Animal Hospital.[8] One-half of the losses during the first week of life were due to cannibalism, dystocia or maternal neglect. Traumas occurring after this time were not defined. Dystocia occurs in less than 2% of births, and so is not the leading cause of traumatic death in kittens.[15] Cannibalism is often associated with nervous or high-strung queens. Cannibalism of sickly kittens is also common, so it may be incorrect to always implicate trauma as the direct cause of death. Maternal neglect is another major trauma to newborn kittens.[16] Like cannibalism, it is often not possible to differentiate maternal neglect of otherwise normal kittens from maternal neglect of sickly kittens, the latter being a programmed response of queens that is akin to cannibalism.

Neonatal isoerythrolysis occurs infrequently among domestic cats, but may be relatively frequent in certain purebred catteries.[1,6] Though the precise mechanism has not been determined, it appears that a proportion of queens with type-B red blood cell antigen, when bred to a blood group-A tom, are at risk. Cats with type-B blood make antibodies against type-A blood group antigen. These antibodies may be passed to the kitten in the colostrum, and if the kitten is blood group A, the antibodies cause rapid destruction of the kitten's red blood cells. Affected kittens are born in apparent good health but fade rapidly during the first 24-72 hours of life and die. The spleen is enlarged, the membranes pale and sometimes yellow-tinged, and the urine may be exceedingly yellow or wine-colored.[1,6] This condition is rare in domestic cats because of the rarity of type-B blood in most outbred cat populations. Less than 1% of the domestic cats in the United States and the Caribbean, 3% in England, 9.7% in Japan, 15% in France and 26.3% in Australia have type-B blood.[4] Therefore, the chance of a type-B domestic queen in the United States being bred to a type-A tom is low. However, this may not be the case in purebred cats; some breeds may have a very high incidence (up to 50%) of type-B blood.[4]

Infectious diseases account for a substantial proportion of kittenhood deaths in the neonatal and post-weaning period. Of 149 kittens between 0 and 24 weeks of life, 121 (81%) died of some infectious disease, most often respiratory or enteric infections.[10] This was similar to the death rate due to infectious diseases of 220 of 359 (61%) reported in 0- to 8-week-old kittens.[8] A few fetal deaths and stillbirths are also due to infections occurring *in utero*. Specific pathogen-free catteries have fewer problems with infectious diseases due to viruses, so kitten mortality is less than in conventional catteries. However, deaths due to ubiquitous bacterial pathogens still remain a problem in SPF catteries, mainly because husbandry is similar.

Common infectious agents that cause *in-utero* or neonatal infections and fetal deaths, stillbirths or fading kittens include hemolytic streptococci, *Mycoplasma* and related organisms, feline herpesvirus type 1, feline panleukopenia virus, feline leukemia virus, feline infectious peritonitis virus and *Toxoplasma*.[17] Additional pathogens that infect and kill neonates include *E coli, Pasteurella,* staphylococci, *Mycoplasma* and *Chlamydia*. Fleas are underestimated pathogens of kittens. Heavy flea infestations cause clinical or subclinical anemia in kittens. In turn, the anemia lowers the kittens' resistance to other pathogens. Common infectious agents of weanling kittens that may contribute to mortality are feline herpesvirus type 1, feline calicivirus, feline panleukopenia virus, feline enteric coronavirus, feline infectious peritonitis virus, feline leukemia virus, *Bordetella, Pasteurella* and *E coli*. Details of these various infections are given in subsequent sections.

Bacterial infection of the blood (septicemia) in neonates is very common and deserves special mention. Coliform septicemia alone has been reported as the cause of death in about 10% of kittens.[3,16] Streptococcal infections may also be a major cause of neonatal kitten deaths in catteries.[17] Kittens that receive insufficient maternal immunity at birth, due to inadequate nursing or poor antibody levels in the queen's colostrum, or kittens exposed to massive levels of pathogenic bacteria in the birth canal or from the mother's mouth or milk are most susceptible to bacterial septicemia. Problem bacteria include hemolytic streptococci, *E coli* (especially hemolytic strains), *Pasteurella multocida,* staphylococci and other miscellaneous enteric bacteria.[17] The bacteria gain access to the kitten's body through mu-

cous membranes of the oropharynx and intestinal or genitourinary tracts, or through the umbilical cord. Mucous membrane infection occurs from exposure to contaminated vaginal secretions (either before or during birth), infected milk (in the case of queens with mastitis), or from saliva (during cleaning of the kitten at the time of birth and chewing off the umbilical cord). The most common route of infection is the umbilical cord.

Infection of the umbilical cord is known as omphalophlebitis. Pathogenic bacteria from the mother's mouth are inoculated into the umbilical cord when the cord is chewed off. The queen normally severs the umbilical cord several centimeters from the body wall. The remnant of the umbilical cord dries up rapidly, which limits bacterial growth in the end of the cord and prevents movement of bacteria up the cord. If the umbilical cord is chewed off too short, especially at the body wall, passage of bacteria into the base of the umbilical cord is unimpeded. Alternatively, if the umbilical cord is left long by the queen and an excessive number of bacteria are deposited in the end of the cord, the chances of bacteria entering the viable portion of the umbilical cord remnant are greatly increased. The net result of the penetration of bacteria into the viable tissue at the base of the cord is an abscess. This abscess often forms just under the skin at the site where the umbilical cord enters the abdomen. Therefore, the umbilical abscess may grow unseen for some time.

Bacteria from the infected umbilical cord have direct access to the bloodstream via the remnant of the umbilical vein. This remnant venous structure stays semi-patent for several days after birth. Once in the bloodstream, the bacteria travel to the lung, spleen, liver, joints and kidneys. Bacteria that enter the body through mucous membranes also spread rapidly into the bloodstream, especially if the kitten's maternal immunity is low. Once again, the lungs, spleen, liver, joints and kidneys are target organs. Kittens with bacterial septicemia usually fade away and die during the first 3-7 days of life.

Some cattery owners sever the umbilical cord themselves, tie it off and dip it in antiseptic. It is uncertain how successful this is in preventing neonatal septicemia. Regardless, it is not a practice that should be routine. Overattention to the kittens and queen during birth by the owner often results in problems that are even more serious than omphalophlebitis. Kittens with umbilical cords chewed off flush with the abdominal wall should immediately receive an injection of short-acting (penicillin K) and long-acting (benzathine penicillin) penicillin, regardless of whether they appear normal or not. This greatly reduces subsequent mortality. The base of the umbilical cord should be periodically examined for swelling, purulent exudation and discoloration. If kittens are weighed daily and their growth rate suddenly falls behind that of littermates, the umbilicus should be hot-packed (with a warm wash cloth) for 10-15 minutes several times a day. This sometimes causes the abscess to appear and come to a head and drain.

Pneumonia is another leading cause of death among kittens.[9,10,15] Bacteria are the major cause of pneumonia in kittens <2 weeks of age, while viruses are more important in kittens >2 weeks.[10] Bacteria commonly involved in kitten pneumonia include *E coli, Bordetella, Pasteurella* and streptococci. *Mycoplasma* and *Chlamydia* may also be involved in neonatal kitten pneumonia. The main viral pathogens causing pneumonia in kittens are feline herpesvirus type 1 and feline calicivirus, with the former being far more important.[10] Bacteria may enter the body through the oropharynx or through the bloodstream. Therefore, bacterial pneumonia may be the sole manifestation of disease or only a part of more widespread septicemia.

Enteritis caused by bacteria or viruses is relatively infrequent in nursing kittens but may be a serious problem in kittens being bottle fed. Enteritis due to bacteria (*E coli, Campylobacter, Salmonella*), viruses (caliciviruses, coronaviruses, rotaviruses, astroviruses, toroviruses), and protozoan parasites (coccidia, *Giardia*, cryptosporidia) is much more common in kittens 4-12 weeks of age than in younger animals.

There are several miscellaneous and poorly understood causes of kitten mortality. For reasons that are not understood, kitten mortality is lowest in 5th litters; first litters and litters after the 5th parity have higher mortality.[7] Midsize queens tend to

have lower kitten losses than large or small queens.[7] Kitten mortality is twice as high in one-kitten litters as in larger litters; the lowest mortality is among litters with 5 kittens.[7] Higher mortality in first-litter queens may be due to maternal neglect, though the reason for optimum survival among 5th litters is not obvious. Small queens may be small because they are sickly, which would explain a higher mortality among their kittens. Higher mortality among overweight queens is more difficult to understand.

Pathologic and Clinicopathologic Features

Kitten mortality appears to be a common and often unavoidable problem with breeding catteries. However, preweaning kitten losses (live-born and stillbirths) >20% and postweaning losses (weaning to 7 months of age) >10% should be reason for concern. Further, disproportional losses to any one factor (for example, congenital defects, specific infectious diseases) greater than those described above are reasons for concern regardless of the overall mortality figures.

If kittenhood mortality is excessive, cattery owners should take the following steps: do not stop breeding, because this will not help diagnose the problem; keep accurate and detailed records of losses, pedigrees of dying kittens, diet and any drugs (vaccines, antifungals, antiparasitics, antibacterials) being administered to the cattery as a whole or to affected queens; and obtain accurate (complete) postmortem examinations on all kittens that die, regardless of age. If these steps are not carried out, it is very difficult to pinpoint the problem.

Obtaining complete and accurate necropsies is the most expensive and crucial aspect of a kitten mortality study. It is preferable to sacrifice the kitten and perform a fresh necropsy as soon as it becomes apparent that death is inevitable. Agonal changes in tissues and the effects of forced feeding and other therapeutic interventions can greatly complicate gross and histopathologic interpretations. For instance, forced feeding of a weakened kitten often results in aspiration pneumonia. Pneumonic lesions may obscure the true cause of the kitten's weakness. Kittens allowed to die often show terminal heart and lung problems, which may also obscure the true cause of death. Kittens that die before they can be euthanized should be immediately refrigerated; freezing ruins tissues for gross and histopathologic examination and should be avoided. If refrigeration of the body is delayed for several hours, especially in warmer weather, autolysis of the tissues can be severe and ruin pathologic studies.

Postmortem examination should be performed by competent people. When possible, necropsies should be done by certified veterinary pathologists or by clinical veterinarians working with such people. Though many practitioners would disagree, most clinical veterinarians are incapable of conducting proper gross, let alone microscopic, tissue examinations. Gross abnormalities are often subtle and go unnoticed by untrained eyes. Representative tissues should be taken as aseptically as possible and frozen for microbiologic (viral, bacterial, fungal cultures) or toxicologic studies, should they prove necessary. A wide sampling of tissues should also be preserved in formalin for histopathologic examination. Formalin-fixed tissues, along with detailed descriptions of gross lesions and clinical histories, should then be forwarded to certified veterinary pathologists for microscopic examination. If tissues indicate an infectious or toxic disease as the cause of death, samples of frozen tissues can then be submitted to competent microbiologists or toxicologists for further study.

After causes of death are determined, it should be possible to integrate all data and diagnose the problem. For instance, if cardiomyopathy was the major cause of death among kittens in a cattery, nutrition and genetics would be 2 major areas for further investigation. Was the outbreak of cardiomyopathy associated with a major change in diet or was it limited only to cats from certain bloodlines or breedings? If infectious diseases were a major cause of kitten losses, did those diseases follow any changes in cattery management? If congenital anomalies were the major problem, was there a possible genetic link, or were certain drugs used in the cattery before the outbreak?

Treatment and Prevention

As previously mentioned, a certain amount of kitten mortality is unavoidable. However, if kitten mortality is excessive, there are only 2 ways to attack the problem: by trial and error or by determining the exact cause and initiating the most appropriate control measures. Unfortunately, most cattery owners choose the first method. Though trial and error is sometimes effective, it is usually not the most efficient or effective technique.

Kitten mortality cannot be treated, but rather it must be diagnosed and prevented. Once the major causes are determined, a concerted effort must be made to eliminate the causative factors before the next breedings. Regardless of the cause of the kitten mortality, prevention ultimately involves either changes in cattery management (to control the spread of infectious diseases or correct nutritional deficiencies) or genetics. Unfortunately, these are 2 areas that cattery owners avoid changing if possible. Environmental changes often involve great costs and basic alterations in breeding practices and philosophies. Many cat breeders avoid the topic of genetic weaknesses altogether because conceding that their bloodlines are weak is an admission that their breeding program has failed. This admission is hard to take for people who have invested large amounts of money, reputation and time in their cats. An admission may also have local, regional, national and international implications, especially if cats of the affected breed or bloodlines have done well in shows.

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Feline Panleukopenia Virus Infection

Cause

Outbreaks of fatal enteritis have been recognized in kittens since the turn of the century. Zschokke suggested *E coli* as a possible cause.[38] The disease was recreated several decades later in healthy cats using filtrates of tissue from affected animals, thus refuting the role of bacteria.[37] The cause of feline enteritis was confirmed to be a virus in the early 1930s.[10,36] The virus was first isolated in tissue culture in 1965.[11] The true identity of the virus as a parvovirus eluded investigators until 1974.[15,17,20,22,34] The name panleukopenia was derived from the very low white blood cell (WBC) count of infected cats.[9]

Feline panleukopenia virus (FPLV) is very hardy and withstands heating to 60 C for 30 minutes.[18] Infectivity decreases only 100-fold after being heated to 75 C for 30 minutes.[12] Partially purified virus has been known to survive for 30 minutes at 80 C. There was no decrease in viral infectivity after storage at 4-25 C for 13 months and

100-fold decrease after storage at 32 C for 6 months.[26] Infectivity of FPLV is not affected by chloroform or acidity (pH 3).[12,14,33] The virus is resistant to most disinfectants, but can be inactivated by 0.5% formalin or 1:32 dilution of commercial hypochlorite (bleach) solution.[31]

Six strains of FPLV have been identified.[13] It grows in cat, mink and ferret cells but not in bovine, dog, monkey or human cells.

Feline panleukopenia virus was originally thought to be the parent of the canine parvovirus that originally appeared in dogs in the late 1970s. However, there are minor, but notable, genetic, antigenic, biochemical and host range differences between the 2 agents.[2,6,21,25,35,39,42]

Pathogenesis

Feline panleukopenia virus infects and causes disease in most Felidae. It infects Mustelidae, such as mink and ferrets, but causes only mild or inapparent disease in these species.[39,42] Procyanidae, including raccoons and coatimundi, are susceptible to infection and disease.[8,14,39,42] Feline panleukopenia virus replicates poorly in dogs and does not cause disease.[42] The red fox and skunk are resistant to infection with FPLV.[39] All other species are also resistant.

Feline panleukopenia virus is shed in the feces during acute illness and for several weeks after clinical signs abate. Low-grade chronic shedding by asymptomatic carriers, probably from the oropharynx, appears likely.[3] Unlike most other viruses of cats, FPLV survives for months or years off the host. Therefore, outbreaks may occur following contact with infected animals or contact with previously contaminated quarters.

Infection occurs in 2 basic forms: fetal and postnatal. Postnatal infection is usually by the oral route, though almost any route of exposure will suffice.[20] The incubation period is 2-10 days.[1,11,20,22,27,34] An initial fever spike occurs during the initial viremic phase. A second fever spike is often seen several days later when the WBC count drops. The virus probably replicates in the oropharynx and spreads systemically to target organs. Though the virus can replicate in virtually any body tissue, cells with high mitotic rates, such as intestinal epithelium or the crypts of Lieberkuhn, bone marrow stem cells and lymphoid cells are the principal targets.

Fetal infection usually occurs mid-gestation.[4,16,18,19] Virus enters the fetus from the maternal circulation. Queens giving birth to affected kittens are rarely clinically ill during pregnancy, suggesting that fetuses are infected by an inapparent primary, secondary or latent maternal infection.

Clinical Features

Classic postnatal FPLV infection usually occurs in kittens 6-14 weeks of age, though cats of all ages may be affected.[7] Because of widespread vaccination, the disease is less prevalent among pet cats and in catteries than in the past. Infection in rural cats often follows local population increases that generate large numbers of susceptible young animals. Conditions in pounds are also ideal for the disease; many unvaccinated older cats and weanling kittens are in close contact with carrier or clinically ill cats and younger susceptible kittens.

Feline panleukopenia virus infection results in inapparent, peracute or subacute disease.[7] There is also a congenital (fetal) form of the infection. Subclinical or inapparent infections are probably common, particularly in older kittens and adult cats.[11]

Peracute disease is characterized by sudden death 4-9 days after exposure and is usually observed in kittens. Infected animals are apparently healthy and then moribund a few hours later. This form is most often mistaken for poisoning. Diarrhea and vomiting are infrequent, but severe abdominal pain may be elicited on palpation. Fever usually goes undetected, and by the time clinical signs are manifested, shock is advanced and the temperature is often subnormal. Death usually ensues within hours. Acute illness is manifested by colic, fever, depression, anorexia and vomiting of a frothy bile-tinged fluid. Abdominal palpation elicits pain. Diarrhea, usually fluid and fetid, follows several hours to a day later. Untreated cats dehydrate rapidly and most die of shock within 24-96 hours.

Subacute disease is manifested by mild depression and diarrhea lasting several days. Chronic diarrhea lasting several weeks to months or more has been observed

after recovery in a small proportion of cats and is due to extensive bowel damage and secondary fibrosis, and not to persistent infection.

The course of the disease in fetal infections differs dramatically from that described for postnatal disease.[12,18,19,34] Fetal infection results in almost selective destruction of the Purkinje cell layer of the cerebellum, and to a lesser extent, the retina. Infected fetuses can be aborted but are usually born alive. Characteristic ataxia is noticed when infected kittens begin to walk. Ataxia is lifelong and associated with hypermetria, dysmetria and incoordination. Kittens with cerebellar hypoplasia are otherwise normal and many become affectionate and functional pets. Retinal involvement is usually of no clinical significance.

Pathologic Features

Gross lesions are observed mainly in the gut and bone marrow.[40] In mild cases, the bowel is fluid filled, and the jejunal and ileal mucosa is reddened. Mesenteric lymph nodes are enlarged, edematous and occasionally hemorrhagic. In severe cases, the mucosa is hemorrhagic and covered with fibrinous exudate. The bowel wall may be so severely affected that fibrinous exudate can be seen on serosal surfaces. The bone marrow may be gelatinous and liquid. The stomach and esophagus in vomiting animals are reddened and bile stained.

Microscopic changes are mainly seen in the mucosa of the small intestine, bone marrow and lymphoid tissues.[40] Necrosis of the intestinal mucosa, beginning in the crypt epithelium, is most prominent in the jejunum and ileum. In severe cases, the mucosa sloughs and is replaced by a fibrinous diphtheritic membrane. Epithelial cells within the crypts of Lieberkuhn are in various stages of damage, ranging from hydropic degeneration to lysis. Eosinophilic intranuclear inclusion bodies are seen within some infected cells.[9,22,23] Inclusion bodies are more evident when tissue is fixed in Bouin's or Zenker's fixatives than in formalin. Bone marrow shows varying degrees of myeloid destruction. Lymphoid tissue can be totally depleted of lymphocytes but show evidence of reticuloendothelial hyperplasia. Leukocytes are almost totally absent in peripheral blood.

Clinicopathologic Features

Leukopenia is a consistent feature of FPLV infection. The drop in the peripheral WBC count parallels the second fever spike and starts as early as 4-6 days post-infection. Cells remaining in the peripheral blood are predominantly lymphocytes. Disease severity tends to parallel the WBC count. Counts above 7000 cells/μl are infrequently associated with clinical signs, while counts of 500-2000 cells/μl are associated with severe disease.

Feline panleukopenia virus can be detected in feces by enzyme-linked immunosorbent assay (ELISA) and electron microscopy. Virus shedding is detected before onset of signs and for a week or more after signs disappear.

Treatment and Prevention

Cats with clinical FPLV infection should be treated supportively and vigorously. Food and water are withheld, especially if colic, vomiting and diarrhea are severe. A balanced fluid and electrolyte solution should be given IV as a continuous drip while clinical signs are present. Fresh whole blood should be given if plasma protein levels fall below 4 g/dl or the WBC count falls below 2000 cells/μl. Broad-spectrum antibiotics should be given parenterally to prevent sepsis and temporarily decrease bacterial overgrowth in the damaged bowel. Supportive treatment decreases mortality by 50% in severe infections.

Vaccination has proven very effective in controlling FPLV infection.[7,26,30] Attenuated live-virus vaccines produce rapid immunity in kittens. Killed-virus vaccines are somewhat slower in producing immunity, are more apt to be blocked by low levels of maternal immunity and induce lower neutralizing antibody titers. In practice, however, killed-virus vaccines provide adequate protection and remain the mainstay of most immunization procedures. Starting at 6-10 weeks of age, 2-3 doses of vaccine should be given at 3-week intervals. Vaccination should not be ended before 12 weeks of age because of the presence of interfering maternal antibodies in younger kittens. For maximum protection, a final immunization at 16 weeks of age has been recommended.[30]

The need for yearly booster immunizations is debatable. Though yearly boosters have been recommended by some groups, experience with disease in the field does not indicate a need for such intensive revaccination.[7] Older cats are much less susceptible to clinical disease, and most cats with access to the outdoors are probably naturally boosted by field exposure.

Infection and Immunity

Maternal antibodies prevent infection in kittens for 6-14 weeks.[24] Maternal FPLV antibodies have a half-life of 9.7 days, and there is a good correlation between passive titers of the kittens and the serum titer of the queen.[30] Passive immunity interferes with the immunizing ability of both live and inactivated FPLV vaccines.[5,24,30,32] Of kittens without maternal FPLV antibodies, 89% responded to vaccination. Only 12% of kittens with maternal titers greater than 1:10 responded. Modified-live FPLV vaccines are more likely to overcome low maternal titers than inactivated-virus vaccines.[30] Vaccination induces both virus neutralizing antibodies and cell-mediated immunity.[41,43]

Feline panleukopenia virus infection can have an immunosuppressive effect on kittens. Fetuses infected in mid-gestation are often born with cerebellar hypoplasia, but are normal otherwise. These kittens continue to harbor and shed virus for extended periods after birth.[19] Therefore, fetal infection induces a form of tolerance to the virus. Fetuses infected at 35 days of gestation have depressed T-lymphocyte-mediated immunity.[29] Infection at 45 days of gestation has no such effect.

Feline panleukopenia virus produces fever, leukopenia and lymphoid lesions when inoculated into germ-free cats, but very little enteritis and no mortality.[27] The mitotic activity of the crypt epithelium of germ-free cats is apparently lower than in conventional cats, thus providing the virus with fewer target cells. It is likely that many mild intestinal pathogens, such as *Giardia*, cryptosporidia, coccidia, ascarids and various enteropathic bacteria can increase the mitotic index of the crypt epithelium and predispose kittens to FPLV-induced disease.

Animal and Public Health Considerations

Feline panleukopenia virus is only infectious to Felidae, Mustelidae and Procyanidae. It is not a human pathogen.

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Feline Herpesvirus Type-1 Infection

Cause

Feline herpesvirus type 1 (FHV-1) was first isolated from nasopharyngeal and conjunctival secretions of a group of 5- to 10-week-old kittens with upper respiratory disease.[12] It was originally called feline rhinotracheitis virus in reference to the type of disease it caused.[9]

Feline herpesvirus type 1 is a double-stranded DNA virus.[5,6,11,14,15] It belongs to the group of alpha herpesviruses. The virus is inactivated by ether, chloroform and almost all common commercial disinfectants, antiseptics, sanitizers and detergents.[1,29,44,46] Infectivity is maintained at 4 C for 154 days or more, but is lost within 33 days at 25 C, 3 hours at 37 C and 4-5 minutes at 56 C.[36] The virus stores well at subzero temperature and withstands lyophilization.

Pathogenesis

Feline herpesvirus type 1 is found throughout the world and infects only domestic and closely related wild Felidae.[8] Healthy-appearing carrier cats and cats with clinically active infections are the principal sources of virus. Carrier cats are latently or actively infected, with considerable interchange between the 2 states. Latent carriers maintain the viral genome in tissues of the nasal passages but do not shed infectious virus.[20,21,23] Under situations of stress or corticosteroid administration, the genome can be activated and intact virus shed.[18,20-22] In a study of over 200 healthy cats in Australia, 1.5% were actively shedding FHV-1 and 25.8% were latent carriers.[17]

Kittens are infected from 3 major sources: the queen; other cats in the environment; or live-virus vaccines. Virus is infectious when placed on almost any mucous membrane, but is not infectious when injected IM.[40] It seems the virus does not replicate at the higher core temperature of the body. Latently infected queens may become transient virus shedders because of the stress of gestation, parturition or lactation.[23] Infection of kittens can occur *in utero*, neonatally or between the ages of 6 and 12 weeks, when maternal immunity wanes.

Asymptomatic or clinically ill kittens and older animals in the same environment constitute a second reservoir of virus. Social and environmental stresses in catteries, multiple-cat households and animal shelters lead to a high level of shedding in resident cats. Conversely, these same stresses lead to decreased resistance in newly introduced animals and make them more susceptible to infection from resident virus shedders.

Outbreaks of feline herpesvirus infection have occasionally followed use of live-virus vaccines in a cattery. This has also been observed on at least 2 occasions in groups of isolated specific-pathogen-free cats in the author's laboratory, thus confirming the vaccine as the source. The importance and frequency of this problem remains to be determined, however.

Contrary to earlier beliefs, infection requires intimate contact between shedding and susceptible cats. Licking, grooming, and eating and drinking from the same food dishes appear more important than aerosol exposure in spreading the infection. Airborne spread via large droplets occurs only over short distances, and sentinel cats that share the same air space but different quarters as virus shedders are infrequently infected.[23]

Virus can be recovered from the nasal passages and oropharynx within 24 hours after intranasal and conjunctival sac inoculation.[47] Recovery of virus from these sites diminishes between days 11 and 14, and ceases by day 15. The virus can be recovered from mononuclear cells in peripheral blood around day 8 postinfection.[47]

Feline herpesvirus type 1 infection has been experimentally reproduced by a number of researchers.[12,13,20-22,25-27,35] Clinical signs usually appear within 2 days in experimentally inoculated cats and persist for 10-14 days. Fever in germ-free cats occurs by the second day postinfection and disappears by the fourth day. A second fever spike follows in natural infections, probably as a result of complicating secondary bacterial involvement.[13,35,39,45]

Clinical disease is more common in environments with a high density of kittens and where stress and other exposure factors are unfavorable. High-incidence environments include catteries, boarding facilities, multiple-cat households, animal pounds and humane shelters. Clinical disease is much less common among relatively free-roaming, solitary household and yard cats.

Clinical Features

At least 7 naturally occurring clinical syndromes are attributed to FHV-1 infection: abortion; neonatal disease; classic rhinotracheitis in kittens; chronic conjunctivitis and keratitis; recurrent disease in older cats; chronic sinusitis; and miscellaneous syndromes.

The role of FHV-1 in abortion in queens was confirmed by experimental studies in which pregnant queens were inoculated IV with infectious virus.[25] Virus was found in the placenta and uterine vessels 6-9 days later. Virus was demonstrated at day 26 in the fetal liver and chorioallantoic membrane. Though abortion was seen occasionally in pregnant queens that had been intranasally infected, no virus was detected in the uterus, placenta or fetuses.[25] Abortion after intranasal inoculation was attributed to nonspecific debilitating effects of the infection. Others were also unable to show *in-utero* transmission following maternal infection.[23]

Neonatal disease seems to be associated with queens that fail to provide maternal immunity or infect their young at birth or shortly thereafter. Neonatal mortality was high among kittens born to queens infected intravaginally with FHV-1 late in gestation.[2] Some of these kittens were born with respiratory disease and the clinical appearance was reminiscent of canine herpesvirus infection. Kittens infected during this neonatal period usually faded away and died over several days.

Classic FHV-1 infection occurs in kittens 6-12 weeks of age, when maternal immunity has waned. Severity of signs varies greatly from outbreak to outbreak and animal to animal. Inapparent infections are common.[23] The most consistent manifestation is rhinitis with sneezing and nasal exudation. Sneezing is particularly pronounced in the early stages of infection. The nasal exudate is serous initially but rapidly becomes purulent and sometimes blood tinged (Figs 1-4). Kittens with mainly rhinitis may have a low-grade fever but usually continue to eat. Clinical signs usually disappear in 7-14 days. A few kittens in an outbreak show rhinitis, pharyngitis, glossitis, tracheitis, high fever, depression, anorexia, open-mouth breathing and drooling (Fig 3). Pneumonia may be seen at necropsy. Mortality, when it occurs, is usually among this latter group of animals. Recovery often takes 2 weeks or more.

Contrary to many published descriptions of the disease, conjunctivitis is less common in FHV-1 infection than rhinitis. When conjunctivitis does occur, it can be mild to severe, and is bilateral (Fig 2, 4). Minimal serous discharge is seen early in the infection but can become more copious and purulent with time. Photophobia, or squinting, is particularly characteristic of FHV-1 keratoconjunctivitis and is due to involvement of the corneal epithelium and possibly the associated nerves (Fig 4). Chronic low-grade conjunctivitis and rhinitis can persist for weeks or months in some cats. Herpetic ulcers can also be a troublesome complication of FHV-1 infection.[37]

Corneal lesions are acute or chronic. Corneal ulcers occurring during the acute stage of illness are often large, superficial and very painful (Fig 3). Chronic lesions are less painful and consist of clusters of small whitish plaques in the central cornea. Limbal blood vessels invade the area in an attempt to heal the ulcer, and pigment is deposited along their paths. Acute herpetic ulcers sometimes enlarge rapidly and perforate the cornea, especially if lesions are secondarily infected with bacteria, and corticosteroids are used topically.

Recurrent disease in older cats is infrequent. It occurs as a result of reinfection in the face of waning or short-lived primary immunity or from stress activation of a latent infection. Recurrent disease can be brought about by corticosteroid injections, social stress associated with cat shows or new environments, surgical stress, chronic debilitating diseases, or the immunosuppressive effects of disease, such as FeLV or FIV infections. Recurrent disease resembles primary disease but is much milder and does not last as long. However, severe re-

Figure 1. Mild recurrent rhinitis, characterized by a slight serous nasal discharge, in an adult cat with herpesvirus type-1 infection. The eyes and mouth are unaffected. Sneezing and nasal exudation lasted about 1 week before resolving.

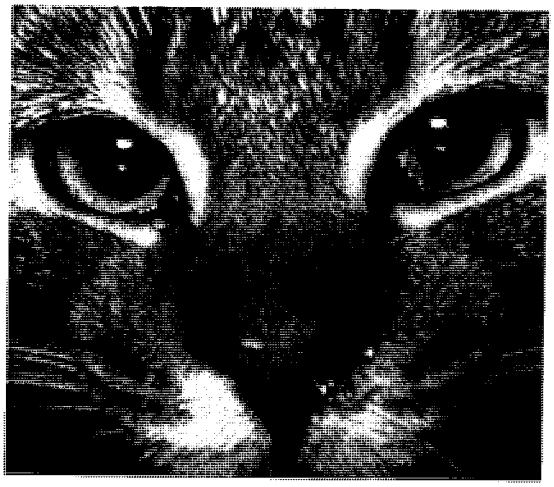
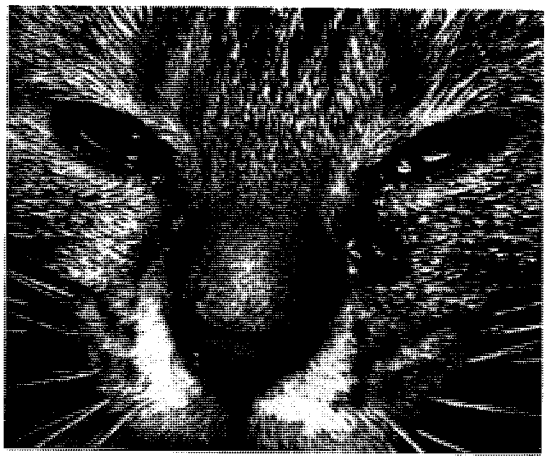


Figure 2. This cat with acute herpesvirus type-1 infection has rhinitis and painful keratoconjunctivitis, but no oral or pharyngeal lesions. Though not evident in this photograph, each eye has a large, superficial corneal ulcer. Such ulcers must be differentiated from the more punctate indolent ulcers associated with herpesvirus keratitis. (From *Virus Infections of Carnivores*, courtesy of Elsevier Science Publishing)



fractory chronic FHV-1 infection can occur in debilitated or immunosuppressed cats.

Chronic rhinitis and sinusitis can be sequelae of severe upper respiratory infections. This complication is much more common in Siamese and related breeds. Turbinate necrosis and damage to the mucosal linings caused by FHV-1 may render the nasal passages permanently prone to chronic infections with bacteria and mycoplasma that normally reside in the area.[26,35] Turbinate atrophy with nasal deformity and chronic epiphora from tear duct obstruction are other uncommon sequelae.

Several miscellaneous disorders have been associated with FHV-1 infection. The virus has been recovered from the brain of kittens, and has been implicated as a cause of CNS disease in experimentally and naturally infected kittens.[8,27] Ulcerative glossitis and skin ulcers due to FHV-1 have been observed in cats without respiratory signs.[30] Severe pancreatitis and pneumonia in a kitten have been associated with FHV-1 infection.[50]

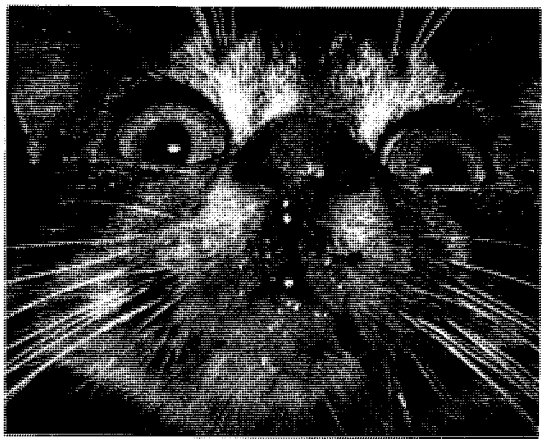
Pathologic Features

Following intranasal infection, the virus causes rapid cytologic infection of the nasal epithelium, with secondary spread to the conjunctival sac, oropharynx, trachea, bronchi and bronchioli. The earliest changes consist of mucosal edema, hyperemia and serous exudation. Focal necrosis of the mucosa follows and the discharges become mucopurulent. Regional lymph nodes and tonsils become enlarged, and small areas of atelectasis may be seen in the lungs.

Microscopic changes in infected epithelial cells resemble those described in cell cultures. Intranuclear inclusion bodies appear in epithelial cells in such areas as the nasal septum, turbinates, bronchi, bronchioli, tongue, conjunctiva and cornea. This is followed by disruption of the epithelium and secondary bacterial invasion. The submucosal tissues become edematous and infiltrated with polymorphonuclear cells. Lymphoid-cell infiltration follows during the recovery stage.

Bone necrosis has been described in kittens inoculated IV with FHV-1.[26] Adult cats do not demonstrate bone lesions following IV challenge, suggesting that growing bone is more susceptible to infection than mature bone. Bone lesions in intranasally infected kittens are limited to the nasal turbinates.[35] Atrophy of the turbinates and gross facial bone deformities may be sequelae of bone necrosis.

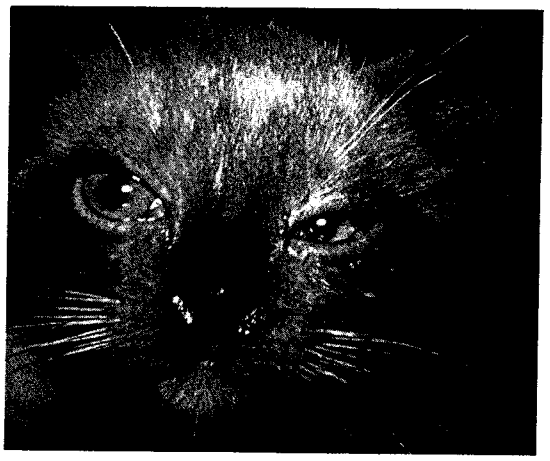
Figure 3. A young cat with herpesvirus type-1 infection. The eyes are unaffected, but the nares are encrusted with exudate. Glossitis and pharyngitis cause drooling. (From *Virus Infections of Carnivores*, courtesy of Elsevier Science Publishing)



Clinicopathologic Features

Feline herpesvirus infection should be suspected in any outbreak of respiratory disease in which rhinitis and sneezing are prominent clinical signs. Conjunctivitis as the only clinical sign is more apt to be due to *Chlamydia* or *Mycoplasma*, especially if

Figure 4. Rhinitis and keratoconjunctivitis in a kitten with herpesvirus type-1 infection. The serous oculonasal discharge often becomes purulent after several days. Squinting indicates painful eyes.



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it initially affects only one eye. Oral ulcers, especially if accompanied by fever and limping and in the absence of conjunctivitis and rhinitis, are more likely to be due to calicivirus.

Feline herpesvirus type 1 can be easily isolated from nasal exudates, conjunctival swabs or oropharyngeal swabs from clinically affected animals. Such material contains large amounts of virus. Cats with positive virus-neutralizing antibody titers should be considered active or latent carriers. However, some latent carriers may not have appreciable antibody titers. The latent carrier state can be detected by treating cats with corticosteroids for several days and culturing oropharyngeal secretions 4-10 days later.[23]

Leukocytosis with absolute neutrophilia is common in the first week of infection. Lymphocytosis may occur in the immediate postrecovery period.[47]

Treatment and Prevention

Treatment of severely affected individuals consists of: keeping the nostrils and eyes clear of discharges; oral or parenteral antibiotics to treat secondary infections; fluid and electrolyte replacement in severe dehydration; oral alimentation when necessary by stomach, nasal or pharyngotomy tube; and specific topical antiherpetic eye medications to treat corneal ulcers. Systemic or topical corticosteroid use should be avoided. Treatment is usually least effective in very young kittens and cats debilitated by other diseases, such as FelV and FIV infections. Recovery from primary infection usually takes a minimum of 2 weeks. Recurrent attacks are generally mild and last 3-10 days.

Feline herpesvirus type 1 is susceptible to systemic antiviral drugs, such as acyclovir and derivatives.[52] However, there is no clinical experience with use of such drugs in treating diseased cats.

Cats can be vaccinated against FHV-1 infection with vaccines containing killed virus, relatively virulent virus given parenterally, or attenuated virus given parenterally or intranasally.[4,32,38,42,51] Parenteral vaccination with killed- or live-virus vaccine gives good systemic immunity but weak local immunity. Such immunity lessens but does not abolish clinical signs resulting from a vigorous challenge with virulent virus and does not prevent latent infection. Experimental intranasal vaccination with avirulent live virus has prevented establishment of the latent carrier state.[38] However, this does not appear to be the case in field situations. Feline herpesvirus vaccines, regardless of type, should not be used as the sole means of disease prevention. In environments with unfavorable stress factors, exposure factors and husbandry practices, FHV-1 vaccines often do a poor job. Vaccination should only supplement good husbandry in such situations (see chapter on cattery design and management).

Live-virus FHV-1 vaccines have been implicated as a cause of outbreaks of upper respiratory disease in catteries. This is more likely to occur in catteries that have been previously free of disease, or catteries in which kittens are under severe stress or are genetically weak. Certain brands of vaccine are more likely to have this side effect than others. The phenomenon probably involves initial infection of a small proportion of vaccinated cats, with subsequent reversion to virulence of the relatively avirulent vaccine strain. At that point, the virulent virus is spread rapidly to other susceptible cats.

Infection and Immunity

The exact nature of FHV immunity is not known; cell-mediated as well as humoral mechanisms are probably involved in cats, as they are in other species.[43,49,51] Similar to other herpesviruses, FHV-1 frequently persists in a nonreplicative or latent state. Latent infections develop in as many as 80% of infected cats. Infectious or latent virus is found mainly in tissues of the head. Of 10 cats, 1 was an active shedder, 7 became active shedders after corticosteroid administration, and 2 cats treated with corticosteroids did not actively shed virus.[22] Feline herpesvirus type 1 was isolated from homogenates of nasal turbinates (9 of 10), soft palates (3 of 10), tonsils (3 of 10), oral mucosa (3 of 10) and tongue (2 of 10). It has been postulated that virus persists in the trigeminal nerve ganglia and other such structures.[22]

Latent carriers have been converted to active virus shedders by giving tham corticosteroids for several days or by stressing them with activities as minor as movement from one animal quarter to another.[20,21]

Virus activation also occurs in queens from stress of parturition and lactation, which may be an important source of infection for kittens.[23] When passive maternal immunity wanes, the kittens become infected.

There does not appear to be a good correlation between maternal virus-neutralizing antibody titers and duration of passive immunity in kittens.[23,41] Some kittens with high maternal titers to FHV-1 become infected, while others with low or undetectable titers resist. Maternal virus-neutralizing titers are usually 1:4 by 2-10 weeks. Kittens may become infected relatively early, while systemic maternal immunity is still present. This may allow the virus to establish itself in the body without clinical illness.[23]

Duration of immunity following experimental infection is variable.[48] Cats are solidly immune 21 days after infection, but most are again susceptible at 150 days. Recurrent disease is much milder and more transient than the primary disease. A similar situation occurs in nature. Recurrent bouts of transient rhinitis and conjunctivitis are common, especially in environments where primary disease is frequent and severe. Protection against recurrent disease is only partially mirrored by serum virus-neutralizing antibody levels.[48] Cats with higher antibody titers tend to be resistant, while previously exposed cats with lower or negative titers may or may not be resistant.

Animal and Public Health Considerations

Cats actively or latently infected with FHV-1 are only health hazards to susceptible domestic cats and closely related species. FHV-1 is not a human pathogen.

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Feline Rotavirus Infection

Cause

Rotaviruses are enveloped RNA viruses with a spoke- or wheel-like appearance, hence the name rotavirus (rota = wheel). Rotaviruses infect most species of mammals, including people. Feline rotavirus infects cats throughout the world. Of 50 cats examined in Louisiana, 23 were seropositive.[2] Similarly, 29 of 94 English cats had rotavirus antibodies.[3] Many normal cats presumably harbor and shed low levels of rotavirus in feces. Virus may also be voided by sick animals into the environment, where it can survive for up to 9 months in dried feces at room temperature.[4]

Clinical Features

Kittens are apparently infected early in life with rotaviruses, but disease signs are minimal or absent. Investigators induced transient diarrhea in 2 3-day-old kittens with fecal extracts.[3] One of the kittens was colostrum deprived while the other was not. Though enteritis was more severe in the colostrum-deprived kitten, both survived after a 1- to 2-day bout of relatively insignificant illness. In contrast to kittens, calves with low maternal globulin developed severe enteritis.[4] Therefore, it seems that rotavirus infection is less severe in carnivores, such as cats, than in herbivores.

Pathologic Features

Gross abnormalities are usually not found in the intestinal tract of affected animals. Virus can be identified by immunofluorescent antibody staining and

electron microscopy in epithelial cells of the jejunum and ileum.[1] Rotavirus can be easily detected in cat stools by electron microscopy or enzyme-linked immunosorbent assays using group-specific antisera.

Treatment and Prevention

Affected kittens seldom require treatment for rotavirus enteritis. If diarrhea is severe, oral food and water should be withheld for 24-48 hours and a balanced electrolyte solution given parenterally. Because the disease is generally of little clinical significance, there has been no impetus to develop vaccines or to devise husbandry procedures to limit its spread.

Animal and Public Health Considerations

As far as is known, feline rotavirus is infectious only to cats. Some animal rotavirus species occasionally cause mild enteritis in people. However, feline and human rotavirus isolates appear to be distinct.[1]

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Feline Enteric Coronavirus Infection

Cause

Feline enteric coronavirus (FECV) is one of the most common viral pathogens of cattery cats.[2,4,5,10,15] It is found in virtually every cattery and multiple-cat household, and infects virtually every cat in such environments. One-fourth or more of outdoor and pet cats have also been exposed to FECV. The virus is not an important cause of disease, however. Its importance lies with its extremely close relationship to the feline infectious peritonitis virus (FIPV).[1,7,13,14] Antibodies to FECV cannot be distinguished from antibodies to FIPV and *vice versa*. This has led to a great deal of confusion on the interpretation of FIP diagnostic tests.

Feline enteric coronavirus is extremely difficult to propagate in culture. To date, only one strain has been propagated *in vitro*, though others have been observed by electron microscope or fluorescent antibody testing.[2-4,11]

Feline enteric coronavirus infection has been studied in 2 relatively closed groups of cats. In the first group, FECV was found to be carried by many healthy seropositive cattery cats and shed in their feces.[10] Kittens in this cattery became seropositive to FIPV antigens at 5-16 weeks of age, usually without any signs of illness. A typical coronavirus was seen in the feces and was found to be distinct from FIPV in its disease-causing spectrum. Kittens in a second cattery also developed antibodies to FIPV antigens after weaning.[15] Adult cats in this environment were seropositive and specific-pathogen-free kittens housed with these animals also became seropositive without noticeable disease. About 25% or more of household pet cats also have antibodies detectable with FIPV tests; most of these cats were probably infected with FECV-type coronaviruses and not with FIPV.[5,10]

Pathogenesis

The major source of FECV is asymptomatic carrier cats that shed the virus in their feces.[10] Kittens in the acute stage of the infection also are a major source of virus within breeding catteries. The virus is passed from cat to cat mainly by the fecal-oral route, though the virus can be tracked from one area to the other by caretakers.[10] Kittens usually become infected between 5 and 16 weeks of age. Systemic passive and lactogenic immunity probably protects the kittens from infection until weaning.

Virus replication occurs predominantly in the small intestine.[3,10,11] There is a minor systemic spread of FECV during initial infection, but the focus of infection is the small intestine.

The acute infection stage of FECV usually goes unnoticed by the owner because of its mild and short course. Following the acute stage of infection, some infected cats

remain carriers for weeks, months or, in some cases, a lifetime. These chronic carriers shed very small amounts of virus as compared to cats in the acute and convalescent stages of the infection.

Clinical Features

Most experimentally infected cats do not develop clinical signs of disease. When present, disease signs are mild and self-limiting and occur 2-7 days after infection. Vomiting is a common initial sign of the infection. Diarrhea follows in 12-24 hours and lasts for 48-96 hours.[10] The stool may be soft and mucus-laden, or fetid and watery. Fatal hemorrhagic diarrhea is very uncommon.[4] Kittens with more severe enteritis may be depressed and anorectic for several days. A transient low-grade fever and leukopenia are often seen in clinically affected animals.[11]

Pathologic Features

Gross lesions in the intestinal tract are usually absent. In severely affected cats, mesenteric lymphadenopathy and edema of the bowel may be apparent.

Clinicopathologic Features

Feline enteric coronavirus should be suspected as the cause of any outbreak of transient enteritis in young cats. The diagnosis can be confirmed by examining stool specimens for virus by electron microscopy.

Serum antibodies appear within 1-2 weeks of infection. Though cats with higher antibody titers are more likely to shed the virus in their stool, there is no accurate serologic test to detect carrier cats.

Treatment and Prevention

Kittens with severe vomiting and diarrhea should not be given food or water for 48 hours and should be given a balanced electrolyte solution parenterally to counteract dehydration and to replace potassium, bicarbonate, sodium and chloride losses. Signs usually abate within 24-48 hours.

Elimination of FECV from catteries is extremely difficult. Serologic tests do not identify carriers, which makes it very difficult to remove or segregate affected animals from the premises. Even if the virus can be eliminated from the cattery, the widespread nature of the infection makes it difficult to keep the virus out.

Infection and Immunity

Though antibodies appear in the serum within a week or so of infection, local rather than systemic immunity is more likely to be involved in recovery and protection against reinfection. Following recovery from the initial infection, serum antibody titers may remain consistently elevated for months or years, or may wane after 2-8 months. Some cats may undergo cyclic and periodic increases and decreases in antibody titers. Circumstantial evidence indicates that cats with persistently high antibody titers are more likely to be carriers that cats that lose their antibodies after a few months. Cyclic increases and decreases of antibody titers probably correlate with infection, loss of the virus from the body, and reinfection.

Immunity to FECV does not extend to the closely related FIPV. In fact, cats with immunity to FECV are more susceptible to FIPV.[8,10,11]

Animal and Public Health Considerations

Feline enteric coronavirus is infectious only for domestic cats and related wild Felidae.

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Feline Infectious Peritonitis Virus Infection

Feline infectious peritonitis (FIP) is a relatively new disease of cats. The definitive reports of FIP were from the United States in the early 1960s.[27] It is doubtful the disease existed much before the early 1950s.[44] The reason for the sudden emergence of FIP is not known. It may be noteworthy that FIP appeared within a decade of the initial descriptions of transmissible gastroenteritis (TGE) of pigs in North America.[17] The causative agents for both diseases, though not identical, are closely related. The dramatic rise in incidence of FIP between 1950 and 1975 coincided with heightened interest in cats as primary pets, increased density of cats in urban areas and catteries, and emergence of such cattery-associated diseases as FeLV infection.[44] Feline infectious peritonitis is now essentially worldwide in distribution.[1,29]

Cause

Feline infectious peritonitis virus (FIPV) is a typical coronavirus with a sun- or crown-like appearance; hence the prefix corona. It is so closely related to TGE virus (TGEV) of swine and canine coronavirus (CCV)that they have all been described as strains of a single virus species.[28,57,64] However, there are distinct differences in the genetic structure of FIPV as compared to other coronaviruses, including TGEV.[10] Feline enteric coronavirus (FECV) is another closely related coronavirus included in this group.[53]

Pathogenesis

Feline infectious peritonitis is mainly a disease of domestic cats. It has also been recognized in the lion, mountain lion, leopard, cheetah, jaguar, lynx, caracal, sand cat and pallas cat.[6,8,14,48,60,61,66,68] Feline infectious peritonitis is seen in cats of all ages, but incidence peaks in cats between 6 months and 5 years of age.[44,48] There is no significant sex predisposition.

In the United States, FIP is more frequent in purebred than domestic cats, and in catteries or multiple-cat households rather than single-cat homes. The incidence of FIP in the United States appears to have plateaued over the last decade. In colder climates of Europe, FIP is seen more often among pet cats and appears to be increasing in frequency.

FIP losses occur as enzootics or epizootics, with the former being much more common. FIP losses are sporadic, unpredictable and infrequent in the enzootic form. Catteries with enzootic FIP may not have any deaths for years; then several cases might be seen in rapid succession. The disease may then disappear, only to reappear months or years later. Overall mortality from enzootic disease is usually 1-5%.

Much higher mortality has been seen in some groups of cats with epizootic FIP, sometimes approaching 25-50% of kittens and adolescent animals.[48,63] Epizootics of FIP seldom last for more than 6-12 months, are relatively uncommon and usually do not strike the same cattery more than once. Following an epizootic of FIP, the disease usually returns to the enzootic form. Enzootic FIP is probably associated with persistence of the same or similar strains of coronaviruses within a population, while epizootics are probably associated with first-time introduction of an FIPV-type coronavirus into the cattery or the introduction of a different strain of the virus.

The precise reservoir of FIPV in cats is not known. Some healthy or subclinically ill cats may harbor and shed FIPV over long periods.[55] Mounting evidence also suggests that FECV carriers may also serve as a reservoir for FIPV. FIPV appears to be a minor

mutant of the more ubiquitous FECV, and hypermutable regions have been observed in the closely related TGEV. Therefore, mutant FECV viruses (*ie*, FIPV) may be shed occasionally by FECV carrier cats or such mutants might be generated *in vivo* in kittens during the course of their FECV infections. FECV-type coronaviruses have been inadvertently introduced into at least 2 large SPF cat colonies. For the first several years no significant disease was seen, but eventually a few cases of FIP began to appear. There also seems to be a relationship between the severity of FECV infection within a cattery and the incidence of FIP. Catteries with a high proportion of cats with high coronavirus antibody titers are more likely to have FIP losses than catteries with cats having low or negative coronavirus antibody titers. There also appears to be a spectrum of FIPV strains, varying from extremely lethal to those that behave almost like FECV (Table 3).[55]

Regardless of the source of FIPV (FIPV carriers, FECV carriers or both), it appears that many cattery cats are infected early in life. Some kittens may be infected *in utero* or as early as the first 5 weeks or life. In some cases, disease is manifested within several days or weeks of infection, but in many cases, disease signs may not appear until many weeks or months later. The highly variable and often long latent period between infection and disease is one of the main reasons that FIP is so feared by cattery owners; it is often impossible to reconstruct whether the infection began in the cattery of origin or was acquired in the new environment after a kitten was sold.

The incubation period and clinical outcome of FIPV infection depend on several complex and incompletely understood factors, including strain of the virus and immunologic responsiveness of the host. The strain of virus is very important and related to immunologic responsiveness. Highly pathogenic strains of FIPV cause fatal FIP in almost all cats, regardless of age, route, inoculation or immunologic responsiveness (Table 3). However, these strains may be largely laboratory artifacts and atypical of most field strains.[55] Outbreaks of FIP with extremely high morbidity and mortality are very uncommon in nature, suggesting that such highly virulent laboratory strains are atypical. In contrast, other strains of FIPV never induce FIP when given by the oral route, though they are infectious and evoke serum antibodies. When given intraperitoneally, they are more virulent, but still only cause FIP in 50% or so of infected cats.[55]

The immunologic responsiveness of the cat also appears to be important in determining the clinical outcome of infection. Most strains of FIPV that exist in nature can be efficiently contained and eventually eliminated by normal cats. After infection, there is a rapid immune response and the virus is contained within local lymph nodes and eliminated over a few weeks or months. Cats that efficiently contain the virus during the initial stage of infection show no clinical signs of illness. However, if this immunity is in some way impeded, the virus is not contained and disease results. High levels of stress, concurrent infectious diseases, malnutrition or specific nutritional deficiencies, trauma (such as elective surgery), pregnancy/parturition/lactation, and genetic weaknesses occurring during the crucial containment period can lead to clinical disease.

The interrelationship of virus strain and host resistance is an important concept. If infected cats develop good resistance and the strain is of low virulence, disease is uncommon even though infection is frequent. At the opposite extreme, if the strain is of greater virulence and the cat's resistance is low, the incidence of FIP is high. This relationship explains why FIP is so unpredictable within catteries where the infection is common.

The initial site of FIPV replication in naturally occurring disease probably varies according to route of infection. Following parenteral infection (all routes other than oral), the virus probably replicates in macrophages within regional lymph nodes. After ingestion, the initial site of replication is probably the intestinal mucosa. Infection can also occur after experimental intratracheal inoculation of FIPV.[33,52]

Clinical disease is associated with dissemination of virus to target tissues via blood-borne phagocytes.[73] FIPV disseminates to tissue rich in phagocytic cells, in which FIPV replicates.[45] Sites particularly rich in target cells include Kupffer cells of the liver, visceral peritoneum and pleura, uveal tract, and the meninges and epen-

dyma of the brain and spinal cord. After dissemination, the ultimate course of disease depends on the type and degree of immunity that develops.

Virus containment is a function of strong cell-mediated immunity; humoral immunity is not protective. Many cats sequester FIPV for a prolonged time after initial infection. These subclinical or latent infections are usually caused by low-virulence strains of FIPV.[55] Maintenance of inactive infections is under immunologic control of the host. Situations interfering with established FIPV immunity can lead to disease.

Clinical Features

Feline infectious peritonitis refers to the principal clinical form of the disease, a transmissible inflammatory condition of the visceral mucosa and omentum.[74] A second form of the disease is characterized by granulomatous involvement of such parenchymatous organs as the kidneys, mesenteric lymph nodes, bowel wall, liver, pancreas, central nervous system and uveal tract of the eyes.[41,44] Granulomatous FIP is called "dry" or noneffusive because there is no inflammatory exudation into body cavities. Classic FIP, which comprises about 75% of cases, is termed "wet" or effusive.

The incubation period (time from infection to disease) of effusive FIP is 2-14 days under experimental conditions.[12,49,52,55] Experimentally induced noneffusive FIP has a longer incubation period. Though the incubation period for experimental FIP is relatively short and constant, the incubation period for FIP in nature can be as short as a few days or as long as a year or more. Feline infectious peritonitis in kittens 4-10 months old is often preceded by a long history of vague ill health and failure to grow at a normal rate. Affected kittens in the incubation stage of FIP may be more susceptible to other common feline diseases, indicating that their resistance is not normal.

At the time clinical signs of FIP are apparent, the disease is of the effusive (three-fourths of cases) or noneffusive (one-fourth of cases) type. However, cats with noneffusive FIP often go through a brief initial bout of effusive FIP weeks or months before death. Conversely, some cats suffer for weeks or months with low-grade noneffus-

Table 3. Variations in infectivity and virulence of various feline coronavirus isolates.

Strain	Infectivity*	Ability to Cause FIP following:	
		oronasal or oral inoculation	intraperitoneal inoculation
FECV-UCD	high	none	none
FECV-79-1685	high	none	none
FIPV-UCD2	high	none	extremely low**
FIPV-TN406 (high passage)	moderate to low	none	extremely low
FIPV-UCD3	high	none	moderate
FIPV-UCD4	high	none	moderate to high
FIPV-UCD1	moderate to low	moderate	high
FIPV-TN406 (low passage)	moderate to low	moderate to high	high
FIPV-79-1146	high	high	high
FIPV-Nor15	high	high	high

* Infectivity is defined as the ability to cause seroconversion following oral or oronasal inoculation.

**Extremely low = less than 1 case in 20-40 inoculated cats.

ive disease and then develop effusive FIP terminally.

The onset of effusive FIP is heralded by a chronic fluctuating fever often associated with a progressive decline in weight, activity and appetite over a 1- to 6-week period. Terminally, affected cats go into shock and die. Peritonitis and ascites are seen in over 90% of cats with effusive FIP; pleuritis with hydrothorax is a sole or accompanying feature in about 40% of cases (Table 4). Ascites leads to abdominal distention (Figs 5, 6) and hydrothorax to dyspnea (difficult breathing). Fluid distention of the pericardial sac, sometimes leading to cardiac tamponade and heart failure, is a rare occurrence.[81] Intact males frequently develop scrotal enlargement due to extension of peritonitis to the tunics surrounding the testes (Fig 5). Peritoneal and pleural exudates are characteristic of the disease. Involvement of other organ systems, such as the eyes and CNS, is clinically apparent in only 10% of cats with effusive disease, though a somewhat higher proportion may have microscopic lesions in these and other nonserosal sites (Table 4).

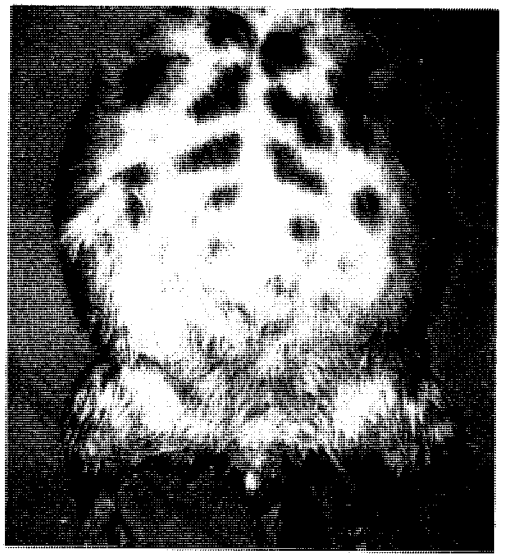
Cats with noneffusive FIP are ill 2-16 weeks or more. As in the effusive form, a chronic fluctuating fever accompanies the disease, along with a progressive decline in general body condition and appetite. Kittens with noneffusive FIP may fail to grow normally, and this may be the sole outward sign for weeks or months. In addition, signs referable to specific organ systems are seen. Peritoneal cavity lesions are found in 50% of cats with noneffusive FIP and pleural cavity lesions in 10% (Table 4). Unlike cats with the effusive form, one-third of cats with noneffusive FIP show signs referable to the central nervous system and have clinically apparent ocular disease (Table 4). Peritoneal cavity lesions in noneffusive FIP usually consist of irregular solitary or multiple masses within the kidneys, or hepatic or mesenteric lymph nodes (Fig 7). Granulomatous lesions in the liver, spleen, pancreas, omentum, serosal surfaces and intestinal walls are less frequent. Testicular enlargement is seen less frequently in cats with noneffusive FIP. Thoracic cavity lesions of noneffusive FIP are usually clinically silent. When present, they are usually on the pleural surface or heart (Fig 8).

Table 4. Variability in clinical signs of noneffusive FIP.

Clinical Signs Referable to Involvement of the:	Number of Cats
Peritoneal cavity	30
CNS	22
Eyes	14
CNS and eyes	8
Peritoneal cavity and eyes	7
Peritoneal and pleural cavities	4
Peritoneal and pleural cavities, CNS	3
Peritoneal and pleural cavities, eyes	2
Peritoneal cavity, CNS, eyes	2
Pleural cavity	1
Pleural cavity, CNS, eyes	1
Total	94

Central nervous system involvement is varied in its clinical expression and is much more likely to be associated with noneffusive FIP. Spinal signs, such as posterior paresis, incoordination, hyperesthesia, and palsy of the brachial, trigeminal, facial and sciatic nerves, have all been described.[25,36,38,44,65] Hydrocephalus, secondary to disease of the choroid and ependyma, has also been reported.[13,23,37] Cranial development can lead to dementia, personality changes (rage, withdrawal) or convulsive disorders. Cerebellar-vestibular signs, such as nystag-

Figure 5. Grossly distended abdomen of a kitten with effusive feline infectious peritonitis. Note the scrotal enlargement.



mus, head tilt or circling, have also been associated with FIP.

Ocular lesions can occur by themselves or in association with lesions in the CNS or peritoneal cavity.[48] Like CNS disease, ocular involvement is more common in noneffusive FIP (Table 4). Uveitis and chorioretinitis are the predominant ocular manifestat ions of the disease (Fig 9).[4,5,11,15,65]

Miscellaneous sites for lesions in noneffusive FIP include the nasal passages, tongue and distal small intestine. Granulomatous colitis due to FIPV has also been described.[82] *In-utero* infections with FIPV result in atypical disease. Pneumonia, pleuritis and hepatitis are the principal lesions in affected kittens.[40]

Pathologic Features

The pyogranuloma is the typical lesion of effusive FIP.[26,73,74] A pyogranuloma consists of necrotic debris and neutrophils, surrounded by a dense accumulation of phagocytic cells interspersed with a few lymphocytes and plasma cells. Considerable amounts of fibrin and protein-rich fluid are also deposited within and around the lesions.[73] Pyogranulomas appear as distinct

Figure 6. Over 600 ml of a yellow, mucinous effusion was removed from the abdomen of the kitten in Figure 5 at necropsy.

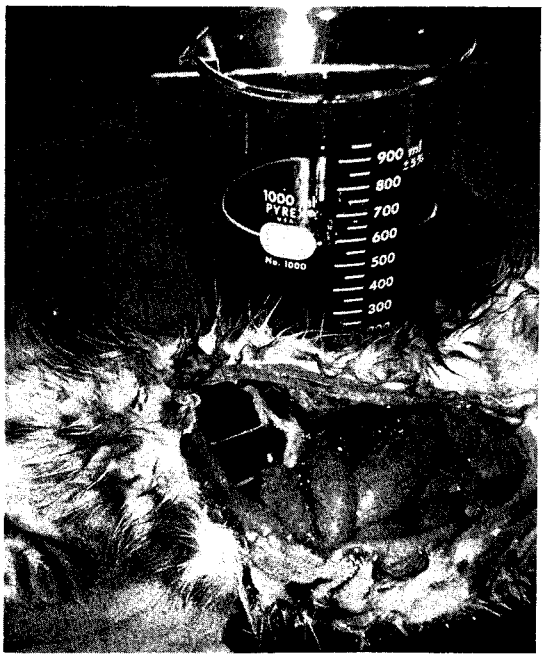


Figure 7. Mesenteric and hepatic lymph nodes and liver from a cat with noneffusive feline infectious peritonitis. The lymph nodes are enlarged and involved with granulomatous adenitis. The liver capsule contains raised, whitish foci 0.5-1 cm in diameter, extending into the underlying parenchyma.

or coalescing serosal plaques 0.5-2 mm or more in diameter (Fig 10). The visceral serosa of the thorax and abdomen is more likely to be involved. The omentum is often thickened, edematous and retracted into a compact mass. Though the pyogranulomatous process is usually surface oriented, a similar inflammatory reaction may extend

Figure 8. Lungs of a cat with noneffusive feline infectious peritonitis. A solitary, whitish granuloma is present on the edge of the left cranial lobe. Lymph node and liver lesions were also present in this cat (Fig 7).

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into underlying tissues along penetrating veins. Focal lesions, often associated with phlebitis and a mixed inflammatory-cell infiltrate, may be seen deep in underlying muscle or organ parenchyma.

Lesions of noneffusive FIP are more typically granulomatous in nature, but nevertheless basically resemble the pyogranulomatous lesions of effusive disease. Granulomatous lesions vary in size, depending on the organ involved.[26,41,65] Ocular and CNS lesions more closely resemble the microscopic or small pyogranulomatous reactions seen in effusive FIP. Serosal, mesenteric and omental lesions also appear as small whitish plaques or nodules. Kidney, liver and mesenteric lymph node lesions are often very large, sometimes exceeding 5 cm in diameter. The outer zone of these granulomas is characteristically more fibrous, and the number of plasma cells and lymphocytes much greater than the pyogranulomas of effusive FIP. Edema, hyperemia, and fibrin and protein exudation are not as pronounced as in the pyogranulomatous lesions of effusive FIP.

Lymphoid lesions are common in effusive and noneffusive FIP. Splenic enlargement may be due to histiocytic and plasmacytic infiltration of the red pulp, hyperplasia of lymphoid elements in the white pulp, necrotizing splenitis with fibrin deposition and

Figure 9. Keratic precipitates on the inner cornea of a cat with noneffusive feline infectious peritonitis. A granuloma on the right side of the iris caused iridial discoloration and an irregular D-shape of the pupil.

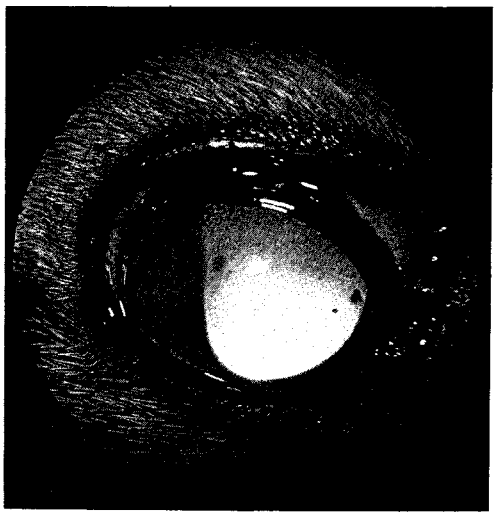
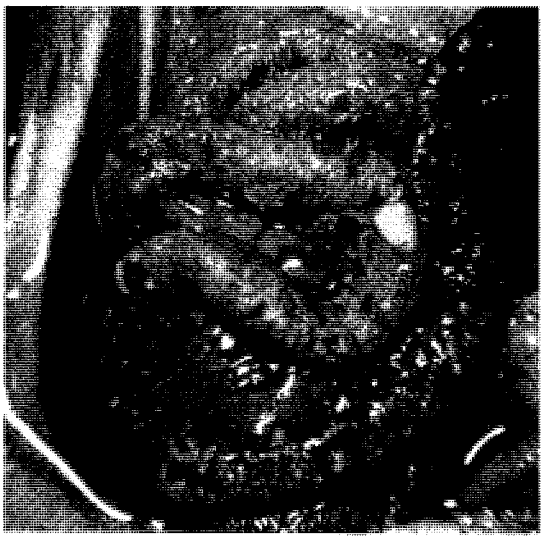


Figure 10. Abdominal viscera of a cat with effusive feline infectious peritonitis. The serosal surface of the intestines and spleen are covered with punctate, coalescing fibrinous plaques, the classic pyogranulomas of effusive FIP. Some peritoneal effusion remains, though most has been removed.



polymorphonuclear cell infiltrates, or by more organized pyogranulomatous reactions. Gross lymph node enlargement is usually limited to thoracic and abdominal nodes and is due to lesions resembling those described for the spleen.

Fluorescent antibody staining of tissue sections from cats with both forms of the disease shows FIPV in the lesions. In effusive FIP, a large amount of viral antigen is contained in phagocytic cells that make up the periphery of the pyogranulomas.[51,52,73] Less viral antigen is present in lesions of noneffusive FIP; it is usually found within a few macrophages adjacent to veins in the center of the lesions.

Clinicopathologic Features

Complete blood counts show similar changes regardless of the disease form. Leukocytosis with neutrophilia and lymphopenia is a common abnormality. In chronic disease, low-grade to moderately severe depression anemia is also seen.

Icteric serum or plasma, with or without evident jaundice of the tissues, is common in cats with FIP, especially the effusive form. In fact, FIP is the most common cause of an icteric serum or plasma in a cat

<3 years of age. The increased level of bilirubin in the blood is usually not due to liver involvement *per se*, but rather to microhemorrhage into tissues and extravascular destruction of red blood cells by phagocytic cells.

Total plasma protein levels are elevated in 50% of cats with effusive FIP and 75% of cats with noneffusive FIP. This increase is due to elevated levels of inflammatory and antibody proteins.

Disseminated intravascular coagulopathy occurs in cats with effusive FIP.[71] It is usually clinically inapparent but may contribute to the production and character of pleural and abdominal effusions.

Ascitic and pleural fluid from cats with effusive FIP is usually pale to dark yellow, and has a sticky, viscous consistency, somewhat like synovial fluid or egg white, with a high protein and WBC count.

Aqueous humor and CSF in cats with ocular or CNS disease also show similar increases in proteins and leukocytes. Synovial fluid from cats with effusive FIP is frequently inflammatory in character.

Following introduction of tests for detection of FeLV infection, 40-50% of cats with FIP were found to have concomitant FeLV infections.[9] With elimination of FeLV from many catteries and pet cat households, and the steady decline in the incidence of FeLV in the entire cat population, the proportion of cats with FIP and concurrent FeLV infections has greatly decreased. At the present, virtually all cases of FIP in purebred cattery-bred cats are FeLV negative, and FeLV infection is detected in 10% or less of domestic pet cats.

Many serum antibody tests have been used for diagnosis of FIP.[1,46] Unfortunately, they do not differentiate between cats infected with FECV and FIP, carrier cats and clinically ill animals, or FIPV shedders and nonshedders.[47,48] Antibody tests are only helpful if the clinician understands the serologic responses of cats experimentally infected with FIPV and related FECV.

When specific-pathogen-free, antibody-negative kittens are infected by oral or intratracheal instillation of FIPV, they react serologically in several ways, depending on the dose and strain of virus.[52,55] Some cats do not develop signs of infection after prolonged exposure and remain antibody negative. Infected cats that do not develop signs of illness show a flat antibody response, while cats that develop FIP show a progressive increase in antibody titer. Virus-neutralizing antibodies tend to correlate with immunofluorescent antibody (IFA) titers in both groups of cats.[49] Some infected cats, however, only develop virus-neutralizing antibodies, and IFA titers are negligible.[47]

Serologic responses are much more difficult to interpret in the field because of the great amount of antigenic similarity between FIPV and FECV, and ubiquitousness of FECV infection in nature. Investigators were unable to show differences in antibody specificity of serum from cats infected with FECV or with various high- and low-pathogenicity FIPV isolates.[3] For this reason, serodiagnosis of FIP in the field is fraught with a great deal of inaccuracy. However, currently used serologic procedures still have some usefulness. Immunofluorescent antibody titers $\geq$1:3200 are usually associated with FIP, frequently of the noneffusive type. Titers this high are uncommon in cats infected with FECV but may occur in healthy cats with subclinical or latent FIPV infections. Titers of 1:100-1:3200 are common in cats with effusive FIP and in a portion of cats with noneffusive disease. Unfortunately, IFA titers of 1:25-1:1024 are also seen in many cats that have had previous FECV infections or inapparent FIPV infections. Diagnosis of FIP in cats with titers in this range depends on the entire clinical and clinicopathologic picture. Positive coronavirus titers should alert clinicians to the possibility of FIP, while negative titers are often helpful in ruling it out. However, some cats with pathologically confirmed FIP have been seronegative by IFA, so a negative IFA titer is not always helpful. Seronegative cats are most likely to be younger and have fulminating effusive FIP. For these reasons, current FIP serologic tests should not be used as a sole diagnostic determinant of FIP in individual cats.

Because of the vagaries and nonspecific nature of FIP serology, FIP antibody testing should also not be used as a means to control FIP in catteries. Vast amounts of money are spent each year by cattery owners on FIP testing. In almost all cases, the results are uninterpretable. Virtually all catteries have 50-80% or more coronavirus seropositive cats. Most of the antibody posi-

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tivity is due to FECV strains and not to FIPV, and the tests do not differentiate one from the other. Moreover, antibody titers do not answer the critical questions: Has this cat been infected with FIPV? Will this cat succumb to FIP in the future? Is this cat carrying FIPV? Is this cat shedding FIPV? As a result of misguided test and elimination programs, more pedigreed cats in the United States probably die each year from FIPV antibody testing than from the actual disease. Ultimately, FIP must be diagnosed by clinical signs, clinicopathologic findings, and ante- or postmortem examination of tissues. Serologic testing should only be used as a general guide to diagnosis.

Treatment and Prevention

No treatment has proven uniformly and consistently effective. Cats that develop FIP usually die in 1-16 weeks. Nevertheless, several cats have reportedly gone into remission after treatment with various drugs. Some cats have gone into remission after treatment with tylosin and prednisolone.[7] This has sparked a decade of tylosin use for treatment of FIP. However, tylosin is now known to have no value whatsoever in treatment of FIP, and the fortuitous response in the original cats was probably due to self-cures or the prednisolone. Some cats went into remission after use of prednisolone and phenylalanine mustard or cyclophosphamide.[44] Another cat was successfully treated with prednisolone and phenylalanine mustard.[39] However, such treatments have also proven to be of limited effectiveness. In my experience, <5% of cats go into brief or sustained remission after treatment with immunosuppressive drugs. Successfully treated cats usually had milder illness, and were still eating and not overly debilitated when treated. Owners were also more apt to administer continuous supportive care in the form of fluid therapy, forced feeding and other such attentions. Debilitated animals inevitably die and drug therapy actually hastens their demise.

A number of dubious treatments have been used for FIP. The FIPV is very sensitive to interferons *in vitro*,[83] but these are ineffective *in vivo*. Various immunostimulants and megadoses of vitamins have also been advocated. These are equally ineffective. Spontaneous remission is a complicating factor in evaluating treatment success. Not every cat with FIP dies. Necropsy of older cats without overt signs of FIP has occasionally demonstrated fibrous lesions on the spleen and liver that indicate past FIP infection. Cats with ocular signs and no other systemic manifestations of FIP have occasionally gone into remission with just topical treatment. Cats with chronic fever, enlarged mesenteric lymph nodes that were histologically compatible with FIP, and high coronavirus titers have spontaneously gone into remission without treatment. Finally, small quiescent lesions in the spleen and mesenteric lymph nodes have been discovered in some infected cats during routine ovariohysterectomies. Therefore, it is sometimes difficult to ascertain whether a treatment is successful or if remission was naturally induced.

Currently, no vaccines are available to prevent FIP. Though FIPV immunizes baby pigs against TGE, initial attempts to immunize cats with TGE virus have been unsuccessful.[67,77] Immunization with killed FIPV has also proven uniformly unsuccessful.[34] Immunity derived from killed vaccines almost always renders cats more susceptible to challenge with the virulent live virus, and the resultant disease is usually more severe and fulminating. A genetically engineered vaccinia virus that expressed the envelope protein of FIPV has been recently tested.[87] It enhanced virulent FIPV infection rather than protecting cats.

Several research groups have been experimenting recently on the use of modified-live-virus vaccines for FIP.[86] When such attenuated virus is given oronasally to susceptible cats, a protective immunity against the virulent parental strain has been evoked. Such vaccines hold the best hope for biological control of FIP, but considerably more safety and efficacy testing remains before they can be licensed.

The incidence of FIP within catteries can be decreased by proper management. Mortality tends to increase as the population of animals, especially kittens, increases. Losses from FIP are also proportional to the severity of other kittenhood diseases, including herpesvirus, calicivirus, chlamydial, mycoplasmal, dermatophyte, parasitic and enteric infections. Kittens kept in crowded

catteries with a large number of other young animals suffer greatly from concurrent diseases. These diseases stress the kittens' immune system and are often associated with a temporary decrease in growth rate and an increase in susceptibility to disease in general. Feline leukemia virus infection, a bane of many catteries in the past, is the single most powerful potentiator of FIP in cats. Elimination of FeLV infection from many catteries has decreased the incidence of clinical FIP. Genetics also play an important role in FIP. Fragile strains of purebred cats are often more susceptible to FIP, probably because of decreased overall disease resistance. Death losses from FIP can sometimes be traced to certain breedings, and further breeding of pairs that produced affected kittens should be avoided. Breeding practices in catteries often result in an abundance of younger breeding animals. Younger animals are more apt to be carriers of disease agents than older animals; the carrier state is often only a protraction of acute illness. This is why catteries with breeding cats 4 years of age and older often have less disease than catteries with younger breeding stock.

Infection and Immunity

Immunity to FIPV appears to be largely cell mediated.[49,51,55] Humoral immunity is not protective or, in some cases, enhances disease.[48,49,51,55,72] The type and strength of immunity also determine the disease form (effusive, noneffusive, recovery or asymptomatic carrier state). Effusive FIP occurs in cats that mount a humoral immune response but fail to develop concurrent protective cell-mediated immunity.[55]

The duration of virus persistence in FIPV-recovered cats is not known. The disease can be reactivated in almost all cats within the first 2 months after infection, but not after 4-6 months.[55,80] This situation resembles that seen in latent FeLV infections.[56] Latency in FeLV infection is merely an extension of the recovery process and usually resolves within 6 months of the disappearance of viremia. This appears to be characteristic of many infectious diseases in which cellular immunity is important for recovery; the longer the period after recovery, the more difficult it is to demonstrate persistence of the agent. Immunity to many infections, including FIP, must be a slow, ongoing process that takes weeks, months or years. In some individuals, the agent may persist for a lifetime. In fact, persistence of the organism in the host may be an essential requirement for perpetuation of immunity.[49,55] Indeed, when latently infected kittens eliminate FIPV, they also lose their immunity.[55]

Animal and Public Health Considerations

Feline infectious peritonitis virus is a naturally occurring infection of domestic and wild Felidae. People are not hosts for the virus. Dogs and swine can be experimentally infected with FIPV; a mild to moderately severe TGE-like syndrome occurs in baby pigs.[76] However, it is doubtful that FIPV is a cause of naturally occurring enteritis in these species. Cats that carry FIPV or those with active disease should be considered infectious to other cats. Fortunately, only a very small percentage of cats naturally infected with FIPV ever develop disease. Further, by the time FIP is first diagnosed in a group of cats, the virus is usually well established. In practice, therefore, disease control by quarantine and isolation of individual animals seldom influences the natural course of disease in a group of cats.

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Feline Calicivirus Infection

Cause

The surface of feline calicivirus (FCV) is made up of cup-shaped depressions.[12] The prefix "calici" is derived from the Greek word *kalyx* for cup or chalice.

Feline calicivirus is not inactivated by lipid solvents, such as ether or chloroform. Infectivity is destroyed by heating to 50 C for 30 minutes. It is inactivated at a pH of 3 but becomes more stable as pH values increase. Infectivity is retained for at least 4 years at -65 C.[3]

Pathogenesis

Feline calicivirus causes disease mainly in domestic cats but has also been associated with illness in some wild Felidae.[11] Clinical illness is more common in catteries and multiple-cat households than in single-cat households. Clinical disease is most common in kittens, and in situations in which other infectious diseases are also likely to be problems. Infections with different serotypes probably occur throughout life but are not likely to be of great clinical significance. It is unlikely that many cats escape infection.

Feline calicivirus persists as an active asymptomatic infection in many recovered cats. In some areas, up to one-third of adult cats are silent oropharyngeal carriers. Virus can be isolated from the tonsillar tissues of recovered cats for at least 34 days.[6] Virus is shed almost continuously from the oropharynx by FCV carriers.[10,14] Maternal immunity protects kittens from infection for the first 3-9 weeks of life.[18] Kittens then become susceptible to infection by virus shed in the saliva of asymptomatic or clinically ill animals. Vaccination with live-virus vaccines is also a frequent cause of disease in kittens.[19,20]

The main route of infection is oral and the initial site of infection is the oropharynx. This localized primary infection is followed by transient viremia, with localization of virus in the epithelium of the nasal passages, conjunctiva, tongue, palate or other tissues. A diphasic temperature response follows experimental aerosol infection. The first temperature rise occurs about 24 hours after infection, and the second occurs between 96 and 168 hours. Recovery is rapid thereafter. Following experimental aerosol exposure, virus can be recovered from the conjunctival sac for 7 days, nasal passages and pharynx for at least 2 weeks, feces for 2 weeks, tonsils for 5 weeks and lungs for 10 days.

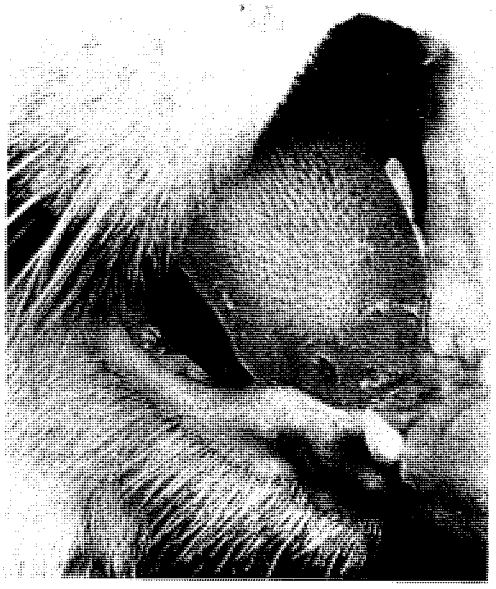
Clinical Features

The predominant clinical signs of naturally occurring FCV infection differ from one report to another. Upper respiratory disease is the principal form of infection described in the literature, but this form has only been partially recreated by massive aerosol exposure.[3] Conjunctivitis is not a common or pronounced feature of experimentally recreated disease and does not persist beyond 13 days. Rhinitis is also uncommon and is most severe by day 6 and disappears by day 10. Small vesicles occur in the palate and tongue of many experimentally infected cats. Vesicles rapidly rupture, leaving shallow erosions (Fig 11). Vesicles and erosions appear toward the end of the disease course and heal rapidly. Focal pneumonia is also a consistent lesion seen in kittens exposed to aerosols. The lungs are mottled with reddish areas of congestion and edema early in the course of infection. After several days, the pneumonic lesions consolidate to form elevated, firm areas in the lung that are pinkish-gray to pale red, have a patchy distribution and usually resolve by day 10.

Recent studies on naturally occurring and experimentally induced FCV infection indicate that upper respiratory disease is not the most common disease manifestation.[9] A transient fever associated with shifting lameness, and lasting 24-72 hours, is a far more common presentation. Oral ulcers are somewhat less frequent.

Caliciviruses have been isolated from feces of pound kittens undergoing epizootics of diarrhea. Though caliciviruses are asso-

Figure 11. Lingual ulcerations associated with acute calicivirus infection. (Courtesy of Dr. R.C. Povey, Langford, Inc, Guelph, Ontario)



ciated with so-called outbreaks of winter dysentery in people, their role in epizootic diarrhea in kittens remains to be determined.

The role of other disease agents in potentiating FCV infection and *vice versa* should not be underestimated. In a study of synergism between FCV and feline panleukopenia virus infections, mortality of 82% was observed in kittens infected with FCV and panleukopenia virus at the same time.[1] In contrast, mortality was only 10% in feline panleukopenia virus-infected cats and only 5% in cats infected with FCV alone. Feline herpesvirus type 1, *Mycoplasma, Chlamydia* and bacteria are all involved in kittenhood infections. The resulting syndromes are often caused by combinations of these and other disease agents.

The role of persistent calicivirus infections in chronic oral cavity disease (gingivitis, periodontitis, stomatitis) of cats is an area of interest. Australian researchers were the first to describe a high incidence of oral calicivirus in cats with chronic gingivitis and stomatitis.[13] Eight of 10 affected cats were culture positive, while 10 healthy controls were negative. Calicivirus infection was linked with FIV infection and chronic stomatitis in cats in the United Kingdom.[7] Seventy-nine and 92% of British cats with stomatitis in 2 different study groups were FCV infected, as compared to 19% of healthy appearing animals. However, 81% of the cats with stomatitis and 16% of the healthy cats were also infected with FIV. In a study of the relationship between gingivitis, periodontitis and stomatitis and chronic calicivirus or FIV in a household of 69 domestic cats in northern California, 27 of the cats had normal mouths and 42 had oral disease ranging in increasing severity from gingivitis (19 of 42), gingivitis and periodontitis (16 of 42), stomatitis and/or cheilitis (5 of 42), and gingivitis, periodontitis and stomatitis and/or cheilitis (5 of 42). Seventeen of the cats were chronic oral carriers of FCV, and 11 were persistent FIV carriers. Of these 28 carrier cats, 4 were coinfected with both viruses. Cats with FCV infection were no more or less likely to have oral disease than FCV-uninfected cats. However, all 11 of the FIV-infected cats had some degree of oral disease. Therefore, it appears that FCV infection alone is not a major cause of chronic oral disease in cats.

Pathologic Features

Focal, interstitial pneumonia is the most consistent lesion seen in experimental disease; rhinitis and conjunctivitis are uncommon and mild when present.[6] Fatal pneumonia is almost always due to complicating secondary bacterial invasion.[3]

Glossal and palatine ulcers are common in both experimental and naturally occurring disease.[4,6] Ulcers have rarely been observed on the footpads and perianal region.[8] The ulcers are derived from fluid-filled vesicles (2-5 mm in diameter) in the epithelium. Oral lesions are more apt to be seen in kittens eating abrasive dried food than in kittens consuming soft canned food.[4]

The cause of the characteristic limping is unknown. Nerves, muscles and joints appear microscopically normal.[9] The number of macrophages in synovial fluid is often increased, however. These macrophages may contain virus-antibody complexes.[19]

Clinicopathologic Features

FCV can be easily isolated on tissue culture from oral swabs of diseased and carrier cats, and from the blood of clinically ill animals.[9] The limping syndrome is associated with moderate to extreme increases in synovial fluid macrophages. The carpal and tarsal joints are most severely affected.

Treatment and Prevention

Fever, joint and muscle pain, and glossal and palatine ulcers disappear within 48-96 hours. Pneumonia, which is an uncommon sequela in nature, is usually due to secondary bacterial invasion of primary viral leions. Likewise, purulent nasal and ocular discharges are almost always associated with complicating bacterial, chlamydial or mycoplasmal infections. Antibiotics are valuable to counteract secondary infections. Though early reports of FCV infection emphasized the seriousness of the disease, the mortality of uncomplicated FCV infection is very low.[9,18]

Because it is virtually impossible to eliminate carrier cats from the environment, control of FCV infection is largely by vaccination. However, FCV can exist in many cat populations without causing serious problems.[18] Concurrent disease, stress and other factors may combine to potentiate disease severity in certain outbreaks.

Though current vaccine strains produce various degrees of cross-protection, the protection they afford is not necessarily against all field isolates.[9,19] The ease with which vaccine-resistant strains can be isolated from catteries indicates that serologic differences are more important than recently believed and immunization less effective than reported.

The effect of long-term calicivirus vaccination on the FCV carrier state was recently questioned. Feline caliciviruses have been isolated with the same frequency from the oral cavities of normal cats today as they were before vaccination was started over a decade ago.[19] The frequency of calicivirus isolation from cats with respiratory infections may even be higher today than in the past.[17] Caliciviruses have been isolated from the oral cavities of 20-30% of normal cats in catteries where vaccination is routinely practiced.[7] It is uncertain whether the strains in catteries are different from the vaccine strains, or if they are identical. It appears certain that both occur. Observations such as these bring into question the benefit of live-virus calicivirus vaccine programs in catteries as well as the general cat population.

Infection and Immunity

Feline calicivirus persists in the oropharynx of many cats and is actively shed in the saliva even with systemic immunity.[15-17] Carrier cats can be classified as low-, medium- or high-level virus shedders.[16] Susceptible cats can be infected in 2-3 days by high-level shedders, and in 11-13 days by low-level shedders. Unlike feline herpesvirus (rhinotracheitis), shedding is not influenced by stress.[16]

Maternal antibodies to FCV have a half-life of 15 days and persist in the serum of kittens for as long as 14 weeks.[5] Antibodies are virus neutralizing and very strain specific, especially when collected soon after infection. Maternal immunity to FCV appears to be incomplete.[2-4] Kittens with maternal immunity can often be infected as young as 3-9 weeks of age.[4,15,18] Even though virus can be isolated from the oropharynx, clinical signs and an active humoral immune response do not occur until maternal immunity declines several weeks later.[4,18] At this point, clinical signs are inapparent or relatively mild, and the resultant primary immune response develops slowly and reaches lower levels than in kittens free of maternal immunity at exposure. In contrast, kittens with very low maternal maternal titers rapidly become ill after infection and the disease is more severe.[4] The immune response also comes on more quickly after infection and reaches higher levels. Maternal immunity may lessen severity of disease in situations with a high level of exposure that occurs early in life.[18] In a small cattery where many of the cats were carriers, kittens showed few signs of illness due to FCV, even though they all became infected at an early age.

Animal and Public Health Considerations

Feline calicivirus is only infectious to domestic and some wild Felidae. It is not a human pathogen.

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Feline Leukemia Virus Infection

Cause

Feline leukemia virus (FeLV) was first identified in cats from a household that had lost several animals to lymphosarcoma.[34] In 1973, an indirect fluorescent antibody (IFA) test was developed that accurately detected viremia in infected cats.[22] The test was rapidly applied to clinical use, mainly as a diagnostic procedure for lymphosarcoma. As a result of clinical testing, FeLV was determined to be: horizontally spread from cat to cat; associated with a great many diseases other than lymphosarcoma; and carried and shed by many apparently healthy cats for long periods before illness developed.[5,9,18,21,24]

Feline leukemia virus does not survive long outside the cat.[12] It loses its infectivity within minutes or hours at room temperature. Some strains even lose considerable infectivity when stored at -70 C. Feline leukemia virus is destroyed within minutes at 56 C and is sensitive to most disinfectants.

Pathogenesis

Feline leukemia virus infects domestic cats throughout the world. Wild cats do not harbor the infection but can be infected when exposed to domestic cats. The incidence of infection is directly related to population density; rural cats have the lowest infection rate and affected cattery or multiple-cat household cats have the highest.[10,60] Urban areas, where many cats live in apartments, condominiums and tenement houses and are still allowed to roam outdoors also have a high incidence of infection.[8] Cats that live their life entirely within high rise apartments, as in New York City, have a very low incidence of infection.[21] These cats are rarely allowed to roam outdoors and have very little exposure to infected animals.

Feline leukemia virus is carried and shed by healthy, subclinically ill or chronically ill cats. In catteries with enzootic FeLV infection, about one-third of the cats are active carriers and shedders.[21,24] The incidence of active carriers in rural areas may be less than 1%, while in most high-density urban and suburban areas the incidence is 2-6%.[31,60] Infected cats have very high levels of virus in their blood and shed almost equal amounts in their saliva.[13,27] Smaller amounts of virus are also found in urine and feces.[27] Tears contain levels of virus about equal to blood levels.[25]

There are 2 basic routes of infection: horizontal via the passage of virus from infected to susceptible cats, and *in utero* from infected queens to their fetuses.[17,24] Though *in-utero* infection results in fetal or neonatal death in 80% of affected queens, 20% of kittens born to FeLV-infected mothers may carry the infection into later life.[48] Queens that have recovered from FeLV infection usually provide their offspring with maternal antibodies that protect them against infection in the first 12 weeks or so of life.[33]

Cats are exposed when they come into contact with infected animals, either while roaming outdoors or when infected and susceptible animals are housed together indoors. In Glasgow, Scotland, the infection rate among free-roaming cats increased progressively with time, and by 3-8 years of age, most cats had been exposed to the virus.[60] Active FeLV infections are uncommon in cats 10 years or older. Cats usually contract the infection early in life and recover or die before they reach later life.

Horizontal spread of FeLV infection requires prolonged intimate contact between cats. The reasons for this are the low stability of the virus in nature, the relatively large dose of virus required to infect by the oral route, and age resistance. Prolonged intimate exposure allows virus spread by mutual grooming and sharing of litter pans. A simple wire partition between cats is sufficient to prevent cross-infections if there is no physical contact between cats or their excretions. Bite wounds are an efficient mode of transmission because a large amount of virus can be injected directly into the body. Infection can also be spread via blood transfusions and reuse of dirty instruments for sequential surgeries.

Resistance to FeLV infection increases with age.[28] Following infection, 70-100% of neonates become persistently viremic for life. Kittens 8-12 weeks of age are much more resistant, and only 30-50% become persistently viremic following exposure.[53] Less than 10-20% of adolescent or adult cats become persistently viremic, and then only after exposure lasting as long as 1.5 years.[15] Age resistance can be virtually abolished by pretreating older cats with corticosteroids at the time of infection.[63] Presumably, natural forms of stress may do the same thing.

Following oral or oronasal instillation, the virus first replicates in regional lymphoid tissue of the oropharynx.[62,64] Virus can be detected within several days in a few circulating mononuclear cells in the blood. These cells apparently carry virus to the target organs in other areas of the body, such as the spleen, lymph nodes, and epithelium of the intestine, bladder and salivary glands. About the same time that virus appears in secretion or excretions from these organs, it also reaches cells in the bone marrow and appears in peripheral blood leukocytes and platelets. Viremia in weanling kittens seldom occurs sooner than 2-4 weeks after infection.[32,53] Viremia and virus shedding persist for less than 1-16 weeks in 70-90% or more of cats.[53] However, when viremia disappears, it usually does so in the first few days or weeks. Cats that remain viremic after 16 weeks usually remain persistently viremic for life, though on occasion viremia disappears after many months or years. Virus shedding usually stops when viremia disappears.[32] In a few instances, virus continues to be shed in tears, urine, milk or saliva for several weeks or months after cessation of viremia.[32,40,48] Eventually, however, even this virus shedding ceases.

Following recovery from viremia, virus persists as a latent infection in the bone marrow.[43,51,65] After 6 months, however, even latent infections become hard to demonstrate in most recovered animals.[51] In this regard, latency appears to be merely an extension of the postviremia recovery process for most animals. However, a small proportion of recovered cats may harbor infectious virus in a latent form for years and become viremic again months or years later. Latent infections can sometimes be converted to active infections by giving the cat glucocorticoids during the immediate postviremic period.[51,56,65] However, activation is very strain dependent, and latent infections with most field strains are activated only with difficulty.[51] Reactivation of latent infections can occur spontaneously up to 6-8 months following recovery in less than 10% of recovered cats.[51]

Most mortality resulting from FeLV infection occurs in persistently viremic cats.[44] Disorders associated with the persistently viremic state can be divided into several categories: *in utero* and neonatal deaths of kittens; lymphoid and myeloid neoplasms, aplastic or hypoplastic anemia, neuropathies or quasi-neoplastic syndromes; secondary or opportunistic infections due to acquired immunodeficiency; and immunologic disorders.

Clinical Features

Feline leukemia virus infection has 2 main clinical stages.[53] The initial stage occurs 2-6 weeks following infection and corresponds to the appearance of virus in the blood, saliva, urine and feces for the first time. This state of the disease is manifested by varying degrees in severity of fever, malaise, generalized lymphadenopathy, leukopenia, thrombocytopenia and anemia. These signs usually persist for 1-16 weeks before all clinical abnormalities disappear. Death is uncommon during this primary stage of disease; when it occurs, it is usually a consequence of sepsis, hemorrhage and anemia. These disorders are usually a result of profound leukopenia, thrombocytopenia and anemia.

Cats that survive the initial stage of infection make a real (true) or apparent (false) recovery.[53] True recovery is manifested by disappearance of virus from the blood, and eventually from other tissues as well. Cats that make an apparent or false recovery appear outwardly normal but remain persistently viremic for life. As a rule, cats that show either mild or inapparent signs during the initial stage of infection are usually among those that make a true recovery. The more severe the clinical signs are during the initial stage of infection, the more likely that the cat will become persistently infected.[53]

Cats that make a true recovery following initial infection usually suffer none of the long-term complications associated with FeLV infection. There is one exception, however. Completely recovered cats still suffer a higher incidence of lymphoid tumors than cats that never were infected.[11] This increased incidence is much less than in persistently viremic cats.

The secondary stage of FeLV occurs months or years after the primary stage and is heralded by the appearance of some FeLV-related disease. The secondary stage is ultimately terminated by death within 1-12 months. Mortality among persistently viremic cats is progressive and relentless, and averages about 50% each year that the cats remain infected. Therefore, most FeLV-infected cats die within 3 years.[44]

FeLV-related disease is either a direct consequence of infection (reproductive problems, lymphoid and myeloid neoplasms, miscellaneous neoplasms, aplastic or hypoplastic anemia, neuropathies or quasi-neoplastic syndromes) or an indirect consequence (immunodeficiency, immune-mediated disorders) of the virus infection itself.

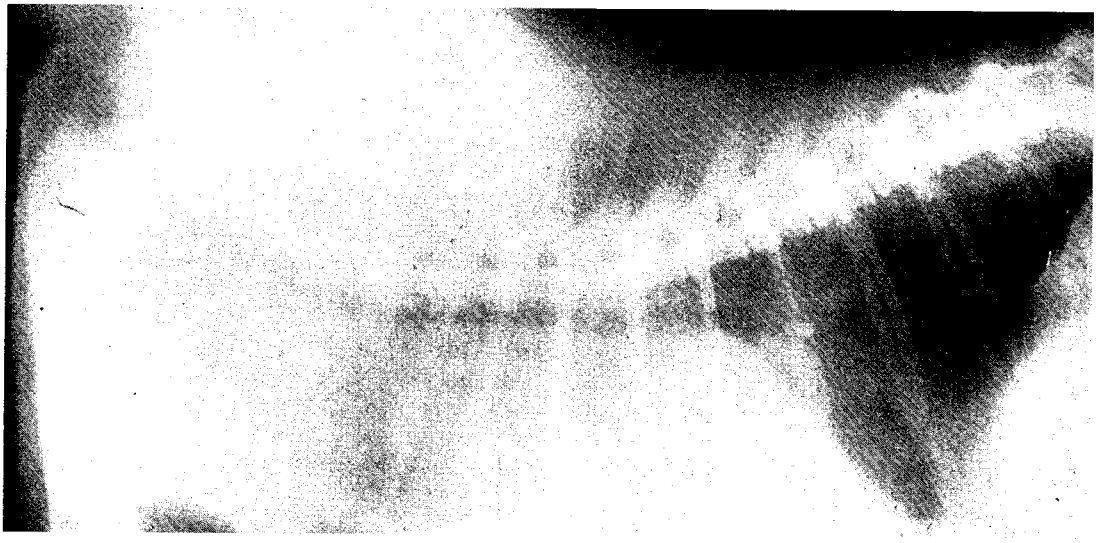
Reproductive problems in infected queens have been widely recognized but poorly documented. Abortion, fetal resorption, stillbirths and neonatal deaths occur in over 80% of viremic queens. However, some kittens are born apparently healthy, but are viremic and carry this viremia into later life. The cause of fetal losses has not been well studied. Virus can be recovered from most fetal tissues and the placenta.[30]

About one-half of FeLV infected cats die of cancer. Cancers related to FeLV-infected cats are of 3 types: lymphoid, myeloid or miscellaneous. Lymphoid tumors account for one-half to two-thirds of the FeLV-related cancer, myeloid tumors (often called myeloproliferative disease) account for about one-fourth to one-third, and miscellaneous cancers for the remainder. Most FeLV-related cancers occur from several months to 3 years or more following infection, and are usually seen in cats less than 6 years of age.[11]

Lymphoid neoplasms can be solid (lymphosarcoma) or more diffuse, with involvement of the blood (lymphocytic leukemia). FeLV-induced lymphosarcoma has been classified as multicentric, thymic, alimentary or miscellaneous.[16] Multicentric lymphosarcomas tend to occur in cats around 4 years of age, and about 90% are associated with FeLV. Thymic lymphosarcomas occur in cats around 2.5 years of age and about 80% are associated with FeLV. Alimentary lymphosarcomas are common in older cats but only about 25% of these cats have active FeLV infections. Miscellaneous lymphosarcomas involve the skin, eyes, kidneys or nervous system. Ocular and neural lymphosarcomas are usually associated with FeLV infection, whereas renal and dermal lymphosarcomas occur more often in FeLV-negative cats. Less than one-third of cats with lymphosarcoma have leukemia (abnormal lymphoid cells in the blood). Leukemia can occur with any of the solid forms of lymphosarcoma but is most frequently associated with multicentric disease.[16] However, some cats may have only blood and marrow involvement.

Cats with thymic lymphosarcoma usually show acute dyspnea and pleural effusion. Abnormal lymphoid cells may be detected in the pleural fluid. Grossly, the thymus often fills the entire cranial thorax and can encircle the heart (Figs 12, 13). Multicentric lymphosarcoma is often manifested by various combinations of generalized lymphadenopathy, anemia, hepatosplenomegaly and renal involvement; abnormal lymphocytes are often seen in the blood and/or pleural effusions. Neural lymphosarcoma is most commonly manifested as acute posterior paresis or paralysis (Fig 14). Generalized CNS disease or more focal peripheral nerve palsies are less commonly observed. Ocular lymphosarcoma can occur by itself or in association with other forms of the disease. Ocular lymphosarcoma is the most frequent

Figure 12. Lateral thoracic radiograph of an FeLV-infected cat with thymic lymphosarcoma. Note the lack of lung detail cranial to the heart, characteristic of a thymic mass. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)



tumor in the eyes of cats and can involve the orbit, nictitating membrane, conjunctiva, cornea, fundus or iris and ciliary body (Fig 15).[71]

Myeloproliferative neoplasms arise from primitive stem cells, granulocytic precursors, erythroid precursors, or less commonly from megakaryocytes. Collectively, these myeloid cancers are called myeloproliferative diseases.[3,16,26] They tend to be seen during the first 6 years of life, with a peak incidence around 4 years of age. Abnormal cells often appear late in the course of disease and the initial clinical signs are usually referable to anemia, hepatosplenomegaly and sometimes icterus. About 70% of animals with myeloproliferative disease are persistently FeLV infected.

Myeloproliferative diseases have been classified into the following types: reticuloendotheliosis; erythremic myelosis; erythroleukemia; myelogenous leukemia; megakaryocytic leukemia; and myelofibrosis.[16] Reticuloendotheliosis is characterized by primitive undifferentiated stem cells in the blood and bone marrow.[14] Erythremic myelosis is a disorder characterized by an increased number of nucleated RBCs without a corresponding increase in more differentiated reticulocytes. The granulocytic cell series is normal. Erythroleukemia is similar to erythremic myelosis except that both immature erythroid and myeloid cells are present in the blood. Myelogenous leukemias induced by FeLV usually arise from precursors of polymorphonuclear neutrophils or monocytes. Eosinophilic, basophilic and mast-cell leukemias are not FeLV-associated disorders. Megakaryocytic leukemia is an uncommon disease manifested by an increase in megakaryocyte and platelet numbers. Myelofibrosis is a terminal state of myeloproliferative disease manifested by marrow hypoplasia and fibrosis.

Figure 13. At necropsy, the thymic tumor filled the cranial thoracic cavity and had invaded the pericardium. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)

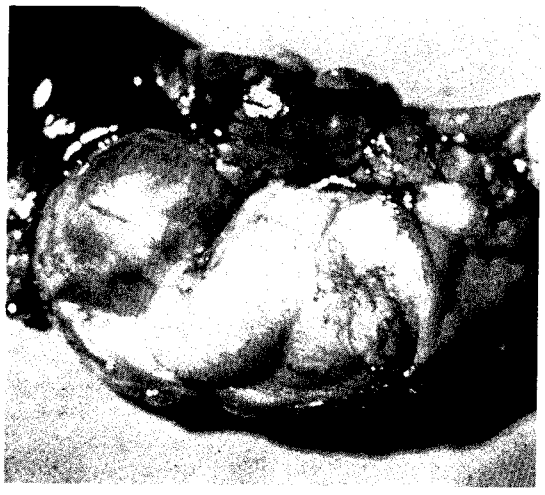
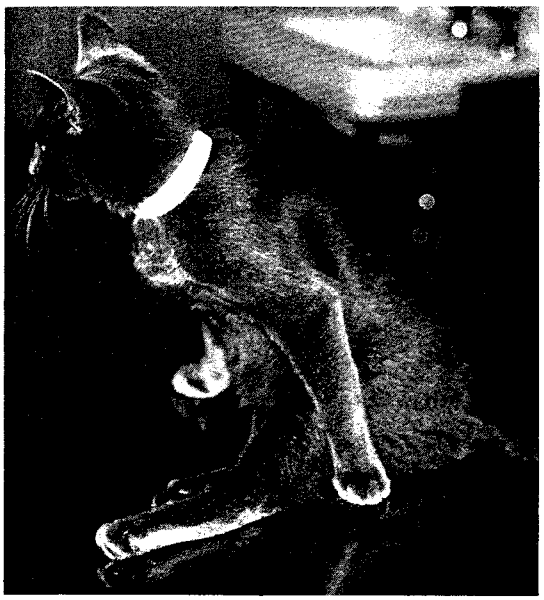


Figure 14. Acute hind limb paralysis in an FeLV-infected cat. Necropsy revealed focal lymphosarcoma of the spinal cord dura mater. (From *Virus Infections of Carnivores*, Elsevier Science Publishing)



There are several miscellaneous quasi-neoplastic or neoplastic syndromes associated with the FeLV carrier state. Though uncommon, they are very flamboyant in clinical expression. Multiple cartilaginous exostoses are seen in younger FeLV-infected cats.[55] Multiple firm pea- to egg-sized growths occur on flat bones of the skull, ribs, scapula, spine and long bones of the limbs. The growths are basically chondromas. Affected cats slowly waste away and die. Benign cutaneous keratin horns on the footpads have also been associated with chronic FeLV infection.[4] They probably represent overgrowth of keratinocytes, similar to the hyperplasia of chondrocytes seen in multiple cartilaginous exostoses. Multicentric rapidly growing fibrosarcomas almost always occur in FeLV-infected cats.[19] A cell-free extract of these tumors induces the same type of tumors when inoculated into susceptible cats. The tumor extract contains two types of viruses, an intact replication-competent FeLV and a replication-incompetent mutant FeLV. This mutant FeLV, called feline sarcoma virus (FeSV), arises within a very small proportion of FeLV-infected cats as a result of genetic recombination between FeLV and normal cat genes. These normal cat genes, called oncogenes, are important for differentiation of cells during embryogenesis. When these genes are incorporated into FeLV, however, they become activated and cause uncontrolled cell differentiation and a fibrosarcoma. Olfactory neuroblastoma, a rare tumor of the brain and nasal cavity of cats, also appears to be an FeLV-related disorder.

Figure 15. Iridal lymphosarcoma in an FeLV-infected cat. (Courtesy of Dr. Ned Buyukumihci, University of California)

Aplastic and hypoplastic anemias are common in chronic FeLV carriers and account for about one-fourth of all FeLV-related deaths. Aplastic anemia is characterized by progressive anemia and subsequent death. More commonly, the anemia is hypoplastic rather than aplastic and the RBC count hovers at a low level for weeks or months, or may also rise or fall in increments. If anemic cats live long enough, many develop myeloproliferative disease. In fact, anemia almost always precedes clinical expression of tumor cells by weeks or months.[53] Anemia is not always the sole abnormality in cats with hypoplastic or aplastic bone marrow. Thrombocytopenia and granulocytopenia are frequent accompanying features. Cats with hypoplastic or aplastic anemia do not usually show clinical signs until the anemia becomes severe. Listlessness, pallor of the mucous membranes and occasionally jaundice are the signs most noticeable to the owner. Hepatomegaly and

splenomegaly are usually detected on physical examination.

Neuropathies are infrequent but important features of chronic FeLV infection. Cats with neuropathies may have no histopathologic abnormalities or may have sparse focal lymphocytic infiltrates into peripheral nerves or the spinal cord. Persistent unilateral mydriasis (anisocoria) in the absence of blindness or intraocular disease is the most common neuropathy seen in FeLV-infected cats (Fig 16). The anisocoria is due to involvement of the short ciliary nerve innervating the muscles of the iris. Urinary incontinence may be another manifestation of neuropathy in infected cats. Of 11 cats with urinary incontinence, 9 were FeLV infected.[2] The cats responded poorly to conventional therapy for urinary incontinence and no lesions were seen on histologic examination of 4 cats necropsied. Some cats with neuropathies show vague pain or hyperesthesia over the spine, or posterior paresis. Acute demyelinating myelopathies have also been seen in FeLV-infected cats.[18]

All of the aforementioned disorders are caused by the direct effect of the virus on certain cells of the body. In contrast, the remaining disorders are indirectly related to FeLV infection and occur because of more complex interactions of the virus and host tissues. Disorders that are indirectly related to the infection are either infectious disease potentiated by FeLV-induced immunosuppression or immune-mediated diseases. Viral diseases potentiated by FeLV include feline infectious peritonitis (FIP) and upper respiratory infection. In the past, about 40% of cats suffering from FIP had concurrent FeLV viremia.[5,47] This relationship is not nearly as common as it used to be, due mainly to a great reduction in the incidence of FeLV infection in catteries and other multiple-cat households. The precise mode of FeLV-induced enhancement of FIP virus infection is unknown, but it appears to be very selective.[49] Severe and intractable rhinotracheitis virus infections have been seen in some FeLV-infected cats, especially debilitated or bone marrow-suppressed animals (Fig 17). FeLV-infected cats also have a higher incidence of viral upper respiratory disease than uninfected cats.[2]

Figure 16. Anisocoria in an FeLV-infected cat. The right pupil did not constrict upon exposure to light.

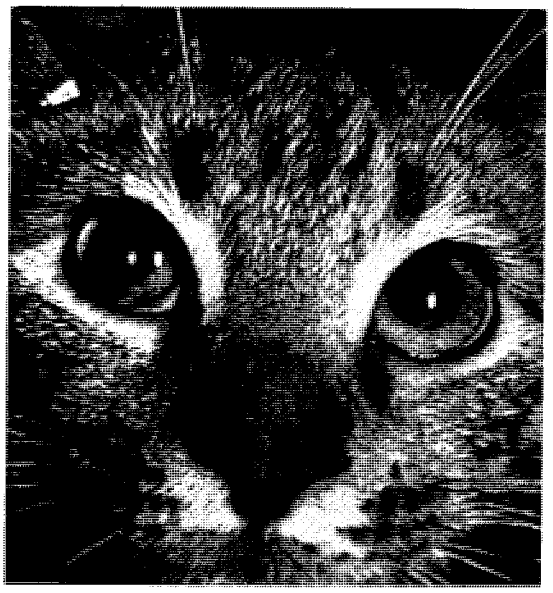
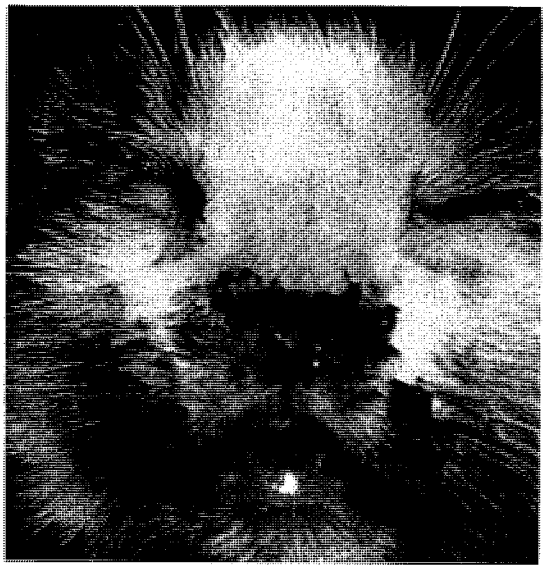


Figure 17. Intractable herpesvirus type-1 infection in an FeLV-infected cat. Squinting is from painful keratoconjunctivitis. The nares are occluded by exudate from herpesvirus-induced rhinitis.



Cats infected with both FeLV and FIV in nature appear to have more severe illnesses than cats naturally infected with either virus alone.[73] FeLV infection was a potentiating cofactor for experimentally induced FIV infection.[74]

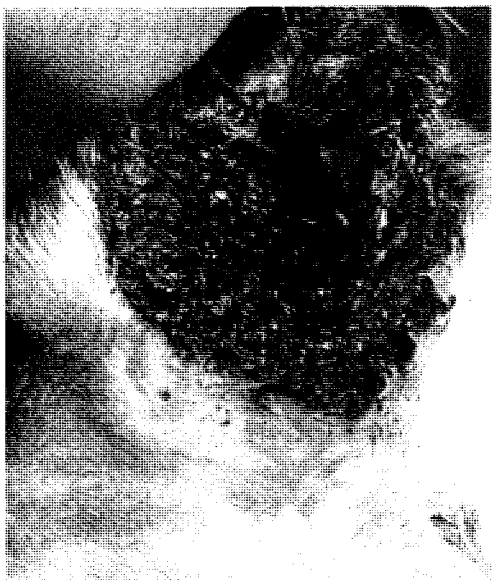
Protozoal diseases enhanced by chronic FeLV infection include toxoplasmosis and hemobartonellosis. Toxoplasmosis is usually not associated with disease in healthy cats

over 8-12 weeks of age, and when it occurs in older animals underlying immunosuppression should be considered (see section on toxoplasmosis).[7] *Hemobartonella felis*, the causative agent of feline infectious anemia (FIA), exists as a subclinical infection in many normal cats. About 50-70% of cats clinically diagnosed with FIA are FeLV infected.[45] Many of these cats have preexisting hypoplastic anemia, or lymphoproliferative or myeloproliferative disorders, so *Hemobartonella* treatment does not always correct the anemia.[57]

FeLV-infected cats have an increased frequency of acute and chronic bacterial diseases.[20,59] Depending on the study, 30-50% of atypical bacterial infections of cats are FeLV associated. Most bacterial diseases occur in cats with subnormal peripheral WBC counts and, as such, a deficiency of phagocytes may be an important underlying cause. However, some FeLV-infected cats also have diminished antibody responses to bacterial antigens.[48] This may contribute to secondary infections. Low-grade proliferative gingivitis is seen in some FeLV-infected cats. Isolated tooth root abscesses and purulent otitis externa are also frequently related to FeLV infection (Fig 18). Peracute enterocolitis (panleukopenia-like syndrome) can be the ultimate cause of death in FeLV-infected cats with myeloproliferative diseases and low WBC counts, or in cats with suppressed cellular and humoral immunity.[58,59] Recurrent abscesses or abscesses that fail to heal normally are frequently associated with chronic FeLV infection. A peculiar necrotizing pneumonia caused by a saprophytic Gram-negative bacterium called EF4 occurs mainly in FeLV-infected cats.

Many immune-mediated diseases are associated with chronic FeLV viremia. Immune-mediated diseases in FeLV-infected cats have 2 major causes: high levels of antigen-antibody complexes circulating in the blood; and interference with normal immunoregulation and autoantibody formation. Immune-complex diseases in FeLV-infected cats are manifested in a number of ways. Many FeLV-infected cats have such vague signs as unthriftiness, episodic depression and minor neurologic problems associated with fine muscle tremors. These signs usually have no histopathologic basis but often subside with continuous use of small doses of corticosteroids. Severe polyneuropathy and myopathy are infrequently associated with FeLV infection. Affected cats develop severe muscle atrophy and myasthenia. This polyneuropathy/myopathy may be due to immune-complex disease.

Figure 18. Severe bacterial infection of the external ear and pinna in an FeLV-infected cat.



About one-third to one-half of cats with autoimmune hemolytic anemia and thrombocytopenia are chronically infected with FeLV. FeLV-related hemolytic anemia in cats is often a prelude to lymphosarcoma or myeloproliferative disease.

Chronic progressive polyarthritis is another disorder potentiated by FeLV infection; about 20% of cats with this disease are FeLV carriers.[52] Chronic progressive polyarthritis is an acute, febrile polyarthritis resembling Reiter's disease in people or a low-grade destructive joint disease resembling human rheumatoid arthritis. The disease is partially responsive to immunosuppressive drug therapy. The precise role of FeLV in chronic progressive polyarthritis is unknown. The disease occurs only in male cats, and all of these cats tested were also infected with feline syncytium-forming virus.

Pathologic Features

Pathologic and histopathologic changes in FeLV-infected cats are as numerous and

diverse as FeLV-related diseases themselves. For this reason, only the salient pathologic features of FeLV-related diseases will be discussed, such as bone marrow dyscrasias, lymphoid and myeloid neoplasms, lymphadenopathy and glomerulonephritis.

Bone marrow abnormalities are seen during the primary phase of the disease, when the host and virus interact for the first time, and in the secondary phase of the illness that occurs months or years later in chronically viremic cats.[53] Anemia, thrombocytopenia and leukopenia in the primary phase of the illness are associated with bone marrow hypoplasia and dysplasia. Anemia later in the course of the disease can have numerous causes.

Lymphoid neoplasms in FeLV-infected cats are comprised of solid masses of cells ranging in maturity from immature lymphoblasts to mature lymphocytes.

Myeloid neoplasms usually originate in the bone marrow and invade the spleen, liver and other tissues to a lesser extent. Myeloid tumors are usually preceded by bone marrow dysplasia or hypoplasia.[53] This suggests that neoplasia is secondary to problems associated with bone marrow maturation. Malignant cells are usually present in the marrow for weeks or months before they appear in the blood. In terminal stages, abnormal cells are released into the marrow in large numbers. The terminal appearance of abnormal cells in the blood of cats with myeloproliferative disorders is reminiscent of the acute blast-cell crisis in leukemic people.

Generalized lymphadenopathy is common in FeLV-infected cats. It is particularly pronounced in the primary phase of infection in younger cats.[53] Lymph nodes may become 0.5-2 cm or so in diameter during this phase, and the increase is due to a reactive lymphoid hyperplasia. Lymphadenopathy in the later stages of infection is frequently due to lymphoid neoplasia.

Clinicopathologic Features

Feline leukemia virus infection is diagnosed by assaying for viral antigens in the blood, by IFA or ELISA tests, or by more laborious tissue-culture isolation procedures from plasma or blood leukocytes. Viremic cats have high levels of viral proteins in their plasma and within the cytoplasm of peripheral blood leukocytes and platelets.

If properly conducted, the IFA test has a high degree of accuracy. False positives are relatively infrequent. However, the IFA procedure is cumbersome to run. It also suffers from a low percentage of false negatives caused by blood smears with inadequate numbers of infected platelets and leukocytes, or by absence of virus in blood cells.

The ELISA is currently the most widely used test for FeLV detection.[36,41,42] The ELISA is simple to run and requires a very small amount of serum or plasma. It has been also adapted for use with tears and saliva.[25,40] Tear or saliva tests detect only about 90% of serum-positive animals and should be used only for rapid or mass screening purposes. ELISA is very sensitive and specific if run properly. However, if the washing steps are not carefully and properly done, or if badly hemolyzed serum or whole blood is used, false positives can occur. This is probably the greatest single weakness of the procedure, but it can be virtually eliminated by proper wash techniques and avoidance of whole blood and hemolyzed serum.[42]

Latent FeLV infection cannot be detected by either ELISA or IFA staining.[51] To detect a latent infection, bone marrow cells must be cultured *in vitro* for up to 6 weeks.[43,51,65] Latent FeLV infections are very uncommon in the cat population, are not associated with illness, and only last for several weeks or months after recovery from initial infection. Therefore, there are no good clinical reasons for testing for latent infections.

Treatment and Prevention

Treatment for FeLV infection is directed at the viral infection itself, and the specific and varied FeLV-related diseases that occur as a result of infection. Treatment of the infection itself has been difficult. Ultimately, control of the infection is totally dependent on the host's ability to mount and sustain an effective immune response. Once the infection becomes persistent, however, the likelihood for eventual self cure is very low. Various immunostimulants, megadoses of multivitamins or vitamin C, and a great number of strange concoctions and proce-

dures have been claimed as cures for FeLV infection; however, none has proven effective. Interferon preparations inhibit the virus in cell cultures, but do not seem to affect the disease in the animal.[70,72] Staphylococcal protein A reportedly cured FeLV infection and/or FeLV-induced tumors in some cats.[6,35,38,70] Anecdotal reports on this treatment were made between 1980 and 1985, but no reconfirmation has appeared since that time and large-scale clinical trials were never conducted. Antiretroviral drugs, such as azidothymidine (AZT), have been used to treat FeLV infection.[29] These drugs inhibit virus replication in the body, but are only effective while they are given, and their toxicity can be severe with chronic use. Many new antiretroviral drugs are under development and testing for treating human AIDS, and some of these drugs may be someday applied to treatment of FeLV-infected cats.

The course of infection in healthy, persistently viremic cats can be influenced by a number of stressful situations. Infected cats living in high-stress, multiple-cat households are more apt to develop complicating disease than cats in single-animal households. Surgical procedures, such as ovariohysterectomy, castration or declawing, can sometimes precipitate crises in otherwise healthy carrier cats, so such procedures should be done with as little stress as possible. Boarding, changes in home environments and other such activities may also shorten the lives of some infected animals. Therefore, it is important to maintain infected cats in environments as free from stress and disease exposure as possible.

Treatments for specific FeLV-related diseases are as varied as the diseases themselves. Lymphoid cancers can be treated with chemotherapy with a reasonable chance for remission but not a cure. However, myeloid cancers respond poorly to treatment. Some secondary infectious diseases, such as hemobartonellosis, tooth infections, abscesses and ear infections, are treatable; others, such as FIP, are not. Immune-mediated disorders, such as autoimmune hemolytic anemia or thrombocytopenia, can be successfully treated with corticosteroids. Cats with aplastic anemia can be kept alive for weeks or months with blood transfusions.

Many FeLV-infected cats suffer from cycles of vague illness manifested by depression, anorexia, vague nervous twitches and weight loss. Such cats benefit greatly from intermittent small doses of glucocorticoids.

Prevention and control of FeLV have been based on routine testing and elimination of carriers.[17] These procedures have been extremely effective in eliminating FeLV infection from confined cat populations, such as in catteries or other multiple pet-cat households. Though testing and elimination have controlled infection in cattery cats, they have had less impact on the spread of disease in the general cat population. In relatively free-roaming cat populations, FeLV infection still remains an important disease.

Testing and eradication consist of 7 steps: test all cats for FeLV infection; remove all FeLV-infected cats from the household; clean all dishes, litter pans and bedding with hot water and soap, and wait 10 days before introducing any new cats; prevent movement of cats in or out of the cattery; retest all quarantined cats 12 weeks after the first test to detect any cats that might have been incubating the infection; lift the quarantine when all cats in the cattery have tested FeLV negative in 2 tests done 12 weeks apart; and test all new cats for FeLV before introduction into the household.[17] In addition, owners of free-roaming cats must be made aware that many cats in the surrounding environments may also be carriers. In this situation, decontamination of the home environment may be of minor importance as compared to limiting direct-contact exposures. Using widespread test and removal, the Dutch have decreased the incidence of FeLV infection among the general cat population in the Netherlands from 9.0% to 3.4% between 1974 and 1985.[69] The incidence in purebred catteries was decreased from 11.5% to 0% between 1974 and 1984.[69] This same pattern of decreasing FeLV infection has also occurred in the United States. Because FeLV infection is so severe when it is introduced into confined cat populations, vigilance by cattery and multiple-cat household owners will be required for as long as the disease continues to exist as an enzootic infection among outdoor cats.

The first vaccine for FeLV infection was marketed in the United States in 1985 (Leukocell: Norden).[67] Two new inactivated whole FeLV vaccines have also been marketed in the United States (Covenant: Diamond Laboratories, VacSyn: Synbiotics). Several more vaccines are at various stages of development and licensing, and will undoubtedly appear on the market in the next few years. Independent efficacy and immunogenicity tests of vaccines currently on the market by the author and other laboratories have not been as positive as tests reported by the manufacturers.[46,48,50] Manufacturers' efficacy claims for FeLV vaccines range from 80% to 90% or more, while independent tests (using USDA test procedures) by the author showed them to be 17-40% effective.[48] One vaccine, tested under natural exposure conditions, was 62% effective.[75] A second group tested the vaccine in essentially the same manner and found it to be totally ineffective.[76] A proportion of cats vaccinated with these products in the field have subsequently become FeLV infected when exposed to infected cats, but the low natural infection rate for FeLV in household pets and cattery cats makes it very difficult to determine whether these cases were exceptions or the rule.

The reasons for discrepancies between independent and manufacturers' test results are not known. However, it is apparent that further independent testing should be done on current and future products. It is hoped that much better vaccines will be forthcoming from worldwide research on FeLV infection and immunity. Until accurate efficacy figures can be obtained for present and future FeLV vaccines, vaccines should not be considered to give total protection. As such, vaccinated cats should not be knowingly exposed to FeLV-infected animals and vaccination should not replace test and elimination procedures for disease control in multiple-cat environments.

Cats have been successfully vaccinated with live-virus vaccines.[17,54] Relatively avirulent strains are available that produce a high degree of protection when given in small doses to older kittens.[54] However, these same strains induce fatal anemia in very young kittens.[28] Also, cats that have recovered from such live-virus vaccinations may be at a much greater risk of developing virus-negative lymphosarcoma later in life.[11,17,23] Doubts expressed by some people about the possible public health hazards of live FeLV have also made it unlikely that a live-virus vaccine will ever by employed for prevention of FeLV infections.[17]

Infection and Immunity

The ultimate outcome (recovery or persistent viremia) of FeLV infection is largely determined by events that occur within the host during the first 16 weeks of infection.[53] Immunity during this critical period is greatly influenced by the age of the cat, dose and virulence of the virus, and stress. Age resistance develops rapidly after 4-8 weeks of age. Cats exposed at a very young ages usually become persistently viremic; older cats usually become aviremic.[28] Age-acquired resistance can be overcome to some extent by increasing the dose of challenge virus and using more virulent strains. It is most easily overcome, however, by subjecting the animal to artificial stress. A single injection of methylprednisolone given within the first 2 weeks after exposure dramatically increases the proportion of cats that become persistently infected.[63]

Termination of viremia appears to be associated with the appearance of virus-neutralizing antibodies in the blood.[31,66] Disappearance of viremia also corresponds with a cessation of virus production by infected cells.

The latent phase of FeLV infection is a transient phase for most cats, and is terminated in most individuals within 1-6 months.[51] It is merely an extension, therefore, of the recovery process. Latency is followed by complete recovery, at which time the virus is no longer present in a form that can be activated in the body.

The persistently viremic state appears to involve some sort of immunologic tolerance. This tolerance develops rather abruptly. At one stage of infection the cat is actively fighting the virus, as evidenced by the pronounced lymphadenopathy. At the other stage, the lymph nodes become quiescent in the face of the same infection that previously evoked an intense immune response. As with any state of immunologic tolerance, it can sometimes be broken. A small proportion of FeLV-infected cats can terminate the persistent viremia after many months or even years. The tolerant

state can sometimes be abrogated by immunologic manipulations.[6,35,38]

Feline leukemia virus infection has been likened to AIDS of people. While human AIDS and FeLV infection have many dissimilarities, there is little doubt that some FeLV-infected cats are immunodeficient. Unlike the immunodeficiency of human AIDS, which involves specific components of the immune system, FeLV infection causes immunodeficiency in many different ways.[20,37,61] Immunodeficiency is not present in all FeLV-infected cats, and is not usually evident until clinical signs of illness appear.

Animal and Public Health Considerations

Feline leukemia virus is found only in domestic cats and some related wild Felidae. The potential health hazard of FeLV-infected cats to people has been controversial.[39,68] This controversy has been an impetus for many research studies. To date, these studies have not shown FeLV to be infectious to people.

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Feline Immunodeficiency Virus Infection

Cause

Feline immunodeficiency virus (FIV) is one of the most recently discovered infectious agents of cats. Though it is a problem in the general cat population, FIV infection is not a cattery disease.[13,29,35] It is a problem mainly of household cats allowed to roam freely outdoors, farm cat populations, and multiple-cat households that adopt free-roaming feral or homeless cats. The disease is discussed herein because of its interesting epidemiologic contrast with FeLV infection (which can be a major cattery problem), the intense interest in the disease by cat owners, and the potential problem with the disease in households with multiple pet cats.

Feline immunodeficiency virus has several biologic features in common with human and simian immunodeficiency viruses (HIV and SIV), which are the causative agents of acquired immunodeficiency syndrome (AIDS) in people.[21]

Pathogenesis

Feline immunodeficiency virus infection was first recognized in cats in Northern California.[21] The infection has been subsequently recognized throughout the United States and Canada, South Africa, Australia, New Zealand, Europe and Japan.[1,2,8,9,12,13,15,25,29,31,33,36] The infection rate varies greatly, depending on environmental factors. Depending on the area, the incidence of FIV among the general cat population ranges from less than 1% to as high as 12%, similar to that of FeLV.[13,15,35] From 4% to 44% of cats with clinical signs suggestive of immunodeficiency test positive for the virus.[13,35] The highest rates of infection are in areas where there is a high density of freely roaming cats. Japan, where there are many freely roaming animals, has a higher incidence than countries where the cat population is less dense and a greater proportion of cats are kept strictly indoors.[13,35] The infection rate seems to be lower in cities than in suburban areas or smaller towns. Purebred catteries have the lowest rate of infection.[13,35]

In every study, male cats have been infected over twice as frequently as females.[1,2,8,11,13,29,35] Most clinically ill cats have been over 5-6 years of age, though infected kittens as young as 6 months have been identified.[13,35] It is not uncommon to find diseased animals that are over 10-15 years of age. This age incidence contrasts with that for FeLV, which is more common in cats less than 5-6 years of age and rare in aged animals. About one-sixth of clinically ill FIV-infected cats are also infected with FeLV.[13,25,27,35]

Feline immunodeficiency virus appears to be transmitted predominantly by bites.[35,36] The virus is shed in the saliva, and puncture of the skin by a canine tooth of an infected cat is highly efficient in transmitting the infection. Clinically ill cats shed much more virus in their saliva than apparently normal infected individuals.[35] The presence of mouth lesions may also increase the infectivity of an infected animal. Transmission by intimate contact in indoor situations, where biting does not usually occur, is very inefficient;[35,36] this is different from FeLV infection.[22] *In-utero* transmission is either nonexistent or uncommon, again different from FeLV infection.[36] Neonatal transmission from infected queens to their kittens, via milk or maternal grooming, also does not occur to any extent.[36] Infected queens, therefore, usually give birth to healthy kittens that remain uninfected. The transmissibility of the virus by blood-sucking insects, such as fleas, remains to be determined.

Infection occurs in 2 stages. The initial stage of the infection has been experimentally studied in specific-pathogen-free kittens.[36] Experimentally infected kittens develop transient leukopenia and fever beginning about 4 weeks after infection. These signs last from several days to 4 weeks. The leukopenia is mainly due to an absolute, and sometimes profound, neutropenia.[36] Platelet and RBC counts remain normal. Generalized lymphadenopathy appears at about the same time and lasts 2-9 months.[36] The initial stage of fever, leukopenia and lymphadenopathy is reminiscent of the initial stage of FeLV infection.[22] The

leukopenia seen in the primary phase of FeLV infection involves other cell types in addition to neutrophils, and is usually accompanied by thrombocytopenia and varying degrees of anemia. The lymphadenopathy of FeLV infection is usually of shorter duration, rarely lasting more than 12-16 weeks.[22]

Most FIV-infected cats recover from the initial stage of the disease after a brief period of malaise; some kittens, however, may succumb to local or generalized sepsis during this period.[36] Sepsis is probably due to the profound neutropenia and not to a more specific immunodeficiency. The initial stage of FIV infection is not dissimilar to the initial stage of HIV infection in people. People infected with HIV develop a transient mononucleosis-like illness several weeks after infection. They then return to a state of normal or near-normal health that lasts until the secondary, or AIDS stage, of illness appears.

Most FIV-infected cats are seen in the so-called AIDS-like phase of the illness, when secondary and opportunistic infections, neurologic signs and myeloid or lymphoid tumors are seen. The levels of T_4 (helper) lymphocytes slowly decline over months or years.[38] Significant decreases ($\leq 1000/\mu l$) are often reached after 24-36 months after infection. Clinical signs of AIDS-like disease are expected as levels decrease below this point. This feature of FIV infection is identical to that of HIV infection of people and human AIDS. The AIDS phase of HIV infection of people occurs on the average of 6 years after initial infection. As in infected people, FIV-infected cats entering the AIDS-stage of illness become progressively more immunocompromised with time.

Clinical Features

Numerous distinct and intertwined disease syndromes have been observed in FIV-infected cats, and these syndromes are similar to those seen in HIV-infected people. Signs referable to an AIDS-like syndrome occur in one-half or more of sick FIV-infected animals. About one-half again of the cats with AIDS-like disease develop chronic and progressive infections of the mouth, including the gingiva, periodontal tissues, cheeks, oral fauces or tongue (Figs 19, 20).[11,13,14,29,35] Oral lesions may be present for months or years before the diagnosis is made. Though chronic oral cavity infections are a common feature of FIV infection, not every cat with severe mouth disease is FIV infected. Less than one-fourth of the cats with severe mouth infections in the United States are FIV positive. In a study in the United Kingdom, three-fourths of a group of cats with chronic stomatitis were infected.[14]

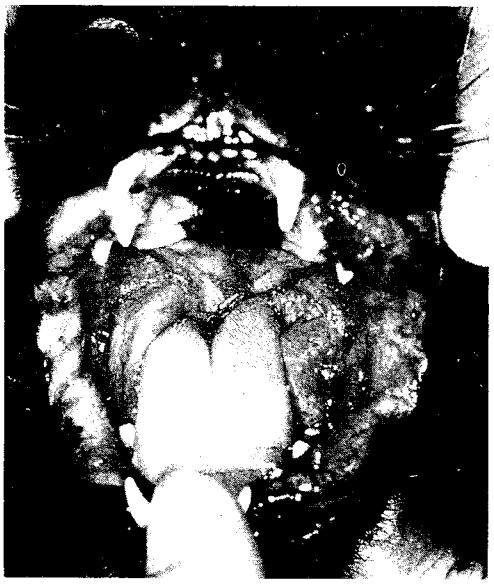
About one-fourth of FIV-infected cats with AIDS-like disease have chronic upper or lower respiratory infections (rhinitis, conjunctivitis, bronchitis, pneumonitis, bronchiolitis) (Fig 20).[2,11,13,21,31,35] Respiratory signs can occur by themselves or in association with infections in other areas of the body. It must be remembered, however, that chronic rhinitis and sinusitis commonly seen in cattery-reared cats is not an FIV-related disease. This condition usually begins as a kittenhood viral respiratory infection that leads to permanent damage to the nasal and sinus membranes and chronic secondary bacterial infections (see section on feline herpesvirus).

One-sixth of FIV-infected cats with AIDS-like disease develop chronic infections of the skin, including the ear canals.[13,21,35] Bacterial skin lesions are usually associated with staphylococcal infections. Chronic abscesses have also been observed in FIV-infected animals.[8,13,29] Generalized mange mite infestations (demodectic and notoedric) tend to be concentrated in FIV-infected cats.[6,13]

Chronic enteritis, usually manifested by diarrhea and weight loss, is the main clinical complaint in about 10% of FIV-infected cats with AIDS-like disease.[1,11-13,21,31,35] Bowel disease in FIV-infected cats is probably more common than indicated; many cat owners do not examine their cat's stools and diarrhea in cats is not as obvious as in other species. Chronic infections of the upper and lower urinary tract are seen in only a small proportion of FIV-infected animals.[8]

Numerous opportunistic infections have been identified in FIV-infected cats with AIDS-like disease. These include feline calicivirus, poxvirus infection, toxoplasmosis, cryptococcosis, candidiasis, mycobacteriosis, demodectic and notoedric mange, and hemobartonellosis.[1,4,8,11-14,31,34]

Figure 19. Severe stomatitis, periodontitis and tooth loss in a cat with chronic FIV infection. (Courtesy of Dr. Takuo Ishida, Nippon Veterinary and Zootechnical College, Tokyo, Japan)



Feline infectious peritonitis, which is often linked with FeLV infection, has yet to be linked with FIV.[13]

One-third of all clinically ill FIV-infected cats show vague signs of illness, such as recurrent fevers, leukopenia, anemia, lymphadenopathy, unthriftiness, inappetence, weight loss or ill-defined behavioral abnormalities.[1,11,13,31,35]

About 5% of all clinically ill FIV-infected cats have neurologic problems as the predominant clinical feature of illness.[29,31,35] An equal or greater proportion of infected animals has neurologic signs as one feature of their illness.[9,21,29] Neurologic signs can be either a direct effect of the virus (most commonly), or due to other opportunistic organisms (less commonly). Most FIV-related lesions are in the cerebral cortex and clinical signs are more behavioral or psychomotor than motor. Dementia, twitching movements of the face and tongue, psychotic behavior (hiding, rage, aggression), loss of toilet training and compulsive roaming have all been observed in FIV-infected cats. Convulsions, nystagmus, intention tremors and ataxia have also been observed in a smaller number of cats.

Chronic progressive renal disease has been a complicating feature of FIV infection in some cats.[1,13] It is uncertain whether this is merely a reflection of old age (both FIV infection and renal disease tend to occur in older animals), or whether there is a cause and effect relationship.

Inflammatory disease of the eye, in particular the anterior uveal tract, has been seen in several FIV-infected cats. There is some indication that some of these animals have active toxoplasmosis.

Immune-mediated diseases may be associated with FIV infection. Some anemic FIV-infected cats are Coombs' test positive. Several cats with FIV infection and thrombocytopenia have also been observed. An inflammatory arthritis has also been seen in FIV-infected cats.[11]

Hematologic abnormalities are common in sick FIV-infected cats.[1,8,11,13,26,29,31,35] The main abnormalities are leukopenia and/or anemia.

Lymphosarcomas have been observed in a number of FeLV-negative, FIV-positive cats.[1,11-13,25,28,29,35] This relationship is more than chance.[27] The relative risks for developing leukemia/lymphoma were 5.6, 62.1 and 77.3 times greater in cats infected with FIV, FeLV or FeLV/FIV, respectively, than in uninfected animals. Lymphoid tumors in FIV-infected cats have often occurred in the

Figure 20. Chronic rhinitis and periodontitis in a cat with chronic FIV infection. (Courtesy of Dr. Takuo Ishida, Nippon Veterinary and Zootechnical College, Tokyo, Japan)

head and neck. Lymphoid tumors of the nasal passages may arise from surrounding chronic plasmacytic-lymphocytic inflammation.

Myeloproliferative disorders have been reported in some FeLV-negative, FIV-positive cats with severe anemia and leukopenias.[1,13,35] A myeloproliferative disorder has been induced in specific-pathogen-free cats infected only with FIV.[21,36] Myeloid neoplasms and myelodysplasias (preleukemias?) are common in cats, and only 70% have been linked with FeLV infection.[3] A portion of the remainder may well be FIV induced.

FIV infection has been diagnosed in some older cats with squamous-cell and mammary-gland carcinomas.[11,13] The rate of FIV infection among cats with squamous-cell carcinomas of the mouth and skin at the School of Veterinary Medicine, University of California, Davis, has been around 10-20%. However, cats with squamous-cell carcinomas tend to be old and mainly outdoor roaming. Both of these are also significant risk factors for FIV infection, so more epidemiologic studies must be done before a real relationship can be determined. A number of other seemingly rare types of tumors have been reported in FIV-infected cats, but again, a cause and effect relationship has yet to be determined.[11-13]

Pathologic Features

The principal lesions seen in the terminal stages of FIV infection are concentrated in the digestive tract. Mild to severe gingivitis, periodontitis and stomatitis are the most common features of FIV infection. Diffuse enterocolitis is common.

Respiratory tract lesions are usually suppurative, with underlying necrosis.

Lymphoid lesions vary greatly, depending on the stage of the disease. In the initial stages of infection, lymphadenopathy is prominent.[36] The secondary or AIDS stage of the disease is characterized by a wider spectrum of lymphoid changes. Thymic lesions are difficult to evaluate in older cats that normally have atrophic thymuses. However, thymic atrophy is profound in younger animals that would normally have considerable amounts of thymic tissue.

Clinicopathologic Features

Any cat with chronic, poorly responsive or refractory infections should be tested for FIV infection. Cats with infectious diseases that are of an opportunistic nature should also be tested. Because FeLV and FIV infections often coexist, it is important to test such animals for both viruses. At the present time, most tests for FIV infection involve antibody detection. Because the presence of serum antibodies is directly related to persistent infection, antibody tests accurately detect almost all infected individuals.

Three basic procedures are used to test for FIV antibodies: enzyme-linked immunosorbent assay (ELISA); indirect immunofluorescent antibody assay (IFA); and Western blotting.[10,21,34,35] Currently available ELISA procedures are highly sensitive in detecting antibodies and are probably over 98% specific when used to test high-risk populations, that is, cats with signs of the disease or cats in contact with known infected individuals. A greater proportion of nonspecific (false) positive test results may occur in low-risk groups, that is, cats kept strictly indoors, cats with no known exposure, or purebred cattery cats. False positives are generally associated with antibodies that react with minor cell culture contaminants in the ELISA antigen. Because many feline vaccines contain these contaminating antigens, heavily vaccinated cats are more likely to have false-positive reactions than cats that are infrequently vaccinated. False-positive reactions are generally weak; some true positives may also be weak, however.

The ELISA is the assay of choice for high-risk animals. When used on such populations, further confirmatory testing is probably not necessary. Confirmatory testing, either by IFA or Western blotting, should be considered for weakly or or suspicious positive samples from cats in low-risk categories. The IFA procedure is slightly less sensitive than ELISA and may give a low percentage of false negatives. If properly conducted, however, it rarely gives a false-positive reaction. The same can be said for Western blotting.

A small proportion of FIV-infected cats may have too little antibody to be detected.[21,22] Such cats may be in an early

stage of infection or in the AIDS phase of illness, in which there is a state of antigen excess with suppression of antibody production. Perhaps tests will be devised to detect such animals.

Hematologic abnormalities are common in both the initial stage of the infection and in the secondary or AIDS stage of illness. Varying degrees of leukopenia, seldom lower than 3000 cells/μl, are seen transiently in the initial stage of infection.[21] This is usually associated with mild to profound neutropenia. The RBC and platelet counts are usually normal.[21] Anemia and leukopenia are seen in about one-third of cats in the terminal AIDS stage of illness. The leukopenia is usually associated with neutropenia and/or lymphopenia.[20] The anemia is usually mild and of the depression type. In some cats with myeloproliferative disorders, the anemia is often profound and may be associated with varying degrees of leukopenia and anemia.

Cats coinfected with both FIV and FeLV tend to be younger than cats infected only with FIV, have more severe disease signs, and die earlier.[7,36] The disease potentiation of dual FeLV/FIV infections has also been experimentally documented.[37] Feline immunodeficiency virus infection is also strongly linked to feline syncytium-forming virus (FeSFV) infection.[20] Three-fourths of a group of FeSFV-infected cats in one study were coinfected with FIV. This high rate of coinfection of cats with FeSFV and FIV probably results from the common modes of transmission of these 2 agents. FeSFV is also spread by bites and the same animals at risk for FIV infection are at risk for FeSFV infection.[20]

Treatment and Prevention

Only cats in the AIDS stage of disease should be treated. Treatment is largely supportive and symptomatic, and directed primarily at secondary or opportunistic infections. Cats in the earlier phases of AIDS-like illness often respond favorably to such treatment. As the disease progresses, however, the response becomes less favorable. The usefulness of human anti-HIV drugs, such as azidothymidine, lymphokines, interferons and immunostimulants, has not yet been adequately explored in cats.

The most successful way to prevent infection is by not allowing cats to run free. Even if a susceptible cat is housed indoors with an infected individual, the likelihood of transmission is small. Strictly indoor cats rarely resort to biting, and biting is the principal mode of infection. Casual transmission, though uncommon, has been described in at least one closed cattery that took in homeless outdoor cats.[12] Contact transmission is much less efficient than with FeLV, and infected and uninfected cats can live together indoors with a lower risk for disease spread than with FeLV.

Infection and Immunity

Whether or not FIV infection of cats is analogous in all aspects to HIV infection in people remains to be determined. However, there are great similarities in progression of disease in HIV-infected people and FIV-infected cats. Both diseases start with a brief, self-limiting illness. Following this initial bout of disease, infected people and cats return to a state of normalcy or near normalcy. With time, usually many months or years, the immune system deteriorates and secondary or opportunistic infections begin to appear.[15] These respond initially to symptomatic treatment, but as the immune system becomes progressively more crippled, treatment becomes less and less effective.

Opportunistic infections seen in human AIDS patients are usually associated with organisms that tend to be intracellular, thus requiring cellular immunity for elimination. Mycobacteria, *Toxoplasma, Cryptococcus, Pneumocystis carinii,* cytomegalovirus, Epstein-Barr virus and hepatitis B virus are just a few. Identical or related types of organisms have been associated with disease in FIV-infected cats.[7]

Cats experimentally infected with FIV begin to make antibodies 2 weeks after infection.[21] The titer of these antibodies rises rapidly and then plateaus. Cats with naturally acquired FIV infection and in the AIDS stage of illness tend to have lower antibody levels than experimentally infected cats in the asymptomatic stage of infection. This observation suggests that FIV antibodies in cats behave similarly to HIV antibodies in people over the course of the respective infections.

Similar to HIV-infected people, FIV-infected cats appear to be infected for life. This is typical of all lentivirus infections; the chance of recovery, even in the face of immunity, is virtually nil. This feature of lentivirus infections makes them resistant to known vaccine strategies. It is difficult to develop a vaccine for an infection against which the host cannot immunize itself, even in a small percentage of cases.

Animal and Public Health Considerations

Feline immunodeficiency virus has a distant genetic relationship to HIV of people.[19,31] It is one member of a large group of lentiviruses that appear to have adapted themselves species by species over eons of time. The adaptation of HIV to people is a very recent event in lentivirus evolution. The current theory is that HIV is a mutant of simian immunodeficiency virus. Though lentiviruses have apparently adapted themselves to a number of species of animals by mutation, once that adaptation occurs, they become very species specific. Lentiviruses of one species of animals do not readily infect a divergent species of animals. This high degree of species specificity obviates FIVs being a public health concern. Preliminary studies have failed to identify FIV antibodies in the blood of people in intimate contact with infected cats, inadvertently bitten by infected cats, or accidently injected with infectious materials.[21]

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Campylobacteriosis

Cause

Campylobacter species are Gram-negative curved bacterial rods.[2] *Campylobacter jejuni* is the main pathogen in this genus. Organisms remain viable at 4 C for 3 weeks in feces and 5 weeks in urine, and for less time at 25 C.[1] Viable organisms were still present in bile kept at 37 C for 2 months.

Pathogenesis

Campylobacter jejuni is found worldwide and carried by many different species of animals, including poultry, wild and caged birds, sheep, goats, dogs, cats, swine, hamsters, primates and people. Infected animals shed the organism in their feces. Canine and feline isolates are identical to human isolates.[13]

The incidence of *C jejuni* infection in dogs and cats is difficult to determine due to variations in isolation rates. The highest recovery rates are from animals that are young or housed in high-density environments. Isolation rates vary from 0.5% to 45% or more in dogs and from 2% to 45% in cats.[7] However, isolation rates in cats in most concurrent studies are usually only a fraction of those in dogs.

The relatively high incidence of *C jejuni* infections in kittens from high-density environments is compatible with what is known about infectious diseases in general. Young animals are most susceptible to infection and continue to shed organisms until good immunity develops, a process that sometimes takes many weeks. Hamsters and ferrets experimentally infected with *C jejuni* shed organisms for several months.[6] Puppies have shed organisms for at least 40 days.[5] Environmental factors favoring serious infection include: overcrowding with increased contact between animals; poor sanitation and increased fecal contamination of the environment; large numbers of kittens and a proportionate increase in carrier individuals; concurrent diseases and lowered resistance; and increased stresses in the population.[6,12]

The role of *C jejuni* in disease has only recently been demonstrated. It causes vibrionic hepatitis in poultry and transient enterocolitis in animals and people.[16] However, epidemiologic studies have had variable success in linking *C jejuni* to disease in dogs and cats. Some studies show the same incidence of infection in dogs or cats with diarrhea and asymptomatic animals.[8,9] In other studies, however, the infection rate is considerably higher in animals with diarrhea than in asymptomatic animals.[7] Cats with acute diarrhea, cats in the postinfection convalescent stage of disease, and chronic asymptomatic carriers are sources of the bacteria. Outbreaks usually occur when susceptible and infected cats commingle.[12]

Infection with *C jejuni* is by the fecal-oral route. The infection is generally limited to the cecum and colon, though bacteremias are sometimes associated with severe primary bowel disease. The incubation period is 3-7 days.

Clinical Features

Clinical signs of *C jejuni* infection are seen mainly in 6- to 12-week-old kittens during the postweaning period. However, whether the infection is clinically apparent is related to a variety of poorly understood factors. The level of infecting organisms, nutritional status, presence of concurrent diseases, and status of passive and active immunities all play some role in the disease outcome. It is not unusual that the disease strikes weanling kittens that have stopped nursing. The kittens suddenly lose the passive local (lactogenic) immunity provided by their mother's milk. Their passive systemic immunity also wanes, their diet is markedly changed, they are exposed to other young animals, and the stress level is high.

Diarrhea, which is sometimes profuse and watery but more often soft and mucoid, is the predominant sign of *C jejuni* infection in kittens.[12] Fever is generally absent and anorexia mild. Vomiting and colic are sometimes observed in the acute stages of illness. Dehydration can be rapid and severe in young kittens with profuse watery diarrhea. Death has been occasionally reported in severely affected kittens.[14] The diarrhea usually subsides within 3-7 days, but the stool may remain somewhat soft for 2-4 weeks. Bloody diarrhea is not a common sign of *C jejuni* enterocolitis in kittens.

Pathologic Features

Lesions in cats have not been described, but changes are identical in most species that have been studied. Gross changes are limited to the distal intestinal tract, particularly the colon, and include mild redness of the mucosa.

Clinicopathologic Features

Highly motile spiral or S-shaped organisms can be seen in fresh fecal suspensions viewed by phase or subdued-light (contrast) microscopy. This can be of some value in tentatively diagnosing *C jejuni* enterocolitis. The organism can be readily isolated on selective *Campylobacter* media. Small, flat, grayish, mucoid colonies appear within 24-48 hours. Typical Gram-negative spiral or S-shaped organisms are seen in stained smears.

Overinterpretation of culture results should be avoided. Many healthy kittens in the same environment also shed organisms, and a number of other enteric pathogens can cause similar disease signs. These other diseases also tend to occur in the postweaning period. A rapid response to specific antibiotic therapy can be helpful in confirming *C jejuni* as the responsible organism.

Treatment and Prevention

Campylobacter jejuni is resistant to penicillin, cephalosporins and trimethoprim.[2,12] Sensitivity to ampicillin, trimethoprim-sulfonamides and metronidazole is intermediate. Almost all *C jejuni* isolates are sensitive to erythromycin, which is considered the drug of choice.[12] Erythromycin is given PO at 20-40 mg/kg divided 3 times daily for 5 days. Tetracycline, aminoglycosides, clindamycin, chloramphenicol and furazolidone are also effective.

Kittens with severe and profuse diarrhea should not be given food or water for 24-72 hours. Fluids and electrolytes should be given parenterally. *Campylobacter jejuni* enterocolitis usually responds well to treatment, and clinical signs resolve within 2-5 days. Cats with milder signs do not necessarily require treatment; signs usually resolve after a few days to a week.

Prevention of *C jejuni* infection in catteries usually requires drastic changes in environment and husbandry. The disease is most severe in situations in which many breeding cats and kittens are crowded into inadequate quarters.

Infection and Immunity

Most *C jejuni* isolates are obtained from animals less than 6 months of age.[7] Bacterial shedding continues for up to 2 months or more after infection, indicating that development of complete immunity is a slow process. This is true of many enteric infections of dogs and cats. Shedding of *Salmonella* also continues for weeks or months after initial infection. Interference with the natural course of salmonellosis with antibiotics can actually prolong the carrier state by removing the stimulation necessary to evoke protective immunity. Animals that have not established immunity immediately become reinfected with *Salmonella* follow-

ing cessation of antibiotic treatment. Experience with human campylobacteriosis suggests that antibiotic therapy does not have a similar effect. Cultures done several weeks to months after treatment are usually negative.[11]

Animal and Public Health Considerations

Campylobacter jejuni is a cause of severe acute enterocolitis in people, especially in children. In underdeveloped areas of the world, person-to-person transmission by the fecal-oral route is common. Human infection in more-developed countries is usually associated with ingestion of contaminated lamb, beef, pork, poultry or unpasteurized milk. Contaminated water is another common source of human infection. Exposure to infected dogs and cats has been estimated to account for no more than 5% of human infections.[17] Dogs are generally more infectious to people than cats, largely due to their higher incidence of infection.[18] Puppies and kittens are more infectious than older animals and diarrheic individuals are more of a health hazard than asymptomatic individuals.[3,10,18,19] Young kittens and puppies are more apt to harbor the infection. Animals with diarrhea shed more organisms and are more likely to contaminate the environment.

People, especially children, who develop acute enterocolitis after contact with a diarrheic kitten should be checked by their physicians for *C jejuni*. If positive cultures are obtained from the patient, fecal cultures from the pets might be warranted. Pets shedding *C jejuni* should not be destroyed without good reason. The infection is self-limiting in both people and animals, and the number of people infected by pets is relatively small. Infected animals can be isolated from people for 40 days or so, and then samples obtained for culture. Alternatively, animals shedding *C jejuni* can be treated with erythromycin for 5 days.

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Streptococcosis

Cause

Streptococci are Gram-positive spherical bacteria that form long chains under optimum growth conditions. Streptococci are commensal organisms that live on mucous membranes of the nasal passages, oropharynx, colon and distal genitourinary tract (urethra, vagina, prepuce). Both pathogenic and nonpathogenic species of streptococci coexist in healthy animals and people. The most common isolate from cats is *S canis*.[1]

Healthy cats are the primary source of streptococci. The level of bacterial growth

in mucous membranes of the mouth, nasal passages and distal genitourinary tissues varies greatly, depending on the age of the animals. Of female cats <2 years of age in the Davis, California, area, 50% carried *S canis* in their vaginal tract.[1] The carrier rate in older cats was lower.

Pathogenesis

Three main forms of streptococcal infections have been recognized in cats: epizootic, neonatal and localized. Each form of the disease will be discussed as a distinct clinical entity, though the various forms often occur together in the same environment. Streptococcal infections are enhanced by a number of unfavorable environmental factors that are most likely to occur in catteries, multiple-cat households and animal facilities (pounds, humane shelters, laboratory animal facilities).

Clinical Features

The epizootic form of streptococcosis has been seen mainly in large experimental cat colonies.[1,4,7-9] This form occurs less frequently in catteries and is virtually nonexistent in normal outdoor/indoor pet cat populations. Outbreaks usually occur among cats kept in close confinement and in free-housed groups of 4 or more animals, rather than in individually caged cats. Animals affected with epizootic streptococcosis were usually fed from common bulk feeders.

Infection rates vary from 2.3% to 28% over several months. The highest incidence of disease is in the postweaning period from 8-10 weeks of age or in new animals introduced into an enzootic environment.

The most common clinical signs associated with this form of infection are acute fever, submandibular edema and lymphadenopathy. The mandibular lymph nodes often spontaneously rupture and drain, or require lancing. Conjunctivitis, sinusitis and abscesses on the feet and legs develop in some animals. Dyspnea, due to a severe suppurative pleuritis and hydrothorax, occurs in a small proportion of affected cats. The epizootic form of the disease has been experimentally recreated.[4] Adolescent and adult cats fed organisms became febrile on day 2, with anorexia, listlessness, and swelling and edema of the mandibular lymph nodes. Draining abscesses often occurred in the area of the enlarged nodes over the following 24 hours. Conjunctivitis, laryngitis and tracheitis were associated signs. Streptococci ingested with food rapidly colonized the tonsils and disseminated via the lymphatics to regional lymph nodes in the head and neck.[7] Purulent inflammation of the lymph nodes was followed by toxemia and fever.

The neonatal form of streptococcal infection occurs more frequently in large breeding catteries.[1,10] Sporadic cases of epizootic disease in weanling and adolescent kittens are often seen in the same environment. The disease has a predilection for kittens born to primiparous queens.[1] Kittens are usually infected during birth from vaginal secretions or when the queen severs the umbilical cord. Umbilical vein infections are more frequent when the umbilical cord is chewed off at the level of the abdominal wall. If the umbilical cord is left long, infection is limited to the dried-up portion and cannot travel up the cord and reach the patent part of the vein. Kittens infected at or shortly after birth often develop a small abscess of the umbilical vein in the inner abdominal wall. Infection at this site is seldom apparent on gross examination. The infection then showers organisms directly into the bloodstream. Infected kittens usually become listless within the first week of life and fade away and die over the next few days. It is not uncommon for entire litters to be affected. Subsequent litters are less likely to succumb from the infection.

Streptococci can be isolated from several localized pyogenic processes, in pure form or as mixed bacterial infections. Abscesses of the skin and subcutis, conjunctivitis, mastitis and uterine, vaginal, oral, ear and wound infections are just a few processes associated with streptococci.[3]

Pathologic Features

Pathologic findings in epizootic streptococcosis are relatively stereotyped. Many affected cats have tonsillitis, with acute inflammation and microabscess formation in the lymph nodes of the head and neck. Acute rhinitis, unilateral or bilateral otitis media, acute splenitis and reactive hyperplasia and histiocytosis of lymphoid tissue throughout the body are associated findings.[8,9]

Pathologic features of neonatal streptococcosis include omphalophlebitis and thrombosing bacteremia.[1] Gross or microscopic abscessation of the abdominal portion of the umbilical vein is common, and bacterial thrombi are observed within vessels in the liver, spleen, lungs and kidneys. Gross and microscopic abscesses are seen in the liver; suppurative meningoencephalitis is common.

Clinicopathologic Features

Epizootic streptococcal lymphadenitis is easily diagnosed on the basis of clinical history (environment, feeding practices) and signs of acute fever and adenitis of the lymph nodes of the head and neck. Pure cultures of beta-hemolytic streptococci are obtained from lymph node exudates.

Neonatal streptococcosis must be differentiated from the myriad diseases that cause mortality in kittens during the first 2 weeks of life. Careful necropsy, histopathologic examination of tissues, and bacterial cultures usually pinpoint the problem. Special attention should be given to examination and culture of the umbilical cord remnant within and outside of the abdomen.

Treatment and Prevention

Streptococci are sensitive to a number of antibiotics, but penicillin is the drug of choice. Antibiotic therapy should be combined with drainage of abscessed lymph nodes and evacuation of pleural exudate in cats that also have streptococcal pleuritis. If neonatal streptococcal infections are a problem, prophylactic treatment of all kittens born to primiparous queens is indicated. A single subcutaneous injection of benzathine penicillin at 35,000 IU/kg at birth often prevents systemic disease and decreases mortality.

An outbreak of streptococcal lymphadenitis in a cat colony was successfully halted by treating all animals in the group with 150,000 IU procaine penicillin and 150,000 IU benzathine penicillin subcutaneously.[9,10] However, such treatment will not eliminate the organism from the premises. Prevention of infection involves changes in husbandry practices to prevent overcrowding and maintain clean feeders. Infected cats should be segregated from uninfected cats. Elimination of communal bulk feeders and use of individual caging also help prevent spread of disease during an outbreak.

Infection and Immunity

Pathogenic strains of streptococci cause similar syndromes in people and many species of animals. Streptococcal diseases of animals are usually related to certain husbandry practices. Overcrowding of animals, infrequently cleaned communal feeders, and premises with a high proportion of younger animals are common predisposing factors. Such conditions favor an increasing level of streptococci in the environment and a higher primary infection rate. The larger the exposure dose of pathogenic streptococci, the higher the incidence and severity of primary infections. An increased incidence of primary infection leads to a higher proportion of cats that carry and shed the organism during the primary phase of illness and in the postconvalescent period.

The severity of pathogenic streptococcal infections in a group of cats is proportional to the percentage of asymptomatic cats that carry the organism in the oropharynx, prepuce and vagina. The reason for higher incidence of streptococcal infections in neonatal kittens born to primiparous queens is not completely understood. Queens less than 2 years of age harbored significant levels of *S canis* in their vaginal canals throughout pregnancy and at parturition.[1]

In contrast, queens greater than 2 years of age had progressively decreasing levels of vaginal streptococci beginning at mid-gestation. Cultures from older queens at parturition were often negative.

The basis of the effect of pregnancy on vaginal populations of streptococci is unknown. Pregnancy, at least in relation to herpesvirus and *Toxocara* infections of cats, is usually immunosuppressive. The immunosuppressive effect of pregnancy is also well recognized in people. Therefore, it is unlikely the pregnancy-associated decrease in streptococcal vaginal populations in older cats is due solely to immunologic mechanisms. Hormonal effects of pregnancy may alter the nature of the membranes and secretions of the vaginal tract and make the local environment less favorable for bacterial growth.

Animal and Public Health Considerations

Pathogenic streptococci vary among animal species. Streptococcal diseases are associated with different groups of streptococci in people more so than in cats. Streptococci isolated from people are usually of human and not animal origin. Occasionally, however, group-G beta-hemolytic streptococci are isolated from infants with neonatal septicemia and from local purulent processes of adult people.

Cats have been implicated as asymptomatic reservoirs for group-A streptococci of people.[2,5] Group-A streptococci are the main cause of pharyngitis in children. It is possible, however, that the cats were infected by the children. Cats shed group-A streptococci for 1, 2 or 3 weeks after being removed from homes where human outbreaks were occurring.[5] *Streptococcus pneumoniae* was isolated from an aged cat with acute fever, septicemia and septic arthritis. An infant in the household had a cold for 3 weeks and was also culture positive. This was almost certainly an incident of person-to-cat transmission.

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Bordetellosis

Cause

Bordetella bronchiseptica is a small, aerobic Gram-negative spherical bacterium. It is a normal inhabitant of the upper respiratory tract of many species of animals and people.

Pathogenesis

Bordetella bronchiseptica is associated with a disease called "kennel cough" in dogs, a condition manifested by tracheobronchitis and a chronic dry cough. In cats, however, it is more often isolated from animals with clinical or subclinical pneumonia.[1,5] The organism can be routinely isolated from oropharyngeal swabs in 3-10% of normal cats.[5,6] Disease appears to be triggered by crowding and stress, and is usually recognized in laboratory cat colonies and catteries.[1,5] The carrier rate increased rapidly from 10% to 48% in a group of randomly obtained cats kept in close confinement for 3 weeks.[5] Disease results from increased colonization of the upper respiratory tract with the bacterium, coupled with other stresses that lower local membrane immunity. The predisposing role of respiratory viruses, such as feline herpesvirus or calicivirus, has not been elucidated. Viral infections can set the stage for *B bronchiseptica*-induced tracheobronchitis in dogs.[7] Of 7 cats with *B bronchiseptica* pneumonia, 3 had concurrent viral rhinotracheitis.[5]

Clinical Features

Pneumonia induced in cats by *B bronchiseptica* can be generalized or focal in nature. Therefore, clinical signs are variable. Manifestations of clinical signs is further obscured by normal feline behavior. Cats with pneumonia often do not show typical pneumonic signs, such as a cough and dyspnea (difficult breathing), even when severely affected. Of 10 cats with fatal *B bronchiseptica* pneumonia, only 7 were noticeably ill before death.[5] Of these 7 cats, 3 had signs of rhinotracheitis, 1 had a cough, and 1 behaved as if it had chronic pneumonia. Of the 7 remaining cats, 2 showed nonspecific signs of listlessness, anorexia, dehydration and emaciation before death. All 10

cats had gross lesions of pneumonia in their lungs at the time of necropsy.

Pathologic Features

Primary lesions of *B bronchiseptica* infection in cats are limited mainly to the lungs. Gross lesions consist of reddish areas of consolidation involving 1 or more lung lobes. Large, firm, grayish nodules 2-5 mm in diameter are occasionally seen in the lungs of some animals. Purulent exudate can be seen on the cut surfaces of affected lungs in about one-third of the cases. Histopathologic findings are compatible with bronchopneumonia. Interstitial disease is less common. The pulmonary parenchyma is congested and edematous, with focal necrotic areas surrounding bronchioli.

Clinicopathologic Features

Recognition of existing pneumonia is the first and most difficult step in diagnosing bordetellosis in cats. In certain catteries where disease is common, the pattern of disease in younger cats is stereotypic. The bronchopneumonia usually is diagnosed by thoracic radiography rather than physical examination. Tracheal aspiration and culture usually confirm the presence of *B bronchiseptica* in large numbers and pure form. Isolation of *B bronchiseptica* from oropharyngeal swabs should be interpreted with more caution; many cats, especially those living in problem environments, are asymptomatic carriers.

Treatment and Prevention

Bordetella bronchiseptica is susceptible to antibiotics, such as chloramphenicol, gentamicin, kanamycin and tetracycline.[2] Therapy should be continued for about 10-14 days. The prognosis is good if the pneumonia is mild, but can be poor in severely affected cats.

Problems with *B bronchiseptica* can be minimized with proper husbandry. Overcrowding of animals, stress on the population and the presence of numerous animals kept in poorly cleaned and ventilated quarters are major factors in the disease. Bordetellosis can be a complication of feline herpesvirus and calicivirus infections; these diseases are also likely to be more severe under poor husbandry conditions.

Avirulent live and inactivated *B bronchiseptica* vaccines are available for prevention of "kennel cough" in dogs.[3,4] The former is given intranasally and the latter by injection. The avirulent live vaccine appears to be much more effective, however. Both of these vaccines have been used by some cat breeders but their safety and efficacy for cats have not been determined.

Infection and Immunity

Bordetellosis is largely an environmentally potentiated disease. A percentage of normal animals carry small numbers of the bacterium in their oropharynx for months and years. In highly stressful, overcrowded, poorly cleaned and improperly ventilated environments, the levels of organisms can increase dramatically. Exposure to small numbers of organisms favors asymptomatic colonization of the oropharynx with no disease, while exposure to large numbers of organisms favors colonization of the upper respiratory tract (trachea and mainstem bronchi) and invasion of the mucous membranes, especially if coupled with stress. Viral infections, which can temporarily damage mucociliary-clearance mechanisms and induce microscopic areas of interstitial pneumonia, may allow *Bordetella* to move from the upper to the lower airways (bronchioles, alveoli) and invade virus-damaged tissues.

Animal and Public Health Considerations

Bordetella bronchiseptica infection is relatively common in many species but clinical disease is uncommon. For this reason, infected cats should not be considered human or animal health hazards.

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Pasteurellosis

Cause

Pasteurella is a small, nonmotile, Gram-negative, ovoid bacterial rod. The organism is a commensal parasite of the oral cavity of many species of animals, including cats.[10] *Pasteurella multocida* has been isolated from 80% of swabs taken from the canine teeth and adjacent gingiva of normal cats. *Pasteurella* was isolated from the oral cavity and upper respiratory tract of 60-75% of normal cats.[5,6] The rate of isolation is higher from animals with dental tartar and gingival disease than from animals with clean teeth.[1]

Pathogenesis

Pasteurella species exist in a number of different serotypes that differ greatly in virulence in mouse-inoculation tests. Of 8 mouth isolates from healthy cats, all were nonpathogenic, while 4 of 10 isolates from wounds and abscesses were pathogenic.[9] Of 6 oropharyngeal isolates from normal cats, 3 were nonpathogenic to mice, 1 was weakly pathogenic and 2 were highly pathogenic.[3]

Clinical Features

Pasteurella is most frequently isolated as a facultative anaerobe along with other anaerobic bacteria from infected wounds and abscesses in cats (see discussion of anaerobic bacteria). It has also been isolated from purulent infections of the external ear canals, conjunctiva, nasal passages and sinuses, tooth root abscesses, periodontal infections and surgical wounds. Omphalophlebitis in kittens can be caused by *Pasteurella.* Similar to *Bordetella, Pasteurella* species are commonly associated with pneumonia in colony- or laboratory-reared cats.[8] *Pasteurella* species are frequent secondary invaders in cats with primary viral pneumonia and are commonly isolated from thoracic exudates in cats with empyema (purulent infections of chest cavity).

Pasteurella organisms enter tissues by licking of wounds or bites. Organisms are frequently isolated from the claws of cats, but cat scratches are less apt to be associated with infections than bites.[1] *Pasteurella multocida* was isolated from 24 of 46 infected cat-fight wounds and abscesses.[9] It has also been isolated from the spinal cord of a cat that developed ascending meningomyelitis after being bitten in the caudal back by another cat.[2]

Pathologic Features

Lesions caused by *P multocida* often exude a great deal of grayish pus. Pasteurella infections in cats tend to remain localized. Local tissue necrosis is usually minimal; when necrosis does occur, it is generally localized to the skin overlying the abscess. There are no specific pathologic features of *Pasteurella* infections in cats. Disease processes associated with these organisms are generally of a purulent nature.

Clinicopathologic Features

Pasteurella infections are easily diagnosed by routine cultures of purulent exudates.

Treatment and Prevention

Fresh wounds should be cleansed. Purulent infections should be opened to allow drainage of the exudate and then cleansed periodically until exudation ceases and the wounds begin to heal. Systemic antibiotics are an important part of treatment and should be given for 5-10 days. Feline isolates of *P multocida* are most sensitive to tetracycline and chloramphenicol, only moderately or relatively sensitive to penicillin, and more or less resistant to sulfas.[1] Trimethoprim-sulfonamides are effective for treatment of *Pasteurella* respiratory infections.[4]

Infection and Immunity

Pasteurella infections in cats are interesting in 2 respects. First, cats seem resistant to the septicemic forms (hemorrhagic fever) of pasteurellosis that are common in

other species. Second, though cats are notorious carriers of pathogenic strains of *Pasteurella*, they seem fairly susceptible to wound infections with the organism.

Animal and Public Health Considerations

Pasteurella species are transmitted from cat to cat almost exclusively by bites. Therefore, affected cats are not a hazard to other cats.

Pasteurellosis is probably the most common zoonotic disease passed from cat to people.[10] Pasteurellosis exists in people in 2 clinical forms: localized infection caused by animal bites, usually from cats; and a systemic form manifested variably as sinusitis, pneumonia, empyema, puerperal sepsis, bacteremia or brain abscess. The origin of *P multocida* in the systemic form is usually unknown, though many affected people have a history of animal exposure.

Cat bites preceded 301 of 1234 (24.3%) human *Pasteurella* infections reported in the British Isles from 1975 to 1979.[3] A high proportion of veterinary students developed *Pasteurella* infections following cat bites.[5] Of human *Pasteurella* infections caused by animal scratches or bites, 60-80% were associated with cats.[10]

Localized pasteurellosis in people occurs at the site of the bite, usually in soft tissues of the hand. Joint infections can be a serious consequence of bites that penetrate into the synovial spaces. The wound becomes painful and inflamed within a few hours.[10] The infection spreads rapidly to surrounding tissues and along lymphatics to the regional lymph nodes. The most common local complications are abscess formation and tenosynovitis.[10] The condition is most severe after the first bite; subsequent bites are less likely to become infected. Cat-bite wounds should be cleansed as soon as possible. If pain, redness and swelling begin to develop at the site after a few hours, medical attention should be sought as soon as possible.

In a study of the role of healthy cats in the spread of *Pasteurella* to turkeys, *P multocida* was readily recovered from the throats of cats on poultry farms, but only some isolates could cause pasteurellosis in chicks.[3] Feline strains were invariably more closely related to the strains isolated from rats on the farms than from those associated with outbreaks of pasteurellosis among turkeys.

Cat bites can also have a devastating effect on small birds. It has been estimated that 60% of wild birds rescued from the jaws of cats die from pasteurellosis.[7] This suggests that prophylactic antibiotic therapy for birds undergoing such trauma is almost mandatory.

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Anaerobic Bacterial Infections

Cause

Anaerobic bacteria grow only under conditions of low oxygen and play a major role in many suppurative infections of people and animals. Most of the species involved are normal inhabitants of the mouth and distal intestinal and genitourinary tracts. The most commonly isolated anaerobic bacteria belong to the genera *Bacteroides* and *Fusobacterium*. *Bacteroides* species are straight or curved rod-shaped bacteria. *Fusobacterium* species are highly pleomorphic, existing in rod and filamentous forms.

Bacteroides species involved in suppurative processes of cats include *B tectum, B fragilis, B asaccharolyticus, B disiens, B bivius, B salivosus, B heparinolyicus, B melaninogenicus/intermedius, B zoogleoformans, B distasonis, B vulgatus, B gingivalis,* pigmented group, and so-called corroding strains.[2,3,6-8,11,13,14] Many unspeciated strains also exist.[7] *Fusobacterium* species include *F russii, F necrophorum, F naviforme and F symbiosum.*[2,8,12-14]

Another common anaerobe isolated from suppurative processes in cats is *Peptostreptococcus anaerobius.*[1,6,9,12,14] Motile *Borrelia*-like organisms have also been occasionally isolated.[4] *Clostridium villosum* is another anaerobe frequently recovered from pyogenic processes in cats.[6,12]

Pathogenesis

Anaerobic organisms are frequently isolated as mixed cultures from pyogenic processes in cats, often in association with facultative anaerobes. Common facultative anaerobes isolated in combination with anaerobic bacteria include *Pasteurella multocida, Corynebacterium pyogenes, Actinomyces meyeri, A viscosus* and *A odontolyticus.*[1,2,4,5,9,12] *Actinomyces*-like organisms are sometimes seen on stained smears of pus but have not been isolated.[9] Streptococci, lactobacilli and *E coli* are facultative anaerobes less frequently isolated from feline pus.[9]

Of 87 bacterial strains isolated from 19 cats with empyema (pyothorax), 80.5% were anaerobes and 19.5% were facultative anaerobes.[12] *Bacteroides* spp comprised 42.5% of anaerobic isolates, followed by *Clostridium villosum* at 16.1% and *Peptostreptococcus anaerobius* at 12.6%. *Clostridium villosum* was the most commonly isolated species of anaerobic bacterium. *Pasteurella multocida* was the most common facultative anaerobe, comprising 64.7% of the isolates. In a second study, *Bacteroides* species were isolated from 19 of 21 pyothoraxes, predominantly *B tectum* and *B heparinolyticus.*[7]

Of 36 cat abscesses cultured, 32 contained 8 species of anaerobes per culture.[8] Species of *Bacteroides, Fusobacterium, Peptostreptococcus, Clostridium* and *Propionibacterium* comprised 95.8% of anaerobic isolates. *Bifidobacterium, Lactobacillus* and *Eubacterium* comprised the remainder. Facultative anaerobes were isolated from about 28% of the samples. *Pasteurella multocida, Actinomyces* and streptococci made up the bulk of facultative anaerobic isolates. Lactobacilli and *E coli* were uncommon isolates.

Gingivitis, periodontal disease, stomatitis, cheilitis and glossitis are common lesions in cats. Anaerobic bacteria play an important primary or opportunistic role in such lesions. It is therefore surprising that *Bacteroides* species were isolated less frequently from diseased gingiva than from normal gingiva.[7] However, *B tectum* is more frequently isolated from diseased oral tissues of cats than from normal mouths, while *B fragilis* is almost absent from oral lesions.[7]

Infections caused by anaerobic and facultative anaerobic bacteria are almost always highly suppurative. They usually involve the nasal passages (chronic rhinitis and sinusitis), oral cavity (chronic gingivitis, periodontitis), subcutaneous tissues (abscesses, cellulitis) or bone (osteomyelitis). They are usually opportunistic and either secondarily invade tissue damaged by other pathologic processes, or are inoculated directly into tissues in which they are not normally found. For instance, accumulation of dental tartar often leads to gingivitis and eventual periodontitis. When the periodontitis becomes severe, tooth root abscessation is common. Herpesvirus infection can damage the nasal passages and sinuses and predispose to chronic bacterial invasion. Cat bites can directly inoculate oral bacteria into the subcutaneous tissues and bone. Immunosuppressive diseases, especially feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infections, can predispose the nasal, oral, skin and intestinal tissues to infection by resident flora. Foreign bodies, such as pieces of plant material or bone, can also transport infection by normal bacterial flora into deeper sites.

Pyothorax (pus in the chest) in cats occurs by 3 possible routes: cat bites that penetrate the chest cavity; opportunistic bacterial infections of primary pneumonic processes, with spread to the pleura and chest cavity; and migrating foreign bodies. Most cases of pyothorax in the cat begin

with primary sites of pneumonia, with secondary spread of infection to the pleura and into the chest cavity.

Clinical Features

Infections caused by various anaerobic and facultative anaerobic organisms are either acute or chronic. Cat-bite abscesses and pyothorax are usually acute, while nasal and oral cavity diseases are usually chronic. Suppurative peritonitis associated with normal oral flora has been described in 2 cats.[14] In 1 of these cats, the disease was insidious and may have been present for almost 2 years. The second cat had more acute bacterial peritonitis that occurred several weeks after a suppurative cat-bite abscess on the flank was treated. Chronic osteomyelitis of the radius (after a cat bite) and mandible (after a tooth root infection) in 2 cats has also been associated with anaerobic organisms.[5]

The clinical presentation of animals with pyogenic anaerobic bacterial infections depends on the site of involvement. Cats with pyothorax usually show acute dyspnea and fever. Cats with bacterial peritonitis may have a much more chronic course of fever, depression, weight loss and abdominal distension. Cat-bite abscesses or cellulitis usually cause acute depression, fever, focal swelling (edema, hemorrhage, exudation), redness and pain. The most common sites for cat-bite abscesses or cellulitis are the distal limbs, tail and tailhead, and around the face and neck.

Pathologic Features

Pyogenic processes caused by anaerobic and facultative anaerobic bacteria range from highly suppurative and necrotizing to pyogranulomatous in nature, depending on chronicity.

Clinicopathologic Features

Purulent exudates range from yellow to yellow-green or reddish. They are often malodorous and may contain sulfur-like granules if actinomycetes are present. The characteristic putrid odor of anaerobic bacterial infections is due to production of volatile fatty acids.

Most *Bacteroides* and *Fusobacterium* species are Gram negative, while *Clostridium, Actinomyces* and *Peptostreptococcus* species are Gram positive.

Anaerobic bacteria, such as *Bacteroides, Fusobacterium* and *Clostridium* species, require special culture conditions and are often slow to grow. Isolation of anaerobic and facultative anaerobic organisms may be of doubtful significance, depending of the site of isolation. For instance, isolation of anaerobic bacteria from swabs of the mouth or superficial wounds (which cats often lick) may be meaningless. However, isolation of anaerobic organisms from abscesses, peritoneal and pleural exudates, or curetted bone is much more meaningful.

Prevention and Treatment

Most anaerobic organisms are susceptible to penicillin, ampicillin, chloramphenicol, cephalosporins, clindamycin and metronidazole. They tend to be resistant to aminoglycosides, such as gentamicin and amikacin. The response is not always good if underlying reasons for the infection are not also treated. Severe periodontal disease cannot be cured in the face of chronic tooth-root abscesses. If infections are secondary to immunosuppressive disease, therapy is only palliative. In chronic bone infections with sequestrum formation, therapy should include curettage of devitalized bone.[6]

Infection and Immunity

Infections with anaerobic and facultative anaerobic organisms are usually opportunistic. Infection depends on the breakdown of normal local or systemic defense barriers (as in chronic oral and nasal cavity disease) or inoculation of organisms into tissues where they do not normally exist (as in pyothorax, osteomyelitis, peritonitis, subcutaneous abscesses).

The additive or synergistic role of individual bacterial species in mixed anaerobic infections (the rule rather than the exception) needs further study. A *Borrelia*-like organism and *Corynebacterium pyogenes* were isolated from the thoracic exudate of a cat with pyothorax.[4] Isolates were not particularly pathogenic by themselves but were very pathogenic when inoculated in combination into cats. Facultative anaerobes are hardly ever the sole isolate from pyogenic processes of this type and are always accompanied by a type of anaerobic bacteria.

It may be possible that most aerobic organisms obtain some sort of nutritional supplementation from the coinfecting anaerobes or vice versa. Indeed, *B melaninogenicus* growth is greatly facilitated by vitamin K, a substance produced by some strains of bacteria. One strain of organism might also elaborate toxins that cause necrosis and local tissue hypoxia, thus favoring anaerobic conditions. Other anaerobic bacteria may produce penicillinase that lessens the effectiveness of antibiotic therapy.

Animal and Public Health Considerations

Anaerobic infections, being largely opportunistic in nature, are a minimal animal and public health hazard. Anaerobic strains of bacteria may also be fairly species specific.[8]

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Salmonellosis

Cause

Salmonella species are motile, Gram-negative bacterial rods that inhabit the intestinal tracts of a wide range of mammals, birds, amphibians and reptiles. *Salmonella choleraesuis, S arizonae, S typhimurium* and *S enteritidis* are the most important species in veterinary medicine. *Salmonella enteritidis* occurs in hundreds of different serotypes that are often named after localities in which they were identified, such as Dublin, Khartoum, Minnesota, Chester, Manhattan and Newport. *Salmonella typhimurium* is the most important pathogen of the genus.

Many *Salmonella* species have been isolated from the feces of normal cats. However, isolation rates have varied from virtually 0% to 44%, depending on the source and locality. Isolation rates from normal free-roaming cats are generally 5% or less.[1,2,10,15,19] Isolation rates are high among random-source cats purchased for experimental use. One-third of the shipments of cats sent to research institutions contained infected cats; overall, 10.6% of such cats were carrying *Salmonella*.[5]

Pathogenesis

Salmonella organisms are passed from animal to animal by the fecal-oral route. *Salmonella* can also grow in pet foods; this can be another source of infection. Organisms can survive for some time on objects in the environment. Environmental and fecal contamination are considered synonymous. An outbreak of *Salmonella* infection in cats has been linked to an epidemic of salmonellosis in migratory song birds in the northeastern United States.[13] Cats apparently contracted the infection by preying on diseased birds or by hunting in areas where birds congregated.

Salmonella replicates initially in the GI tract. However, GI tract colonization following ingestion requires quite large doses of organisms.[16] This is probably why salmonellosis is more apt to be seen in dense populations of cats and in conditions of close confinement and poor sanitation. If enough organisms escape the acidic environment of the stomach, they attach to the ileal villi. They then invade and multiply within the villi and reach the mesenteric lymph nodes. Bacteremia is infrequent in asymptomatic infections but is common in clinically affected animals.

Clinical Features

Infection with *Salmonella* is usually inapparent. In high-stress situations and environments that favor massive exposure, infection can be clinically apparent. Kittens are also more likely to be clinically affected than adult cats.[3] Therefore, clinical outbreaks of salmonellosis have largely been limited to hospitalized populations of cats or cats in high-density colony-type environments.[5,18] Spontaneous outbreaks of salmonellosis in individual pet animals are uncommon.[6-8,11,12]

The most common clinical form of salmonellosis in cats is acute gastroenteritis, resembling feline panleukopenia, usually manifested by sudden onset of vomiting, diarrhea, fever and depression 2-5 days after exposure.[4,13] The clinical course lasts 2-7 days in most cases.[13] However, clinical signs in some infected cats are subacute to chronic, with nonspecific signs (fever, anorexia, depression).[4] Acute salmonellosis is more apt to be primary and uncomplicated, while subacute and chronic infections more often occur for some underlying reason (nosocomial or opportunistic infections). In severely affected cats, the disease is rapidly terminated by bacteremia and endotoxic shock.[11,17] Neurologic signs have been associated with intestinal signs in at least 1 kitten.[11] One kitten had intestinal signs and hemolytic anemia. Recovery following milder disease occurs in 3-5 days.[12,13]

Miscellaneous forms of salmonellosis have been also observed in cats. Purulent conjunctivitis associated with salmonellosis has been seen in a cat and experimentally recreated in kittens.[5,6] Acute peritonitis associated with *S typhimurium* has been observed in a kitten.[8] *Salmonella choleraesuis* has been associated with abortion in a queen.[7] Salmonellosis was a complicating bacterial infection in two cats following fracture repair and colonic resection.[4]

Pathologic Features

Cats with *Salmonella* gastroenteritis demonstrate reddening of the intestinal mucosa, as well as congestion and reddening of the mesenteric lymph nodes. In septicemic cats, petechial and ecchymotic hemorrhages, vascular thrombosis, and focal necrosis are seen in the liver, spleen, heart, lungs and brain.[4,11,17]

Clinicopathologic Features

Cats with acute salmonellosis are often leukopenic.[4,13,17] The clinical signs, coupled with leukopenia, resemble those of panleukopenia virus infection. The organism is readily isolated from affected organs and rectal swabs. Bacteremia is present in many cats with salmonellosis; therefore, blood cultures are warranted in any cat with specific or vague GI signs and/or leukopenia.

Treatment and Prevention

Outbreaks of salmonellosis in hospitals and similar settings are often associated with antibiotic-resistant strains. Chloramphenicol and trimethoprim-sulfonamides are the drugs of choice.[4] However, there is some controversy about use of antibiotics to treat uncomplicated cases of *Salmonella* gastroenteritis. Antibiotics can actually favor the growth of antibiotic-resistant *Salmonella* and depress the normal inhibitory flora. Antibiotic therapy also delays establishment of immunity and prolongs fecal shedding in many cats. Such cats should be treated supportively by withholding food or water during the period of vomiting and diarrhea, administering parenteral fluids and enforcing rest. Unfortunately, clinical salmonellosis in cats is often acute and severe, and a decision to treat is often made before a diagnosis is confirmed by culture. Mortality was 61% among affected cats in one outbreak.[18] Therefore, acute salmonellosis in cats should not be viewed lightly.

Infection and Immunity

Clinical salmonellosis is difficult to recreate experimentally. Cats can be experimentally infected by oral inoculation with virulent *Salmonella,* but they shed the organisms without becoming ill.[18] This suggests that factors in addition to the dose of organisms are important in causing disease. Cats experimentally infected with *Salmonella* shed organisms for only about 10 days, though an occasional cat sheds for 4 weeks or more.[17]

Immunity to *Salmonella* infection appears to be mainly cell mediated. Organisms often persist following establishment of immunity in intestinal epithelial cells and mononuclear cells within mesenteric lymph nodes. Stress factors can delay development of cellular immunity, thus increasing the duration and severity of infection and likelihood of bacteremia. Severe stress or use of corticosteroids can also transiently depress immunity and allow reactivation of bacterial shedding in latent carriers. Persistent feline leukemia virus (FeLV) infection and noninfectious immunosuppressive diseases, such as diabetes mellitus, can also lower resistance in some cats and predispose them to fatal salmonellosis.[4] The possible relationship between FIV infection and salmonellosis must be determined, especially in cats with more chronic and atypical forms of the disease.

Animal and Public Health Considerations

There is little doubt that cats can carry and shed *Salmonella* in their stool. Serotypes found in cats are often identical to those that are pathogenic to people and other animals.[9,10,12,14] Considering the number of cats that are carriers of *Salmonella,* however, there are relatively few reports of people infected by exposure to cats. People are more often infected by other types of animals, and cats and people in the same household may both become infected at the same time from a common source.[9,12]

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Colibacillosis

Cause

Escherichia coli is the only important member of the genus. It is a variably motile, Gram-negative bacterial rod that inhabits the distal digestive tract. Similar to *Salmonella, E coli* resists environmental destruction and can survive outside the animal for long periods.

Pathogenesis

Escherichia coli, a natural inhabitant of intestinal tract of all animals, is pathogenic only under certain conditions. Massive initial colonization of the gut with enterotoxigenic strains, especially in young suscepti-

ble animals, can lead to severe and acute gastroenteritis. *Escherichia coli* can secondarily complicate other diseases (wounds, colonization of damaged heart valves, etc). Septicemic *E coli* infections also occur in immunocompromised hosts or following severe damage to the bowel mucosa.

The pathogenesis of neonatal *E coli* infections is unknown. The high frequency of bacterial pyelonephritis and/or pneumonia in kittens with *E coli* septicemia suggests that the infection either ascends the urinary tract or enters through the upper respiratory tract.[5] Alternatively, the pyelonephritis and pneumonia may be secondary to a primary blood-borne infection. Hematogenous spread of *E coli* may also be associated with a primary umbilical vein infection. Carrier cats serve as a ready source of infection for susceptible cats brought into the cattery. Conversely, new cats may introduce different pathogenic strains of *E coli*.

Clinical Features

Escherichia coli infections of cats are generally of 4 types: bacteremia in neonatal kittens; transient gastroenteritis in weanling kittens; bacteremia in older immunocompromised hosts; and localized infection.

Neonatal colibacillosis is common in kittens. From 10-20% of the neonatal kitten deaths in 2 specific-pathogen-free breeding colonies were due to *E coli* septicemia.[4,14] Hemolytic strains of *E coli* were the most consistent bacterial isolates from kittens that died during the first weeks of life.[13] This form of disease can affect all or part of a litter. One queen had a history of entire litters of fading kittens, and one of the kittens that was necropsied had *E coli* septicemia.[5]

Transient gastroenteritis associated with pathogenic strains of *E coli* has been infrequently described in young cats,[8,11] but is probably common. Following ingestion, enteropathogenic strains of *E coli* attach to intestinal mucosal cells and secrete enterotoxins. The toxin causes transient osmotic diarrhea. Infection is terminated when local immunity is established and bacteria-coated intestinal epithelial cells slough, usually after 3-7 days. Very young animals, which are more sensitive to acute fluid and electrolyte imbalances, are more apt to be clinically affected than older animals. Prerequisites for coliform enteritis include exposure to very large numbers of toxin-producing *E coli* and exposure to strains against which the animal has little or no previous immunity. Therefore, disease is more likely in high-density populations where sanitation is poor and fecal contamination is high, and in environments with a frequent influx of animals from different sources. Each environment may have a different strain of enteropathogenic *E coli* to which it is resistant. If a cat carrying one strain is introduced into a cattery that has never experienced infection with that strain, a brief epizootic of enteritis may follow. The same is true of the susceptible newcomer that is exposed to a resident population of cats carrying their uniquely different strains of *E coli*. For these reasons, cattery environments are much more apt to have transient outbreaks of *E coli* gastroenteritis than households.

Fulminating bacterial septicemia, often due to *E coli*, is common in immunocompromised cats. Predisposing conditions include antibody deficiency in neonates that have not received colostrum, feline panleukopenia and various forms of feline leukemia virus (FeLV) infection. Feline panleukopenia is associated with profound depletion of WBCs and severe intestinal damage. Both situations favor rapid movement of bacteria from the intestine to the bloodstream. Cats with myeloproliferative disease, aplastic anemia and various preleukemic (myelodysplastic) disorders often have profound leukopenia and diminished immunoresponsiveness. Such animals may develop severe enterocolitis and bacteremia.

Escherichia coli have been associated with a number of localized infectious processes in cats. Acute and chronic pyelonephritis in mature cats, though uncommon, is often associated with *E coli*. *Escherichia coli* has also been isolated from cat-bite abscesses and wound infections. Septic endometritis has been associated with *E coli*.[8,13] *Escherichia coli* has also been commonly associated with pyometra in cats.[2,6] Though *E coli* is frequently associated with cystitis in dogs, it is rarely associated with cystitis in cats.[12] *Escherichia coli* has occasionally been isolated from cats with gallbladder infections. Several weanling kittens with *E coli* pneumonia and septicemia have been observed. Fulminating

necrotic colitis has been attributed to *E coli*, though definitive proof is lacking.[3]

Pathologic Features

Lesions caused by *E coli* infection are highly variable, consistent with the numerous clinical forms. Kittens with pyelonephritis have pronounced kidney enlargement and suppurative parenchymal disease. Septicemic forms are also frequently associated with thrombotic phenomena and necrosis. Intestinal disease associated with enterotoxigenic strains usually causes mild or inapparent tissue changes.

Clinicopathologic Features

Escherichia coli is readily isolated from affected tissues, and frequently from the blood in fulminating cases of colibacillosis in kittens or immunocompromised adults.

Treatment and Prevention

In a study of the pattern of antibiotic resistance of *E coli* isolated from rectal swabs taken from 93 cats in the Brisbane area, *E coli* strains resistant to common antibacterials (tetracycline, streptomycin, ampicillin, sulfanilamides) were obtained from 26% of the cats sampled.[10] Cephalosporins, aminoglycosides and chloramphenicol were usually effective against most isolates. An aminoglycoside antibiotic, such as amikacin or gentamicin, combined with a penicillin, such as ampicillin, is a particularly effective treatment for coliform septicemia in young kittens.

Infection and Immunity

Similar to the pattern of infection caused by normal commensal bacteria, *E coli* is only pathogenic under conditions that increase the degree of exposure, or damage local and systemic immune defenses. There is some indication, but no definitive proof, that kittens succumbing to coliform septicemias in the first 1-2 weeks of life may be deficient in passive maternal immunity.

Animal and Public Health Considerations

Escherichia coli is ubiquitous and pathogenic strains are widespread. Affected or healthy cats carrying potentially pathogenic serotypes are not considered a public or animal health hazard.

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Cat Scratch Disease (Cat Scratch Fever)

Cat scratch disease is a condition mainly of people rather than of cats. It is mentioned here because it is one of the most important zoonotic (animal to person) diseases of cats. Cats are implicated in most cases of the disease, and veterinarians are often called upon to advise clients on the disorder. Recent studies indicate that the cat scratch bacillus may also cause idiopathic lymphadenopathy in cats.[4,5]

Cause

The causative agent of cat scratch disease is a small Gram-negative bacterial rod that has only been recently cultured *in*

vitro.[4,12] It is often observed within capillary walls in involved regional lymph nodes and, on occasion, in tissues at the primary inoculation site.[9,12] About 90% of human infections result from a scratch, lick or bite from a cat, usually a kitten.[10,11] The disease has been observed less commonly following dog bites, or from puncture wounds associated with thorns, wood splinters or fish bones. Epidemiologic studies indicate that cats may be mechanical vectors and not hosts of the organism for the following reasons: cats implicated as the source of human infection fail to react to cat scratch antigen when skin-tested; involved cats appear to only transmit the causative agent for a brief period, usually 2-3 weeks; and attempts to isolate the causative agent from cat saliva or claws have been unsuccessful.[10] It is also possible that the agent is a part of the normal oral flora of some cats.[5] The organism would then be transmitted to the claws during grooming and from cat-to-cat or cat-to-person by scratching or biting.

Pathogenesis

Cat scratch disease of people occurs throughout the world, more commonly in children than adults, and more frequently in males than females.[10,11] Most cases occur in fall and winter in cooler climates, while seasonal variation is minimal in the tropics. About 2000 cases are reported annually in the United States but the true incidence is unknown. Positive skin tests for the infection are seen in 12-29% of veterinarians and less than 5% of healthy people in other occupations, indicating that subclinical or mild infections are common.

The organism can apparently enter the body through broken skin or by mucous membrane contact. About 90% of patients have primary skin infections, 7% have primary conjunctival infections, and 2% have primary infections of other mucous membranes.[10,11]

The disease begins at the site of initial contact.[10,11] The earliest skin lesion is a single small papule or pustule, or a number of erythematous macules. Conjunctivitis is common in individuals exposed by the conjunctival route, while small mucosal granulomas are associated with primary infection of the mucous membranes. Infection spreads via lymphatics to the regional lymph nodes. However, lymphangitis is not a feature of the disease. Regional lymphadenitis occurs 3-50 days after exposure.[10,11]

Cat scratch disease is usually limited to the site of infection and the regional lymph node(s). Systemic spread has been observed in less than 5% of individuals.[10,11] Systemic manifestations usually result from involvement of the CNS, lungs, liver or bone.[3,10]

Clinical Features

Most patients are not seen until regional lymphadenopathy becomes prominent. An erythematous papular or pustular lesion at the site of infection is detectable in 54-96% of affected people after careful examination.[10,11] Fever, malaise and influenza-like symptoms lasting 1-3 weeks are seen at onset of lymphadenopathy in less than 50% of affected individuals. More widespread skin disorders, characterized by maculopapules, petechiae, erythema nodosum or erythema multiforme exanthema, are associated with the disease in less than 5% of patients. Splenomegaly is detected in about 16% of affected people.[10]

The involved lymph nodes are usually in the axilla, neck or groin, variably tender on palpation and 1-8 cm in diameter. Lymph node enlargement usually persists for 2-4 months and rarely for up to 2 years. Suppuration, detected by needle aspiration, occurs later in the course of the disease in 13% of patients.[10] Spontaneous rupture and drainage of a suppurative node occurs in less than 6% of patients.

In people with primary conjunctival lesions, infection often spreads to the lymph nodes of the head and neck and results in a condition called the oculoglandular syndrome of Parinaud. The parotid area is often swollen due to periauricular lymph node enlargement.[2]

When central nervous system involvement occurs, it appears within 1-6 weeks of the adenopathy. The encephalitic form of the disease may be manifested (in order of frequency) by coma, convulsions, encephalopathy, meningitis, radiculitis, polyneuritis, myelitis with paraplegia, and lethargy and/or confusion.[10] Neurologic manifestations progress over 1-2 weeks and then gradually resolve over the next 1-6 months.

Atypical pneumonia and localized osteomyelitis are uncommon systemic manifestations of the disease.[3,10] Osteomyelitis can result from hematogenous spread or extension from adjacent affected lymph nodes.[3] Hepatic abscesses have also been associated with the cat scratch agent.

The full spectrum of cat scratch disease in cats has not yet been defined. A syndrome of idiopathic generalized lymphadenopathy has been the only disease condition linked to the agent.[4,5]

Pathologic Features

Characteristic lesions of cat scratch disease are seen mainly in affected lymph nodes. Multiple microabscesses appear in the nodes later in the course of disease, only to be replaced by frank abscess formation. Differential diagnoses in the latter stages include tularemia, brucellosis, tuberculosis or sarcoidosis.[4,10]

Hodgkins' disease is the main differential diagnosis in the earlier stages of infection.[7] Cat scratch disease has also mimicked malignant lymphoma in some individuals.[8]

Clinicopathologic Features

Cat scratch disease should be strongly considered in any child or adolescent with persistent localized lymphadenopathy lasting longer than 3 weeks.[10,11] The diagnosis is strengthened by the presence of dermal or conjunctival lesions and history of exposure to a cat within the previous 2 weeks. The diagnosis is less readily made in patients with atypical forms of the disease. Diagnosis of cat scratch disease is usually confirmed when 3 of the following 4 findings are present: history of contact with an animal, usually a cat, and presence of a primary dermal or eye lesion; aspiration of sterile pus from an involved lymph node or laboratory tests that exclude other causes of adenopathy; a positive delayed-hypersensitivity reaction in the skin to cat scratch antigen; and a node biopsy revealing characteristic histopathologic changes, especially if organisms can be identified with Warthin-Starry silver stain.[10]

The cat scratch skin test is positive in about 90% of affected individuals, providing that the duration of illness has been at least 3-4 weeks. The antigen for the test is made from pus collected from patients. A positive reaction consists of a wheal or papule occurring 48-72 hours after intradermal inoculation.

There is no known way to identify whether a cat is harboring the causative agent. Cats invariably react negatively to cat scratch antigen, and the causative agent has not been identified in saliva or on the claws of potentially infectious cats.

Treatment and Prevention

The course of cat scratch disease is usually benign and the disease spontaneously resolves within 2-3 months. Aspiration of pus from suppurated nodes may be necessary to relieve pain and discomfort.

With the isolation of the organism in culture, it has been possible to conduct antibiotic sensitivities on the cat scratch bacillus. It is sensitive *in vitro* to cefoxitin sodium, gentamicin sulfate, amikacin sulfate, tobramycin sulfate, netilmicin sulfate and mezlocilin sodium.[4] *In-vivo* studies appear to confirm the sensitivity of the agent to these antibiotics.[1] Therefore, antibiotic therapy will probably become the treatment of choice for cat scratch disease in people.

Infection and Immunity

Cat scratch disease is typical of a number of bacterial and fungal infections that enter the body through skin abrasions or mucous membranes and spread slowly to regional lymph nodes. Immunity remains strong for many years following recovery.[10]

Animal and Public Health Considerations

Though cat scratch disease can be reproduced with pus in people, monkeys, baboons and the Hartley strain of guinea pigs, there is no evidence of natural person-to-person transmission. It remains to be determined whether diseased cats are any greater risk to other cats or people than asymptomatic animals.

Veterinarians are often called upon to pass judgment on cats associated with human exposure. This is probably best left to people who are considered experts in the disease. Cats only appear to transmit the organism for 2- to 3-week periods or less.[10]

If this is the case, implicated cats can be loosely quarantined from children and adolescents for 2-3 weeks and then allowed to live a normal life. The disease is also very sporadic, and only an infinitesimally small portion of cat bites, scratches or licks lead to the disease. It has also been noted that 12-29% of veterinarians test positive with the cat scratch antigen, as compared to less than 5% of other healthy people and family contacts.[10] Therefore, many veterinarians have been unknowingly infected with the organism at some stage in their careers. Given this information, it is wise not to overreact to the disease or condemn the cat.

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Chlamydiosis

Cause

Chlamydia psittaci variety *felis* parasitizes living cells like a virus, but the organism is more closely related to bacteria. The feline organism can be differentiated from the more virulent avian strains.[1,6] Unlike bacteria, *Chlamydia* depends on host cells for energy. Like bacteria, it is inhibited by certain antibiotics.

Chlamydia psittaci of cats is primarily an inhabitant of mucosal cells of the conjunctiva and genital tract. Yet unclassified *Chlamydia* species inhabit the gastric mucosa of many normal cats.[9] Though gastric isolates cause mild upper respiratory diseasae and gastritis in highly immunocompromised cats, its role in classic feline chlamydiosis has not been determined.[7] In all likelihood, chlamydial isolates from the stomach are either identical or closely related to those found in the conjunctiva and genital tract.

Chlamydia psittaci has been isolated from diseased cats in the United States, Canada, Australia, England and Iran.[3,8,11, 15,18,19] It is found in most cattery populations and is widespread among groups of free-roaming domestic and feral cats.[3,8,18,20]

The organism is carried by clinically ill as well as asymptomatic cats within the epithelial cells of the conjunctiva and gastrointestinal and distal genital tracts. These carrier cats shed low levels of organisms in secretions and feces, but shedding may be greatly increased in situations of heavy stress.[15] Transmission is horizontal from clinical, subclinical or asymptomatic carriers to susceptible animals, and occurs at birth or in the postweaning period when maternal immunity has waned. Some chlamydial vaccines have also been linked to outbreaks of chlamydiosis in cats.

Pathogenesis

Infection requires intimate exposure; fleeting contacts or aerosol exposure over a distance are not usually sufficient. Spread via contaminated objects is also unlikely. *Chlamydia* attach themselves to mucosal cells following contact and are taken into the cell. The organisms infect adjacent epithelial cells and the cycle of replication and infection continues until it is suppressed by host immunity.

Clinical Features

There has been some confusion on the precise types of diseases caused by *C psittaci* in cats. The organism was first isolated from cats with so-called "pneumonitis."[2] This term was used to describe what is now called upper respiratory infection (conjunctivitis, rhinitis, sneezing) or "URI."

Pneumonitis, in its strictest meaning, is a pathologic term that means "inflammation of the lungs." After its discovery, *C psittaci* was thought to be the cause of most upper respiratory disease in cats. With the subsequent discovery of respiratory viruses, it was realized that respiratory disease of cats was in truth multifactorial. In many cases, especially in kittens, multiple agents could be isolated simultaneously from the same animals. When *Chlamydia* was inoculated into susceptible cats by itself, it produced a relatively mild disease manifested mainly by conjunctivitis. With these discoveries, the importance of *Chlamydia* in feline respiratory disease was deemphasized in favor of viruses. This was unfortunate, because chlamydiosis is still an extremely troublesome infection of cats kept in high-density, high-stress multiple-cat environments.

Chlamydia psittaci variety *felis* has been associated with 2 major and several minor disease syndromes of cats. The 2 major disease syndromes include ophthalmitis neonatorum (neonatal conjunctivitis) in neonates (0-2 weeks of age) and conjunctivitis in postweanling (6-12 weeks) kittens. Minor syndromes include fatal neonatal pneumonia, abortion, stillbirths and possibly infertility. All of these syndromes are analogous to forms of human chlamydiosis.

Neonatal conjunctivitis can affect entire litters of kittens, and may be particularly troublesome and recurrent in certain younger queens. The neonates are thought to be infected by the passage of contaminated birthing fluids up the nostrils and nasolacrimal ducts. Conjunctivitis then develops behind the closed eyelids and is usually exudative in nature. The first noticeable sign of the disease is a delay in opening one or both of the eyelids at the normal age of 7-10 days (Fig 21). Bulging of the closed eyelids is often seen, and is due to accumulation of exudate. There is frequently a crusting of honey-like exudate along the closed or partially opened lid margins. When the eyelids are forced open, a copious amount of whitish to grayish mucoid material is exuded. The underlying conjunctivitis is noticeable when the exudate is carefully cleaned away (Fig 21). Failure to open the eyelids and drain the exudates can result in corneal ulcers, some of which may perforate. Aside from the ocular disease, affected kittens appear otherwise normal and grow at a normal rate. The conjunctivitis persists for as long as 2-4 weeks if untreated.

Conjunctivitis in 6- to 12-week old kittens is the most common clinical manifestation of chlamydiosis in cats.[3,10] This form of the disease has been experimentally recreated on several occasions.[4,10,15] Conjunctivitis appears 5-10 days after aerosol exposure.[10] This is followed by a low-grade fever on days 11-15, which lasts for 3-8 days. The fever is likely to go unnoticed, especially because most kittens continue to eat and act otherwise normal. The conjunctivitis is often unilateral in both natural and experimentally induced infections (Fig 22). Even when the disease is bilateral, one eye is often more seriously affected. Rhinitis is usually mild or inapparent, and sneezing is therefore infrequent. The course of primary disease is 2-6 weeks in kittens and 2 weeks or less in older cats.

Chronic chlamydial conjunctivitis sometimes occurs in cats with abnormal ocular conformation. One adult Persian with severe facial foreshortening, exophthalmos, lagophthalmos and chronic tearing had associated bacterial and chlamydial infections (Fig 23).

Recurrent bouts of chlamydial conjunctivitis have been observed in some older cats. Recurrent disease can be due to reactiva-

Figure 21. Kitten with ophthalmitis neonatorum. The first signs are failure of the eyes to open at the normal time, bulging of the closed eyelids, and a honey-colored exudate along the lid margins. If the eyelids are forced open, a typical mucinous, cloudy exudate is evident behind the eyelids. The underlying conjunctivitis is apparent when the exudate is wiped away.

tion of a low-grade asymptomatic infection in a carrier cat, or from reinfection during waning immunity. Recurrent attacks of chlamydial conjunctivitis are seldom as severe as primary attacks, and usually last no longer than 5-10 days.

Chlamydia is a common cause of severe systemic diseases (pneumonia, arthritis) in young livestock, such as foals, calves, lambs, kids and poults. Systemic disease is associated with hematogenous spread of the organism from localized sites of infection in the mucous membranes. Paradoxically, kittens often have severe localized infections but systemic spread is very uncommon. Nevertheless, *Chlamydia* has been isolated from the lungs of 3 kittens from a litter of 6 that died within the first few days of life.[15] The lungs appeared to be grossly consolidated. This condition may be analogous to chlamydial neonatal pneumonitis in human infants.

Chlamydia is emerging as an important cause of abortion and infertility (chronic infection of Fallopian tubes) in people and certain livestock species. However, the role of *Chlamydia* in such diseases of cats is presently unknown. A high incidence of abortion has been associated with outbreaks of chlamydial conjunctivitis in a cattery.[15]

Figure 22. Typical chlamydial conjunctivitis in an 8-week-old kitten. The conjunctivitis is usually unilateral in the early stages, with pronounced epiphora and conjunctival swelling.

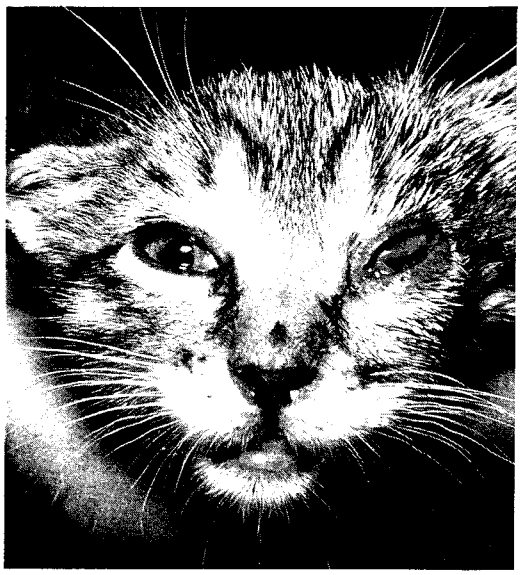

Figure 23. Adult Persian cat with long-standing bilateral conjunctivitis. *Chlamydia psittaci* was seen in conjunctival scrapings. The conjunctivitis cleared with use of tetracycline ophthalmic ointment. However, reinfection is common after therapy is discontinued. Cats with compressed faces may be predisposed to chronic bacterial, mycoplasmal and chlamydial infections because of the relative dryness of their central cornea (lagophthalmos) and excessive tear spillage from abnormal lacrimal apparatus anatomy.

More research is needed in this area of feline reproduction.

Pathologic Features

Conjunctival inflammation changes to prominent lymphoid nodules late in the disease and before recovery begins.

Lung lesions are not significant, but small foci of pneumonia are seen in some animals.[10]

Clinicopathologic Features

Conjunctivitis that usually starts in one eye is presumptive evidence for chlamydial infection, especially if it occurs in weanling kittens from a cattery environment or in older cats under recent stress. The main differential diagnosis in kittens is mycoplasmal conjunctivitis, which can appear in an identical form. In fact, mycoplasmal and chlamydial diseases are often concurrent.[4] Older cats with acute unilateral conjunctivitis should be examined closely for foreign bodies.

Definitive diagnosis of chlamydiosis is by identification of the organism in epithelial cells or by isolation in culture. Conjunctival

scrapings can be stained by conventional or immunofluorescent antibody techniques, the latter being more sensitive.[4]

Treatment and Prevention

Tetracycline is the drug of choice for treatment of cats with *C psittaci* infection. Cats should be treated mainly with topical tetracycline ophthalmic ointments 3-5 times daily for 2 weeks. Response is prompt but recurrences are sometimes seen when the medication is withdrawn. Tetracycline and related antibiotics inhibit growth of the organism, but ultimate recovery depends on development of host immunity, a process that can take 6 weeks or more. Withdrawal of the medication before immunity is established can allow the organisms to proliferate. Systemic therapy is questionable in cats with localized disease. Systemic tetracycline can discolor the erupting permanent teeth if given to kittens. Systemic tetracycline also can cause fever and anorexia as a side effect. The infection is usually superficial, and the potential side effects of systemic therapy are not compensated for by any added therapeutic benefits. However, systemic therapy is warranted in cases where systemic disease or infertility are suspected.[11]

Several vaccines are available for prevention of *C psittaci* infection in cats. Chlamydial vaccines usually contain attenuated living organisms and are generally given in combination with other feline vaccines.[12,13] Despite considerable favorable advertising claims, chlamydial vaccines should be considered poor at best.[5,16,22] This relatively poor efficacy is not a factor of the vaccine itself, but is due to the nature of chlamydial immunity. Natural infection evokes weak and often transient immunity. A chronic carrier state in the face of immunity is the rule rather than the exception. Given these circumstances, it should not be surprising that artificially induced immunity would be more effective.

Chlamydial vaccines decrease the severity of the primary infection but do not prevent colonization of the conjunctiva, gastrointestinal or genital tracts with virulent organisms and the chronic carrier state.[14,20] Even their efficacy against primary disease is lessened if the exposure is high and stress factors are unfavorable. As such, chlamydial vaccines appear to perform much better in environments and under conditions in which disease is not severe anyway. They perform poorly in high-density situations where disease is most severe. This is supported by experimental evidence; cats vaccinated with live chlamydial vaccines developed incomplete resistance to challenge-exposure.[16,22] Though clinical signs of primary infection were diminished, two-thirds of vaccinated cats shed virulent organisms for 21-35 days after challenge and one-third for 61 days or longer.[16]

Control of chlamydiosis in problem catteries must rely heavily on environmental control. Properly managed catteries with low stress levels have very few problems with chlamydiosis even though the infection may be enzootic (see chapter on cattery design and management).

Infection and Immunity

Chlamydial infection stimulates both humoral and cellular immunity.[17] In spite of such immunity, recovery from clinical infection is slow, and persistence of the organism in epithelial cells is common. Once immunity develops, it is generally weak and of relatively short duration. Protective immunity is easily overcome by severe challenge-exposure and is rapidly suppressed by stress. Therefore, recurrent disease is common in the same environments where primary disease is frequent and severe. Recurrent disease results from reinfection in the face of weak immunity and high exposure, or from reactivation of subclinical infections. Recurrent infections are more likely within the first 1-2 years following primary disease. Cats older than 2 years are much more resistant to recurrent disease. Cellular immunity is often slow to develop and takes many months or even years to become solid enough to overcome severe exposure or stress-induced immunosuppression.

The effects of stress on chlamydiosis can be mimicked by corticosteroid administration. Corticosteroids given 40-44 days after infection increased the severity of chlamydial conjunctivitis in cats, an effect that lasted for 4-5 days. Corticosteroids also increase shedding of *Chlamydia* by carrier cats.[15] Therefore, stressful environments are not only more conducive to spread of the organism but are also more apt to produce clinically apparent disease.

Animal and Public Health Considerations

Feline strains of *C psittaci* cause disease in cats and people. However, their role in other species has not been determined.[8] People exposed to cats with active *C psittaci* conjunctivitis have developed conjunctivitis themselves.[14] Human cases of conjunctivitis due to feline chlamydia resemble the feline disease in most respects, except that the duration is usually shorter. It often involves only one eye, the conjunctiva is reddened and edematous, and there is a considerable amount of tearing and irritation. Untreated, the disease lasts 1-2 weeks.

It is doubtful whether *C psittaci* of feline origin is associated with any other chlamydial disease of people. Trachoma, neonatal chlamydiosis, genital infections and ornithosis are all caused by different strains or species of *Chlamydia* than those found in cats.

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Mycoplasmosis

Cause

Mycoplasma and *Mycoplasma*-like organisms belong to 3 groups: *Mycoplasma*; *Ureaplasma* or *T-mycoplasma*; and *Acholeplasma* species. *Mycoplasma*, *Ureaplasma* (*T-mycoplasma*) and *Acholeplasma* species are all commonly isolated from domestic cats. *Mycoplasma felis* and *M gatea* are the most prevalent mycoplasmas in cats.[1,2,12,29]

Pathogenesis

The pathogenicity of mycoplasmal strains varies greatly in cats. *Mycoplasma felis* has been isolated 7-8 times more frequently from cats with respiratory disorders than from normal animals. *Mycoplasma arginini* was isolated at about the same rate in sick and normal animals.[30] The lack of pathogenicity of *M arginini* for cats was reconfirmed.[26] Likewise, *A laidlawii* appears to be nonpathogenic for cats and probably exists as a saprophyte in many species of animals.[30] *Mycoplasma gatea* was isolated more often from normal than sick cats.[26] However, *M gatea* has been isolated from an older animal with widespread arthritis

and tenosynovitis. This appeared to have been an opportunistic infection in an immunocompromised animal.[19]

Mycoplasmal infections are probably acquired at a relatively young age. Many older animals harbor the organisms in the mucous linings of the conjunctival sac, oropharynx and genital tracts (prepuce and vagina). Infection of kittens may occur at birth or shortly thereafter through exposure to vaginal or oropharyngeal secretions from the queen. If kittens are not infected at birth or within the first few weeks of life, they almost certainly are exposed to the organisms as they contact carrier animals after weaning. Following infection, the subsequent course of disease is probably influenced by the animal's immunologic status. Animals most susceptible to disease include fetuses that are not immunologically competent, neonates that have immature immune systems and low levels of maternal antibodies, and postweaning kittens that are partially immunologically competent but have lost their maternal immunity. Older cats that have become immunocompromised through some other primary illness may also be at risk.

Clinical Features

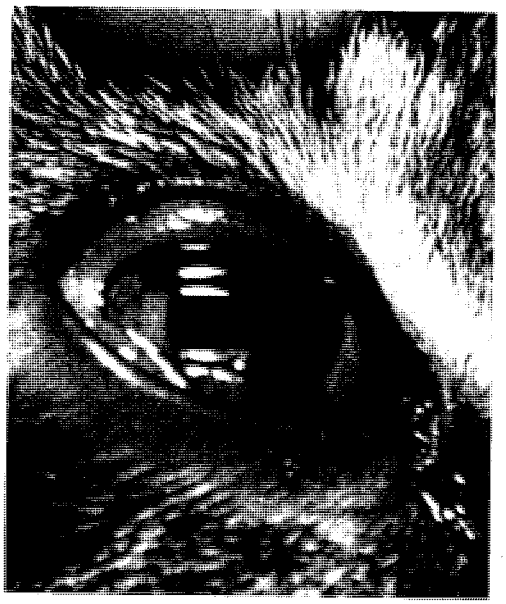
Mycoplasma and *Mycoplasma*-like organisms are important pathogens in lambs, kids, calves, foals and poults. Infections in these species are initially localized but frequently disseminate hematogenously to the lungs and joints. The disease-causing potential of mycoplasmal organisms in cats appears to be much less. Initial infections remain localized and disseminated disease is uncommon in immunocompetent individuals. Conjunctivitis is the most common clinical manifestation of mycoplasmosis in cats.

Mycoplasma isolated from naturally diseased animals did not cause conjunctivitis in normal cats but readily did so in animals that had first received an intrapalpebral inoculation of corticosteroids.[5] Subsequent studies linked *Mycoplasma* to conjunctivitis merely because it was isolated more frequently from inflamed eyes than normal eyes.[10,17,27,32] However, those studies did not consider primary infection and coinfection with other agents, such as herpesvirus or *Chlamydia*.[2,20]

It was not until 1974 that conclusive evidence was obtained for the role of *Mycoplasma* in conjunctivitis.[24] These latter experiments involved kittens, which are more sensitive to infection than adults.

Mycoplasmal conjunctivitis is most frequently caused by *M felis*.[29] It is predominantly a cattery disease and is seldom seen in kittens from single-cat homes. It usually develops shortly after kittens are weaned, around 8-12 weeks of age. The earliest signs are acute swelling and reddening of the conjunctiva in 1 or both eyes (Fig 24). Conjunctivitis may be associated with some squinting and photophobia. Inflammation of the conjunctiva varies greatly; conjunctival membranes may be only slightly reddened or may be so swollen that the globe is barely visible. Early in the disease, the exudate is usually serous but it may become somewhat purulent with time. A diphtheritic or fibrinous coating may sometimes be seen on the inflamed conjunctiva and is highly conducive to formation of conjunctival-corneal adhesions. Sneezing is either mild or not seen and, if present, is more apt to be due to excessive nasolacrimal drainage from the inflamed conjunctiva than from rhinitis. Severe concurrent sneezing and nasal discharge in kittens with unilateral

Figure 24. Mycoplasmal conjunctivitis in a cat. The conjunctiva is swollen and glistening, and the hair around the lower eyelid is wet from the serous discharge.



conjunctivitis usually indicate a complicating herpesvirus infection.

Mycoplasma organisms tend to disappear from the conjunctival sac upon recovery but may persist in the oropharynx. Conjunctivitis may recur in older cats, especially following stress or major disease outbreaks among younger animals. Recurrent disease resembles the primary infection but is usually milder and seldom lasts longer than 7-10 days.

Corneal-conjunctival adhesions may be important sequelae in cats with diphtheritic inflammation. Secondary infections of the conjunctiva with staphylococci or *Pseudomonas* can sometimes occur and, if improperly treated, can lead to corneal ulceration and even perforation.

Mycoplasmal conjunctivitis in cats is often associated with chlamydial conjunctivitis.[6,7] Chlamydial conjunctivitis has virtually the same pathogenesis as mycoplasmal conjunctivitis. Therefore, it is not surprising that *Mycoplasma* and *Chlamydia* infections often occur together.

Pneumonia is an important systemic complication of localized mycoplasmosis in many species of animals but is surprisingly uncommon in cats. The author observed an outbreak of mycoplasmal pneumonia and conjunctivitis in 6 adult cats that had received an injection of long-acting methylprednisolone 2 weeks earlier and in a litter of 4-week-old kittens.

Arthritis and tenosynovitis, though common in other domestic species, are uncommon manifestations of mycoplasmosis in cats. This again indicates the marked resistance that cats have to systemic spread of *Mycoplasma*. *Mycoplasma gatea* was isolated from the synovium of an 8-year-old cat with chronic fibrinopurulent tenosynovitis.[19] This infection appeared to be opportunistic because the cat also had a chronic nasal infection and hypogammaglobulinemia. Though the cat was feline leukemia virus (FeLV) negative, the possibility of some other concurrent virus-induced immunosuppression (feline immunodeficiency virus infection) or nonviral immunocompromising disease was not established. Mycoplasmal polyarthritis has been observed in a second severely immunocompromised cat.[15] Mycoplasmal polyarthritis has also been observed in 2 aged cats seen at the Veterinary Medical Teaching Hospital, University of California, Davis. Both cats had advanced cancer and were undergoing extensive therapy when arthritis occurred.

Urethritis and cystitis have been associated with *Mycoplasma* and *Ureaplasma* in people. They have also been isolated infrequently from dogs with cystitis. Though they have been frequently isolated from the distal genital tracts of male and female cats, they have not been associated with disease. They have not been isolated from cats with feline urologic syndrome, a disease that is probably of dietary origin.

Mycoplasma has caused fetal death and abortions in people, cattle and sheep. Given the high incidence of mycoplasmal infection in catteries and the established role of the organism in fetal disease in other species (and possibly cats), further studies of the role of these organisms in feline abortions are needed.

Pathologic Features

Mycoplasmal organisms cause purulent and fibrinopurulent inflammatory reactions early in the course of primary or systemic infection.

Clinicopathologic Features

Organisms can be identified in conjunctival scrapings stained with Giemsa or Macchiavello stains. Mycoplasmal organisms can be cultured using specific types of agar and broth enriched with equine serum. Identification of *Mycoplasma*, *Ureaplasma* or *Acholeplasma* is by colony size and morphology on agar, susceptibility to various antibiotics, serologic reactions or responses in selective biochemical media.[9,13]

Treatment and Prevention

Mycoplasmal conjunctivitis is treated topically with appropriate nonsteroidal ophthalmic ointments. For best results, medication should be applied 4 times daily or more frequently. Tetracycline is preferred for initial treatment. They are also active against *Chlamydia*, which often complicates mycoplasmal conjunctivitis in cats. Some mycoplasmal isolates are resistant to tetracycline. Erythromycin or spectinomycin should be used in such cases. *Mycoplasma* is resistant to penicillins, cepha-

losporins and aminoglycosides. Systemic antibiotic treatment is not warranted in kittens with localized disease. It only adds to the stress of the condition and may induce intestinal upset. Therapy should be continued for at least 3-5 days after conjunctivitis has completely resolved. Conjunctivitis, especially in kittens, may recur after therapy is discontinued. Therapy must be reinstituted in such cases. If systemic infections are suspected, oral or parenteral tetracyclines are the drugs of choice. However, they can permanently discolor the permanent teeth when given to kittens.

Mycoplasmosis in catteries can be controlled to a great extent with proper design and management. This includes limiting stress and numbers of kittens, and isolating kittens by litters from other young cats.

Infection and Immunity

Cats appear to have a great deal of natural resistance to systemic spread of mycoplasmal infections from primary disease sites in the upper respiratory tract. Therefore, cats are spared from the most serious manifestations of the disease. The reason for this species resistance is not known but it also extends to chlamydial immunity. *Chlamydia* and *Mycoplasma* are responsible for virtually the same type of localized and systemic diseases in cats and other animals. Therefore, it is not surprising that cats show a similar type of resistance to both organisms.

Opportunistic mycoplasmal infections have been seen in older immunocompromised cats. They mimic systemic forms of infection, such as arthritis and serosal disease, seen in susceptible species of animals. The author has observed severe mycoplasmal pneumonia and conjunctivitis in 6 adult cats that received an injection of repository methylprednisolone 2 weeks previously.

Animal and Public Health Considerations

Cats with mycoplasmal infections are not considered public health hazards. The main pathogenic *Mycoplasma* species is *M felis*, an inhabitant of cats that has not been identified in other species. Therefore, cats are the principal reservoir for their own infections. Though cats apparently spread the infection to each other, the myriad environmental and host-resistance factors that influence disease are probably more important than actual exposure in determining the clinical outcome of mycoplasmosis.

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Dermatomycosis (Ringworm)

Cause

Dermatomycosis (ringworm, tinea or dermatophytosis) is a skin condition caused by a group of fungi known as dermatophytes. Dermatophytes penetrate and parasitize keratinous body tissue, such as skin, hair, feathers, horns or nails. There are presently over 35 species of dermatophytes belonging to 3 genera: *Epidermophyton, Microsporum* and *Trichophyton*. Some species of dermatophytes are zoophilic (live on animals), some are anthrophilic (live on people), and others are geophilic (live in soil) (Table 5).[10,16] Among the 35 or so species, only 6 are of particular interest to cats. These 6 species include *Microsporum canis*, *M distortum*, *M gypseum*, *Trichophyton mentagrophytes*, *T verrucosum* and *T rubrum*.[1,3,4,6,14,19,23,30,34,38,42] *Microsporum cookei* and *M gallinae* have been rarely implicated with dermatomycosis in cats.[10] *Trichophyton terrestre* has been associated with ringworm in a cat from the United States.[45] However, it usually is present on the cat's fur as a contaminant or inapparent infection.[2]

Microsporum canis accounts for 75-98% of ringworm seen in cats in most parts of the world.[1,6,18,20,21,38,43] *Microsporum distortum* is a major cause of feline ringworm in Southern New Zealand but is uncommon elsewhere in the world. *Microsporum gypseum* accounts for 0.5-30% of the cases of feline ringworm.[6,18-20,34] Various species of *Trichophyton* account for less than 1% of the cases of feline ringworm; they are more common in dogs or livestock.

Because *Microsporum* species account for almost all feline ringworm in catteries, and *M canis* is by far the most serious pathogen, the remainder of this discussion will apply mainly to this organism. The pathogenesis of other species of dermatophytes is virtually identical, except for the most common reservoir for spore forms in nature. *Microsporum canis* causes disease in a wide number of animal species and in people. However, despite what its name might suggest, the principal host and victim of *M canis* is the cat.

Pathogenesis

Cats are exposed to dermatophytes from spores shed into the environment by infected animals or by direct animal-to-animal contact. Spores of *M canis* have survived in the environment for as long as 13 months.[22] The degree of environmental contamination is proportional to the numbers of kittens raised in the area, density of cats in the quarters, degree of sanitation (removal of hair, keratinous debris), and level and type of disinfection.

Animal-to-animal contact occurs between clinically affected and susceptible cats or between inapparent carriers and susceptible animals. Though cats with clinical lesions are more apt to shed large numbers of spores, and to be more infectious, up to 40% or more of normal cats in an enzootic environment can also be infected.[3,12,40,48] In a survey of *M canis* infection among 1059 cats seen by veterinarians for various reasons, 5.9% were infected.[23] The infection rate among domestic shorthaired cats was 3.8%, while among purebred cats it was 16.9% in Persians and 38.8% in Siamese.

The greater incidence of dermatophytes in cattery-bred cats as compared to regular household pets underscores the importance of the environment in the spread of ringworm. Age is also an important consideration. The highest isolation rate among random-source cats was in kittens less than 3 months of age (12.6%).[23] The infection rate in this study remained constant at 3-5% in cats up to 4 years of age. The isolation rate drops precipitously to less than 1% in cats older than 4 years of age. This great decrease in infection after 4 years of age is also reflected in a marked drop in the incidence of active lesions in older cats.[32]

Infection usually involves dermal contact with spores in the environment or spores shed from infected animals. *Microsporum canis* spores remain viable on affected hairs for 315-422 days at room temperature.[22] Kittens born in catteries where ringworm is enzootic are usually infected shortly after birth, while kittens born into dermatophyte-free environments do not get infected until they are placed into new homes.

The severity of clinical disease depends on many factors. Kittens that are malnourished, sickly or concurrently infected with viral, bacterial and parasitic agents, kittens that live in stressful conditions, or kittens born in badly contaminated environments develop much more severe disease than kittens born in normal environments. Genetics also appear to play a role. Persian cats have a much higher incidence of clinically apparent infections and the disease course is more severe and protracted in Persians than in other breeds.

Ringworm lesions slowly expand by horizontal and centrifugal growth within the interfollicular keratin layer of the skin and vertical and downward growth along the intrafollicular hair shaft.[41] The actual ringworm lesion only comprises a portion of the infected areas; fluorescent hairs often extend many millimeters around the lesion. Typical ringworm lesions occur because of loss of diseased hairs by early breakage, increased desquamation of keratinized skin, host inflammatory responses, and in some cases, by secondary bacterial infection.

Spread of ringworm infection appears to be halted by immunologic means around day 30 after clinical lesions appear.[41] However, this event can be greatly delayed in sickly, malnourished or heavily stressed kittens with impaired immune responsiveness. Large numbers of infectious spores remain on the hairs after recovery, and these are only lost when the hairs grow out and are shed. This process can take another month or more. Even though recovery is widespread and very dramatic, it is not always complete. Small numbers of chronically infected hair follicles can remain for many more months or years.

Clinical Features

Lesions in naturally infected kittens often begin to appear as early as the second or third week of life. The earliest lesions tend to concentrate on the face and paws, but any area of the body can be affected.[5-7,17,32] Early lesions consist of small plaques that are somewhat erythematous. Eventually hairs in the central part of the lesions are lost, while hairs around the periphery appear discolored and otherwise dead (Fig 25). Lesions slowly expand and coalesce to form large, scaly, grayish-brown areas of

Table 5. Principal environmental reservoirs of common and uncommon dermatophytes of people and animals.

Genus	Animals	People	Soil
Trichophyton	*T equinum* *T mentagrophytes* (several varieties)	*T rubrum*	*T terrestre*
Microsporum	*M canis* *M distortum* *M equinum* *T gallinae*	*M audouinii*	*M gypsum-complex* *M nanum* *M cookei*

hyperkeratosis and alopecia (Fig 25). Over time, hairs in the center part of the lesions begin to regenerate. This central area of hair regrowth, surrounded by a zone of hair loss, which in turn is surrounded by a zone of dead hairs, gives lesions their ring-like appearance.

Involvement of the whiskers and eyelashes is especially severe (Fig 26).[5] The hairs are weakened and shed early in the disease course. Extensive hair involvement around the eyelids can also lead to pronounced depilation and a mild conjunctivitis-like syndrome (Fig 26).

Lesions are frequently found in the skin around the toes and nails. The keratin layer of the nail may be involved and lead to nail deformities.[28] The number of lesions on the body is highly variable. Lesions often remain relatively small and localized; they may not be clinically apparent unless closely inspected. In severe cases, a large proportion of the body can be affected. Such severe cases are least likely to respond to therapy and often persist for months before resolving. Cats with smaller and more localized lesions usually recover spontaneously within a month or so.

Deeper nodular skin lesions called mycetomas have been associated with *M canis* infection in cats.[4,33,46] Persian cats are especially prone to this condition. The lesions were poorly circumscribed, solid or cystic in nature, and granulomatous in appearance on histologic examination. Mycetomas can be particularly extensive and severe in some animals.[33]

Figure 25. Persian kitten with a chronic ringworm lesion behind the ear. The lesion is scaly and pigmented. Hair has been lost from the center of the lesion, while peripheral hairs are thinned and apparently dead. (Courtesy of Dr. Peter Ihrke, University of California, Davis)

Figure 26. Litter of kittens with severe acute dermatomycosis caused by *Microsporum canis*. Note the concentration of lesions around the head, loss of whiskers and eyelashes, and low-grade conjunctivitis. (Courtesy of Dr. Peter Ihrke, University of California, Davis)

Pathologic Features

Dermatophytes are essentially parasites of keratin.[27] Early hair loss is caused by massive invasion and weakening of the hair cuticle. Infection spares the nonkeratinized bulb from which the hair grows, thus ensuring a continued substrate for fungal growth.[27] Involvement of the skin's keratin layer leads to an increased rate of keratin sloughing and formation (hyperkeratosis). Inflammatory reactions in tissues surrounding infected hairs are mild in *M canis* infections.

Clinicopathologic Features

Lesions of many different skin disorders can be mistaken for ringworm. Biopsies are essential when the clinical history, age of the animal, appearance and progression of the lesions, and fluorescence studies do not

clearly indicate a diagnosis of ringworm. When the disease course and history are typical, very little diagnostic testing is needed. A minimum workup should consist of a Wood's lamp fluorescence and examination of hairs by light microscopy.[13]

Fungal elements of *M canis* and *M distortum* within hair shafts fluoresce a whitish to bluish-green when examined closely under a Wood's lamp. Hairs at the periphery of the lesions are most likely to fluoresce. Fluorescence is usually concentrated on the proximal ends of the hairs, but can extend the entire length.

Skin scrapings containing hairs, or hairs pulled from the periphery of lesions, can be examined microscopically for fungi. Visualization of fungi can be aided by partially dissolving the hairs to be examined in 10% KOH. Heating the mixture briefly under a flame hastens the process. Branching hyphae that sometimes invade the hair structure, as well as spores, can be readily identified with some experience.

Treatment and Prevention

Treatment and prevention of ringworm in catteries are directed at individual infected animals, potential carriers, and the environment. Treatment and prevention of ringworm in ordinary household pet cats are directed almost entirely at the affected animal.

Treatment of individual cats with ringworm has consisted of systemic antifungal medications, topical treatments and/or combinations of the 2. All 3 approaches have proven effective in individual animals. However, the efficacy of any particular treatment regimen must be evaluated in context of natural immunity and "self-cures." Many articles on ringworm treatment describe complete cures within 30 days, the same length of time that most lesions take to spontaneously resolve. The true test of any treatment regimen is its ability to cure ringworm in cats with chronic and severe disease.

Griseofulvin has been commonly used for treatment of feline dermatomycosis.[9,17,36] It is usually given orally and is carried systemically to keratinized cells, where it is deposited. An oral dosage of 25 mg/kg, divided twice a day, preferably with a fatty meal, for as long as 8 weeks has been recommended for cats. The efficacy of griseofulvin has been reportedly increased by shaving the animal to remove dead hair and including topical antifungal therapy.[36] Resistance to griseofulvin has been occasionally observed.

Griseofulvin given at the newer recommended dosages has limited toxicity for cats. Toxicity appears to be idiosyncratic and not dose related.[25] It has caused pruritic drug reactions to the skin, angioneurotic edema of the skin, mucous membranes or viscera, fever, lethargy, diarrhea, vomiting, developmental anomalies in kittens born to queens treated during pregnancy, anemia, leukopenia, neurologic problems, weight loss and anorexia.[15,25,44]

Ketoconazole is the newest systemic drug used to treat dermatomycosis in cats.[8,47] The suggested dosage is 10 mg/kg orally once a day for up to 8 weeks. Ketoconazole provided much quicker regression of ringworm lesions than griseofulvin.[39] The drug can irritate the GI tract and suppress the adrenal glands. Toxic signs include anorexia, fever, depression and diarrhea. Newer, safer and more effective imidazole compounds are currently appearing on the market.

Topical treatment is commonly used for localized ringworm, or in combination with systemic drugs in severe generalized disease. In one study, the time for resolution of lesions was reduced by more than one-half in cats that received both topical and systemic treatment, versus that in cats that received systemic therapy alone.[5] Many substances have activity against dermatomycosis, including undecylenic acid, mercaptan, tolnaftate, iodophor, iodochlorhydroxyquin, chlorhexidine, nystatin, thiabendazole, clotrimazole, miconazole and numerous other new topical imidazoles, dilute chlorine solutions, and organic and inorganic iodides. If lesions are extensive, total body clipping of hair facilitates treatment and eliminates a great amount of infectious hairs from the environment. As in systemic therapy, topical treatment is more successful in cats with milder and more acute infections than in cats with severe and chronic disease.

Mycetomas due to *M canis* are very difficult to treat medically and they frequently recur following surgical removal. Ketoconazole and amphotericin B plus griseo-

fulvin have proven unsuccessful in 2 cats, and 3 of 4 cats treated surgically have had recurrences.[4,33,46]

Identification and elimination of carrier cats have been elusive for many veterinarians and cat breeders. Carriers can be identified by using the "brush technique," in which large areas of the body can be sampled.[3,7] Carrier cats, when identified, are usually less than 4 years of age. In many enzootic households, 5-40% or more of younger breeding cats may be carriers.

Many veterinarians and cattery owners have recognized the difficulty and expense of mass culturing, and have attempted to eliminate carrier cats by treating all of the cats in the environment with some systemic antimycotic, such as griseofulvin.[7] Such attempts are usually doomed to failure and may even be deleterious to the health of cats being treated and to the unborn fetus. Systemic antimycotics may temporarily clear the infection but do nothing for bolstering immunity to prevent reinfection when drug therapy is stopped. Topical treatment of all cats in the environment is also likely to fail for the same reasons. Moreover, drug therapy is often done in lieu of environmental control measures, which in the long run may be far more effective.

Environmental factors are of paramount importance in ringworm control programs. Spores of most dermatophytes survive for a year or more in the environment and are very difficult to kill with disinfectants and heat treatment. This is especially true if they are protected by porous surfaces, dust, dirt and other debris. Therefore, the emphasis of spore reduction should be on preventing their accumulation in the first place. When possible, cages should be constructed of impermeable materials that can be easily washed down with soap and hot water. This loosens the spores and allows them to be washed away. Hair, dander and other litter should be swept or vacuumed up as often as possible between washings.

The second important step in ringworm control is to reduce spore shedding by infected animals. This can be done by decreasing the total numbers of cats in the environment (which also reduces stress and hastens recovery), decreasing the numbers of cats less than 4 years of age, decreasing the numbers of kittens, and taking special precautions on reintroducing ringworm into a cattery.

Ultimately, cattery owners must realize that ringworm is enzootic in most environments where large numbers of cats (especially young cats) are kept. However, whether or not the organism causes clinical disease following infection is often more a function of environment and genetics than the disease-causing potential of the organism itself. Cattery owners are often quick to blame outside cats for bringing in the infection, when in truth it is often present continuously in the cattery in a fairly innocuous state. Sudden or gradual changes in the cattery may allow this innocuous infection to increase in severity and eventually become clinically apparent. Catteries with relatively few breeding animals, especially if they are older, have far fewer disease problems with ringworm than catteries with many younger breeding cats. Younger breeding cats may serve as a reservoir for the organism, their kittens being infected at a young age. These infected kittens shed far more spores than their parents and become amplifiers for the organism. New litters that are born shortly thereafter are then exposed to far more fungal spores than the initial litters and as a result of increased exposure they develop even more severe clinical signs. Each subsequent litter further amplifies the infection for those that follow. Segregating litters, maintaining the best sanitation possible, and limiting the number of breeding animals all help to break this amplification process.

The clinical severity of ringworm in a cattery is enhanced by factors that lower young animals' resistance. Upper respiratory and enteric infections, ear mite and flea infestations, genetic predisposition (as seen in the Persian breed), nutritional status, unfavorable temperature and humidity, and overall stress levels associated with overcrowding all contribute to more severe disease. Ultimately, it may not be possible to rid an environment entirely of ringworm. However, it is definitely possible to create an environment in which disease is inapparent or mild and self-limiting.

Vaccines for dermatophyte infections have been widely touted during the last decade and are seeing more and more use. There is no experimental evidence that such

vaccines positively affect the course of ringworm in a cattery. Several vaccinated cats have even developed more severe forms of ringworm. Like many infectious diseases of cats, there is an overreliance on vaccination to cure the problem. This is understandable because vaccination is infinitely easier than the alternative of environmental control.

Infection and Immunity

Dermatophytes are superficial parasites of the keratin layer of skin and hair. They do not invade deeply and are slow to elicit host immunity. Moreover, their location away from living tissues makes it difficult for the host to bring blood-borne immunity into contact with the organism. Nevertheless, some type of immunity develops following infection.

Immunity to dermatophyte infection is not complete when clinical lesions disappear. Infected hair follicles remain for many months, and perhaps years, in some individuals. The numbers of infected hairs are far fewer in "recovered" cats than in animals with active lesions, however. The proportion of infected cats that remain carriers decreases with time. By 4 years of age, hardly any of the cats that were infected as kittens remain carriers.[23] This slow decrease in the carrier rate indicates that total immunity can take many months or years to develop, or that repeated reexposures over a long period of time may be required for complete immunization.

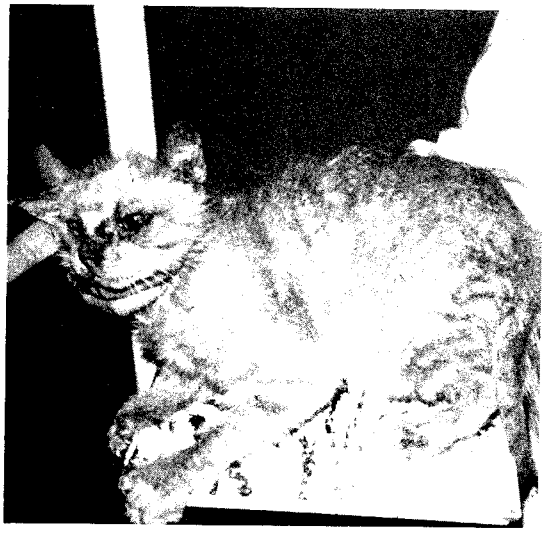
Recurrent infections are seen in both human and feline dermatomycosis. Recurrent disease, unless associated with some immunosuppressive condition, is generally much milder, more localized and more transient than primary disease. Only 1 in 7 recovered kittens is totally resistant to reinfection when exposed 3 months later. Lesions in reinfected kittens also were relatively small, did not tend to spread to secondary sites, and did not last as long as primary lesions.[41]

These findings suggest that immunity to ringworm can be very tenuous in the early stages.

Corticosteroid treatment in the first 1-4 months following recovery may lead to a severe recurrence of disease (Fig 27). Corticosteroid therapy after this time is less apt to cause recurrence. This suggests that a substantial proportion of ultimate ringworm immunity develops in the first few months following infection. Reactivation of disease is particularly severe when long-acting corticosteroids, such as methylprednisolone, are used. Similar to corticosteroids, chronic stress can greatly delay natural recovery from both the initial clinical stage of disease and the subsequent carrier state. It can lead to a higher incidence of clinically apparent infections, more severe disease signs, greater proportion of carriers after recovery, and a longer carrier period. Congenital or acquired diseases can also have a similar effect.

Genetic factors also play a role in ringworm of cats. Individual cats of the Persian breed are especially prone to clinical disease following infection with ringworm spores. Lesions in some Persians tend to be more widespread and to resolve more slowly with or without therapy. Persians are also much more prone to develop more deeply seated lesions (mycetomas) than other breeds.[4,33,46] This predisposition extends even to dermatophytes other than *M canis*.[2] The nature of this increased susceptibility is unknown.

Figure 27. This 8-month-old cat had dermatomycosis (*Microsporum canis*) at 3-4 months of age. The cat was apparently fully recovered until it received an IM injection of repository methylprednisolone at 10 mg/kg. Dermatomycosis reappeared on the face within 2 weeks, and spread rapidly to the remainder of the body. Note the poor haircoat, extensive hair loss on the head, and low-grade conjunctivitis.



Animal and Public Health Considerations

Microsporum canis is the most important cause of ringworm (tinea) in people, and cats are the major reservoir.[10,12,16,18,26,29,32,35,37,43] Cat-to-people transmission of ringworm due to *Trichophyton* is uncommon.[42] Kittens, with or without clinical lesions, are the most common reservoir for *M canis* infection of people, and children are much more commonly affected than adults.[24,26,29,35] The highest infection rate is among children 10 years of age or younger. The incidence declines rapidly in children over 11 years of age. Most adults are resistant to infection or, if infected, lesions are often small, localized and transient. Infected children are not very infectious to other children. The disease course in people, though not as severe as in cats, is surprisingly similar. Lesions in people tend to concentrate on the scalp, forearm, trunk and neck. Recurrent infections throughout life occur in some individuals, while others resist all subsequent exposures. Like cats, some people develop a strong immunity, while in others the it is short-lived and/or tenuous. Secondary infections, similar to those of cats, are more localized, mild and transient than primary infections.

To limit spread of infection from cats with clinical lesions to susceptible people, infected animals should be clipped as close as possible to remove all infected hairs. They should then be dipped periodically over a 2- to 4-week period in some topical antifungal solution to destroy as many remaining surface spores as possible. Infected cats should be handled mainly by adults or older children, who are usually immune or more resistant.

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Coccidiosis

Cause

Coccidiosis is a term used to describe intestinal infections caused by a number of different coccidia. Species of coccidia infecting cats belong to the genera *Isospora, Hammondia, Besnoitia* and *Sarcocystis.*[10] However, classification of these organisms changes rapidly. It has been proposed that *Isospora* species, such as *I felis*, be classified in a new genus called *Cystispora.*[8] Changes in names and classification can be expected as more is learned about individual coccidia.

Various species of intestinal coccidia are found in cats throughout the world. In a survey of cats in the general population in Illinois, Kansas, Missouri, Ohio and Hawaii, 0-1.5% were infected with coccidia that appeared similar to *Toxoplasma* or *Hammondia*, 6-22% with *I felis*, 3-22% with *I rivolta* and 0-0.8% with *Sarcocystis.*[2] However, the precise genera and species of coccidia found within specific groups of cats varies greatly according to their environment and feeding habits. *Isospora* species are the sole or predominant coccidia found within confined cattery cats fed entirely commercial food or cooked meat. *Besnoitia, Hammondia* and *Sarcocystis* are found only in cats allowed to prey on wildlife or that are fed raw or undercooked meat. These differences are due to the life cycles of the various coccidia; only *Isospora* can be spread efficiently from cat to cat (see below). The infection rate of *Isospora* within closely confined groups of cats is also increased because of poor sanitation, overcrowding and stress. Subclinical infection with *I felis* was observed in 49 of 58 cats in a single colony.[15]

Cats are infected with *Isospora* by ingesting sporulated oocysts (shed by other cats) or by eating tissues of prey animals that contain encysted forms of the organism.[2,4,6,9] When oocysts are the source of infection, organisms appear in the feces 12-48 hours later.[4] Infectious forms released from the cysts or oocysts infect intestinal mucosal cells, which later shed unsporulated oocysts. Oocysts sporulate in the environment within a day or less under optimum conditions. Mammalian intermediate hosts

are infected upon ingestion of sporulated oocysts.

Besnoitia and *Hammondia* differ from *Isospora* in their absolute requirement for a nonfeline intermediate host (rodents).[2,6,13,14] Cats can only be infected by eating encysted forms of the organism and not by ingestion of sporulated oocysts. Coccidial replication occurs in the cat following ingestion of infected prey. Unsporulated oocysts appear in the feces 5-9 days after ingestion of cysts and are shed for 1-2 weeks or longer.

Like *Besnoitia* and *Hammondia, Sarcocystis* requires nonfeline intermediate hosts for development (rodents, small and large ruminants).[2,12] Unlike other coccidia, shedding of *Sarcocystis* oocysts is very prolonged, lasting 60 days or longer.[11,12] Infection of intermediate hosts can be particularly widespread and severe.

Pathogenesis

Coccidiosis is probably one of the least understood yet most commonly diagnosed intestinal infections of dogs and cats. Diarrhea is common in cats, and coccidia are commonly found in the stool at the same time, especially in kittens. However, shedding of coccidia is usually totally unrelated to the presenting clinical syndrome.

Clinical coccidiosis has only been observed in very young animals infected with relatively large numbers of cysts.[4] *Isospora* is the only coccidian (in this group) that is also infectious for cats in the oocyst form. Severe coccidial enteritis has been experimentally induced in newborn kittens and immunosuppressed animals.[4,10]

Clinical Features

Experimentally induced coccidiosis in weanling kittens is inapparent or relatively mild.[10] Clinical signs in natural infections consist mainly of diarrhea that lasts for several days. In severely affected animals, the stool is mucus laden and may contain some blood.[15] Rarely, intestinal infection is widespread and severe, and hemorrhagic diarrhea may develop. *In-utero* transmission from the queen to fetus has not been observed with coccidia.[3]

Clinicopathologic Features

Coccidiosis should not be automatically diagnosed in every cat that has diarrhea and organisms in the feces. This is especially true if it is a young purebred cat from a cattery, or young animals from other multiple cat environments (pounds, shelters, pet stores). Every attempt should be made to rule out other causes of diarrhea before diagnosing the condition as coccidiosis.

Coccidia are easily detected in fecal flotations. Some coccidia are of characteristic size or morphology and easily identified.[2] Others are difficult to distinguish from each other and can only be identified by experts or from animal inoculation studies. Coccidia are 10 μ (*H hammondi*) to 35-40 μ (*I felis, H pardalis*) long (Fig 28). Smaller forms of *Besnoitia* and *Hammondia* may be particularly hard to differentiate from oocysts of *Toxoplasma gondii* (Fig 29). Oocysts of *Sarcocystis* are also small like those of *Toxoplasma* (Fig 30).

Treatment and Prevention

The usual treatment for coccidiosis in cats is sulfadiazine, sulfadimidine or sul-

Figure 28. Smear from fecal flotation from a cat infected with *Ancylostoma tubaeformes, Isospora felis* and *Hammondia*-like coccidia. The embryonated ova of *A tubaeformes* (A) are easily distinguished from the smaller oocysts of *I felis* (B). The *Hammondia*-like oocysts (C) are less than half the size (10 μ) of *I felis* oocysts (30-40 μ). (Courtesy of College of Veterinary Medicine, Texas A&M University)

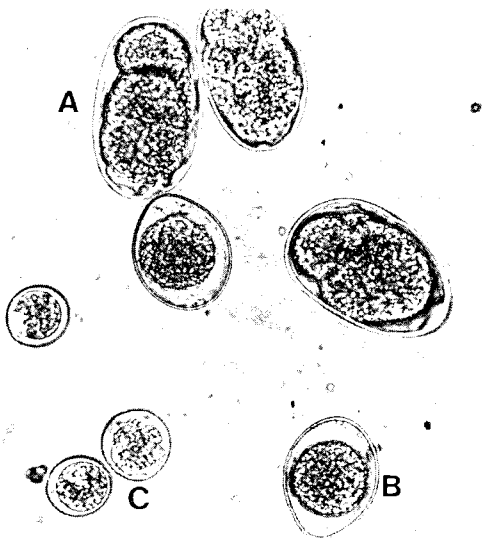
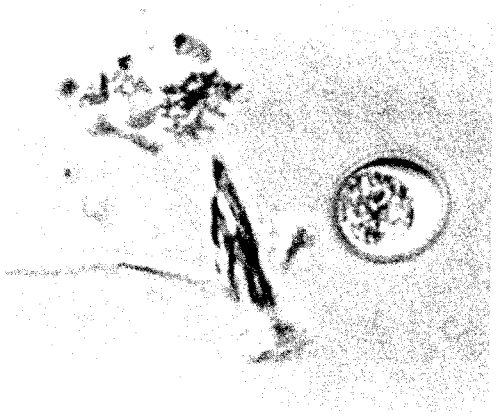


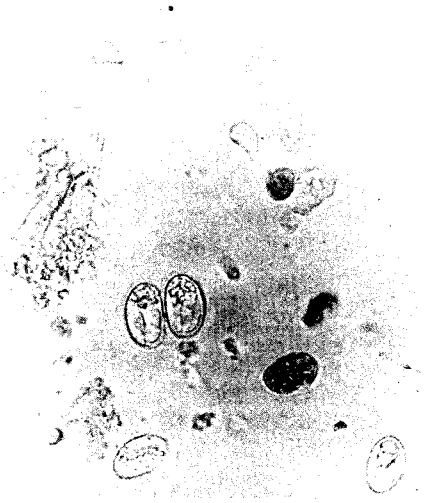
Figure 29. Unsporulated oocyst of *Toxoplasma gondii*. The oocyst is 10-12 μ in diameter and virtually impossible to distinguish from oocysts of *Hammondia* and *Besnoitia*. (Courtesy of Drs. Jerry Theis and Norman Baker, University of California, Davis)



fadimethoxine orally at a dosage of 50 mg/kg daily or divided twice daily for 14 days.[15] Nitrofurazone at 15 mg/kg daily is an alternative treatment. All drugs that show activity against coccidia are coccidiastatic and not coccidiacidal.

Total elimination of coccidia from a closed cattery by improved hygiene and sulfa treatment has been reported by Wilkinson.[15] However, dramatic or long-term successes with such approaches are uncommon.

Figure 30. Oocysts of *Sarcocystis* in cat feces. *Sarcocystis* oocysts are 10-15 μ in diameter and easily distinguished from the oocysts of other coccidia. (Courtesy of Dr. Norman Baker, University of California, Davis)



Infection and Immunity

Immunity to coccidia is the same as described for toxoplasmosis. Immunity appears species specific. Cats infected sequentially with *T gondii, I felis, I rivolta* and *H hammondi* shed oocysts of the respective organism within 11 days postinoculation.[3] Immunity to the intestinal stages is usually acquired within about 2 weeks. Immunity appears tenuous or short-lived because reinfections are common.[2] This differs from toxoplasmal immunity, which is usually more stable.[1]

Sarcocystis appears to elicit little or no immunity in carnivore hosts, which can be infected repeatedly.[12] Immunity to *Besnoitia* spp appears similar.

Animal and Public Health Considerations

Only cats that shed *Isospora* are infectious to other cats. Oocysts of *Hammondia, Besnoitia* and *Sarcocystis* are only infectious for the appropriate intermediate hosts; cats are infected by eating tissues containing encysted organisms. Feline species of these coccidia are not pathogenic to people.[12]

Cats may play an important role in the pathogenesis of *Sarcocystis* infections of livestock.[11,12] Cats frequently defecate in barn litter and feed bunkers, and contaminate livestock forage with oocysts. A small number of *Sarcocystis* oocysts can cause severe systemic disease in calves. Systemic disease in cattle resembles systemic toxoplasmosis to some extent. Disease in older cattle is often less fulminating and frequently goes unnoticed except for the presence of numerous cysts at slaughter.

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Toxoplasmosis

Toxoplasmosis is important to cats and cat owners for 4 reasons: it is one of the most important zoonotic diseases of people; the human disease affects mainly the unborn and newborn child, which impacts strongly on women (the main owners of cats) and human emotions; cats are the sole definitive host for the causative agent and are one source of human infection; and occasional cats suffer from clinical toxoplasmosis. However, the infection is virtually nonexistent in closed cat populations that are not allowed to hunt, or that are not fed raw or undercooked meat.

Cause

Toxoplasma gondii is a complex intracellular parasite. It occurs throughout the world and is responsible for clinical illness in a wide range of animals, both domestic and wild.

Toxoplasma gondii is unique among coccidian parasites of cats and other animals. Though many different animals can serve as intermediate hosts, the entire life cycle can be completed within cats. In this regard, it resembles *Cryptosporidium* and *Isospora*.

Pathogenesis

Cats are the only recognized definitive hosts for *T gondii*. However, literally thousands of species of fish, amphibians, birds and mammals may serve as intermediate hosts. Clinical disease can occur in either definitive or intermediate hosts, making *T gondii* one of the most important pathogenic coccidian parasites of people and animals.

The incidence of toxoplasmal infection in cats varies greatly from country to country and from one subpopulation to another, depending on the incidence of the infection in wildlife and the importance of raw meat (wild-caught or domestic) in their diet. Morbidity also varies with age. Antibodies were found in up to 10% of kittens younger than 10 weeks of age, 16.2% of 11- to 26-week-old domiciled kittens, 37.5% of adult house cats, and 57.9% of adult stray cats.[4] In Washington, the incidence of toxoplasmal antibodies was 31% in cats from animal pounds.[23] Morbidity was higher in house cats that owners relinquished than in strays. Incidences of this magnitude are common among domestic cats throughout the world.

The primary sources of infection for cats are probably small birds, rodents and reptiles containing encysted forms of the organism. Cats can also be infected by ingesting sporulated oocysts shed by other cats. However, a significantly lower percentage of cats will shed oocysts after having been infected with oocysts rather than cysts.

The life cycle of *T gondii* in the definitive host is complex. It usually begins when cats ingest freshly killed prey, or raw or undercooked meat containing encysted forms of the organism. Cats can also be infected with oocysts shed in the feces of other cats. However, this means of transmission is not nearly as efficient.

Encysted forms of *T gondii* are found in highest concentration in the muscle of intermediate hosts. Cysts remain relatively inactive in the muscles until the muscle is ingested by a carnivore or omnivore. Proteolytic enzymes within the digestive tract

of the carnivore or omnivore break down the cyst wall and release the enclosed bradyzoites. Bradyzoites transform into tachyzoites, which infect the intestinal epithelium. Some tachyzoites undergo sexual division intestinal cells and become fertile oocysts. Others spread throughout the body, divide asexually and ultimately become cysts.

Oocysts are passed in the feces at up to 10,000 per day during initial infection. Oocysts generally appear in the feces after 3-10 days when cysts are ingested, or after 20 days or longer when oocysts are the source of infection.

Cats usually shed oocysts for 5-14 days after primary infection. Oocysts passed in the feces of cats are unsporulated. In this form, oocysts of *T gondii* are very difficult to differentiate from those of *Hammondia* and *Besnoitia* (see Figs 28-30). Oocysts are relatively resistant and can survive in soil, especially if warm and moist, for at least 1 year.

Intermediate hosts (usually omnivores or herbivores) are infected by ingestion of sporulated oocysts. Cysts form in the diaphragm, brain, lungs, abdominal muscles and heart. They are found less frequently in the stomach, small and large intestines, mesenteric lymph nodes, spleen and gallbladder.[22] It must be remembered that people, being omnivorous, can be infected either by eating cysts or by ingesting oocysts. Therefore, cats are not the sole source of human toxoplasmosis. Further, because people did not evolve as a natural prey species of cats, they are a "dead-end host" for toxoplasmosis.

Clinical Features

Clinical signs related to *Toxoplasma* infection are infrequently observed in cats. When disease occurs, it is associated with 4 distinct phases of infection: intestinal disease related to intraepithelial replication during primary infection; systemic disease resulting from extraintestinal replication of the organism during primary infection; secondary disease associated with reactivation of encysted organisms; and neonatal disease associated with maternal transmission either in utero or at parturition.

Clinical signs related to primary intestinal replication are uncommon in cats. Though intestinal signs can be experimentally induced in kittens, naturally occurring cases of *Toxoplasma* enteritis have not been recognized.

Signs of systemic toxoplasmosis occurring during or shortly after primary infection are uncommon. The severity of this form of disease is proportional to the extent of extraintestinal proliferation of organisms after initial infection. This is age related. Cysts can be recovered from only about 10% of cats infected after 8 weeks of age but can be isolated from most kittens infected before this time.[10] Of 12 cats with acute toxoplasmosis, most had negative *Toxoplasma* antibody titers.[28] The ages of these cats ranged from 3 months to 15 years, and the most common presenting signs were anorexia, lethargy, fever and dyspnea. Cats with dyspnea had harsh bronchial lung sounds, tachypnea and deep abdominal breathing, but only a mild or inapparent cough. Two cats had signs similar to those of feline panleukopenia, that is, fever, vomiting or diarrhea, anorexia, abdominal pain on palpation, and enlarged mesenteric lymph nodes. Of the 12 cats, 2 had uveitis along with other signs, and 2 were obviously jaundiced. One cat aborted during the course of illness. The clinical course in these cats was 3-19 days (usually 3-8 days) and the disease was fatal in all 12 animals.

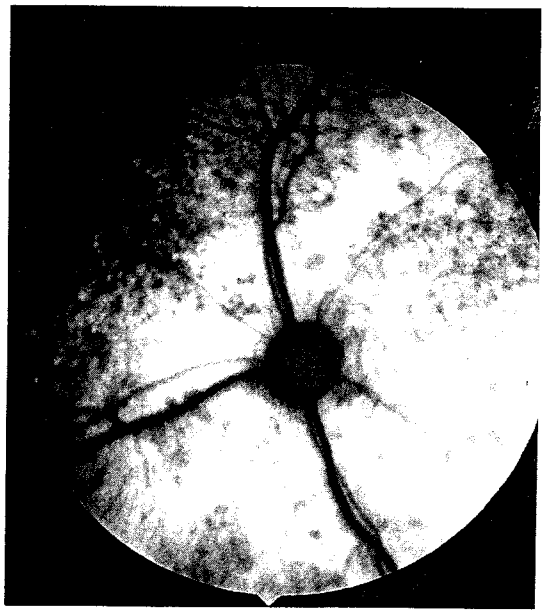
Secondary toxoplasmosis, resulting from reactivation of encysted organisms, is probably the most common clinical form of the disease in cats. Evidence that this type of disease is caused by reactivation of latent organisms rather than primary extraintestinal infections is circumstantial and includes the following: the disease course is more apt to be chronic; toxoplasmal antibody titers are often high when animals are seen; it often occurs in conjunction with other debilitating or immunosuppressive diseases; both encysted and actively replicating forms of the organisms are often seen within the same animal; and many asymptomatic cats have subclinical foci of chronic inflammation associated with cysts in the brain.[8]

The secondary form of toxoplasmosis, referred to as chronic toxoplasmosis, has been reported on numerous occasions.[1,2,20,21,26,28,29,31] This form of toxoplasmosis is often associated with fever, abortion, vomiting, diarrhea, anterior and/or posterior uveitis

(Fig 31), anemia, myocardial disease, CNS signs, lymphadenopathy and respiratory signs of varying durations and intervals (weeks, months and sometimes years). Feline leukemia virus and feline immunodeficiency virus infections may predispose cats to secondary toxoplasmosis by their immunosuppressive effects.

Neonatal toxoplasmosis has been observed on several occasions, but whether the disease is transmitted *in utero* or shortly after birth has not been determined. Fetal infection is common in animals or people in which active intestinal replication of the organism occurs during gestation. In dogs, this can lead to abortion or progressive central nervous system (CNS) and muscle disease manifested shortly after birth.[17] Human infants, depending on the stage of gestation in which they are infected and the dose of organisms, are born: healthy with protective immunity; with severe disease manifested at birth by ocular and CNS abnormalities; healthy but with disease signs developing during the first few weeks of life; or healthy but with low-grade chronic disease that can lead to disease signs as late as the third or fourth decade.[24] More severely affected fetuses are stillborn or aborted.

Figure 31. Chorioretinitis in a cat with systemic toxoplasmosis. (Courtesy of Dr. Ned Buyukmihci, Univ California, Davis)



Queens appear much more resistant to maternal transmission than bitches or human mothers. Queens exposed to *T gondii* during weeks 1-7 of gestation did not have any infected fetuses or newborn kittens.[9] However, 3 kittens born to these queens developed neonatal toxoplasmosis. The route of transmission in this instance was not determined but was postulated to involve transfer from mother to kitten in the milk. Milk-borne transmission of toxoplasmosis is also a serious problem in dairy goat kids. *In-utero* transmission of toxoplasmosis by queens was suggested by an outbreak.[11] Of 7 littermate kittens, 3 developed toxoplasmosis and died at 16-32 days of age with dyspnea, mucopurulent nasal and ocular discharges, and progressive neurologic disease. Pneumonitis, hepatitis, myocarditis, retinitis and encephalitis were evident on microscopic examination of tissue. The presence of encysted organisms in the brain indicated that primary infection occurred before birth. Cell cultures from fetal kittens have occasionally contained *Toxoplasma*, again suggesting that toxoplasmosis can occur as an *in-utero* infection in cats.

Most cases of maternally transmitted toxoplasmosis manifest themselves before weaning. The most common sign of toxoplasmosis in kittens up to 3 weeks of age was sudden death or rapidly developing "sickness."[27] Fever, depression, body tremors, dyspnea, paralysis and diarrhea were more apt to be seen in kittens between 5 and 8 weeks of age.

Pathologic Features

Lesions of active toxoplasmosis are widespread in the body but tend to be most concentrated in the lungs, followed by the liver and CNS.[19,26-28] Involvement of the alimentary tract is less frequent.

Gross lesions are most noticeable in the lungs. Lung lesions consist of edema and diffuse or focal firmness and reddening. Diffuse white and yellow foci are scattered throughout the parenchyma. Subpleural hemorrhages are sometimes seen, along with small amounts of free reddish pleural fluid or blood. The liver is often pale and mottled yellow-brown, or may contain small whitish foci. When involved, the pancreas is edematous and bordered by necrotic fat containing whitish or yellowish foci. Mesen-

teric lymph nodes are occasionally enlarged and edematous. Focal thickening of bowel walls has also been observed in some cats with predominantly GI disease. Likewise, the spleen is often enlarged and meatier than normal.

Clinicopathologic Features

Toxoplasmosis should be suspected in younger cats dying of vague illnesses and in animals with disease involving the lungs, CNS or eyes. Toxoplasmosis should also be considered in cats with acute GI disease, especially if associated with mesenteric lymphadenopathy, pneumonia and hepatitis.

Toxoplasmosis is often suspected before death but almost always diagnosed postmortem necropsy. Cats with acute primary toxoplasmosis may have had insufficient time to produce serum antibodies; antibody titers in cats with chronic or reactivated toxoplasmosis are often high. Cats with primary toxoplasmosis are often shedding oocysts when presented, while cats with recurrent disease are often nonshedders. Further, *T gondii* oocysts are not significantly different in appearance from those of *Hammondia* or *Besnoitia*. Accurate identification by inexperienced investigators is difficult. Definitive identification of oocysts is by mouse inoculation, after allowing time for oocyst sporulation. Oocysts may not be present in the feces of cats with chronic or maternally transmitted toxoplasmosis.

Serum antibodies appear within 7 days after primary infection.[32] These antibodies can be measured by the Sabin-Feldman dye exclusion test, indirect fluorescent antibody (IFA) procedure, indirect hemagglutination test, complement-fixation or enzyme-linked immunosorbent assay (ELISA). The Sabin-Feldman dye exclusion test is considered the most reliable in all species, including cats, though the IFA test is the most widely used and an acceptable alternative. Antibody levels rise rapidly during the course of disease and reach levels somewhat proportional to the severity of extraintestinal replication and cyst formation.

A single antibody titer, regardless of magnitude, is of very little diagnostic value. As many as 60% of normal adult cats have positive antibody titers, some being very high. Therefore, it is important to use serologic test results wisely in making a diagnosis. A 4-fold rise in the IgG antibody titer over a 2-week period has been used by some clinicians to diagnose toxoplasmosis. Measurement of specific IgM antibodies may be an accurate way to diagnose the disease; only active infections induce such antibodies. While this is acceptable in cats with active primary infections, it may not be diagnostic in cats with chronic or reactivated disease.

The radiographic appearance of lung lesions of toxoplasmosis may be quite specific.[1] Radiographic changes mirror the focal alveolar nature of the infection. Ill-defined, coalescent, patchy densities appear throughout the lung parenchyma. Densities tend to adjoin bronchi. Air bronchograms become more noticeable as the disease progresses due to consolidation of parenchyma around air-filled bronchi. This reaction may extend down into the alveoli and lead to the appearance of air alveolograms.

Though variable blood and serum abnormalities are seen in cats with toxoplasmosis, none is specific for the disease. White blood cell numbers vary from low to high, the PCV is usually normal, liver enzymes are elevated with hepatic involvement, and urine and serum bilirubin levels are elevated in a few cats. Platelet counts are normal or decreased.

Cats showing signs compatible with toxoplasmosis should be tested for FeLV and FIV infections. About one-half or more of cats with toxoplasmosis may be FeLV or FIV positive. As in people, toxoplasmosis of cats is mainly an opportunistic disease.

Treatment and Prevention

The disease can be prevented by not allowing cats to eat raw and undercooked meat (especially from swine, goats and sheep) or milk, hunt or contact sporulated oocysts shed by other cats. These steps are seldom practical, so the disease cycle is difficult to break. Freezing meat at -20 C, a temperature not always achieved by home freezers, inactivates the organism, as does cooking meat at temperatures above 60 C.

Treatment of naturally occurring toxoplasmosis has had limited success. This may partly be because many cases occur in immunocompromised hosts, in which treatment is not as effective. Further, many cats are treated for toxoplasmosis because they

have compatible signs and positive antibody titers when, in fact, they actually have other illnesses. The oldest treatment is a combination of pyrimethamine and sulfadiazine.[12] Sulfadiazine is given orally at 100 mg/kg divided 3 or 4 times a day. Pyrimethamine is given in conjunction at 1 mg/kg daily. Treatment is continued for 2 weeks. Folinic acid or bakers' yeast is sometimes given to counteract the side effects of pyrimethamine without interfering with treatment. Trimethoprim-sulfa is similar to the above drug combination and has been used to treat some animals. Clindamycin IM at 5 mg/kg 4 times daily has been used to treat dogs with toxoplasmosis and is probably the treatment of choice.[16,25]

Infections and Immunity

After primary infection, oocysts are shed for 4-16 days.[10] Oocyst production apparently ceases as a result of local immune mechanisms at about the same time that systemic immunity is developing and extraintestinal replication is halted. Systemic immunity causes the rapidly dividing tachyzoites to become slowly dividing bradyzoites and to encyst in muscles.[14]

Even during the active shedding stage, oocyst production appears regulated to some extent by various host factors. Male cats appear to shed more oocysts after ingesting infected mice than females, and cats under 12 months of age shed more than older cats.[10] Even though oocyst production ceases with development of local immunity, some organisms remain inactive in the epithelium.

Immunity to reinfection occurs after initial recovery from oocyst shedding. This immunity is somewhat age dependent. About 60% of cats <13 weeks of age when initially infected subsequently shed oocysts when fed infected mice; immunity in cats initially infected after 13 weeks of age is much better.[6,10] Oocysts are more apt to be shed after ingestion of cysts than sporulated oocysts, and oocysts are shed after a longer latent period and for a briefer duration than in primary infection. Immunity to subsequent bouts of extraintestinal replication appears more solid than local immunity to oocyst shedding.

The nature of immunity to toxoplasmosis is not entirely understood. However, the level of serum antibody at challenge bears no relationship to the degree of immunity.[8,10] Toxoplasmosis in people and cats is usually associated with immunosuppressive diseases, particularly those that profoundly affect cellular immunity. Infections with FeLV and FIV underlie one-half or more of the cases of feline toxoplasmosis.

Reactivation of latent organisms in intestinal and extraintestinal sites, resulting in oocyst reshedding and even clinical disease, has been induced in carrier cats by corticosteroid administration.[8] Such immunosuppression can result from a wide range of stressful and debilitating diseases in cats.

Certain manipulations have activated latent organisms in the intestinal tract. If a cat has not been previously infected with *Isospora,* infection with this organism causes transient shedding of *T gondii* oocysts as well.[5] Primary infection with *Isospora* apparently interferes with established local immunity to *T gondii.*

Animal and Public Health Considerations

Cats are much less infectious to other cats than to other species of animals. Cat-to-cat infection occurs exclusively by ingestion of sporulated oocysts, a relatively inefficient mode of infection. Because cats are the definitive host for the organism, they play an important role in transmitting the disease to many types of animals, particularly herbivores. Carnivorous and omnivorous animals are not only infected by ingesting oocysts from cats, but also by ingestion of encysted forms in the muscles of a multitude of intermediate hosts.

Farm cats are a common source of infection for cattle, sheep, goats and swine.[33] Defecation in feed bunkers, barnyard litter and soil can lead to a large accumulation of oocysts. Transmission of toxoplasmosis from cats to other animals may be particularly severe in goat dairies, where cats are an important source of infection. Maternal transmission to newborn goats via milk is an important link in the disease cycle in this species.

People are infected with toxoplasmosis by ingesting sporulated oocysts from cats, raw milk (especially from goats), or uncooked or poorly cooked meat, especially lamb, pork and goat meat. In fact, in North

America and western Europe, where cats are kept more closely confined and fed largely processed foods, consumption of infected meat by people is probably of greater public health importance than contact with cats.[24,30]

The frequency of infection in the human population in the United States varies greatly according to sociologic, economic and environmental factors. Morbidity and seropositivity increase with age. Less than 1% of infants are congenitally infected. The infection rate is low in young children, but rises abruptly in teenagers. Morbidity rises about 1% each year from the ages of 15 to 50.[24]

The most important form of human toxoplasmosis is associated with transplacental transmission. Such infection results from extraintestinal replication of organisms in the mother during pregnancy. About 0.5-1% of women in the US and Europe show rising titers during pregnancy. This indicates active infection, but only about 40% of these infections are transmitted to the fetus.[24] Moreover, only a small proportion of the infected fetuses have significant clinical disease.

Veterinarians are frequently called upon to give advice to pregnant women with cats or to clients contemplating pregnancy. Medical advice to clients should be limited to steps needed to prevent cat-to-person transmission. Prenatal exposure advice is better left to experts on the human disease, and not to general medical practitioners or obstetricians. The last 2 groups often view the disease and the cat in an overly and unduly negative light. Most important, clients can be comforted that cats are only one of many reservoirs for toxoplasmosis, that only a small fraction of infants are ultimately infected, and that even a much smaller percentage of infants are clinically affected.

Human exposure by cats to toxoplasmosis can be minimized by reducing the chances of infection in cats.[13,17,18] This can be done by confining cats to prevent hunting, feeding cats only processed meats, and changing litter boxes daily to prevent sporulation of oocysts. Oocysts must sporulate before becoming infectious, a process that takes several days. Litter should be discarded in a sealed plastic bag (not buried in the garden). People should eat only thoroughly cooked or processed meat, wash hands thoroughly after handling raw meat and uncooked home-raised vegetables, wear gloves when working in yards likely to be contaminated with cat feces, prevent cats from defecating in children's sand boxes, have someone other than the expectant mother change the litter box daily, and avoid raw milk (especially from goats).

Oocyst shedding by cats has been suppressed by feeding cats 0.02% monensin with their dried food.[15] Kittens appear to tolerate the medicated food well. However, use of such treatment to prevent oocyst shedding has not been widely applied in the field. Immunization of cats against toxoplasmal shedding has been attempted.[14]

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Cryptosporidiosis

Cause

Cryptosporidium is a protozoan that is similar to coccidia. Cryptosporidial infections are apparently common and widespread among animals and people throughout the world.[1,5,16]

Infection occurs by ingestion of thick-walled oocysts. Oocyst shedding in the feces in normal immunocompetent hosts begins as early as 5 days after infection and continues for a 2- to 3-week period.[10] Unlike other coccidia, many species of animals act as definitive hosts and cross-infection between species is common.[3,8,9,12-15]

Pathogenesis

Infections are often limited to the ileum but can involve virtually the entire bowel in massive exposures in neonates and immunocompromised individuals. Clinical signs are seen only when a substantial part of the bowel is affected.

Clinical Features

The importance of *Cryptosporidium* in enteric diseases of cats is uncertain. Many cats shed organisms in the feces, kittens more so than adults. However, oocyst shedding is often unrelated to concurrent intestinal disease. Adult cats fed large numbers of *Cryptosporidium* showed no signs of illness.[6]

Severe cryptosporidiosis has been described in an adult cat with chronic diarrhea, anorexia, weight loss and bowel thickening.[13] The disease in this cat was clinically and histopathologically similar to plasmacytic-lymphocytic enteritis, a disease of allergic or pre-lymphomatous origin. Feline immunodeficiency virus (FIV) infection of cats produces a similar intestinal disorder.

Pathologic Features

Most of what is known about cryptosporidiosis has come from experimental transmission studies in lambs or swine.[8,12,14] However, disease in these species is considerably more severe than naturally occurring infections of carnivores, which are usually inapparent.

Clinicopathologic Features

As in coccidiosis, every attempt should be made to eliminate other causes of enteritis before diagnosing cryptosporidiosis in cats with positive fecal examinations. This includes use of hypoallergenic diets to rule out food allergy, which is the most common cause of diarrhea in cats. Older cats with chronic diarrhea and cryptosporidia in their stool should also be tested for FeLV and FIV infections.

The Sheather's sugar flotation method has been used to concentrate oocysts from fecal specimens.[5] Oocysts are very small and difficult to see without phase microscopy or special contrast staining. They resemble miniature coccidia in morphology.

Treatment and Prevention

Standard anticoccidial drugs have no effect on *Cryptosporidium*. In fact, no single treatment has proven uniformly effective. Infection in healthy cats is usually subclinical or mild, and is self-limiting. For this reason, treatment is not generally recommended except in cats with particularly severe infections and there is a high likelihood that cryptosporidia are the cause of the enteritis.

Spiramycin has proven effective in some people with congenital or acquired immunodeficiency and severe cryptosporidiosis.[15] However, spiramycin is not available in the United States, and its efficacy against animal cases of cryptosporidiosis is unknown. Oral clindamycin and quinine have proven less effective in people and are associated with many more side effects.

Oocysts of *Cryptosporidium* are relatively resistant to disinfectants.[2] Cresylic acid (3%), hypochlorite (2-5%), benzalkonium chloride (5%), sodium hydroxide (0.02 M) and isophore (1-4%) failed to inactivate oocysts after 18 hours. However, oocysts are sensitive to ammonia (5-10%) and formaldehyde (10%).

Infection and Immunity

Immunity to *Cryptosporidium* appears within 1-2 weeks in normal individuals but is tenuous and short-lived. The poor post-infection immunity to cryptosporidiosis may be due to the superficial nature of infection in the bowel. Debilitating diseases and excessive stress can lower resistance and further increase the incidence of recurrent infections.

Animals that are debilitated or immunocompromised by other diseases often shed greater numbers of oocysts for a more prolonged period. If the infection is particularly severe and persistent, it can contribute to clinical signs. An FeLV-infected cat had acute signs apparently due to chronic cryptosporidiosis.[7] Another cat appeared to be suffering from concurrent cryptosporidiosis and lymphocytic-plasmacytic enteritis of unknown origin.[11]

Animal and Public Health Considerations

Infected cats are hazards to human and animal health only in that they serve as one of hundreds of different mammalian, avian and human hosts. Cryptosporidiosis as a clinical entity is seen mainly in neonatal ruminants and immunocompromised people. Mild to moderately severe enteritis has been induced in neonatal lambs and there seems little doubt that cryptosporidiosis is an important natural cause of diarrhea in very young calves.[10,12] Cryptosporidiosis in calves is considered an important source of human infection.

Cryptosporidiosis in normal people is characterized by acute diarrhea and abdominal cramps lasting 1-10 days.[4] Clinical signs usually begin within 5 days or sooner after exposure. A severe and potentially fatal form of intestinal cryptosporidiosis has been seen in people with acquired or congenital immunodeficiency syndromes.[4] Opportunistic cryptosporidiosis appears particularly prevalent and severe among people with AIDS.[15]

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Giardiasis

Cause

Giardia species are droplet-shaped protozoan parasites that are found throughout the world. They are found most consistently in the duodenum and jejunum of most species of animals. However, they are more common in the distal jejunum and proximal ileum in cats.[12,13] They do not invade mucosal cell surfaces, and obtain nutrients directly from intestinal contents.

Encysted and non-encysted forms of the organism are passed in the stool. Encysted forms are quite resistant to environmental degradation and can survive for weeks or months under cool and moist conditions. Non-encysted forms die rapidly after being passed in the stool.

Pathogenesis

Surveys in different countries show an infection rate of 1-11% in cats.[11] Younger cats and kittens are more likely to be clinically infected than older cats.[11,15,22] Giardiasis is most prevalent in high-density and closely confined populations. Infection occurs by direct animal-to-animal transmission (fecal-oral) or contamination of drinking water with cyst forms. Fecal-oral transmission is probably the most important route in cats, while water-borne transmission is the most common route in people.[7,9,10] Ingested cysts are partially dissolved by stomach acids and cysts appear in the feces within 5-16 days.[11]

Large numbers of organisms in the small intestine damage underlying epithelial cells. The mechanism of this effect is not understood but may include mechanical interference, elaboration of a yet-unidentified soluble toxin, competition between parasites and epithelial cells for essential nutrients, direct damage of epithelial cells by adherent organisms, changes in the microenvironment favoring bacterial overgrowth, and secondary damage to the epithelium caused by host immunity against the parasites.[1,8,24,25] Intestinal disease caused by *Giardia* is of a malabsorption type.[25]

Clinical Features

Giardial infections of cats are usually subclinical. Clinical signs are most often seen in younger animals from multiple-cat households and catteries. Outbreaks of disease are often associated with introduction of new animals into the environment. The introduced cat develops signs from exposure to the household cats, or is the vehicle for infecting the resident population. In its most severe form, infection is characterized by loose, mucoid and frequently foul-smelling stools, steatorrhea, flatulence, abdominal distension and poor haircoat.[6,9,11,13,15,18,22,23,28]

The course of the disease in untreated individuals varies from less than a week to several months.

Pathologic Features

Pathologic changes are limited to the intestinal tract, mainly the jejunum. Gross anomalies are not seen and histopathologic changes vary from nonexistent to marked.

Clinicopathologic Features

Giardiasis is diagnosed by demonstrating cysts in the stool. However, organisms are often shed sporadically and are not always easy to identify. Direct examination of fresh fecal smears is the simplest procedure. A small amount of feces is diluted with saline, mixed with a drop of Lugol's iodine solution and examined by conventional light microscopy. Cysts can be concentrated from feces by zinc sulfate centrifugal flotation but not with flotation procedures using sugar or other salts. Diagnosis of giardiasis is complicated by the cyclic nature of cyst shed-

ding.[13] Therefore, at least 3 collections must be examined before declaring a fecal sample negative.

Treatment and Prevention

A favorable response to treatment is often the most accurate way to diagnose clinical giardiasis in animals and people. This is because some animals with giardiasis do not have demonstrable numbers of organisms in their stool, while others have demonstrable organisms but suffer from totally unrelated problems. Quinacrine hydrochloride, orally at 1.5 mg/kg 3 times daily for 10 days, is the treatment of choice for people. In cats, a dosage of 11 mg/kg daily for 12 days eliminated clinical signs but not shedding of cysts.[6] Metronidazole orally at 8 mg/kg twice daily for 10 days eliminated both clinical signs and fecal organisms in 2 cats.[18] Similar success was reported in a cat given metronidazole at 25 mg/kg BID for 5 days.[28] Experimental studies in cats showed good results with metronidazole at 10 mg/kg twice daily for 5 days or furazolidone given orally at 4 mg/kg twice daily for 5 days.[13]

Infection and Immunity

Immunity to *Giardia* is probably similar to that of *Cryptosporidium*. Both cellular and humoral immunity appear involved in resistance,[2,21,24,26] as further supported by the high incidence of infection in people with combined or specific IgA immunodeficiencies.[24]

Immunity in mice appears to be highly controlled by genetics.[4,20,21] Under normal circumstances, immunity to infection develops in several weeks. Infection can be greatly prolonged by stress and debilitating diseases. Glucocorticoid treatment has prolonged the course of primary infection and triggered reactivation of low-grade or latent infection in mice.[17]

Shedding of cysts increased more than 100-fold 2 days after an injection of glucocorticoids in 1 cat; other cats given lower daily oral dosages of prednisolone for 5 days did not shed more organisms until after therapy was stopped.[13] Once established, immunity is probably tenuous and short-lived. Therefore, reinfection with episodic shedding of organisms is probably common.

Animal and Public Health Considerations

Though cats apparently carry many strains of *Giardia* that antigenically resemble those found in other species, feline strains are probably more pathogenic for cats than for other animals.[7,27] Therefore, cats are the greatest health hazard to other cats. Human isolates of *Giardia* appear to be minimally infectious or noninfectious for cats.[14] The converse situation has not been studied, so the exact public health significance of infected cats is not known. Only 2 instances of concurrent human and feline giardiasis in the same households have been reported.[7] Until more information is obtained, infected cats should be considered as potential, but probably not important, reservoirs for human giardiasis.

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Toxocariasis (Roundworm Infection)

Ascarids, or roundworms, are the most common helminth parasites of cats. They are one of the few helminths that persist in closed catteries; most other such parasites require several species of vertebrate or invertebrate animals as intermediate hosts and are usually ingested by cats during hunting. Roundworms, such as *Toxocara cati*, can complete their entire life cycle in cats, and though rodent intermediate hosts can be involved, they are not essential.[8] As with many other infectious diseases involving cat-to-cat transmission, ascarid infections are most severe in high-density environments where fecal contamination is high, where conditions are favorable for survival of ascarid eggs, and where many susceptible (young) cats are present.

Cause

Toxocara cati is the principal ascarid that infects cats and is found throughout the world. It is found as an adult in the small intestine of domestic and wild Felidae.[8] Adult male worms are 3-6 cm long, while females are 4-10 cm long. Eggs laid by female worms are shed in the feces in relatively large numbers. Ascarid eggs can survive several months or longer in the environment.

In Iowa, the proportion of infected cats was 0% in newborns, 4.3% in 0.5- to 2-week-old kittens, 5.8% in 2- to 6-week-old kittens, 1.9-2.1% in 0.5- to 4-year-old cats, and 0.8-1.3% in 4- to 15-year-old cats.[5] No infections were seen in cats over 15 years of age. These percentages are considerably lower than those reported in other studies. In Missouri, the rate of infection was 24.4%.[10] Australian studies reported 20.3% infection among urban cats in western Australia, 24.5% infection in Brisbane and 21.9% infection in New South Wales.[6,7,12] In southwest England, 63% of farm cats were infected.[3]

Pathogenesis

Cats are infected when they inadvertently consume ascarid eggs that are shed into the environment by other cats, or by ingestion of encysted larvae in the tissues of rodent prey. Eggs passed in the feces of infected cats contain fully developed second-stage larvae. Following ingestion by other cats, the second-stage larvae are released from the egg and enter the stomach wall, where they remain for 1-2 days. Larvae migrate to the liver in the mesenteric veins, and then enter the bloodstream and are carried to the lungs. They exit the pulmonary vasculature and enter the alveoli, bronchioli and trachea, where they form third-stage larvae. Then they are coughed up and swallowed, and reenter the stomach wall. Following further maturation, they migrate to the lumen of the small intestine, where egg laying occurs. This entire migration can take place in as short a time as 10 days.

Transmission of *T cati* through ingestion of intermediate hosts is important for hunt-

ing cats. Eggs passed by the cat are ingested by rodents, and second-stage infectious larvae are released in the intestinal tract and migrate to various tissues, particularly the liver. Because rodents are not the definitive host, larval development is arrested and encystation occurs. Rodents are referred to as paratenic hosts because no essential developmental stages occur in them. Encysted second-stage larvae can remain alive for months in rodent tissues. When a cat eats the rodent, second-stage larvae are released from the cysts by digestive enzymes and enter the stomach wall, where they develop to third-stage larvae over a 6-day period. They then reenter the stomach, where they become fourth-stage larvae. These make their way to the small intestine, where they become adults. Following ingestion of paratenic hosts, the entire cycle takes about 3 weeks. Larval migration through the liver and lungs does not occur in cats infected with encysted worms.

In addition to being infected by eggs or encysted second-stage larvae, kittens can be infected through nursing. Larval forms may be encysted in the tissues of the queen as a result of an earlier primary infection. For reasons that are not completely understood, pregnancy causes some of the encysted worms to excyst and enter the bloodstream. They then find their way to the mammary glands and are secreted in the milk. Transmammary infection is a continuous phenomenon; larval ascarids are present in the milk throughout lactation, not just in colostrum.[9] Larvae ingested by the kittens while nursing develop in the same manner as larvae acquired by eating infected rodents.

Clinical Features

Clinical signs of *T cati* infections are mainly caused by visceral migration. Pulmonary changes occur over a 2-month period or longer following exposure.[11] Irritation to gastric and intestinal walls, aberrant migrations into such sites as the bile ducts, and mechanical obstruction of the bowel can also cause clinical signs.

Clinical signs associated with *T cati* infections are limited mainly to kittens and to cats in environments in which exposures and worm egg numbers are high. The most prominent feature of severe infections is generalized unthriftiness manifested by delayed growth, a poor haircoat, and a pot-bellied appearance due to generalized muscle thinning caused by malnutrition. Acute colic, peritonitis and death have been associated with intestinal blockage by masses of adult worms. In kittens, this can be associated with perforation of the proximal small intestine. Pulmonary changes due to visceral larval migrans, though severe at times, usually are not clinically apparent.

Pathologic Features

Lesions within the intestinal tract are absent or mild. Reddening of the gastric and small intestinal walls is the predominant gross change. Likewise, changes in the liver are usually not grossly apparent or consist only of subcapsular scarring. Pulmonary changes can be severe in some animals and occur within 2 weeks of infection.[10] Multiple tan lesions 1-2 mm in diameter may be observed throughout the lung parenchyma, particularly on the pleural surfaces. Some foci may be hemorrhagic.

Clinicopathologic Features

Ascarid infections are diagnosed by examination of feces for typical eggs. In kittens with visceral larval migrans, eosinophilia may be pronounced.

Treatment and Prevention

Prevention of environmental egg contamination is an essential part of disease control. To minimize egg accumulation, cattery surfaces should be as impervious as possible to allow for thorough cleaning with soap and water.

Numerous drugs are effective against adult and immature intestinal stages of the worm. The most popular are various piperazine salts. A single oral treatment with piperazine adipate at 200 mg/kg removes both immature and adult forms from the intestine. Dichlorvos is also highly effective but has been associated with severe diarrhea and, occasionally, rectal prolapse in some kittens. Fenbendazole, orally at 10 mg/kg twice daily for 2 days or at 100 mg/kg orally as a single treatment, and pyrantel pamoate at 5 mg/kg orally as a single treatment, are also effective. Fenbendazole may also reduce the number of larvae in tissues of bitches with *T canis*

infections.[2] The efficacy of fenbendazole against tissue stages in cats is unknown. Ivermectin, given once subcutaneously at 200 g/kg, has also eliminated all egg shedding in infected cats.[4] Its effect against the larval stages is unknown, but may be substantial. If this is so, ivermectin may ultimately be the drug of choice.

Infection and Immunity

Immunity to ascarid infection develops over time. The infection rate was 39.9% in 6- to 8-week-old kittens, 41.2% in 5- to 8-month-old kittens, 21.1% in 10- to 15-month-old cats and 4.6% in cats over 2 years of age.[12] This immunity is directed against both tissue-migrating forms and stages confined to the intestinal tract.

Immunity may explain why ascarids are much more common in cats younger than 6 months of age than in older animals. Neutered cats also appear to have about half the ascarid load of intact cats, perhaps because of some hormonal influence on immunity.[10]

Animal and Public Health Considerations

Cats that shed *Toxocara* eggs are the principal reservoir for infection of other cats. However, when cats hunt freely, paratenic hosts (rodents) also constitute an important reservoir.

Visceral larval migrans is a potentially serious disease that occurs mainly in children. *Toxocara canis* is a far more common cause of this disease than *T cati*.[8] Nevertheless, a wide range of roundworms has been incriminated at times with the human syndrome. These include *Toxascaris leonina* and *Toxocara cati*. Visceral larval migrans in children is similar to the somatic infection seen in rodents infected with *T cati*. Larval forms are apt to migrate to the liver, lungs, brain and eyes. Encysted or dying organisms in human tissues provoke an eosinophilic granulomatous response and, if sufficiently severe, clinical signs. Clinical signs include fever, coughing, asthma-like wheezing, malaise, weight loss, hepatomegaly, central nervous system disturbances, and eye disease ranging from retinal granulomas to severe exudative enophthalmitis.[1] Eosinophilia is very pronounced. The ocular lesions can be particularly severe in people and lead to blindness or enucleation because of misdiagnosis as an ocular tumor.

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Stomach Worm Infection

Like other helminth infections of cats, only certain types of stomach worms are a problem for catteries. The troublesome species are those that can complete their entire life cycles within cats. Those that involve other animal hosts in their life cycles are usually only a problem with cats allowed to hunt.

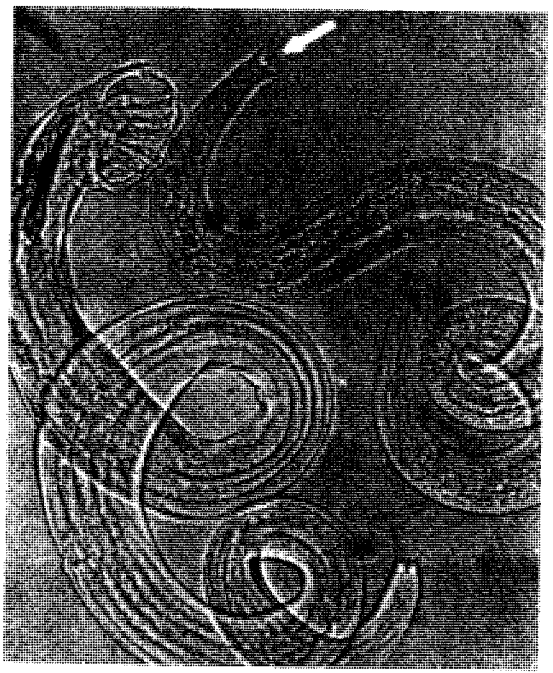
At least 8 nematodes parasitize the stomach of domestic cats. These include the trichostrongyloid worm *Ollulanus tricuspis*, the spiruroid worms *Cyathospirura dasyuridis* and *Cylicospirura felineus,* the physalopterid worms *Physaloptera praeputialis, P felidis, P pseudopraeputialis* and *P canis,* and *Gnathostoma spinigerum*.[17] Only one of these worms, Ollulanus tricuspis, is likely to be a problem among cattery-confined

cats. The others occur sporadically among free-roaming cats that are more likely to prey upon the reservoir species (arthropods, insects, fish, reptiles, amphibians).[17,18] For these reasons, the remainder of the discussion will be concerned with *Ollulanus tricuspis*.

Cause

Ollulanus tricuspis has been recognized in Europe, North America, Australia and Chile.[14] Male worms are 0.7-0.8 mm and females are 0.8-1.0 mm long (Fig 32). In addition to domestic cats, they also infect wild Felidae, foxes and pigs. The incidence of infection has been reported as 6.1% in indoor pet cats and about 40% in free-roaming outdoor cats in Germany, 42.8% in feral cats in Australia, 30% in outdoor cats in Greece, 18.3% in Turkey, and 27% in cats in the United States.[1,4,10,13-16] The overall infection rate is reportedly higher in catteryhoused cats than among individual pet and free-roaming animals.[2,12,16] However, the clinical importance of stomach worm infection in cattery populations has yet to be determined.

Figure 32. Adult male and female *Ollulanus tricuspis*. The male worm (left) has a well-formed bursa, while the female has a tricuspid tail (arrow). (Courtesy of Dr. A. Hargis and *Veterinary Pathology*)



Pathogenesis

Adult worms are found in the stomach, and do not penetrate or firmly attach to the mucosa.[3] In severe infections, worms may also be found in the most proximal part of the duodenum. The female worm is viviparous. Large eggs formed in the single uterus hatch within the reproductive tract and develop through first and second stages before release as third-stage larvae into the gastric lumen. Third- and fourth-stage larvae develop free in the stomach. Sexual differentiation is complete in fourth-stage larvae, which rapidly mature to adults within the stomach. Third- and fourth-stage larvae that pass into the intestinal tract are rapidly destroyed by digestive processes and intact worms are not seen in the feces except when transit time is decreased. However, infectious third- and fourth-stage larvae are present in vomitus. Susceptible animals are apparently infected when they ingest infectious larvae that have been expelled in this manner into the environment.

The exact pathogenic effect of *Ollulanus* infection of cats is debatable. It is probably related to the degree of infection and chronicity. Even with large worm burdens, infection is often asymptomatic. When clinical signs occur, they are usually associated with chronic irritation, inflammation, increased mucus secretion and vomiting associated with the presence of worms adjacent to the mucosa and in gastric glands.

Clinical Features

Infection with *O tricuspis* is widespread and often asymptomatic.[10,12] Periodic vomiting is the most frequent clinical sign.[2,3,5,12,19] Vomiting is first seen within 4 months of infection and correlates within a week or so to detection of worms in gastric contents.[18] Vomiting is usually intermittent, occurring every 1-93 days (mean of 12 days).[19] Vomiting usually occurs 10-15 minutes after eating. A mild intermittent diarrhea has been seen in several cases, though whether the infection was the cause was not determined.[2,9]

A more severe fibrosing or sclerosing gastritis has been associated with *O tricuspis* infection in both wild and domestic Felidae.[7,11,14] Clinical signs include vomiting, chronic weight loss, poor coat condition and, in some instances, death.

Pathologic Features

Gross and microscopic lesions of *O tricuspis* infection have been well documented.[2,7,10,12,14] Gross lesions are seen in less than 5% of infected cats. The gastric wall in such cases appears thickened and the rugal folds much more prominent. Mucosal fibrosis that progresses at times to sclerosis may be evident in severe cases. More mildly affected cats may show some mucosal reddening, with excessive mucus production.

Clinicopathologic Features

Diagnosis of *Ollulanus tricuspis* infection requires a high index of suspicion. Larvae of the parasite are destroyed by digestive enzymes in the intestines and do not usually appear in the feces. An exception is when transit time decreases, such as in diarrhea.[9] Adult female worms are about 1 mm long and have 3 major cusps or projections on their caudal end. Males are slightly smaller and have a caudal bursa. Larvae can be very small and difficult to visualize. Larvae can only be observed in the gastric mucosa, gastric contents or vomitus.[6,14]

Cats are usually induced to vomit 1-2 hours after feeding using xylazine at 2.2 mg/kg IM. If vomiting cannot be induced, a stomach wash is obtained with a large tube. Gastric contents are strained through coarse gauze or a kitchen strainer to remove particulate debris and examined under a dissecting microscope.

Treatment and Prevention

Ollulanus infection has reportedly responded to a single dose of tetramisole at 5 mg/kg orally or dichlorvos at 11 mg/kg.[5,14]

Prevention of *Ollulanus* infection in catteries and closely confined groups of cats can be attempted in enzootic environments. Thorough deworming of all animals, coupled with increased cleanliness and reduced population density, greatly reduces the problem. Special attention should be paid to cats that vomit more frequently than expected; such animals are the main source of environmental contamination with infectious larvae.

Infection and Immunity

Nothing is directly known about immunity to *O tricuspis* infections. However, immunity to *Ollulanus* appears quite minimal. Some groups of cats develop many chronic infections, and average worm burdens are often very large.

Animal and Public Health Considerations

Cats infected with *O tricuspis* are health hazards only to other cats.

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Tapeworm Infection

Tapeworms have ribbon-like bodies and lack an alimentary canal.[9] They are composed of tens to thousands of connected segments. The head segment, or scolex, attaches to the mucosa of the small intestine. The adjacent neck segment serves as the germinative center for subsequent reproductive segments, called proglottids. As new proglottids are formed from the neck segment, older proglottids move caudally. Terminal proglottids break off and are shed in the feces.

Tapeworms are hermaphroditic; each proglottid has both testes and ovaries. Mature proglottids contain from 10 to several thousand elongated eggs. In some cases, all of the eggs are released through the lateral pores of the proglottids during passage down the intestine and intact proglottids are not seen in the feces. In other cases, only part of the eggs are released and eggs appear both free and within motile proglottids in the stool.

Tapeworms can live 2-3 years and reach 50 cm to several meters in length, depending on the species. Though some species of tapeworms have cats as their definitive hosts, only 9 have been commonly described in the literature.[9] Several other species of tapeworms can have cats as aberrant intermediate hosts. The life cycles, geographic distribution and incidence of infection for tapeworms of domestic cats are quite variable.[9]

Dipylidium caninum is the most common tapeworm of cats and dogs found throughout the world. It is one of the few feline tapeworms found more commonly in urban areas than among rural populations.[1,5,7] It is the only tapeworm that occurs among closely confined cattery-reared cats. This is because the cat flea is the intermediate host, and fleas abound within many catteries. The 8 other species of tapeworms are seen only among cats allowed to hunt small reptiles and rodents, which are essential intermediate hosts. For these reasons, the remainder of the discussion will be on *D caninum*. However, the same basic principles apply to all species of tapeworms.

Cause

Adult *Dipylidium caninum* are up to 50 cm long and attach to the wall of the small intestine. The average worm burden in heavily infected cats is 46-256.[5] A dozen or more proglottids, each containing 30 or more eggs, are passed in the feces each day.

Eggs are released during passage of proglottids down the intestine or from desiccated proglottids on the ground. Eggs are ingested by the larvae of several species of fleas (*Ctenocephalides canis, C felis, Pulex irritans*) or lice (*Trichodectes canis*).[9] The infectious form develops within fleas and lice.

Pathogenesis

The infection rate for *Dipylidium caninum* is intimately related to the type of environment. The more fleas, dogs and cats in a closed area, the more likely that tapeworm-infected fleas will be present, and the more infected fleas that will be ingested. One study found one-third of the urban cats in Australia to be infected, while the infection in feral cats in Australia was only 2-11.6%.[1,5,16]

Cats are usually infected with *Dipylidium caninum* when they ingest adult fleas during grooming. Infectious forms are released in the digestive tract, attach themselves to the small intestinal mucosa by their scolex and develop to adults in several weeks. Tapeworms obtain nutrients by diffusion from intestinal contents. They do not usually cause clinical signs in the host. If infection is massive, there may be some competition for nutrients between the host and worms. Irritation and inflammation in the intestinal wall may be seen with heavy infestations.

Clinical Features

Adult tapeworms in the intestinal tract of cats usually do not cause clinical signs. However, diarrhea attributable to tapeworm infection has been described. Owners usually notice motile or desiccated proglottids around the anus of the cat and in the stools, which is aesthetically displeasing. Massive infections may cause cats to be nutritionally deprived and somewhat thin and rough in appearance.[9]

Clinicopathologic Features

Intestinal tapeworm infections are usually diagnosed by grossly visualizing proglottids around the anus or on the feces, or by visualizing microscopic eggs or egg-packets in fecal flotations. Freshly passed *Dipylidium* segments resemble small pumpkin seeds that move slowly in inchworm fashion. However, they rapidly become desiccated and immobile. Dried proglottids look more like small brownish kernels of rice. Tapeworm eggs are also present in the feces, having been released from proglottids during their passage down the digestive tract.

Treatment and Prevention

Prevention of tapeworm infection involves eliminating intermediate hosts from feline habitats or preventing cats from entering environments where intermediate hosts are found. In the case of *Dipylidium caninum*, this involves flea control.

Several drugs are effective against intestinal tapeworms. Perhaps the safest and most effective is praziquantel.[6,8] Oral or subcutaneous dosages of 4.2-12.7 mg/kg given once are safe and effective; 5 mg/kg is the recommended dosage. Alternative drugs commonly used to treat intestinal tapeworm infections include a single treatment of niclosamide orally at 100-150 mg/kg or dichlorophene orally at 0.1-0.2 mg/kg. Mebendazole is also used orally at 100-200 mg twice daily for 5 days.

Infection and Immunity

Cats mount very little immunity to adult tapeworms in the intestine, and worms appear to die within 1-3 years from natural aging.[10] No or only minimal immunity to reinfection develops after natural or drug-induced death of worms.[10] However, it appears that some mechanism prevents massive accumulations of organisms associated with continuous reexposure. Numbers of tapeworms found in intestines of cats remain fairly constant even though animals in certain environments are continuously reexposed to infected intermediate hosts.[5] A similar phenomenon may explain why animals cannot be superinfected. Immunity may vary greatly from one cat to another, similar to strain variations that have been recognized in rodents.[4] Acquired immunity has been recognized in dogs and appears to interfere with development during the parasite's rapid growth stage. It has less effect on the more stable adults.[2]

Animal and Public Health Considerations

Cats infected with *Dipylidium caninum* are not directly infectious for other cats. Eggs shed by cats must first be ingested by appropriate intermediate hosts, in which essential developmental stages occur.

Some tapeworms of cats are infectious to people, including *Dipylidium caninum*, and adult tapeworms are found infrequently in the alimentary tract of people, particularly children.[11] Infection is by eating infected intermediate hosts and not eggs, so the flea rather than the cat is the source of infection.

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Ear Mite Infestation

Cause

Otodectes cynotis commonly infests the external ear canals of dogs, cats, foxes, rac-

coons, ferrets and other carnivores.[5] The mite is found throughout the world and is particularly prevalent among cats kept in cattery-type environments.

Adult mites live mainly in the middle to proximal portion of the external ear canals and inner pinnae, where they feed on epidermal debris and inflammatory exudate. Eggs are laid singly and hatch in 1-3 days.[5] Larval mites molt at least twice during a 5- to 7-day period and become sexually competent young adults. Mating occurs shortly after the second molt. Gravid young female mites molt a third time 2 days after mating and begin to lay eggs 1 day later. Therefore, the period from hatching to egg laying is as short as 9 days. Adult mites live for a month or more and lay 2-3 eggs per day.

Pathogenesis

Ear mite infestations are very common among cats, especially those housed in catteries or cattery-like environments. The extent and severity of infestation within a closely confined group of cats are usually directly proportional to incidence of other common cattery problems, such as flea infestation, ringworm and viral upper respiratory diseases. Stress, environmental contamination and husbandry practices that favor infectious diseases in general also appear to favor large mite accumulations.

The route of transmission from cat to cat has not been precisely determined. Infestation is much more severe when multiple animals are closely confined. This indicates that transmission is direct and by close contact. Mites may then transport themselves from host to host, or from environment to host, and migrate to the external ear canals. Mites feed on inflammatory products stimulated by the mites themselves.[3] Inflammation of feline ear canals, regardless of cause, also causes eventual exhaustion of sebaceous glands, hypersecretions of apocrine glands, and increased secretions of acidic lipids, acid mucopolysaccharides, protein-bound lipids and carbohydrates.[2] Such inflammatory products are probably more desirable for mite nutrition than normal sebaceous-gland secretions (cerumen).

Mite infestations are first noticed in 2- to 6-week-old kittens. Infestation is usually less severe in adult cats than in kittens and adolescent animals. It is also less severe in females than males. The severity of infestations also varies greatly from animal to animal within the same environment. Certain animals have severe infestations, while others have light infestations or are completely free of mites.

Ear mites occasionally cause pruritic miliary lesions distant from the ears. In a study of cats with miliary dermatitis, 4 of 133 had ear mite infestations.[4]

Clinical Features

Cats with ear mite infestations may show no outward signs or may scratch at their ears. Close examination of the proximal part of the external ear canals and inner pinnae often demonstrates darkening and thickening of the epidermis and greatly increased amounts of blackish, flaky or granular sebaceous exudate. Scratch marks and small sores may be seen on the more sparsely haired region in front of the ears and on the inner pinnae. If secondary bacterial infection occurs, the exudate may be purulent and the ear canals are much more inflamed.

Clinicopathologic Features

A presumptive diagnosis of ear mite infestation can be made on the basis of the characteristic appearance of involved tissues of the ear and associated exudate. Ear mites are often seen grossly within the exudate, appearing as small whitish specks that move slowly under bright light and low magnification with a hand lens. Exudate can also be smeared onto a slide and examined microscopically under low power. Eggs and adult, nymphal and larval mites are readily observed in most cases (Fig 33).

Treatment and Prevention

Infested ears should be cleansed of exudates by instilling a few drops of warm mineral oil or ceruminolytic ear drops into each ear canal and gently massaging the base of each ear. This loosens the exudate, which can then be gently removed with cotton swabs. Following exudate removal, the ears are treated daily for 10-14 days with mineral oil, commercial oil-based acaricidal preparations, or a 20% suspension of benzyl benzoate. A short repeat treatment is often done 9-10 days later. Organophosphate-im-

pregnated flea and tick collars are not effective against ear mites.[6]

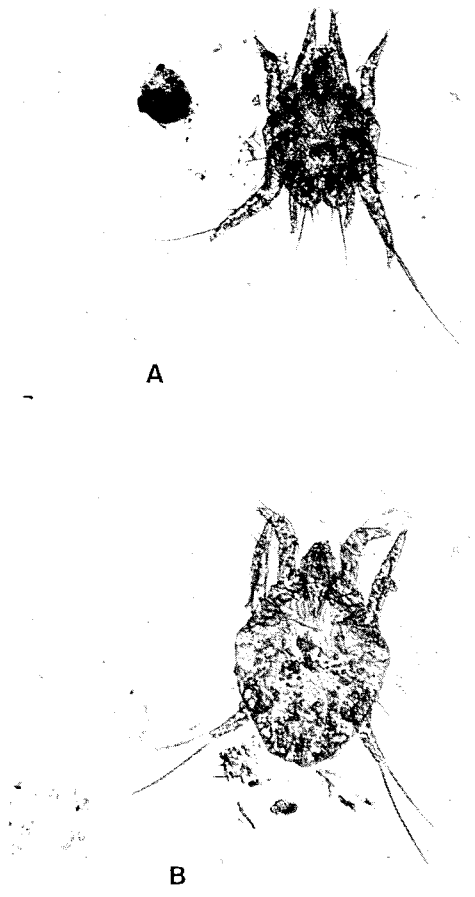
Ivermectin is effective in treatment of ear mites in dogs and cats and is probably the treatment of choice.[1,7] A single subcutaneous dose of ivermectin at 200-1330 μg/kg (400 μg/kg preferred) has been highly effective.

Topical antibacterial medications are sometimes required for ear infestations with a secondary bacterial component.

With repeated use, topical ear medications can elicit hypersensitivity reactions that may mimic the original mite infestation. With ear mite infestations that appear refractory to treatment or recur despite continuous therapy, such reactions should be suspected. If the true cause of the otitis is doubtful, therapy should be discontinued for several weeks. Otitis externa rapidly resolves following discontinuation of treatment if drug hypersensitivity is causing the problem.

Elimination of ear mites from catteries is difficult with topical medications. The mites persist on normal untreated parts of the body and in the environment. Use of ivermectin has facilitated eradication. All cats should be treated as described for individual infestations, with treatment repeated in 2 weeks. The cats are then monitored at monthly intervals and treated again if new mite infestations are detected.

Figure 33. Adult male (A) and female (B) *Otodectes cynotis* in exudate from the ear of a cat. (Courtesy of Dr. Norman Baker, University of California, Davis)



Infection and Immunity

Cats vary greatly in their resistance to ear mite infestations. However, the nature of this resistance is not clearly understood. Ear mite infestations are more common among younger cats and declines as they become older.[3]

Animal and Public Health Considerations

Otodectes cynotis can be transmitted between dogs and cats. However, people cannot become infested.

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Flea Infestation

Cause

Fleas are wingless insects 1.5-4 mm long, with a chitinous covering. Their long strong legs are well adapted to jumping and for

continuous movement between their hosts and the environment.

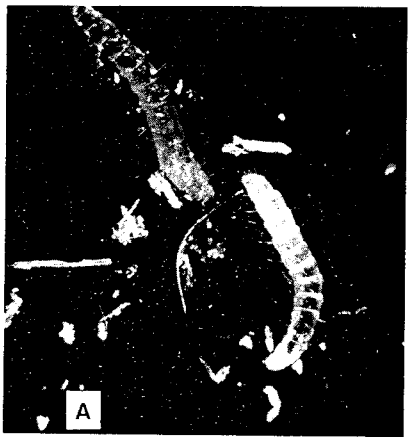
Ctenocephalides felis is the principal flea of cats.[17] Cats may also be infested with the dog flea (*C canis*) and human flea (*Pulex irritans*).

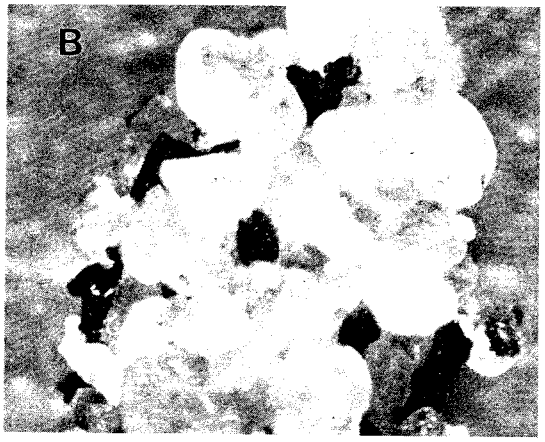
Adult fleas live on the skin of the cat and obtain nutrients by sucking blood. Most of the adult flea's life is spent on the animal.[2] After mating, female fleas lay 400-500 eggs during their lifetime. Eggs are laid in clutches of 20 or more while the females are off the host. After egg laying, fleas return to the cat for feeding until the next egg-laying cycle. Adult fleas live 58 days off the host if fed, and 234 days if unfed.[17] Eggs are usually laid in the dust and dirt in carpeting, bedding or yards. Larvae hatch in 2-16 days, depending on temperature and humidity. Larval fleas are maggot-like and feed on organic matter (Fig 34A). Flea feces, which are rich in nutrients and continually shed from the coat of infested animals, may be a particularly good source of nutrition. Within about 10 days, mature maggots spin a cocoon that quickly becomes camouflaged by dust and debris adhering to its sticky surface (Fig 34B). The pupal stage lasts 10 days to several months, depending on temperature and humidity. Young fleas then emerge and jump onto a cat, where they feed and complete their life cycle (Fig 34C). The remainder of their lives is spent on and off the cat.

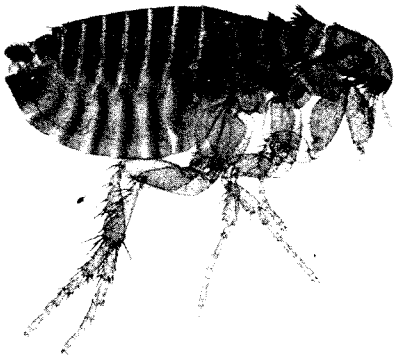
Pathogenesis

Fleas are found throughout the world but are particularly prevalent in warmer and more humid climates. Extremely cold or hot and dry climates limit accumulations of fleas by killing or impeding development of both adult and immature forms. Fleas have adapted for survival and reproduction both within dwellings and in the environment. Seasonality may be less evident when animals are continuously kept in air-conditioned environments. Extremely large flea accumulations can occur when climate, humidity and host numbers are favorable. Therefore, fleas are more apt to be a problem within catteries, multiple-cat households, or urban and suburban environments where climate and humidity are favorable and the feline population is dense.

Figure 34. Various stages in the life cycle of the cat flea, *Ctenocephalides felis*. Maggot-like larvae (A) are found free in the cat's environment. The pupa (B) is very sticky and accumulates a coating of debris, which makes it difficult to distinguish from house dust. The adult (C) is the most likely form to be found on an infested cat. (Courtesy of Dr. Lorry Dunning, University of California, Davis)







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Clinical Signs

Clinical signs associated with flea infestations vary greatly, depending on numbers of fleas and whether the animal becomes hypersensitized (allergic) to flea saliva. Severe anemia and death have been associated with massive flea infestations in kittens. Such infestations are more apt to be seen among confined cat populations. The anemia in such infestations is of the blood-loss type and associated with feeding by adult fleas.

Most healthy cats infested with fleas maintain a small and relatively stable resident population and do not show marked clinical signs. The natural grooming behavior of cats usually keeps numbers of fleas at a minimum, providing that the flea population in the environment is not overwhelming. However, if cats become sick for any reason and stop grooming, flea numbers on the cat can greatly increase. Excessive numbers of feeding fleas can further drain an ill cat of energy and contribute to the overall disease.

Cats that become allergic to flea bites show considerably more clinical signs, the severity of which depends on the degree of hypersensitivity and numbers of feeding fleas. Flea allergies usually develop in cats after 3 years of age.[14] Initial lesions consist of small erythematous papules on the skin at the site of flea bites. These are most prevalent around the tailhead, inner thighs, abdomen, and head and neck. Lesions are usually pruritic. Lesions resemble those described for miliary dermatitis; 55% of cats presented with miliary dermatitis in one study were suffering from flea-bite hypersensitivity.[14] Appearance of the lesion can be greatly altered by self-excoriation and secondary bacterial infection due to chewing, biting and scratching. In severe and chronic infestations on sensitized animals, the involved skin becomes thickened, crusty, scabby, darkened and alopecic (Fig 35). Peripheral lymphadenopathy is common in such animals.[14]

Clinicopathologic Features

Flea infestations are easily diagnosed by close examination of the skin and coat for adult fleas or flea feces. In mild infestations, fleas and flea feces may be hard to visualize. Diagnosis can be facilitated by vigorously rubbing the coat while the animal is standing over a moistened white paper towel. After 20-30 seconds, the paper towel is examined for small black specks, which are flea feces. Within a minute or longer, reddish discoloration emanates from the specks due to dissolution of the blood in the flea feces.

Cats with severe flea allergic dermatitis often have mild to severe eosinophilia that is proportional to the chronicity and severity of the skin lesions.[14]

Intradermal skin testing appears to have more value for diagnosing flea allergies in cats than it does for desensitization.

Treatment and Prevention

Treatment and prevention of flea infestations require patience, persistence and expense. Control of fleas on premises should be directed to 4 areas: controlling flea populations by environmental manipulation; killing adult fleas on all host animals; destroying adult and larval flea populations within the home; and killing adult fleas in surrounding yards.

Figure 35. Back of a cat with severe, chronic flea-bite hypersensitivity dermatitis. The skin is thickened, darkly pigmented, scabby and depilated. Secondary bacterial infection may be manifested as pustules.

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Several studies have dealt with survival of adult and immature fleas in the environment and how environmental factors apply to flea control. Temperature and relative humidity are the 2 most important environmental variables for flea growth and survival. Adults and immature forms survive best in warm, but not exceptionally hot, environments with high relative humidity. Survival of cat fleas at ambient temperatures of 21-32 C (70-89 F) and 80% relative humidity was 90-99%.[5] Adult emergence from pupae was almost totally inhibited when relative humidity fell below 45% and ambient temperatures were greater than 32.2 C (89 F). The lower and upper ambient temperature limits for optimal flea development were 13 C (55 F) and 32 C (89 F), respectively.[16] Relative humidities from 50% to 92% within this temperature range resulted in greater than 80% flea egg hatch, 100% larval development and 90% pupal survival.

Studies on optimum temperature and humidity do not explain flea survival in semi-arid climates. Pupae survived outdoors most of the year in semi-arid southern California, except for July and August, when ambient temperatures often exceeded 35 C (96 F) and relative humidities were low.[15] Pupal survival decreased dramatically at ambient temperatures as low as 27 C (81 F) when relative humidities fell below 33%. At 27 C (81 F), relative humidities of 12% and 33% killed 97% and 100% of pupae, respectively, over a period as short as 16 hours. However, larval survival at warmer ambient temperatures was greatly increased when humidity of the air or microenvironment rose above 50%. Larvae could also survive in the ground at high temperatures and low relative humidity if soil moisture was 1-10%. However, soil moistures from 20% to 50% were deleterious. Exposure to ambient temperatures from -1 C (30 F) to 3 C (37 F) killed all immature stages of the flea within 5-10 days, respectively.

In another study of flea populations in southern California, more fleas were found in living rooms and bedrooms, and in carpeted rooms than in uncarpeted rooms.[12] Fleas were found in the yards of only 8 of 50 infested residences. Flea control should be concentrated in areas where most fleas are found.

Knowledge of the optimum ambient temperatures and relative humidity for flea development can be used in some areas for environmental flea control. For instance, in semi-arid and arid regions, catteries should be kept dry. Yards around the catteries should be planted with vegetation requiring as little irrigation as possible. Lawns should not be planted around the cattery, and swamp water coolers should not be used for air-conditioning. Cats should be kept outdoors in open catteries rather than indoors. Indoor environments are often cooler and more humid because of air conditioning and other factors (running water, washing, cooking, toilets, baths, poor ventilation, respiration).

In cooler regions, the ambient temperature in the cattery should be maintained as low as possible. Cats easily acclimate to ambient temperatures as low as 55 F, which inhibit flea growth. However, flea control by environmental manipulation is virtually impossible if cats are maintained in homes. People usually maintain the home environment at a temperature and humidity that is comfortable to them and ideal for flea development, thus negating any beneficial effect of outside temperature and humidity.

Fleas on animals can usually be killed with appropriate insecticidal powders, sprays or shampoos. Active ingredients within these preparations vary greatly. New insecticides are also continuously being developed and incorporated into flea-control products. Preparation changes are mandated mainly by safety to cats and developing drug resistance of fleas. Drug resistance occurs commonly, necessitating incorporation of new insecticides.

Insecticides are generally active against adult fleas (adulticides) or larvae (larvicides). Adulticides currently used belong to 1 of 4 groups of drugs: carbamates, organophosphates, chlorinated hydrocarbons and botanical compounds.[9] Carbamates are cholinesterase inhibitors, which fortunately are more toxic to fleas than to host animals. The 2 most commonly used carbamates in cats are carbaryl and propoxur. Carbaryl is a common insecticide in garden powders. It has a relatively low toxicity for cats but tends to stain fur, furniture and rugs. Propoxur is popular in many commercial flea preparations and has good residual action.

Organophosphates are also cholinesterase inhibitors. Organophosphates used in cats include dichlorvos (a component of many flea collars), dioxathion, malathion, naled, phosmet, ronnel, temephos and tetrachlorovinphos. Organophosphates tend to be much more toxic to cats than carbamates, even though their mode of action is similar. Though they are used routinely in cats, careful attention must be given to concentration of the compounds used, total amount applied, and amount of residual insecticide on the fur. Toxic signs include vomiting, diarrhea, sweating, dyspnea, miosis and, in severe cases, death. Atropine sulfate at 0.2 mg/kg IM is considered the best of readily available antidotes for organophosphate or carbamate poisoning. Poisoned cats should be thoroughly washed to remove residual insecticide on the fur.

Fenthion (20%) is being increasingly used for flea control in cats. About 0.3 ml is applied to the top of the head, behind the ears, or in the ears. This is repeated every 1-2 weeks initially, then every 4-6 weeks as needed to keep the cats flea free. Use of such a potent organophosphate in cats is questionable. Signs of organophosphate poisoning are subtle at this dosage but nevertheless common. Deaths have been reported in catteries using fenthion in this manner. These may have resulted, however, from incorrect dosage of the drug. Chronic neurotoxicity has been reported in people exposed to fenthion, as well as other potent organophosphates. Dogs may develop a similar syndrome after brief or prolonged use of fenthion. Use of such compounds as fenthion in this manner is reminiscent of the military tactic of directing artillery on your own position when it is being overrun by the enemy. It is a desperation measure that is no replacement for more conservative regimens.

Chlorinated hydrocarbons are selectively more neurotoxic to fleas than to host animals. Many forms of chlorinated hydrocarbons, such as DDT or chlordane, are no longer permitted in many countries because of environmental hazards. Lindane and methoxychlor are 2 chlorinated hydrocarbons that are still used for flea control in cats. Other environmentally acceptable chlorinated hydrocarbons are considered too toxic for animals. Similar to organophosphates, chlorinated hydrocarbons have a lower safety margin for cats than other species. Serious toxicities have even been seen in some cats following use of approved products. Toxic signs include hyperexcitability, inappetence, muscle weakness, tremors, convulsions, paralysis and death. Mildly toxic animals should be treated with diazepam; more severely affected animals should be treated with phenobarbital. The fur should also be thoroughly washed to eliminate drug residues.

Botanical compounds are of plant origin and include rotenone, d-limonene and pyrethrin. D-limonene has not proven nearly as effective as pyrethrins.[14] Synthetic pyrethrin-like compounds include allethrin, d-trans allethrin, fenvalerate, d-phenothrin, resmethrin and tetramethrin. Both natural and synthetic compounds in this class have a high margin of safety. Potency and residual effect of natural pyrethrins can be "potentiated" by addition of piperonyl butoxide. Some synthetic pyrethrins are naturally potentiated.[9]

The effectiveness of many adulticides has been limited by emergence of drug-resistant strains of fleas. This is especially true for carbamates and chlorinated hydrocarbons. Pyrethrins and pyrethrin-like compounds are much less likely to evoke drug resistance. Resistant strains of fleas are usually found in areas where flea populations accumulate all year and use of insecticides is heavy. Due to problems with low drug resistance of and toxicity to cats, natural and synthetic pyrethrins are preferred. Their organic or "natural" composition also makes them much more acceptable to people concerned with environmental accumulation of toxic chemicals. A potentiated or long-acting pyrethrin compound should be applied to infested cats every 3-7 days during the flea season in temperate climates and throughout the year in more tropical areas.

Flea collars impregnated with organophosphate adulticides are very popular with cat owners but are becoming less and less effective as resistant fleas appear. Fresh flea collars can cause mild signs of poisoning when used in kittens. Severe contact allergies of the skin have been occasionally

described; the allergy appears to be due to resins in the plastic.

Adult and larval fleas living in the environment, usually in carpeting, bedding and dusty areas, should also be eliminated with appropriate insecticides. If possible, this should be done by experienced pest exterminators. Nevertheless, various compounds incorporating both adulticides and larvicides are available as over-the-counter preparations for home use. These various preparations are administered as powders, sprays or aerosol "bombs" that can be set off after the house is temporarily vacated of people and animals.

Adulticides used indoors usually kill fleas quickly but have a short residual action. However, the larvicide portion of such preparations usually has a very long residual effect. The most popular larvicide is a synthetic hormone called methoprene.[4] This compound has a residual effect of 75-90 days and prevents pupation of fourth-stage larvae. Methoprene is virtually nontoxic for other living organisms, including adult fleas and flea eggs. Home environments should be retreated with adulticide-larvicide combinations every 75 days during the flea season in seasonal areas and all year in more tropical climates. Methoprene combined with pyrethrins has proven completely effective in controlling fleas within homes.[12]

Fleas in surrounding yards can be killed with chlorpyrifos or diazinon. Both have relatively long residual effects. Diazinon is also available in microencapsulated form. Malathion is also effective against fleas but has a very short residual effect. Yards should be treated 3 times at 10- to 14-day intervals during the height of flea season or all year in more tropical climates.

Flea repellents have emerged again as a popular means to control fleas. Early preparations were not highly effective and quite messy to use. Recently, however, more effective and aesthetically pleasing preparations, such as N,N-diethyl-m-toluamide (Deet), have been developed and sold commercially. Repellents are usually combined with an adulticide. Though relatively safe when used separately, combinations of Deet and fenvalerate can sometimes cause toxicity and death when used heavily on kittens and adult cats.[18]

Contrary to common myths, fleas are not repelled by feeding brewers' yeast or thiamin.[1,7] Likewise, special collars that use ultrasonic sound waves to repel fleas have proven totally ineffective on cats.[6] Use of flea repellents in a good flea-control program in a cattery is questionable. The object of flea control is to lower numbers, not merely redistribute fleas from one animal to another. It is also highly unlikely that any flea repellent will be 100% effective, especially in areas with large flea numbers. Repellents may be most helpful in limiting the numbers of fleas that cats bring into the home from outside.

Persistent treatment of fleas on the animals and in the home and environment can greatly reduce flea problems. In more temperate climates, such methods may effectively eliminate the problem. In more tropical areas, where fleas are rampant and drug resistance is high, control is less successful even when rigorously applied. Moreover, many people are not prepared to spend the time and money required to continuously control fleas in highly enzootic areas. In these areas, it is important to prevent fleas from initially entering the environment. Cat owners moving into flea-free homes and environments should maintain flea control at all times and not wait until infestation occurs. This is especially true in tropical climates where flea problems can sometimes be overwhelming. The importance of designing cattery quarters to prevent flea infestations cannot be overemphasized (see chapter on cattery design and management). Proper cattery design can mean the difference between success and failure in flea control. The problem of flea control in these areas is compounded by cats roaming outside and large flea-infested feral cat populations.

When it is impossible to eliminate fleas from the environment of animals suffering from flea-bite allergies, the skin itself may require direct treatment. This has been approached in 2 ways: treatment of the allergy with drugs, usually glucocorticoids; and desensitization of the animal with injections of flea proteins. Drug treatment usually consists of prednisolone or prednisone at an initial dosage of 2-4 mg/kg daily for 7-14 days, then 2 mg/kg every other day. Once

the condition is under control, the lowest possible dosage of glucocorticoid should be used to maintain remission. Cats are reportedly much easier to desensitize with flea-antigen extracts than dogs.[11,13] However, such optimism has not been borne out by well-controlled hyposensitization trials in cats.[8,14] Therefore, desensitization should still be considered as an experimental approach to control of flea allergic dermatitis in cats.

Infection and Immunity

The absolute number of fleas on any given animal often remains constant; however, flea numbers differ greatly from cat to cat. This implies that some cats are naturally more resistant to fleas than others; the nature of this immunity is not known. Flea numbers on cats increase dramatically when they become ill and stop grooming. Whether fleas are ingested during grooming or inhibited by proteinaceous products in saliva has not been determined.

Factors that cause some animals, and not others, to become sensitized to fleas have not been determined.

Animal and Public Health Considerations

Cat fleas can be a major problem to dogs that live in the same environment. Dogs appear much more susceptible to flea-bite allergies than cats. Therefore, it is common to have households of animals in which the cats serve as reservoirs, while the dogs suffer most with clinical disease. Cat fleas are also the principal intermediate host of the dog and cat tapeworm, *Dipylidium caninum*. Repeated infection with this tapeworm is inevitable as long as fleas exist in the same environment.

Cat fleas attack people when other suitable hosts are not available. Human bites most often occur when a flea-infested house has been left vacated of people and animals for several weeks or more. People returning from a vacation or moving into such a home or apartment may be greeted by a hungry population of fleas. Bites occur around the ankles and lower legs. People can also become sensitized to flea bites, and repeated exposure may elicit large and highly pruritic lesions.

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Chapter 5

Behavior

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As of 1989, 57,500,000 cats were kept as household pets in the United States.[85] The number of cats kept as pets increased by 7,500,000 in the period between 1985 and 1989, and the sale of cat food grew by 50% from 1981 to 1989.[85] Of these cat-owning households, 1 in 4 has more than 1 cat; the usual multi-cat household averages 3 animals.[72] This increased popularity of cats as pets has brought about a greater need to understand normal feline behavior. Unfortunately, the increased amount of cat/human contact, and the tendency to have many cats in the same or immediate environment, have also increased the likelihood that people will be confronted with a behavioral problem.

Behavioral problems of cats are usually manifestations of normal behavioral traits. These normal traits evolved over eons of time, mainly when cats were undomesticated. Cats have been domesticated relatively recently and, unlike more domesticated species, cats have only a thin veneer of domestication that has been superimposed on a stronger core of wild traits.

In the recent past, cats usually lived in a feral or semi-feral state in the wild, on farms, or in and about cities. They lived and reproduced without much direct human contact. Cats often survived and prospered in this state because people and their activities often brought supplies of food, usually in the form of rodents and other pests. Except for a brief period in the Dark Ages, when cats were associated with evil and were destroyed in large numbers, people have appreciated cats for vermin control and for their grace and beauty. Though some early cats were somewhat domesticated by people, they were always allowed to roam more or less freely and infrequently achieved the status of full-fledged family members. People were not concerned, therefore, about whether or not their cats used litter boxes, marked their territory with urine, fought with other cats or were aggressive toward people.

This attitude is rapidly changing as cats have become the most common nonhuman household companions in cities and suburbs. As an intimate member of the family, the cat's behavior is under much closer scrutiny than it has been in the past. Desirable behavioral patterns, such as seeking or expressing affection from people and being fastidious in eliminative behavior, are sought for obvious reasons. Such problem behaviors as urine spraying, inappropriate elimination, scratching furniture, killing songbirds, and fighting with other cats can be extremely disconcerting to cat owners. In fact, inappropriate behavior is the major reason why many cats are destroyed or abandoned by their owners. To solve a behavioral problem and save a cat from euthanasia or abandonment is as meaningful, therefore, as treating a life-threatening health problem surgically or medically.

To understand problem feline behavior, it is necessary to first understand normal behavior. The first section of this chapter covers various aspects of normal feline behavior. Additional information on the nor-

mal behavior of cats is available in a large number of reviews and individual articles.[6,27,31,53,54,67]

The second section discusses the analysis and treatment of common behavioral problems. For a more detailed and broader discussion of behavioral therapeutic techniques, as applied to both cats or dogs, readers may find it useful to consult books on animal behavior.[6,31,82]

The behavior of sick cats is discussed to provide a behavioral perspective on the course and signs of infectious disease. The last section deals briefly with the phenomenon of large multi-cat households.

NORMAL BEHAVIOR

Understanding normal feline behavior is a prerequisite to understanding problem behavior. Most problem behavior of cats is based on normal wild-type behavior. Cats were the most recently domesticated of all common domestic animals (about 2000 BC in Egypt), and their behavior is probably the least genetically altered by selective breeding of all domestic animal species. Therefore, our understanding of the behavior of domestic cats could be much enhanced by information about the cat's wild ancestors, *Felis libyca* and the closely related *F sylvestris*. Unfortunately, there is practically no information about the behavior of *F libyca* in the wild. Many of the current perspectives about normal behavior are based on observations of free-living feral cats, normal household cats, and cats in breeding colonies. As new information is obtained, we can expect some of our perspectives to change.

Social Evolution

There are 3 levels of pets: primary, secondary and tertiary. Primary pets are family members or surrogate children. Primary pets live intimately with their owners and are imbued with many human-like qualities, some deserved and some unrealistic. The owners invest a great deal of emotion, time and expense in the relationship, and the grief is often considerable when a primary pet dies.

Secondary pets round out the family circle, but do not command the same degree of family status. They are fed, protected and given routine medical care (neutering, vaccinations, treatment of simple medical conditions), but are not kept alive or healthy at all possible cost. Grief upon their passing is not as great as for the primary pet.

Tertiary pets are kept for their beauty or mystique, but are totally expendable. They are easily obtained and easily replaced. Their parting is not associated with undue emotion, and most owners are unwilling to expend much time or expense on their medical care. Aquarium fish and small birds are examples of common tertiary pets in many homes.

In the past, cats were considered to be either secondary or tertiary pets by most people, while dogs were the main primary pet. This has rapidly changed over the last 2 decades, and cats now have replaced dogs as the main primary pet in many industrialized countries of the world. In 1989, there were 57,500,00 cats in American homes versus 49,900,000 dogs.[85]

The reasons for the cat's belated rise to primary pet status are numerous and have more to do with changes in the lifestyle of their masters than changes in the makeup of the cat. Our modern society has rapidly changed from a rural to an urban setting. Farm cats, which were largely secondary or tertiary pets, have evolved into the more pampered primary household pet. In environments where single family dwellings predominate, cats are still allowed to roam more or less freely from indoors to outdoors. As apartment houses, tenements and condominiums have replaced the single-family home, cats have moved more and more indoors. Unlike the dog, which tends to be loud, messy and somewhat destructive when left alone, the cat has proven ideal for apartment house, condominium, mobile home and recreation vehicle living. Cats readily adapt to being left alone because they are basically solitary animals by evolution.

Though cats can live in social networks with other cats, they do not have a social nature going back to the pack life, such as dogs. Cats are thus a more ideal pet for a person who must leave a pet alone for much of the day, rather than a dog, who might show anxiety when isolated from people or

other dogs. Cats are also relatively quiet, clean in their personal habits and small, and eat less food. Even if they are allowed to roam free, they usually go about their way unobtrusively at night while people sleep.

The ease by which cats can be trained to use litter boxes, which greatly simplifies waste disposal, also makes them a particularly attractive pet as compared to a dog. Their habit of defecting and urinating in less obvious spots, and burying their wastes, is held in high favor. Dogs in many cities have to be walked on a leash, and their waste picked up and disposed of so it does not contaminate streets and yards. Finally, though cats may not be as sociable to people as are dogs, they are much less likely to show aggressive behavior toward people. Dogs aggressively defend their homes against unfamiliar people, and the problems of rabies exposure and biting are far more frequent and serious with dogs than cats. Aggressive behavior is particularly troublesome as people are forced to live closer and closer together.

Though cats can have a social hierarchy, groups of cats do not have a rigid social structure comparable to the dog pack.[13,50,52] The highest degree of social structure has been observed among farm cats.[54] Female farm cats interacted with each other at close proximity, engaging in mutual licking and displaying a type of social hierarchy that was reinforced by subordinate cats rubbing the perioral and cheek regions against the bodies of dominant cats. Female cats in the central parts of farms were very aggressive to cats peripheral to the main group cats. Farm cats have even been observed to nurse each others' kittens.[54]

Tomcats do not tolerate or seek social contact with other males as one might find in canine or primate social groups. Another interesting social phenomenon observed is a "brotherhood of males."[52] Tomcats come together at some neutral spot at night and sit in close proximity. After midnight, the gatherings break up and each cat returns to its own territory. A dominance hierarchy among toms may serve to prevent fighting during their gatherings.

Felis libyca characteristically lived a relatively solitary life, implying that the progenitors of domestic cats had little social interaction. This is perhaps an overstatement, because the closely related European wild cat (*F sylvestris*) sometimes seeks the company of domestic cats and other cats of its species.[87] Domestic cats often share the same home, and even appear to enjoy each others' company. Such clear-cut socializing is probably fostered by plentiful food and shelter. With focused and abundant resources, as would be seen in certain farms, homes or neighborhoods (and occasionally in the wild), social patterns may emerge wherein cats, especially those raised together, seek each others' company and establish a dominance hierarchy. Socialization appears strongest among female cats.[54] Castrated male cats may act generally as females with regard to socialization, while intact males remain intolerant of other males. If the food supply is sparse and fewer cats can be sustained in a given area, the pressure would be against such social interactions.

Though domesticated cats may be either social or intolerant of other cats, they are usually social toward owners. Some behaviorists believe that cats react toward people as a kitten would react to its mother. Thus, cats purr when we pet them, knead our laps with their paws, or nurse on our clothing.

In understanding and dealing with problem behavior of cats, the concept of social evolution discussed above is important. About half of all pet cats live in multi-cat homes. Data from a survey on cats in northern California revealed that while only about one-fourth of cat-owning households have more than 1 cat, multi-cat homes had an average of 3 cats.[72] Thus, any particular cat has about a 50% chance of coming from a multi-cat home. Many feline behavioral problems, especially those involving aggression, spraying and eliminative problems, stem from our practice of maintaining cats in multi-cat households. Though cats can live happily in such social orders, communal living can be a considerable strain on their unpredictable social behavior and a stimulus to their deeper and more highly evolved solitary or asocial nature.

Given the premise that cats are basically asocial animals, it would be logical to assume that cats would resist socialization

even when forced to live together. Indeed, this appears to be true. Cats in high-density environments use overlapping or even temporary territories to avoid social conflict.[52] Some cats use an area in the morning and others use the same area later in the day. Free-roaming cats tend to avoid each other in pathways and thus reduce social encounters. Cats within a region of overlapping territories are well aware of the paths of movement and timetables of other cats in the same region, thus, further avoiding conflict.[53]

Social Hierarchies

Domestic cats, whether owned, semi-wild or feral, can develop a hierarchy from the most dominant to the most submissive animal.[11,13] Intact female cats develop a hierarchy based on having kittens. Each subsequent litter increases the social status of the female cat. Following birthing, queens gain rapidly in social status irrespective of the number of litters that they have had in the past. When queens stop having kittens, usually because of neutering, their social status rapidly declines. Female cats neutered before they have kittens are at the lowest social status. Neutering a male cat is associated with a rapid decline in their dominance ranking, and this decline parallels the fall in testosterone levels. As with females, male cats neutered before joining the hierarchy are at the lowest end of the dominance spectrum.

The male hierarchy is based on the physical attributes of strength, tenacity, bluster and cunning. When new tomcats enter the neighborhood or an adolescent animal reaches maturity, he is tested by established males. After several encounters, some of which may involve fighting, the newcomer's rank is set. No further battles or confrontations are necessary, provided new tomcats do not enter the area, a dominant tom does not decline in vigor, or younger cats do not try to improve their rankings.

Tomcats may become belligerent once again when females are in heat. They fight each other for the female cat's affections; they often assemble together outside the home of the female and successively take each other on in tirades of crying and snarling. A greater proportion of such encounters ends in actual fights. Though toms fight for the favor of the estrous queen, she is free to choose whichever male she wants. This does not always include the winning male.

When many intact cats are placed in the same environment, a single cat becomes dominant and reigns over all others in all aspects of life. At the opposite extreme, a few cats in the household or cattery group become so submissive as to be the butt of the others' frustrations. Most are of middle rank and somehow stay out of ongoing social problems.

Communication

Cats communicate with each other by scent, vocalization, and body motions. Scent is one of the most important means of communication, and characteristic body odors (body excretions and secretions) make each cat in an area aware of others.[81] Marking of territorial boundaries by urine spraying, scratching or rubbing is an important part of this long-distance communication. Short-distance olfactory communication involves direct body contact. Cats previously acquainted often greet each other by touching noses, rubbing cheeks and bodies together, or sniffing at the head and anogenital area.

Cats also communicate with each other through a variety of sounds and tones. These vocalizations consist of soft murmurs, clear vowel-like sounds, and shrill shrieks, cries and screams.[87] Soft sounds, such as purring, usually reflect contentment. Vowel-like sounds (meows) vary in duration and tone according to the animal's desire. Certain types of meows are recognized by the cat's owner to indicate a need for food, a welcome greeting, a desire to be held or played with, or permission to enter or leave. The more shrill sounds are usually associated with cat-to-cat communication and such activities as fighting and mating.

Vocal communication is both a learned and genetically ingrained faculty. Kittens instinctively know how to spit and hiss when approached by strangers or in unfamiliar situations. Even cats raised alone in an indoor situation learn to communicate their needs and desires.

Body language is also an important means of communication. Most cat owners

learn, knowingly or unknowingly, what various body, tail and facial expressions mean. An upright carriage of the tail is a friendly sign, often seen as cats approach their owners or kittens approach their mothers. If the cat wants to threaten, the tail is also vertical but the hairs are bristling. Aggressive behavior of an offensive nature is manifested by a low crouch of the body with the tail held horizontal or low, with the tip of the tail often twitching from side to side. If the tail is arched, the body in an upright and arched position or in a crouch, and the hairs of the tail and back bristling, the cat is in a defensive mode.

Facial features also change, depending on the emotional state of the cat. A cat in an undisturbed state has its ears wide apart and upright, whiskers relaxed in an outward position, and the pupils of normal size (depending on the amount of light). Anger is manifested by a wrinkling of the forehead (bringing the ears closer together) and furling of the ears in an upright position. The pupils are constricted and the whiskers come forward. A frightened or defensive cat has dilated pupils, and flattened ears and whiskers. Baring of the teeth and hissing can communicate either defensive or offensive behavior; the more pronounced they are, however, the more defensive the intended communication. As with people, the more bluster and noise that is made, the more frightened the individual.

Body language is often used to communicate things to the owner and to other cats. If the cat comes to the owner with tail upright and rubs against his or her leg, this is an obvious request for attention. If the owner approaches the cat and the cat retreats, this is a clear signal that the cat does not want to be handled at that time. If the owner is petting the cat and the cat does not want to be petted, the tail may twitch in an offensive manner. If the petting is continued, the cat may hiss or growl. In some cases, the cat may grasp the owner's hand briefly in its mouth with the intention of warning but not injuring.

Some cats stalk their owners, even leaping out at them, as if the owner was prey. Play-fighting is another common behavior between people and cats, especially kittens and adolescents. The cat rolls on its back and grasps the owner's hand to its abdomen. The hand is grasped with the front paw and mock-bitten; at the same time, the hand is raked with the back paws. The claws are guarded, however, and the canine teeth grasp the flesh but do not puncture it. Kittens and some older cats also love to strike at objects or owners with their paws.

Territoriality

Territoriality is a feature of all domestic cats.[87] A cat's territory is the area in which the cat spends most of its time and is willing to defend. Territoriality is undoubtedly a holdover from the behavior of wild progenitors, such as *Felis libyca* and *F sylvestris*. The territory occupied by each cat is usually well defined and built around a safe spot or home base. Home base may be a single spot, or a series of spots. It is a place for eating, drinking, sleeping, napping, watching the world or playing. For most owned cats, home base is closely aligned to the owner's home. Home bases for free-roaming cats are usually within the owner's home or surrounding yards. Cats kept strictly indoors still have a home base, even though it may be a specific perch, windowsill, piece of furniture or room. The actual territory or home range radiates from the home base.

Home ranges for domestic cats, as for their wild relatives, are always defined by availability of food, shelter and water. If conditions are good, as with owned or feral cats living near people, hundreds of cats may be found in a single square kilometer. If food, water and shelter are sparse, far fewer cats occupy an area and the home ranges for each animal are larger. In such circumstances, a single animal may roam over many acres. The size of the individual territory may also vary with the sex of the cats. Intact females and neutered male and female cats have more compact ranges than intact males. Intact males do a lot more roaming and their territories are larger and less defined. If food is hard to find within the home range, cats may move into more distant hunting ranges. Hunting ranges are connected to home ranges by regularly used paths. These paths are selected carefully to avoid the home ranges of other cats and, as such, are often long and circuitous.

It is important to remember that feral and owned cats often share the same home and hunting ranges. In the case of feral cats, the ranges are defined by a process of natural selection. Owned cats may be guaranteed a home base and a ready food supply, but they do not have their owner's help in establishing home and hunting ranges. Owned and feral cats must compete equally for such space. It is also important to remember that although a new homeowner is guaranteed rights to a piece of property, his or her cat has no predefined territorial rights. Domesticated cats that have owners usually stake out territories that center around their owner's home. The new territory may be a part of another cat's range, which can be a source of initial conflict.

Most domestic cats with owners live in areas of high human and cat density. It is not possible, therefore, for every cat to have its own territory. It is equally impossible for such cats to continuously defend their territories against this large number of neighboring animals. Territorial and defense requirements are met in interesting ways. Territories are often overlapping and may be 3 dimensional as well as 2 dimensional.[87] For instance, higher ground, such as fences, roofs and trees, may belong to different cats than the ground below. Territories may be shared by a small group of cats at the same time, or one cat may dominate at one time of the day and another cat at a different time. Complex but well-defined pathways may allow cats to circumvent the home ranges of other cats. Cats may be familiar with the movement patterns and time schedules of other animals in their area.[53] They quickly learn to time their use of such pathways to avoid other cats that have a different schedule. On community pathways, the cat already on the path has right of way over cats that are entering.

A cat's territorial claims must be staked, and claim staking involves physical confrontation. Confrontation is not always violent, however. Cats often use intimidation and nonphysical aggressive behavior; actual fighting is reserved for situations where diplomacy and bluff fail. Nonphysical aggression ranges from a brief staring episode to a more vocal and visual demonstration of offensive posturing (repositioning of the ears, eyes, tail and vibrissae to appear ferocious, piloerection over the back and tail, showing fangs, spatting, snarling, crying, hissing and clawing movements). Such matches usually last less than a minute. One of the participants usually realizes that it is weaker and rapidly retreats. The winner may half-heartedly chase after the loser for a short distance to flaunt its victory. Conditions leading to actual combat are less understood. Female cats with kittens vigorously fight to protect their kittens. They attack without fear and preliminary warning. Tomcats also attack with less preliminary ritual. Even then, actual fights rarely last for more than a few seconds.

Attacks are directed at the head or tail region, depending on the relative strengths of combatants. Head wounds indicate that the cat was on offense, while tail and lower back wounds indicate that the cat was defensive or trying to escape. Leg wounds are usually received when cats attempt to deflect a blow. Wounds are inflicted by claws and canine teeth. Once a wound is inflicted, the wounded animal rapidly retreats. Cats rarely induce multiple wounds and they rarely fight to the death, as can dogs. Intact females and neutered males and females less rigorously defend their smaller and more compact territories against all comers, and are less often successful, especially if pitted against intact animals. Intact male cats defend larger, more diffuse territories; however, they pick their fights more carefully and are more often successful.

Once a conflict between 2 cats is resolved, it is seldom repeated. The dominance pattern is set for those animals and is not renegotiated until there is a definite tip in the status quo, such as when a younger cat becomes stronger with time or the dominant male is weakened by age or disease. Dominance is most apparent among intact male cats. Every intact male cat in a given area has achieved a precise niche in the social order, and new tomcats (introduced or adolescents reaching adulthood) are rapidly tested over a period of several nights by established males. Once the newcomer's rank is determined, fighting does not recur unless he attempts to move up in the hierarchy or is himself challenged.

The dominant tomcat usually has the largest territory. Unlike in other species,

however, this may have nothing to do with his sexual prowess. Local females are not obliged to accept the dominant male as a mate. Fighting over females in estrus may not always be sexually motivated, therefore. Sexual aggression may also result when outside toms trespass on foreign territories while being attracted by estrous females.

Territoriality brings a aggressive behavior. One factor that keeps an animal's territory intact is its aggressive disposition toward other cats. That is why it is difficult, and sometimes impossible, for an adult cat in a household to accept new cats, even kittens. Many prefer to avoid each other, but if one intrudes into another's territory or if they are forced together, fighting can occur. If dominance is not established, they may remain intolerant of each other almost permanently. Both males and females tend to be aggressive toward intruders or strangers.

The tendency of males to be drawn into fights with other males is termed intermale aggressive behavior.[59] This type of aggressive behavior is facilitated or enhanced by postpubertal secretion of testosterone. When male cats are castrated after or before puberty, their tendency to fight is markedly reduced.

Territoriality brings certain marking behaviors, in which the cat seems to excel. Two principal types of this have been recognized. They include scratching prominent objects to leave a visual and a chemical mark, and urine spraying. Cheek and head rubbing on vertical objects, a third type of marking, is a type of scent marking by glandular secretions from cutaneous areas around the corners of the lips and behind the eye. Cheek rubbing is more commonly a response to dominant individuals, and rubbing performed on the owner's legs is probably a representation of the relationship between cats and their owners. Urine spraying and scratching on household walls or furniture, can create serious problems for the owner and for the cat (see Management of Behavioral Problems).

Urine spraying is a type of scent marking used mostly by tomcats. Under natural conditions, urine spraying is used near boundaries with the neighbor's territory, on frequented pathways or at crossing points. If cats are like other domestic animals, we would expect that urine marks indicate the sex and identity of the spraying cat.[27] Cats may thus keep track of the movements or presence of neighboring cats by these marks. During the mating season, urine marks left by males or females would also help bring the 2 sexes together.

Another role of urine spraying is to familiarize cats with their home ranges. Cats spray urine more when they encounter new or unfamiliar scents, or if they are alarmed. Thus, cats may spray outdoors after an unfamiliar cat has sprayed in its territory, or in the house when such objects as new furniture or grocery bags are brought into the home. Moving to a new house often evokes spraying. Urine marking is also performed in situations that evoke anxiety or aggression. Since anxious or aggressive behavior often occurs near a neighboring cat's territory, urine spraying is usually concentrated around territorial boundaries.[18] Once routine urine spraying points have been established, these spots tend to be repeatedly renewed without provocation by strange objects or interactions with other cats.

Of the 3 types of chemical marking, urine marking is the only one that is sexually dimorphic and performed more by males than by females. When males are castrated, before or after puberty, they tend to spray much less. If females or castrated males are spraying, one may have to look at factors in the environment that are anxiety-provoking or involve alterations in a cat's territory. Sexual reasons for spraying would likely be eliminated or lessened by neutering, depending on the levels of sex hormones produced by nongonadal organs.

Sexual Behavior

Though cats are comparatively silent and timid in their daily activities, feline courtship is far from a silent and private affair. Since cats are nocturnal, many of their sexual interactions take place at night. Therefore, many cat owners have not seen cats court and mate; veterinarians and other feline care specialists are often called upon for advice.

Female Behavior

Like females of many of our domestic species, a female cat in estrus displays dis-

tinct behavior, including heightened activity and nervousness. Vocalizations attract male cats, and sexual attractants (pheromones) in the urine stimulate visiting males to stay around. Owners of estrous female cats sometimes complain that unfamiliar tomcats appear uninvited at their doorstep and yowl to communicate their sexual interest in the female.

In the presence of one or more males, the female, even if she can only hear or smell the males, may assume a receptive posture, with elevation of the pelvic region, deviation of the tail to one side, and treading of the back legs. Once a male is next to her and starts to mount, these responses often become more intense. Pelvic elevation, treading of the back legs and tail deviation can often be induced by the owner's stroking the back of the female cat and touching the perineal region. The response may be intensified by grasping the skin over the back of the neck while also stroking the perineal region with the other hand. This test of female's receptivity is not completely accurate, however, in detecting heat. Some female cats may show pelvic elevation, tail deviation and treading, particularly if the stimulation is rather vigorous, even though they are not receptive. Other female cats may not exhibit this response when handled by the owner, even though they are sexually receptive toward male cats.

During copulation, the female cat typically turns aggressively upon the male just a second or so after he achieves penetration and ejaculates. After the male quickly dismounts, she often grooms her genitalia and rubs and rolls on the floor in what is called the "after reaction." The after reaction is a prelude to activation of the neuroendocrine system and ovulation.

Male Behavior

If a male cat is comfortable with the surroundings, it approaches a female and usually engages in nose-to-nose greeting, and then genital investigation. Genital investigation by the male is often followed by a flehmen response, manifested by curling of the upper lip, elevating the head and extending the neck.[34] The posture is maintained for several seconds. This response is believed to be involved with sex pheromones or sex attractants from the female. Flehmen behavior is sexually dimorphic and virtually always shown by males. The flehmen response may be seen in females that have investigated places where males had been urine spraying.[34]

During copulation, the male takes a neck grip on the female with his teeth and immediately engages in some treading of the back legs as he mounts. Since the initial mount is usually somewhat forward on the female's back, he usually slides backward while leg treading until there is genital contact. Leg treading by the female, along with the pelvic elevation, usually aids genital contact. When the male achieves intromission (penile insertion), there is a deep pelvic thrust and the male remains motionless for a 1-2 seconds. During this time, excitement seems to build up in the female, as evidenced by pupillary dilation. Almost immediately the male ejaculates, and the female disengages from the male and emits a loud cry. She typically turns to hit at the male as he moves aside or springs back. The male then retreats a safe distance from the female to wash his paws and penis.

Though the urge to mate is strong in both male and female cats, both sexes often exhibit some degree of selection. Some males will not breed certain females, even though the female is in full estrus and is positioning herself for breeding. Likewise, some females will not accept certain males even though they are fully receptive to other males. Some females in estrus are so aggressive to the male, even before breeding, that the male is intimidated. Conversely, some males force themselves on the female regardless of how hard she tries to repel him. Other males are cautious, staying near the queen for hours until she accepts him for breeding. Aggressiveness is not always beneficial to the male; some coy and reserved males may enjoy great success with certain females.

Maternal Behavior

Maternal behavior of cats has been examined and described in some detail.[73] A marvel of animal behavior is that a new mother can perform a relatively complex set of maternal behaviors without prior experience or training. Moreover, maternal be-

havior of the queen must change at each stage in the life of her kittens. Among all of our domesticated animals, the female cat is the most capable of going through parturition and raising its young without human care or intervention. In fact, some mother cats may first reveal their young to owners 3-4 weeks after they have been born. More commonly, however, female cats give birth to their kittens in the midst of a concerned family audience or under the watchful eyes of a cattery owner.

Behavior Before and During Parturition

Shortly before parturition, the queen usually seeks out a dark and relatively undisturbed area to deliver her young. Cats that are more strongly attached to their owners usually choose a location within the home or immediate vicinity. If the pregnant queen is allowed to roam freely in the house and is not confined during the later stages of gestation, the owner's bed or closet are likely delivery sites. Many cats may show nesting behavior several days before delivery. They actively search for an appropriate spot to deliver their kittens. Once this spot is selected, some modifications to the area may be carried out. This may include moving items or shredding cloth or paper. Some cats may become irritable or even aggressive as parturition nears. Like other species, female cats often become somewhat less active as parturition approaches and spend more time licking the abdominal and genital areas of their bodies.

Parturition occurs over four recognizable stages: contraction, delivery of the fetus, delivery of the placenta, and interval between deliveries. During the intervals between deliveries, some aspects of maternal care are initiated.

Uterine contractions mark the beginning of parturition. Most cats lie down during this stage and get up from time to time only to change positions. As the fetus enters the pelvic canal, abdominal muscle contractions and contractions of the uterus become more intense. When the head or buttocks of the fetus appears at the vulva, the female often reaches back with her head through her back legs and breaks the fetal membrane with her teeth. At times, she may actually pull the fetus through the birth canal by tugging on the membranes. The mother then consumes the fetal membranes and begins licking the newborn vigorously, causing the first respiratory movements. The third stage of labor involves delivery of the placenta. The placenta is usually eaten by the mother as it is passed.

The queen continues to lick the newborn for some time after it is born. While doing this she usually bites off the umbilical cord several centimeters from the body wall. Severing the umbilical cord at the body wall is abnormal and often leads to an umbilical abscess and death within a few days because of bacterial septicemia. Cutting the umbilical cord is associated with minimal bleeding. The umbilical blood vessels constrict at birth and the blood vessels retract inward as soon as they are cut.

The fourth stage of labor, consisting of intervals between deliveries, is when the mother grooms the newborn and her own genital region. She often cleans the bed that has been soiled with amniotic fluids. By eating the placenta, the mother gains extra nutrients and water, and maintains a clean nest. There is no evidence that eating the placenta contributes important hormones to the mother or that there is any difference in maternal responsiveness, whether or not the mothers are allowed to eat the placenta.[42,90] If the intervals between deliveries are long, the queen often nurses the kittens that have been delivered. If they are short, she begins to nurse the kittens in 1-2 hours of the last delivery.

The stages of labor may vary considerably from cat to cat, with the stage of contraction ranging from a few seconds to more than an hour. The actual delivery may take 30-60 minutes once heavy labor begins.

Postparturient Care

Mother cats usually remain close to their litters for the first 2 days after parturition, but then break away more and more frequently thereafter. The amount of time a mother spends nursing kittens in the first couple weeks after parturition may relate to the size of the litter. A queen may spend 70% of her time nursing if she has a litter of several kittens, but considerably less if she has only one kitten.[73]

Kittens receive a great deal of grooming from their mothers during the first 2-4 weeks after birth, especially over the anogenital area. This anogenital grooming evokes elimination, and the fecal material and urine are consumed by the mother. Since kittens are stimulated to urinate or defecate by anogenital licking, this maternal behavior is effective in keeping the nest clean. Later, as the young are able to leave the nest area, anogenital licking subsides and the young deposit feces and urine on one side of the nest area or even in the room away from the nest.

A question that frequently arises is whether there are differences in maternal behavior between females giving birth to their first litter (primiparous) and those that have given birth to one or more litters. Only minor differences have been observed among primiparous, uniparous and multiparous queens. Experienced mothers are somewhat more responsive to environmental events, and to the neonates by licking, grooming and retrieving them.[73]

A queen may carry her kittens by the scruff or nape of the neck when moving them from one location to another or when retrieving an errant kitten. Mother cats typically do not retrieve their young on sight, but rather respond to their vocalizations. Marooned kittens emitting the loudest stress vocalizations are the most likely to be retrieved. Quiet kittens are less likely to be retrieved.

The tendency for a mother cat to shift her litter from one spot to another, sometimes in response to environmental disturbances, is apparently strongest between 25 and 35 days after birth.[73] Environmental disturbances may be related to nearby dogs, other cats, and overly attentive people. Some queens do not like the spot selected for them; the owner and cat often become very frustrated trying to move the kittens to the site deemed most appropriate to each of them. Some frustrated queens have moved their kittens some distance from the home to seek solitude, and only bring their kittens back when they are nearing weaning age. If the queen is forced to move the kittens too many times, especially when they are very young, the skin of the kittens' head and neck may become abraded and raw. This may lead to serious infections, hemorrhage or cannibalism of the kittens by the queen.

The tendency for kittens to become limp and draw the tail upward when grasped by the nape of the neck is a reflex intimately associated with movement of the kittens by the mother. The same behavior may be evoked in adult cats by grasping them by the nape of the neck. Adult cats held in this manner usually become passively immobile. Veterinarians or animal handlers can take advantage of this behavior to obtain a rectal temperature, examine such sensitive areas as the genitalia, and to give injections, providing that the injections are not very painful.[21] This method of restraint for adult cats may be very effective, but some cat owners may be upset, feeling incorrectly that such a practice is painful.

It is important to remember that this type of feline restraint is not total; cats can still quite easily raise their back legs and inflict serious severe lacerations on the holder's hands. When carrying cats by the nape of the neck, it may be best to place a hand beneath the sternum to help support the weight or lay the cat on its side on an examination table.

As is true of most polytocous species, mother cats readily accept alien kittens, even if they are of a somewhat different age than their own kittens. In a large cattery operation, this trait is useful for fostering kittens of excessively large litters or orphaned kittens. The foster kitten may need some assistance in adapting to suckling from the new mother. Kittens removed from their mothers for several days may take several hours to resume normal suckling behavior upon being returned to the litter.[73] The same could be expected with transferring kittens to a foster mother.

The Nursing Relationship

The major interaction of a mother and her kittens after birth occurs during nursing. Kittens begin to nurse within 1-2 hours after birth, though earlier-born kittens may not be nursed until the last kitten is born. Newborn kittens have no problem finding a teat. The mother lies on her side, partially encircling the kittens. Kittens are further attracted by the warmth of the mother's

body. Moving its head from side to side while burrowing forward, the kitten eventually comes into contact with the mother's abdomen. They nuzzle into the mother's fur and quickly locate a nipple. Though kittens are born with their eyes closed and ears not functioning, they can detect thermal and olfactory stimuli.[71]

The nursing-suckling relationship occurs over 3 stages. In the beginning, the queen initiates each nursing episode. She arouses the kittens by licking them and then encircles them with her body. After an initial bit of searching, the kittens quickly respond to the mother's arousal behavior and begin nursing

The importance of saliva as an olfactory cue for blind newborn animals to locate a teat has been studied in rats, and what is known about baby rats may well apply to kittens. Queens actively lick their own nipples as well as those of the newborn. The saliva may leave a scent for the newborn to follow.[7] Washing the teats of rats inhibits nursing by neonatal rat pups. Conversely, suckling can be reinitiated by painting the washed teats with amniotic fluid or saliva from the mother.[79] Saliva and amniotic fluid not only lead rat pups to the teats, but cause them to open their mouths and extend their tongues. Saliva from newborn rats, when painted on the teats, also promotes attachment of the rat pups to the teats. Secretions from the nipple induced by oxytocin production in the mother also stimulate rat pups to attach to a teat.[77]

The second stage of the nursing-suckling relationship occurs after the second or third week, when the kitten's eyes and ears are functioning and they can interact with the mother both outside and inside of the nest. At this stage, the young kittens also initiate some of the nursing episodes. The mother generally cooperates by lying down and taking up the nursing position.

In the third stage, starting at about the fifth week after parturition, the kittens initiate virtually all nursing. The mother becomes more evasive and uncooperative as this stage progresses. Near the end of this stage, the mother begins weaning her kittens by becoming less and less available to them. She may even be aggressive toward their pleadings. In wild felids, this is typically the time when the mother begins to provide them with fresh killed prey.

Feeding and Hunting Behavior

Cats spend only a small fraction of their waking hours eating. However, the cat's evolutionary history as a predator is directly related to the small bit of time invested in feeding. The wild ancestor of the domestic cat, the small north African felid (*Felis libyca*), preyed upon small rodents, birds and insects, much as cats do today. In the wild ancestor, the main dietary item was small rodents. Rather than living a feast-or-famine type of existence characteristic of the larger cats, such as lions and tigers, domestic cats and their wild relatives tend to take smaller meals more frequently.

Feeding Patterns

When given access to a complete cat food on an ad lib basis, a group of cats ate as many as 13 times a day at evenly spaced intervals.[64] Whether the food was canned, semi-dry or moist did not affect the frequency of meals. Co-feeding of several cats had very little influence on the pattern and frequency of meal taking.

Most cat owners have a tendency to keep food out in front of their cats throughout the day. It is perhaps surprising then that cats are not more commonly overweight. Like other animals, cats have a number of physiologic controls over the amount of food they consume. Over the long term, their body weight is maintained within narrow limits. Factors involved in control of food intake include passage of food through the mouth and digestive tract, distension of the stomach, release of such substances as glucose, amino acids or fatty acids into the blood, and stimulation of chemoreceptors. This stimulation causes release of humoral factors that give the animal a feeling of satiety. Osmotic changes in the body caused by movement of water into the gut during eating and digestion also give the animal a feeling of satiety.[27]

Though cats consume a fixed amount of food when fed the same food, the appetite may be increased when a novel food is introduced. One could take advantage of this tendency and increase caloric intake of cats

by providing the animals with a variety of different foods.[64]

Among active free-roaming cats, there is a definite seasonal cycle in food consumption, weight gain or loss, and thickness of haircoat. These changes are probably related to the relative amount of daylight. Active cats often begin to eat more food and gain weight toward the end of summer. At the same time, their haircoats become thicker and more luxuriant. By autumn and early winter, the cats reach their maximum weight. Beginning in early spring, and associated with increased outdoor roaming and hunting activities, the cats rapidly lose weight, and by early summer some cats may even appear overly thin to their owners. These cyclic changes in fat stores and coat character have obvious evolutionary benefits. Wild cats often have to rely heavily on fat stores, the most efficient source of calories, to tide them over the winter months when game is more sparse. The thickened coat is also an obvious preparation for the colder winter months. In addition to these changes, some cats become noticeably more lethargic during winter months. This is also an adaptation to conserve energy and is akin to the more flamboyant hibernations of other species.

Food Aversions

Cats are notoriously finicky eaters and hardly ever eat tainted, spoiled or bad tasting food. This is one reason why cats are so rarely poisoned. Cats, like other animals, can sometimes develop food aversions; however, the aversion is to the taste or smell of the food. This can occur when a particular food is paired with a substance that tastes bad or causes nausea after eating. This may be caused by certain bacterial endotoxins and some drugs that may be given with food. It can also occur when a certain food is fed too long; a cat may seemingly enjoy a new food for a period and then suddenly refuse to eat it anymore. Laboratory-induced aversions have been retained for as long as 40 days.[64] In nature, food aversions may prevent reingestion of prey or parts of prey that are potentially injurious.

Hormonal Effects on Food Intake

Most domestic pet cats are castrated or spayed, and there has been some question as to whether these operations promote overeating or obesity. In mammals, ovariectomy leads to an increase in body weight as a result of hypoestrogenism.[88] The laboratory rat, for example, may gain as much as 25% following ovariectomy.[49] Increased food intake and a change in energy balance within the body are responsible for this weight gain. Much of the increase in weight is due to enhanced fat deposition.[49,51] In male rats, the picture is a little bit different. Castrated rats have reduced food intake and decreased body weight; however, the weight loss is due to reduction in muscle mass.[19] The percentage of body weight in fat actually increases.[58]

If we were to extrapolate research findings from rats to cats, we would predict that spaying female cats would also lead to obesity. However, it must be remembered that the normal female rat continually cycles throughout the year on a 4- to 5-day basis and is subjected to estrogen surges much more frequently than a female cat, which cycles only on a seasonal basis. Thus, we would expect to find a much greater effect of ovariohysterectomy in rats than in cats, which only cycle several times during a single season. Indeed, female cats with cystic ovaries and persistent estrus tend to become very thin. Though there are no good experimental data, there is circumstantial evidence that spayed cats tend to be less active and heavier than their intact counterparts. It is not a universal finding, however, and there are many exceptions. In one clinical survey, owners felt that castration had little effect on weight gain.[29] Adjusting the neutered cat's diet to counteract any modest hormonal alterations should easily control the animal's weight.

Progestin compounds increase appetite and promote some gain in body weight. When a progestin, such as medroxyprogesterone acetate or megestrol acetate, is used to treat problem behavior, clients should be advised of possible weight gain. Cats that are somewhat borderline in terms of excessive body weight should be watched carefully when put on progestin therapy.

Hunting

Rats and mice are natural prey of cats. Cats have also been known to kill and eat a

range of prey, including rabbits, birds, grasshoppers, lizards, snakes and squirrels.[1] Feral cats make about 3 attempts before catching a mouse.[53] If a rat is cornered by a cat, it may jump defensively at the cat, causing most cats to back off. Cats will not directly attack a rodent as large as a Norway rat, but rather will sit back and strike at the rat with their forepaws. A series of blows in rapid succession cannot be tolerated indefinitely by the rat, and soon it becomes disoriented or exhausted and tries to escape. When the rat turns its back to run, the cat seizes it by the nape of the neck.[53] Cats usually bite their prey in the neck and kill it immediately. The cat's canine teeth, when inserted into the intervertebral spaces, seem to be well adapted for piercing the tendons and ligaments of the neck and severing the cervical spinal cord of their prey.[53]

The effect of feral cats on rodent populations can be quite substantial. In a survey of meadow mice in a park in northern California, feral cats ate 88% of the mouse population.[66] It is estimated that normally only 4-18% of feral cats' diets consist of small birds.[38] However, in neighborhoods where the rodent population is under good control, it is argued that cats are more likely to pursue songbirds.

The role of the mother in teaching kittens to hunt has attracted some attention from behaviorists. As kittens approach the time of weaning, feral mother cats usually begin the process by bringing dead prey to the kittens and eating it in front of them. Later they bring the prey and, rather than eating it themselves, try to interest the kittens in it. Somewhat later, the queens bring in live or wounded prey and allow their kittens to play with them, standing close by so that they can recapture the prey if it attempts to escape. The latter process is eventually phased into a more supervisory role on the part of the mother as the kittens learn to stalk and to capture prey on their own. Interestingly, kittens that watched their mothers hunt and retrieve prey were more efficient predators as adults, but the experience had little carryover to prey types that their mothers did not hunt.[9,10]

Though maternal training might hone, modify or hasten development of hunting skills, hunting is more an instinctive than an acquired trait. Cats raised for generations in catteries can become hunters when returned to the outside environment.

To what degree does hunger affect a cat's tendency to hunt? This has naturally been of interest to people who want their cats to catch rodents around the home or, conversely, not to catch certain prey, such as songbirds. Casual observations by cat owners and experimental studies have revealed that cats may kill prey without eating it immediately afterward, or that they may kill more animals than they can possibly consume. In one study, hungry cats were allowed to eat a preferred food, and then a rat was released in their vicinity. Cats generally stopped eating, travelled several feet to attack and kill the rat, brought the rat back to their food, and then resumed eating their preferred food.[1] There are no logical reasons, therefore, to keep cats particularly hungry so that they will hunt better or more often. Conversely, feeding by the owners will not abrogate hunting behavior when cessation of this activity is desired.

Almost everyone has observed the tendency of cats to play with their prey before killing and eating it. Many owners take great offense at this seemingly sadistic behavior. The prey may be tossed into the air, batted around with the paws, rolled on, or clasped and kicked with hind claws. The prey animal may even be allowed to roam away from the cat for a distance and is then recaptured. There has not been a very satisfactory explanation for this behavior. The behavior may represent the release of pent-up energy stimulated by hunting.[53] One investigator envisioned a neuronal system for predation that is activated by stalking, pouncing and seizing prey, and tends to remain activated once it is aroused. This investigator hesitated to refer to playing with prey as something that cats "enjoy."[53]

There is no evidence that the initial capture is itself pleasurable. However, once the prey is wounded or stunned, subsequent actions appear to be highly stimulatory. These actions are akin to those evoked by catnip. Regardless of its origin, there is no doubt from watching cats playing with their prey that the habit is deeply embedded in the feline neuronal network.

Purring

Purring is a peculiar sound emitted by domestic and some wild species of cats.[5,78] The exact purpose of purring is unknown, though it appears to be a sign of contentment. It has been heard, however, in cats that are obviously ill and sometimes in seeming discomfort. Purring occurs only when cats are awake. It is widely believed that purring is a reflex act induced when cats are around people. People are not essential for purring, however. Cats may purr during mating, when they are around other cats, and while nursing.

The physiologic and anatomic basis for purring has been extensively studied.[69] Investigators found that purring consisted of regular bursts of sound (150-200 cycles/second) occurring every 30-40 milliseconds during, but not between, the inspiratory and expiratory phases of respiration.[69] Purring was caused by pronounced, cyclic and rapid pressure changes in the trachea that were superimposed upon normal breathing. These pressure changes caused turbulence in air flow through the airways, and was the source of the purring sound. These pressure changes were caused by short 10- to 15-millisecond bouts of stimulation of the laryngeal muscles every 30-40 milliseconds. Stimulation of the laryngeal musculature alternated with 10- to 20-millisecond bursts of diaphragmatic muscle activity every 40 milliseconds.

The purring sound is actually generated in 3 stages. In the first stage (20-30 milliseconds), the glottis is narrowed by stimulation of the laryngeal musculature, causing increased transglottal pressure. In the second phase (5-10 milliseconds), the vocal cords open and air is rapidly dissipated, causing resonance. In the final phase (5-10 milliseconds), the glottis remains open, permitting normal airflow in or out of the trachea. Both diaphragmatic and laryngeal stages can generate sound independently of each other. This probably explains why purring sounds are often heard or felt from both the chest and throat region at the same time.

As might be supposed, purring does affect normal respiration. Both the heart and respiratory rates increase during periods of purring. The minute volume of air almost doubles as a result of increased respiration, but tidal volume remains the same. The hyperventilation resulting from purring causes a 20% decrease in the carbon dioxide content of the blood.

The stimulus for purring appears to originate within the central nervous system itself, as sectioning of afferent nerves from the muscles of the diaphragm and larynx does not stop purring activity.[69] Stimulation of the infundibular region of the midbrain causes a cat to purr.

Grooming

Cats spend a considerable amount of time grooming their coats. Grooming consists of licking, washing and biting movements. Washing movements involve use of the paw as a washcloth. The paw is wetted by licking and then rubbed on the fur. Licking movements are used to groom all of the body except for the face, while washing movements are used for facial cleaning. Biting movements are used to remove larger particulate material from the coat. Such objects as grass awns are grasped with the teeth and pulled from the coat.

The feline tongue is well suited for grooming. The dorsal surface of the tongue contains many stiff, backward-facing papillae that act as a brush to remove loose hairs and other foreign material from the coat. The tongue also serves to transfer saliva from the mouth to the coat. It is estimated that grooming consumes about one-third of the nonevaporative water loss of a rat.[70] Cats groom themselves as much or more than rats, so it can be assumed that cats also use a significant portion of their daily water intake in grooming.

Grooming serves several functions. It is important for removal of dead hair. Cats' coats shed more or less continuously, and hair loss in cats seems inordinately large as compared to that in other species. Grooming also cleanses the hairs of impurities. The cleansing action of grooming is highly efficient; impurities on the coat are quickly dissolved or loosened, transferred to the tongue and oral cavity, and swallowed. If the impurities in the coat are locally toxic or irritating, mucosal sloughs of the palate and tip of the tongue may result. If the impurities are systemic poisons, such as insecti-

cides, a systemic reaction may result from ingestion of the material.

Grooming is essential for maintenance of the coat's health and luster. Cats that fail to groom themselves, for example, through illness, rapidly develop a dry, lusterless coat, with excessive amounts of dead hair. How grooming maintains the quality of the coat is not precisely known. The saliva placed on the coat through grooming contains a large number of proteins, some of which may play a role in conditioning the hair. The stimulating action of the tongue, or substances in the saliva, may also be essential to normal elaboration of beneficial glandular secretions from the skin.

Grooming also plays an essential role in keeping flea populations under control. A healthy cat maintains a relatively stable population of fleas on its body. If the cat becomes sick and stops grooming itself, the resident population of fleas increases rapidly to levels many times greater than normal. It is not known how grooming keeps flea numbers on the cat under control. Some fleas may be removed during grooming and swallowed. Saliva may also have a repellent or destructive action on fleas, but this also remains to be determined.

Grooming is one of the principal reasons behind human allergies to cats. Nearly 10% of people are allergic to cats. Most allergic people are sensitive to a single protein in feline saliva. The protein is placed on the hair by grooming, and is dispersed in the environment when dead hairs are shed.

Hairballs

A hairball is a loose aggregation of hair. It may consist of a few individual hairs or may be as large as an unshelled almond. They are frequently thrown up or passed in the stool. In the not too distant past, "hairballs" were the most common diagnosis in feline medicine. As our understanding of cats has increased, however, the diagnosis is made much less commonly. Cats normally swallow large amounts of hair while grooming. The swallowed hair either is periodically vomited from the stomach, regurgitated from the esophagus or oropharynx, or passed into the intestinal tract and voided with the feces. The thicker the cat's coat, the more fastidious the cat in its grooming behavior, and the longer the hairs, the more hairball-related signs that are seen.

The most commonly observed abnormality associated with grooming and hair swallowing is periodic gagging and retching. This is due to hair caught in the back of the throat or upper esophagus, and is much more commonly observed in long-haired cats. Excessive amounts of hair in the stomach can lead to loose accumulations of hair and mucus. When these become large enough, they are either thrown up or passed into the intestine. Retching, with vomiting or regurgitation of hair and mucus (usually not containing food or bile), is common in such animals.

Trichobezoars, or true hair balls, are large hard concretions of hair and mineral. They probably begin as hairballs. They are relatively uncommon as compared to hairballs, but are more likely to cause disease. If they are large enough, they can obstruct outflow of food from the stomach and cause periodic vomiting. Occasionally, a smaller trichobezoar is passed into the intestine. Passage of such a hard mass can lead to colic, inappetence and localized pain for a day or so while it is being passed.

Too much clinical importance should not be put on hairballs and their associated signs. In most cases, clinical signs are slight and can be considered a normal part of grooming and hair swallowing. They certainly do not cause serious clinical problems, and should not be used to explain more severe vomiting and weight loss, or other signs of illness. Since signs related to hairballs are so common in cats, it is almost always possible for the owner to temporally associate hairball-related signs with any disease, regardless of its true etiology. It is also hard to justify overtreatment of hairballs with chronic administration of oils, laxatives and other such products. Many normal cats are given such products every day of their life for no good reason.

The Catnip Response

Most people are familiar with the behavioral reaction of cats that smell, chew or eat catnip. There is even a whole industry built around marketing dried catnip leaves, catnip-stuffed toys, or aerosol cans containing

catnip extracts. Most felids apparently respond to catnip. This plant has been used on occasion by hunters in North America to attract bobcat or lynx. Lions, leopards, jaguars, pumas, ocelots, and several of the small wild felids also respond to catnip.[37]

Cats are drawn to catnip leaves or extract by its odor. They sniff it for a brief period, and then lick or chew it. The cat rubs its cheeks or chin over the catnip source. This rubbing frequently becomes very intense, and the cat may end up rubbing and rolling its entire body on the floor or ground next to the catnip. Cats frequently bat or paw at the catnip source and sometimes grasp it with their front paws and claw at it with their back feet. The response usually lasts from 5-15 minutes, followed by a period of satiation lasting an hour or more.

Response to catnip is apparently a genetic trait. Only 50% of cats respond to catnip.[65] There appears to be no difference in the proportion of responders among females and males, intact and neutered animals, and different breeds. Age is a factor, however. Kittens under 2 months of age usually do not respond to catnip, and may even fear or avoid it.

The catnip plant (*Nepeta cataria*) is a member of the mint family and is easily cultivated in the home. It grows as a weed in certain parts of the US, such as the upper Midwest. Catnip extract is obtained from volatile oils distilled from crushed catnip leaves. The active ingredient of catnip, nepatalactone, is found in these oils. It was initially thought that a cat's reaction to catnip was a co-evolved function and that perhaps the plant used the cat for seed dispersal. However, felidae can be found both in the southern and northern hemispheres, while the plant is indigenous to the southern hemisphere. Thus, felids display the catnip response even though they were not always exposed to a natural source of nepetalactone during their evolution.

Cats' response to catnip is mediated through the olfactory system. Cats unable to smell no longer respond to catnip.[33] Ingestion of catnip leaves does not provoke the reaction. The aromatic and volatile oils are probably taken into the olfactory system and trigger neuronal responses relating to sexuality, predation, play, chewing and eating. Hence, catnip evokes a random assortment of the rolling and rubbing that normally occurs in female cats during courtship, between cats at play, between a cat and its injured prey, or in cats that are eating.

Catnip is biochemically related to marijuana and some psychedelic drugs. It is interesting to speculate, therefore, that the behavioral reaction of cats to catnip is similar to the pleasurable response that people get from psychedelic drugs. Marijuana-like reactions have been reported by people who smoke catnip.[40]

ANALYSIS AND TREATMENT OF BEHAVIORAL PROBLEMS

Such problems as urine spraying, inappropriate elimination, aggression toward other cats, and destructive scratching of objects in households are not inappropriate for cats living outdoors or in the wild, and are, in fact, essential for survival and reproduction in nature. Thus, it may be more appropriate to use the term "maladaptive or problem behavior," rather than "abnormal behavior." The term "problem behavior" refers to normal behavior that occurs at an inappropriate time or place, is misdirected, or is too flamboyant. It is also important to remember that cats live in a wide range of environments from farms to small apartments, and a behavioral pattern that may cause severe problems for someone in an apartment may go unnoticed by people living on a farm.

Behavioral problems in cats usually have a much different basis than behavioral problems in dogs. Dogs interact socially much more with people, and human-canine problems usually involve dominance-subordination relationships.[31] Since cats are not usually drawn into such relationships with people, we generally do not see the problems centering around dominance-related aggressive behavior with cats.

Urine Spraying

Urine spraying is the most common behavioral problem of domestic cats. This behavior is normal for gonadally intact adult males; most tomcats spray their territory as a type of marking. However, females and

castrated males may also engage in urine spraying. Urine spraying of vertical surfaces is initiated by the cat's smelling the target area and then turning and directing a urine stream toward it. The target area is often a foot or so off of the ground. Frequent targets inside the home are kitchen appliances, furniture, bookcases, draperies, windows and interior walls. Outdoor targets include automobile tires, windows and windshields, doorsteps, bushes, trees and fences. Horizontal surfaces are sprayed from a normal squatting position. Frequent targets for horizontal urine spraying are carpets, clothes of a family member or the owner's bed.

Determinants of Urine Spraying

One of the determinants of spraying behavior is the gonadal status of the cat. Castration greatly lessens urine spraying. However, this behavior is not fully under hormonal control. About 10% of prepubertally castrated cats and 5% of prepubertally spayed cats are problem urine sprayers.[30] Spraying, which is normally expected of tomcats, increases during the breeding season. This may be partially a function of a seasonal increase in testosterone secretion.[2] Though castrated males are much less likely to spray than intact males, the onset of a breeding season and interaction with intact males and females may induce spraying in a castrated male. Urine spraying occurs infrequently in neutered females but is expected in some intact females, especially during the breeding season. A female may attract male cats to her vicinity by depositing urine, which contains sexual attractants, on vertical objects around her home range.[4]

Urine spraying is not just a sexually provoked response. It also can also result from chronic or excessive anxiety. Events that are frustrating or upsettling to cats, therefore, also predispose to spraying. For example, when owners move to a new house and the cat's territorial identification is altered, there may be a transient period of adjustment for the new cat, during which spraying may occur. When the cat adjusts to the new environment, it often stops spraying. In other instances, however, spraying may continue long after the adjustment appears to have been made.

Making an outdoor cat an indoor cat has also led to spraying. Owners changing their working hours or taking a trip for a few days may come home to find urine odor on their bed, clothing or shoes. Introduction of a child into the home, a new mate or friend, or other such social changes by the owner may also provoke urine spraying.

Understanding the environmental changes that may lead to spraying helps determine if the cat can eventually adjust to the new situation, or if precipitating factors are likely to continue. If adjustments can be made, one would be more optimistic about therapeutic approaches. One of the major causes of anxiety and urine spraying is introduction of other cats into the household. Spraying in male cats is greatly enhanced by the presence of female housemates, and less so by males.[30]

Diagnostic Factors

It is necessary to distinguish urine spraying from inappropriate urination (see below) or even some physical abnormality, such as from congenital anomalies, urinary tract infection, feline urologic syndrome or neurologic incontinence. Frequent urination, excessive amounts of urine production, urinary incontinence, pain or straining while urinating, and blood in the urine are usually associated with physical abnormalities. In almost all of these physical abnormalities, the urine is deposited on a flat surface. Spray marks on a vertical surface a foot or so off the ground indicate spraying. In urine spraying, certain target areas are repeatedly hit, such as a specific place on the carpet or the owner's clothes. Cats with inappropriate urination may be attracted to the texture of the substrate, as with carpet pile or planter soil, whereas a cat that is spraying continues to use the litter box for elimination when not engaged in marking.

A special problem arises in multi-cat households, where it may be difficult to identify the offending cat. Though one cat may have been observed spraying, other residents may also be involved. A logical approach is to ask the owner to separate the cats so that each may be monitored sepa-

rately. This physical separation and added attention may alter the spraying practice, however, especially if the spraying is induced by anxiety.

A method has been developed to mark the urine of a cat engaging in urine spraying without altering its environment. A dye, sodium fluorescein, which is used to reveal corneal ulcers, can be given to cats suspected of urine spraying. The dye is readily excreted in the urine, and urine-marked spots retain the dye for several days. The dye appears in the urine within 2 hours of subcutaneous or oral administration. When diluted in urine, sodium fluorescein, does not discolor fabrics and is water soluble. An ultraviolet light (Wood's lamp) can be used in the darkened room to detect the dye. Positive urine spots fluoresce a bright apple green. If the spot fluoresces, the urine came from the cat that was given the dye. The dosage of fluorescein is 0.5 ml of 10% sodium fluorescein solution orally in the afternoon. If the solution is not available, 6 strips of ophthalmic test paper inserted in gelatin capsules may also be used. For subcutaneous administration, 0.3 ml of sterile 10% sodium fluorescein dye can be given in the afternoon. Urine deposited that night or the next morning is usually labelled. If the urine spot is negative for the dye, the owner must wait 2 days for the dye to be cleared by the first cat, and another cat is treated. This is repeated until the owner has discovered which cat(s) is doing the spraying.[32]

Prepubertal Versus Postpubertal Castration

Castration alters the predisposition of male cats to spray, and eliminates much of the objectionable odor of tomcat urine. Testicular androgens cause the particular odor of tomcat urine, but the nature and source of the odor are not known.[4] About 80% of adult male cats have a rapid and significant decline in spraying behavior following castration, and an additional 10% experience a more gradual improvement. About 10% of male cats castrated as adults persist in spraying behavior indefinitely.[20,29] This persistence in spraying behavior is not due to residual amounts of testosterone because the concentration of testosterone in the blood is reduced to levels similar to those in long-term castrates within 8-16 hours after castration.[22]

The question often arises as to whether prepubertal castration is more effective in preventing urine spraying later in life than postpubertal castration is in treating the objectionable behavior after it occurs. In a retrospective clinical survey, there was no relationship between the likelihood of spraying as adults and the age (range 6-10 mo) at the time of castration.[30] About 10% of prepubertally castrated cats in the survey became problem urine sprayers at one time or another as adults. Also, 10% of adult male cats persisted in urine spraying after castration. With regard to female cats, the incidence of problem spraying by prepubertally ovariohysterectomized cats was about 5% overall, and was not related to age at the time of surgery.[30]

Behavioral Conditioning and Management

Physical threats, such as yelling at the cat or throwing an object at it while it is spraying, are usually ineffective. Where it has seemed to work, the cats often learned not to spray when the owners were around and sprayed when they were alone. Most people understand the futility of bringing a cat to a urine-soiled spot to scold it or rub the cat's nose in it. This type of punishment is more likely to make cats wary of their owner.

If cats mark or spray in only 1-2 spots, it is sometimes helpful to provide feed and water for the animal at these spots. Cats, like other animals, are hesitant to eliminate in places where they eat. A behavioral conditioning procedure that is also useful in such a situation is to produce an aversion to those spots by remote punishment. Ambushing a cat with a water sprayer when it approaches a target area may be effective. This type of remote punishment should be delivered without the cat's knowing that the owner is involved in squirting it. Use of inverted mouse traps, fixed so that they easily trigger when touched by the cat, is a form of remote punishment that many cat owners have found useful in producing aversions to certain areas. Attaching a motion sensor alarm to the area sprayed may also serve as effective remote punishment.

A discussion of the principles of aversion conditioning is available elsewhere.[31] Allowing cats more outdoor freedom has also been effective for some animals.

Management and conditioning procedures should always be tried first in preventing urine spraying. However, in most instances, spraying behavior seems to be highly motivated and behavioral approaches to control are often disappointing. If an aversion is produced to one area, cats often find new areas to spray or mark. When management and conditioning procedures fail, it is necessary to approach the problem medically. Surgical approaches are to be reserved to the most refractory cases.

Progestin Therapy

Progestins have been the mainstay of treatment for urine spraying and marking, though enthusiasm for these drugs has waned as side effects (lethargy, obesity, diabetes mellitus, mammary hyperplasia, mammary cancer) of chronic therapy have become evident and other treatments have been discovered. Progestins seem to mimic effects of castration in reducing male-like or sexually dimorphic behaviors, such as mounting, roaming, intermale fighting and spraying.[22] Given that spraying can be a manifestation of anxiety or tomcat-like expression of sexuality, it is likely that progestins are not so effective against spraying related to anxiety. Progestin is available through injectable medroxyprogesterone (Depo-Provera: Upjohn) and oral megestrol acetate (Ovaban: Schering; Megase: Mead Johnson). One injection or series of oral treatments may eliminate spraying, especially if environmental factors that evoked it are transient, or repeated injections or oral treatments may be necessary to suppress the behavior. Chronic treatment increases the risk of side effects, however.

About 30% of spraying cats are successfully treated with progestins.[24] The sex of the cat, and the number of cats in the household, are important factors in success or failure. Males respond favorably more often than females, and cats from single-cat households more often than those from multi-cat households. The highest success rate was 80% for males in single-cat households. There was virtually no success in progestin treatment with females from multi-cat households. These clinical findings also suggest that in females, spraying is more related to anxiety than being an expression of male-like behavior.

Both medroxyprogesterone acetate and megestrol acetate are equally effective in the initial treatment of spraying. With long-acting injectable progestins, the client does not have to observe a complex dosage regimen. The customary dose of medroxyprogesterone acetate is 100 mg for a male cat and 50 mg for a female cat (10-20 mg/kg). The drug should be given intramuscularly or subcutaneously. If given subcutaneously, the injection should be in the inguinal region because occasionally there is some hair loss or change in hair pigmentation at the injection site.

Positive results, if they occur, should be evident in one week. If there is no response in one week, another approach should be tried. The injection should be repeated when the objectionable behavior returns. When megestrol acetate is given orally, the initial dosage is 5 mg/day for 7 days. If the progestin therapy is effective, improvement should be evident within 7 days. If improvement is not seen in one week, megestrol acetate treatment should not be continued. If effective, the dosage should be gradually reduced over 2-4 weeks to 5 mg once a week, and treatment terminated in 2-6 months. Continuous treatment beyond this point greatly increases the chances of side effects.

Since progestins are steroids, they have a tendency to suppress the adrenal cortex by virtue of negative feedback on ACTH production by the pituitary gland. Progestins may also cause mammary gland hyperplasia and increased incidence of mammary gland tumors.[23,24] Another side effect is precipitation of diabetes mellitus in cats that are prediabetic. These are usually middle-aged, obese and sedentary cats. More frequent but less serious side effects are an increase in appetite (seen in 30% of cats treated) and depression (seen in 30% of treated cats).[24] In some instances, depression is severe enough to require cessation of treatment.

Antianxiety Drug Therapy

Diazepam, given at a dosage of 1-2 mg per os twice a day, has proven effective in

eliminating urine spraying in cats. Some cats may show excessive sedation or ataxia at the initial dosage. In such cases the dosage should be reduced to the least effective level. Sedation and ataxia tend to subside with time, even though the antianxiety effect remains. The effectiveness of diazepam, a widely recognized antianxiety drug, in reducing urine spraying is a further indication of the importance of anxiety as a cause of urine spraying in cats. Unpublished clinical case reports, indicate that diazepam is more effective in reducing or eliminating urine spraying than progestin therapy, especially in cats from multi-cat households. For this reason, and because of fewer major side effects, diazepam is probably the treatment of choice for spraying.

Neurosurgical Approach

Olfactory tractotomy, which is a simple neurosurgical procedure carrying little surgical or recovery risk, has been used successfully to reduce urine spraying or marking in cats that do not respond to progestin treatment.[25,26] The need for this surgery has not been reevaluated since the advent of antianxiety therapy, however. This operation may appeal to some cat owners who wish to consider a more extreme measure to resolve a spraying or marking problem when progestin or antianxiety therapy has not succeeded. Little in the way of specialized instruments is required. This operation has been effective in almost all female cats and about 50% of male cats that have undergone the operation. The reason for the difference between males and females is not known. Interestingly, the success of this operation with regard to males versus females is the opposite of the success rate with progestin therapy.

The surgery involves removal of the olfactory tracts and caudal parts of the olfactory bulbs through a small dorsal hole in the frontal sinus.[25] No major undesirable side effects are seen following the operation. About half of the treated cats showed little interest in food following surgery but were coaxed to resume eating by placing meat-like baby food in their mouths or smearing food on their lips. Subsequently the cat would accept the usual semimoist or dry cat food. In terms of long-term changes in eating behavior, a few cats were willing to consume a greater variety of food postoperatively than preoperatively, while some cats became more finicky eaters.

Inappropriate Elimination

Cats are generally fastidious and one of the few species that bury their waste. The evolutionary background for development of this behavior is unclear, but this trait certainly makes cats good house pets for apartment dwellers. The owner only needs to provide a discreetly placed litter box and keep it clean. It is such a natural tendency for most kittens to urinate and defecate in sand or loose dirt that it is usually not necessary to use any kind of housebreaking or training. A few cats, however, are not as fastidious as others and either refuse to use their litter boxes or, more commonly, use them erratically.

Analysis and Diagnosis

Elimination problems in cats are multifactorial and can reflect behavioral or medical-physical causes. As mentioned with the diagnosis of urine spraying, it is important to rule out medical or physical factors. Cats with diseases that cause diarrhea, increased amounts of urine formation, urinary or fecal urgency, urinary or fecal incontinence, or nerve, muscle, bone or joint pain may have difficulties in using the litter box normally. Some purebred cats, in particular certain types of Persians, may be difficult to litter train.

Once medical and physical causes of the elimination problem are excluded, behavioral causes can be examined in detail. The diagnosis of urine spraying is discussed above. When the elimination problem is not a manifestation of urine spraying but has a behavioral basis relating to aversion to the litter box, aversion to outside toilet areas or attraction to unacceptable areas in the house, the problem is referred to as inappropriate elimination.

Aversion to the Litter Box

Aversion to the litter box is a common cause of inappropriate elimination behavior. Some cats may have an aversion to going outdoors in rainy weather, causing an otherwise healthy cat to inappropriately elimi-

nate within the house. Cats that are repeatedly frightened by dogs may also be driven to eliminate inside. Aversions to litter boxes may occur if the litter box has not been cleaned frequently enough or when a new cat has been added and one litter box is insufficient. Once-a-day cleaning may be sufficient for one cat, but not for 2-3 cats. Certain litter additives may cause aversion in some cats. Some cats may develop an aversion to the litter box because they have been bothered by young children while using it. Some kittens, especially purebreds of certain longhaired breeds, are litter trained with paper rather than typical cat litter. Paper is used because it does not collect on the fur. Cats trained on paper may have trouble adjusting to other types of litter.

Attraction to Alternate Toilet Areas

Though owners may provide their cats a litter box filled with fresh litter, not all cats decide that it is the preferred site for their urination or defecation. Fireplace ashes or planter boxes in the house may be so attractive that cats use them in preference to a litter box or going outdoors. The texture of a carpet may make it irresistible. It may be necessary, therefore, to make these desirable areas unattractive to the cat. Putting aluminum foil cloth around the base of plants in a planter box is an example. Remote punishment may be effective when only 1-2 locations are involved. Placing loaded inverted mouse traps in the off-limit areas is one example. Other procedures take advantage of the latest in home security electronic products, such as use of a motion sensor alarm on the target area or an infrared photorelay alarm system connected to a loud siren, which is triggered by approach of the cat.

Establishing New Litter Box Habits

To establish new litter box habits, the new litter material must be as attractive to the cat as possible, as cats have differing preferences. If the cat objects to deodorizing additives, it may be necessary to shift to unadulterated clay-like litter. The best way to identify preferred litter is to provide a number of litter boxes at the same time, each containing a different litter. Over several weeks, it should be possible to determine which litter is used most frequently. If given a choice, many cats prefer plain sand. It is possible, therefore, to arbitrarily start litter box retraining with sand. Once litter box habits are established again, the sand could be gradually phased out and commercial litter phased in by mixing more and more commercial litter with the sand.

As a part of retraining, the cat should be confined to an area where there is a high probability that it will use the litter box rather than the floor. Bathrooms or utility rooms with vinyl or tile floors are generally not attractive elimination areas and in such places a cat is more likely to use a litter box. As the cat begins to use the litter box, it can be allowed gradual access to other parts of the house. The cat can first be allowed into an adjacent room or hallway in addition to the confined area. If this goes well, it can be gradually allowed access to other parts of the house. Alternatively, the cat might be allowed free run of the house for a couple of hours, during which it can be carefully watched, and then returned to the confined area. If things go well, it can be allowed longer and longer access to the rest of the house.

Plush carpets are an attractive alternative to a litter box for some cats and it may be necessary to cover the carpet in some rooms with a plastic sheet. The sheet can be gradually trimmed away as the cat continues to use the litter box. In some instances, carpet soiling has been so extensive that it must be replaced. Some owners have had success in covering the bottom of the litter box with a piece of the old carpet, and once the cat starts to use that litter box, the actual litter material is gradually added until the old carpet is uniformly buried. As the cat continues to use the litter box, the carpet is gradually trimmed away. The secret of maintaining good litter box habits once the habit is reestablished is not to change the environment, social life or litter box too rapidly. For example, if the litter box should be moved to a new location, this should be done gradually, only a few inches at a time.

Establishing Eliminative Behavior Outdoors

Sometimes the problem, or solution to the problem, of indoor litter box problems is

altering a cat's eliminative behavior outside the house. It may be helpful to create a litter area outside the house by digging a shallow hole and filling it with sand. Cats are attracted to such areas (as many a child's sandbox owner will attest), and the sand area is cleaned the same as one would clean an inside litter box. Such a sandy elimination area should be sheltered from the rain, readily accessible to the cat, and in a place where the cat will not be harassed by dogs. Unfortunately, it will probably be used by other cats as well.

Some cats have been trained to use a human toilet. This procedure works for cats that are strictly house cats, and may even eliminate the necessity of a litter box in the house. The technique requires some conditioning and is described elsewhere.[31]

Aggressive Behavior

Though cats are frequently aggressive toward each other, aggressive behavior toward people is less common for cats than dogs. Cats may be aggressive toward people out of fear, but they can easily hide or escape from people that evoke such a response. Cats are usually not forced to interact with people as much as dogs. Most aggression is directed to other cats rather than to people. In one study, 80% of cats hissed and 85% swatted at other cats, and 70% fought with each other occasionally.[8] In contrast, only 25% of cats growled or hissed periodically at people in the house, and 23% broke the skin with claw or tooth.

During roaming, tomcats get into serious fights with other cats and sustain injuries more frequently than dogs or female cats. Female cats fight more frequently with other feline housemates. Aggression may even occur among siblings raised in a household from kittenhood. It may occur spontaneously, or when one cat is removed from the household for a while and then reintroduced. In the wild, this family fighting is an apparent expression of the dispersal phenomenon that drives emerging adults away from their natal territory. In households, this dispersion is often delayed or even suppressed far beyond kittenhood. When it does occur, the cats' owners may not understand what is going on. They are surprised to see cats that previously got along quite well suddenly falling into continuous belligerency.

Treatment of Aggression Toward Other Cats

Intermale fighting is clearly enhanced or facilitated by postpubertal androgen secretion. Hence, fighting occurs more often in tomcats after they have reached puberty. Castration usually prevents intermale fighting. A clinical survey indicated that about 90% of cats castrated in adulthood for problem fighting stopped fighting; about half these castrated cats showed a rapid decline in fighting, though it was more gradual in the rest.[29] For castrated cats that continue fighting, progestin therapy, as outlined for spraying behavior, has proven somewhat effective.

Progestin therapy may be effective for household cats fighting with each other. When this is not effective, one useful approach is to create separate territories. This involves providing separate feeding stations for the 2 cats, providing separate litter boxes, and otherwise arranging it so that the cats can live with minimal contact with each other. It may be necessary to use an antianxiety drug, such as diazepam (Valium: Roche), or a tranquilizer, such as acepromazine, for a short time to suppress the aggressive behavior while the cats establish a type of peaceful coexistence. The dosage is gradually lowered as the undesirable behavior abates.

Treatment of Aggression Toward People

Occasionally cats scratch or bite a person when the owner attempts to pet or hold the cat, or during play. Interestingly, family members are 3 times more likely to receive a skin-breaking scratch or bite than a stranger.[8] Growls or hisses, however, are just as likely to be directed at a stranger as a family member. About 23% of household cats in one study broke the skin of a family member by clawing or biting on at least one occasion.[8] About 9% of household cats have broken the skin of a family member 5 or more times, and 5% of cats have done it more than 8 times.

Cats often enjoy petting and handling, but have a certain threshold for human con-

tact. Once this threshold is reached, the cat may suddenly turn and attack. Anxiety may also lead to biting behavior, and in some cases it is directed toward specific people. Knowingly or unknowingly, these people are often the source of the anxiety. Attacks on people are usually muted.

If the attacks are not serious, but are somewhat frequent, use of an aversive stimulus when the cat turns to bite or scratch may be effective. This may involve the person tapping the cat on the nose with a finger. Probably the best way to discourage this type of aggression is to stage the misbehavior while having an accomplice in the room with a water sprayer to squirt the cat in the back of the head when it becomes aggressive. If the technique works, sessions should be staged repeatedly until the cat no longer turns and acts aggressive when being handled or carried. Progestin or diazepam therapy, as outlined for treating spraying behavior, has been useful in treating aggressive behavior in some instances where punishment is not effective.

It must be remembered that each cat has its own threshold for human contact, and that the owner and cat must both make adjustments. This threshold is obviously low for the feral cat that shuns people and fights ferociously when trapped. Some of these apparently antisocial cats rapidly become well socialized pets, while others resist all attempts to tame them. Most cats communicate to their owners by voice or body language if and when they want to be handled. Most owners learn to interact on the cat's terms, rather than their own.

Many cats are extremely sensitive about being scratched on the lower back. Rough petting or scratching of the lower back of such animals elicits an aggressive response toward the person doing the petting. Though some physical problems lead to increased sensitivity over the lower back, most such cats are physically normal, and the behavior does not progress with time as it would if associated with disease. Cats that are anxious, ill or irritated may also become nonspecifically hyperirritable when touched on the back. How or why lower back scratching elicits aggression in such cats is not understood.

Aggression redirected toward people is not uncommon. Cats that have been emotionally agitated by aggressive or defensive encounters with other cats or dogs, or cats that have encountered some physical trauma, may react aggressively toward their owners for a short time after such encounters.[8] It is wise, therefore, for people to avoid immediately picking up cats that are obviously emotionally or physically agitated. It is important to remember that redirected aggression toward people is more reflexive than deliberate.

Some cat handlers and veterinarians believe that kittens subjected to rough play may be more aggressive to people as adult cats. Though there is little evidence to support this assumption, it seems prudent to discourage overly rough play with kittens.

Feeding Problems

Problems with ingestive behavior that one may see include anorexia, wool chewing and eating house plants. Anorexia is covered under the discussion of the ill cat.

Wool Chewing

This is one of the few feline behavioral problems that is totally abnormal. Wool chewing appears to have no particular value to the domesticated or wild cat, and no counterpart in the wild. This behavior involves sucking, chewing and possibly ingesting chunks of wool from such items as stockings or sweaters. The behavior is seen almost always in Siamese or Siamese crosses, and begins at about the time of puberty. Though wool seems to be preferred by many Siamese cats, others progress to cotton (terry cloth towels) and even synthetic materials. Most cats give up wool chewing within 1-2 years, but occasionally a cat continues to cause so much damage that it cannot be kept as an indoor cat. There has been no indication that the behavior stems from any kind of nutritional deficiency. The fact that the behavior is most common in Siamese suggests a predisposing genetic trait. No universally successful treatment is recognized.

Eating House Plants

As most cat owners are aware, eating grass is a natural behavior for cats, though

the function or basis for this behavior is not understood. Some cat owners claim that their cats seek out grass when they have an apparent gastrointestinal disturbance. They may vomit after eating the grass, suggesting that stimulation of the stomach by the grass induced the vomiting. Others note that cats eat grass when they seem to be perfectly healthy. Whatever the reason for eating grass, this is relatively normal behavior, and some cats do it more than others.

Given the habit of cats to chew on grass, it is understandable that some house cats would also chew on potted plants. Though there are many articles on the potential toxicity of common houseplants, other than *Dieffenbachia* and some types of philodendrons, which are oral and laryngeal irritants, cats are almost never poisoned by eating house plants.

Scratching Problems

A perfectly normal behavior of cats, but one which can cost cat owners hundreds or thousands of dollars, is the scratching of furniture, drapes or other household items. Though declawing is a justifiable, safe and highly effective means of dealing with scratching problems, some cat owners are repulsed by this idea. Others consider it only as a last resort. Therefore, it is probably worth trying behavioral modification before the declawing option is accepted.

Natural Scratching Behavior

By watching cats scratching outdoors, we can understand why cats scratch certain objects inside and what can be done to alter this behavior. Many cats have one or more scratching trees on which they repeatedly scratch, making the tree a readily visible territorial marker. In the process of scratching, the cat also apparently rubs secretions from its feet onto the tree trunk so that the scratched area gains a distinct olfactory character that may be recognized by other cats in the territory.[31] Thus, the tree provides both a chemical and a visual mark of the resident cat, and the animal returns to repeatedly scratch the same spots on the same trees to freshen up these visual and chemical marks. Scratching also removes the worn outer layers of the claws, exposing a new sharp claw underneath. Thus, a cat's claws are not sharpened in the traditional sense as one would sharpen a cutting instrument. The inherited predisposition to scratch is so strong that some declawed cats still routinely make scratching motions.

Many owners provide their cats with a scratching post, usually covered by carpet and placed in an inconspicuous area. Some scratching posts have a compartment for catnip to attract the cat to the post, where it will then engage in scratching. As pointed out above, however, cats have a tendency to establish their territorial marks (scratches) on prominent vertical objects. Therefore, the corner of a chair or couch, which juts into the room and is most visible, is a preferred site. Cats certainly do not discriminate between a scratching object purchased for them at the pet shop and one that is available to them as a corner of a couch or chair. After cats start scratching a particular object, they tend to persist.

Therapeutic Approaches

Training a cat to stop scratching requires that the targeted objects be removed or covered with plastic so that they are unavailable for scratching. Alternate fixtures, such as scratching posts, are then installed. The texture of the intended scratching post is an important consideration. Cats like to take long vertical strokes when dragging their claws through material. Unfortunately, the coverings of many commercial scratching posts do not lend themselves to such vertical drags. Commercial posts can be recovered with an upholstery material with vertically oriented threads.

Posts of soft wood, such as redwood or pine, may also work if they are first roughed up with a wire brush. Many experienced cat owners prefer a board attached to the wall rather than a free-standing post. It may be useful to gently rub a cat's feet on the intended scratching object to rub off secretions from the feet of the cat onto the post. Attaching catnip to a post or putting catnip in a compartment provided at the top of the post is not recommended. Even if the catnip produces a reaction, there is no reason to believe this will encourage scratching.

To train a cat to use a particular scratching post or board, the object should be placed in a prominent area until it is scratched regularly. Once a cat starts scratching the post, it can be gradually moved to the side of a room.

Sexual Behavior Problems

These types of problems include objectionable sexual mounting of other cats or people, or lack of sexual interest toward the opposite sex.

Objectionable Mounting

Castrated cats, and sometimes females, may persistently mount other cats in a household. Mounting is in the normal behavioral repertoire of cats, and is highly instinctive. For some reason, the neural circuitry underlying mounting behavior in these cats is sometimes activated at inappropriate times or directed at inappropriate objects (people, other cats not in estrus). One approach in eliminating inappropriate mounting is to reduce the motivation for such activity. This may be done by administration of the long-acting progestins, using the same regimen used for treating urine spraying. Another approach is to make mounting unpleasant for the cat being mounted so that the problem cat has no cat to mount. Remote punishment with a water sprayer to punish the cat that is mounted may engender aggression toward the cat that is doing the mounting. It is important that the cats do not know that a person is involved in delivering the remote punishment. During this conditioning the cats should not be allowed together unless someone is there to deliver the punishment.

Lack of Sexual Interest by Breeding Males

Strange Environment: Males may be reluctant to breed females for a variety of reasons. Male cats in a strange environment may be uncomfortable or anxious, and may require several days or sometimes a month, to acclimate and breed normally. Females do not seem to require this degree of adaptation. For this reason, it is advisable to bring females to the male for mating.

Inexperience: For young males, lack of experience in performing the right mating movements may be a factor. The only therapeutic measure here is time and experience. Mating is a strongly instinctive trait, but inexperienced toms can benefit from trial-and-error learning. Instead of putting the tom in with the queen for a brief period, they might be left together for several days, or at least overnight.

Penile Hair Ring: A problem that is sometimes confused with lack of experience in executing the right movements is a hair ring around the glans penis that prevents intromission and successful mating.[35] The penis of the male cat is covered with epithelial papillae that project toward the body. These papillae gradually collect hairs that eventually form a ring around the penis. Male cats with this condition continuously perform correctly oriented pelvic thrusting but cannot insert their penis. The hair rings are sometimes removed by the male cats themselves. The hair ring can be removed by gently sliding it over the penis.

Lack of Libido: Many breeders and veterinarians sometimes believe that lack of libido in a tom is caused by abnormally low blood concentrations of testosterone. Testosterone levels can be evaluated by measuring levels of the hormone in blood and comparing these to the levels in normal toms. It is necessary however, to collect several blood samples throughout the day for such an analysis, since testosterone blood concentrations fluctuate. Results from a sample taken at a particularly low or high point in the fluctuation may be misleading. Work on laboratory animals indicates that testosterone levels have to be markedly depressed to contribute to a male's lack of sexual interest.[22] There is evidence that males with less than half the usual level of testosterone still maintain normal copulatory activity. Thus, low testosterone is not a likely factor in inadequate sexual interest of breeding males.

Males do apparently undergo some seasonal fluctuations in testosterone levels that can influence libido. Seasonal fluctuations in testosterone levels are usually not a problem in a cattery because females are usually not in estrus when a male's testosterone levels might be at a low point. Seasonal

fluctuation might be considered a factor in an otherwise unexplained reduction of sexual interest by a breeding male out of the normal breeding season.

Individual Preferences: Though mating is a strong instinctive trait in both male and female cats, actual mating preferences involve more than instinct and desire. Both the male and female cats may have definite preferences for an intended mate. Some males will not breed certain females even though they have a good libido toward other females. The opposite is also true. If the male is particularly aggressive, he may forcefully overcome the female's objections, but the mating is often quarrelsome. Some toms are very patient with queens and mating may not occur until hours after initial contact.

Breeding Problems with Females

Most owners of breeding females can detect changes in a female cat's behavior as she comes into estrus. Her vocalizations increase and she rubs and rolls on the floor. These signs are more pronounced when the female hears or smells a tomcat. Petting the estrous female on the back and rubbing the perineal area evoke or intensify the sexual crouch, elevate the genital area, and induce treading of the back legs and deviation of the tail to the side. Unless one knows the exact sexual behavior of each particular female, it would be a mistake to rely on such behavioral changes as the sole indicator of estrus. Some female cats will not show these sexual responses unless they are in the vicinity of a sexually active male, while others demonstrate them for no apparent reason.

Queens may appear to be in full estrus to the human observer yet will not readily accept a male's sexual advances. Sometimes restraining the reluctant female will be helpful. In these instances, one might try breeding the female with a male cat that is particularly sexually vigorous and does not feel intimidated in mating with a female cat that is restrained by a person. One might also resort to leaving a male and female alone for several hours or overnight. Some females reject certain males. As most successful cat breeders recognize, breeding cats involves dealing with a number of individual feline idiosyncrasies and sensitivities. Patience and persistence are invaluable in managing this aspect of a cat's life.

Occasionally people want to keep a female for breeding, but are bothered by the female's estrous behavior in the interim period. Cats are reflex ovulators, and the duration and number of estrous periods in cats during the breeding season depend on whether a female has mated. Estrus lasts 4-6 days if mating, or the mating reflex, occurs. If it does not occur, estrus may last up to 10 days. Cats continue to come into estrus during each breeding period as long as ovulation is not induced. Subsequent estrous periods occur at intervals of 2-3 weeks if the female is not mated. After several estrous cycles, cats not bred go out of estrus until the next season.

Gently probing the vagina of a female cat with a blunt instrument, such as a glass rod or stout rectal thermometer, can induce ovulation and shorten the estrous period in the same manner as mating. Several insertions of the glass rod of about 10 seconds' duration and 5 minutes apart over 2 successive days are usually sufficient to induce ovulation. Sometimes females display the characteristic copulatory after reaction to these insertions.[14]

Maternal Behavior Problems

Cats are considered to be excellent mothers. We are puzzled, therefore, by queens that ignore their kittens from birth or cannibalize their offspring. There are explanations for these alterations in maternal behavior other than inexperience. Though mothering reflects some degree of learning or experience, it is a strongly instinctive trait. In fact, the best predictor of mothering is a queen's past performance in maternal care.

Maternal Neglect

About 8% of kittens die from inadequate maternal care.[31] In such situations, kittens die for several reasons, including failure of the mother to remove fetal membranes and lick the kittens dry. Hypothermia also occurs if kittens stray away from the other kittens and are not retrieved, or if the mother does not stay in contact with them

enough in the first few days after birth. Some queens do not properly nurse their kittens at birth, which quickly leads to starvation and increased susceptibility to bacterial infections due to a failure of passive systemic immunity gained from colostrum.

Failure of a queen to care for her kittens has several causes. Some primiparous queens seem to lack maternal instincts, or have not yet fully developed them. Many queens that are poor mothers initially become good mothers with time. A small percentage of queens are never good mothers. If the kittens are physically abnormal, premature or otherwise weak at birth, the queen may ignore them or, as will be discussed, destroys them by cannibalism. Some queens are overly anxious during parturition, because of unfamiliarity with the situation, serious distractions or environmental stress. If the queen is constantly disturbed by people, she may not settle down to the task at hand.

The fact that environmental stress may play a role in some kitten abandonments is supported by a peculiar behavior of many queens. Some queens deliberately deliver their kittens away from the home and people's overwatchful and interfering influences. The kittens are kept hidden until they began to require solid food, at which time they are proudly presented to the owners. The fact that cats demonstrate this behavior indicates the importance of quiet and solitude in kitten rearing, at least during the first several weeks of life.

Cannibalism

Some queens may cannibalize one or more of their kittens. Cannibalism may occur during a second pregnancy in the season, with the first kitten born, with a litter that is larger than usual, or with kittens that are ill. Cannibalism does not appear to be a reflection of inexperience in mother cats. It may also result from anxiety brought on by too much human interference, or the stresses of other cats or dogs in the immediate environment.

Cannibalizing of ill kittens has an evolutionary advantage. By killing and eating a kitten that is likely to die, the mother keeps the nest from being soiled by a dead kitten. The mother cat is also able to use the protein and water from the dead kitten to the benefit of surviving kittens. Further, the mother, by reacting to early signs of disease, such as inactivity, hypothermia or respiratory distress, may actually remove the affected kitten before it becomes infectious to the other kittens. Depositing the dead kitten outside the nest would attract scavengers, so the mother, by consuming it, avoids this problem also.

Wild felids apparently have the instinct for cannibalism, and in nature cannibalism can be triggered by deviations from the norm. If a kitten has impaired immunity and develops a full-blown disease, even involving opportunistic pathogens to which other kittens in the litter may be immune, the sick kitten could act as a reservoir of the pathogen sufficient to overwhelm the healthy littermates. For this protective strategy to work, cannibalistic behavior of the mother must be triggered by very subtle changes in the kittens or the environment. In domestic cats, cannibalism may be triggered in an inappropriate manner. Thus, kittens that are not sick are occasionally killed and eaten by the mother.

Some queens may be cannibalistic or aggressive to their first-born kittens, even after having had several previous litters. In such cases, the first kitten may be greeted with anger, apprehension or fear. The queen may traumatize the kitten or kill and eat it. If the first kitten is treated aggressively, it should be removed along with subsequent kittens and the litter reunited with the queen after the last kitten is born.

Tomcats also may kill kittens. When kittens of mothers bred by another tom are killed, the females soon come into estrus again, and the male can breed them and sire the next round of offspring. This type of behavior is commonly seen in lions, and has been also reported in tomcats.[54] Strange tomcats should be kept away from lactating female cats with litters. One would expect a resident tomcat, such as one that belongs to a cattery, to be quite safe around kittens. This is what some breeders have found.

Queen-Kitten Interactions

Interaction of the mother cat with her newborn kittens is almost continuous for the first 2 weeks of life. It is not surprising,

therefore, that insufficient maternal-neonatal interactions may have a significant impact on behavior of such kittens when they become adults. Kittens weaned at 2 weeks of age and raised away from their siblings and mother are more suspicious, cautious and aggressive as adults than kittens weaned at the usual age of 6-8 weeks.[74]

If possible, orphaned kittens should not be raised in a totally isolated fashion. Ideally, orphaned kittens should be fostered onto other mother cats that also have kittens. If this is impossible, hand-reared kittens should interact as much as possible with their littermates or other kittens for at least the first 4-6 weeks of life. Interactions with other kittens can apparently take the place of maternal interactions. Raising an orphaned kitten with no contact with other cats is the least desirable option, though the behavioral side effects are much less serious than might be imagined for a comparable lack of human infant-mother interactions.

Despite the fact that removal of young from the nest for prolonged periods can theoretically have an adverse effect on the behavior of the kittens as adults, brief interludes for a few minutes each day have no deleterious effects. In fact, brief handling of kittens within the first 2 weeks after birth can promote slightly more rapid development. As adults, kittens that were handled by people were less emotional in strange environments. The importance of early experience in development of cats is discussed in detail elsewhere.[31]

BEHAVIOR OF SICK CATS

Signs of Illness

It is often difficult to obtain accurate clinical information about the course of a cat's illness. This is due in part to the ability of cats to feign health in the face of disease, the tremendous stamina of cats (the legendary 9 lives), normal cat behavior, unique anatomic and physiologic characteristics, and inattentiveness of some owners.

Severely ill cats can appear healthy from all outward appearances. They often do not show signs of illness until organ damage is significant and their organ reserves are exhausted. Once this point is reached, they rapidly deteriorate in condition. Therefore, many cat illnesses, though chronic in nature, appear relatively acute to the owner. The origin of this trait is not known, but it is common among many wild species. The ability to appear healthy despite illness may protect the cat from potential enemies and other competing cats.

Regardless of the purpose of such behavior, it has important clinical implications. First, it means that a sick cat is often seriously diseased by the time it is seen. This might be the origin of the old saying that "a sick cat is a dead cat," muttered so often by veterinarians of the past. Though this saying may have had its roots partly in the behavior of sick cats, it was probably equally due to our rudimentary understanding of cat diseases in previous decades.

Normal cat behavioral traits also serve to mask disease signs. Cats are very fastidious about defecating and urinating. Not only do they bury their excreta, but they also clean themselves well after elimination. Owners frequently do not notice that their cats have diarrhea, if the stools contain blood or mucus, or if the stools have an abnormal color or shape. The evidence is usually buried in the yard or litter box, and very few owners dig through sand and litter to examine the stool. Further, because of cats' fastidious nature, fecal soiling of the perineum is not usually as noticeable in diarrheic cats as it is in diarrheic dogs.

Cats often lead a relatively sedentary life during the day and do most of their roaming at night. This is opposite to the lifestyle of most people, and signs of illness may go unnoticed. Likewise, increased water consumption and urination may go unnoticed. Cats allowed access to the outside will drink water from sources other than the water bowl. Urination and defecation are conducted in private and the evidence buried. Anorexia is also difficult to appreciate at times. Cats are often fed *ad libitum*, and it is not unusual for them to eat at irregular schedules or to occasionally miss a meal. Any anorexia or decreased food consumption may not be immediately noticed.

Due to unique anatomic and physiologic characteristics of cats, certain physical signs may also not be manifested as well in cats as in dogs and people. For instance,

coughing is a much less common sign of respiratory disease in cats than in dogs or people. Joint pain is also less likely to be manifested by lameness or stiffness in cats than in dogs. Cats with severe arthritis may still climb fences and hunt, while dogs with a similar degree of changes are often incapacitated. Cats, being desert animals by evolution, have a marked ability to concentrate their urine and conserve fecal water. A cat in renal failure may have a much higher specific gravity in its urine, therefore, than a dog in a similar state of disease. Such animals may not drink or urinate as much as similarly affected dogs. Diarrheic stools in a cat may contain far less water, and be noticeably more formed, than diarrheic stools from a dog with the same type and severity of bowel disease.

Because cats can appear healthy in the face of progressive disease and mask signs by behavioral and physiologic means, and because of inattentiveness by the owner, sick cats often tend to look outwardly the same regardless of the cause of their illness. Some signs, however, are common to many sick cats. These signs include anorexia, weight loss, change in the haircoat, recuperative hiding, fever and depression.

Anorexia

Anorexia often occurs in progressive stages over days, weeks or months, depending on the illness. Early in the course of disease, sick cats lose their appetite for their usual foods. They may go to their food pan and even appear to be hungry. They sniff their food, or even take some into their mouth, but then rapidly turn away. They can still be tempted to eat some foods, however. A new brand of commercial food, or a special flavor, may entice them to eat. The favorable response to a change in diet is usually short lived. Within a few days, even the new food is shunned. As their appetite continues to diminish, the sick cat eats only small amounts of highly palatable food. The most palatable food is usually raw liver. Once they lose their appetite for highly palatable morsels, their anorexia is complete. Thereafter they shun food, even sometimes when it is forced upon them. Most cats die within a few days to 2 weeks when this stage of illness is reached. Many cats seem to rally as death approaches. They suddenly become more alert and attentive, and may even attempt to eat. Death usually occurs within the next 12-24 hours, however.

Anorexia, though viewed as a detrimental sign, may have a protective effect on acutely ill animals. Anorexia may benefit a sick cat during the short term in 2 possible ways. By not consuming food, the cat reduces the chance of raising the blood concentration of iron. Low iron blood concentrations inhibit the growth of pathogenic bacteria.[17,46,63] Because febrile cats sequester iron in the spleen and liver, the influx of new iron into the bloodstream would be counterproductive. Also, if a cat does not feel hungry, it has little motivation to move about in search of food. Thus, it would stay in one place curled up, insulating itself from heat loss. There would also be reduced muscular activity and conservation of the body's energy reserves. Studies in mice showed that mortality is increased and survival time decreased if animals are force-fed during a bacterial infection.[60,61] On the other hand, if the mice are deprived of food for 2-3 days before a bacterial infection, survival rates are increased.[86]

Weight Loss

Sick cats lose weight in a different manner than most other species. With cessation of food intake, cats immediately begin to catabolize their own protein. This usually takes the form of muscle atrophy. Fat stores are for some reason not efficiently used. Obese cats that become ill often remain obese in outward appearance even though they are rapidly losing weight, therefore. Muscle atrophy and retention of internal and external fat stores cause many sick cats to feel "mushy." Many owners and veterinarians mistakenly underestimate the severity of a cat's weight loss based on the apparent gross retention of fat. Fat is much less dense than muscle, and marked weight loss can be associated with a relatively small amount of muscle loss.

The loss of elasticity often seen in the skin of a chronically ill cat is due in part to dehydration but more often to a change in the physical character of the skin and subcutaneous tissue because of protein catabolism. Skin turgor cannot be used, therefore,

as a measure of dehydration in chronically ill and wasted cats.

Change in Haircoat

One of the earliest signs of illness in a cat is a change in the character of the haircoat. Haircoat changes can occur within days of the onset of illness. There are several possible reasons why a cat's coat deteriorates so rapidly following the onset of illness. A proportion of a cat's daily protein intake is expended on replacing shedding hair and salivary proteins placed on the coat during grooming. Cats use dietary protein inefficiently even when normal (see chapter on Nutrition). When they are not consuming protein in their diet, they rapidly turn to endogenous sources of protein to supply their vital needs. Many sick cats decrease the amount of grooming, or stop grooming altogether. Grooming also plays an important role in maintaining the quality of the haircoat, and has a pronounced inhibitory effect on flea infestations. This inhibitory effect on grooming has been experimentally confirmed for ectoparasite infestations in rodents.[62,84]

The reasons that ill cats cease grooming are not known. One obvious reason is that the cats are too weak, depressed or nauseated to carry out such a function. In some cases, however, cessation of grooming may have a beneficial effect on recuperation, at least in the short term. Cessation of grooming conserves body heat, energy and water. Grooming takes a great deal of body movement, which generates heat and uses energy. A great deal of water is also lost on the fur during grooming. In rats, which have a grooming ritual similar to that of cats, up to one-third of nonevaporative water loss is through grooming.[70]

Though cessation of grooming may be helpful in the short term, it can have a detrimental effect in the long term. Ectoparasitism, especially flea infestations, increases dramatically with time in cats that fail to groom themselves. Massive flea infestations, which are not uncommon in chronically ill cats living in flea-infested environments, can literally drain cats white of blood and serum protein.

Recuperative Hiding

Some clinical signs of illness involve traits peculiar to cats. Sick indoor cats often retreat to certain areas of the home to recuperate. When free-roaming cats become seriously ill, they often leave their home base and take up refuge in specific hiding places. These hiding places may be a long distance from their homes, and are often in neighboring shrubbery or buildings. The reason for this peculiar behavior is unknown, but may be involved with the sick cat's desire to be alone where it can concentrate its recuperative powers. Sick cats that disappear from home may die while in hiding, recuperate and return home, or get slowly worse.

If they are still able, many runaway sick cats attempt to return to their homes as death approaches. The owner is then faced with a cat that has been missing for days or weeks and returns in a severe state of debilitation and disease. What has taken place in the interim is usually a mystery. Occasionally neighbors may find the sick cat hiding under shrubbery or in buildings. Such people are at even greater loss to explain what has happened, because more often than not, the cat is a complete stranger to them. Such cats are often taken to veterinarians for treatment. This poses an even greater dilemma for the veterinarians because they have no history of the animal or its condition, no obvious owner, and a moral obligation to the animal and the people that brought the cat to them.

Fever

Fever often accompanies inflammatory diseases. Inflammation can be caused by myriad different diseases, many of which are infectious and a few that are noninfectious. In the past, fever has been viewed as a deleterious side effect of disease, and a great deal of effort has been invested in lowering body temperature to normal as a part of therapy. Currently, however, the fever response is thought to have protective and therapeutic value, and is tampered with only when it becomes dangerously high.[12,28]

The normal body temperature of a cat is 100-102.5 F, and fevers of 103-106.5 F are not unusual in many diseases. A tempera-

ture of 106.5 F is only a temperature rise of 4.5-6.0 F for a cat. This would be comparable to a fever of 103.1-104.6 F in a person. Though this may seem high to a person who does not take into account the higher normal temperature of a cat, this would not usually be considered dangerous, and there is no need to suppress it if there are no good indications to do so.

The fever response is brought on ultimately by the release of endogenous pyrogens. Pyrogens are released from several sources, including circulating leukocytes and tissue macrophages. Infections, hypersensitivities and tissue necrosis, to name a few, cause release of endogenous pyrogens. Endogenous pyrogens have more recently been equated with a lymphokine called interleukin-1 (IL-1).[15] The febrile response caused by release of IL-1 is due to changes brought about in the hypothalamic thermoregulatory set-point.

Increased heat is generated both by conservation of existing heat and production of more heat. Heat is conserved by shunting of blood from peripheral tissues to internal organs. Sick cats often seek warm environments and curl up to reduce the exposed body surface area and reduce heat loss. Heat also is produced by shivering.[36] IL-1 is also involved in other fever-related responses, such as lowering the plasma concentration of iron and increasing synthesis of certain proteins from the liver, including haptoglobin, ceruloplasmin and c-reactive proteins.[15,68] The proteins produced by the liver are referred to as acute-phase proteins. Sometimes the physiologic responses that occur during fever are referred to as the acute-phase response.

The fever response plays an important beneficial role in disease, at least during the short term. The clearest evidence of the role of elevated body temperature in fighting acute disease involved experimental use of cold-blooded reptiles, whose body temperature can be artificially varied by experimental means.[43-45] Lizards kept in cold rather than warm environments had impaired survival when subjected to infection. Similar experiments have involved rabbits infected with Pasteurella multocida. Rabbits whose fever was suppressed were more likely to die of pasteurellosis than control subjects allowed to develop a fever.[47] In another study, ferrets infected with influenza virus shed much less virus when their fever response was not blocked.[39] Though fever may be beneficial in acute diseases, its beneficial effects might be overcome by negative effects over a longer period.

Changes during fever promote the body's ability to deal with infectious disease in two ways. One is by the influence of IL-1 in potentiating antibody synthesis and lymphocyte proliferative responses to antigens or mitogens.[3,41,55,76] There is a direct suppressive effect of temperature elevation on growth of some microorganisms. Fever responses are also accompanied by reduction in plasma iron and zinc levels by sequestration in the liver and spleen. Iron and zinc are essential nutrients for the growth of some microorganisms. A reduction in iron and an increase in body temperature have a synergistic inhibitory effect on growth of some bacteria.[17,46]

Generating a fever is an expensive proposition for most animals, including cats. For every 1 degree C increase in temperature, metabolism must be increased by about 10-13%.[16] Further, if the animal must rely on shivering to raise body temperature, the basal metabolic rate is increased 2-5 times above the resting level.[36] Cats with febrile diseases lose weight much faster, therefore, than nonfebrile diseased animals. Febrile animals also require several times more calories per day to maintain condition than normal cats or cats with nonfebrile illnesses. For these reasons, fever is more beneficial for acute than chronic disease.

The occurrence of anorexia in febrile cats, as in other animals, seems somewhat paradoxic to clinicians. The febrile animal not only needs calories to maintain the elevated body temperature, but it needs replacement protein for tissue breakdown from the direct effects of the disease-causing organism. It is possible, however, that anorexia, like fever, can be beneficial in the short term and that both work together (see section on Anorexia). Research studies indicate that IL-1, and not fever per se, mediates the loss of appetite in febrile individuals.[56] It seems unlikely that both responses would work against each other.

Depression

Sick cats are typically depressed and inactive, and seem to lose interest in their surroundings. There is a tendency, perhaps, to think of this behavior as reflecting the debilitating aspects of a disease, and this may be the case for very prolonged illnesses. However, like fever, anorexia and cessation of grooming, depression may be beneficial in acute disease. A depressed cat is less motivated to move about, using energy that would otherwise go into production of body heat. It instead curls up and insulates itself to conserve body heat. Depression reflects a survival strategy in the sense that the animal's chances of survival are better in the depression mode than in the flight-fight mode, which expends energy.

The most common element of depression is increased sleepiness or a tendency to sleep during normal periods of wakefulness. Interestingly, the sleepiness during disease, like fever and anorexia, may also be stimulated by IL-1. In rabbits and rats, administration of IL-1 causes prolonged slow-wave sleep.[48,80,83] Like fever and anorexia, it is doubtful that depression continues to be helpful after a certain time.

THE MULTIPLE-CAT HOUSEHOLD

Multiple-cat households may refer to catteries, farms, research animal colonies, pounds and shelters, and the single-family home. The term is generally reserved for the last situation, however. Multiple-cat households in the form of catteries are covered elsewhere (see sections on Cattery Design and Management and Cattery Diseases). The following discussion concerns mainly single family homes with more than one cat. Particularly troublesome are households containing 5 or more cats, which is a common situation.

How and why do some people keep large numbers of cats? Cats are relatively easy to keep as compared to dogs, and bring very little attention upon themselves. Cats are also comparatively clean and nondestructive to their surroundings, and are easily cared for with litter box, and food and water provided ad libitum. It is easy, therefore, to keep several cats in the same home without attracting the attention of neighbors and friends. Some people enjoy having several cats in their home. They like cats and appreciate the differences in personality of each animal. Others are trapped into having more than one cat for a number of reasons. Many people believe that their cats get lonely without the company of other cats. As we have already mentioned, this is far from correct. Cats enjoy solitude, and the social stress of too many cats in a home can cause anxiety and lead to behavioral problems. Some people, because they like cats so much, take in new cats because they are abandoned and would suffer or be destroyed if not sheltered and cared for by someone.

A type of multiple-cat household that deserves special attention is that containing 30-60 cats. Almost every city in industrialized countries has people that keep large numbers of cats. These people are usually older women who live a solitary life in a large, older home in a single-family or tenement-house neighborhood. They often began by feeding stray cats, which eventually become tame or semi-tame. They often do so because of their concern for the health of the animals and an honest desire to make the cats' lives better. With time, however, they often collect more and more cats, and within a few years the numbers peak at 50-60 animals. This number appears to be near the maximum that can be sustained in such an environment.

Cats are usually left to "do their own thing" in such homes. Some stay strictly indoors as pets, others come and go, and still others are loosely attached to the periphery of the group as feral or semi-tame cats. In many instances, some of the cats remain intact and a number of kittens are born on the premises each year.

Accumulation of cats in such a multiple-animal household is inevitable. Feral cats on farms move rapidly into areas where food is most accessible.[75] If the animals are no longer fed, they just as rapidly disperse to other areas. People that feed stray or feral cats keep acquiring new animals as long as they continue to provide food. As the numbers of cats increase in such households, there is a tendency for many of the owners to become more and more reclusive.

The physical condition of the home and yard often deteriorates as more of their income and time is spent caring for the cats. It is uncertain whether their cat-accumulating behavior is the cause or effect of the personality and lifestyle changes.

There are 2 complications of multiple-cat households. Behavioral problems are often rampant, and urine spraying and abnormal elimination lead to tremendous sanitation problems and odors within the home and surrounding areas. The most important problem, however, is an increased incidence of infectious disease.[67] The stress and close proximity of animals to each other intensifies the rate of infection and severity of the resulting disease. Factors behind the spread of disease in multi-cat households are discussed in the section on Common Cattery Diseases.

One aspect of disease in the open multi-cat household pertains to changes in the hunting behavior of sick cats. For instance, a higher than expected proportion of stray or feral cats tamed by people are infected with chronic disease-causing agents, such as feline immunodeficiency or leukemia viruses.[67] The owner notices a feral cat hanging around the yard and slowly tames it with food. When the cat becomes domesticated, it is found to be chronically ill and is taken to a veterinarian. The veterinarian often discovers an underlying feline immunodeficiency or leukemia virus infection. The conclusion is that feral cats, when chronically ill, seek food where it is easier to obtain.

The chronically ill feral cat is taming itself, rather than the other way around. This phenomenon is akin to the aged or diseased tigers that start to prey on people rather than animals. People are easier to prey upon than animals, and tigers that cannot hunt their preferred prey put aside their fear of people and change their hunting patterns. Though this has been shown to be especially true for feline immunodeficiency virus infection, it likely applies to chronic diseases of many other types.[89] Bringing in feral or stray cats to existing households is a high-risk activity, therefore. If they are suffering from low-grade infections, they bring these diseases into the household with them. If the diseases are made worse by physical and social factors, the result may be outbreaks of disease within the household that are far more severe than in nature. This seems to be particularly true for such diseases as feline leukemia virus infection, which is enzootic in a small number of feral and stray cats and from which most free-roaming cats easily recover.[67] Introduction of feline leukemia virus into a multi-cat household can cause serious disease problems, with a high infection rate and a much lower rate of recovery.

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Chapter 6

Nutrition and Nutritional Disorders

C.A. Buffington

Normal Feline Nutrition

Cats are unique among the common household pets in that they are pure carnivores. As T.S. Elliot said, "So first, your memory I'll jog, and say: a cat is not a dog."[31] Dogs and cats diverged in evolution over 30 million years ago; dogs became members of the family Canidae, and cats the family Felidae.[20] This divergence had important nutritional consequences. Cats became true (metabolic) carnivores, meaning they require animal products in their diet to meet their nutritional needs. This unique aspect of cat nutrition is evident in their water, protein, amino acid, fat and vitamin metabolism.

Though people and cats have closely interacted for the last 3000 or more years, the nutritional requirements of the domestic cat have been of particular importance only during the last 3 decades. Before this time, cats were not as popular as primary pets, and relatively few of them were kept indoors away from their normal prey. They tended to be fed homemade diets rich in meat, and commercial cat foods contained mainly animal meat. In fact, the principal dietary problem of the past was feeding too much animal tissues. Cats fed mainly red meat received an improper balance of calcium and phosphorus and developed a bone disorder known as nutritional secondary hyperparathyroidism. Many of the recent dietary problems have paradoxically involved feeding too little animal meats, a genuine necessity created by the great increase of cats as household pets.

Cats have increased dramatically in numbers in the United States in the last several decades, and as of 1989, 57.5 million cats were kept as pets.[95] Cats surpassed dogs as the principal household pet in 1985, when there were 50 million cats and 49 million dogs. The trend toward greater numbers of cats as pets has been associated with an increasing reliance on use of commercial foods as the principal or sole source of nutrition. There was a 50% increase in cat food sales between 1981 and 1989 in the United States alone, and $2.19 billion worth of cat food was sold in 1988.[95]

As the demand for commercial foods grew, animal food companies have increasingly relied on nonanimal meat sources to provide plentiful and cheap supplies of cat food; animal-derived nutrients tend to be too expensive. In spite of intense nutritional research, a number of nutritionally related diseases have developed over the last few years as a result of the search for palatable, nutritious and economical food. These dietary problems can be traced to 3 factors: a relatively poor understanding of the unique dietary requirements of cats; a greater dependence on commercially prepared foods; and a trend away from dietary ingredients against which cats evolved, *ie,* only animal tissues.

The discussion that follows is concerned first with the normal nutritional requirements of cats, and what is known about them. This will be followed by a discussion of modern cat food preparation and diseases caused by improper diets. The final portion

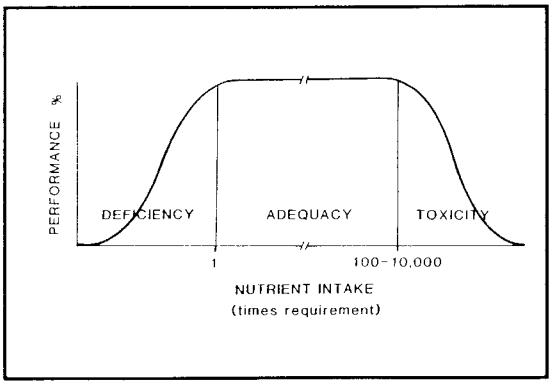
of the chapter is concerned with the nutritional needs of the ill and anorectic cat.

NRC Recommendations

Dietary nutrients have a range of effects on the animal, depending on their level in the diet (Fig 1). The minimum nutrient requirements of the cat are established by an expert committee and published in The Nutrient Requirements of Cats by the National Research Council (NRC) of the National Academy of Sciences.[67] The NRC presents a summary of the minimum requirements for dietary essential nutrients, compiled from currently available published research information, for cat growth. The research basis upon which each recommendation is made is presented, along with physical signs of deficiency and excess of the nutrients. The NRC also provides the nutrient composition of many ingredients used in cat foods and the characteristics of the 3 classes of commercial cat foods: dry, semimoist and canned.

The NRC recommendations thus summarize the scientific basis for our current understanding of the cat's nutritional requirements. The term "requirement," however, has occasionally led to confusion by those who have misinterpreted the intended use of the term by the NRC. As the authors caution in the NRC introduction, "A margin of safety was not intentionally incorporated into these recommendations. It is important to note that the requirements for many of the nutrients . . . have been established using purified diets (*eg*, amino acid diets were used in determining the amino acid requirements), and therefore an allowance for a product of lower digestibility (and/or availability) should be used when the nutrients are supplied by foodstuffs . . . . Finally, these nutrient requirements are based on the best information available; modifications should be made as environmental or other circumstances may warrant."[67]

Figure 1. Performance outcome of a nutrient compared to its level of intake. If a nutrient is given at less than its required level, signs of specific deficiency develop, while at excessive levels the nutrient may be toxic. Fortunately, the range of the adequacy for most nutrients is very wide, making deficiency or toxicity unlikely.



Current recommendations are presented in Table 1. As just stated, many of the studies upon which the recommendations were made were conducted with purified diets from which nutrients are readily available. Nutrient availability is influenced by interactions among nutrients in natural food ingredients and by diet digestibility. Minimum requirements should be increased, therefore, by 20-100% (the "correction factor" in Table 1) to ensure dietary sufficiency of practical diets.

Characteristics of a Satisfactory Diet

Cats require a satisfactory diet to maintain normal structure and function at all stages of life. A satisfactory diet is one that is complete, balanced, digestible and palatable. "Complete" means that the diet provides adequate levels of all the nutrient classes. The nutrients must also be present in the proper proportions, because excesses of some nutrients may cause deficiencies of others. A diet containing the correct proportions of each nutrient is called balanced. The completeness and balance of a diet are often evaluated by comparing the chemical composition of the diet with the cat's nutrient requirements.

Regardless of the chemical composition of the diet, the nutrients must be present in forms that are digestible enough to be made available to the animal. Nutrient digestibility is measured by deducting the amount of the nutrient found in the feces from that present in the food.[60] The difference, for fat and carbohydrate, is assumed to have been absorbed by the animal. Protein presents a special case because amino acids not immediately used for protein synthesis after absorption are degraded. The carbon skeleton is metabolized to provide energy and nitrogen is excreted in the urine. Thus, the amount of usable protein available to the

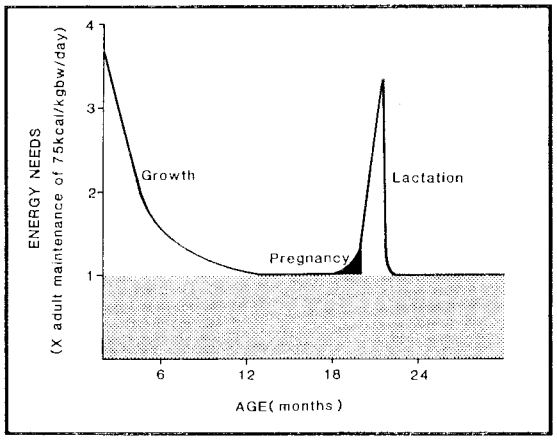
animal is the difference between the dietary level and the sum of fecal and urinary nitrogen losses. While a diet must be complete, balanced and digestible, it is of no value if the cat will not eat it; it must also be sufficiently palatable to be eaten in quantities great enough to support normal function.

It is important to realize that a satisfactory diet for one life stage may be inadequate for another. As Figure 2 shows, the dietary energy requirement varies with the stage of the cat's life, with the needs for lactation and early growth being nearly 3 times greater than for maintenance as adults. Changes in the level of need for other nutrients at different life stages are not as well understood, but are probably similar to the pattern seen with energy re-

Table 1. Current NRC and corrected recommendations for the nutrient content of cat food based per kg of body weight and per 300 Kcal of energy required.

Nutrient	Unit	Per kg	NRC Recommended Amount/300 Kcal	Correction Factor	Corrected Recommended Amount/300 Kcal
Protein	g	240	14.4	1.3	18.7
Arginine	g	10	2.0	1.3	2.6
Histidine	g	3	0.6	1.3	0.8
Isoleucine	g	5	1.0	1.3	1.3
Leucine	g	12	2.4	1.3	3.1
Lysine	g	8	1.6	1.3	2.1
SAA	g	7.5	1.5	1.3	2.0
Methionine	g	4	0.8	1.3	1.0
Phe + Tyr	g	8.5	1.7	1.3	2.2
Phenylalanine	g	4	0.8	1.3	1.0
Taurine	mg	400	80.0	10.0	800.0
Threonine	g	7	1.4	1.3	1.8
Tryptophan	g	1.5	0.3	1.3	0.4
Valine	g	6	1.2	1.3	1.6
Fat	g	100	20.0	1.0	20.0
Arachidonic acid	mg	200	40.0	1.5	60.0
Linoleic acid	g	5	1.0	1.5	1.5
Calcium	g	8	1.6	1.0	1.6
Phosphorus	g	6	1.2	1.0	1.2
Magnesium	mg	400	80.0	1.0	80.0
Potassium	g	4	0.8	1.0	0.8
Sodium	mg	500	100.0	1.0	100.0
Chloride	g	1.9	0.4	1.0	0.4
Iron	mg	80.0	16.0	1.3	20.8
Copper	mg	5.0	1.0	1.3	1.3
Iodine	μg	350.0	70.0	1.3	91.0
Zinc	mg	50.0	10.0	1.5	1.5
Manganese	mg	5.0	1.0	1.5	1.5
Selenium	μg	100.0	20.0	1.0	20.0
Vitamin A	IU	3333.0	666.0	1.5	1000.0
Vitamin D	IU	500.0	100.0	1.5	150.0
Vitamin E	IU	30.0	6.0	2.0	12.0
Vitamin K	μg	100.0	20.0	1.0	20.0
Thiamin	mg	5.0	1.0	10.0	10.0
Riboflavin	mg	4.0	0.8	1.6	1.3
Pyridoxine	mg	4.0	0.8	1.6	1.3
Niacin	mg	40.0	8.0	1.6	12.8
Pantothenic acid	mg	5.0	1.0	1.6	1.6
Folic acid	ug	800.0	160.0	1.6	256.0
Biotin	ug	70.0	14.0	1.6	22.4
Vitamin B_{12}	ug	20.0	4.0	1.6	6.4
Choline	g	2.4	0.5	1.6	0.8

Figure 2. The energy requirement of a cat during various stages of life. Over 3 times more energy is required to satisfy the additional requirements of rapid growth and lactation.



quirements. Subtle dietary nutritional defects are often apparent only during these periods of greatest nutritional stress, when one must be most careful with the quality of the diet provided.

Nutrient Classes

Cats, like all animals, require 6 classes of nutrients: water, energy, protein, essential fatty acids, minerals and vitamins. The following discussion presents a general overview of each class. Detailed presentations of the nutrition of each individual nutrient in the cat are available elsewhere.[61,67]

Water: Water is the medium in which the reactions that maintain life occur. Animals can live for many weeks without food but die in 2-3 weeks, or sooner, without water.[74] While cats appear to tolerate dehydration better than dogs do, acute loss of 20% of body water is usually fatal. By contrast, they can survive the loss of nearly all their glycogen and fat reserves and half their protein mass. Because of the importance of adequate water intake, a constant source of fresh, clear water should still always be provided, regardless of the food source.

Daily water needs are estimated by assuming that the water needed in milliliters is equal to the metabolizable energy requirement in kilocalories. Animals get water from 3 sources: water contained in the food, drinking water, and water produced in the body when foods are metabolized. Canned diets provide enough water so that cats consuming them may rarely drink;[49] drinking is the primary route of water intake in cats fed dry or soft-moist diets. This may create problems because cats are relatively insensitive to dehydration. Dogs drink when as little as 4% of normal body water is lost, while cats may lose as much as 8% of body water before drinking.[74] The ratio of water to food intake of cats fed dry diets is about half that seen when canned foods are fed.[49] The relative lack of thirst sensitivity may be one reason why cats form sterile struvite crystals in the urinary bladder more readily than other species. Their urine tends to be much more concentrated than the urine of many other species, and this increases the solute concentration and favors crystal formation.

In addition to the water cats take in with food or by drinking, "metabolic water" from the metabolism of nutrients provides about 10% of the total daily water intake.[2] About 10-13 g of water are produced from oxidation of each 100 kcal of metabolizable energy in a mixed ration.

Water is lost in 2 different ways: direct urinary and fecal losses (approximately 75%), and "insensible losses" of evaporation from the respiratory tract, mucous membranes and skin. Cats, having a metabolism similar to that of desert animals, evolved to conserve water. They can concentrate their urine to very high levels (1.080 g/ml) and absorb fecal water in their lower small bowel as well as in their colon. Evaporation of water from the skin and mucous membranes of the oral and respiratory cavities is minimal. These physiologic features tend to protect them from excessive water loss.

The rate of insensible water loss is determined primarily by the environmental temperature and amount of exercise. Water loss from the kidneys and bowel varies greatly, depending on the dietary intake of water and the level of insensible loss. In normal animals, water intake and excretion balance vary closely, with daily body weight usually varying less than 1%.[17] In addition to normal losses, increased water loss in ill animals can occur from vomiting, diarrhea, burns and hemorrhage. Water loss by insensible routes is increased by fever, hyperventilation and burn wounds.

Energy: The primary drive for food intake in cats is to meet energy needs. When

energy needs are met, cats stop eating. As the current high incidence of feline obesity demonstrates, this statement says nothing about at which state of body condition energy "needs" are met. Essential nutrients must be present in the diet in amounts sufficient to meet the animal's needs before the point where the energy requirement is met. Nutrient requirements are presented in Table 1 as a percentage of the energy requirement to reflect this basic relationship. If over 100% of the energy requirement is consumed before the required amount of a given nutrient is provided, the diet is deficient in that nutrient.

Energy is required for all functions of the body, and needs are met in the order of priority for survival. Basal metabolism is the energy required for maintenance of muscle tone and transmembrane gradients, and for protein turnover. The basal energy requirement makes up about two-thirds of the total amount of energy needed for maintenance of the cat.[61] Basal metabolism and work associated with food assimilation, temperature maintenance and minimal activity make up the animal's maintenance energy requirement. It is only after maintenance energy needs are met that growth, reproduction or work can occur. Maintenance energy requirements of cats are presented in Table 2, as are the increments in the requirement for various productive activities.

Energy is derived from the catabolism of ingested carbohydrate, protein and fat. The energy content of a food can be expressed as gross energy, digestible energy or metabolizable energy. Gross energy is the amount of heat given off when the food is combusted in a calorimeter. Digestible energy is the gross energy of the food minus the gross energy of the feces, and metabolizable energy is the gross energy of the food minus the sum of fecal and urinary energy.[68]

Digestible and metabolizable energy values are equivalent for carbohydrate and fat. Energy lost in urinary nitrogen, however, results in metabolizable energy values of protein that are about 90% of digestible energy values. Carbohydrate and protein in commercial foods provide about 3.5 kilocalories (kcal) of metabolizable energy per gram of nutrient, while fat provides about 8.5 kcal per gram.[64]

There is no recognized requirement for carbohydrate as an energy source, but the same is not true for protein and fat. Protein provides amino acids and nitrogen for synthesis of many compounds in the body, while fat provides essential fatty acids, insulation and a storage form of energy. It is important to remember, however, that all energy sources are equal until energy needs are met. Protein and fat are used for energy until the basal need for energy is met, and only thereafter can they fulfill their unique nutritional functions.

Commercial dry cat foods contain about 3.5-5 kcal, semimoist foods about 2.7 kcal, and canned foods 1.0-1.5 kcal per gram food. The variation within types of food is primarily due to differences in fat content. A 4-kilogram adult cat (9 lbs) at maintenance requiring 300 kcal per day (75 kcal/kg body weight) would thus consume about 100 g (1 cup) of dry or semimoist food, or 300 g (2 6-oz cans) of canned food per day. The actual amount of food eaten varies among cats of equal weight because of differences in metabolic rate and activity level.

Table 2. Daily energy intake requirements for cats of different ages, gender and activity.

	MALES		FEMALES	
Age	Wt (lb)	Kcal/day	Wt (lb)	Kcal/day
10 wks	2.4	275	2.0	225
20 wks	5.5	325	4.0	250
30 wks	7.5	350	6.0	270
40 wks	9.0	320	6.5	240
Adult				
inactive	32 Kcal/lb/day		32 Kcal/lb/day	
active	36 Kcal/lb/day		36 Kcal/lb/day	
pregnant	——		45 Kcal/lb/day	
lactating	——		64-128 Kcal/lb/day	

Protein: Protein is required to maintain the supporting structure of the animal (muscle, bone, ligaments, tendons). Many of the functional components of the body, including enzymes, plasma proteins, many hormones and some neurotransmitters, are also proteins. Body proteins are in a "dynamic steady state" of constant synthesis and breakdown. The greater the importance of a protein in metabolic regulation, the more rapid its turnover.[82] Such proteins as enzymes and hormones turn over much more rapidly, therefore, than structural proteins. Rapid turnover ensures prompt response to changing situations and enables a limited amino acid pool to be used with optimal efficiency.[86] Reuse of amino acids as new protein is not completely efficient, however, so some protein is constantly lost from the body. The more rapid the turnover rate, the more rapidly amino acids are lost.[92] During growth or healing, protein turnover and related processes can account for as much as 40% of the total resting energy expenditure.[93]

Dietary protein provides 2 essential components, amino acids and nitrogen, for synthesis of the many nitrogen-containing compounds of the body. Cats require 20 amino acids to synthesize all the needed body proteins. Of these, 10 can be synthesized in the liver from carbon and nitrogen. These are called dispensable amino acids because they need not be present in the diet. The other 10 cannot be produced in sufficient quantities (or not at all) to meet the animal's needs, and are thus called indispensable amino acids. For 2 of the indispensable amino acids, phenylalanine and methionine, about half of the requirement may be met by the dispensable amino acids tyrosine and cystine, respectively. Concentrations of the indispensable amino acids required for growth in the cat are presented in Table 1.

The dietary protein requirement of cats depends on the digestibility, amino acid pattern and quality of the protein. Protein digestibility in pet foods is about 80% for dry foods, 85% for semimoist and canned foods containing large amounts of cereal grains, and 90% for canned diets with meat as the primary protein source. Digestibility is influenced both by the source of the protein and how it is processed. Use of excessive heat during food processing can result in cross-linking of amino acids and sugars, which decreases their availability. Proteins can also be oxidized by high dietary levels of polyunsaturated fatty acids, reducing the availability of histidine, methionine and tryptophan.

The higher the digestibility of the dietary protein and the more closely its amino acids match the animal's needs, the higher the protein quality of a food. Protein quality is sometimes evaluated using the biologic value of the protein, which is the amount of the protein retained by the body divided by the amount absorbed. Some examples are egg, 100% (by definition); fish, 92%; beef, 78%; soybean meal, 67%; whole wheat, 48%; and whole corn, 45%.[60]

Protein in cat foods comes from animal and plant sources. Animal protein is generally more expensive and often, but not always, of higher quality than plant proteins. The amino acid requirements presented by the NRC were determined by feeding highly purified diets to growing animals and measuring nitrogen (protein) retention. Protein in commercial cat foods originates from a variety of plant and animal sources of differing digestibility and quality. The amount of protein in commercial diets is higher than the NRC minimum to account for these differences and to provide a "margin of safety" over the requirement.

Minimum protein requirements for growth and maintenance are about 17% and 10% of energy (kcal ME), respectively.[61] These values are half or less of protein levels seen in common cat foods. A safe assumption is that pet foods are about 80% digestible, overall, and that protein is at least 80% usable. If one divides the minimum requirements for growth and nitrogen balance by 0.64 (0.8 x 0.8), one gets minimum protein needs of 27% and 16% of calories for growth and maintenance, respectively. Protein needs for late gestation and lactation are at least as great as growth requirements. About 1-1.5 times these minimums, depending on the quality of protein, should meet the needs of nearly all cats.

The relatively high minimum protein requirement of cats provides another example of their metabolic uniqueness. The minimum protein requirement of cats for growth is twice, and for maintenance 3 times, the requirement of dogs. Most of the

increased requirement is for nitrogen, because cats are unable to adjust the levels of liver enzymes responsible for ureagenesis in response to changes in dietary protein levels.[79] While requirements for most amino acids are similar, cats require more arginine than dogs due to lower levels of intestinal enzymes for synthesis of arginine precursors.[64,78] The beta-amino acid taurine is also required in the diet of cats because of inadequate synthesis and obligatory intestinal losses. Though other species produce both glycine and taurine conjugates of cholesterol for secretion as bile acids, cats can only use taurine. Bile reabsorption is not 100% efficient, so some taurine is continually lost via the intestine.

Fats and essential fatty acids: Fats are esters of fatty acids and glycerol. They provide a concentrated source of energy, improve palatability, facilitate absorption of the fat-soluble vitamins and provide essential fatty acids. Essential fatty acids are required for normal membrane function, reproduction and skin integrity. Dietary fat is derived from both animal and vegetable sources.

Feline dietary fat requirements depend upon the function of interest. No fat requirements have been determined for energy, which may be provided completely from carbohydrate and protein in the diet. Palatability is enhanced by increasing levels of some fats, but cats have been maintained on very low fat diets at acceptable levels of intake. While the essential fatty acid requirements of cats have not been determined exactly, they are about 2.5% of dietary energy for linoleic acid and 0.04% for arachidonic acid.[61] Amounts of dietary fat that would provide these levels of essential fatty acids would also ensure adequate absorption of fat soluble vitamins.

Commercial cat diets generally contain 9-20% crude fat, though cats have been fed diets with fat levels as high as 64% without evidence of maldigestion or cardiovascular disease. Fat digestibility may depend on both the composition and method of processing involved in production of the diet. The apparent digestibilities of "ether extracts" were 79% for dry foods, 88% for canned foods and 92% for semimoist foods.[54] Thus, a dry diet (350 kcal/100 g dry matter) containing 10% fat that was 80% digestible would contain 8 g of usable fat per 100 g of food. This amount of fat would supply about 20% of the dietary energy, since fat provides about 9 kcal/g, more than twice the amount provided by carbohydrate or protein.

Both the type and dietary level of fat influence the palatability of cat foods. Animal fats improve the palatability of cat diets.[48] One study showed that cats tend to prefer unbleached tallow and yellow grease over bleached tallow, and diets containing bleached tallow are preferred to those with butter, oil or chicken fat.[51] No preference was found between bleached tallow and (partially hydrogenated) vegetable oil. They also found that cats preferred yellow grease at a dietary level of 25% over 10% or 40%. When bleached tallow was the fat source, 40% was preferred over 12% or 25%. This may have been due to effects of the type of fat on the texture of the resulting diet. It is worth noting that the diet of feral cats probably contains about 40% fat, virtually all of animal origin.

Some dietary fat is required for normal absorption of fat-soluble vitamins because ingestion of fat stimulates release of lipases from the pancreas and bile from the gallbladder. Taurocholic acid in bile emulsifies ingested fats, allowing the lipases to hydrolyze triglycerides to 2-monoglycerides and free fatty acids. These form particles called micelles that are absorbed into intestinal mucosal cells. Micelle formation is also required for fat-soluble vitamin absorption. Absorbed fatty acids and fat-soluble vitamins are esterified by small intestinal mucosal cells into chylomicrons, the form in which triglycerides are transported from mucosal cells through the lymphatics to the systemic circulation. Defects in fat digestion, absorption or lymphatic transport may predispose cats to deficiencies of fat-soluble vitamins if the condition is chronic.

The essential fatty acid requirements of cats are another demonstration of the uniqueness of their carnivorous lifestyle. The cat requires a dietary source of both linoleic acid and arachidonic acid, a requirement it shares with other species, such as the lion, turbot and mosquito.[61] The requirement for both fatty acids (noncarnivorous species appear to require only linoleic acid) by carnivores arises from their inade-

quate enzymatic capacity to synthesize arachidonic acid from linoleic acid. In the liver of most mammals, arachidonic acid synthesis from linoleic acid occurs first by addition of another double bond, addition of a 2-carbon fragment, and finally another double bond. Cats and other carnivores lack the ability to add the first double bond. Studies using isotopically labeled linoleic acid have shown that less than 0.5% of the label appeared in fatty acids containing 4 double bonds.[85] Arachidonic acid is found only in animal tissues, while linoleic acid is present in both animal fats and plant oils.

Minerals: Mineral nutrients are divided into 2 classes: macrominerals (>0.05% of the diet) and microminerals (<0.05% of the diet). Macrominerals comprise the mineralized portion of the skeleton, maintain electrolyte and acid-base balance, and provide electrochemical gradients for nerve cell function. Microminerals are primarily enzyme cofactors. While mineral requirements for growth have been estimated for cats (Table 1), there is very little information available on needs for other life stages. Cats receive minerals via the diet or from supplements provided by the owner. Dietary sources include minerals present in natural ingredients and those added by the manufacturer to meet recommended allowances.

Mineral nutrition is complex because many interactions among minerals may affect absorption from the intestine. For example, dietary excesses of calcium or phosphorus may bind to each other in the intestine, reducing their availability. Because of this interaction, calcium and phosphorus should be present in diets in a ratio of 0.9:1 to 2:1, and at 1-1.5 times the minimum recommended levels. Excesses of macrominerals also reduce availability of micromineral divalent cations, such as copper, zinc and manganese. The source of dietary minerals also affects their availability;[67] calcium and phosphorus are more readily absorbed from animal than plant sources and organic (heme) iron is more bioavailable than iron from inorganic sources. These interactions help explain the necessity for balance among nutrients; excesses, deficiencies and imbalances all have pathologic consequences.

Vitamins: Vitamins are also divided into 2 broad groups: fat-soluble vitamins A, D, E and K; and the water-soluble or B-complex vitamins thiamin, riboflavin, niacin, pantothenic acid, pyridoxine, folic acid, biotin and B_{12}. Vitamin C, also a water-soluble vitamin, is unnecessary in the diet of cats because adequate amounts are synthesized in the liver.

Vitamins are required in minute amounts for normal membrane function (vitamins A and E), bone metabolism (vitamin D), antioxidation (vitamin E), blood clotting (vitamin K), as enzyme cofactors (vitamin B complex), and collagen integrity (vitamin C). Vitamin nutrition in cats is even less understood than mineral nutrition, as few controlled studies have been conducted. As a practical matter, vitamins A and D are of primary concern because of the potential for toxicity if excessive amounts are consumed.

The minimum requirements of cats for the B vitamins thiamin and niacin are high. While part of the niacin requirement of dogs may be met by tryptophan, niacin from this source is not available to cats because of the rapid removal of a metabolic pathway intermediate. Cats also lack the intestinal enzyme dioxygenase that converts carotene, a plant precursor of vitamin A, into the vitamin A molecule. Thus, cats require preformed vitamin A, which is found only in animal tissues.

Feeding Behavior

The feeding behavior of cats does not appear to follow the daily rhythmicity seen in other species. When fed *ad libitum*, cats generally eat 12-20 meals per day, evenly spaced over the 24-hour period.[51,65] In feral cats, these meals consist of small birds, mammals and insects. Mice are common prey of domestic cats, and each mouse provides about 30 kcal of food energy. The average adult cat would thus need to consume 10-15 mice per day to meet the daily energy requirement. This behavior pattern is quite different from that of infrequent consumption of large meals seen in great cats.[34]

Cats appear to control their food intake based on caloric needs, though they appear to be more sensitive to the taste and physical form of the diet than other species.[51] Cats generally choose foods with a flavor or physical character that is novel to them. Some cats, however, refuse to eat novel

foods, particularly if they have been fed a single food source previously. A natural aversion may make it difficult to introduce new foods into the cat's diet. If a diet change must be instituted, the new food should be offered as an increasing proportion of the previous diet over a period of a few days. Alternatively, the diet may be switched abruptly. If no food is consumed for 3 days, one should return to the previously accepted diet for 3-4 days before reintroducing the new food. The new food should be accepted after 2-3 such introductions, by which time it will no longer be novel.

Palatability of cat foods is enhanced by moisture, animal fats, protein hydrolysates, meat extracts, the amino acids alanine, histidine, proline and lysine, and acidity.[94] The preference for protein breakdown products and acidity may explain the use of "digest" as an ingredient in nearly all dry and semimoist cat foods. Digest is "a microbiologically stable material resulting from digesting animal tissues . . . ."[3] Digest is produced by enzymatic hydrolysis of animal tissues and byproducts that yields a viscous solution of amino acids, peptides and fatty acids. Digest also contains significant quantities of phosphoric acid, which is added to stop the enzymatic degradation process and to preserve the product. Digest is sprayed onto the outside of cat foods at four to ten percent of the final finished product, or is incorporated directly into the food. Digest can enhance the palatability of foods by as much as 4-10% over the uncoated product.[98]

Preparation of Cat Foods

Types of Cat Food

There are basically 3 forms of cat food: dry, semimoist and moist (canned). In 1986, $250 million worth of semimoist cat food, $750 million worth of dry food, and $1.2 billion worth of canned cat food were sold in the United States.[95] Proportionately more canned food has been fed to cats over the last few years, probably because of its greater palatability and consumer appeal. Each type of food uses a standard method for controlling spoilage. Since the quality of cat food does not depend on its physical form, good and bad types of all 3 forms are sold.

Dry, semimoist and canned foods differ greatly in their average energy, water, protein and fat content (Table 3). Since the physical forms of dry, semimoist and canned foods are very different, making direct comparisons of levels of energy, protein and fat among these different forms of food may be quite misleading. For example, the amount of protein per unit of product weight in dry cat foods is about 35%, and in canned foods about 10%. Canned foods contain more water. A much more accurate way to compare the nutrient content of different forms of cat food is on a dry-matter basis.

To compare nutrient contents on a dry-matter basis, one divides the nutrient of interest by the total dry matter. For example, dry foods are about 90% dry matter, so 35% protein divided by 90% dry matter equals 38% protein on a dry-matter basis. Canned foods are closer to 25% dry matter, so 10% protein divided by 25% is equal to 40% protein on a dry-matter basis. Calculated this way, canned food actually contains more protein than the dry food on a dry-weight-adjusted basis (Table 3). Canned foods are more expensive, however, because the consumer is also paying for the water and additional processing.

Another way to compare dietary constituents is on an energy basis. Using metabolizable energy estimates of 3.5 kcal/g for dry and 1 kcal/g for canned food, 100 g of dry food provides 350 kcal of energy, while the same amount of canned food only provides 100 kcal of energy. Therefore, 3.5 times more canned food than dry food must be fed to provide the same amount of energy. Because nutrient needs can only be met once energy requirements are provided, and because of variations in the nutrient and moisture content among diets, nutrient

Table 3. Average nutrient content of US cat foods.

Form	Energy (Kcal/100 g)	Water (%)	Protein (% Dry Matter)	Fat
Dry	350	10	25	10
Semi-moist	280	35	30	12
Canned "ration"	125	75	35	15
Canned "gourmet"	140	75	50	25

comparisons between foods are most meaningful when made on an energy basis.

Each form of cat food has advantages and disadvantages. Dry foods are predominantly extruded, expanded products. Extrusion is a process whereby dry ingredients are cooked with steam and pressure to improve the digestibility of the ingredients and kill any dangerous bacteria. The heated food is then forced (extruded) through a small opening in the end of the pressure chamber. The sudden change in pressure when the food exits the chamber causes the gelatinized carbohydrate to expand.

The major advantages of dry foods are lower cost, greater convenience and contribution to dental health. Dry foods may be left out for the cat to "self-feed" for longer periods than other forms without spoiling, and their dryness "brushes" the animal's teeth, reducing tartar accumulation and dental disease. Disadvantages of dry foods include the generally lower energy density and the possibility of decreased palatability and digestibility of the dry ingredients commonly used in these formulas. Further, the level of available energy in some dry foods may make it difficult for the animal to eat enough food to meet its needs during periods of nutritional stress, such as rapid growth and lactation. Unopened packages of dry foods tend to spoil more quickly than semimoist or canned foods in humid climates.

Semimoist foods are produced by similar processes as those for dry foods. The primary difference is that chemical preservatives are added to prevent spoiling while retaining a soft, moist character. Compounds used to preserve semimoist foods include propylene glycol, acid and sorbitol. Propylene glycol binds water to make it unavailable for bacterial growth. Phosphoric, hydrochloric and malic acids are added to bind water and inhibit bacterial growth. Sorbitol is added to decrease fungal growth. These compounds make it difficult to make recommendations about semimoist foods for cats. Their acidity makes bladder stones in cats fed these foods highly unlikely, but propylene glycol may cause oxidative damage to the red blood cells of some cats (though the clinical significance of this is not clear). As with dry foods, semimoist foods may be self-fed. They are highly digestible and palatable, and can be formulated to include fresh animal tissue. The disadvantages of semimoist foods are that they may be expensive and do not help keep the teeth clean.

Canned foods are also palatable and digestible. Any ingredient may be used in canned foods because heat and pressure are applied to sealed cans to ensure sterility. This method of processing also generally results in the greatest loss of nutrients, which must be compensated for in product formulation. Two major forms of canned food are produced for cats: "ration" diets, which are made up of animal tissue, soy and cereal grains, and "gourmet" diets, which are primarily meat with vitamins and minerals added to balance the diet. Gourmet products must be carefully formulated because muscle meat is a poorly balanced, incomplete food by itself. Cats in the wild eat parts of the viscera and bone of prey, which results in a more balanced diet. Advantages and disadvantages of canned foods are the same as for semimoist foods, with the additional disadvantage that if they are opened and left out they will spoil.

Variability in Commercial Cat Food

Some pet food manufacturers use what is known as "least-cost formulation" to compound their diets. This means that the proportion and quality of ingredients may fluctuate with ingredient prices. The final formula at any given time thus depends on a computer program, which may or may not generate the same formulation as the one originally tested. While variations are generally minor, least-cost formulation may explain why some variability from batch to batch is noted by the observant owner. Manufacturers of premium cat foods use fixed formulas, which do not change according to ingredient prices. This is one of the reasons for the higher price of these foods, which are often sold only by pet shops.

Cat Food Labeling

The label on a package or can of cat food is a legal document, and pet food labeling in the United States is based on rules established by the Association of American Feed Control Officials (AAFCO) to ensure compliance with federal and state feed regulations. Regulations that apply to pet food la-

beling and testing of foods for nutritional adequacy are published in the AAFCO manual.[98] This manual, updated yearly, also provides definitions of terms. For example, "complete" is defined as "a nutritionally adequate feed for animals other than man; the specific formula is compounded to be fed as the sole ration and is capable of maintaining life and/or promoting production without any additional substance being consumed except water." "Balanced" is a term that may be applied to a diet, ration, or feed having all the required nutrients in proper amount and proportion based upon recommendations of recognized authorities in the field of animal nutrition, such as the National Research Council, for a given set of physiological animal requirements. "The species for which it is intended and the functions such as maintenance or maintenance plus production (growth, fetus, fat, milk, eggs, wool, feathers, work) shall be specified." Though label information is important, it must be remembered that the amounts of all of the 43 required nutrients are not listed on the label of cat foods, and even if they were, labels do not in themselves provide all the information necessary to evaluate a food properly.

The label of commercial cat foods must include the product name, guaranteed analysis, ingredient content, manufacturer's or distributor's name and address, net weight, and "a claim that the pet food meets or exceeds the requirements of one or more of the recognized categories of nutritional adequacy: gestation, lactation, growth, maintenance, and complete for all life stages, as those categories are set forth in regulations PF2(L) and (M) unless the food is designated solely for intermittent or supplemental feeding, or to be used on the advice of a veterinarian."

The required claim of nutritional adequacy may be met in either of 2 ways. The first is by analysis. This means that if chemical analysis of the food shows that it contains levels of nutrients that exceed the NRC recommended minimums, it may claim nutritional adequacy. Unfortunately, chemical analysis is of very little practical value. There is no way to know if the nutrients are present in the forms that are available to the animal, if nutrient excesses or other toxic substances are present, or if the animal would eat the food if it were presented. The other method of establishing a nutritional claim is by passing a protocol test. These feeding tests are the only valid way to ensure that the food can actually meet the nutritional needs of cats to which it is fed. The problem with the label assurance as it is currently required is that there is no way to tell how it was met. Until the regulation is changed to correct this problem, the only way to know for sure that the food has passed protocol tests is to write the manufacturer (whose address must be on the label).

A list of ingredients must also be present on the label. Listed ingredients fall into 4 major categories: water, energy sources, protein sources, and vitamins and minerals added to balance the food. Table 4 shows the major sources of energy and protein in United States pet foods for 1982 (the most recently available figures). Ingredient names have specific legal definitions, which are also presented in the AAFCO manual. Examples of some of these definitions are presented in Figure 3. The definitions are somewhat imprecise to allow for normal variation in feedstuffs and processing procedures. AAFCO also requires that ingredients be listed "in descending order by their predominance by weight." "Descending order" must be evaluated carefully, however, because ingredient lists can be misleading. For example, a meat protein source followed on the list by 2-3 separate grain sources may indicate that total grain, not meat, is the primary ingredient!

A guaranteed analysis that lists minimum amounts of crude protein and fat and maximum amounts of crude fiber and moisture present in the product must also be on the label. While a legal requirement, the guaranteed analysis is of little value for a variety of reasons: analyses for fat and protein are nonspecific, and crude fiber underestimates the indigestible fraction of the food for cats. Further, the numbers are not meant to represent the amount of nutrient present, only the minimum or maximum. More accurate analyses are often available on written request from manufacturers.

Feeding Management

The recommended amounts of various types of food to feed cats of different sizes for adult maintenance activity are given in

Figure 3. Examples of official definitions of feed ingredients established by AAFCO.

48.8 Corn Flour is the fine-sized hard flinty portions of ground corn containing little or none of the bran or germ.

93.2 Wheat Flour consists principally of wheat flour together with fine particles of wheat bran, wheat germ, and the offal from the "tail of the mill." This product must be obtained in the usual process of commercial milling and must contain not more than 1.5% crude fiber.

84.61 Soybean Meal, Solvent Extracted, is the product obtained by grinding the flakes which remain after removal of most of the oil from soybeans by a solvent extraction process. It must contain not more than 7% crude fiber. It may contain an inert non-toxic conditioning agent either nutritive or non-nutritive and combination thereof, to reduce caking and improve flowability in an amount not to exceed that necessary to accomplish its intended effect and in no case exceed 0.5%. The name of the conditioning agent must be shown as an added ingredient. The words "Solvent Extracted" are not required when listing as an ingredient in a manufactured food.

9.2 Meat is the clean flesh derived from slaughtered mammals and is limited to that part of the striate muscle which is skeletal or that which is found in the tongue, in the diaphragm, in the heart, or in the esophagus; with or without the accompanying and overlying fat and the portions of the skin, sinew, nerve, and blood vessels which normally accompany the flesh. It shall be suitable for use in animal food. If it bears a name descriptive of its kind, it must correspond thereto.

9.3 Meat By-Product is the nonrendered, clean parts, other than meat, derived from slaughtered mammals. It includes, but is not limited to, lungs, spleen, kidneys, brain, liver, blood, bone, partially defatted low temperature fatty tissue, and stomachs and intestines freed of their contents. It does not include hair, horns, teeth and hoofs. It shall be suitable for use in animal food. If it bears a name descriptive of its kind, it must correspond thereto.

9.14 Poultry By-Products must consist of non-rendered clean parts of carcasses of slaughtered poultry such as heads, feet, viscera, free from fecal content and foreign matter except in such trace amounts as might occur unavoidably in good factory practice.

51.14 Fish Meal is the clean, dried, ground tissue of undecomposed whole fish or fish cuttings, either or both, with or without the extraction of part of the oil. It must contain not more than 10% moisture. If it contains more than 3% salt (NaCl), the amount of salt must constitute a part of the brand name, provided that in no case must the salt content of this product exceed 7%.

48.14 Corn Gluten Meal is the dried residue from corn after the removal of the larger part of the starch or germ, and the separation of the bran by the process employed in the wet milling manufacture of corn starch or syrup, or by enzymatic treatment of the endosperm. It may contain fermented corn extractives and/or corn germ meal. (Adopted 1936, Amended 1960)

58.18 Bone Meal, Steamed, is the dried and ground products sterilized by cooking undecomposed bones with steam under pressure. Grease, gelatin, and meat fiber may or may not be removed. It must be labeled with guarantees for phosphorus (P) and calcium (Ca). Steamed bone meal must be used in all labeling.

Table 5. Considerably more food is required for nonmaintenance activities, such as pregnancy and lactation (see Table 2). Cats may be fed free choice (*ad libitum*), where food is available at all times, or they may be fed by hand, with the owner determining the size of each meal. Self-feeding is more convenient and in group feeding situations ensures that timid animals are not denied access to food. It has the disadvantage of reducing owner contact with the pet. If cats tend to overeat, however, they should be fed by hand twice daily. Cats vary widely in the amount of food required to maintain normal body weight and should be fed whatever is necessary to maintain optimum body condition. This condition is present when the ribs cannot be seen but are easily felt and the abdomen is trim and not flabby.

Nutrition and Disease

The cause of a nutrition-associated disease may lie with either the diet or the animal. Diet-related nutritional diseases include nutrient imbalances, excesses or deficiencies, and chemical or microbiologic intoxications. These are diet-induced diseases.

Table 4. Ingredients used in pet foods (1982).

Energy Sources	Quantity (tons)	Value (millions of $)
Corn	1348	137
Wheat	422	50
Fats & oils	178	63
Oats	55	7
Brewers & distillers grains	20	6
Protein Sources		
Soybean meal	725	148
Meat, meal & byproducts	528	114
Corn gluten meal	248	48
Poultry, feather & byproducts	119	35
Fish, meal & byproducts	55	18

Many animal diseases are also related to nutrition, but the problem is caused not by the food *per se* but by an adverse response of an individual to an otherwise satisfactory diet. These diseases are called nutrition sensitive. Nutrition-sensitive diseases include obesity, food allergy and primary organ system diseases such as pancreatic, liver or kidney disease. Differentiation between diet-induced and nutrition-sensitive diseases is important because lack of a clear understanding of the distinction between the 2 has resulted in confusion and unfounded nutritional advice. For example, to say that "sugar" is bad for diabetics has led many to draw the (inappropriate) conclusion that "sugar" causes diabetes. Diet-induced nutritional diseases are treated by replacing the defective diet with a diet known to be satisfactory. Attempts to supplement inadequate diets are of no value because if one deficiency is recognized the diet is probably defective in other ways, too. Proper management of nutrition-sensitive disease is more complex, and is an important part of veterinary clinical medicine.

Diet-Induced Diseases

Diet-induced diseases generally result from feeding errors committed by well-meaning owners. Knowledge about cat nutrition and its incorporation into the manufacture of dietarily sound commercial cat foods has been acquired only recently. Many currently inappropriate feeding practices were developed before high-quality proprietary cat foods were available. Adult animals have relatively low nutrient requirements (Table 1), and many survive ingestion of imbalanced diets for years. Poor feeding practices are often recognized only in lactating queens and young growing kittens.

Oversupplementation with vitamins and minerals is a common problem. It is neither economical nor sensible to supplement a poor-quality food, which should be discarded in favor of a high-quality food that needs no supplementation. Another common problem is feeding only one food item, generally meat. Feeding meat as the sole diet causes metabolic bone disease in cats. Cats may also become "addicted" to highly palatable, unbalanced food items, making it extremely difficult to switch them to a satisfactory diet. Feeding large amounts of table scraps is occasionally a problem. Table scraps are rarely nutritionally balanced, and they may upset the balance of a satisfactory cat food. Feeding cats dog food can also result in nutritional deficiencies. The cat's unique nutritional requirements may not be met by dog foods made with insufficient amounts of animal products. In addition to these general problems, a number of specific nutrient deficiencies and excesses may result in diet-induced disease.

Table 5. Amounts of US cat foods to feed per day for maintenance. There is some variation between brands; this represents only a guideline.

Body Weight (kg)	Body Weight (lb)	TYPE OF FOOD Dry (g)	Semimoist (g)	Canned (g)
2	4.4	45	60	130
3	6.6	70	85	190
5	11.0	115	140	320

Hypervitaminosis A: One of the many nutritional peculiarities of cats is their dietary requirement for preformed vitamin A. Neither oral nor intravenously administered beta-carotene, the plant precursor of vitamin A, can be converted to vitamin A.[40] Most mammals have an intestinal enzyme that cleaves dietary beta-carotene into 2 molecules of vitamin A, which are absorbed. This enzyme is absent from the intestine of cats.

The vitamin A requirement of cats in the wild is met by consumption of animal tissue, especially liver. In the late 1950s and 1960s, vitamin A toxicity in cats fed diets made up mainly of liver was reported from areas of South America and Australia.[16,32] The disorder was extensively studied after these reports. Though vitamin A toxicity is currently a minor veterinary problem, it still occurs in cats fed large amounts of liver and/or cod liver oil for months to years. Liver is highly palatable to cats, and many owners trap themselves into feeding large amounts of liver because they want to please their cats. It has also been seen on occasion in cattery cats whose diet is supplemented by so-called "pet mixes" obtained from butchers. Such mixes often contain relatively large amounts of liver, which

some cats may selectively pick out of their diet.

The initial signs of vitamin A toxicity are cervical stiffness and forelimb lameness. The signs are due to new periosteal bone production that restricts joint movement and may pinch spinal nerves exiting from the vertebral foramina (Fig 4). Affected cats resist movement and resent handling. With continued exposure to excessive amounts of vitamin A, the bony changes may extend to the sternebrae, ribs, scapulae, long bones and pelvis. Ankylosis of cervical vertebrae and elbow joints may occur, and affected cats are typically unkempt because the movements of the head necessary for grooming become impossible. Detailed pathologic descriptions of vitamin A toxicity have been presented by a number of workers.[32,83] Switching the cat to a nutritionally satisfactory diet early in the course of the disease may resolve the stiffness and discomfort if ankylosis has not yet occurred.

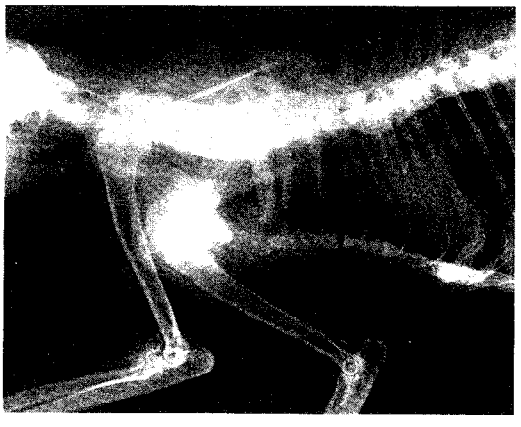
Vitamin E and Thiamin Deficiencies: Diets containing large amounts of fish can cause vitamin deficiencies in cats. Many fish contain a thiaminase in their tissues that destroys thiamin. Improperly processed foods containing fish have caused thiamin deficiency and even death in cats. Cooking destroys the enzyme, thus protecting thiamin. Some processing techniques, especially canning, can also destroy large amounts of thiamin, so manufacturers must add excesses to the diet to ensure adequacy. In addition, some cats may have genetic defects that make them more susceptible to diets that are relatively deficient or borderline in thiamin content (see chapter on genetic diseases).

Signs of thiamin deficiency include an initial period of decreased food intake and salivation that may appear within 1-2 weeks of ingestion of a deficient diet and last for several days.[33,46] This is followed by a period of brief seizures. During this period, ventroflexion of the head and loss of normal righting reflexes may occur. Retinal veins are dilated and retinal hemorrhages may be seen. Abnormalities of the heart have also been reported during this stage, including sinus irregularity and (usually) bradycardia.[46] Treatment during this period with thiamin, 5 mg orally or 1 mg parenterally, results in disappearance of all signs within 24 hours. Untreated cats develop extensor rigidity, subside into coma and die within 48 hours of these terminal signs.

High levels of fish in cat food can also cause deficiency of vitamin E.[19,22] Fish contain high concentrations of polyunsaturated fatty acids, which are easily oxidized. A primary function of vitamin E is to prevent this oxidation, and in the process excessive amounts of vitamin E are consumed. It must be added in larger amounts by the manufacturer to all-fish diets to ensure that a deficiency does not occur. Vitamin E deficiency causes steatitis or yellow fat disease.[22] Signs of steatitis include depressed appetite and hypersensitivity to touch. The fever usually present does not respond to antibiotics. As the disease progresses the subcutaneous fat becomes firm and nodular due to accumulation of peroxidized polyunsaturated fats and the abdominal fat often feels like rolled-up wads of cellophane. Inflammation and necrosis are also present. Treatment consists of a change in diet, with enteral nutritional support until the appetite returns. Corticosteroids should be administered to decrease the inflammatory reaction. Vitamin E acetate may be given at 100 mg per day for 1-2 weeks to replace body stores.

Taurine Deficiency: The beta-amino acid taurine is required in the diet of cats. Taurine is normally synthesized from methionine via cysteine in the liver and other tis-

Figure 4. Radiograph of an adult cat that had been fed only liver for several years shows bridging ossification of axial and appendicular joints. Many of the cervical and thoracic vertebrae are fused, and such joints as the elbow and shoulder are badly affected. (Courtesy of Dept Radiol, Sch Vet Med, Univ California, Davis)



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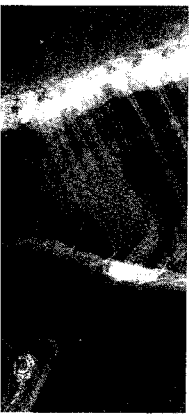


sues of mammals. This synthesis occurs in the cat, but not at a rate sufficient to maintain adequate stores.[7] Additionally, bile salt production in the cat is an obligatory route of excretion for taurine because cholesterol is conjugated only with taurine, rather than glycine and taurine as in other species. The taurine requirement is also influenced by the dietary concentrations of methionine and cysteine, decreasing with increasing levels of sulfur-containing amino acids.

Taurine deficiency has resulted in central retinal degeneration in cats.[42,43] The disease occurs in older kittens (>6 months) and adult cats because months are required for the deficiency to develop. Electroretinographic abnormalities are the first lesions to appear (3 months), with ophthalmologically observable damage to the reflective tapetum, darkening followed by hyperreflectivity, occurring only after neural damage is extensive (6 months) (Fig 5). Total blindness may take 2 years to develop.

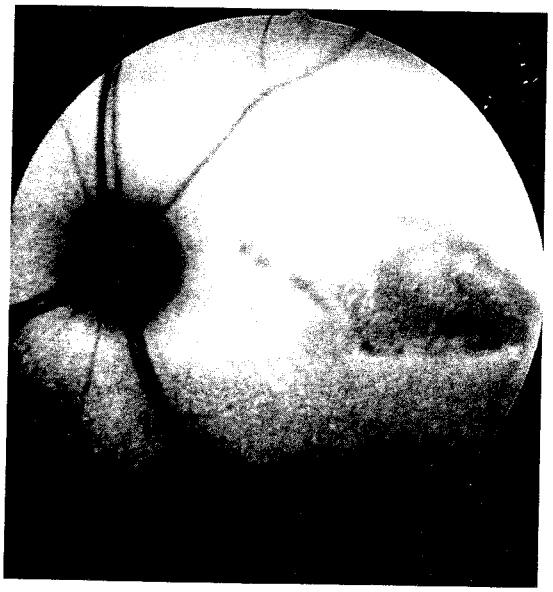
Clinical cases of central retinal degeneration have resulted from feeding cereal-based dog foods to cats for prolonged periods.[1] Taurine is present only in animal tissues, with high concentrations present in meat (200-400 mg/kg) and very high concentrations in shellfish (up to 2500 mg/kg).[76] Thus, the carnivorous nature of cats would prevent development of dietary taurine deficiency in the wild. The 1986 revision of the NRC nutrient requirements of cats suggested a requirement of 400 mg taurine/kg of diet for growth and maintenance, and 500 mg/kg diet for reproduction.

The above recommended amounts of taurine may be sufficient to prevent retinal damage but are inadequate to prevent other manifestations of taurine deficiency in cats. One study showed that a previously recognized disease of the heart muscle (idiopathic dilated cardiomyopathy) was associated with low plasma taurine concentrations and was treatable by oral administration of taurine.[71] This disease had been called idiopathic because its cause was unknown. Before 1988, it was the cause of many thousands of deaths each year among kittens and adult cats. Taurine concentrations in the plasma of cats presented for treatment of dilated cardiomyopathy were only 10% of normal levels, and some of these cats also had the eye lesions characteristic of taurine deficiency. The affected cats had been fed a variety of commercial diets, which by analysis contained "adequate" or NRC recommended concentrations of taurine. When the cats were provided supplemental taurine (500 mg twice daily) and drugs to control signs of heart failure, all were clinically improved during the first 2 weeks of taurine supplementation. Echocardiographic signs of damage to the heart muscle began to diminish after 3-4 weeks of supplementation. When pet food companies added more taurine to their diets, the taurine concentrations returned to normal and the incidence of cardiomyopathy plummeted.

Dilative cardiomyopathy due to deficient dietary taurine is manifested anytime from before birth to late life. Severely affected fetuses die *in utero* or kittens die during the first few weeks of life. Cardiomyopathy in kittens is manifested mainly by failure to thrive, acute congestive heart failure and death. Some affected kittens have difficulty breathing and are cyanotic and depressed with fluid flowing from their mouth and nostrils. Most affected kittens die quickly without specific signs of heart disease.

Older cats show more chronic signs of heart failure, including exercise intolerance,

Figure 5. Retina of a cat fed a taurine-deficient diet. The lesion consists of a circular, darkened and thinned area in the area centralis of the retina; hence the name central retinal degeneration.



fatigue, difficulty in breathing and fluid effusions in the chest and/or abdominal cavity. The heart beat is often rapid, with weak pulses. The heart is grossly enlarged on thoracic radiographs. On postmortem examination, the heart is dilated, flabby and thin-walled, and the inner heart surfaces are whitened by increased elastic tissue formation (Fig 6). The liver is often enlarged, congested and mottled (nutmeg-like), and small to large amounts of red-tinged fluid may be present in the pericardial sac, chest cavity or abdomen.

Nutritional Secondary Hyperparathyroidism: The most common diet-induced disease of cats related to mineral nutrition is nutritional secondary hyperparathyroidism (NSHP).[6,70] This is a metabolic bone disease caused by consumption of homemade diets, usually all meat, that are absolutely or relatively (excess phosphorus to calcium ratio) deficient in calcium.[70] Though the dangers of overfeeding cats meat has long been stressed, the problem still occurs from time to time in catteries.[70] Supplementation of kittens' diets with meat often causes them to grow more rapidly and to appear more robust. Most cattery owners do not deliberately feed all meat to their kittens, but rather mix it with commercial food. The meat component is usually much more palatable than the commercial food, however, and the kittens selectively pick out the meat portion to eat.

Since the queen's milk is nutritionally sound, NSHP occurs only after the kittens are weaned onto solid food. Most affected kittens are 10-16 weeks of age when the first clinical signs appear. Kittens with NSHP usually show generalized stiffness, lameness (usually more prominent in the hind limbs) and joint pain on palpation. Constipation and abdominal distention may also be observed.[70] The constipation may be due to decreased function of the intestinal smooth musculature and, in some cases, narrowing of the pelvic canal. Clinical signs are due to generalized demineralization of bone, pathologic fractures (usually of long bones) and generalized myopathy.[70]

When animals are fed diets relatively or absolutely deficient in calcium, extracellular calcium concentrations decline, causing the parathyroid glands to secrete parathyroid hormone (PTH). PTH stimulates resorption of bone calcium and phosphorus. PTH also acts on the kidney to enhance phosphorus excretion and calcium retention, thus returning extracellular fluid calcium concentrations to normal.[80] Resorption of bone mineral in growing kittens with calcium deficiency does not inhibit production of the organic bone matrix (thus the name osteitis fibrosa).[56] The precise mechanism for the myopathy is unknown.[70]

Nutritional secondary hyperparathyroidism is diagnosed on the basis of nutritional history and radiographic signs. Bone demineralization results in progressively decreased skeletal radiodensity, bowing and folding of long bones, narrowing of the pelvic canal, and vertebral compression fractures in advanced cases (Fig 7). Serum biochemistry assays are of little value due to normal variation in plasma calcium, phosphorus and alkaline phosphatase concentrations.[70]

Nutritional secondary hyperparathyroidism is treated by providing a nutritionally satisfactory diet for the animal's age. Much of the generalized soreness and lack of bowel emptying disappears within 48 hours of feeding a normal diet due to rapid resolution of the myopathic portion of the disease.[70] If the pelvic canal is greatly narrowed, which it often is in severe and protracted cases, constipation may be a long-term or even permanent complication. The stools of cats with a badly narrowed pelvis may be angular or ribbon-like. Intact female cats with permanent narrowing of the pelvis also frequently have problems with dys-

Figure 6. Heart from a 5-week-old Himalayan kitten that died suddenly. The kitten's dam was fed a diet deficient in taurine. The heart is very enlarged, thin-walled and flabby.

tocia when giving birth. Following remineralization of the bone, which may take several weeks, there is often permanent bowing of the long bones of the limbs, and kyphosis and lordosis of the spine. Supplemental calcium has been advocated but is probably unnecessary. Dietary change results in rapid improvement of stiffness and pain, but constipation and bone abnormalities resolve more slowly and may be permanent.

Nutritional secondary hyperparathyroidism is a disease better prevented than treated. Breeders and cattery owners should be interviewed about nutritional practices early in the doctor-client relationship and the hazards of inappropriate diets explained. Reliance on excellent-quality commercial cat foods without supplementation is the best insurance against nutritional secondary hyperparathyroidism during the critical nutritional period of early growth.

Feline Urologic Syndrome: Feline urologic syndrome (FUS) is a disease well known to veterinary practitioners and cat owners, even though only 1% of the total cat population is at risk. The syndrome has been recognized for over 100 years, but its cause is still not completely understood. The disease occurs more frequently in cats 2-6 years of age, more often in obese and sedentary cats than in athletic and lean animals, more frequently in neutered than intact cats, and more often in cats fed dry rather than moist foods. Clusters of cases in the same geographic area often occur after prolonged periods of unusually cold or damp weather that prevents the cats from going outdoors, and sometimes after boarding or other social stress. Presumably, these stresses prevent normal voiding of urine and decreased water consumption. Retention of urine increases the time the concentrated urine is in contact with the bladder wall, while decreased water consumption increases urine specific gravity.

Both male and female cats suffer from FUS, but the disease is more serious in males due to the added complication of urethral obstruction. Attacks of FUS begin abruptly with frequent urination, straining to urinate and, in many cases, bloody urine. Male cats often become obstructed soon after onset of signs due to intraurethral concretions of crystals, proteinaceous debris, and inflammatory cells. Obstructed males try repeatedly to urinate, usually to no avail. Their abdomens become acutely painful and tense as the bladder swells with urine. If they are not unblocked, obstructed male cats die within 72 hours. Typical affected female cats (and unobstructed males) have palpably thickened bladders containing very little urine. The irritation of even small amounts of urine in the bladder leads to frequent voiding. Even limited pressure on the empty bladder causes voiding of a small amount of urine.

Episodes of FUS, if not complicated by urethral obstruction, usually subside spontaneously within 5-8 days. About 70% of affected cats suffer only one attack, while the remainder have multiple attacks at intervals of weeks, months or years. A small percentage of affected animals have chronic disease.

Feline urologic syndrome is thought to be a dietary disease that occurs in a small subpopulation of predisposed cats. Acute bladder inflammation is thought to be caused by irritation from excessive amounts of microscopic or macroscopic struvite (magnesium-ammonium-phosphate) crystals. In some cats, struvite crystals eventually form into a larger struvite calculus or stone. Struvite urolithiasis causes more chronic and low-grade urinary tract signs than FUS.

Components of the diet that may predispose to struvite urolithiasis and FUS include ash, magnesium, moisture and fiber. While ash *per se* was shown 30 years ago to have no effect on struvite crystallization, it is still mentioned as a causative factor.[27] The quantity of ash in the diet has an effect on struvite urolithiasis, but only in the context of its macromineral composition. High ash content may either promote, inhibit or have no effect on struvite crystallization, depending on what minerals it contains. While components of ash may be significant, their influence cannot be predicted reliably from the dietary ash level. For example, sodium chloride (salt), added to food to stimulate drinking and promote increased urine volume, increases the dietary ash content, even though in this case it may be beneficial. The major component of ash associated with FUS is magnesium. This association was based on experiments that demonstrated that addition of magnesium,

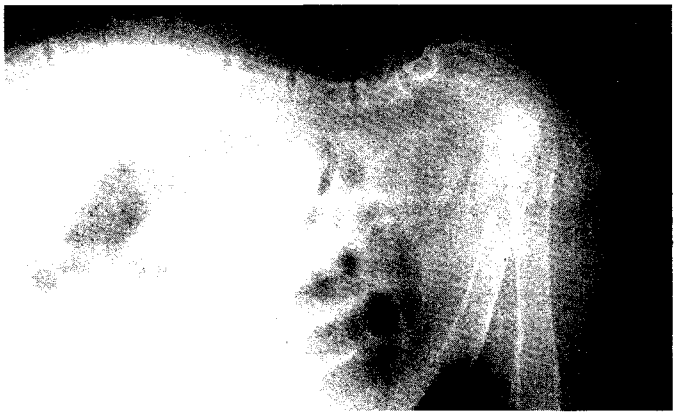


Figure 7. Radiograph of a 12-week-old Persian kitten with nutritional secondary hyperparathyroidism. The kitten had been on a diet consisting primarily of horse meat since weaning at 6 weeks of age. The bones are very lucent due to lack of calcium deposition. The spine is abnormally curved at points of gravitational stress, such as at the sacrum, and there is a pathologic fracture of the proximal femur. The abdomen is distended with loops of bowel filled with gas and feces.

usually at 3-10 times the concentrations found in commercial cat foods, would cause struvite stones to form in the bladder of cats.[47,59,75]

More recently it has been shown that struvite uroliths in the bladders of cats fed high-magnesium diets (3 times commercial concentrations) dissolved when the urine was acidified with ammonium chloride, suggesting that the effect of magnesium on struvite urolithiasis and FUS might be more related to urinary pH than excessive dietary levels.[88] Further research indicated that urine pH could also be dramatically altered by changing the chemical composition of the magnesium supplement. Magnesium had always been added to experimental or commercial diets as the oxide or carbonate salt. While these salts increase urinary magnesium concentrations, they also raise the urinary pH. When magnesium was added to experimental diets as chloride in subsequent studies, no increase in pH or struvite crystalluria occurred.[11] These studies demonstrated that struvite crystal formation is only enhanced by increasing concentrations of dietary magnesium when urinary pH was not controlled.

The reason that struvite crystal formation depends on magnesium only when urinary pH is not controlled is explained by the components of the stone: magnesium, ammonium ion and the trivalent phosphate anion (PO_4^{-3}). The trivalent phosphate anion is present to any significant extent only in alkaline solution, because addition of hydrogen ions, *ie,* lowering urinary pH, promotes formation of HPO_4^{-2} and $H_2PO_4^{-}$, which cannot precipitate as struvite. At urinary pH less than approximately 6.5, struvite crystal formation is negligible at the concentrations of magnesium found in commercial diets.

Urine volume (or more specifically, urine specific gravity or concentration) also influences struvite crystallization because it determines the relative levels of Mg^{+2}, NH_4^{+} and PO_4^{-3} in the urine. The greater the urine volume, the lower the urine specific gravity (more dilute), and the lower the relative concentrations of mineral ions. Crystal formation is favored when concentrations of mineral ions are high, so dilute urine is less crystal-forming than concentrated urine. Urine pH also affects the solubility of minerals. A low (acid) pH favors the ionic or soluble form of struvite, and a high (alkaline) pH favors crystal formation. Because the urine volume can be changed only about 4-fold, and urinary hydrogen ion concentration can change by nearly 1000-fold (3 pH units), the potential influence of pH is much greater than that of urine volume. The effects are also interrelated, because dietary urinary acidifiers may induce diuresis as well.

Fiber content of the diet also may influence the incidence of struvite urolithiasis and FUS by changes in the route of water excretion or by influencing gastric acid secretion.[11] Dietary fiber favors intestinal secretion of dietary and metabolic water,

which concentrates urine and predisposes to struvite crystal formation. Changes in gastric acid secretion would be predicted to influence renal acid secretion, and thereby urine pH.

Diet-induced struvite urolithiasis and FUS can be largely prevented by offering foods that maintain a urine pH between 6.0 and 6.5. This fact is significant because it is easier for commercial manufacturers to adjust food formulations to acidify urine than it is to remove magnesium or fiber. In fact, one manufacturer has demonstrated that their dry food maintains a low urine pH, presumably by addition of corn gluten meal and digest.[50] Semimoist foods also produce acidic urine (often <pH 6), due mainly to the large amounts of phosphoric acid used as a preservative. Corn gluten meal, animal digest (preserved with phosphoric acid) and d,l-methionine are all used by pet food manufacturers to prevent diet-induced increases in urine pH.

One consequence of addition of acid-forming ingredients to commercial diets is that great care must be used in prescription of urine acidifiers to avoid acidosis.[37] Urinary acidifiers should *only* be prescribed if the measured *ad libitum* bicarbonate is greater than 18 mmol/L. The pH of urine of fasted animals may range from less than 6 to greater than 7, depending on previous diet and duration of food deprivation, making measurements of urine pH from fasted animals difficult to evaluate. Overacidification may result in depressed growth, hypokalemia, increased urinary excretion of potassium and calcium, and possibly bone demineralization.[9,29,36]

Recognition of the predominant influence of urinary pH on struvite crystal formation should provide new opportunities for prevention of struvite urolithiasis and FUS. To what extent the overall incidence of struvite urolithiasis and FUS will be reduced by lowering the urinary pH remains to be seen, though preliminary evidence is that it is substantial.

Calcium Oxalate Urolithiasis: The increased incidence of calcium oxalate urolithiasis in cats may be a consequence of hypercalciuria induced by acidification of cat foods, and of reduced magnesium content (magnesium is an inhibitor of calcium oxalate crystal formation).[69] This is paradoxic, because diets formulated to solve one problem induce yet others, indicating the difficulties nutritionists have in understanding the unique nutritional requirements of cats. Fortunately, it appears that the antiFUS and antistruvite urolithiasis effects of acidifying diets are more important than the complication of calcium oxalate urolithiasis.

Hypokalemia: Lower than normal blood potassium concentrations are commonly seen in chronically ill cats. In one study, 186 of 501 (37%) of cats seen over a 3-year period at a veterinary teaching hospital had serum potassium concentrations <4.1 mEq/L.[30] Diseases significantly associated with hypokalemia included chronic renal failure, hepatic disease, systemic infectious diseases (viral or bacterial) and neuromuscular or CNS disease. Interestingly, diseased cats fed 2 commonly used commercial diets (since modified) were 4 times more likely to be hypokalemic.[30] It was not certain from this study whether disease, diet or diet plus disease were the major causes of the hypokalemia.

In a second study, hypokalemia in a group of cats with renal insufficiency was attributed to the combined effects of inadequate dietary potassium and excessive renal tubular potassium loss.[29] This suggests that diseased cats are prone to hypokalemia, especially those with renal insufficiency, and that the hypokalemia may be of clinical importance if the diet does not adequately compensate for the potassium drain. In some cats with renal insufficiency and hypokalemia, there was an improvement in renal function when the cats' diets were supplemented with potassium. Though no explanation was given, it seems likely that certain types of diets (especially urinary acidifying diets) may have actually induced (or added to preexisting damage) renal tubular damage through their tubular acidifying effect, and this damage was compounded by the resultant increased urinary potassium loss and hypokalemia. Urinary acidifying diets implicated in this problem have since been modified to contain greater levels of potassium.[29]

Hypokalemic Polymyopathy: A few cats fed certain commercial diets relatively deficient in potassium and supplemented in such a way as to acidify the urine (antiFUS

diets) have developed severe and often fatal polymyopathy.[28] Cats with this disorder developed acute generalized weakness, muscle pain manifested by stiffness, stilted gait and pain on muscle palpation, and muscular weakness manifested by persistent ventroflexion (drooping) of the neck, sometimes complicated by renal disease. The severe hypokalemia in these animals probably resulted from chronic renal tubular acidosis and resultant excessive loss of potassium in the urine. Tissues become badly depleted in intracellular potassium over a long period, which may be responsible ultimately for the tissue damage. Some urine acidifying diets were also relatively deficient in potassium, which probably compounded the problem. In addition to low serum potassium concentrations, the cats had extremely elevated levels of serum creatinine phosphokinase. Muscle damage was submicroscopic, however, and muscle biopsies showed only mild necrosis. Nephrosis was sometimes severe, due either to hypokalemia or myoglobin-related tubular damage. Clinical signs and hypokalemia rapidly resolved when potassium supplements were given and reappeared when the cats were again fed the original diets.

Nutrition-Sensitive Disease

Nutrition-sensitive diseases are those for which dietary management is part of the treatment of the disease. These include a wide range of problems, such as food allergy, obesity and primary organ system diseases. Consumption of a satisfactory diet by cats with nutrition-sensitive diseases may exacerbate the problem even though there is nothing intrinsically wrong with the diet. Dietary modifications in such cases are necessary to maintain nutritional homeostasis in the face of organ system malfunction.

Food Intolerance and Allergy:[4,87,91] Idiosyncratic adverse reactions to foods occasionally occur in cats. These reactions may be divided into 2 broad categories: food intolerance and food hypersensitivity or allergy. Food intolerance includes all nonimmunologic adverse responses to foods, while food allergy is an adverse response to some dietary component mediated by the immune system. Food intolerances are caused by inappropriate metabolic and biochemical interactions between the host's digestive system and ingredients in the food. Examples of food intolerance are lactase deficiency, in which lactose or milk sugars cannot be properly metabolized. Overfeeding with carbohydrates may lead to overproduction of gas in the colon and bacterial overgrowth in the lower small bowel. Vegetarian diets, popular among some cat owners, may induce chronic diarrhea due in large part to food intolerance. Food intolerances are uncommon in cats. Food allergies, on the other hand, are very common.

Food allergies probably occur to one degree or another in roughly 10% of cats on commercial diets. The allergies are usually to proteins and smaller peptides within the food, or created in the digestive tract as a result of digestive processes. Food allergens are usually animal or vegetable proteins never used by cats during their evolution. These include fish, beef, whale, soybean protein, bovine milk proteins, egg proteins and wheat proteins.

Food allergies are manifested in various parts of the intestinal tract and/or in the skin. Gastrointestinal allergies are caused by direct contact between the food-borne allergen and sensitized mast cells within the gastrointestinal mucosa, while skin allergies are due to interaction of allergens carried via the bloodstream from the intestinal tract to sensitized mast cells in the skin. Vomiting, usually of mucus or bile- tinged fluid, is the most common manifestation of allergies in the stomach or upper small intestine. Vomition occurs from 1-5 times or more a week, usually several hours after eating. The cats are usually otherwise healthy, unless skin or lower bowel allergies are also present. Allergies in the lower small intestine of cats are associated with intermittent diarrhea and, if severe, to varying degrees of weight loss and eosinophilia. Small bowel allergies are more likely to be accompanied by skin lesions than allergies higher or lower in the intestinal tract. Allergies in the colon are usually manifested by small amounts of blood and/or mucus in the stool. In severe cases, bowel movements are greatly increased in frequency and the stool is loose or semiformed.

Skin lesions caused by food allergies are usually of 2 types: mildly pruritic miliary

scab-like lesions throughout the coat (but concentrated about the head), or much larger, severely pruritic plaque excoriations about the face and neck. The pruritus is nonseasonal and frequently refractory to corticosteroid therapy.

Because food allergy is a common cause of skin or intestinal disease in otherwise healthy cats, allergies should be ruled out before a search for other causes is undertaken. Food allergies may be suspected when signs occur early in life and are nonseasonal. However, signs may or may not be temporally associated with food intake. Though various diagnostic tests have been devised, elimination diets remain the only reliable method of diagnosing food allergy. If food allergy is suspected, the cat should be provided with distilled water to eliminate the possibility of a water-borne agent. All food should be withheld for 2-3 days, and only a hypoallergenic diet should be fed in a stainless-steel bowl for 3 weeks. The stainless-steel bowel eliminates a source of potential allergens in plastics or crockery. It is important that *no* other food treat, vitamin or nutrient supplement be given.

Hypoallergenic diets for cats should be as close to what wild cats eat as possible, *ie,* all animal meat. Lamb, turkey and rabbit are preferred because they are usually readily available fresh or frozen and less apt to have been a part of previous diets. The meat should be cooked and shredded or ground before being fed. Prepared baby food is a convenient, though much more expensive, alternative source of lamb or turkey. Beef and chicken or their byproducts are frequently incorporated into commercial foods, and cats have been known to develop allergies to them. For this reason, they would not be ideal first choices for a hypoallergenic diet. A volume of cooked meat equal to that offered as canned food should be fed. There is no need to supplement the meat with minerals or vitamins for the 3-week test period. A dramatic improvement in the cat's skin and/or intestinal problems should be seen within 7-14 days. If there is no improvement with one type of animal meat (such as lamb), change the diet to a second animal meat (turkey or rabbit) for an additional 2 weeks. If there is no change in the condition with either diet, it is prudent to investigate causes other than allergies.

If the skin and/or intestinal problems resolve with the hypoallergenic diet, a mineral and vitamin supplement is added and the diet continued for a month or more. Bonemeal, about 1/4 teaspoon per day, is an ideal mineral source. Human pediatric or pet (nonmeat flavored) multivitamin supplements should be used for the vitamin source. If the allergies are under control after a month, one new animal meat source can be added to the diet each month. If allergic signs recur when the new meat is introduced, withdraw it from the diet and try another type of meat.

Obesity: Obesity is a problem that appears to be increasing. This may be due to recent advances in diet palatability or to greater numbers of neutered cats maintained in relatively confined and sedentary environments. While much has been written about obesity in dogs, the disease has not been well studied in cats.[68] Common therapeutic recommendations include diet and exercise. For dogs, dietary restriction to one-half the calories required for the desired body weight is recommended. Even complete restriction of food intake (fasting) in dogs has been shown to be a safe and effective method of weight control. In obese cats, however, excessive food restriction may cause a fatal fatty liver syndrome called idiopathic hepatic lipidosis. Because of the risk of hepatic lipidosis, *obese cats should not be fasted for weight reduction.* Caloric intake should not be reduced to less than the maintenance requirement at the desired weight (about 75 kcal x desired body weight in kilograms). Under no circumstances should the caloric intake be decreased more than two-thirds of the prior intake, regardless of the calculated value. Also, changes in diet should not be abrupt, because such changes can induce transient anorexia.

Idiopathic Hepatic Lipidosis: Idiopathic hepatic lipidosis is a potential complication of acute anorexia in certain predisposed cats.[5,89] Most, but not all, cats that develop fatty liver syndrome are obese and of middle age before onset of disease. About two-thirds of affected cats experience some predisposing stress that caused them to become briefly anorectic. Common stresses include transient illness, boarding or sudden changes in environment or human and animal companions. Though cats often become

anorectic from a variety of illnesses, hepatic lipidosis is not generally an important complication in obese cats suffering from other diseases. Paradoxically, hepatic lipidosis can be experimentally recreated by making cats obese on a high-caloric-density diet and then suddenly curtailing their food intake by one-half or more. The clinical changes are usually not as severe as in the natural disease, however.

The pathogenesis of hepatic lipidosis is not known. Acute anorexia or dieting appears to set off a sudden metabolic derangement that has its greatest impact on hepatocytes. The disease involves a vicious cycle, beginning with acute anorexia, nutritional and metabolic perturbations, hepatic lipidosis, and more anorexia due to liver derangement. The fatty liver may develop from a decreased rate of fatty acid oxidation, increased rate of hepatic lipogenesis, reduced rate of triglyceride secretion, or reduced clearance of circulating triglycerides.

Affected cats show progressive anorexia, generalized weakness, muscle wasting, and weight loss of variable duration. Icterus appears after several weeks and becomes severe during the terminal stages. Laboratory evaluation commonly reveals progressively increasing serum levels of ammonia, liver-specific enzymes and bilirubin. Serum cholesterol and triglyceride levels are sometimes elevated. Plasma protein levels are usually normal.

The only available therapy is forced feeding and provision of lipotropic factors, such as methionine. Because cats with hepatic lipidosis are usually totally anorectic, forced feeding is mandatory. This can be done through an implanted pharyngostomy tube, nasogastric tube, gastrostomy tube or jejunal catheter. Nasogastric tubes are more difficult to maintain and require the diet be filtered or given in the form of commercial high-caloric liquids, such as Pulmocare (Ross) or Traumacal (Mead-Johnson) supplemented with protein powder. Such commercial preparations are expensive. Pharyngostomy tubes are more difficult to keep in place, prone to infection, and easily displaced. Gastrostomy tubes are the safest, most effective and cheapest to maintain. Special catheters of the balloon (Foley) or mushroom type can be installed under anesthesia by gastroscopy. Because the tubes are of large diameter, it is possible to use regular commercial cat food, well blended with water to make a slurry. Jejunostomy tubes are indicated only when vomiting is a problem.

Though high-carbohydrate diets have been advocated for cats with hepatic lipidosis, their use seems illogical, as they are lipogenic.[89] If the problem is due to prolonged food deprivation, force feeding a diet containing at least 30% of the kilocalories as protein would seem to be indicated in the absence of hepatic encephalopathy. Paradoxically, the diets can also be high in lipids as an energy source. Diets that meet these criteria are available commercially (Feline p/d or Feline c/d, Hill's). Since cats respond to starvation by depleting urea cycle intermediates, rather than urea cycle enzymes as most omnivores do, feeding high-protein diets should be relatively safe. Response to therapy is variable, probably because of differences in the stage of the disease at presentation. Without forced feeding, the condition is usually fatal. Even with forced feeding, about 50% of treated cats may still die. Clinical improvement, to the point that the cat eats on its own, can take as long as 6-8 weeks. Pathologic findings include periacinar hepatocellular necrosis of variable severity, parenchymal-cell fat accumulation and bile pigment accumulation.

Diet in Chronic Liver and Kidney Disease: Chronic liver diseases, other than idiopathic hepatic lipidosis and chronic biliary cirrhosis, are not as common in cats as in some other species. Chronic kidney disease is present to some degree in over half of cats >10 years of age, however, and is one of the leading causes of death in aged indoor cats. Because of their metabolic peculiarities and the low palatability of reduced-protein diets, nutritional management of cats with chronic liver or kidney disease is a dietetic challenge. It is easy to justify the need for a special diet for cats with chronic liver or kidney disease, but it is yet another thing to formulate a diet that is low in protein and adequate in energy, and that cats will eat.

Energy and protein needs for cats with kidney and liver disease are similar, so that diets for one can be used for the other. Pro-

tein is reduced in the diet of cats with kidney disease because of reduced ability to excrete waste products of protein catabolism. As with liver disease, frequent feedings of small meals should be offered to maximize protein utilization.

Energy needs for maintenance of cats with liver disease are assumed to be the same as for normal animals. Protein needs should be met with proteins of high biologic value (usually egg and milk protein) fed at levels close to the minimum requirement. The minimum protein requirement for nitrogen balance of adult cats fed purified diets is about 140 g protein (nitrogen x 6.25) per kg diet, or 11% of metabolizable energy.[67] Diets comprised of whole foods are less efficient at providing usable amino acids, so minimum protein needs for conventional diets are probably closer to 15-20%. This amount of dietary protein can be met by commercially available therapeutic diets, dilution of commercial diets with fat and carbohydrates, or formulation of a homemade diet.

An example of diluting a commercial diet with fat and carbohydrates is as follows: A 180-g (6-oz) can of commercial canned cat food contains about 180 kcal and 18 g protein. The protein content comprises 35% of the kcal (18 g protein x 3.5 kcal/g protein = 63 kcal or 35% of the total 180 kcal). To reduce the protein content to 20% of kcal, 135 kcal/can must be added, which is 1 tablespoon of fat or cooking oil or 2/3 cup of cooked rice or pasta per 6-oz can. The total kcal in this reformulation is 135 kcal, which meets the requirement for a 9-lb (4-kg) cat for a day.

Though it is important to reduce protein intake, excessive reduction of dietary protein may cause weight loss, decreased muscle mass, hypoalbuminemia and depressed immune response. The protein portion of total calories should be reduced below 20% only if the animal can tolerate this level. The diet should be fed as small meals over the course of the day to minimize the amount of protein that escapes digestion in the small bowel. Undigested protein is fermented in the large bowel, with production and absorption of such toxic metabolites as ammonia and mercaptans, which are not detoxified by the diseased liver.

Nutritional Support of Sick Cats[10,24]

Lack of desire to eat is called anorexia, which results from some interruption of the normal mechanisms of food intake control. Anorexia can be caused by a wide variety of medical problems, including organic disease, inflammation, trauma and neoplasia. Pain, fear and stress also inhibit food intake. Patients with chronic diseases often have a diminished appetite and become nutrient depleted as the disease progresses. Cats with facial injuries or obstruction of the gastrointestinal tract may not eat because they are physically incapable of ingestion, chewing or swallowing food. Infections of the nasal passages, which are particularly common in kittens, can lead to impaired sense of smell. Cats depend strongly on the smell of their food for palatability, and if they cannot smell properly, their food may be ignored.

Metabolic Response to Starvation

Normal animals can survive relatively long periods of food deprivation.[68,81] Healthy animals respond to starvation primarily by changes in the proportions of circulating insulin and glucagon.[13,25,53] Blood glucose concentrations begin to decline within hours after the last meal, which stimulates glucagon production and a decline in the plasma insulin:glucagon ratio. This hormonal shift attempts to restore normal blood glucose levels by stimulating glycogen breakdown, fatty acid and glycerol release from adipose tissue, and amino acid release from tissue protein catabolism. Released amino acids and fatty acids provide the precursors for gluconeogenesis and ketone body production in the liver, which is also enhanced by glucagon. Ketone bodies provide an alternate metabolic fuel source for extrahepatic tissues, which decreases the peripheral demand for glucose. Rising blood glucose and ketone body concentrations stimulate insulin release, thus completing the feedback loop and minimizing breakdown of protein for energy production. The animal's metabolic rate declines due to lost tissue mass, decreased physical activity and decreased thyroid ac-

tivity, all of which help conserve body substance.

The normal metabolic response to starvation does not occur in diseased animals that are anorectic. Hormonal changes accompanying severe disease include increased production of growth hormone, catecholamines, corticosteroids, antidiuretic hormone and aldosterone, in addition to glucagon. Combined release of these hormones increases fat, glycogen and protein breakdown in proportion to the severity of disease. High rates of glucose production resulting from these alterations may cause hyperglycemia, possibly due to inadequate insulin production. While fatty acid release from adipose tissue also occurs at a high rate, ketone body production is often depressed in severe trauma and infection, which deprives the animal of an important fuel source.

Increases in metabolic rate also occur with disease due to altered hormone concentrations, fever and increased tissue demands. If exogenous nutrients are not provided, high metabolic rates result in rapid weight loss. Major body functions become affected when more than 10% of the body cell mass is lost. Loss of 30-50% of lean body weight may result in death.

Treatment of anorexia should begin early in the course of therapy. Clinical circumstances where fasting is indicated are few (though it has been suggested that severely depleted patients with infections should be repleted carefully to avoid reemergence of "dormant" pathogens).[66] *The appropriate decision is not whether the patient should be fed, but whether it should be starved.* Nutrients should always be provided by the most physiologic route available.

Energy Requirements of Sick Cats

The difference in rate of tissue loss between normal and sick animals can be quite dramatic. For example, a 1-kg weight loss results in liberation of about 3300 kcal.[21] For a normal, fasting 4-kg cat this would represent a 2-week energy supply. If the cat were severely ill, this amount of energy would last less than 1 week. This "autocannibalism" or disease-induced hypermetabolism emphasizes the need for early nutritional support. When animals are anorectic, energy needs must be met by body stores of glycogen, fat and protein. As long as glycogen is available for energy, protein is spared. Once it is depleted, however, protein and fat are catabolized for energy to perform essential body functions.

Protein Requirements of Sick Cats

Anorectic cats, unlike people and dogs, do not usually draw first on stored fat reserves. Rather, they rapidly catabolize body stores of protein. Since fat reserves are considerable in many cats, starving cats may not appear thin to their owners for some time. During the early stages of anorexia, plasma glucose and amino acid concentrations are maintained at the expense of labile proteins in the liver, kidney and gastrointestinal tract. After the first 2-3 days of anorexia, muscle proteins begin to be broken down as well.[38] By carefully measuring the quantity of nitrogen excreted, the amount of protein lost may be estimated by multiplying grams nitrogen excreted by 6.25 (assuming body protein is 16% nitrogen). Normal animals lose approximately 1.2-1.6 g protein per kg body weight per day when adapted to starvation, about half the loss incurred at the onset of anorexia. Due to the rapid wasting of muscles and retention of fat depots, starving cats often have a "mushy" feeling. The starving cat is essentially a ball of fat encased in a thin veneer of atrophic and toneless muscles.

Because sick cats do not adapt to starvation, large losses of nitrogen may occur. With severe stress, such as from major burns, trauma or sepsis, patients may be unable to provide sufficient amino acids for high-priority protein synthesis, resulting in impaired wound healing, erythropoiesis and immune function. Animals with chronic diseases may be protein depleted at the time of presentation due to decreased food intake in the face of ongoing or increased nitrogen losses caused by the disease. Calculation of precise protein needs in disease is difficult due to uncertainties in the previous nutritional status of the patient, effect of the disease on protein metabolism, and severity of the insult. In a number of conditions, such as fever, fracture, burns and surgical trauma, protein is lost extensively during the acute phase of the disease. In human patients, basal nitrogen requirements may increase 2-3.5 times, depending on the severity of the disease.

Vitamin and Mineral Requirements of Sick Cats

Specific vitamin and mineral needs depend on the type and severity of the disease. For short-term nutritional supplementation, sodium, chloride, potassium, phosphate, calcium and magnesium should be provided. Provision of supplemental zinc should also be considered, especially in anorectic patients with gastrointestinal disease, where losses may be increased. Zinc is also important because of its role in protein synthesis, immune function, *in-vitro* phagocytic activity, taste and smell.[72] Supplementation of 1 mg zinc/kg/day (4 mg/kg $ZnSO_4$) may be instituted until the animal resumes eating. Very little research has been conducted on the effect of various diseases on vitamin requirements, but providing vitamins at or near the NRC recommendations is reasonable.[84]

Nutritional Assessment of Sick Cats

Malnutrition should be suspected in cats with recent weight loss of greater than 10%, recent major surgery, complete anorexia of longer than 7 days' duration or excessive nutrient losses from the gastrointestinal tract, burns or wounds. Increased needs due to fever, infection or trauma may also result in rapid losses of body stores, as can chronic administration of corticosteroids, diuretics, laxatives and other drugs with antinutrient activity.[77] Chronic diseases also generally result in depressed food intake and ultimately malnutrition. A diet history should be obtained, including the amount and types of food eaten (an adult cat should eat about 1 cup of dry food, 3 packages of soft moist food or 2 6-oz cans of canned food per day), assessment of the cat's appetite and a specific question regarding use of supplements. A response indicating the cat is fed a homemade diet should raise one's suspicion of dietary inadequacy because many people have incorrect beliefs about the appropriate nutrient content of diets for cats; all-meat and vegetarian diets are particularly detrimental.

The extent that a cat is over- or underweight is assessed during the physical examination. Muscle wasting, edema or lack of subcutaneous fat indicates chronic malnutrition. Because obesity can mask lean tissue depletion, obese patients must be carefully examined.

It is important to remember that malnutrition, even if not present on admission, may occur during hospitalization. Failure to maintain daily records of weight and food intake, prolonged food deprivation before diagnostic tests and/or surgery, and failure to recognize disease-related increases in nutrient needs are all causes of malnutrition during hospitalization.[12] Many laboratory values can be affected by malnutrition, but few changes are specific. Serum albumin concentrations and total lymphocyte counts are 2 parameters that may provide information about nutritional status. Albumin is commonly used in human patients to indicate visceral protein depletion, with <20%, 20-40%, and >40% decreases in normal values indicating mild, moderate and severe depletion, respectively.[41] The plasma half-life of albumin is about 8 days in cats, which is short enough for decreases to be seen before severe nutritional depletion occurs. Serum albumin concentrations are also affected by hydration status, and by the presence of gastrointestinal, liver and kidney disease.[52]

Starvation may interfere with normal immune function, making sick cats more susceptible to secondary or opportunistic infections. The only readily available assessment of immune status is total lymphocyte count, which may be depressed by protein depletion. Stress and immunosuppressive drugs can also decrease lymphocyte numbers. Further, even if total numbers are in the normal range, functional abnormalities may adversely affect immune competence.[44]

Feeding Techniques for Sick Cats

Provision of calories, protein, vitamins and minerals may be provided as soon as volume, electrolyte and acid-base abnormalities have been corrected. There are basically 2 ways of providing nutrients: parenterally or via some access to the gastrointestinal tract (Fig 5). The rule is, "if the gut works, use it." The gut works a surprisingly large percentage of the time.[44] There are situations, however, in which food cannot be given by the digestive tract, such as with vomiting, diarrhea, intestinal malabsorption and possibly pancreatitis.[63,97]

Nonforced Feeding: A number of techniques may be used to induce hospitalized cats to eat. Staying with the cat when food is offered and encouraging it to eat is the simplest method. Inappetence is to be expected when cats are in unfamiliar surroundings among strangers and are being subjected to unpleasant diagnostic procedures. Petting and vocal reassurance may be all that is necessary to encourage the cat to begin eating again. Warming the food to enhance aroma may also help; sick animals often have diminished senses of taste and smell that make food less desirable. A change in the type of food offered can also be tried. If dry foods have been offered, switch to canned meat or fish, which may be more palatable. Meat baby foods or such things as smoked oysters, while not nutritionally balanced, are quite palatable and adequate for a few days. If the cat will not eat from a bowl, it may take food if offered on one's finger. If these methods are unsuccessful, the owner can be asked to come in to feed the animal its usual food. One or two days of this treatment are usually sufficient; once the animal resumes eating, it may continue on its own.

Drugs may also be used to stimulate feeding. Diazepam (Valium) can stimulate food intake in normal cats at oral dosages of 2 mg/kg. However, tranquilization and ataxia may occur for up to 2 hours after these doses.[15] A dosage of 0.05-0.4 mg/kg may be more appropriate for sick cats.[26] Whether the use of drugs has any advantage over behavioral approaches to stress reduction to stimulate food intake is open to question.[62]

Forced Handfeeding: If all attempts to induce the cat to eat fail, it may be force-fed by hand. This technique can be used for 1-3 days. A convenient method of force feeding is to cut off the end of a disposable syringe and cut a core of food from a can of pet food. The syringe plunger is then used to force the food into the cat's mouth. While forced feeding provides some nutrition, the difficulty of providing sufficient nutrients to meet increased requirements of disease and stress makes the technique of limited usefulness in severely debilitated animals. The main danger of this approach is aspiration pneumonia. If the cat is extremely weak and has impaired gag and cough reflexes, or if too much food is given too rapidly, food may pass into the trachea and lungs. If aspirated food contains a lot of lipids, which many high-calorie preparations do contain, severe pneumonia may be a sequela.

Stomach Tube Feeding: The next most invasive method of force feeding is to pass a feeding tube into the stomach for each feeding. Passing an orogastric or stomach tube is a very simple procedure. The most important criterion of success is the gentleness with which the maneuver proceeds. Limited restraint and opening the mouth just far enough to introduce the tube will minimize the animal's objections to the procedure. One must be careful to avoid damaging the pharyngeal and esophageal mucosa or intubating the trachea when passing the tube. The equipment needed for orogastric intubation commonly found in most hospitals or can be readily obtained from surgical supply firms. Disposable equipment suitable for artificial oral alimentation is also available.

Nasogastric Tube Feeding: If the patient is too debilitated to tolerate repeated tube feedings, if feeding must be continued for more than 3 days, or if the disease prevents periodic intubation, a nasogastric tube may be placed. Placement of a nasogastric tube is very simple and allows oral nutritional support for extended periods. Polyvinyl tubes are the least expensive and work quite well for nasogastric feeding. The biggest problem with nasogastric tubes is keeping them in place for a long period of time, such as would be required to treat a cat with hepatic lipidosis. As the cat begins to feel better, it increasingly resents the indwelling nasogastric tube. The tube can also be relatively easily dislodged by coughing or vomiting.

The technique of passing a nasogastric tube is quite simple.[14,18] A topical anesthetic, such as 4-5 drops of 0.5% proparacaine HCl (Ophthetic, Allergan), is first instilled into a nostril. A 5- or 8-French feeding tube (Becton, Dickinson) is passed caudally through the ventral meatus and nasopharynx into the esophagus. The tube is unlikely to enter the trachea if the head is held at the normal angle of articulation. Once the tube is placed, its position in the stomach is confirmed by injecting a small amount of sterile water through the tube, which causes the animal to cough if the

tube has been placed into the lungs. A radiograph may be used to confirm placement of the tube if uncertainty persists. The tube is then sutured in place and fixed to an Elizabethan collar.

Pharyngostomy Tube Feeding: If the nature of the disease or injury obviates use of the nasogastric route or a prolonged course of enteral feeding is anticipated, a feeding pharyngostomy tube may be implanted.[24] Tube placement via pharyngotomy may be used for patients undergoing operation for disease or trauma of the maxillofacial region or with impaired swallowing secondary to neuromuscular disorders. This procedure requires general anesthesia or heavy sedation and is well described in the veterinary literature.[39] Potential complications include infection at the operative site, hemorrhage from major vessels in the area, and aspiration of food materials.

Gastrostomy Tube Feeding: Gastrostomy is the other common feeding enterostomy. This route is used for postoperative nutritional support in medical or surgical problems of the mouth, larynx, pharynx or esophagus. Foley mushroom-type gastrostomy catheters can be placed via trocar using gastroscopy and stomach insufflation with air.[8,67] Such safe and effective tube placement procedures have made gastrostomy tube feeding the preferred method for chronic enteral nutrition in cats.

Jejunostomy Tube Feeding: In circumstances of vomiting or gastric ileus, nutrients must be introduced distal to the pylorus. There are several situations in which a jejunostomy would be performed instead of a gastrostomy. Obstruction of the stomach, duodenum or proximal jejunum is an absolute contraindication to gastrostomy feeding. The primary advantage of postpyloric feeding is decreased gastric reflux, which reduces risk of aspiration. Only isotonic feeding solutions should be used for postpyloric feeding.[67] Complications of jejunostomy (in people) include hemorrhage, infection, catheter dislodgement, persistent fistulas and small bowel obstruction from adhesions around the enterostomy site, though they are uncommon.

How Much to Feed Sick Cats

To determine the energy needs of a sick cat, one must estimate the effect of the disease on energy expenditure. A cat resting in a hospital cage probably expends about 60-70 kcal/kg body weight daily. Mild, moderate or severe degrees of hypermetabolism increase this level of energy expenditure by about 25%, 50% or 100%, respectively. Protein needs are estimated at 20-30% of calories, depending on the extent of protein catabolism and loss, and the presence of any diseases requiring protein restriction. These values equal current nutritional goals. Nutritional support should attempt to reach these goals 24-72 hours after institution of therapy, depending on patient response. These levels of nutrient intake are well below those required to restore body mass lost rapidly during the course of disease. The immediate goal of nutritional support is to support protein synthesis and to attempt to reverse disease-induced catabolism; repletion of body substance may be deferred until the disease is under control.

Diets for Sick Cats

Foods for inappetent cats should supply the important nutrients required during disease, convalescence and healing without causing digestive disturbances. Nutrients should be supplied in a form that is easily digested, readily assimilated and efficiently metabolized with a minimum of waste products. The ideal food for anorectic animals should be so well tolerated by the gastrointestinal mucosa that it can be administered to cats with gastritis, enteritis or colitis without producing additional irritation. It should be in a form that is easily administered, yet should be palatable enough to be eaten voluntarily by healthy cats. Injured or diseased animals should not lose weight while being fed the diet in the recommended quantities.

Many liquids are satisfactory for providing nutrients to cats not eating. The nutrients in liquids are easily digested and readily assimilated. The dosage can be measured accurately and the liquid given to depressed or comatose animals if proper precautions are taken to prevent regurgitation and aspiration. Many commercial products for enteral support are available. Most of the products fall into 1 of 3 groups. As with most therapies, one should choose a small number of formulations and concentrate on gaining experience with them.

Meal-Replacement Formula: The first group is the meal-replacement formula for use in patients with nearly normal gastrointestinal function. These products are polymeric mixtures containing protein (usually casein, soy or egg albumin), fats (about 30% of calories) and carbohydrates. Nutrients are provided in high-molecular-weight forms to reduce osmolarity to about 350 mOsm/L. These are low-lactose and low-residue products. Meal-replacement formulas are adequate for most clinical situations.[23]

Peptide and Elemental Diets: Peptide and elemental diets are essentially monomeric forms of meal-replacement diets. Protein is present in the form of peptides or amino acids and carbohydrate as oligo- or monosaccharides. These diets are usually low in fat, part of which may be present as medium-chain triglycerides to enhance absorption. Because of the inclusion of low-molecular-weight nutrients, the osmolality of these solutions may be higher (450-850 mOsm/L) than meal-replacement formulas. These diets have been recommended for patients with abnormal gastrointestinal functions, as in inflammatory bowel disease and pancreatic insufficiency.[55]

Feeding Modules: The third class of enteral product is the feeding module, which is a concentrated source of one nutrient: protein, fat or carbohydrate. Modules may be added to formula diets to increase specific nutrient concentrations or to reduce the required volumes. They also generally increase the osmolarity of the formulation. Unless a contraindication exists, such products as Pulmocare (Ross) or Traumacal (Mead-Johnson), supplemented with 5-15 g protein powder per 8-oz can, are preferred.

Commercial nutritional products are generally available at large commercial pharmacies or by contacting the manufacturer. One may also contact local human hospital dietetics personnel. These professionals have nutritional products and delivery apparatus available, and have extensive training and experience in nutritional support.

Rate and Volume of Forced or Tube Feeding

Cats that have been anorectic for any length of time are expected to have decreased stomach volume and small intestinal absorptive capacity.[35] Normal cats can tolerate volumes of about 50 ml/kg body weight at one time without obvious discomfort.[10] If a solution containing 1 kcal/ml food were fed, the entire day's nutrient and water requirement could thus be given in one feeding. Dividing this volume into 2-4 feedings should enhance utilization. With sick animals, one should approach the calculated goal for nutrient and fluids over 24-72 hours to avoid causing the animal abdominal discomfort or diarrhea. Initially, an isotonic solution should be fed at half the desired rate.

For intragastric feeding, nutrient concentration is increased to the desired level, after which the rate is increased. Feeding small volumes at slow rates enhances nutrient absorption and minimizes the problems of diarrhea and cramping. Reservoirs and delivery tubes for feeding solutions are available from a number of manufacturers. "Hanging" small volumes of fluids (<12-hour supply) in a fluid therapy burette, gravity feeder (Ross), or feeding bag with built-in burette (Norwich Eaton) minimizes the possiblity of overdosing the animal with an excessive volume of feeding solution. Instructions for bolus feeding are presented in Table 5.

Problems with Enteral Tube Feeding

Problems with enteral feeding may be mechanical, gastrointestinal or metabolic (Table 5). Mechanical problems are those related to placement and maintenance of the tube. When a tube is placed into the stomach or duodenum, its position must be verified to avoid tracheal intubation. Tube placement must be checked before feeding if an intermittent schedule is used. Indwelling tubes may become occluded if coarse food materials are infused. They can cause reflux esophagitis, and their presence through the cardioesophageal junction may predispose to aspiration. Esophagitis and aspiration are usually the result of the use of large-diameter tubes.[39] This problem can be minimized by using smaller tubes, such as human nasoenteral tubes, available from 3.5 to 12 French. Smaller tubes have the further advantage of allowing the animal to begin to eat on its own with the tube still in place. These tubes clog easily, however, and make use of blenderized cat food impossible.

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Other problems associated with feeding tubes include regurgitation of the tube and infection at pharyngostomy sites. Good nursing care should make infection at the site of tube entry unlikely. No food material should be allowed to collect at the pharyngotomy site, and the tube should be kept tightly capped when not in use.

Most of the gastrointestinal problems caused by enteral feeding are due to overly rapid administration of the solution, administration of solutions of high osmolality (Table 5). When nutrient solutions enter the duodenum too rapidly, they can cause vomiting, cramps and diarrhea by overwhelming the normal neural and endocrine gastrointestinal mechanisms.

Hyperosmolar solutions cause rapid fluid and electrolyte influx into the gut lumen, leading to cramping and abdominal distention. Serum albumin levels of less than 2 g/dl may also result in decreased nutrient absorption due to inadequate plasma oncotic pressure.[24] These gastrointestinal problems are managed by reducing the solution concentration or rate of feeding.[35]

Metabolic problems include rapid absorption of high-carbohydrate solutions which may result in hyperglycemia, osmotic diuresis and ultimately nonketotic hyperosmolar coma (Table 5). Fortunately, these are not common problems. Metabolism of glucose also results in production of CO_2 and metabolic water. Excessive CO_2 production can further compromise patients with pulmonary disease; if metabolic water is retained, it can contribute to hyponatremia and edema. Most of these complications can be

Table 5. Bolus feeding instructions for *each feeding.*

Feeding Procedure

1. Auscult abdomen for gut sounds. Do not feed if gut sounds are not heard.
2. Inject 2 ml of water through the tube. This induces coughing if the tube has been misplaced or repositioned itself into the trachea.
3. When satisfied that the animal can be fed, check the feeding orders before proceeding, because the diet and amount fed change with the patient's condition. If necessary, place the animal in sternal recumbency. Solution should be warm, at least room temperature, and fed *slowly*. Feed no more than 20 ml per minute to prevent vomiting. IF THE ANIMAL VOMITS, STOP FEEDING.
4. After feeding, flush the tube with 2-5 ml of warm water and replace the tube cover, leaving the tube full of water.
5. Observe the animal for discomfort, colic or diarrhea for a few minutes.
6. Record all feedings, including any problems.
7. Nothing is to be administered via the tube except the feeding solution without permission of the clinician in charge.

Potential Complications and Their Management

Type of Complication	Frequency	Therapeutic Response
Mechanical		
Tube lumen clogged	Infrequent	Flush with water, replace tube if needed
Pulmonary aspiration of stomach contents	Rare	Discontinue feeding
Esophageal erosion	Rare	Remove tube
Gastrointestinal Signs		
Vomiting and bloating	10-15%	Reduce flow rate, discontinue if needed
Diarrhea and cramps	10-20%	Reduce flow rate, dilute solution, consider different type of solution, add antidiarrheal drug
Metabolic, Fluid and Electrolyte Abnormalities		
Hyperglycemia, glucosuria	10-15%	Reduce flow, administer insulin
Hyperosmolar coma	Rare	Discontinue
Edema	20-25%	Reduce solute content, slow feeding rate, use diuretics
Congestive heart failure	1-5%	Slow feeding rate, administer diuretics and other heart medications
Hypernatremia, hypercalcemia	5%	Adjust electrolyte content of feeding solution

avoided by slow rates of administration acclimatizing the patient to the feeding solution.

While anorexia is common and associated with myriad diseases, it is important to recognize that anorexia is much more than a nonspecific sign of disease. Prolonged absence of food intake adversely affects all body systems, making it more difficult for the animal to resist the effects of disease and respond to treatment.

Few contraindications exist to feeding hospitalized patients, and a broad range of maneuvers can be used to ensure adequate intake of food. Nutrients are available in forms ranging from standard commercial diets to the most elemental forms of glucose and amino acids.

Remember that supplemental nutrition is adjunctive therapy. Without antibiotics, all the food in the world will not cure septicemia. Without surgical intervention, damaged parts may not heal. Supplemental nutrition attenuates the severity of disease in otherwise well-managed patients. It also reduces the number of disease-related complications, and may shorten healing time. When the limitations are understood and the advantages weighed against the potential complications, nutritional support can make an important contribution to recovery of the patient.

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Chapter 7

Toxicology

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Among common pets, cats represent a large and unique group. They are often kept indoors in close association with their owners. Their natural curiosity and athletic ability give them both the reason and the ability to encounter a variety of plants, medications and environmental chemicals not readily available to other pets. In addition, their predatory nature induces them to catch and eat a variety of insects and small mammals that may themselves have been poisoned, giving rise naturally to the possibility of secondary poisoning.[1,2,8]

Certain innate characteristics of behavior may lead to increased susceptibility to intoxication.[1,8,22,43] Dermal preparations applied to cats may be ingested as part of the grooming process. Generally, products ingested are much more readily absorbed than if exposure is only dermal. Powders, sprays or spilled chemicals may cling to footpads and paws and are thus ingested in substantial amounts during grooming.

In spite of some types of behavior that may render cats more susceptible to poisoning, their discretion regarding food may lessen their exposure to chemicals.[1,2,8,43] Cats often closely inspect any potential food and may reject it because of objectionable taste or odor. It is comonly held that cats chew their food longer and more thoroughly than dogs, and this may allow for better detection of unusual tastes or odors. However, others have observed that this is not a universal characteristic of cats, and some cats may ingest food quite rapidly with little or no mastication. Another protective behavior of cats is their habit of consuming small amounts at any one time. This obviously reduces the total dose of a chemical as well as the rate of exposure. Further, since nausea and vomiting are a common response to many chemicals, ingestion of small amounts may only cause vomiting, thus reducing exposure and preventing further consumption.

Incidence of Poisoning

Several sources of information have improved our ability to evaluate the incidence of poisoning by or exposure to drugs and chemicals.[4,22,23,28,36,42] The Center for Veterinary Medicine of the Food and Drug Administration maintains a record of reported adverse reactions to therapeutic drugs. Veterinarians are encouraged to report adverse reactions as part of this system. Recently, Poison Control Centers in human hospitals have developed some interest in exposure of pets to drugs and chemicals, since animals have considerable value as sentinels of potential human exposure.[22] All states have some system of veterinary diagnostic services and some of these have active toxicology units with board-certified veterinary toxicologists on duty.[34] Veterinary colleges in North America also receive reports of toxicosis in cats as well as other species. Recently, one veterinary college has established a telephone referral center for questions related to toxicology.[4] Questions about cats and their exposure to drugs and chemicals constitute 20.7% of the calls received. By comparison, calls with questions about dogs involve 63.4% of total inquiries.

From these sources, it is apparent that cats are potentially exposed to a wide variety of synthetic and natural toxicants. Many of the exposures do not result in proven toxicoses, but the combined data provide some information about the risk of poisoning in cats.

Susceptibility of Cats to Poisoning

Cats are commonly believed to be more susceptible to poisoning on a comparative dosage basis than other species. This belief probably arises from the notable sensitivity of cats to certain compounds.[1,2,12] While cats have less of certain metabolic capabilities than many other species, one must not generalize too broadly about their susceptibility to poisoning, keeping in mind that many of their behavioral characteristics may mitigate the increased sensitivity due to biochemical differences.

Three mechanisms may lead to a high degree of sensitivity to certain drugs in cats.[1] These include: relatively slow rate of drug biotransformation; species-specific sensitivity to Heinz body formation, methemoglobinemia and hemolytic anemia; and unusual sensitivity of certain drug receptor sites. Each of these will be considered briefly.

Drug Metabolism

Many drugs are metabolized in 2 phases. Phase-I reactions are commonly oxidations.[1,34] Oxidation prepares the drug for further reaction with a variety of agents that can conjugate with the Phase-I product. The conjugated (Phase-II) chemical is generally less lipophilic and more polar and water soluble, leading to more rapid and complete excretion, mainly in urine. Cats are deficient in at least one important conjugating system (glucuronidation), since they have insufficient enzyme glucuronyl transferase. Compounds detoxified by this pathway include acetaminophen, aspirin, phenols, alcohols and aromatic carboxylic acids.[1,8]

Because cats cannot readily eliminate Phase-I metabolites by conversion to Phase-II products, there may be elevated and/or prolonged concentrations of Phase-I compounds. Phase-I metabolism often activates or increases the toxicity to common toxicants, such as acetaminophen. This results in persistence of a compound that is often even more toxic than the absorbed parent compound.[1,34]

Feline erythrocytes have at least 2 biochemical liabilities with respect to certain drugs, especially those with oxidant activity.[1] Feline hemoglobin has a relatively high sulfhydryl content, which may be reflected in greater susceptibility to oxidative damage. Increased oxidative damage leads to Heinz body formation and eventual damage to the erythrocyte membrane. Feline erythrocytes are also deficient in methemoglobin reductase, which is the enzyme responsible for converting oxidized hemoglobin (methemoglobin) back to reduced form. For example, acetaminophen (Tylenol, *etc*) induces methemoglobin that, if not corrected, leads to Heinz body formation, eventual erythrocyte membrane damage and hemolysis.[1]

The response of cats to receptor site stimulation may be different from that in other animals.[1,38] Cats respond to increasing doses of morphine by becoming excited rather than depressed. However, cats can respond favorably to morphine in small doses, the response being dependent on a dose that allows adequate metabolism and elimination of morphine.[14] Reserpine effects persist for only 1-2 days in most species but for as long as a month in cats. Cats appear to recover more slowly from the nicotinic effects of some organophosphate insecticides, though this susceptibility could be at the receptor site or in metabolism of the insecticide.

Diagnosis of Poisoning

Though the clinician often is forced to treat acute illness symptomatically, therapy is most effective when a chemical specific diagnosis can be made.[1,33,34] When poisoning is suspected, one should attempt to gather information about specific exposure. A quick but thorough review of the circumstances and environment should be made. Important information includes changes in diet or location, freedom to roam, recently applied or administered medications, use of cleaners or pesticides on the premises, open containers of drugs or household chemicals, availability of house or garden plants, and

presence of projects that use chemicals (photographic development, furniture refinishing, etc). Any suspicious labels or containers should be brought with the affected animal, since the ingredient label often contains information important to diagnosis. The information sources discussed earlier may be helpful in evaluating potential effects of active ingredients.

Clinical signs are important in diagnosing intoxication. Such signs as sudden death, acute seizures, blindness, ataxia, acute gastroenteritis, icterus, hemolysis, hemoglobinuria and cyanosis traditionally have been associated with poisoning. However, one can be misled by clinical signs.[34] With only a limited number of body systems and thousands of disease entities and chemicals, distinctive responses are often difficult to obtain. Further, many chemical intoxications cause only vague and generalized clinical signs. The clinician must attempt to relate available clinical evidence to a field of potential toxicants. With the field thus narrowed, one can go on to more specific procedures that may lead to a specific chemical diagnosis.

In fatal cases, necropsy should always be encouraged.[33,34] Specific lesions are caused by many toxicants, while lack of gross lesions is characteristic of others. Necropsy provides access to organs valuable for chemical analysis to confirm or deny the clinical diagnosis. Liver, kidney, stomach and intestinal contents, urine, fat and brain usually provide the specimens needed to consider a wide array of toxicologic possibilities. If owners wish to dispose of the remains themselves, a cosmetic necropsy can easily be done and samples from all the tissues listed readily obtained.

Diagnosis is important, not only for the improved outcome of an individual case, but to provide counseling and prevention of further losses. In addition, the close association of cats with their owners suggests that what is a danger to the cat could also be a potential for harm to children or others in the household.

Treatment of Poisoning

Animal toxicoses often are manifested as acute, serious clinical disorders in which prompt supportive and symptomatic therapy is essential. If circumstances or clinical signs suggest that toxicosis is involved, cerain important guidelines should be kept in mind.[3,5,14,34] Proper management of toxicologic emergencies should include:

- Emergency and supportive therapy to sustain life.
- Prompt evaluation of the animal's pathophysiologic status.
- Detoxification appropriate to the probable route of exposure.
- Appropriate supportive and antidotal procedures.
- Monitoring of clinical progress.
- Enhancing the body's natural detoxification and elimination mechanisms.

Beyond these immediate and life-saving steps, appropriate diagnostic and prophylactic measures should be implemented to prevent future instances of poisoning. One should attempt to confirm the chemical or agent responsible as quickly as possible. This helps determine the source of toxicant so that one may instruct clients in the avoidance of such instances.

A telephone call may be the first contact with the owner of an animal that may have been poisoned.[3,34] During the telephone conversation, questions should be asked to determine the cat's clinical condition and major clinical responses. If exposure to a specific agent is known or suspected, ask the owner to read the ingredients from the label or describe as accurately as possible the material or plant to which the animal was exposed. If possible, the owner should be instructed to collect any vomitus, bait or other suspected material and bring them with the animal for possible identification or analysis.

If the patient has not vomited and is asymptomatic, quick calculation of the probable dose received may help establish a prognosis. However, usually owners are not aware of the amount ingested or degree of exposure.

It is generally difficult or impossible for owners to administer oral emetics to cats. The best action usually is to have the cat promptly brought in for examination by a veterinarian. Cats may be allowed to drink water voluntarily, since this will dilute any

ingested toxicants and could stimulate vomiting. If the cat will voluntarily consume egg white, this may help bind and thus retard absorption of certain intoxicants.[34] However, the efficacy of this procedure for a wide variety of toxicants is not well established.

With dermal exposure to a toxic chemical, owners should be warned to protect themselves from potential exposure while handling the cat.[3,16,34] However, prompt washing with warm water and a mild detergent to remove highly toxic materials, such as pesticides, may be quite beneficial and even life saving. If protective clothing and gloves are not immediately available to the owner, it may be best to wrap the cat in a blanket or sheet and bring it immediately for veterinary attention. These cats should be bathed with large volumes of warm water. Many dermal toxicants are lipophilic and not readily removed by water alone. Use of an appropriate shampoo or mild detergent helps remove lipid-soluble toxicants, such as pesticides. Veterinarians and their assistants should also take care to prevent dermal or ocular exposure to themselves during this washing.

A recently ingested toxicant may still be in the stomach. Some toxicants, such as alcohol, are directly absorbed from the stomach.[1] Since ingesta may move from the stomach to the intestine within 30 minutes to several hours, prompt gastrointestinal detoxification is important.[3,14,34] Methods generally used to decrease absorption from the gastrointestinal tract include emesis, gastric lavage, containment in a nonabsorbable form, catharsis and direct removal.

Inducing Emesis

Inducing emesis is effective but is of limited benefit if performed more than 4 hours after ingestion.[3,16,34] Emesis is contraindicated if an animal has ingested corrosive agents or volatile hydrocarbons or petroleum distillates. Further, emesis should not be used in unconscious or semicomatose patients that do not have an active cough reflex. Finally, emesis should not be attempted in convulsing animals unless convulsions are controlled. For some toxicants causing hyperirritability (*eg*, strychnine or chlorinated hydrocarbon insecticides), vomiting may trigger seizures.

Emesis is most effective when the stomach contains food material or liquids.[1,3,34] While apomorphine is generally an effective emetic, it may increase CNS and respiratory depression caused by the toxicants. Further, a safe dosage of apomorphine has not been established for cats, and use of this drug is generallly not recomended.[1,3,14,16] Syrup of ipecac (7% in glycerol), diluted 1:1 and given PO at 2.2-6.6 mg/kg body weight, is the preferred emetic.[1,14,16] Both hydrogen peroxide (1 teaspoonful) and liquid dishwashing detergent have been used successfully as emetics in dogs. The usefulness and safety of these agents in cats has not been determined.

Gastric Lavage

An alternative to emesis is gastric lavage.[3,14,16,34] This is most effective if done within 2 hours after ingestion of the toxicant. Animals must be maintained under anesthesia with a cuffed endotracheal tube in place. The tube should extend at least 2 inches rostrally beyond the teeth to prevent aspiration. The largest-bore stomach tube possible for the size of animal should be used.

Premeasure the tube from the nose to the last rib. The cat should be inclined slightly with the head somewhat lower than the body. The lubricated tube should be inserted gently and carefully without undue force. A lavage solution dosage of 5-10 ml/kg body weight is recommended for each washing, being introduced under low pressure. After a brief time in the stomach, the fluid should aspirate with a large bulb or 60-ml syringe. This procedure should be repeated at least 10 times or until the lavage fluid is essentially clear. Remember that induction of emesis or use of gastric lavage even immediately after ingestion removes no more than 60-70% of gastric contents. Lavage fluids may be either tap water or saline solution. Gastric lavage may be contraindicated after ingestion of caustic or corrosive agents.

Containment

Because neither emesis nor gastric lavage is completely effective, and in some cases may be contraindicated, an additional or alternative detoxification procedure is containment of the toxicant in a nonabsorb-

able form.[3,34] This is generally done with an adsorbing agent, such as activated or superactivated charcoal. Adsorption therapy involves physical binding of toxicant molecules to a nonabsorbable carrier (*eg*, charcoal), which is then eliminated from the intestinal tract. Activated charcoal is effective for adsorbing a variety of heavy metals and organic toxicants and drugs. It is relatively ineffective against cyanide and ammonia.

Several convenient adsorbing products are currently available for use in small animals. The potency of different products may vary, but the principle involved and overall effect are similar. Activated charcoal can be given as a slurry consisting of 1 g of activated charcoal and 5 ml of water. The recommended dosage is 10 ml slurry/kg body weight. It may be useful to follow administration of charcoal about 30 minutes later with a saline cathartic. Of the available cathartics, sodium sulfate is generally recommended. The dosage is about 1 g/kg PO.

Adjunctive Therapy

Adjuncts to effective therapy include procedures that hasten elimination of absorbed toxicant from the body.[3,16,34] Most toxicants are metabolized and excreted in the bile or, more commonly, in the urine. Animals should be monitored closely to maintain renal function and urine output. Fluid therapy consistent with the animal's pathophysiologic status is important. Diuretics may hasten urinary elimination of toxicants. Animals must be well hydrated before diuresis begins. Mannitol should be given IV at 2 mg/kg/hour. Alternatively, furosemide may be given IV at 4 mg/kg. Since many toxicants cause renal shutdown because of nephrotoxicosis or hypovolemia, maintenance of hydration, blood pressure and urinary output is extremely important.

Ion trapping is sometimes recommended as a useful adjunct to toxicologic therapy.[1,3,34] Compounds pass cell membranes less readily when ionized. Therefore, ionized toxicants are less readily absorbed by renal tubules. Alkaline urine facilitates ionization of acidic compounds, such as aspirin or barbiturates. Use of sodium bicarbonate IV at 5 mEq/kg/hour has been recommended. Basic compounds are ionized in acidic urine. Strychnine, amphetamines and other alkaloids are thus more readily excreted when urine is acidified. Ammonium chloride, given PO at 200 mg/kg/day in divided doses, facilitates ionization of basic compounds.

In some cases peritoneal dialysis may be an alternative in toxicologic therapy, particularly if renal function is compromised. Peritoneal dialysis helps remove endogenous toxins from animals with toxic renal failure.[16] In addition, many exogenous toxicants may be removed by peritoneal dialysis.

Application of a specific antidote to chemically combat a specific toxicant is an ideal goal. Unfortunately, few effective specific antidotes are available, as compared to the wide array of toxicants to which cats may be exposed. Appropriate specific antidotes are probably available for less than 5% of clinically significant intoxicants. In our experience, effective antidotes include mainly the following:[16,34]

- Atropine for cholinesterase inhibitors
- Acetylcysteine for acetaminophen
- EDTA for lead
- Ethanol for ethylene glycol
- Penicillamine for arsenic and copper
- Vitamin K_1 for anticoagulant rodenticides

Individualized supportive therapy is probably the most important aspect of emergency toxicologic treatment. Respiratory and cardiovascular support, maintenance of body temperature, control of CNS function and alleviation of pain allow time for the animal to metabolize and eliminate toxicants and initiate important homeostasis and repair functions in major organs.[1,3,16,34] Only a few generalized suggestions are given here, since individual decisions about supportive therapy are the province of the clinician and will vary greatly in each individual situation.

Seizure or CNS hyperactivity should be controlled with 2.5-5 mg diazepam (Valium: Roche) given IV. If IV administration is not possible, intraperitoneal injection is a practical alternative; the drug is absorbed from the peritoneum within 10-15 minutes after IP injection. Diazepam administration may

be required every 3-4 hours until clinical signs abate. Phenobarbital is also effective in controlling seizures, generally IV at 2-4 mg/kg. Phenobarbital may be used cautiously by IV injection given to effect. Though dosage guidelines are given for drugs controlling CNS activity, clinicians must use individual judgment and administer only what is necessasry on an as-needed basis. A complication of many intoxications is respiratory depression, which may be complicated by administration of drugs used to control seizures. Since some seizures may be associated with cerebral edema, appropriate therapy with mannitol and/or dexamethasone may be indicated.

Pain in conscious animals may be alleviated in part by meperidine IM at 1-2 mg/kg body weight.[3,16]

Intoxication by Rodenticides

Rodenticides are designed to kill mammals, and exposure of domestic animals may lead to toxicosis. Some highly toxic rodenticides, such as fluoroacetate and strychnine, induce secondary poisoning (also known as relay toxicosis) in carnivores, such as cats, that consume poisoned rodents.[34,37]

Rodent-control chemicals are commonly available as baits or tracking powders.[34] Tracking powders are placed in locations of rodent traffic. Rodents that contact the powders ingest them involuntarily during grooming. Cats frequenting such areas also are at risk to intoxication by tracking powders because of their habit of frequent cleaning and grooming of their paws and haircoat.

Toxic baits are designed to be attractive to mammalian pests.[34] They may be incorporated into paraffinized or microencapsulated forms that increase their stability under a wide range of environmental conditions. The flavors and odors used may be attractive to dogs and cats as well as rodents. Careless placement, overuse or failure to remove poisoned rodents may result in accidental exposure of cats or other domestic animals. Since rodenticides are commonly recognized as toxic, they may be used for malicious poisoning as well.

A wide variety of commercially available rodenticides is available. Those of greatest concern are a hazard because of widespread use or high toxicity. By far the most common rodenticides are the anticoagulants.[4,29,34] Other agents still in routine but less frequent use are strychnine and zinc or aluminum phosphide. Two new rodenticides, bromethalin and cholecalciferol (vitamin D_3) are becoming increasingly available. In reports on the incidence of poisoning in small animals, cats are much less frequently victims of rodenticide poisoning than are dogs.[4,11]

Anticoagulant Rodenticides

Types: Anticoagulant rodenticides are commonly used by professional exterminators and laypersons.[8,29,34] The product in greatest general use is warfarin. Concentrations of warfarin in commercial products range from 0.025% in baits to 1% in throw packs. These products are recognized by the term "4-hydroxycoumarin" as part of the active ingredient listing. Some commercial preparations include sulfaquinoxalin to enhance anticoagulant activity by inhibiting synthesis of vitamin K in the small intestine and colon.

Other common anticoagulants are the indandiones. These include diphacinone, chlorphacinone, valone and pindone. Of these, diphacinone is the most commonly used and has a very extended half-life, resulting in a much longer anticoagulant effect than warfarin. Blood levlels of diphacinone may be detectable for 3-4 weeks after ingestion of a toxic dose.[29] A group of anticoagulant rodenticides known as second-generation coumarins includes brodifacoum and bromadiolone. These are available to pest-control professionals and over the counter. These compounds are generally much more toxic than first-generation rodenticides and may induce poisoning from a single ingestion. The effects of brodifacoum are much more prolonged than for bromadiolone.

High dietary fat, prolonged antibiotic therapy, liver disease and concurrent presence of such drugs as phenylbutazone, sulfonamides and corticosteroids may enhance the toxicity of anticoagulant rodenticides.[29,34]

Clinical Signs: The anti-vitamin K rodenticides interfere with vitamin K epoxide

reductase, preventing the regeneration of the "active" or hydroquinone form of vitamin K.[29,34] Because coagulation factor synthesis depends on the presence of active vitamin K, continued interference results in eventual decay and loss of vitamin K-dependent coagulation factors (II, VII, IX, X). Even massive exposure to coumarin anticoagulants requires a latent period, during which coagulation factors decrease below critical levels. Clinical signs generally occur after 1-3 days of exposure.

Clinical signs are manifestations of hemorrhage.[1,5,8,29,34] Occasionally the onset of signs may be acute, with hemorrhage occurring in the cerebral vasculature, pericardial sac, mediastinum or thorax. More commonly animals develop pale mucous membranes, dyspnea, hematemesis, epistaxis and bloody feces. Subcutaneous hematomas, hemarthrosis and hemorrhage in the anterior chamber of the eye may also occur. If the clinical course is longer than several days, icterus may develop as a result of autolysis of impounded blood.

Necropsy reveals sites of hemorrhage throughout the body. Hemopericardium, pulmonary hemorrhage and edema, subpleural and subperitoneal ecchymoses and suffusions, subcutaneous hematomas, hemarthrosis and hemorrhagic intestinal contents are common. Laboratory examination of blood may confirm an anti-vitamin K coagulopathy. Depression of vitamin K-dependent factors results in elevated bleeding time, increased clotting time and prolonged one-stage prothrombin time and activated partial thromboplastin time.[29,34]

Chemical detection of anticoagulants in baits or vomitus may confirm recent exposure.[29,34] However, the stomach is often cleared of anticoagulant well before clinical signs are evident. With the exception of bromadiolone, most common anticoagulants can be detected in specimens of whole blood or liver. An anticoagulant may not be detected because the rodenticide may be metabolized and excreted while clotting defects persist.

Treatment: Treatment decisions generally involve 2 types of patients. The first is a patient with clinical signs or complications of coagulopathy. The second is an asymptomatic patient presented within several hours of suspected or confirmed exposure.[5]

Animals with severe coagulopathy should be handled carefully to avoid additional traumatic hemorrhage. If severe hypovolemia is present, transfuse fresh whole blood IV at 20 ml/kg. Infuse half rapidly and the remainder by slow IV drip. Providing prothrombin and other clotting factors in whole blood immediately restores coagulation function. As a followup, or when blood loss is not critical, vitamin K_1 is the most effective therapeutic agent. An injectable product (Aquamephyton: Merck, Sharp and Dohme) contains 10 mg vitamin K_1/ml. Administration should be SC at 5 mg/kg every 12 hours until coagulation times return to normal. Reversal of hypoprothrombinemia begins within 30 minutes and is maximal within several hours. Synthetic vitamin K (menadione) is less effective than vitamin K_1 and should not be used when clinical signs are serious.[5,29,34]

If dyspnea persists as a clinical sign, radiography of the thorax may demonstrate significant thoracic hemorrhage.[34] Thoracentesis to remove excess blood may be life saving. Convalescent animals should be given vitamin K_1 for at least 4-6 days PO at 1.0-2.5 mg/kg divided TID or BID. If poisoning by diphacinone or brodifacoum is confirmed or suspected, the prothrombin time should be reevaluated weekly; therapy may be needed for as long as 3-4 weeks.

If the patient is asymptomatic when presented, emesis should be induced if exposure was less than 3 hours previously.[5] Administer activated charcoal PO at 1 g/kg body weight and follow in 30 minutes with a saline cathartic PO at .25-0.5 g/kg dissolved in at least 5 volumes of water. If substantial exposure is known or calculated, a loading dosage of vitamin K_1 (2.5 mg/kg SC) may be given and oral vitamin K_1 dispensed for home administration. If the cat remains asymptomatic for 3 days, it may be maintained on oral vitamin K_1 for an additional week. It may be wise to perform an activated clotting time and/or one-stage prothrombin time a week later.[5,29]

Strychnine

Strychnine is most commonly used to control gophers and chipmunks.[34] Its use is

restricted to preparations containing less than 0.5% strychnine for subsoil use. While strychnine remains a relatively common source of poisoning in dogs, it is an uncommon cause of poisoning in cats. Strychnine is highly toxic to most mammals. The estimated lethal oral dosage in cats is about 2 mg/kg.

Strychnine is readily absorbed from the intestinal tract but poorly absorbed from the stomach.[1,34] The highest concentrations are in blood, liver and kidney. Metabolites are excreted primarily in the urine.

Clinical Signs: Strychnine affects the central nervous system by selectively antagonizing postsynaptic inhibition in the spinal cord and medulla.[1,34] With the moderating and controlling effects on reflex arcs eliminated, massive spinal reflex activity results in generalized rigidity and tonic seizures. All striated muscle groups are affected, but relatively more powerful extensors predominate to produce the characteristic extensor rigidity and tetany of strychnine poisoning.

Other effects of strychnine include elevated blood pressure, heart rate and right ventricular pressure. These responses appear to be mediated through the medulla, and persist even when seizures are prevented by curare and hypoxia is alleviated with artificial respiration.[1,5]

Clinical signs appear within 10-120 minutes after ingestion. Affected animals are first apprehensive, nervous, tense and stiff. Palpation reveals a tense abdomen and rigid cervical musculature. External stimuli, such as touch, sound or sudden light, may initiate a spontaneous tetanic seizure. Animals may assume a "saw-horse" stance, with the legs and body stiff, neck arched, ears erect and lips pulled back from the teeth. Breathing may cease momentarily, and death is often a result of respiratory arrest during a seizure. Dilated pupils and cyanotic membranes occur during the seizures.

Diagnosis: Rigor mortis occurs rapidly after death. There are no gross or microscopic lesions characteristic of strychnine poisoning.[34] Often, however, the stomach of strychnine poisoned animals is still filled with food or bait, since strychnine does not generally cause vomiting. Strychnine toxicosis is commonly suspected when animals die suddenly in tetanic seizures or when they are found dead with no premonitory signs. Similar acute clinical neurologic signs may be caused by chlorinated hydrocarbon insecticides, metaldehyde, hypocalcemia, 4-aminopyridine, amphetamine or caffeine toxicosis.

Liver, stomach contents and urine are preferred specimens for chemical analysis.

Treatment: Treatment of strychnine poisoning depends primarily on maintenance of relaxation and prevention of asphyxia.[1,5,34] The first priority should be to prevent serious seizures, which are life threatening. A variety of sedatives, anesthetics and muscle relaxants may be used. An IV dose of 2.5-5 mg diazepam (Valium: Roche) is often recommended as initial treatment, for controlling seizures. Administration must be repeated frequently to maintain relaxation. Anesthesia with IV pentobarbital is often required to prevent seizures. Barbiturates should also be administered cautiously and only in doses sufficient to control seizures, taking care to avoid the respiratory depression that may accompany barbiturate use. When the patient is relaxed, a cuffed endotracheal tube may be placed to ensure a patent airway. Muscle relaxation can also be induced with inhalation anesthesia, methocarbamol (Robaxin: Robins) IM at 150 mg/kg, or continued use of IV Valium. With seizures controlled and the endotracheal tube in place, gastric lavage may be used to remove stomach contents, which are the source of the toxicant. After lavage, activated charcoal may be given PO, followed with a saline cathartic.

Cardiovascular function and temperature should be monitored and maintained during therapy and convalescence. With good oral detoxification and relaxation, cats can be expected to recover in 24-48 hours, requiring no medication after that time.

Zinc and Aluminum Phosphide

Zinc phosphide and aluminum phosphide are alternatives to anticoagulant rodenticides. They are generally used by professional exterminators in this regard, but are not widely used by laypersons. These dull grayish-black powders are unstable in water or acids, but are environmentally stable for

about 2 weeks. Commercially and individually compounded baits contain concentrations of 2-5%. Phosphide has a faint odor of acetylene.

The specific toxicity of phosphides to cats is unknown, but most animals including dogs are poisoned by dosages of about 40 mg/kg body weight. Consumption of food before ingestion of zinc phosphide stimulates gastric hydrochloric acid secretion and increases susceptibility by enhancing hydrolysis to phosphine, which is responsible for the acute toxic effects. Zinc phosphide often causes vomiting in nonrodents, and thus does not consistently cause fatal poisoning.[1,5,14,34,37]

Clinical Signs: Both phosphine and zinc phosphide are absorbed from the gastrointestinal tract. Enteric irritation, pulmonary irritation and CNS effects occur. The mechanism of poisoning is not fully known, but acidosis and hypocalcemia are seen.

Clinical signs usually occur 15 minutes to 4 hours after ingestion but may be delayed as long as 18 hours.[5,34] Large doses may cause death within 3-5 hours. Severely poisoned animals rarely survive more than 48 hours. Emesis is common and the vomitus often contains dark blood. Early signs of anorexia and lethargy are followed by rapid deep respiration. Abdominal pain is evident. Ataxia, weakness and recumbency are followed by terminal hypoxia, gasping for breath and agonal struggling. Hyperesthesia or seizures occur occasionally. Some reports in dogs have described hyperesthesia and running similar to the clinical syndrome seen with fluoroacetate toxicosis.

Diagnosis: Zinc or aluminum phosphide poisoning is difficult to diagnose.[34] A history of exposure, accompanied by rapid onset of clinical signs including dyspnea, vomiting and variable nervous signs, may suggest phosphide toxicosis. Chemical analyses for zinc phosphide in stomach contents are somewhat unreliable. Zinc concentrations in blood, liver, kidney or stomach contents may be elevated, but background concentrations and ranges are not well established. Acetylene odor of the breath or stomach contents may also suggest zinc phosphide poisoning. All specimens should be rapidly frozen and maintained frozen until arrival at a diagnostic laboratory. Zinc concentrations may also be affected by sample containers. Rubber stoppers in blood or serum vials, as well as gaskets of plastic syringes, may be coated with zinc stearate, which can affect the analysis of zinc. Therefore, any samples for zinc analysis should be collected in glass or all-plastic syringes and stored in all-glass or all-plastic vials.[5]

Treatment: There is no specific treatment for zinc phosphide poisoning.[1,5,34] Therapy is directed against acidosis, hypocalcemia and liver damage. Oral detoxification using emesis or gastric lavage may be attempted. Hydrolysis of zinc phosphide to phosphine is retarded by gastric lavage with 5% sodium bicarbonate. Calcium gluconate and 1/6 Molar sodium lactate are recommended to counteract hypocalcemia or acidosis, respectively. Sodium thiosulfate (10% solution), B vitamins and dextrose have also been recommended.

Bromethalin

Bromethalin is a relatively new rodenticide available in pelleted grain baits at a concentration of 0.01%.[24] It is currently marketed in 1.5-oz place packs under the trade names Assault and Vengeance. The acute oral LD_{50} for bromethalin in cats is 1.8 mg/kg body weight. On this basis a 7-lb cat would consume an LD_{50} dose in 54 g of bait (about 1 1/4 place packs). Thus, while specific toxicoses are not currently apparent, the potential exists for serious toxicosis from careless use of this rodenticide. Bromethalin is rapidly absorbed from the gastrointestinal tract. In rats, plasma levels peak in about 4 hours. The plasma half-life is 5.6 days.

Bromethalin is thought to uncouple oxidative phosphorylation in CNS mitochondria. There may be decreased ATP production with reduced Na-K ATPase, resulting in fluid accumulation in the CNS. Cerebrospinal fluid presssure is increased 3-4 times above normal, resulting in cerebral edema. There is an increase in the water and Na content of white matter, with development of vacuolation similar to lesions produced by trialkyl tin or hexachlorophene toxicosis.

Clinical Signs: Both acute and chronic poisoning may occur. Doses in excess of twice the LD_{50} cause acute signs, including

tremors, clonic convulsions, prostration and death, often within 18 hours after consumption of bait. Subacute or chronic signs may result from multiple smaller doses and are characterized by lethargy, posterior weakness, reduced muscle tone and paralysis. Effects are generally reversible if exposure is avoided.

Diagnosis: Diagnosis depends on a history of exposure correlated with characteristic clinical signs. Bromethalin may be detected in baits or stomach contents, but tissue residues and their diagnostic significance are not yet established.

Treatment: There is no specific antidote for bromethalin. Treatment should include counteracting cerebral edema. This may be accomplished by using an osmotic diuretic, such as mannitol, followed with corticosteroid therapy (*eg,* dexamethasone).[24] Prompt therapy may reduce CSF pressure to normal levels within 30 minutes. Untreated animals may have elevated CSF pressure for as long as 7 days.

Cholecalciferol (Vitamin D_3)

Cholecalciferol has been used as a new chemical approach to rodent control. Cholecalciferol is incorporated at 0.075% into commercial baits and marketed under such trade names as Quintox and Rampage.

The rationale for use of cholecalciferol baits is that they are either single-feeding or multiple-feeding rodenticides, for controlling anticoagulant-resistant species. Consumption of a single lethal dose results in death 3-4 days after first ingestion. Once a lethal dose is consumed, food intake generally ceases.

Toxicity of cholecalciferol is not well established in a wide variety of mammals. However, the single acute oral LD_{50} in rats is 43.6 mg/kg. For dogs the oral LD_{50} is 88 mg/kg body weight. In the absence of data for cats, it is assumed the toxic dose in in the same range. Recent evidence from field cases indicates that a nonlethal toxic dosage may be as low as 2-3 mg/kg body weight, or about 1 g of bait/kg body weight.[53]

Clinical Signs: Cholecalciferol mobilizes Ca and P from the skeletal system.[5,8] In addition, large doses may cause direct cellular damage to liver and kidney. Persistent hypercalcemia leads to calcification of blood vessels, kidney and heart. Clinical signs of acute toxicosis include generalized weakness, nausea, vomiting, constipation, polyuria, dehydration, hypercalcemia and hyperphosphatemia. Hypercalcemic heart failure may be the cause of acute death.

Prominent gross lesions are myocardial necrosis with white streaks throughout the myocardium, hemorrhagic gastroenteritis and mild pulmonary edema. Histologic lesions include mineralization of vasculature, necrosis and mineralization of myocardial fibers, subintimal mineralization of myocardial vasculature, hyaline degeneration of kidney tubules, mineralization of Bowman's capsule and glomeruli, and pulmonary bronchial mineralization.

Diagnosis: Diagnosis depends on correlating clinical and pathologic effects of vitamin D toxicosis with a known exposure, or confirmation of elevated levels of hydroxylated metabolites in blood or tissues. Analysis of metabolites is not readily available. Clinicopathologic changes, including hypercalcemia and hyperphosphatemia, may strongly suggest vitamin D toxicosis.

Treatment: Treatment should include prompt removal from any source of vitamin D. Affected animals should be placed on a low-Ca diet. In affected people, prednisone (1 mg/kg/day) is recommended to reduce Ca absorption and decrease Ca mobilization from bone. If hypercalcemia is life threatening, calcitonin (Calcimar) at 2-4 IU/kg helps reduce serum Ca to near normal levels. Saline infusion IV may improve glomerular filtration and reduce renal tubular resorption of Ca but must be used cautiously if cardiac or renal impairment is present.[5]

Minor Rodenticides

Because of tight controls or very limited commercial availability, various minor rodenticides do not constitute a significant threat to cats. These include alpha chloralose, ANTU, fluoroacetate, thallium and pyriminil. Characteristics of these rodenticides are listed briefly in Table 1.

Intoxication by Insecticides

Various insecticidal preparations are used widely to control ectoparasites on cats, and to control pests in premises and

yards.[1,8,11,28,34] Common sources of exposure of cats to insecticides include excessive application by dipping or spraying, inhalation or dermal exposure when houses are treated with sprays or fumigants, and occasionally by ingestion of large amounts of poisoned insects, such as crickets, grasshoppers or roaches. Among insecticides, the most commonly used include organophosphates and pyrethrins. Chlorinated hydrocarbons are generally unavailable and so cause only occasional accidental exposures. Products containing limonene, a citrus extract, are used with increasing frequency but are relatively nontoxic.[5] Two highly toxic insecticidal compounds, nicotine and arsenic, are very rarely used. Their toxicity will be discussed with the natural toxicants and metals, respectively.

Chlorinated Hydrocarbons

Cats are commonly considered more susceptible than other animals to chlorinated hydrocarbons.[1,34] However, documentation of this belief for a variety of chlorinated hydrocarbon insecticides is difficult to find. Chlorinated hydrocarbon insecticides used extensively in the past included DDT, aldrin, dieldrin, endrin, benzene hexachloride, chlordane, heptachlor and methoxychlor. Currently only limited use of lindane and methoxychlor is allowed for the public. However, neither of these products is currently recommended for cats. Therefore, exposure is expected only when accidental access is gained to old products or when owners may carelessly or naively use products not recommended for cats.

The specific mechanism of action of chlorinated hydrocarbon insecticides remains obscure. Generally they may interfere with metabolic reactions in neurons and/or affect ionic exchange at the axonal membrane.[1,5,34]

Clinical Signs: Toxicity of chlorinated hydrocarbon insecticides varies widely, with LD_{50} values ranging from <10 mg/kg for highly toxic compounds, such as endrin, to >1000 mg/kg for methoxychlor.[34] Toxicosis is characterized generally by CNS stimulation.[8,13,34] Early signs may include apprehension, tremors, intermittent spasms of cervical muscles, blepharospasm, champing and mild hypersalivation. Clonic seizures occur intermittently. Between seizures animals may rest and appear near normal. Marked incoordination may interfere with an animal's ability to eat or drink. In cats, dieldrin, endrin and lindane are most rapid acting and have the highest potential for producing seizures. Hepatotoxicity, renal damage and myocardial damage may occur. These are more likely from exposure to toxaphene and chlordane.

Diagnosis: Chlorinated hydrocarbon insecticide toxicosis can be readily diagnosed.[34] Characteristic intermittent clonic seizures may suggest exposure. Vomitus, hair or blood from live animals may be submitted for gas chromatographic detection of a specific insecticide. Specific quantitation is not always correlated with the severity of clinical signs. An organochlorine pesticide level of >1 ppm in blood strongly suggests serious exposure. In animals that die from acute intoxication, liver is generally the most reliable specimen for analysis. With chronic poisoning and accumulation, the lipophilic nature of chlorinated hydrocarbon insecticides makes adipose tissue the specimen of choice.

Treatment: Treatment of poisoned animals is primarily symptomatic.[3,8,34] Animals with seizures or other neuromuscular hyperactivity should be lightly anesthetized with a barbiturate. An oral dose of 15-60 mg given twice daily, can control hyperactivity due to chlorinated hydrocarbons. An IV dose of 2.5-5 mg diazepam (Valium: Roche) is also effective and does not produce respiratory depression characteristic of the barbiturates. It is important to determine the route by which contamination occurred. Appropriate detoxification should be matched to the route of exposure. Failure to detoxify an animal dermally may result in continued absorption and prolongation of clinical signs.

Animals known to have been exposed to chlorinated hydrocarbon insecticides should be considered sentinels for potential human exposure. Every effort should be made to ascertain the source of exposure to prevent potential human access to the same toxicant. For example, prior improper or heavy use of chlorinated hydrocarbons for termite control can result in long-term contamination of soil, crawl spaces and buildings,

Table 1. Characteristics of selected rodenticides.

Ingredient	Common Trade Names	Concentration in Baits	Toxic Dosage (mg/kg)	Clinical/Diagnostic Features	Therapy
Alpha chloralose	Alphakil, Glucochloralose	1-3%	100 (LD_{50})	Very limited use in US. Depresses neurons of ascending reticular formation, suppressing arousal. Ataxia. Aggression, progressing to weakness, prostration. Sensitive to stimuli.	Restrain and/or sedate (diazepam). Evacuate & detoxify GI tract. Maintain temperature & support respiration.
Alpha chlorhydrin	Epibloc	1-3%	188 (LD_{50})	Available only to certified pest control operators. Sterility at sublethal doses. Produces anorexia & diuresis.	None specific. Oral detoxification may be useful.
ANTU	Anturat, Bantic, Rattract, Krysid	1-2%	75-100	Old rodenticide. Little used. Early salivation & vomiting. Causes marked pulmonary edema & hydrothorax. Cyanosis. Death by anoxia.	Oral detoxification early. Symptomatic therapy for pulmonary edema. Thoracentesis to relieve hydrothorax.
Crimidine	Castrix	0.1%	1.5 (rat)	Convulsant. Rapid onset & short course of seizures. Exact toxicity & features for cats not available.	Diazepam or barbiturates for seizures. Pyridoxine HCl (20 mg/kg IV).
Fluoroacetate & fluoroacetamide	Compound 1080 Compound 1081	0.12-2.2% 2%	0.2 (LD_{50})	Very toxic. Secondary poisoning may occur. Hyperirritable, restless in early stages. Repeated vomiting & defecation. Vocalization. Hyperesthesia. Cardiac arrhythmia.	Usually not successful after signs appear. Use symptomatic & detoxification procedures. Glycerol monoacetate (monoacetin) at 0.55 g/kg IM recommended but efficacy not established.
Norbormide	Shoxin, Raticate	0.5-1.0%	>1000	Toxicosis not likely in cats or dogs. Rats are restless, ataxic, dyspneic, become prostrate & die.	None described. Toxicosis unlikely.
Phosacetin	Gophacide	0.3%	3.7-7.5 (LD_{50} rat)	Organophosphate. Not currently marketed. Old supplies could be available. Signs of organophosphate toxicosis.	See organophosphates.
Phosphorus	Yellow Phosphorus, White Phosphorus, Bonide Blue Death, Sterns Electric Paste, Rat-Nip	1-2%	about 0.2	Not commonly available. Bait has garlic odor, also apparent on breath of intoxicated animal. Early vomiting & watery to hemorrhagic diarrhea. Later signs (3-5 days) are icterus, liver failure. Necropsy lesions are hepatosis, nephrosis, fatty change & hemorrhagic enteritis.	Gastric lavage. Follow with mineral oil. Treat for shock, hemorrhage, liver failure. Monitor blood glucose & renal function.
Pyriminil	Vacor, DLP 787	2%	62-200	Agent is nicotinamide antagonist. No longer marketed. Nausea, colic, vomiting, anorexia, depression. Tremors, lethargy, visual disturbances.	Oral detoxification. 25-50 mg nicotinamide IM every 4 hrs up to 8 injections. Follow orally with same dosage for 7-10 days.

which may also be a source of exposure to human beings.

Organophosphates and Carbamates

Organophosphates and carbamates are still the most commonly used and widely available insecticides for use on plants, animals, soils or households.[4,8,9,28,34] Gardening, lawn care, ectoparasite control and flea control commonly result in potential exposure to organophosphate or carbamate compounds. Flea collars impregnated with organophosphates, carbamates or other compounds are an additional source.

Spilled or improperly stored insecticides in basements, garages or lawns constitute a hazard of poisoning. Cats may lap up liquid concentrates or track through dry powders spread carelessly in the environment. Miscalculation of concentrations used for ectoparasite dips or sprays is a common source of overdosage. In addition, some organophosphate products are used at lower concentrations for cats than for dogs. Use of a product that is recommended for dogs may result in mild or moderate toxicosis if applied to cats at the same rate.

Clinical Signs: Organophosphate and carbamate insecticides inhibit the enzyme cholinesterase, inactivating synaptic neurotransmitter acetylcholine.[9,34] Acetylcholine released at synapses of parasympathetic nerves and myoneural junctions normally is quickly hydrolyzed by cholinesterase. When cholinesterase is inhibited, persistence of acetylcholine causes continued nerve stimulation, resulting in clinical signs characteristic of organophosphate and carbamate poisoning. Effects of acetylcholine stimulation are muscarinic (parasympathetic) and nicotinic (neuromuscular).

Clinical signs produced by the most common organophosphate and carbamate insecticides are similar.[1,5,9,34,37] There is overstimulation of the parasympathetic nervous system and skeletal muscles. Occasionally there may be mild involvement of the CNS. Early signs of acute cholinesterase inhibition are uneasiness or apprehension, increased skeletal muscle tone and isolated mild muscle fasciculations. Increased urination, defecation and vomiting may occur. As neuromuscular signs become more pronounced, the animal walks with a stilted, stiff-legged or "sawhorse" gait. Early parasympathetic signs may include mild salivation, but normal licking and swallowing may mask this effect for some time.

As toxicosis becomes more advanced, excessive salivation is evident and increased respiratory secretions result in coughing, moist rales and dyspnea.[34] Respiratory effects may become severe enough to produce cyanosis and serious respiratory embarrassment. Hypermotility of the gastrointestinal tract, in combination with excessive gastrointestinal secretions as a result of parasympathetic stimulation, results in diarrhea and straining. Other signs include excessive lacrimation, miosis and urinary incontinence. Muscular hyperactivity may progress to ataxia, weakness and paralysis as acetylcholine effects become fully manifested. Occasionally cats may exhibit increased CNS stimulation with what appears to be clonic seizures. More often however, severe CNS depression is evident. Pronounced miosis may cause animals to appear somewhat blind.

In acute cases, death likely results from hypoxia due to excessive respiratory tract secretions and bronchoconstriction coupled with bradycardia. Cats may die within 1-2 hours or survive for as long as 48-72 hours with marked clinical signs. For most organophosphate exposures, signs begin to abate after 48 hours. Recovery from carbamate toxicosis may occur in 6-24 hours because of the rapid reversal of inhibition by carbamates.

In some poisoned cats, muscarinic signs abate within a few days, but severe depression and mild nicotinic signs persist for several weeks. There is prolonged anorexia and dehydration. In spite of aggressive intervention these cats sometimes die after prolonged illness.

Diagnosis: The diagnosis is often strongly suggested by a history of exposure to organophosphate or carbamate insecticides, coupled with characteristic clinical signs of parasympathetic stimulation and nicotinic effects.[1,5,34] Rapid tentative confirmation of diagnosis can be obtained by cholinesterase determination in whole blood. Many clinical laboratories can run cholinesterase determinations. Whole blood is the specimen of choice. Whole blood cholinester-

ase values of poisoned animals generally are <20% of normal for control values. In cats, plasma pseudocholinesterase constitutes most of the whole blood cholinesterase activity.[5] Thus, cholinesterase values in cats may be markedly depressed even when serious clinical toxicosis has not occurred. In dead animals, brain is the best tissue to evaluate anticholinesterase exposure.

Detection of organophosphates in tissues of poisoned animals is usually not rewarding. Organophosphates are rapidly metabolized and low or undetectable tissue residues often occur even when acute and lethal toxicosis is evident.[34]

Treatment: Treatment of severe organophosphate poisoning should be handled as a medical emergency. The goal is to control excessive muscarinic activity, administer a cholinesterase reactivator if possible, maintain respiratory function and decontaminate the animal as soon as possible.

Control of muscarinic activity is generally accomplished with atropine. Atropine sulfate antagonizes the effect of acetylcholine in the autonomic nervous system.[1,5,9,34] Substantial doses are required, as atropine competitively blocks acetylcholine receptors. With mild clinical signs or doubt about diagnosis, a preanesthetic dosage of atropine (0.044 mg/kg) can be given SC. If this does not produce signs of atropinization (mydriasis, tachycardia, dry mouth), a presumptive diagnosis of organophosphate toxicosis can be made. Atropine dosage up to 0.2 mg/kg body weight is recommended if needed to control marked clinical signs. If cats are cyanotic, the oxygen deficit should be corrected before administration of atropine. Administer no more than one-fourth of the recommended dose IV. Full atropinization should be achieved in at least 15-20 minutes. The balance of the required dosage may be given IM or SC. Atropine administration may need to be repeated because the drug is metabolized in 4-6 hours, and severe clinical signs of organophosphate toxicosis could return after that time.[1,5,34] Remember that atropine does not antagonize nicotinic effects. Severe nicotinic effects can cause respiratory paralysis, and artificial respiration may be necessary.

Administration of a cholinesterase reactivator is recommended.[1,5,9,34] Use of hydroxamic acid derivatives (oximes), such as pralidoxime chloride or 2-PAM chloride (Protopam), has been recommended IV, IM or SC at 20 mg/kg body weight. This compound acts on the organophosphate-cholinesterase complex to free cholinesterase, allowing it to resume its normal function. However, if treatment is delayed for several hours, the organophosphate-enzyme complex stabilizes (known as "aging") and becomes more refractory to dissociation. Thus, for oximes to be most effective, they should be given as soon after exposure as possible, since aging increases with time. Reactivation of cholinesterase is beneficial because nicotinic effects of poisoning are also counteracted. However, the highly ionized oximes do not distribute to the brain and, thus, any CNS effects of organophosphates are not counteracted.

Administration of 2-PAM can be repeated every 12 hours as needed. Oximes are generally not recommended for carbamate toxicosis. In some cases, such as with poisoning by the insecticide Sevin, their use is contraindicated.

Nicotinic signs may also be counteracted by diphenhydramine (Benadryl), given PO at 1-4 mg/kg TID. This treatment, originally documented experimentally in dogs, has also been used successfully in clinical organophosphate toxicosis of cats.[54]

Decontamination to prevent further absorption is extremely important in organophosphate poisoning. Prompt administration of activated charcoal by drench or stomach tube markedly reduces additional absorption. With dermal exposure, the skin should be cleansed thoroughly with soap and water and rinsed with a dilute alkaline solution (*eg*, dilute Hilex liquid bleach). Organophosphates are readily hydrolyzed and detoxified under alkaline conditions.

Complicating pathophysiologic features of organophosphate toxicosis include respiratory failure and dehydration from continued vomiting and diarrhea. Supportive therapy, including artificial respiration and fluid and elecrolyte support, should be provided as appropriate.

Pyrethrins and Pyrethroids

Pyrethrins are natural insecticides produced by certain exotic *Chrysanthemum*

flowers.[5,34] Insecticidal properties of pyrethrum flowers have been known for years. They are relatively nontoxic and rather unstable in light and air. Recently, synthesis of more stable pyrethroid molecules has led to commercial introduction of a new generation of insecticides characterized by high toxicity in insects and fish, and low toxicity in birds and mammals.

Pyrethroids kill insects by severely disrupting nerve function. They prolong the transient increase in Na conductance of the nerve membrane. This leads to repetitive activity. The Na channel is stabilized with the Na gate in an "open" position, leading to prolonged influxes of Na and subsequent disruption of the action potential.

Numerous commercial pyrethroids are now available.[34] Some of these include allethrin, cypermethrin, decamethrin, fenvalerate, flucythrinate, flumethrin, permethrin, resmethrin and tetramethrin. Toxicity of these compounds in cats has not been reported. The oral LD_{50} for rats ranges from as low as 450 mg/kg for fenvalerate to well over 10,000 mg/kg for flumethrin. Pyrethrins and pyrethroids are commonly used with synergists, such as piperonyl butoxide, N-octyl bicycloheptane dicarboximide and others, which enhance toxicity in insects and mammals by prolonging the life of the intact, active form of the insecticide. Among domestic animals, cats are commonly considered more at risk to pyrethroid poisoning. In particular, use of fenvalerate as an insecticidal spray for cats has caused some adverse reactions.[6]

Clinical Signs: Clinical signs of pyrethroid toxicity appear to be characterized by 2 syndromes, the T syndrome and the CS syndrome. The T syndrome is characterized by increased sensitivity to external stimuli, fine muscle tremors, and eventual progression to whole-body tremors and prostration. It is observed generally in poisoning with pyrethroids not containing the cyano group, such as permethrin terallethrin and tetramethrin. The CS syndrome involves pawing and burrowing behavior in rodents, salivation, coarse tremors progressing to sinuous writhing, and clonic seizures. This syndrome is associated with poisoning by cyano-group pyrethroids, such as allethrin, cyfluthrin, cyprimethrin, decamethrin, fenvalerate and flucythrinate. Paraesthesia of the skin has been described in affected people, but this effect is not known to occur in animals. There appear to be no persistent or pathologic effects, but this may be a pharmacologic response to transient increases in Na conductance in sensory nerves.

Toxicosis is most often associated with vigorous or excessive insecticidal treatment directly applied to animals.[5] Some believe it may be due, in part, to larger amounts of synergists in the insecticide formulation. This is supported by recent reports of enhanced toxicity associated with use of an insecticide (fenvalerate) and repellent (Deet) combination.[55] Such combined products are widely available as over-the-counter preparations.

Treatment: There is no specific antidotal treatment. Topical exposure should be treated by bathing with detergent to remove residual insecticide. Recent oral exposures can be counteracted by appropriate administration of emetics, activated charcoal and saline cathartics. With severe CNS stimulation, sedation may be accomplished with small doses of short-acting or ultrashort-acting barbiturates. Diazepam (Valium: Roche) may also be effective for neurologic signs. Atropine blocks salivation produced by pyrethrins, but does not protect against other clinical signs.

Rotenone

Rotenone is a natural botanic insecticide derived from the roots of the *Derris* plant.[5,34] Historically it has been used as a fish poison as well as an insecticide for ectoparasite control. It has been formulated into products for use in gardens and on dogs and cats as dips, sprays and powders.

Oral lethal doses used in animals ranged from 50 mg/kg in guinea pigs to 3000 mg/kg in rabbits.[5,34] The specific toxic dosage for cats has not been reported, but cats are most often affected after deliberate use of rotenone products against ectoparasites.[5] In normal use, rotenone is of low toxicity because the concentrations are usually 1% or less. It appears to act by blocking NAD-flavin-dependent electron transport.

Clinical Signs: With oral exposure, gastric irritation is followed by vomiting. Oral toxicity is relatively low, probably because of poor gastrointestinal absorption in con-

junction with gastric irritation, resulting in vomiting that limits availability. Dermal exposure occasionally has been associated with problems in cats. There may be skin irritation and pulmonary irritation from inhalation of dust. Signs have included vomiting, lethargy, tremors, repeated clonic convulsions, respiratory failure, dyspnea and death.

Treatment: With oral exposure, recommended treatment is to avoid fatty or oily foods that may enhance absorption. Other procedures include use of emetics, gastric lavage, activated charcoal and saline cathartics. Animals exposed dermally should be bathed with a detergent. Blood glucose levels should be monitored, since hypoglycemia may occur. Glucose should be administered as needed.

Citrus Oil

Two products based on citrus oil extracts are available for small animals. In one form, crude citrus oil extracts are formulated into products labelled to "control itching" associated with common ectoparasites, such as fleas, ticks and lice. Other products contain a purified citrus extract, d-limonene.[5]

Dermal application of some citrus extracts results in absorption through the skin. The citrus derivative linalool is metabolized by glucuronide or sulfate conjugation and excreted primarily in the urine. Thus, one would expect products of this nature to be hazardous to cats.

Specific toxic concentrations of citrus oil extracts are not described. However, intoxication has resulted from using citrus oil extracts at recommended concentrations on cats. Cats appear to be highly tolerant of d-limonene, the purified extract used in commercial insecticidal preparations. Cats treated with 15 times the recommended concentration on the final dip solution survived with no supportive or detoxification treatment, though they showed dramatic but transient signs of toxicosis. Cats given combinations of d-limonene, linalool and piperonyl butoxide developed serious clinical signs at 10 times the recommended concentration.[5]

Clinical Signs: Clinical signs of toxicosis by citrus-based insecticides include ataxia, depression, occasional profound hypothermia and sometimes generalized paralysis.[5] There are no chemically induced lesions, but excessive use has been associated with self-induced traumatic scrotal and perineal dermatitis in male cats.

Treatment: Treatment is aimed at general detoxification, combined with supportive and symptomatic therapy. Removal of insecticide residue by bathing in liquid dish detergent is recommended. Atropine should not be given to affected animals.

Intoxication by Herbicides

Herbicides are perhaps the most broadly used class of common pesticides available in the United States.[34] Selective herbicides are commonly used to control broad-leaf weeds on private lawns, public parks and roadways. Pre-emergent herbicides may be used in gardens to control weeds, and nonselective herbicides may be applied to prevent growth of all vegetation along fence rows, on driveways or in other areas where no plant growth is desired.

Because of their widespread use in many areas inhabited by cats, herbicides are the subject of many questions from pet owners and practicing veterinarians. However, available evidence indicates that few serious exposures to herbicides occur in cats. Only very limited instances of toxicosis are documented. In particular, the herbicides commonly used by homeowners and municipalities are organic synthetic compounds with relatively low toxicity. When used as directed they are of very low hazard and unlikely to cause toxicosis. Unfortunately, a very limited amount of specific information on the toxicity of herbicides to cats is available. Some common herbicides have been studied in dogs, and questions about effects or toxicity are currently best answered by referring to literature cited for dogs.

Arsenical herbicides, composed of inorganic arsenic salts or combinations of arsenic with organic molecules, are sometimes used for crabgrass control. Arsenic is highly toxic to cats; its effects will be discussed with the metallic poisons.[34]

Chlorates

Chlorate salts are sometimes used to nonselectively prevent all plant growth in

an area.[34] Heavy applications of dry granules could result in contamination of a cat's paws if they are allowed access to treated areas. Exposure would then be as a natural consequence of grooming and cleaning of the feet. The toxicity of chlorates for dogs is about 0.5 g/kg body weight. However, the toxicity may be higher in cats, since chlorates are strong oxidizing agents that induce methemoglobinemia. Cats are highly sensitive to methemoglobin formation and might be poisoned by substantially smaller amounts.[5,8,34] Lacking specific evidence, it would be wise to consider chlorates as potentially hazardous to cats.

Clinical Signs: Methemoglobinemia results in dyspnea, increased respiratory effort and cyanosis. Blood with elevated concentrations of methemoglobin has a characteristic chocolate brown color, and this color is imparted to tissues and mucous membranes both before and after death. Chlorate salts may also irritate the intestinal tract, resulting in diarrhea.

Treatment: Cats suspected of consuming chlorate salts should be promptly detoxified by appropriate oral or dermal methods. If methemoglobin is a serious clinical consideration, ascorbic acid (30 mg/kg PO every 6 hours for up to 7 treatments) may help convert methemoglobin to oxyhemoglobin. A 1% solution of sodium thiosulfate PO is also recommended in chlorate poisoning.[8]

Dipyridyl Herbicides

Paraquat and diquat are dipyridyl herbicides used to rapidly kill plants where nonselective vegetation control is desired. Commercial preparations for home use by spot application are available. Paraquat is most commonly available and has a reported LD_{50} in cats of about 50 mg/kg body weight.[26,34]

Paraquat concentrates in lung tissue, where it is converted to a paraquat-free radical in type-I alveolar cells.[34] This initiates a chain of oxidation reactions that eventually lead to membrane destruction, with cell dysfunction and death. This chain of events can be countered with vitamin E and selenium, which help maintain reduced glutathione and provide a scavenger system for peroxides and free radicals.

Clinical Signs: Because of the concentration of paraquat in the lung, clinical signs are primarily respiratory. Early effects of intoxication include vomiting and depression within 1-3 days after consumption of a toxic dose. Respiratory signs begin 2-7 days after exposure. Signs include rapid respiration, dyspnea, cyanotic mucous membranes and moist rales. Pneumothorax may develop as a consequence of respiratory distress. Animals that survive the acute effects develop progressive respiratory distress that may continue until death 10-21 days after initial exposure.[26,34]

Lesions reflect pulmonary damage. Acute lesions include dark, congested and hemorrhagic lungs, atelectasis and bullous emphysema. In chronically affected animals, the lungs are shrunken and fibrotic. Microscopically there are intraalveolar hemorrhages and edema. Animals surviving 7-21 days have moderate to marked alveolar and interstitial fibrosis.

Knowledge of exposure to paraquat and signs of acute respiratory distress suggest a grave prognosis. Determining the herbicide content of suspected chemicals, plant tissue or stomach contents in acute cases may help to establish the degree of exposure. Because of substantial urinary excretion, chemical analysis of urine from a suspect animal may aid diagnosis.

Treatment: Treatment depends primarily on prompt gastrointestinal detoxification.[8,26,34] Vomiting should be induced as soon as possible after ingestion. Oral detoxification is recommended using Fuller's earth or bentonite PO at 5 g/kg body weight. These adsorbent clays are more effective than activated charcoal in binding dipyridyl herbicides. Adsorbent therapy is most useful if given within 4 hours after ingestion of herbicide. Administraton of the adsorbent may be followed with an appropriate dose of saline cathartic. Supportive therapy includes diuresis, monitoring of urinary function, respiratory support and possibly peritoneal dialysis. Some sources report that corticosteroids benefit cats poisoned with paraquat. Superoxide dismutase is being evaluated as a possible therapeutic aid in diminishing the superoxide anion produced in the lungs.

Intoxication by Fungicides

A wide variety of organic chemicals is used as fungicides.[8,34] Those used in agriculture and food processing vary in toxicity. Their use patterns, restrictions and generally low toxicity make poisoning in animals generally uncommon. Available information indicates a very low incidence of questions or reported problems associated with common organic fungicides. Though toxicity figures are not available generally for cats, organic synthetic fungicides used by homeowners are of low toxicity and appear to present little hazard to cats. Three products with somewhat greater toxicity to cats will be discussed briefly.

Hexachlorobenzene

Hexachlorobenzene has been used as a fungicide in treatment of seeds. The oral LD_{50} for cats is 1700 mg/kg body weight.[8] Hexachlorobenzene is irritating to the skin and in toxic doses may cause liver and kidney damage, porphyria, blood cell disorders, neurologic dysfunction and weight loss. Chronic intake in dosages as low as 10 mg/kg body weight per day in cats may cause adverse effects. Exposure to treated seed would not be a likely hazard in most cats unless they are free roaming in rural areas or have access to concentrations used for seed treatment. There are no reported antidotes, and therapy would be strictly symptomatic and supportive.

Dinitrophenol

Dinitro derivatives of phenol and cresol are used as fungicides, and occasionally as insecticides or herbicides.[5] Dinitro compounds are nonselective biocides applied directly to plants.

The toxic dosage of dinitrophenol and dinitroorthocresol is 20-50 mg/kg body weight, though specific toxicity for cats is not apparent.[5,34] Because cats have difficulty metabolizing phenol and cresol compounds, they would be expected to be at greater risk than other species. These compounds uncouple oxidative phosphorylation, reducing the synthesis of adenosine triphosphate (ATP). Thus, metabolism is accelerated but energy production is converted into heat instead of being stored as high-energy phosphate bonds.

Clinical Signs: Toxicity is enhanced by elevated environmental temperatures. Conversely, low environmental temperatures reduce overall toxicity. Clinical signs include listlessness, anorexia, lethargy, deep rapid respiration, thirst, oliguria, weakness and eventual prostration and death. Hyperthermia is a common sign.

Diagnosis: Dinitro compounds are a bright yellow and may stain the skin or hair.[5] This staining may persist for weeks or months, and a yellow stain does not necessarily indicate recent exposure. There may also be a yellowish-green color to the urine. Chemical analysis of stomach contents, liver or urine may be helpful for diagnosis.

Treatment: Antidotes for poisoning with dinitrophenols are not available. Treatment is based on detoxification and symptomatic and supportive therapy.[5] This should include control of hyperthermia. The animal should be kept in a cool environment and provided with water or, if necessary, IV fluids to combat dehydration. If hyperthermia is excessive (>105-106 F), cold water baths may be appropriate. Though some affected animals may seem agitated, sedatives should be used carefully. In people, chlorpromazine potentiates the action of some dinitro compounds.

Pentachlorophenol

Pentachlorophenol has been widely used as a fungicide, particularly for treatment of lumber.[8,34] Until recently, commercial preparatioins of pentachlorophenol dissolved in hydrocarbon solvents were widely available for lay use. Pentachlorophenol is rapidly absorbed after dermal contact. Freshly treated wood may "bleed" pentachlorophenol after pressure application. This leaves a residue of pentachlorophenol in oil at the surface of treated wood. After treated wood has weathered for some months, bleeding usually ceases and surface residues of pentachlorophenol are much lower.

Specific toxic dosage figures for pentachlorophenol in cats are not available. An acute oral or dermal LD_{50} in most species evaluated is 100-200 mg/kg. A multiple-exposure lethal dosage is estimated at 30-50 mg/kg.[34] As with other phenolic compounds, cats would be expected to be more susceptible to pentachlorophenol than other com-

mon species. Commercial pentachlorophenol recently available has contained contaminants known as chlorinated dibenzo-p-dioxins and chlorinated dibenzofurans. With chronic long-term exposure, toxicosis is more likely from the dibenzo-p-dioxin and dibenzofuran accumulation than from pentachlorophenol. Recent restrictions on the availability and use of pentachlorophenol have reduced its somewhat limited hazard to small animals even further.

Clinical Signs: Expected effects of pentachlorophenol result from its mechanism of action as an oxidative uncoupling agent. It also inhibits a number of cellular enzymes.[8,34]

Direct exposure to pentachlorophenol results in irritation of mucous membranes, respiratory tract and skin. Early signs of mild intoxication include weakness, anorexia and lethargy. More advanced effects include accelerated respiration, hyperthermia, hyperglycemia, glycosuria and dehydration. Renal damage is reflected as proteinuria and elevated blood urea nitrogen levels.[5,30,34]

Diagnosis: The diagnosis is suggested by acute onset of hyperthermia and lethargy associated with respiratory and renal dysfunction. Pentachlorophenol can be readily detected in blood and urine, which is the excretory route. Background levels of pentachlorophenol in blood may range as high as 2 ppm. Acute intoxication is suggested by blood levels >100 ppm and tissue levels >200 ppm.[34]

Treatment: No antidotes are available for pentachlorophenol toxicosis. Appropriate detoxification and supportive therapy is recommended. This would include attention to fluid and electrolyte status and control of body temperature. Therapeutic principles are generally similar to those described for dinitrophenol.

Intoxication by Avicides

Several commercial products are available for chemical control or elimination of pest birds.[37] Common active ingredients include 4-aminopyridine (Avitrol), endrin (Rid A Bird), fenthion, strychnine, and 3-chloro-p-toluidine (Starlicide). Endrin is considered with the chlorinated hydrocarbon insecticides. Fenthion is an organophosphate and strychnine is an alkaloid.

4-Aminopyridine

This is used as a bird repellent. Cracked corn or other grains are used as baits, with 4-aminopyridine concentrations ranging from 0.5% to 3.0%. Effects in birds include involuntary muscle contractions, disorientation, pronounced vocalization (distress cry) and other erratic activities that cause other members of a flock to leave.[34] The compound is of relatively low lethality for birds but rather toxic to mammals. An acute oral LD_{50} for dogs has been estimated at 4 mg/kg body weight. Assuming this same toxicity for cats, the toxic dose of 0.5% bait in a 4-kg cat would be 16 mg of 4-aminopyridine or 3.2 g of bait. Thus, consumption of small amounts of baits could be hazardous to cats.

Clinical Signs: 4-aminopyridine enhances transmission at neuromuscular junctions and synapses.[34] Clinical signs include salivation, hyperexcitability, muscle tremors, incoordination, seizures and cardiac or respiratory arrest. Similar clinical signs are produced by amphetamines, caffeine, organochlorine insecticides, acute lead toxicosis, nicotine, metaldehyde and strychnine. Clinical differentiation without a history of exposure would be very difficult.

Diagnosis: The diagnosis may be confirmed by analysis of stomach contents or liver.

Treatment: A specific antidote against 4-aminopyridine has not been established for small animals. If ingestion is recent, emesis or gastric lavage and other appropriate oral detoxification procedures should be promptly initiated. Propranolol (Inderal) has shown some effect in blocking cardiac arrhythmias. The dosage for this purpose has not been established in cats, but IV administration at 0.1-1.0 mg/kg body weight in dogs has suppressed catecholamine-induced arrhythmias.[5,37] The standard dosage for cats is 0.25 mg in 1.0 ml of saline, given IV in 0.2-ml boluses of the mixture. Diazepam, given IV at 2.5-5 mg, may be used to control seizures. Though not tested in cats, heavy sedation with xylazine provided relief in horses from excitement and muscle tremors induced by 4-aminopyridine.

3-Chloro-p-toluidine

3-chloro-p-toluidine (Starlicide) is used against such pests as starlings, crows and

blackbirds.[37] The oral LD_{50} for avian species is <4 g/kg body weight. The acute oral LD_{50} for rats is 655 mg/kg body weight. The toxic dosage for dogs and cats has not been established. If the acute oral toxic dose were similar to that for rats, and assuming that 10% of the LD_{50} could cause lethality, then a lethal dose for a 5-kg cat could be as little as 1 ounce of bait. In addition, clinical signs of 3-chloro-p-toluidine are a result of methemoglobinemia and Heinz body formation. With the sensitivity of cats to these effects, cats may be at greater risk than rats to toxicosis by this avicide. Thus, based on limited evidence, it would be wise to consider 3-chloro-p-toluidine hazardous to cats if bait is consumed directly.

Treatment: No specific treatment has been established. Recent consumption of baits should be treated with oral detoxification procedures. If methemoglobinemia develops, supportive treatment and administration of ascorbic acid as described for chlorate herbicides may be attempted.

Intoxication by Metals

Arsenic

Arsenic compounds are now much less commonly used than in past years. However, sources still available to homeowners include ant and snail baits and arsenical crabgrass killers. Also, arsenicals are occasionally used to treat heartworm infection or hemobartonellosis in cats. Soluble trivalent inorganic arsenic compounds, such as sodium arsenite, are considered more toxic than pentavalent or organic forms. However, cats appear highly susceptible to both trivalent and pentavalent arsenicals.[1,5,34]

An oral lethal dosage of arsenic in cats is about 20 mg/kg body weight.[1,8,34] Clinical signs may be induced by as little as 5 mg/kg. At a 1% concentration in ant baits, each gram of bait contains 10 mg of sodium arsenate. A lethal dose of sodium arsenate in a 3-kg cat would be 60 mg. Thus, 6 g or about 1 teaspoonful of arsenical bait could potentially be lethal if ingested by a cat.

Arsenic acts by combining with sulfhydryl groups at active sites of many enzymes (*eg,* as pyruvate enters the tricarboxylic acid cycle). Cells with active metabolism and rapid turnover appear to be most susceptible.[34] In addition, asenic is a potent capillary poison affecting especially the splanchnic vasculature. The combination of metabolic and vascular derangement damages cells of the gastrointestinal mucosa and renal tubules.

Clinical Signs: Clinical arsenic toxicosis in cats is primarily a gastrointestinal disturbance.[1,5,34] Within a few minutes after consuming an arsenical bait, cats show signs of nausea and may vomit several times. Attempts to vomit may be repetitive and continue for several hours. Abdominal pain is evident and some cats may vocalize as evidence of this pain. In serious poisoning, cats rapidly become depressed and dehydrated. Prostration may occur in 1-6 hours. If the clinical course is prolonged for several hours, watery diarrhea may develop. This may also progress to contain blood and shreds of intestinal mucosa. However, most cats with acute poisoning die before intestinal hemorrhage and necrosis are evident. Shock usually develops during the course of arsenic poisoning. The rare animal that survives for several days may develop renal failure as a result of tubular necrosis.

Clinicopathologic changes reflect diarrhea, vomiting and shock. Hemoconcentration, dehydration and electrolyte changes are consistent with the clinical response.

Diagnosis: Antemortem diagnosis of arsenic poisoning is suggested by profound clinical signs of shock accompanied by persistent vomiting, dehydration and diarrhea. Samples of vomitus or urine may be analyzed for arsenic content to establish exposure. Blood concentrations of arsenic are not useful in establishing a diagnosis, since arsenic rapidly leaves the blood, even in acute poisoning. In fatal cases, analysis of liver and kidney for arsenic content is useful. If animals survive for several days, however, the arsenic content of tissues diminishes rapidly.

Treatment: Treatment of advanced clinical arsenic poisoning is difficult. The prognosis should be guarded to grave. Dimercaprol (British antilewisite, BAL) is a classic antidote for arsenic poisoning.[1,3,5,8] The recommended dosage is 3 mg/kg given IM every 4 hours for the first 2 days, every 6 hours on the third day, and every 12 hours for the next 10 days or until recovery.[1] Sup-

portive therapy is essential to survival. Close attention should be paid to IV fluid and electrolyte therapy, maintenance of urine flow, and blood transfusions if needed because of intestinal blood loss. Adjuncts to therapy include vitamin B complex and antibacterial agents to control secondary infection. Morphine sulfate (0.1 mg/kg) has been recommended to control abdominal pain. Work summarized in recent reviews indicates IM administration of 20% thioctic acid at 50 mg/kg TID in cattle, dogs and mice has been somewhat effective in prolonging survival in acute arsenic poisoning.[1,34] Its usefulness in cats has not been established.

Bismuth

Acute nephrosis may occur after administration of bismuth sodium triglycollamate in cats.[1] A dose of 150 mg per day for 3 days induced anorexia, oliguria and severe depression. Renal damage was confirmed by elevated serum creatinine levels and cellular casts in urine sediment.

Lead

Lead poisoning occasionally occurs in cats. Judging from various surveys, available literature and our own experience, however, lead poisoning in cats is not common.[34,39,44]

Sources of lead include lead-based interior and exterior paints, linoleum, putty, lubricating agents and lead objects, such as fishing sinkers and drapery weights.[34] Less common sources of lead for small animals have included driveways treated with ash from a lead smelter, and the dust and soil around homes in the vicinity of a lead smelter.

Reasons for the low incidence of lead poisoning in cats as compared to that in dogs and cattle are not known. However, the grooming habits of cats may provide for inadvertent poisoning. It is also possible that the array of clinical signs associated with feline lead toxicosis is not recognized.

Clinical Signs: Lead poisoning is generally described as a syndrome involving the central nervous system, gastrointestinal system and hematopoietic system.[1,34] Descriptions of characteristic clinical signs of lead poisoning in cats have varied. Some consider it to be primarily a neurologic condition, while others recognize mainly a gastrointestinal syndrome.[39,44] Changes in the hematopoietic system to this point have not been well described.

In our experience, clinical lead poisoning in cats has been mainly characterized by signs of lethargy, anorexia, intermittent vomiting and depression. Recently, clinical lead poisoning has been produced in cats given various doses of dietary lead.[25] A dose-related behavioral change, including seizures, nervousness and fear of people, was exhibited in cats given lead at >1000 ppm dietary equivalent. This is equivalent to a dosage of about 3 mg/kg body weight. Other characteristic signs included projectile vomiting and excessive salivation.

Based on accumulated clinical evidence, it seems likely that early clinical effects of moderately severe intoxication are characterized primarily by gastrointestinal signs. However, advanced cases or excessive exposure can result in acute neurologic and behavioral changes.

Diagnosis: Estimating dosage intake for small animals is generally not practical. Thus, the primary goal of the clinician should be to establish potential exposure to lead and demonstrate clinical signs compatible with lead toxicosis.

Various laboratory indicators of lead toxicosis may be used.[25,26] Zinc protoporphyrin is significantly increased, even at lead exposures that do not induce clinical toxicosis. This sensitive index would detect low-level exposure but could not be used to differentiate clinical lead poisoning. Amino levulinic acid dehydratase (ALAD) decreases proportionately as lead dosage increases. As with zinc protoporphyrin, its main value would be to indicate a wide range of lead exposure.

In contrast to those in dogs, anemia and reticulocyte counts in lead-poisoned cats do not vary from normal.[25]

Blood lead levels increase in proportion to lead dosage during chronic exposure. There is probably no single blood lead concentration that can be used to confirm toxicosis.[25,26,34,39,44] Generally, however, normal cats not exposed to unusual amounts of environmental or dietary lead have blood lead values <0.2 ppm (μg/g). Blood lead levels in affected or exposed cats may range from 0.3

ppm to as high as 1.0 ppm. The value of blood lead determinations is to establish that significant exposure beyond normal has occurred. The diagnosis must then be based on correlation of exposure with occurrence of typical clinical signs.

If serious questions exist about a diagnosis of lead toxicosis, a urine sample may be analyzed for lead concentration. This is followed by injection of a dose of calcium EDTA and collection of a second urine sample 24 hours later.[1,26,34] In lead-poisoned animals, there should be a 10- to 20-fold or greater rise in urinary lead after treatment with calcium EDTA.

Treatment: Specific treatment procedures for lead poisoning in cats have not been developed. However, guidelines described for dogs will be summarized. For a more extensive discussion, the reader is referred to additional references on dogs.

Detoxification therapy is important in lead poisoning. Unabsorbed lead can be removed from the gastrointestinal tract before chelation therapy using enemas, emetics and cathartics. Magnesium sulfate (Epsom salt) is the agent of choice, since it precipitates lead as insoluble lead sulfate. An abdominal radiograph should be made to indicate if solid particles of lead are remaining in the gastrointestinal tract. Such items as fishing sinkers or drapery weights may have to be removed surgically. If signs of cerebral edema are evident, IV mannitol and/or dexamethasone may help reduce brain swelling. Most lead-poisoned animals are anorectic, so a combination of parenteral and/or forced oral feeding may be necessary as convalescence progresses. Oral feeding, however, will not be effective until vomiting is controlled.

A specific antidote is available for mobilization and excretion of lead from the body.[1,26,34] The commonly recommended drug is calcium ethylenediaminetetraacetate (Ca EDTA). Satisfactory results in dogs have been produced with daily SC injections of Ca EDTA at 110 mg/kg divided into 4 daily doses given for 5 days. Commercial preparations should be diluted to 10 mg/ml (1% w/v) for SC injections. This dilution minimizes pain at the injection site. If 6.6% Ca EDTA (Havidote: Haver-Lockhart) is used, a volume of 100 ml of 1% solution containing Ca EDTA at 10 mg/ml can be made by diluting 15 ml of Havidote with 85 ml of 5% dextrose solution. Chelation therapy should be discontinued after 5 days and the animal reevaluated for lead status and clinical effects. A 5-day rest period should be allowed before any additional course of therapy is used.

In dogs, Ca EDTA may cause depression, vomiting and diarrhea, followed sometimes by renal changes. The susceptibility of cats to Ca EDTA is not well documented. Ca EDTA is no longer available for veterinary use.

An alternative chelating agent for lead poisoning is penicillamine.[26,34] As with Ca EDTA, the dosage and effectiveness of penicillamine in cats have not been established. Penicillamine is available in 125-mg capsules (Cupramine: Merck). Dosages of 33-55 mg/kg daily are tolerated by dogs. Oral administration of penicillamine may be useful when animals cannot be hospitalized or as a followup to Ca EDTA therapy when continued longer-term chelation seems desirable. Remember that chelation therapy can alter the balance of other divalent cations, especially calcium, zinc and copper. Further, the safety and efficacy of these agents in cats are not fully documented. Therefore, chelation therapy should be carefully discussed with the client.

Veterinarians diagnosing lead poisoning in animals should consider the public health implications. Experience in dogs indicates that geographic, seasonal and economic conditions for lead poisoning in dogs are often similar to those seen for people. Clients should be advised of the potential hazard for lead exposure; assistance from public health or medical authorities may be recommended.

Mercury

Mercury poisoning has been extensively studied in cats. The history and background of mercurialism in cats are well documented.[1,8,34] In North America, access of cats to significant sources of mercury contamination is considered very rare.

Clinical Signs: Clinical effects of methylmercurism in cats are primarily neurologic.[1,34] A dosage of 0.6-1.3 mg/kg body weight produces anorexia, ataxia, hyper-

metria, proprioceptive impairment, blindness, vertical nystagmus and convulsions. Clinical signs commonly occur within 15-60 days after initial exposure. Microscopic lesions, including neuronal necrosis and vascular degeneration, are seen in the central nervous system. Tissues contain elevated concentrations of mercury, ranging generally from 40-80 ppm in liver and kidney.

Clinical signs of inorganic mercury poisoning consist primarily of acute gastroenteritis, with vomiting and diarrhea that may appear somewhat similar to that seen with acute arsenic poisoning. If affected animals live more than several days, toxic tubular necrosis may result in renal failure.

Treatment: Treatment for mercury poisoning is dimercaprol (see Arsenic Poisoning above). N-acetyl-d-l-penicillamine and/or 2,3-dimercaptosuccinic acid have also been used, but their dosages have not been established for cats.[1,5,8,34] Realistically, treatment of methylmercury intoxication is not successful because neurologic lesions are irreversible and generally well advanced before clinical signs are evident.

Cats and people may be exposed to mercury from similar sources. Confirmation of mercury poisoning in cats warrants careful evaluation of the environment to suggest possible sources of human exposure as well.

Plant Poisoning

There are relatively few references on plant poisoning in cats.[15,19] Cats housed indoors commonly chew on leaves of various houseplants, some of which may contain toxic or irritant compounds. Though reports of plant ingestions and/or chewing are fairly common, few of these appear to result in overt or serious clinical toxicosis.[2,4,36,43] Few documented reports are available concerning plant toxicosis in cats. Even fewer are confirmed by experimental reproduction of a toxic syndrome using known poisonous plants. Toxic plants specifically associated with adverse reactions in cats include laurel, philodendron, dieffenbachia, pine trees, poinsettias and *Amanita* mushroom poisoning.[1]

Characteristics of intoxication by these plants are reviewed briefly in Table 2. In addition, selected ornamental plants potentially toxic to cats or other small animals are presented briefly.

With plant poisoning, it is important that owners and veterinarians understand which toxic plants are popular and/or indigenous to their area. Familiarity with those plants and how to prevent plant poisoning often eliminates or reduces serious problems. A general reference useful to small animal practice has been prepared.[15]

Treatment of plant poisoning rarely involves specific antidotes. Good oral detoxification therapy, coupled with appropriate clinical supportive and symptomatic therapy, is most important.

Information about plant poisoning is filled with folklore, misinformation and many undocumented or circumstantial reports. While it is probably wise to err on the side of conservatism, one should realize that absolute diagnosis of plant toxicosis based on today's information is extremely difficult.

Intoxication by Animal Toxins

Relatively few instances of animal toxin problems involving cats are recorded. The effects of these few animal toxins specifically associated with cats have been reviewed.[1] Of the animal toxins, only snake bite will be presented here.

Snake Bites

There are over 3500 species of snakes in the world, 375 of which are poisonous to people and animals.[50] Only a few species, however, account for most animal and human bites (Table 3). The most troublesome species for animals are found in 3 major taxonomic groups: Crotalidae, Viperidae and Elapidae. These snakes are more plentiful, more poisonous, more accessible, more aggressive or more efficient in injecting their venom into tissue than other species of poisonous snakes. The incidence of snake bite poisoning in cats is low. Cats are less likely to be bitten by snakes than dogs, even though they often prey upon snakes. They are also more resistant to the effects of snake venom.[50]

The venom of snakes, even from the same individual or species, is a complex mixture of protein and polypeptide sub-

stances. At least 25 different enzymes have been recognized in snake venom, though no single venom contains all of them.[50] Snake venom contains large proteins that act as proteolytic enzymes, arginine ester hydrolases, thrombin-like enzymes, collagenases, hyaluronidases, phospholipases A, B and C, lactate dehydrogenase, phosphomonoesterases, phosphodiesterase, RNase, DNase, 5'-nucleotidase, NAD-nucleotidase, and L-amino acid oxidase. In addition to these enzymes, snake venom also contains smaller polypeptides that do not have enzymatic activity. Most of these polypeptides affect the nervous system and have been collectively called "neurotoxins."

Clinical Signs: Snake venom causes disease in 4 basic ways: Varying degrees of severity of local edema and tissue necrosis; systemic shock-like reactions; coagulopathies that may or may not be associated with hemolysis or hemorrhage; and neurologic signs. In general, Elapid snake venom contains less enzymatic activity than Crotalid or Viperid venom but has much more neurotoxin. Crotalid and Viperid venom have low levels of neurotoxins and high levels of various enzymes. Therefore, bites from Crotalids and Viperids are more likely to cause local swelling, shock, tissue necrosis, coagulopathies and hemolysis than bites from Elapids, and are less likely to cause paralysis. There are exceptions, however. Australian black, copperhead and small-eyed snake venoms contain a higher proportion of cytolysins, hemolysins and myotoxins than other Elapid snake toxins.[49] Because death is more likely to result from paralysis than enzymatic effects, and because cats are relatively more resistant to death from enzyme-induced tissue necrosis, shock, hemorrhage and hemolysis than other animals, Elapid snake bites are more apt to be fatal to cats than bites from Crotalid or Viperid snakes.

The clinical signs of snake bite poisoning in cats vary greatly with the species of snake, the site of the bite, and the amount of venom injected.[49] Almost all cats are bitten on the skin around the face or on the hind limbs. Bites may also occur inside the mouth, particularly on the tongue.[51] Swelling is usually seen at the site within 5-10 minutes, especially with bites of Crotalid or Viperid snakes. Swelling may not be noticeable with Elapid snake bites. In the case of Crotalid and Viperid snakes, local swelling is a major sign. The fang marks may become noticeable within a few hours or a day, and often ooze serosanguineous fluid. Cats bitten by Crotalid or Viperid snakes are often depressed for 24-96 hours or more. Facial swelling may also be associated with obstruction of breathing, either from swelling in the neck region or swelling of the mouth and around the nares.

Shock may be apparent for the first few hours, but usually is mild or self-limiting. Shock usually is associated with the initial edema at the site of inoculation, rapid and shallow breathing, and hemoconcentration. Coagulopathy associated with localized and generalized hemorrhage of skin and mucosal surfaces is sometimes seen, depending largely on the dose of venom and type of snake. Hemolysis, when it occurs, is seen within several hours of the bite. Hemolysis and hemorrhage are associated with a rapid drop in the hematocrit, sometimes associated with hemoglobinuria. Hemolysis associated with Crotalid toxins is uncommon in cats but has been experimentally recreated with relatively large doses of toxin.[50] Myoglobinuria associated with myotoxicity has been observed in some animals. Most cats that show mainly localized swelling survive with limited treatment, though complete recovery may take several days.

Cats bitten by Elapid snakes are much more likely to have only neurologic signs, with signs appearing within minutes to 2 hours. Clinical signs include pupillary dilation, diminished pupillary light reflex, depression, fever, generalized weakness, hind limb ataxia, lateral recumbency, tachypnea and dyspnea, and paralysis of the pharynx and larynx.[46] Complete flaccid paralysis and subnormal temperature are seen in severe cases. Recovery periods range from 1 to 14 days, with a mean of 4 days.[47]

Diagnosis: Diagnosis of snake bite poisoning in cats can be difficult, especially in animals with mainly neurologic signs. Only 16% of affected cats were observed with snakes, as compared to 64% of bitten dogs.[46,47] The time of the year can be of some importance; most bites occur during the warmest 6 months of the year. Specific enzyme-linked immunosorbent assays have been developed to detect Australian Elapid

Table 2. Effects of selected toxic plants.

Clinical Response	Common Name	Scientific Name	Toxic Parts	Comments
		Stomatitis, Pharyngitis, Salivation		
Plants in this group produce burning sensation in the mouth, local irritation, salivation. In some cases there is acute inflammatory swelling of mucous membranes & submucosa with airway interference.	Caladium	*Caladium* spp	All parts	These plants contain calcium oxalate. Spicules (raphides) may be direct irritant & eject other toxins as well. Alkaloid trigonelline in leaves & seeds is irritant *and* purgative. Antihistamines & general symptomatic & supportive care recommended.
	Calla lily	*Zantedeschia aethiopica*	All parts	
	Christmas rose	*Heleborus niger*	Rootstocks, leaves	
	Dumbcane	*Dieffenbachia* spp	All parts	
	Elephants ear	*Colacasia* spp	All parts	
	Four o'clock	*Miribilis jalapa*	Leaves, seeds	
	Jack in the pulpit	*Arisema triphyllum*	Rhizome	
	Philodendron	*Philodendron* spp	All parts	
		Conjunctivitis, Gastroenteritis		
Direct contact with milky sap ("latex") can cause conjunctivitis, keratitis, stomatitis, gastroenteritis & (rarely) dermatitis.	Crown of thorns	*Euphorbia* spp	Leaves, stems, sap	Leaves, stems & milky sap contain an irritant or vesicant. Response to exposure may vary widely for reasons unknown. Treat by bathing or rinsing as appropriate. Treat irritation symptomatically.
	Pencil cactus	*Euphorbia* spp	Leaves, stems, sap	
	Poinsettia	*Euphorbia* spp	Leaves, stems, sap	
	Snow-on-the-mountain	*Euphorbia* spp	Leaves, stems, sap	
			Leaves, stems, sap	
	Spurge	*Euphorbia* spp	Leaves, stems, sap	
			Leaves, stems, sap	
			Leaves, stems, sap	
			Leaves, stems, sap	
			Leaves, stems, sap	
		Gastrointestinal Upset		
Acute immediate nausea, vomiting	Amaryllis	*Amaryllis* spp	Bulbs	Most members of this group have greatest toxicity in the bulbs, except *Daphne*, in which entire plant, especially berries, is dangerous and Wisteria, in which seeds & fruit are most toxic. Treatment is symptomatic & supportive.
	Daffodil	*Narcissus* spp	Bulbs	
	Hyacinth	*Hyacinth orientalis*	Bulbs	
	Wisteria	*Wisteria* spp	Seeds, fruit	
	Daphne	*Daphne mezereum*	All parts, berries	
	Iris	*Iris* spp	Bulbs	
Nausea, vomiting, abdominal pain. Commonly followed by moderate to severe diarrhea.	Azalea, Rhododendron	*Rhododendron* spp	All parts	Signs delayed 6 hrs. Also mild hepatosis & nephrosis. Cardiac irregular rhythm & rate. Salivation, depression, colic, tenesmus & grinding of teeth common. Therapy is symptomatic, including fluid & electrolyte replacment & maintenance.
	Common box	*Buxus sempervirens*	Leaves	
	Euonymus	*Euonymus* spp	All parts	
	Holly	*Ilex* spp	Berries	
	Honeysuckle	*Lonicera* spp	Berries	
	Mushrooms	*Amanita* spp	All parts	
	Mistletoe	*Phoradendron* spp	Berries	
	Privet	*Ligustrum* spp	All parts, especially berries	

(Table 2 continued)

Clinical Response	Common Name	Scientific Name	Toxic Parts	Comments
Nausea, vomiting (delayed), diarrhea. GI signs accompanied by cardiovascular, renal or other organ involvement (see Comments).	Black locust Castor bean Precatory pea English ivy Nightshades Autumn crocus Yew Mushrooms	 *Ricinus communis* *Abrus precatorius* *Hedera helix* *Solanum* spp *Colchicum autumnale* *Taxus* spp *Amanita* spp	 Seed Seed Foliage Foliage, fruit Bulb Foliage All parts	May be 18- to 24-hr latent period. Severe purgation. May be renal damage (locust, castor bean, rosary pea). Neurologic signs may accompany or follow nightshade ingestion. *Taxus* causes cardiac irregularities & collapse. *Amanita phalloides* mushrooms are hepatotoxic.
		Cardiovascular Disturbances		
Digitalis-like glycosides. Often first response is nausea & vomiting 2-3 hrs after ingestion. Diarrhea & tenesmus may follow. Cardiac changes are due to digitalis-type toxins. Effects include arrhythmia, dropped beats, blockades, fibrillation. Respiratory rate increases & extremities become cool. Anoxic struggling (not true seizures) may occur terminally. Course is usually <24 hrs.	Foxglove Lily-of-the-valley Oleander Yellow oleander	*Digitalis purpurea* *Convallaria majalis* *Nerium oleander* *Thevetia peruviana*	Leaves, seeds Leaves, flowers, roots All parts All parts, especially fruit	These plants are highly toxic. Consumption of small amounts could be lethal. Treat by oral detoxification. Apply antidotal procedures as for digitalis overdose. Includes potassium chloride (carefully), procainamide. Consult pharmacology or medicine references for digitalis countertherapy.
Polycyclic diterpene alkaloid (aconitine) causes vagal stimulation & brachycardia.	Monkshood	*Aconitum napellus*	Roots, seeds, leaves	This is an outdoor cultivated garden plant.
Sudden death, trembling, dyspnea, collapse. Systolic heart block.	Yew	*Taxus* spp	Needles, bark, seeds	Alkaloid in needles, bark & seed. Very small doses may be lethal. Common outdoor ornamental.
		Neurologic Signs		
Atropine-like action is common to several plants. Signs occur quickly after ingestion. Early signs are thirst, disturbed vision due to mydriasis, dry mucous membranes, tachycardia, bradypnea, convulsions & eventual coma may occur.	Angel's trumpet Belladonna Jimson weed Thornapple	*Datura arborea* *Atropa belladonna* *Datura stramonium* *Datura meteloides*	Leaves, flowers, seeds Leaves, flowers, seeds Leaves, flowers, seeds Leaves, flowers, seeds	Sometimes used by people as intentional hallucinogen, using "teas" or extracts of seeds. Treat for atropine overdose with parasympathomimetic drug (neostigmine, physostigmine). Consult pharmacology reference for full details. Oral detoxification necessary.

(Table 2 continued)

Clinical Response	Common Name	Scientific Name	Toxic Parts	Comments
Nicotinic action. Pyridine & piperidine alkaloids of several plants. Produce early signs of nausea, salivation, lacrimation, muscle tremors, stilted gait. Large doses or late stages cause weakness, paralysis, respiratory failure.	Cardinal flower Goldenchain tree Poison hemlock Tobacco	*Lobelia* spp *Laburnum anagyroides* *Conium maculatum* *Nicotiana* spp	All parts All parts All parts All parts	Nicotine & related alkaloids act very quickly. Treatment may not be successful. Detoxify orally. Use artificial respiration (endotracheal tube, positive pressure). Toxic principle is rapidly metabolized.
		Convulsions		
Various toxic principles, but signs generally include staggering, tremors, ataxia, tonic seizures.	Bleeding heart Buckeye Chinaberry Moonseed	*Dicentra* spp *Aesculus* spp *Melia azedarach* *Menisperumum canadense*	Foliage, roots Leaves, seeds Fruit Seed	No specific therapy except oral detoxification. Administer sedatives if seizures are severe. Support vital signs.
Nux vomica causes violent, tetanic seizures (see strychnine in text).	Nux vomica	*Strychnos nux vomica*	Seed	
		Hallucinations		
Variety of psychotropic signs. Difficult to differentiate in animals. Look for derangement, apparent hallucinations, marked changes in behavior, altered sensory perception. Some may lapse into coma-like state.	Marijuana Morning glory Periwinkle Nutmeg Peyote	*Cannabis sativa* *Ipomea* spp *Vinca rosea* *Myristica fragrans* *Lopophora williamsii*	Leaves, flowers Seeds Seeds All parts	Animals usually gain access accidentally or by intention of owner. Poisoning from natural exposure not expected. No specific therapy. Detoxify orally, control clinical signs.

snake toxins in blood or urine.[49] These tests may not determine the exact snake responsible for the bite, but they help confirm the diagnosis of snake bite and guide the use of appropriate type of antivenin.

Treatment: Treatment of snake bites is directed at the localized swelling, shock-like syndrome, tissue necrosis, hemorrhage and hemolysis (Crotalid and Viperid snakes), or at neurologic abnormalities (Elapid snakes). Glucocorticoids are largely ineffective in treating the localized tissue damage and systemic shock associated with certain types of snake venom. Antihistamines may be helpful, however. It is most important to treat the animal with IV fluids to counteract any shock, and to maintain a patent airway. Blood transfusions to counteract internal hemorrhage and hemolysis are indicated if the hematocrit falls rapidly.

Treatment of neurotoxic envenomation is also supportive. Respiration must be maintained and hydration closely monitored. Snake bites are occasionally secondarily infected with bacteria, so it is important to treat bitten animals with a broad-spectrum antibiotic for several days. Administration of tetanus antitoxin or toxoid is unnecessary for cats. Tetanus is an uncommon sequel of snake bite, and cats are much more resistant to tetanus toxin than people or other animal species.

Antivenin is available for many common types of snake venom. Practitioners should familiarize themselves with the types of snakes in their area, and the source and

dosages of available antivenin. The usefulness or necessity of antivenin therapy for cats bitten by Crotalid or Viperid snakes is somewhat debatable. Snakebitten cats often are presented many hours after the bite, a mean of 21 hours for cats in one study as compared to 5.8 hours for dogs.[47] Antivenin is less effective when given so late. Further, most cats bitten by Crotalid or Viperid snakes recover without complications in 2-4 days with nothing more than supportive care and rest. Antivenin is often made of horse serum, and some cats have acute anaphylactic reactions to the material. Unless antivenin can be given soon after the bite, it is conceivable that antivenin could be of more harm than benefit.

The usefulness of antivenin in Elapid snake bite is a little more proven, but the benefit may not be as great as imagined. Of 97 cats treated with antivenin for snake bites in Australia, 84 (86.6%) survived.[48] Of 12 untreated cats, 9 (75%) survived. In another report, 31 (89%) of 35 cats survived when treated with antivenin for Elapid snake bites.[46] Also, 2 of 2 cats died after their owners declined treatment with antivenin. Cats with complete flaccid paralysis and subnormal temperatures usually died despite therapy.[46]

It would seem, therefore, that cats are relatively resistant to snake bites, regardless of the species of snake involved, and that simple supportive care is most important.

Intoxication by Household and Commercial Products

Numerous drugs and chemicals are available in homes and businesses. Many are relatively safe and/or largely inaccessible to companion animals.[4,34,35] Certain products generally available in a home or business environment have been consistently associated with toxicosis in cats. Among the more common of these agents are antifreeze, boric acid, disinfectants, detergents, solvents, thinners, common over-the-counter medications and chocolate. Various other materials have potential toxicity if exposure occurs. In most cases there are no specific treatments for these latter agents. Several of the important agents are discussed in this section. Table 4 summarizes characteristics of potential toxicants for a variety of other household and commercial products.

Antifreeze

The common source of ethylene glycol occasionally available to pets is automobile radiator antifreeze.[1,17,34,40] Exposure generally occurs when antifreeze is being changed and unguarded cans or containers are available. In addition, overflow of radiators can result in pooling of toxic amounts of antifreeze on a floor. A less common source of poisoning is antifreeze used to protect water pipes and toilet bowls from freezing.

The lethal dosage of antifreeze in cats is 1.5 ml/kg body weight. Since radiator mixtures are commonly diluted with equal parts of water, drained antifreeze solution from radiators would be lethal to cats at about 3 ml/kg body weight.

The mechanism of intoxication by ethylene glycol has been extensively studied.[1,17,34,40] Ethylene glycol is readily absorbed in the gastrointestinal tract and rapidly metabolized through a variety of aldehyde and acidic intermediates. The profound metabolic acidosis in ethylene glycol poisoning is attributed primarily to glycolic acid. The interested reader may consult several sources for more detailed reviews of the metabolism and mechanism of action.

Clinical Signs: Initial clinical signs may occur within 30-60 minutes after ingestion of ethylene glycol.[17,40] A transient period of ataxia corresponds to absorption of ethylene glycol and can be roughly compared to ethyl alcohol ingestion. After recovery from this brief inebriation phase, serious clinical signs commence within 1-6 hours after initial ingestion. These effects are the result of metabolic intermediates. Early signs include vomiting, depression, ataxia and incoordination. At this time animals are generally anorectic. As clinical signs progress beyond 6 hours postingestion, animals become depressed, comatose and acidotic. Occasional vomiting may continue. Acute poisoning from massive disturbances in acid-base balance often cause death before renal damage and uremia can occur.

Signs of uremia develop if cats survive longer than 24-36 hours.[5,17,34] A major metabolite, oxalic acid, combines with calcium

Table 3. Medically important poisonous snakes of the world.[50]

Common Names	Geographic Distribution
	Crotalids
Common coontail	Southern Mexico, Guatemala, Nicaragua
American copperhead*	Eastern and southeastern United States
Mamushi	Caspian Sea to Japan
Malayan pit viper	Southeast Asia
Fer-de-lance	Mexico to Peru and northern Brazil
Barba amarilla	Mexico to Peru and northern Brazil
Terciopelo	Mexico to Peru and northern Brazil
Jararaca	Brazil, Paraguay, Argentina
Jararacussu	Brazil, Bolivia, Paraguay, Argentina
Jararaca pintada	Brazil, Bolivia, Paraguay, northern Argentina
Eastern diamondback rattlesnake*	Southeastern United States
Western diamondback rattlesnake*	Southwestern United States to central Mexico
Cottonmouth moccasin*	Southcentral and southeastern United States
Mexican west coast rattlesnake	West coast of Mexico
Habu	Amami and Okinawa Islands
Chinese Habu	Taiwan, southern China, Vietnam, Laos, India
	Viperids
Mole or burrowing viper	Lebanon, Arabia, Africa
Puff adder	Morocco, western Arabia, Africa
Horned puff adder	Angola, Namibia, South Africa
Night adder	Subsaharan Africa
Sahara sand viper	Sahara to Lebanon
Saw-scaled viper	Bengal to Senegal and Ghana, Egypt, western Arabia, Israel
Long-nosed viper	Italy, southeastern Europe, Turkey, Jordan to northwestern Iran
European viper	British Isles and Europe, northern Asia to Korea
Levantine viper	Cyprus to Kashmir
Russell's viper	Indian subcontinent, southeastern China to Taiwan, parts of Indonesia
Near East viper	European Turkey and Asia Minor
	Elapids
Coral snakes*	United States, Asia, Mexico, Central and South America
Cobras	
Ringhals cobra	Southern and southeastern Africa
Egyptian cobra	Northern Africa, Arabia
Chinese cobra	Thailand, southern China, Taiwan
Indian cobra	Indian subcontinent
Spitting cobra	Western Africa and southern Egypt to southern Africa
Central Asian cobra	Pakistan, Iran, southern USSR
Philippine cobra	Philippines
Malayan cobra	Malayan peninsula to Indonesia
Cape cobra	Namibia, Botswana, southern Africa
King cobra	Indian subcontinent, Philippines
Desert cobra	Egypt to Iran
Kraits and Mambas	
Indian krait	India, Pakistan, Sri Lanka, Bangladesh
Malayan krait	Thailand, Malaysia, Indonesia
Many-banded krait	Burma, southern China to Hainan, Taiwan
Black mamba	Ethiopia and Somalia to Angola, Zambia, Namibia, southwestern Africa
	Australian Elapids
Death adder	Australia, Moluccas, New Guinea
Tiger snake	Southeastern Australia
Taipan	Northern coastal Australia, New Guinea
Small-scaled fierce snake	Southwestern Queensland, northwestern New South Wales, South Australia
Red-bellied black snake	Coastal regions Queensland, Victoria, southeastern South Australia
Clarence river snake	Northern New South Wales, Queensland
Small-eyed snake	Coastal Queensland, New South Wales, Victoria
Mulga	Australia except southeastern and southern coasts, New Guinea
Western brown snake	Australia except southeastern and southern coast
Eastern brown snake	Eastern Australia
Australian copperhead	Southeastern coastal Australia and Tasmania

* Common poisonous snakes in the United States.

to form calcium oxalate crystals in renal tubules. Vomiting, anorexia, depression and coma progress over 2-7 days. Oliguria and/or complete anuria often develop, and there are progressive increases in serum urea nitrogen and K levels and serum osmolality.

Laboratory tests are useful and often essential adjuncts in diagnosis of ethylene glycol poisoning.[5,17] Elevated plasma osmolality is characteristic of ethylene glycol intoxication. Detection of increased plasma osmolality is most useful in the early stages of ethylene glycol poisoning when accurate diagnosis is critical. Therapeutic intervention is effective only if begun in the first few hours after ingestion. Ethylene glycol also increases the anion gap as much as 3-5 times greater than normal. Patients poisoned by ethylene glycol are acidotic, often with blood pH values less than 7.1.

As calcium oxalate-related renal disease develops, urine sediment contains large numbers of birefringent or polarizing oxalate crystals.[5,8,17,34] Acute renal damage is accompanied by oliguria, hyperkalemia, hyperphosphatemia and increased serum urea nitrogen levels.

Diagnosis: Antemortem diagnosis of ethylene glycol poisoning is difficult.[17,34] Differential considerations include encephalitis, concussion, acute nephrosis, uremia, foreign body ingestion, leptospirosis and acute gastritis. Ethylene glycol toxicosis should be suspected in cats with emesis, ataxia, convulsions, subnormal temperature and renal failure.

Ethylene glycol and some metabolites (hippurate and oxalate) can be detected by chemical analysis in blood, urine and renal tissue.

At necropsy, impression smears of cut kidney surface can be examined under polarized light. Birefringent crystals are readily apparent in fatal cases of ethylene glycol poisoning.

Treatment: Early diagnosis is the most important aspect of ethylene glycol treatment and prognosis. Oral detoxification, including emesis followed by activated charcoal given <2 hours after ethylene glycol ingestion, markedly increases chances for survival.

Ethyl alcohol is used as a competitive inhibitor to prevent metabolism of ethylene glycol to more toxic products.[5,8,17,34] Ethanol serves as a preferential substrate for alcohol dehydrogenase and allows increased excretion of unmetabolized ethylene glycol from the urine. Parenteral sodium bicarbonate also combats acidosis. A thorough and well-documented regimen of treatment for ethylene glycol poisoning has been published.[17] Recommendations include sodium bicarbonate at 6.2 mEq/kg body weight every 4-6 hours if plasma bicarbonate values are not known. Bicarbonate administration may also be adjusted to maintain urinary pH at or just below 7.5-8.0. The recommended 20% ethanol dosage for cats is 5 ml/kg body weight IV at 6-hour intervals for up to 72 hours. After that, ethanol can be infused every 8 hours for 4 additional treatments. Treatment is most effective if initiated within 2 hours after ingestion. Ethanol dosage is commonly adjusted so the animal is maintained in a comatose or near-comatose state.

Successful treatment includes fluid therapy. However, care should be taken to avoid pulmonary edema from overhydration in animals with oliguric renal failure.[17] Urine output and central venous pressure are helpful in monitoring fluid therapy. Calcium borogluconate may be given to help control seizures that may be related to hypocalcemia. A 10% solution given IV at 0.25 ml/kg body weight daily in 3 divided doses is recommended. Prednisolone (0.25 mg/kg) is useful to alleviate shock and pulmonary edema. Fluid therapy should not contain potassium salts until urine flow is established or the BUN level is near normal.

Experimental work with 4-methylpyrazole, an inhibitor of alcohol dehydrogenase, has given excellent results in dogs. However, the compound is not effective in cats.[17]

Remember that cats with advanced clinical signs of ethylene glycol toxicosis warrant a grave prognosis. Client education is important in prevention. Toxicosis also occurs in people, and clients should be instructed in preventing access of children and pets to antifreeze solutions.

Table 4. Selected household and commercial products that are hazardous to cats.

Category	Toxic Components	Clinical/Diagnostic Features	Therapy
Detergents (anionic)	Sulfonated or phosphorylated forms	Alkaline product. Dermal irritation, vomiting, diarrhea, GI distension. Usually not fatal.	Lavage with water or weak acid (vinegar).
Detergents (cationic)	Quaternary ammonium with alkyl or aryl substituent groups	Vomiting, depression, collapse, coma. May cause corrosive damage to esophagus.	Milk or activated charcoal orally. Soap is also effective. Treat seizures & respiratory depression as needed.
Dry-cleaning fluids	1,1,1 Trichloroethane	Exposure may be dermal, inhalation or oral. Anesthesia, depression, disorientation, narcosis. Occasional ventricular fibrillation. Hepatic and/or renal failure.	Artificial respiration. **DO NOT USE EMESIS OR LAVAGE.** Charcoal for oral exposure. Monitor lungs, use antibiotics & other therapy for hydrocarbon pneumonia.
Fire extinguisher (liquid)	Chlorobromomethane, methyl bromide	Dermal & ocular irritants. Lacrimation, salivation. Metabolized to methanol. Vomiting, impaired vision, dizziness, paresis, coma.	Flush with soap & water. **DO NOT USE EMESIS OR LAVAGE.** Control pulmonary edema, renal failure, acidosis & pneumonia.
Fuels	Petroleum hydrocarbons, ethanol, kerosene, gasoline	Early CNS depression, disorientation, necrosis. Mucosal irritation. Aspiration or hydrocarbon pneumonia.	Prevent aspiration pneumonia. **AVOID GASTRIC LAVAGE OR PROCEED CAUTIOUSLY TO PREVENT ASPIRATION.** Monitor & treat for pneumonia.
Paint & varnish removers	Benzene, methanol, toluene, acetone (10-75%)	Dermal irritation, depression. Narcosis, pneumonia, hepatorenal damage. See Fuels.	See Fuels.
Pine oil disinfectants	Pine oil 5-10%, phenols 2-6%	Gastritis, vomiting, diarrhea followed by CNS depression, occasional mild seizures. Phenols may induce nephrosis.	Gastric lavage with caution to prevent aspiration. Mineral oil or saline cathartic. Monitor pulmonary & renal function.
Shampoo (antidandruff)	Zinc pyridinethione	Progressive blindness with retinal detachment & exudative chorioretinitis.	Prompt oral detoxication therapy. No specific antidote.
Shoe polish	Aniline dyes (3%) in some, small amounts of nitrobenzenes or terpenes	Low concentration of these agents reduces toxicity of product. Aniline & nitrobenzene induce methemoglobinemia. Probability of poisoning is low.	Use ascorbic acid for therapy of methemoglobinemia.
Thawing salt	Calcium chloride	Strong local irritant. Erythema, exfoliation of skin. Vomiting & diarrhea. GI ulceration.	Flush affected area with cold water. Give water or egg white orally.

Benzoic Acid

Cats have been poisoned by benzoic acid and benzoate salts used as food preservatives.[1,8] In most other animals, benzoic acid is conjugated with glycine to form hippuric acid or with glucuronic acid to form benzylglucuronide. Because cats are deficient in glucuronyl transferase, benzoic acid accumulates to toxic levels more readily than in other species.

Clinical Signs: Clinical signs in cats include marked ataxia, mild hyperesthesia, muscle tremors about the head and ears, depression and prostration. Pupils are dilated and fixed before death. Clinical signs may be due to rapid onset of metabolic acidosis. The progression from onset of clinical signs to death occurs within a few hours to as long as 36 hours or longer.

Treatment: Treatment is entirely symptomatic and supportive. Acidosis can be corrected with fluids containing bicarbonate. Ideally, the acid-base balance should be monitored. Artificial respiration occasionally may be required to maintain life until excretion is accomplished and acidosis is corrected.

Boric Acid

Boric acid may be a constituent of roach and ant poisons. Borates are also used in cleaning and washing powders (Borax). Sodium perborate decomposes to form hydrogen peroxide and sodium boride. This is found in some denture cleansers. The toxic dosage is estimated at 0.1-0.5 g/kg; cats appear to be poisoned more often than dogs.[1,5,8,35]

Clinical Signs: Clinical signs include vomiting followed by diarrhea and anorexia. In severe poisoning, weakness, ataxia and occasionally seizures or tremors may be seen. This toxicant appears to concentrate in the kidneys, and oliguria or anuria can develop.

Diagnosis: Lesions at necropsy include gastroenteritis, nephrosis, hepatic fatty degeneration and possibly cerebral edema. Diagnosis would be suggested by characteristic clinical signs and lesions and confirmed by positive analysis for boric acid in urine.

Treatment: Treatment is entirely symptomatic, consisting of fluid diuresis and peritoneal dialysis. If exposure is recent, emesis or gastric lavage and other appropriate oral detoxification therapy, including charcoal administration, is recommended. Diazepam (Valium) can be used to control any seizures.

Caustics and Corrosives

Cats may be exposed to surgical, hospital or household disinfectants, strong bases or strong acids.[1,8,35] The most likely effects are severe skin irritation and occasionally stomatitis, gingivitis, glossitis and pharyngitis (Fig 1). Most cats inadvertently ingest the material while grooming after contact exposure.

Clinical Signs: Because cats are not likely to ingest large quantities of caustics or corrosives quickly, severe damage to the esophagus or stomach is not expected. These compounds are direct irritants and their effects are confined to those areas of local contact, such as the tip of the tongue, hard palate and pharynx.

Treatment: Treatment should include flushing the affected area with large amounts of water. After rinsing the area, any remaining material should be neutralized if possible. Bases are commonly neutralized with vinegar or dilute (5%) acetic acid. For acids, a 5% sodium bicarbonate solution is recommended.[1,5,8,35]

If necrosis or sloughing of skin or mucosa has occurred, affected areas should be cleaned and treated with an antibiotic ointment. Affected areas should be examined daily and treated as needed.

The prognosis is grave with necrotizing damage to the esophagus. In affected people, esophageal scarring and stricture often require extensive management and surgical intervention. Apparently no cases of this type have been documented in cats.

Intoxication by Common Drugs and Medications

Some common drugs available over the counter may pose hazards to cats. Since they are given without veterinary supervision, yet may be accessible or administered intentionally to cats, they will be considered briefly as accidental intoxications.

Aspirin

Aspirin (acetylsalicylic acid) is commonly available as 5- or 7.5-grain (325- and 500-mg) tablets. Aspirin inhibits prostaglandin synthesis and other enzymes in cellular systems. Side effects also include prolongation of bleeding time by prevention of platelet aggregation. Salicylates may also uncouple oxidative phosphorylation, resulting in hyperglycemia and glycosuria.[34]

Aspirin is readily absorbed from the stomach and proximal small intestine. The acidity of the stomach favors an unionized state for salicylate, thus promoting absorption.[1,34]

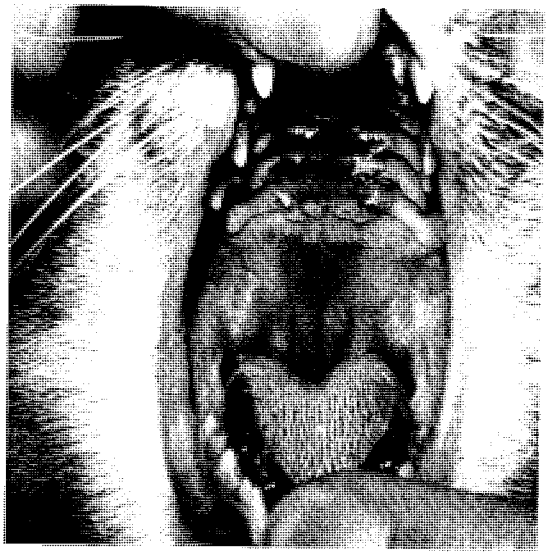
Biotransformation of salicylates occurs primarily by conjugation with glycine or glucuronic acid. Cats are especially sensitive to aspirin toxicosis because of their limited ability to form glucuronides, which are important in rapid excretion of the salicylate.[5,32] An aspirin dosage of 25 mg/kg body weight daily in a cat maintains serum salicylate levels considered therapeutic for people. Cats given this dosage for 15 days had no clinical evidence of toxicosis. Administration of a single 5-gr aspirin tablet (325 mg) daily produces clinical toxicosis within 12 days.

Clinical Signs: Clinical signs include vomiting, depression, anorexia and toxic hepatitis. Additional effects are anemia, gastric ulcers, Heinz body formation and reduced erythrocyte production. There may also be bone marrow hypoplasia.[1,5,8,34]

Diagnosis: If aspirin toxicosis is suspected, determination of serum salicylate levels may be useful in confirming the diagnosis. At necropsy, characteristic lesions include gastric and intestinal ulceration, toxic hepatitis and pulmonary ecchymotic hemorrhages.

Treatment: Treatment for aspirin poisoning should include appropriate evacuation of the gastrointestinal tract, followed by administration of activated charcoal.[1,5,32] It is important to maintain normal body temperature and reestablish normal hydration as well as fluid and electrolyte balance. Therapy is aimed at correcting metabolic acidosis with IV fluids and sodium bicarbonate. In addition, alkalinization of the urine with sodium bicarbonate promotes excretion of salicylate by enhancing the ion-trapping mechanism. Sodium bicarbonate should be administered carefully, with frequent monitoring of urine or blood pH.

Figure 1. Severe necrosis of the epithelium on the tip of the tongue and hard palate from ingestion of a commercial disinfectant containing a phenolic compound. The compound was used to disinfect the animal's quarters. It was then transferred from the haircoat to the mouth by grooming.



Acetaminophen

Acetaminophen (N-acetyl-p-aminophenol) is widely available under a variety of trade names, including Anacin-3, Comtrex, Datril, Excedrin, Tylenol, Vanquish and many others. Acetaminophen is normally biotransformed by hepatic glucuronidation and excreted in the urine. When hepatic capacity for glucuronidation is exceeded, acetaminophen undergoes N-hydroxylation, with spontaneous formation of N-acetyl-p-benzoquinone, which is commonly believed responsible for hepatotoxicity.[1,5,8,32,34]

Toxicosis in cats can be produced by oral administration of a single 325-mg acetaminophen tablet.[32] A second tablet given within 4-24 hours is often lethal.

N-acetyl-p-benzoquinone binds covalently to cellular constituents. If glucuronide formation is ineffective, the drug may be metabolized as a glutathione conjugate. When glutathione stores are exhausted, metabolites then bind with cellular proteins, resulting in liver necrosis.[5,32]

Other metabolic pathways result in accumulation of oxidizing metabolites that induce methemoglobinemia and cause denaturation of other erythrocyte membranes. This constitutes the second avenue of susceptibility of cats, since they have demonstrated tissue sensitivity to Heinz body formation, hemolytic anemia and methemoglobinemia.

Clinical Signs: Acetaminophen overdose results in toxicosis within 4-12 hours after ingestion. Methemoglobin formation is evidenced by cyanosis, which increases in severity with time. The combination of intravascular hemolysis and liver damage results in icterus, hemoglobinuria and anemia. These signs occur within 1-7 days after toxic ingestion of acetaminophen. Cats develop a characteristic edema of the face and paws, which is often attended by lacrimation and pruritus (Fig 2). Affected cats are anorectic and extremely depressed throughout the toxicosis.

Laboratory findings are consistent with methemoglobinemia and liver damage.[5,32,41] Blood is chocolate-brown, and stained blood smears reveal Heinz body formation. Packed cell volume is decreased, and there are increases in serum levels of liver-specific enzymes and both total and direct-reacting bilirubin.

Necropsy findings include facial edema, icterus, chocolate-brown blood, mottled liver and hemoglobinuria.

Treatment: Goals are to prevent development of reactive metabolites and promote their excretion, convert methemoglobin back to oxyhemoglobin and support cardiovascular and respiratory system functions.[5,32,41] To counteract the formation of reactive metabolites, N-acetylcysteine is given PO in cats. Acetylcysteine is effective due to its ability to replenish glutathione or substitute for it functionally. Acetylcysteine (Mucomyst: Mead Johnson) is available as sterile 10% or 20% solution. The initial dosage may range from 140 mg/kg in mild cases to 280 mg/kg in severe cases. This should be followed with 70 mg/kg PO 4 times daily for 3 days. Acetylcysteine also can be given IV at a loading dosage of 140 mg/kg body weight as a 5% solution.[32] This is repeated every 4 hours thereafter at 70 mg/kg for 3-5 more treatments.

If acetylcysteine is unavailable, sodium sulfate may be substituted. Sodium sulfate should be given IV as a 1.6% solution in water at 50 mg/kg body weight every 4 hours for 6 treatments. Animals should be monitored carefully to assure that therapy is not withdrawn too early.

Ascorbic acid (20 mg/kg) may be given parenterally to convert methemoglobin to oxyhemoglobin.[3,5] Methylene blue should not be used for this purpose, since it induces methemoglobinemia in cats.

Supportive therapy should include administration of fluids as needed, respiratory support including oxygen if cyanosis is evident, maintenance of body temperature and monitoring of vital signs.

Caffeine and Related Alkaloids

Coffee, tea and chocolate contain the methylxanthine alkaloids caffeine, theophylline and theobromine, respectively. Sources of methylxanthines associated with poisoning in pets include stimulants ("pep pills") containing caffeine, and excessive consumption of chocolate.[21] One ounce of baking chocolate contains 35 mg of caffeine and 392 mg of theobromine. Methylxanthines cause central nervous system stimulation, diuresis, cardiac muscle stimulation and smooth muscle relaxation. They

Figure 2. Characteristic edema of the face and paws of a cat with acetaminophen toxicosis.

appear to be active in translocation of intracellular calcium, accumulation of cyclic AMP and blockade of adenosine receptors.

These agents are readily absorbed orally or parenterally and widely distributed throughout the body, and are eliminated primarily in the urine.

Clinical Signs: The approximate LD_{50} of caffeine and theobromine in cats is estimated at 100-200 mg/kg.[5,21] Commonly available stimulants or "pep pills" contain 200 mg per tablet. Thus, ingestion or administration of 3 such tablets to a cat would likely be lethal. Early clinical signs are restlessness, hyperactivity, and urinary incontinence or diuresis. Severe effects develop 3-8 hours after ingestion. These include extreme hyperactivity, stiffness, occasional twitching and spastic rigidity of muscles. Seizures are tonic to near tetanic in nature and are difficult to differentiate from those caused by poisoning with strychnine or 4-aminopyridine.

Diagnosis: Methylxanthine poisoning can be confirmed by chemical detection of the alkaloids in stomach contents, serum or urine.

Treatment: Though there is no specific antidote for methylxanthine poisoning, a course of therapy has been recommended. The respiratory and cardiovascular status of the patient should be monitored. Intubation and artificial ventilation, therapy for shock and IV fluid therapy may be necessary.

If ingestion has occurred within 2 hours of presentation, oral detoxification, including emesis, gastric lavage and administration of activated charcoal and a saline cathartic, should be accomplished as described in the general treatment section. Before gastric lavage, any seizures or hyperreflexia must be controlled. For this procedure, diazepam may be given IV in a total dose of 2.5-5 mg. If this is unsuccessful, phenobarbital IV at 6 mg/kg is recommended. This should be repeated 2-4 times daily or as needed. Finally, the electrocardiogram should be monitored. If a beta blocker is indicated, propranolol (Inderal) should be given. The recommended starting dose for propranolol in cats is 0.25 mg in 1 ml saline, followed by 0.2-ml IV boluses to effect. The usefulness of beta blockers for this purpose has been demonstrated in dogs but remains to be established in cats.[21]

Because methylxanthines may be resorbed from the urinary bladder, it may be wise to catheterize the urinary bladder to decrease resorption of these agents or their metabolites from the urine.

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Chapter 8

Cattery Design and Management

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General Concepts

A group of cats brought together for the purpose of raising kittens for show or sale is called a "cattery." A "multiple-cat household" is a home that has at least 2 or more cats not used for breeding purposes. Pounds are public-funded facilities where stray, abandoned or unwanted cats are kept for a finite period, usually less than a week, pending adoption or reclaiming by the owner. If the animals are not reclaimed or adopted, they are destroyed. A "cat shelter" is usually a privately run abode for homeless cats that are kept for an indefinite period pending adoption into permanent homes. If they are not adopted, they often spend the remainder of their lives in the facility. "Boarding kennels" are privately run businesses that house (board) pet cats for short periods for a fee. All of these environments share many of the inherent problems of keeping relatively large numbers of cats in close quarters. The discussion that follows applies more or less to all of these situations, though the emphasis of this chapter is on catteries.

Success in cat breeding is a measurable entity. It is reflected by the numbers of kittens per litter that are successfully weaned, and the magnitude of disease problems that occur in the neonatal (first 2 weeks of life) and postweaning (6-16 weeks) periods. Successful cat breeders also produce high-quality examples of a chosen breed. Success in this area is measured by show wins, bloodline reputation, public demand for kittens of the breed, and production of cats with predictable temperaments and appealing appearance. It is also important to breed cats that are both genetically and phenotypically robust.

Though this balance is difficult to achieve, the triple goals of vigor, proper temperament and breed conformation should not be compromised. Litter sizes should average 3-4 or more kittens (though some breeds have smaller litters), and 90% or more should be healthy at weaning. The incidence of "clinically apparent" infectious disease should also be low. The term "clinically apparent" is stressed because kittens kept in well-managed catteries may be infected with myriad potentially pathogenic agents without becoming ill (see chapter on infectious diseases). Among the infectious diseases of cats, a small number take on serious proportions in catteries that are poorly designed and managed. These diseases, termed "indicator diseases of cattery health," include feline herpesvirus type-1 infection (rhinotracheitis), feline infectious peritonitis, chlamydiosis, ear mite and flea infestations, and dermatomycosis (ringworm). Persistent or recurrent problems with these diseases indicate that cattery design, management and/or genetic vigor of the broodstock are inadequate.

Need for Specially Designed Facilities

The success of any cat breeding program depends on 3 factors: the facilities in which the cats are housed; management and maintenance of the facilities; and care of the animals. As you will see from the following discussion, the last 2 items are totally

dependent on the first. It is important, therefore, for new cat breeders to consider beforehand the need for specially designed facilities to house their animals. Ultimately, cat breeders that start out on the proper footing will enjoy their experience and continue breeding cats. New cat breeders that proceed rapidly forward with too many animals, too many kittens, inadequate facilities, and a poor understanding of proper genetics and cattery management often face severe or even insurmountable disease problems. These problems will either cause them to get out of cat breeding altogether or, even worse, to continue despite disease problems and deplorable environmental conditions. Breeders in the latter category often withdraw inward as their cattery problems increase. With time, many of them become slaves of their situation. The cattery experience should be joyful and allow for a proper balance of human and animal relationships.

Though there are compelling reasons for creating a special cattery facility, only a small proportion of cat breeders actually constructs special quarters for their cats. Indeed, most catteries are within the breeder's home. Homes are used for catteries for several reasons: it is cheaper to purchase and maintain one structure; some cat breeders believe that cats become bored by lack of intimate human contact and that behavior problems can be aggravated by caging the cats; many cat breeders believe that cats must be integrated into households from the day of birth to become socially adjusted to later home life; and cats, even if used for breeding, are also accepted as members of the family (pets) and their owners have no intention of banishing them to private quarters.

Many reasons are used to justify maintaining a cattery in a human abode, but the main tenet of good cattery design and management is that "human homes do not make easily manageable catteries." It is unusual to have more than 5 breeding animals in an unmodified home without creating problems with their care and health. Therefore, unmodified human habitations should not be used to house more than 5 breeding animals. With modifications, a home may be able to handle up to 10 breeding animals; if more animals are desired, specially designed cat quarters should be constructed.

The objections to separate cattery facilities can easily be countered, with the possible exception of economics. Even with economic consideration, however, separate quarters easily pay for themselves in healthier cats, lower veterinary expenses, and a better cattery reputation. It has been our experience over the last 20 years that cats do not need constant attention to become socialized. A few minutes of individualized attention each day during cleaning and feeding produce well-adapted pets.

During the course of feline health-related research dating back to 1967, we have maintained 2 separate cat breeding facilities that have produced over 3500 kittens. Over 1000 of these animals have been placed in homes throughout the world as pets, usually when 8-12 months of age. Many of these animals have been adopted through Save Our Cats and Kittens (SOCK), Walnut Creek, CA, a group dedicated to raising money for feline health research and to finding homes for animals coming out of our studies. Even though these cats were raised in separate quarters and received relatively short periods of daily human attention, the vast majority of people who have adopted these animals said they have never had friendlier and better-adjusted animals.

Many of the suggestions made in this chapter relate to our own experience with raising cats in cattery environments and with assisting hundreds of cattery owners with their problems. In fact, genetic selection for temperament has, in our hands, been a far more positive tool in producing well-socialized animals than hours of daily human handling. The fact that cats are kept in separate quarters does not preclude breeding animals from being treated as pets. It can be argued that 1-2 cats in the house have a far more positive human-pet interaction than 50 cats.

Guidelines for Cattery Design

Before considering design and management of privately owned and maintained catteries, it is important to review some of the United States government guidelines for maintenance of cats used for experimen-

tal purposes. These federal guidelines are not legally applicable to privately run catteries where animals are reared for non-laboratory purposes, but they do reflect the experiences and wisdom acquired by laboratory animal managers and veterinarians over many years. Such federal guidelines will probably be used by state and local legislators to formulate local laws and ordinances that may some day affect cattery owners.

USDA and NIH Guidelines

Detailed guidelines for the care and maintenance of cats in laboratory settings have been provided by the United States Department of Agriculture (USDA) and the National Institutes of Health (NIH).[2,14] Copies of these guidelines can be obtained directly from the Government Printing Office, Washington, DC. Though many of the guidelines given by the USDA refer specifically to laboratory-maintained animals, some of these guidelines have direct application to private cattery design and management (Table 1).

The NIH guidelines for housing experimental cats are similar to USDA guidelines in most aspects.[14] Floor space required for each adult cat is 3 ft ^{2} instead of 2 1/2 ft ^{2} as in the USDA guidelines. The NIH guideline for humidity is 30-70% and optimum dry bulb temperature range of 64.4-84.2 F. Ventilation comparable to 10-15 room air changes per hour has been recommended by the NIH, based on years of experience with experimental animal quarters. The stringency and necessity of such a requirement has been questioned by some who argued that ventilation must also take into account the spatial arrangement of the animals and pens within the building, and that ventilation rate per animal or animal cage is a better measure of effective air flow.[4,22] Despite this criticism, the 10-15 room air changes per hour guideline has been maintained. NIH recommends that air in animal facilities should not be recirculated unless it has been treated to remove particulate debris and waste gases. However, air treatment, in addition to being prohibitively expensive, is likely to be ineffective due to improper or insufficient maintenance of the complex air-treatment systems.[8] NIH is also more explicit about lighting requirements. Illumination levels of 75-100 foot candles have been generally recommended for animal rooms. NIH guidelines also encourage time-controlled lighting systems to provide a regular diurnal (dark-light) lighting cycle.

Revised USDA Guidelines

The USDA is in the process of revising their animal welfare regulations.[3] Though not approved at the time of this writing, most revisions will probably be incorporated into the existing guidelines. Proposed changes are meant to strengthen the previous regulations by defining them better or making them more stringent. The proposed guidelines were formulated to "provide for an environment that better promotes health, comfort and well-being of dogs and cats." The aim of the proposed changes is to make cat facilities not only more healthful for the cats, but more appealing to their human inspectors. For example, if an average cat owner (not necessarily familiar with cattery practices) finds some aspect of the operation troubling, cruel or personally offensive, the cattery design and/or management is probably not acceptable. Though the new welfare guidelines are similar to the old, there are several notable differences:

Food storage areas must be kept free of trash, weeds, discarded material and clutter, including equipment, furniture and other stored materials not essential for proper husbandry practices.

Surfaces of housing facilities must be easily cleaned or sanitized, or be removable or replaceable. Hard surfaces in contact with dogs or cats must be cleaned daily and sanitized at least every 2 weeks. Floors made of dirt, sand, gravel or similar material must be raked or spot-cleaned daily.

All facilities must have electrical power and pressurized potable running water, based on the premise that proper cleaning cannot be done without these commodities. Ventilation must be provided to minimize ammonia levels. Artificial or natural light must be provided for at least 8 hours a day, corresponding to the natural period of daylight.

Indoor floor areas in contact with animals, outdoor floor areas not exposed

Table 1. Summary of USDA guidelines for sheltering cats used for experimental purposes. Only guidelines pertinent to management of privately owned catteries or multiple-cat households are listed.

General Facilities

Structural Strength: Structurally sound and adequately maintained so that animals are protected from injury and cannot escape, and so that other animals may not gain entrance.

Storage: Food and bedding to be protected from infestation with vermin. Refrigeration provided for perishable food.

Waste Disposal: Facilities designed and maintained to minimize vermin infestation, odors and disease hazards.

Indoor Facilities

Heating: Sufficiently heated to protect cats from cold and to provide for health and comfort. The ambient temperature shall not be allowed to fall below 50 F for animals not acclimated to lower temperatures (35 F if acclimated).

Cooling: The maximum temperature for acclimated cats is 95 F, and 85 F for unacclimated animals. Cooling of the air is required for temperatures above 85 or 95 F, respectively.

Ventilation: Facilities are to be provided with fresh air by means of windows, doors, vents or air conditioning, and ventilated as to minimize drafts, odors and moisture condensation. Auxiliary ventilation, such as exhaust fans, vents or air conditioning, shall be provided when the ambient temperature is 85 F or higher.

Lighting: Ample lighting by natural or artificial means shall be provided. Lighting shall be uniformly distributed and of sufficient intensity to permit routine inspection and cleaning during the entire working period. Primary enclosures shall be placed to protect cats from excessive illumination.

Interior Surfaces: Shall be constructed and maintained as to be substantially impervious to moisture and readily sanitized.

Outdoor Facilities

Shelter from Weather: Sufficient shade shall be provided to allow cats protection from direct sunlight. Cats shall be allowed access to shelter so as to remain dry during rain or snow. Shelters shall be provided for all cats kept outdoors when the temperature falls below 50 F. Sufficient clean bedding or other means of protection shall be provided when the ambient temperature falls below the temperature to which a cat is acclimated. Pens should be constructed so as to rapidly eliminate excess water.

Primary Enclosures

General Requirements: Structurally sound and well maintained so as to protect animals from injury, contain them, and keep predators out. Enclosures shall be constructed and maintained so as to keep animals dry and clean, and provide convenient access to clean food and water. Receptacles containing sufficient clean litter shall be provided to contain excreta. Each primary enclosure shall be provided with enough solid resting surfaces (perches) of adequate size to comfortably hold all occupants of the enclosure at the same time. Resting surfaces shall be elevated in all enclosures housing 2 or more cats.

Space Requirements: Enclosures shall provide sufficient space to allow each cat to turn about freely and to easily stand, sit and lie in a comfortable normal position. Each adult cat shall be provided with a minimum of 2 1/2 square feet of floor space, and no more than 12 adult cats shall be housed in the same pen.

(Table 1 continued)

Animal Health and Husbandry Standards

Feeding: Cats shall be fed at least once daily, except as otherwise required to provide adequate veterinary care. Food shall be free from contamination, wholesome, palatable, and of sufficient quantity and nutritive value to meet normal daily requirements for the size and condition (nonpregnant, pregnant, lactating, kittens) of the animals. Food receptacles shall be accessible to all animals in the enclosure and localized so as to minimize contamination by excreta. Feeding pans shall be durable and kept clean and sanitized at least every 2 weeks. Self-feeders may be used for feeding dry food, but must be sanitized regularly to prevent moldiness, deterioration or caking of food. Potable water shall be provided at all times or, if not possible, twice daily for periods of not less than 1 hour. Watering receptacles shall be kept clean and sanitized once every 2 weeks.

Sanitation: Excreta shall be removed from primary enclosures as often as is necessary to prevent contamination of the animals and to reduce disease hazards and odors. When enclosures are hosed down, animals contained in the enclosure being cleaned shall be removed during the cleaning process and measures taken to protect the animals from being contaminated with water and other wastes. Cages, rooms and hard-surfaced pens or runs shall be sanitized by washing them with hot water (180 F) and soap or detergent. This shall be followed by a safe and effective disinfectant. Sanitation of this type shall be conducted every 2 weeks. Pens or runs using gravel, sand or dirt shall be sanitized by removing the soiled gravel, sand or dirt and replacing it as necessary.

Housekeeping: Premises (buildings and grounds) shall be kept clean and in good repair to protect animals from injury and to facilitate prescribed husbandry practices. Premises shall be maintained free of accumulations of trash.

Pest Control: An effective pest-control program shall be established and maintained for control of insects, ectoparasites and avian and mammalian pests.

Classification and Separation: Animals housed in the same enclosure shall be maintained in compatible groups, with the following restrictions: females in estrus shall not be housed in the same enclosures with males except for breeding purposes; any cat exhibiting a vicious disposition shall be housed individually; kittens shall not be housed in the same primary enclosure with adult cats other than their dams, except when maintained in breeding colonies; cats shall not be housed in the same primary enclosure with any other species of animals; and cats showing signs of communicable illness shall be separated from other cats in such a manner as to minimize dissemination of disease.

Veterinary Care: Programs of disease control and prevention, euthanasia, and adequate veterinary care shall be established and maintained under the supervision of a veterinarian. Each cat shall be observed daily by the animal caretaker in charge, or by someone under his/her supervision. Diseased animals shall be provided with veterinary care or euthanized.

to the direct sun or made of a hard material such as wire, wood, metal or concrete that are in contact with the animals, and all walls, boxes, houses, dens and other surfaces in contact with the animals shall be impervious to moisture (ceiling excepted). Outside floor areas in contact with the animals and exposed to the direct sun should consist of compacted earth, sand, grass or gravel.

Outdoor facilities shall: contain a shelter area large enough for all animals in the structure to sit, stand or lie in a normal manner and to turn about freely; provide adequate shelter from cold and heat; have wind and rain breaks at the entrance; contain clean dry bedding material; and contain a separate outside area of shade big enough to contain all animals at one time and protect them from the sun's rays.

The space requirement for cats is increased in the new proposed guidelines.

Weaned cats 4 kg (8.8 lb) shall be provided with 3 ft^2 of floor space and cats 4 kg with 4 ft^2. Queens with kittens are to be supplied with their base space plus 5% of minimum for each nursing kitten. The minimum floor space is exclusive of food, water, litter pans and perches, and would have to be at least 24 inches high.

Queens in heat cannot be housed with sexually mature males, except for breeding. Queens with litters and kittens under 4 months of age cannot be housed in the same primary enclosures with any other adult cats, except when maintained in a breeding colony. Vicious or aggressive cats should be housed separately. All resting surfaces shall be elevated, even if only one animal is in the enclosure.

CFA Cattery Guidelines

The Cat Fanciers' Association (CFA) recently approved what they refer to as *minimum* cattery standards for breeders (Table 2).[4] The purpose of these standards is to provide a basis to judge humane cattery facilities. In particular, they are to provide a means to evaluate complaints of animal abuse against CFA catteries brought by other CFA breeders, the public or local authorities. The minimum nature of these regulations is stressed; they represent a worst-case scenario. Owners of catteries judged not to meet minimum CFA standards would be subject to internal discipline, which would consist mainly of a loss of CFA privileges, such as registration of kittens and certain show privileges.

These standards are based closely on those of NIH and USDA for housing experimental cats, but are stated in much more general terms. Like these other regulations, they stress the point that cats maintained in closed facilities must not only be maintained in good health, but the environment should also have a healthful appearance.

Cattery Design

Preliminary Considerations

It should be evident from USDA, NIH and CFA cattery guidelines that large numbers of breeding cats cannot be maintained in a home or structure that has not been modified in some way to house and maintain cats. It is important, therefore, to consider cattery design.

Good cattery design cannot be accomplished without first considering a few basic requirements: numbers of cats, and space allowed for each animal; purpose of the cattery, such as intensive breeding or occasional breeding, no breeding; external climate; internal climate, such as temperature, lighting, ventilation and humidity; legal requirements for licensing, where applicable; and amount of money available for the project.

The number of animals is the most important consideration in cattery design. Disease problems increase in home-type environments as the number of animals exceeds 6 queens and 3 toms, with each female producing 6-8 kittens a year. It is difficult to maintain optimal cattery husbandry in a home environment for more than this number of adult animals and kittens. If more than this number is kept, it is advisable for the health of the animals, to design separate facilities just for them.

The maximum number of cats that can be maintained in catteries also depends on the time and money a person is willing to expend. As a general rule, a single person acting both as owner and caretaker cannot adequately care for more than 25 breeding animals even in the best of facilities. In fact, most successful owner-operated catteries that we have observed seldom exceed about 9 top-quality breeding animals. A good breeding program can involve as few as 6 females and 3 males, providing only one breed is kept. Some breeds, however, require more than this number. For example, the breeding of Colorpoint Shorthairs includes outcrossing to Siamese. Manx and Scottish Folds require that a certain number of tailed or straight-eared cats be kept. Under the most intensive breeding conditions, a cattery of 6 breeding females and 3 males can produce as many as 36-48 kittens per year. The work required to maintain the comfort, sanitation, nutrition and health of this many young animals is tremendous.

Once a decision has been made on how many animals the cattery will maintain, the

Table 2. Minimum cattery standards adopted by the Cat Fanciers' Association in October, 1989.

Definitions

For the purposes of this standard, the following definitions shall apply:

Person: An individual, firm, partnership, corporation, trust or any association of persons.

CFA Cattery: Any person(s) who has registered a litter of kittens with the Cat Fanciers' Association or who has registered 3 or more cats with the Cat Fanciers' Association or who has registered a cattery name with the Cat Fanciers' Association.

Cattery Facility: A building, room or area used to house cats.

Primary Enclosure: A structure used to immediately restrict 1 or more cats to a limited amount of space, such as a room, pen, run, cage or compartment.

Animal Cruelty: Any inhumane or abusive or neglectful treatment causing harm or death of a cat as determined by local law enforcement authorities.

Cat-in-Distress: A cat that is in jeopardy of life or limb, as determined by a qualified animal-control officer or veterinarian.

Litter: Material used by the cat for defecation or urination.

Litter Pan: An enclosure or area (receptacle) in which litter is placed for the cat's use.

Standards

CFA catteries shall maintain the following *minimum* standards:

Cattery Facility

The cattery facility, whether a private residence, portion of a private residence or separate structure not physically connected to a private residence, shall be structurally sound and maintained in good repair to protect the cats from injury, protect the cats against overexposure to the elements, contain the cats and restrict entrance of other animals.

Supplies of food, bedding and interior building surfaces shall be maintained in a sanitary manner.

Food shall be transported, handled and stored in a manner that prevents introduction of parasites, disease vectors (such as insects) or chemical contaminants. Supplies of dry food shall be stored in areas that are cool, dry, clean and free of vermin and other potential contaminants. Refrigeration shall be provided for supplies of perishable food. Conditions affecting the shelf life of food, such as date of manufacture, exposure to extremes in temperature and humidity, exposure to moisture, unsanitary conditions, exposure to light, exposure to oxygen and exposure to insects, shall be monitored to prevent deterioration of the food's nutrient value.

The facility shall be sufficiently heated and cooled to protect cats from excessive cold and heat. The ambient temperature shall be maintained in a range that ensures that the cats will not suffer from heat stress (heat stroke or hyperthermia) nor from cold stress (frostbite or hypothermia).

The facility shall be adequately ventilated to provide for the health and comfort of cats at all times. The facility shall be provided with a source of fresh air by means of windows, doors or vents and shall be ventilated in a manner that minimizes drafts, odors and moisture condensation.

The facility shall have ample light of good quality by natural or artificial means or both. Lighting shall provide uniformly distributed illumination of sufficient intensity to permit routine inspection and cleaning, and provide for the well-being of the cats. The cats shall be protected from excessive illumination.

When sunlight is likely to cause overheating or discomfort, sufficient shade shall be provided to allow cats to protect themselves from direct rays of the sun.

Access to shelter shall be provided for cats to allow them to remain dry at all times.

(Table 2 continued)

Primary Enclosures

Primary enclosures shall provide a microenvironment that satisfies the standards for the cattery facility, as well as the following additional standards:

A primary enclosure shall be structurally sound and maintained in good repair to protect the cats from injury, to contain them, to keep other animals out, and to enable the cats to remain dry and clean.

A primary enclosure shall provide sufficient space to allow each enclosed cat to turn freely and to easily stand, sit and lie in a comfortable position. The minimum primary enclosure space for a single cat of 4 lb or greater shall be 30 ft^3.* Where the primary enclosure is used for more than one cat, resting perches shall be provided.

A primary enclosure shall be constructed and maintained so that cats have convenient access to clean food, water and litter.

The number of cats in a primary enclosure shall not exceed a number that would prevent proper ventilation and sanitation.

A primary enclosure shall not be constructed or maintained with an exposed wire mesh bottom or any other material that will injure the feet or legs of a cat.

If the primary enclosure is not of sufficient size to allow the cat(s) to express their specialized locomotor patterns, then an additional area shall be made available for the cat(s) to jump, run, exercise and scratch at least once a day.

Feeding and Water

Cats shall be fed at least once each day, except as otherwise required by a veterinarian. The food shall be free from contamination and shall be wholesome, palatable and of sufficient quality and nutritive value to meet the normal daily requirements for the condition and size of the cat. Food shall be provided in sufficient amounts to ensure normal growth of kittens and maintenance of normal body weight in adults.

Food receptacles shall be accessible to all cats and located to prevent contamination by excreta. Feeding dishes shall be kept clean. Self-feeders may be used for feeding of dry food and shall be sanitized regularly to prevent moldiness, deterioration or caking of food.

Cats shall have continuous access to fresh, potable and uncontaminated drinking water.

Cleaning and Sanitation

Primary enclosures, the cattery facility and storage spaces shall be cleaned with appropriate detergents and disinfectants as often as necessary to keep them free of dirt, debris and harmful contamination.

Easily accessible litter pans shall be provided for all cats at all times.

Feces and soiled litter shall be removed from all litter pans at least once a day.

Absorbent litter and/or any other material used to absorb urine shall be changed when 30% saturated with urine.

The cattery facility shall be kept clean and remain free of accumulated debris and excreta.

All primary enclosures and accessory equipment, such as feeding bowls and watering devices, shall be washed and sanitized frequently to keep them clean and free from contamination.

An effective program for control of insects, ectoparasites and mammalian pests, if present, shall be established and maintained using safe products.

* 30 ft^3 = a space with dimensions of 3.3 x 3 x 3 ft.

(Table 2 continued)

Health Care

The cattery shall promptly provide medical care to any cat-in-distress and/or any cat exhibiting signs of severe illness.

Cats shall be observed daily and diseased cats shall promptly be provided with medical care.

A vaccination program, under the advice of a veterinarian, is recommended.

Cats shall be kept clean and free of severe coat mats, and generally groomed sufficiently to maintain a healthy condition.

Cruelty

Cats residing in the cattery facility shall be treated humanely and without neglect.

Catteries shall not allow a cat to be deprived of necessary sustenance, deprived of potable water, deprived of clean quarters, deprived of protection from weather, beaten, mutilated or cruelly treated, and shall not allow, through neglect, any situation to exist or persist that would cause a cat-in-distress condition to occur or persist.

next step is to assign a given amount of space for each animal and for each function (breeding, maintenance, rearing of young). The first rule for assigning space is that "no cat will ever be housed individually in small cages of less than USDA, NIH or CFA standards except for transport or temporary (<24 hours) housing." Small cages are extremely stressful on cats, especially if placed in rooms where other animals are allowed to roam free. Whenever possible, cats should be housed in larger open rooms that allow an opportunity for movement and a degree of privacy.

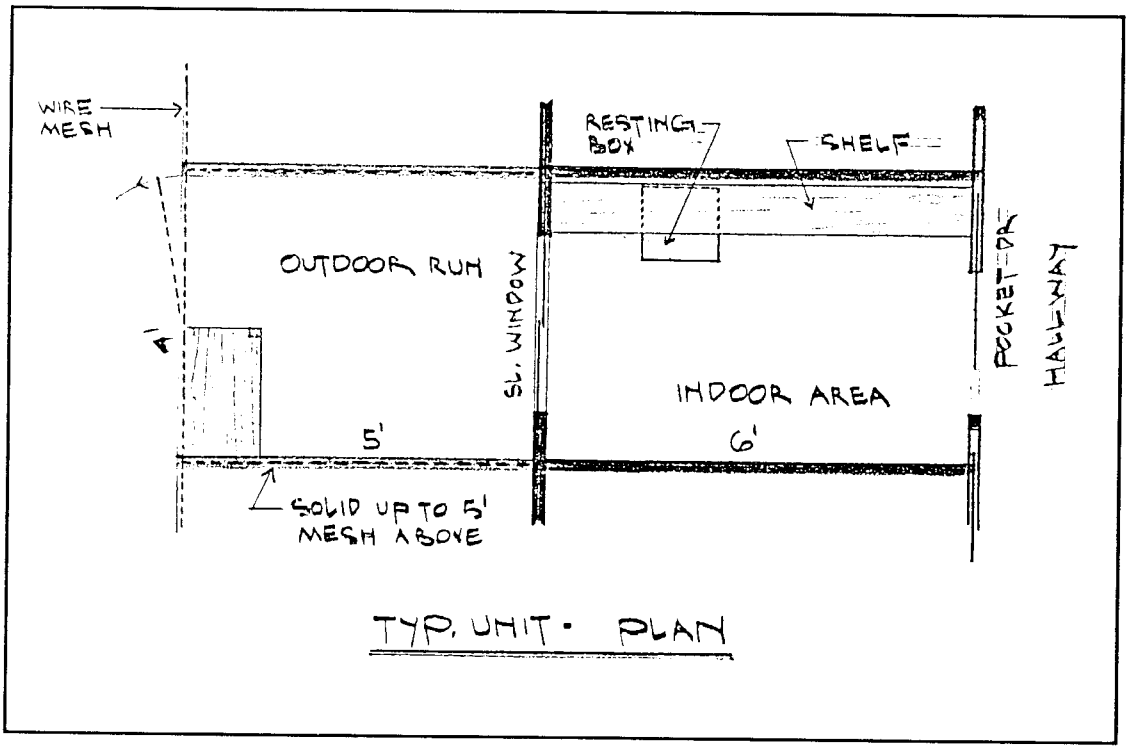
Basic Animal Containment Unit

In designing catteries, it is important to think in terms of a "basic animal containment unit" or "primary enclosure." Research and commercial-type breeding colonies and successful private catteries have certain points in common. Independently of each other, owners and operators of these various types of cat facilities have developed basic designs for catteries that have universal applicability. Depending on garnishings, such facilities are within the financial grasp of most cattery owners.

A basic animal containment unit is shown in Figure 1. This unit can be variable in size, but should be somewhere near 4 feet wide, 7-8 feet high and 8-12 feet long. The outer one-half to two-thirds of the unit should be relatively open to the elements, and the inner portion more or less closed off and protected from the elements. In warmer climates, the outside runs can be larger, while in cold climates more room should be provided inside. Access from the inner to the outer unit can be provided by anything from regular doors to small openings. At least one perch for each animal should be attached at various heights to the walls in each of the inner and outer portions. The floors and at least the lowest 2 feet of the walls should be constructed of solid concrete, with the concrete sealed or covered to prevent water penetration.

A single unit of the above dimensions can serve any of the following functions: as holding quarters for no more than 4 adult cats during the period when they are not breeding or for the first 40 days of gestation; as holding quarters for 1-2 male cats, depending on temperament, when they are not being used for breeding; as a breeding room; as a delivery and nursery room, where a single female is placed 2-3 weeks before parturition and allowed to deliver and rear its young in isolation until its kittens are weaned; as a rearing room, where weaned kittens are kept in isolation until they are sold or reach 16 weeks of age; and as a room for cats currently being shown. If outside stud service is provided, 1 unit will be required for isolation and holding of visiting females.

Figure 1A. (top) Floorplan of a basic animal containment unit. B. (bottom) Floorplan of a cattery made up of a common central hallway and 12 basic animal containment units. The unit may be contiguous with a private home. It is important to surround the cattery with a barrier fence to prevent contact with free-roaming cats.



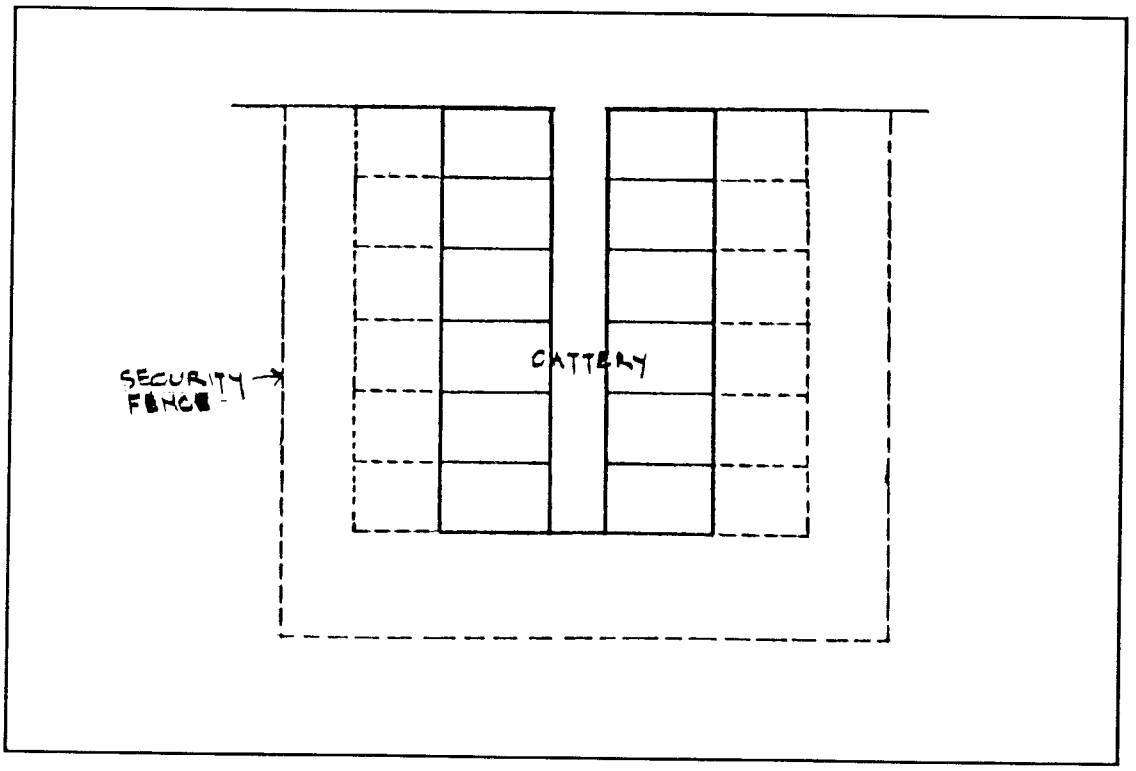
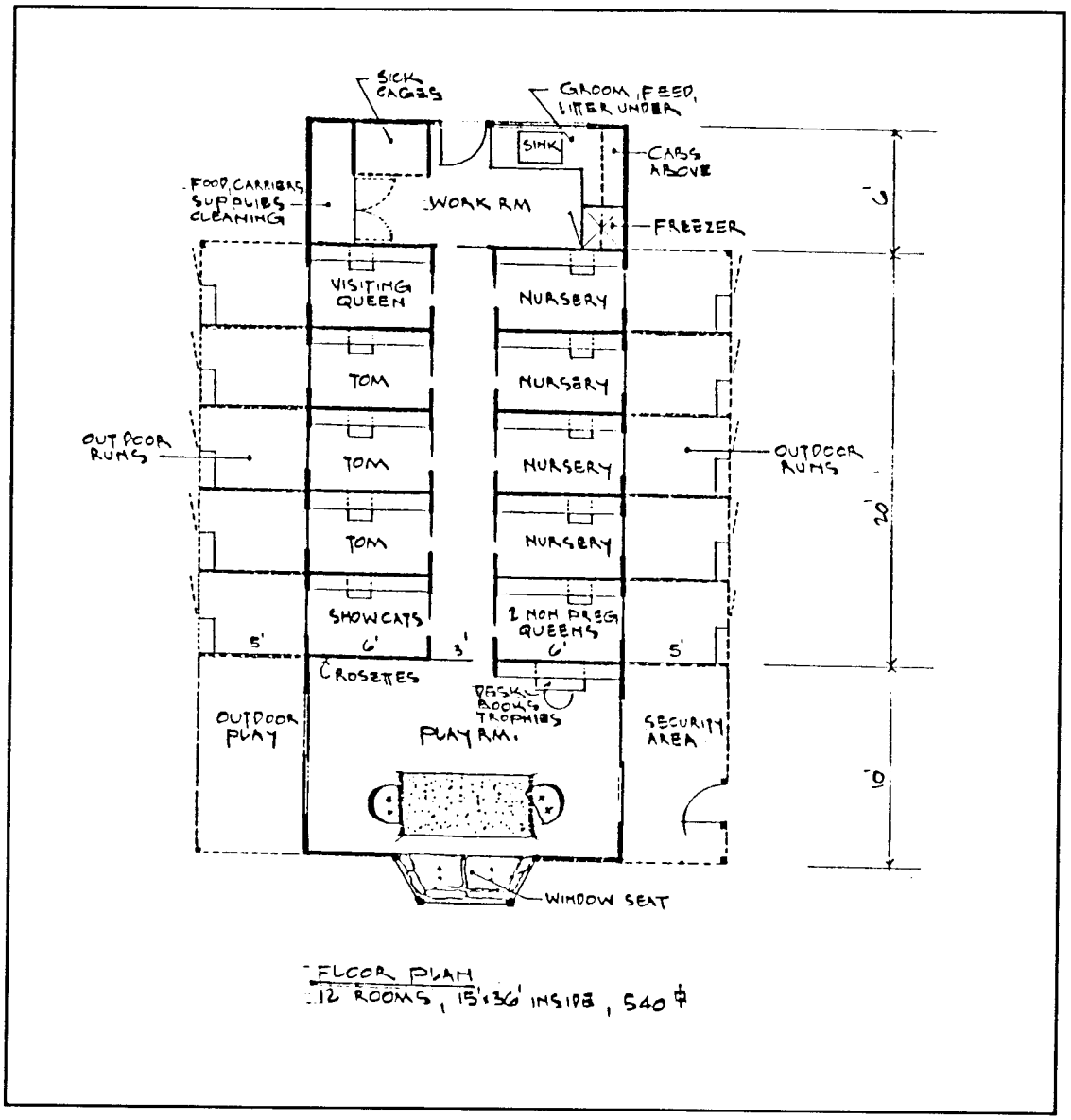


Figure 1C. Floorplan of a cattery with space for ancillary functions.



With this information, it is easy to calculate the number of basic units required for a given cattery. For instance, if a cattery contains 3 breeding males and 6 females, and each female produces 2 litters a year, the following number of units will be required: 2 rooms for nonpregnant and early-gestation queens, 1 breeding room (or room to isolate visiting queens), 3 rooms for toms, and 6 nursery and rearing rooms.

Once the number of units has been determined, it is possible to design the entire cattery. The cattery design depends on ingenuity, aesthetic considerations, and financial and space constraints. Figure 1 shows how 12 basic animal containment units can be put together to provide maximum use of space. In this basic plan, 6 units are placed on each side of a central corridor, with the interior or enclosed part of the unit facing inward. A second cat-proof fence is placed around the outside of the unit to prevent contact between cattery cats and feral animals, and to provide escape-proof access to

the outer portions of the units. The enclosed portions of the basic animal containment units can also be incorporated within homes or garages.

Once the design is created, special provisions should be made for sanitation, ventilation, climate control and ancillary functions. The success or failure of the cattery depends a great deal on how well these various functions are met. Unfortunately, these are the most expensive items in cattery construction and are most likely ignored.

Sanitation

Sanitation refers to the housekeeping functions necessary to maintain an environment that is as free of contagious agents as possible. Contagion arises in 3 ways: exposure to microorganisms in body excretions (urine, feces), secretions (saliva), and exfoliations (hair, dander); direct contact with other cats in the cattery;and contact with outside animals or contaminated air and objects. Because cats are the main source of infection for other cats, indirect exposure to body excretions, secretions and exfoliations, or direct contact between animals, accounts for most spread of disease.

Contact between animals can be controlled by proper cattery design and management, and is the most important means to control infection. Accumulation of excretions, secretions and exfoliations can be prevented by cleaning. Individual units within the cattery should be designed for rapid and efficient cleaning and waste disposal. When possible, the floors and lowest 1-2 feet of the walls should be cast as one piece of concrete. The concrete should be smoothly finished and the foundation sufficiently reinforced to prevent cracking. Nonporous flooring may be used *in lieu* of solid concrete, provided that the joints are well sealed. Because cat urine can spoil many surfaces, care must be taken in selecting floor coverings. Sheet linoleum of the type approved for hospitals is most ideal. Regular linoleum is quickly damaged by urine, water, and the disinfectants and soaps so frequently used in a cattery.

If floors are to be hosed down, floors should slope toward one end of the unit, usually the outer or unenclosed portion. A shallow gutter should be placed at right angles to the floor at the lowest point. Common gutters should slope, in turn, to a common drain at one end of the building (Fig 2). Movement of waste water from the inside to the outside part of the enclosure can be facilitated by a narrow swinging door at the base of the dividing wall. Waste water should never travel through one pen to another. Gutters should be constructed outside of the actual enclosures or a single gutter and drain provided for each run. Drains and drain pipes should be large enough to handle larger particles of litter and excreta. If drains are inside the pens, they should be covered with movable screens to prevent smaller kittens from falling into them.

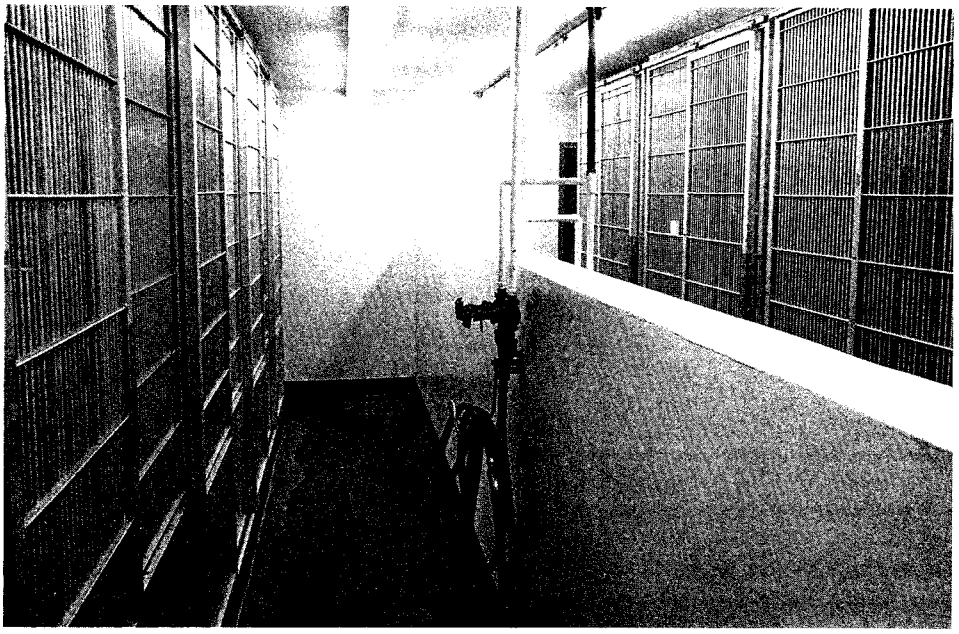
The remainder of the walls in the enclosed portion of each containment unit should be constructed of marine plywood painted with several coats of an epoxy-type paint, or preferably covered by masonite, laminated plastic or comparable impermeable surfaces. It is important to install all impermeable wall and floor surfaces in such a way as to prevent water intrusion. Flooring material should extend onto the walls (to avoid corner seams) and wall siding should extend downward over the flooring, rather than under it (to prevent water from running down the walls and under the flooring). Commercial caging made of anodized aluminum can also be designed as panels that can be assembled. The assembled cage can then fit on top of prepared concrete floors and pre-walls (Fig 2). Though the initial investment is higher, commercial caging may be less expensive and more easily cleaned and maintained over the long term.

The side panels of each internally situated unit should be solid. This prevents nose-to-nose contact between runs and allows the same wall to be shared by adjoining units. The outward-facing walls of end runs can be made of wire. The front of each unit should be screened for easy view of the animals and fitted with entry doors. Doors may be of a sliding type to save space and provide for rapid and safe closure.

Perches should be provided for each animal, but should be large enough to hold 2 animals if necessary. A narrow space should be left between the perch and wall to prevent urine or water pooling. Perches should also be made from impermeable substances

Figure 2A. (top) Inside of an experimental cat housing facility at the University of California, Davis. Two banks of cages (primary enclosure units) are found in each room; each bank of 4 units is separated by a 4-foot-high concrete divider. The facility is made of waterproof materials and designed for rapid cleaning. The cages themselves were custom made from anodized aluminum by a commercial caging contractor and delivered as flat panels that were assembled on a preformed concrete pad. B. (bottom left) Sliding doors are used for entrance into the primary enclosures. Sliding doors save room and are easier to close rapidly; this helps prevent animals from being injured by closing doors. Each bank of primary enclosures is placed on top of a 4-inch raised concrete pad that slopes slightly to the back. The floors are made from a mixture of epoxy and sand for durability and to facilitate cleaning and drying. C. (bottom right) Inside appearance of a primary enclosure unit. Notice the plastic perches attached to the side wall at varying heights. Plastic trays are used for litter pans and stainless-steel bowls for food and water.

A.



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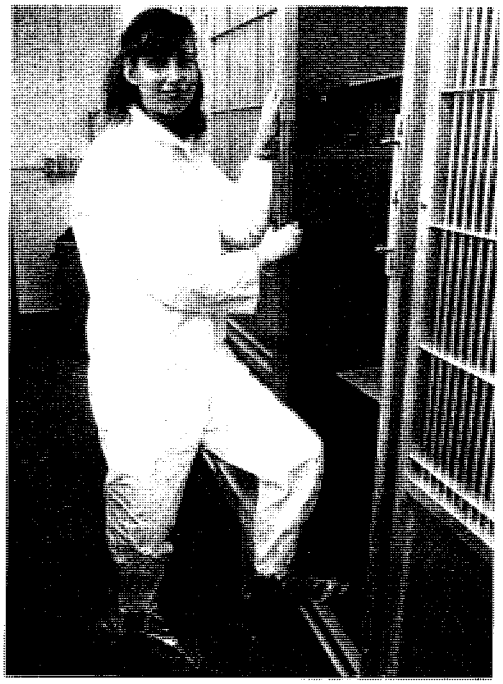

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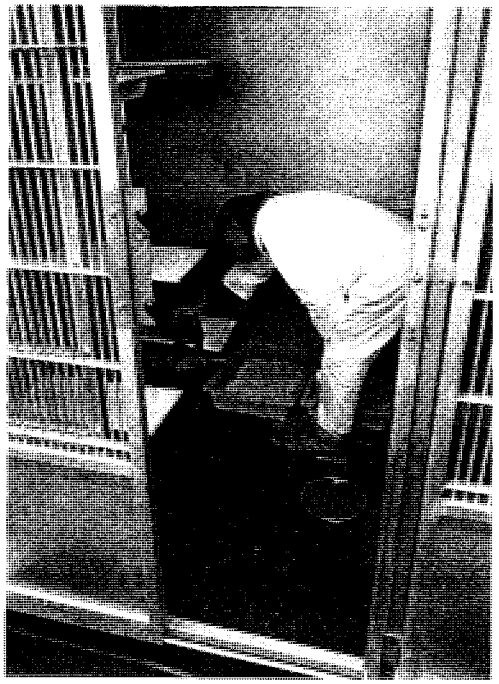
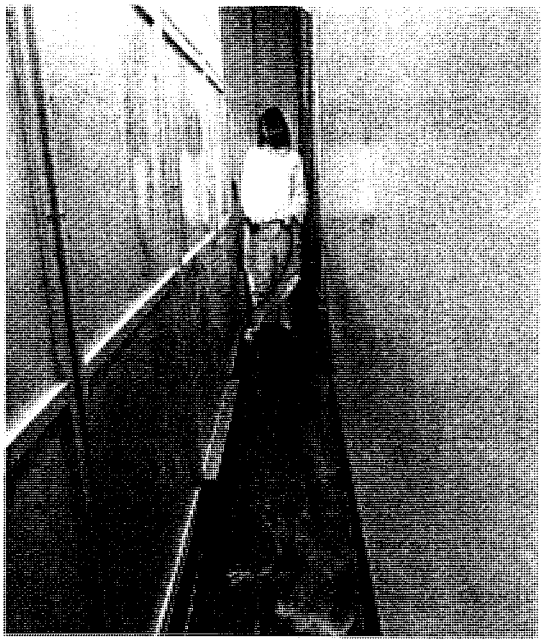


Figure 2D. (left) The lower side of the back wall of each primary containment unit contains a built-in hinged door that can be raised for cleaning. The door is being opened in preparation for washing. Waste is washed under the opening, into a common gutter in the back of the bank of primary enclosures. Notice again the plastic perches for the cats. During washing, the cats move up onto the higher perches away from the water. E. (right) A narrow common alleyway and gutter is located at the back of each bank of primary enclosure units. The common gutter slopes gently away from the animal caretaker to a common drain that is out of view at the bottom of the photograph.



rather than wood. An unpainted wooden scratching post or small movable hemp rugs on the floor can be provided for claw sharpening. The hemp rugs can be washed several times before being replaced. Carpeted scratching posts, while a nice personal touch, should be avoided, as they cannot be cleaned. They provide ideal homes for flea larvae and pupae, and only encourage cats to scratch on furniture when the cats are subsequently placed in homes.

Smaller secondary enclosures within the larger primary enclosures are commonly found in private catteries (Fig 3). Such structures usually contain several openings and compartments at different levels through which the cats can enter and leave. Cats often use such enclosures for privacy and rest. Many innovative designs ranging from miniature mansions to hollow trees are used for such structures; the design is more likely to strike the fancy of the owner than the cat. Though secondary enclosures are appreciated by cats, they are difficult to clean properly and are not essential. If they are used, they should be kept as simple and easy to clean as possible. Fancy paint, window shades, curtains, doors, carpeting and wall covers should be avoided because they prevent adequate cleaning, especially with soap and water, disinfectants or steam.

Ventilation

Ventilation is one of the most important requirements for a cattery. Good ventilation removes odors and accumulations of waste gases, and dilutes and flushes out air-borne pathogens. NIH regulations for housing experimental cats call for 10-15 complete air changes per hour.[6] This means that 10-15 times the volume of the enclosures should be replaced with fresh or reconditioned (filtered) air each hour. Filtration of air requires special particulate and toxic gas filters that are prohibitively expensive for most cattery owners, and they also tend to be unreliable.[3]

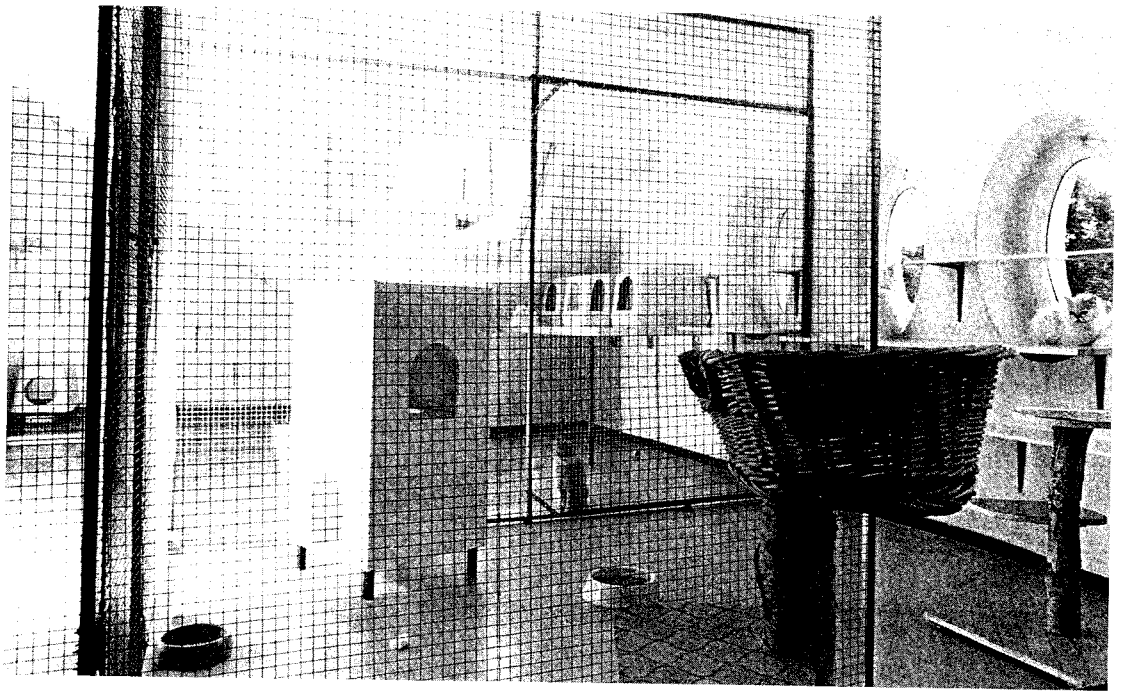
Alternatively, if the air is completely exhausted, there is the added expense of heating or cooling the new air that is brought into the unit or installing a heat-recovery system. It is not usually possible, therefore,

for private catteries to meet the ventilation standards set by the government. Fortunately, it is not necessary to do so. Most pathogenic organisms are transmitted by direct contact or through ingestion, while air-borne transmission is much less important. Sanitation and control of animal movement are more important for disease control than superior ventilation. Moreover, even if NIH ventilation standards were met, they would not effectively reduce disease problems if sanitation remained inadequate.

The least expensive and most effective type of ventilation is provided by free movement (sometimes aided by fans during still days) of outside ambient air through the animal containment units. Catteries should be designed, therefore, to take advantage of passive ventilation as much as possible. Well-designed catteries can be opened up during favorable weather to allow for maximum movement of air and penetration of sunlight. This can be accomplished by using wire screening for the walls of the outer portion of the animal containment units. Screens can be blocked with solid storm doors or windows during cold or wet weather. Side-to-side air movement is more difficult to obtain because of the need to prevent nose-to-nose contact between pens. Open screens can be placed on adjoining walls if the bottom two-thirds of the wall are left solid. Perches should then be placed only on the solid parts of the intervening walls or on unshared back walls. If perches are low enough and there are no window sills on which to perch, nose-to-nose contact is prevented. Lateral air movement can also be provided by using a common ventilated attic and wire tops on each run. The cattery should be positioned in such a way as to take maximal advantage of prevailing winds.

Sunlight is almost as important as adequate air flow, and is considered one aspect of proper ventilation. Animal containment units should be constructed, therefore, to provide for access of sunlight. Sunlight has a pronounced inhibitory effect on many microorganisms, in addition to its direct health-promoting effect on the animals

Figure 3. This large, airy cattery contains smaller, secondary enclosures inside the main enclosures. The structure on the left is a 2-story "apartment." A wicker laundry basket in the foreground serves as a napping place. Note the linoleum-covered steps leading to the perches, and the windows with perches. (Courtesy of Elke and Norbert Deutschmann, Essen, West Germany)



themselves. Windows and skylights should be used as much as possible in the cattery and positioned in such a way as to take advantage of both summer and winter sun. Cats like to sit by windows, and window sills on the outward-facing walls can double as perches if properly constructed (Fig 3). Outdoor runs can be partially shaded from summer sun in warmer climates with loosely foliaged deciduous trees. During winter months, these same runs will be exposed fully to the sun, and on warmer winter days, cats can be allowed to move from indoor to outdoor areas.

In areas with no prevailing breezes, ventilation fans should be installed to encourage movement of air. They are particularly beneficial if an attic-type construction is used. Fans should pull air from the attic portion to the outside. Air is then drawn through the front of the cattery, upward into the attic, and then to the outside. Air does not flow from run to run.

The requirement for clean and odor-free air in the home or cattery is of more than aesthetic importance. Ammonia gas is a common contaminant of the atmosphere in environments where many animals are closely confined.[28,32,34] Ammonia gas (NH_3) is a product of bacterial breakdown of fecal and urinary urea. This breakdown process is accentuated by conditions of high temperature and humidity, accumulation of waste material (infrequent cleaning of litter boxes), litter favoring bacterial growth, allowing urine to accumulate until litter is soaked, too many animals per litter box, permeable surfaces where urine can accumulate, and inadequate ventilation.

Ammonia gas is detectable to the human nose at about 5 parts per million (ppm) in the air.[23] People usually begin to complain about the ammoniacal odor when the levels reach 20-25 ppm. Irritation to the eyes and nose may follow exposure to levels greater than 50 ppm, though people in continuous contact to irritating levels often become tolerant of the effects of ammonia. Levels of ammonia gas ranging from 2-720 ppm have been recorded in many experimental rat-holding facilities.[32] Even in environmentally regulated swine barns, ammonia gas levels frequently reach 13-76 ppm.[28] Based on detectable ammoniacal odors, many densely populated and poorly ventilated catteries reach ammonia gas levels of 25 ppm or greater. Attempts to mask ammoniacal odors in catteries with perfumes and air deodorizers should be avoided. Such measures may confound the normal physical senses necessary to detect the problem and to gauge its severity.

Ammonia gas is absorbed readily through the mucosa of the nasal passages and upper airways. The levels of ammonia in the blood of animals housed in contaminated environments increase in direct proportion to the levels in the surrounding air. Ammonia is potentially toxic to animals once inhaled. The concentration of ammonia gas required to kill 50% of test mice following 1 hour of exposure and again 14 days later is 4230 ppm or greater.[30] Acute mortality is not seen in mice exposed to ammonia gas levels under 3500 ppm for 1 hour. Obviously, such high levels of ammonia gas are not seen in nature, except for rare industrial accidents. However, much lower levels of ammonia gas can affect the animals' health in myriad and subtle ways.[32,34]

The severity of mycoplasmal, viral and secondary bacterial infections of the respiratory tract has been enhanced in chickens and rats exposed to common environmental levels (20 ppm or higher) of ammonia gas in poultry houses and laboratory animal holding facilities.[24,25] Impairment in reproductive performance and delayed puberty have been observed in cattle and swine exposed to common environmental levels of ammonia gas.[31,34] Ammonia also has a toxic effect on the nervous and endocrine systems. It is logical to assume that cats would also suffer the same problems from ammonia toxicity as other species. Indeed, cats (especially kittens) quickly develop signs of ammonia toxicosis when fed inordinately large amounts of ammonium chloride as a urinary acidifier.[26]

In addition to its effects on animals, ammonia gas poses an identical health risk to people that share the same air space. The American Conference of Governmental and Industrial Hygienists has set the minimum safe level for ammonia gas at 25 ppm, a level also adopted by most other countries.[23] However, it must be remembered that toxicity may be a factor of both levels of ammonia gas and duration of exposure. Chickens exposed to ammonia levels of 20 ppm for

less than 6 weeks showed no effects, while chickens exposed for greater than 6 weeks had lung abnormalities.[24] Further, even if the air in the home or cattery has ammonia levels below 25 ppm, cats kept in individual or group cages within premises may be exposed to several times this level. People began to complain about ammoniacal odors at 25 ppm. Because cat owners often develop a tolerance to the odor, complaints of ammoniacal odors by visitors should be taken seriously. If there is irritation to the nose or eyes, levels of ammonia gas above 50 ppm are present, which is a dangerous situation.

The only sure way to eliminate ammonia gas from the environment is to increase ventilation and the frequency of litter box changes. Litter boxes should be well washed to remove all remnants of liquid waste, and periodically disinfected. Remaining waste serves as a bacterial inoculum for the new litter and accelerates the ammonification process. The alternative is to greatly decrease the number of animals.

Animal holding rooms should not be overheated, and the humidity of the air in the cattery should be kept as low as possible. Heat and humidity enhance ammonification. Urine spraying outside the litter box, which can be a big problem in some multiple-cat households, is a source of ammonia gas that is less amenable to litter box cleaning. Urine spraying can be decreased by minimizing social and sexual stress within the cattery (see the chapter on Behavior) and by constructing pens with impervious surfaces that resist urine soaking and that can be more efficiently cleaned. Some newer types of litter material greatly inhibit ammonia gas production. However, such materials are usually expensive. They may also allow for a greater buildup of microbial pathogens, as there is a tendency to change them less often. It may some day be possible to treat litter with certain additives to decrease ammonia production, something that has worked on a limited basis with poultry.[7]

Climate Control

Climate control is essential for cats housed in regions of excessive humidity and cold. The need for auxiliary air conditioning in a cattery depends on its design and external climate patterns. Cats do best in warmer and less humid conditions.

Cold weather, if it is dry, is of little concern. However, cold weather accompanied by excessive dampness is associated with the greatest amount of disease.

Cats, having evolved in desert climates, can tolerate a wide extreme of temperature. Cats can tolerate temperature ranges from 35 to 100 F and average humidities of 10-70%. Though cats can tolerate a wide range of climates, they need time to adjust to seasonal temperature and humidity variations. Cats naturally begin to store subcutaneous and intraabdominal fat and their coats become much thicker as daylight hours shorten in late summer. It is important, therefore, to design catteries so cats can be given adequate exposure to changes in seasonal lighting and temperature. Cats allowed to acclimate themselves to seasonal temperature changes can survive amazingly well in almost all regions of the world with minimum artificial climate control, provided they also have access to protective bedding and shelter. Boxes or small barrels with small openings can be hung on the walls. The openings should be placed away from prevailing winds.

Though most domestic and purebred cats can be kept in environments varying greatly in temperature and humidity, certain breeds require climate control. For example, short-coated cats, such as Cornish and Devon Rex breeds, do not adapt as well to cold as heavy-coated Persians.

Though the temperature and humidity in open parts of the animal containment units can be allowed to fluctuate greatly, the climate within the enclosed part of the unit should be kept within a narrower range. Temperatures of 50-85 F and humidities of 10-50% are optimal.

Temperatures and humidities within this range can usually be maintained in warmer and dryer climates with passive air conditioning and minimal mechanical equipment. The more time that the external climate is outside of this range, the more elaborate the air conditioning requirements become. To minimize the expense of such artificial climate control, many catteries rely on heavier insulation and more re-

stricted air movement. Unfortunately, catteries cannot be constructed like thermos bottles. Air movement must be maintained as much as possible, even during cold weather.

Given these constraints, how can the temperature be maintained during the coldest part of the year when heating is necessary? Indoor portions of the animal containment units should be well insulated yet allow as much free air to enter and leave as possible. To minimize costs, incoming air need only be heated to 50-60 F if the cats have been allowed to become naturally acclimatized. Supplemental heating can be provided by focal heat sources, such as heat lamps. Plugs and wires should come from the ceiling to prevent the cats' chewing on the wires or urinating on the plugs. Wall heaters can also be placed under perches so that the heat radiates upward and warms the perch from the bottom. Again, heaters should be positioned so they cannot be accidentally wet by the hose or urinated upon.

Focal heating sources allow the animals to seek their own optimum temperatures by getting as close to or far from them as they desire. Focal heating is more healthful than overheating the entire cattery. If air is overheated, there is a tendency for less ventilation and more marked fluctuations in temperatures. Overheating of the air also adds appreciably to the humidity, which in turn adds to the problem of contagion. Overheating, especially if accomplished with fuel oil or coal, can also diminish the oxygen content of the air and bring the danger of toxic accumulations of harmful gases, such as carbon monoxide. To further compensate for lower winter temperatures, it is prudent to reduce the density of numbers of animals within the cattery during winter months. Cat numbers can be decreased during this period by breeding queens mainly in the spring, so that most of the kittens are well past weaning or have been sold by the onset of winter.

Cattery owners in colder climates often believe that outdoor runs are not acceptable. Even in the coldest climates, however, outdoor or feral cats can survive if they are properly adapted and have shelter from cold winds, snow and dampness. Fortunately, such shelter is usually abundant in nature. If outdoor cats are allowed to acclimate themselves, their coats become quite thick, providing a great deal of protection against the cold. Moreover, even in cold climates, the weather is still reasonably favorable for 7-8 months or more of the year. Basements are a feature of homes in most cold climates and are commonly used for catteries in such areas. If the basements have ground-level windows, as most do, the windows can serve as access doors to above-ground runs built on the side of the house.

Flea Control

Cattery owners are often reluctant to build separate facilities for their cats in warmer and more humid climates where fleas abound. This attitude is hard to understand, as flea control is much more difficult in a home than in a well-designed outdoor cattery. The most effective way to control fleas is to create an environment in which they cannot reproduce. If surfaces are constructed so they do not collect dust and dander, and they can be readily vacuumed, cleaned and hosed down, the life cycle of the flea is interrupted. Such surfaces do not exist in the average human abode.

One innovation in flea control, especially in warm and humid climates, is to build all or part of the cattery on stilts 18-24 inches off the ground (Fig 4). Since fleas cannot jump over this height, access to the building is limited. The floors in such a raised building can be solid, provided that they can be washed down. They can also be covered with sturdy 1/8- to 1/4 inch mesh, with narrow solid walkways between runs. Female fleas dropping off the cats then fall through the wire or are washed out during cleaning. If the ground under the pen is covered by smooth concrete, it can be readily hosed down or sprayed without disturbing the cats above. Adult fleas dropping off the animals lay their eggs at ground level, rather than on the cattery floor above.

A concrete-lined shallow water moat around the cattery, with retractable drawbridge, may prove equally useful in limiting movement of fleas from surrounding yards. After gross litter and excrement are removed,the cattery floors can be hosed out and the drainage allowed to flow into the moat. The moat can also serve a dual role as a fish or aquatic plant pond, if excessive

amounts of toxic materials (nonbotanical insecticides, disinfectants, excrement) are not allowed to enter the pond.

In hot and dry climates, the ground around the cattery should be left bare or planted with vegetation requiring little superficial watering (see section on fleas). Dark-colored gravel placed around the cattery absorbs heat and inhibits flea development. In cold climates, cat runs should be maintained at temperatures of 55 F or lower. These low temperatures are inhibitory to flea development. Surrounding yards can also be periodically sprayed with insecticide to maintain a relatively flea-free zone around the cattery. A high perimeter fence with a 12-inch smooth metal strip at the top (to prevent cats from climbing over the top) placed 5 feet or more back from the cattery also prevents contact between feral or outdoor pet cats and cattery animals. Outdoor animals constitute an important reservoir of fleas. If a cattery maintains a number of pet cats that are allowed to roam freely, flea control is almost impossible. Such cats continually bring fleas back with them. Though these pet cats may have no direct access to the cattery cats, the fleas have no such limitations.

Lighting

Lighting is also an important consideration. Like heating and cooling, it can be done passively through well-designed windows, screened enclosures and skylights, or mechanically with light fixtures. Sunlight, if unimpeded by glass, inhibits growth of pathogens that accumulate in the environment. Sunlight filtered through glass windows also generates heat by the so-called "greenhouse effect."

In addition to its heating and antimicrobial effects, lighting plays an important role in cat breeding. Cats are seasonally polyestrous and are brought into heat in spring and fall by relative changes in the hours of daylight and darkness. Cats can be artificially brought into season by manipulating the hours of light and dark through artificial lighting.

If units are kept artificially lighted for 12 hours or more each day throughout the year, the cats show no seasonality of estrus, but come into heat as their litters are born and weaned. The intensity of lighting within a cattery need not be high. Light intensity equal to that of a well-lit room is usually sufficient.

Ancillary Functions

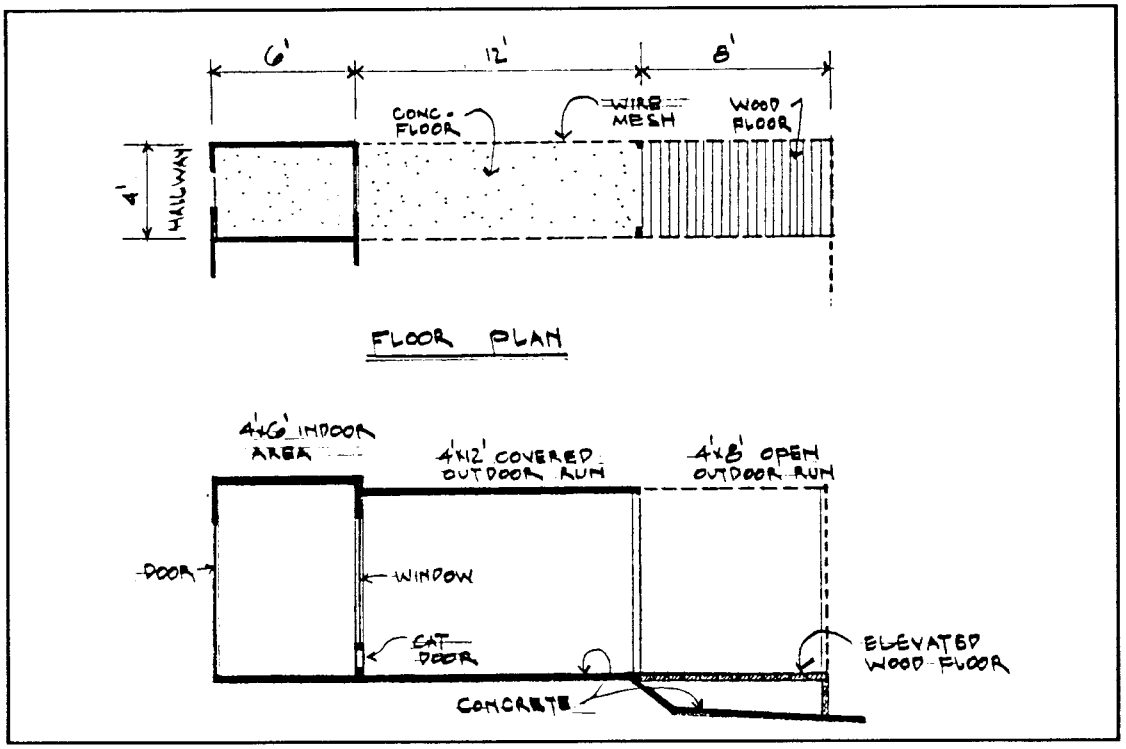
In addition to the basic housing units, good catteries often provide space for other functions. A room to store cleaning equipment is necessary, as well as a room to shelter food and litter from water and vermin. A treatment and grooming room is also a nice touch. It is essential to have excellent lighting in the treatment room to better observe eye, dental or other problems. The treatment room can contain several individual cages for care of sick animals, the only small individual cages that should be allowed in the cattery. These cages can be obtained from veterinary supply houses and should have impermeable and easily disinfected surfaces. Many cat breeders like to have a "play room" where the owner and guests can commingle temporarily with their animals. This might also be a good place to display trophies, ribbons, pictures and other mementoes. With such auxiliary space, a basic cattery may appear like the one shown in Figure 1C. However, some breeders believe such an arrangement exposes kittens to potentially pathogenic organisms. These breeders use a display cage instead.

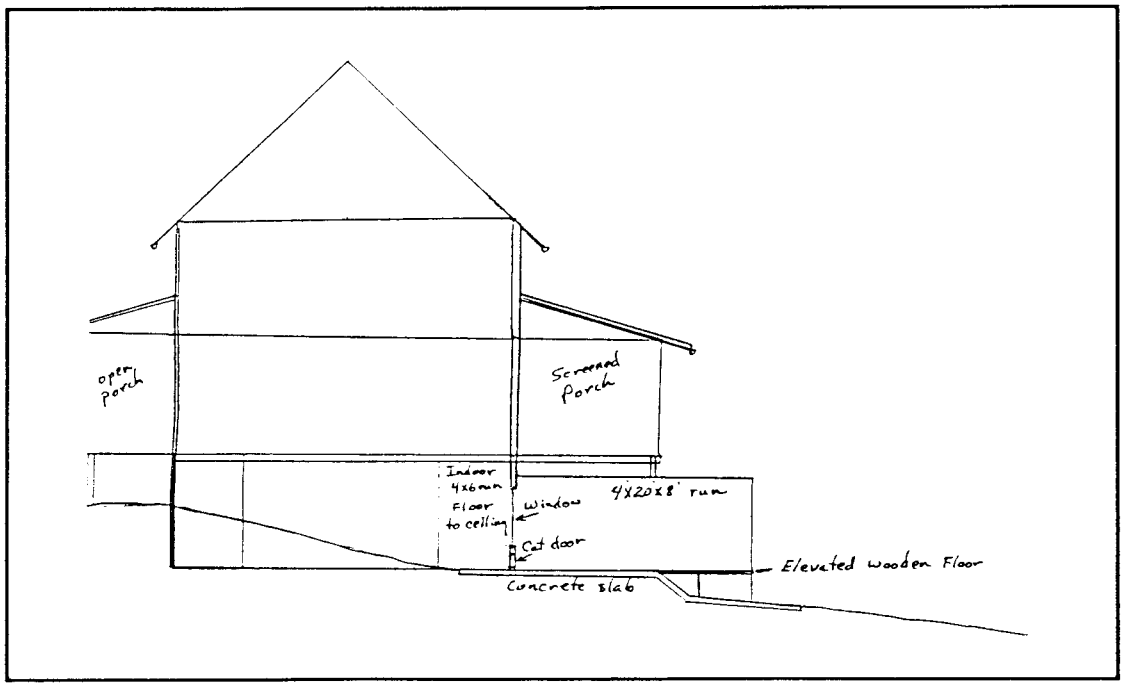
At this point, many potential cattery owners might be taken aback by the apparent complexity and cost of a well-designed cattery facility. With time, ingenuity and donated labor, however, home- built cattery facilities can be constructed relatively inexpensively (Fig 5). Readers interested in cattery facilities designed and built by ordinary cattery owners should also refer to a number of excellent articles that have appeared in lay magazines over the last decade.[1,5-7,10,13,15-18,21]

Cattery Design in Great Britain

There are no specific guidelines for cattery design and management in Great Britain; however, general guidelines are provided in the Animal Boarding Establishment Act of 1963. Though these guidelines are for animal boarding facilities and not technically for feline breeding establish-

Figure 4A. (top) Floor plan of a basic animal containment unit in a cattery, specifically designed to aid flea control. The cattery was designed and owned by Jim Rambo of Rambo Cattery, Atlanta, Georgia. The basic animal containment unit in this plan consists of 3 sections. The inner section is part of the basement of the home, the central unit is a screened run covered by the porch, and the outer unit is a completely open run with wire walls and ceiling. The outer run has a slatted wood floor elevated several feet over a concrete floor that is part of the home's foundation. B. (bottom) Side view showing the relative position of the basic animal containment units to the existing home, basement, foundation and porch.





aid flea control.
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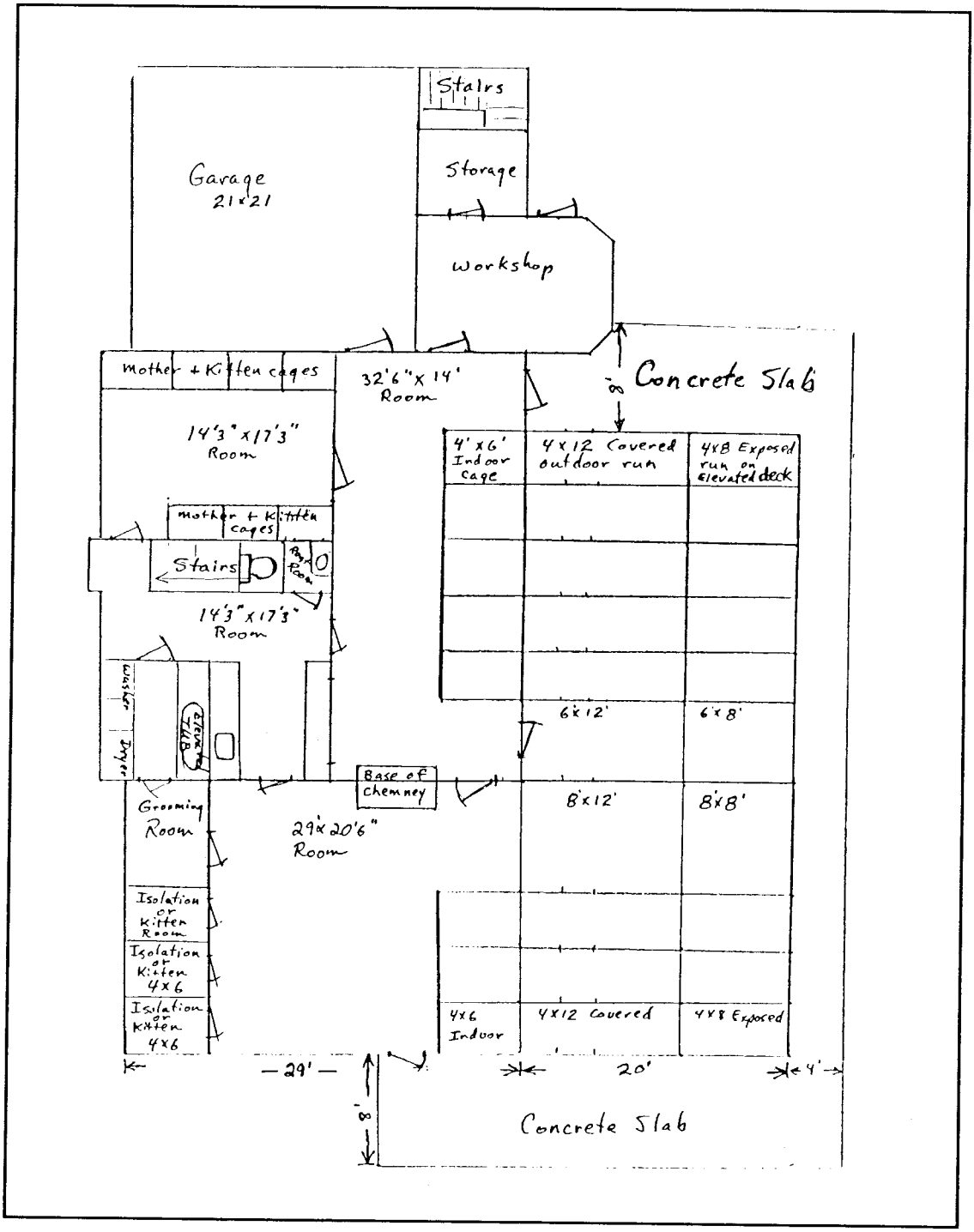
Figure 4C. Floor plan showing the relative position of the basic animal containment units to each other and to ancillary rooms. The basic animal containment units are constructed to allow the floors to be swept and washed down from the inside toward the outside. Weather permitting, cats spend most of their time in the outer open run. During the heat of the day or during inclement but not severe weather, cats spend most of their time in the central run. Adult fleas are swept or hosed into the outer run, or drop directly from the cats through the slatted floors. Since fleas cannot jump the distance from the concrete to the slattedwood floor, they cannot reenter the cattery. The lower concrete floor can be easily cleaned and sprayed with insecticide, and is not a good environment for flea eggs to hatch and larval stages to develop.



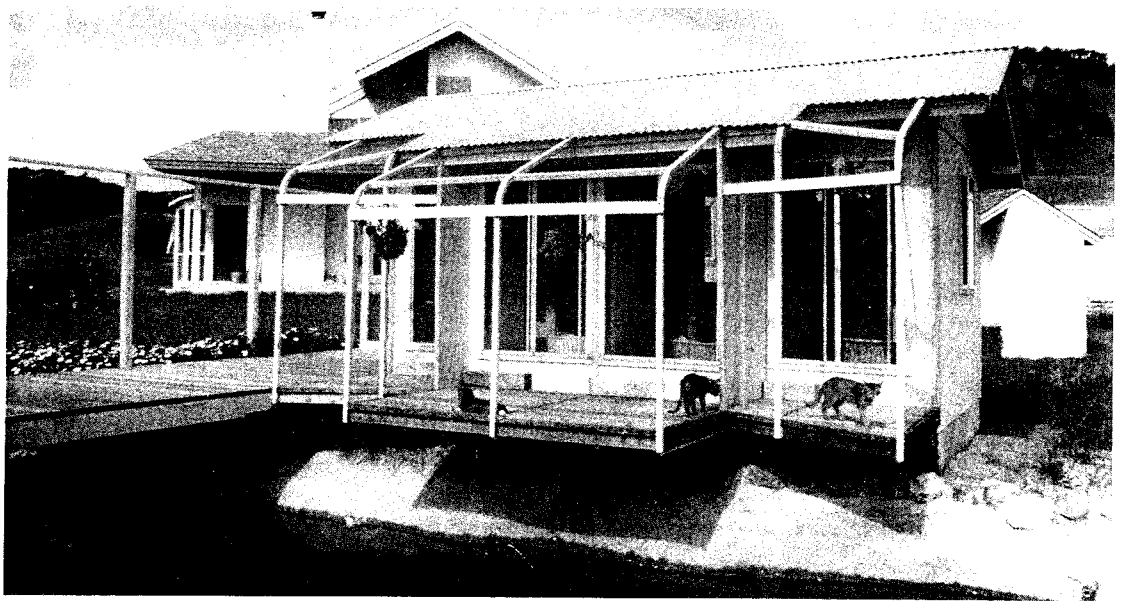
ments, the guidelines are often applied to both situations.

"Under the Animal Boarding Establishment Act of 1963, no person should keep a boarding establishment for animals except under a license granted by the Local Authority. In determining whether to grant a license, the Local Authority must have regard to the need for ensuring: a) that all animals will at all times be kept in accommodations suitable as respects construction, size of quarters, number of occupants, exercising facilities, temperatures, lighting, ventilation and cleanliness; b) that animals will be adequately supplied with suitable food, drink and bedding material and, so far as necessary, visited at suitable intervals; c) that all reasonable precautions will be taken to prevent and control the spread among animals of infectious diseases, including the provision of adequate isolation facilities; d) that appropriate steps will be taken for the protection of the animals in case of fire or other emergency; and e) that a register be kept containing the description of any animal received into the establishment, date of arrival and departure, and name and address of the owners. Such register is to be available for inspection at all times by an officer of the Local Authority, veterinary surgeon or veterinary practitioner authorized under Section 2(1) of this Act and without prejudice to their right to withhold a license on other grounds."

These general guidelines are vague because such terms as suitable, adequate, reasonable, appropriate, as far as necessary, intervals, temperatures, lighting, ventilation and cleanliness are not strictly defined and are therefore subject to a great range of interpretations, depending on the "Local Authority." Nevertheless, these guidelines provide a reasonable basis for proper animal facilities and management.

Facilities that meet the above requirements are not described by the British government, but guidelines have been made available in the form of a pamphlet by the Feline Advisory Bureau (*Boarding Cattery Construction and Management,* 1 Church Close, Orcheston, Nr Salisbury, Wilts SP3 4RP, United Kingdom), a private registered charity organization, in consultation with the British Small Animal Veterinary Association. While the Bureau's recommendations are not legally binding, they are widely ad-

Figure 5. Containment units, designed by Joan and Alfred Wastlhuber. The cattery is built on a small island surrounded by a moat. Wood decking is suspended over concrete and water.



vocated by governmental and professional organizations. Though the pamphlet describes a boarding facility, the principles are frequently applied to purebred catteries as well. The facilities are remarkably similar to those previously described, again indicating the universality of thought on good cattery design and management.

The authors of this pamphlet (Sophie Hamilton-Moore and Caryl Cruickshank) believe that a well-run, efficient boarding cattery should accommodate no more than 45-50 cats. Their design calls for construction of a single outdoor (preferred) or indoor facility made up of no more than 25 individual animal-holding units, called "chalets." The figure of 25 is about the number of units that 2 people can care for properly in a day, with each chalet housing 1-4 cats, depending on its size.

The size of each chalet is predicated on its use. A 2-room chalet, with each room having a dimension of 44 1/4 inches long, 44 1/4 inches wide and 71 inches high is suitable for 1 or 2 small to regular-sized cats from the same household (remembering that this cattery is designed as a boarding facility for household pets). A chalet with each room measuring 48 inches long, 44 1/4 inches wide and 71 inches high is sufficient for 1 or 2 large cats from the same household. A chalet with each room measuring 60 inches long, 44 1/4 inches wide and 71 inches high is sufficient to hold 3 or 4 cats from the same household. The number of small, middle-sized or large chalets incorporated into the boarding facility depends on the proportion of the clientele that have single, double or multiple cats in their homes.

Each chalet consists of an indoor or closed section with solid walls and roof, and a single window and access door, and a contiguous open section with wire sides and translucent plastic roof (Figs 6A, B). This basic 2-room chalet is very similar to the basic animal containment unit described earlier. Individual units are positioned on a sturdy sloping concrete floor with at least 2 feet of space between each of them. The units are arranged in either a "C" or "L" shape (for outdoor catteries), with the open-wired portions of the chalets facing south for maximum effect (Fig 6C). For indoor catteries, the units are positioned in a manner identical to that described earlier in Figure 1C and are enclosed under a single roof. To prevent animal escape or entrance of unwanted animals, a 4-foot-wide safety passage is constructed around the outside perimeter of the entire complex (Figs 6A-C).

Cat fanciers desiring detailed construction information on this type of cattery should write to the Feline Advisory Board of Great Britain for their *Boarding Cattery Construction and Management* book. In addition to construction details, the pamphlet contains information on cattery management practices.

Cattery Management

The main goal of all cattery managers is to create a healthy environment, in which animals are stressed as little as possible, properly protected from the elements, and allowed to produce large litters of robust kittens that are free from disease.

The most essential step toward this goal is to have properly designed facilities. The second step is to manage those facilities in a proper manner. The third is to breed only genetically sound animals, regardless of what prevailing show standards might suggest. These 3 things require careful appraisal of the goals of the cattery and implementation of rules to see that those goals are met.

Management of a cattery can consume a great deal of time. It is important, therefore, to design and manage the cattery to lessen the time spent in management. Cattery management involves a variety of areas, including: cattery goals and rules; cleaning and litter disposal; disinfection; feeding and nutrition; breeding and production of kittens; medical care; (preventive and therapeutic); weaning kittens; litterbox training; teaching proper nail scratching; showing of kittens; preventing disease at shows; procurement and sale of animals; showing of adult cats; and purchase, leasing, co-ownership and sale of cats.

Population Control

Though the basic rules of cattery management vary somewhat according to the goals of the cattery, a few rules should be kept more or less sacred. The first and foremost rule is, "Never keep more cats than the facility can handle or the manager can

Figure 6A. Schematic drawing of small and large chalets.[35] Each chalet consists of an enclosed section and a contiguous open wire run. Each unit is positioned at least 2 feet apart to prevent aerosol contamination between runs. The single window in the enclosed section of the chalet opens into the wire run. The base of the chalets is raised by narrow plastic or hardwood blocks, creating a narrow space for the hosing off of waste materials and preventing water damage to the wood baseboards. Each chalet is joined by a perimeter or safety enclosure. Access to each chalet is through a door opening into the safety passageway. (Adapted from *Boarding Cattery Construction and Management*, by S. Hamilton-Moore and C. Cruickshank, courtesy of the authors and the Feline Advisory Bureau)

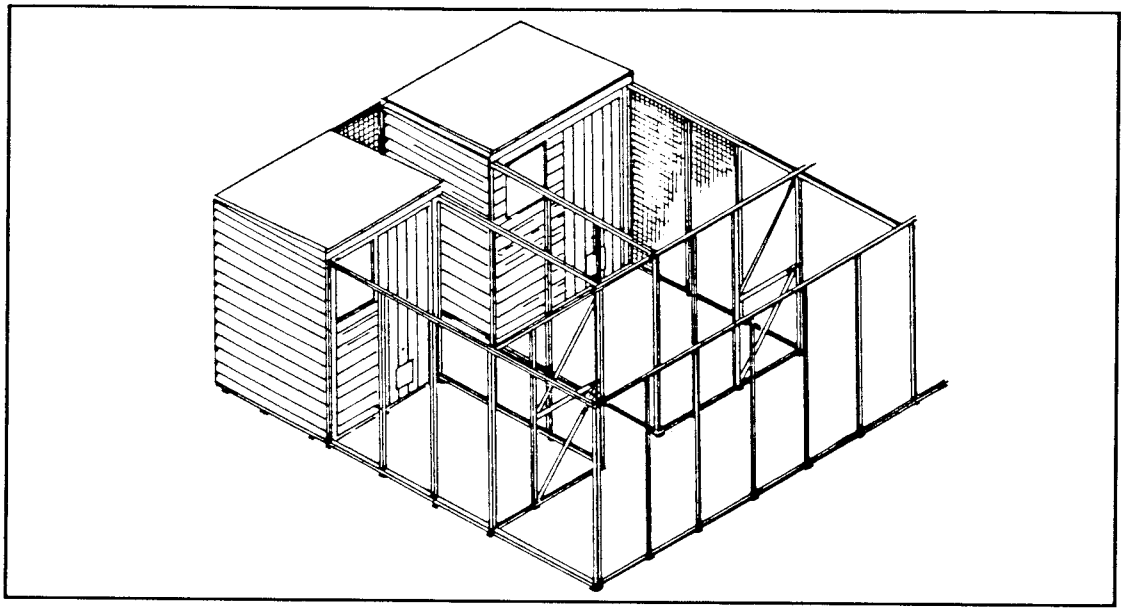


Figure 6B. An endwise cutaway view of a bank of chalets.[35] This view provides more details of the fixtures to be found within the enclosed section of each chalet. Note the heat lamp suspended from the ceiling; plugs and wires are not accessible to the animals. Also note the position of the perch, which is just under the window. The solid door has a smaller access door, which allows cats to move back and forth from one section to the other without opening the main door. The roof of the enclosed section is solid, while the roof of the open run and safety enclosure is made of semi-translucent plastic. This allows the runs to be illuminated and heated by the sun, yet protects against overexposure. (Adapted from *Boarding Cattery Construction and Management*, by S. Hamilton-Moore and C. Cruickshank, courtesy of the authors and the Feline Advisory Bureau)

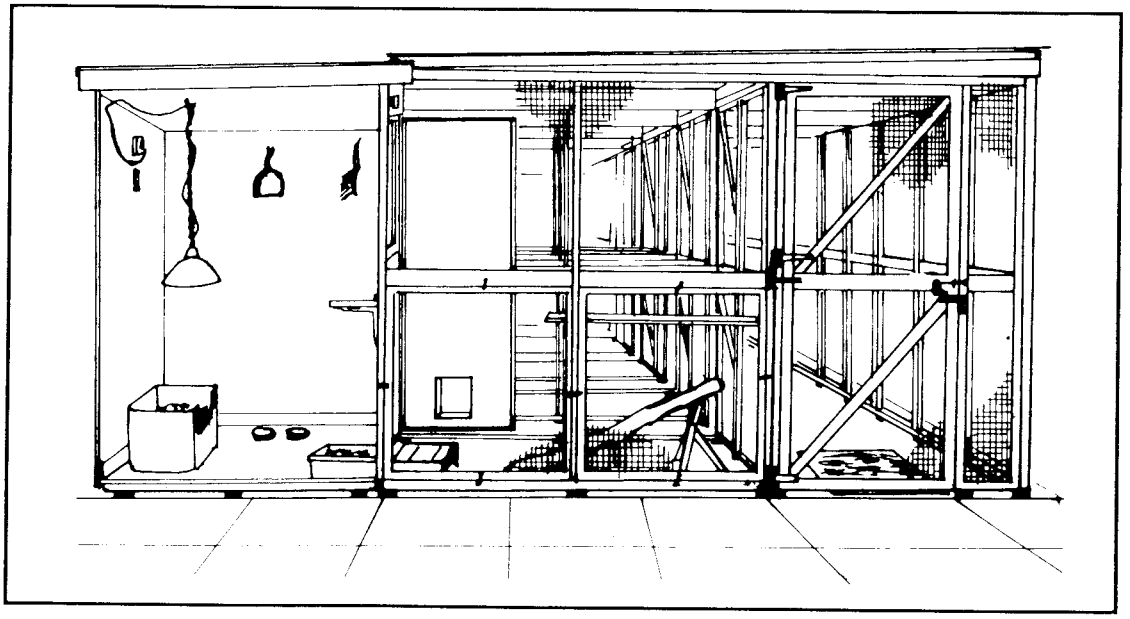
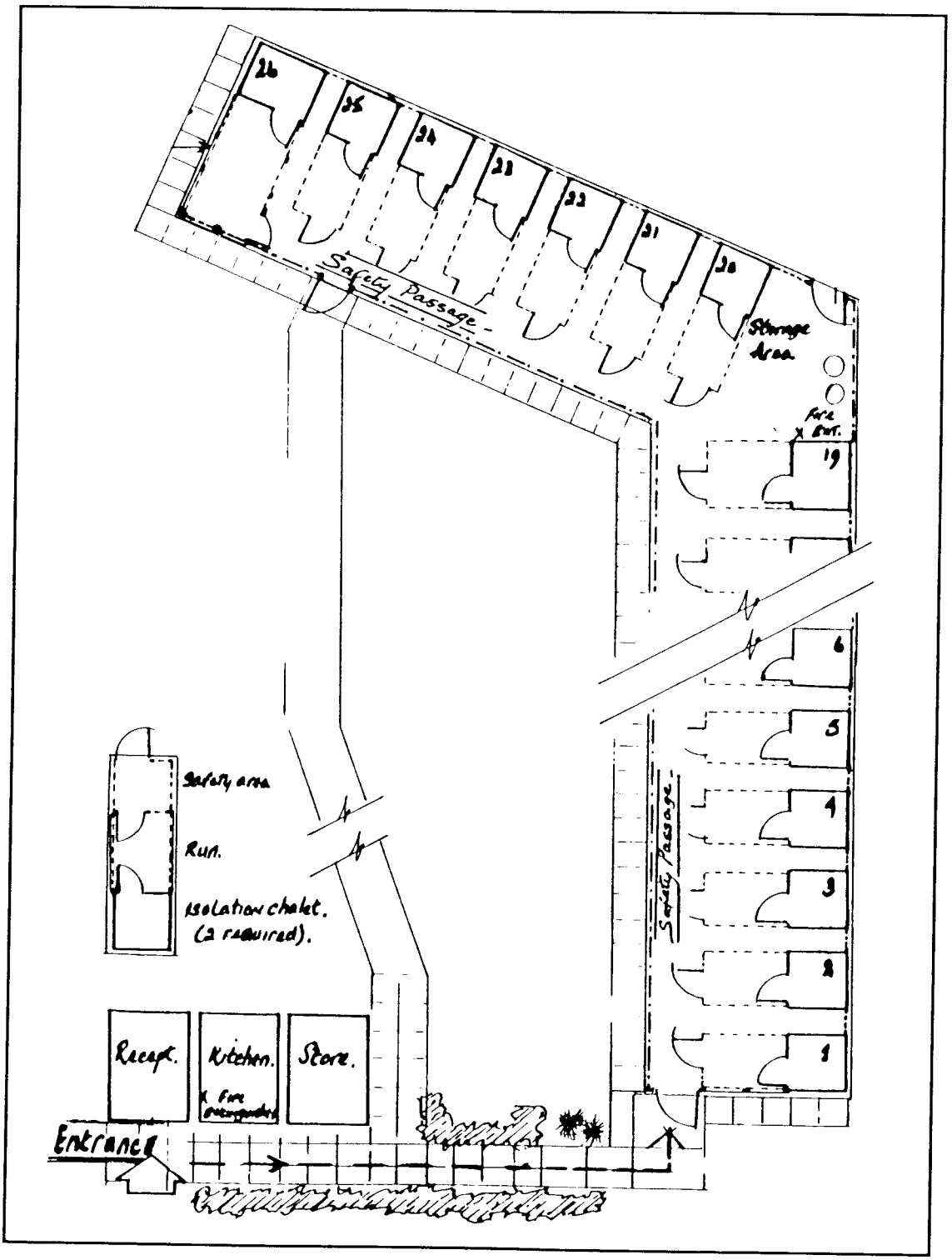


Figure 6C. Schematic drawing of the layout of an L-shaped outdoor boarding cattery containing 26 chalets and several unattached rooms for ancillary functions.[35] The building is positioned so that the open runs have maximum exposure to the sun. Note the relationship of the safety passageway to the chalets. (Adapted from *Boarding Cattery Construction and Management*, by S. Hamilton-Moore and C. Cruickshank, courtesy of the authors and the Feline Advisory Bureau)



properly care for, given the time delegated to the task." It is also important to allow for vacation or business time away from the cattery. The larger or more unmanageable the cattery, the more difficult to find good temporary help. Problems with disease and ill health increase dramatically as the numbers of breeding cats increase. Most cattery managers realize that the numbers of animals should be limited, but eventually compromise themselves by gradually accumulating more and more cats. The second rule is to maintain a closed cattery population. The third rule is to keep the numbers of young animals and kittens as low as possible. The fourth rule is to segregate litters of kittens from each other until they are at least 12-16 weeks of age.

Control of Cattery Population: Accumulation of too many cats is usually not planned. Cat breeders are often highly competitive, especially the newer breeders who have never experienced the long-term hardships of cattery management. In their quest for winning show cats, caution is often thrown to the wind. For instance, it is not usually prudent to breed cats with poor conformational traits. Too often, however, pedigrees are viewed as more important than physical attributes. The premise is that any relative of a winning cat, no matter how poor a specimen, has the genetic potential to produce an animal with winning characteristics. Marginal or unacceptable cats, if they have good pedigrees, often are kept for this reason.

There is also the tendency to breed poorly conformed queens to stud cats with winning conformation, especially if the queen is from the same winning bloodline. Unfortunately, this encourages inbreeding and retention of animals that would better be neutered and sold as pets. Doubly unfortunate, breeding marginal queens to show-winning toms occasionally pays off with show-winning kittens. This only encourages people to keep more and more queens, a decision that is more often based on gambling intuition and hunches than sound reasoning.

Another factor leading to accumulation of too many cats is the practice of keeping kittens until they are mature in the hopes that they will eventually develop winning form. While this may occur with some individuals, it often does not pay off. Cattery owners confronted with sexually mature cats with characteristics that did not develop as anticipated sometimes keep the animals rather than sell them. The fact that such cats are often more sound in pedigree than in reality ensures their maintenance in the cattery.

There is also the problem of kittens returned by the new owner for myriad reasons. If these cats are returned because of bad habits (poor litter box training, poor temperament), illness or for other reasons, the cattery owner is not anxious to place them in another home where the same complaints might arise. They also do not want to have them destroyed, and as a result these animals accumulate in the breeder's home as neutered pets.

Accumulation of too many cats also occurs when several different breeds or bloodlines within a breed are kept in the cattery. Successful cattery owners maintain the cats at healthful numbers. Good breeders usually concentrate on one breed of cats and a minimum of bloodlines. They also scrupulously cull poorer animals and carefully plan matings to increase the odds of producing good show-winning kittens.

The problem of too many cats in an environment is not unique to breeding catteries. Overcrowding also exists in many pounds, shelters and multiple-cat households. Extremely large households of cats exist in many communities, often comprising 20-60 or more animals. The owner of such a household is usually a middle-aged or older single woman who has dedicated her life to sheltering unwanted cats. The numbers of animals in such households increases rapidly to 20-60 or so animals, at which point such factors as disease, limited feed supply, and the owner's inability to provide even rudimentary care tend to hold the numbers steady. Cat numbers rise because of the tendency of feral or unwanted cats to leave areas of poor food supply and migrate to areas where food is more available.[20] It is an unfortunate fact that the more homeless cats that are fed in an area, the more homeless cats will move into that area.

Overcrowding is a serious problem for a number of reasons, but has a particular effect on the incidence of infectious diseases.

Overcrowding imposes tremendous stress on animals that evolved as solitary and territorial creatures. Stress in cat populations not only causes a higher frequency of aberrant social behavior (fighting, urine spraying, defecation outside of litter pans), but also lowers resistance to disease.

Chronic stress affects the incidence of disease in 2 important ways. It makes cats more susceptible to infection and it increases the amount of pathogens shed into the environment. Depression of established immunity activates latent infections, especially herpesvirus, leading to virus shedding from the nasal passages. If the reactivation is particularly severe, clinical signs may recur. Active infections are also affected, leading to a higher than normal rate of microorganism shedding. Examples of these types of agents include calicivirus, chlamydia and ringworm. Overcrowding also increases the number of infected (asymptomatic or diseased) individuals in the area and provides a greater reservoir of susceptible animals. Because more animals are crowded into the same area, the chances for intimate contact and potential transmission of infectious agents increase.

Overcrowding can also influence nutrition. Though malnutrition is more apt to be seen in multiple-cat households than catteries or shelters, it can occur in any large animal population. If the owner has a limited income, which is commonly the case with individuals that keep large numbers of homeless cats, it becomes economically impossible to provide adequate nutrition to every animal. When there is not enough food to go around, pregnant queens, lactating queens, kittens and chronically ill animals are most vulnerable. They are often at the lower end of the social order, but have the greatest nutritional needs. Malnutrition has a profound effect on susceptibility to disease.[19] Malnutrition is particularly devastating in kittens, which not only have the highest nutritional requirements but also are most vulnerable to infection.

Maintaining a Closed Cattery: The second rule for good cattery management is to maintain cat populations as closed as possible. Each population of animals has its own resident microbial flora, said to be enzootic or resident. Cats within such environments have a high state of resistance to the resident microbial flora, and this immunity is passed on to their kittens genetically (genetic resistance) and in the colostrum and milk (maternal immunity). New cats introduced into the environment bring with them their own flora.

If these new microbes are substantially different from the resident flora, infection and disease occur in resident animals. This infection spreads rapidly because of the uniform susceptibility of the population. Infections of this type are referred to as epizootics. Not only are resident cats susceptible to infection from newly introduced animals, but the new cat is susceptible to the unique flora of the resident cats.

Introduction of new animals can also have profound social effects on the entire population, transiently increasing the level of cattery stress. Cats have well-established social orders of dominance that are disturbed when new animals are introduced. This stress acts like other stresses in increasing the animals' susceptibility to infection and the level of pathogenic organisms shed into the environment. Given the problems with introducing new animals into the household, it is wise to minimize this.

Successful cattery managers recognize the problems with introducing new animals and limit the numbers of animals introduced into the cattery.

The number of animals that enter the cattery is best limited by having a well-conceived breeding program, rather than one that is entirely haphazard. Many cattery owners, especially newer ones, cannot resist the temptation to bring in new animals. This is done because of a desire to be competitive. The more cats brought in, the more bloodlines represented, the more breeds that are kept, and the greater the perceived chance of breeding show-winning kittens.

Control of the Kitten Population: The third rule of cattery management is to limit as much as possible the numbers of kittens reared in the cattery. Kittens are the most susceptible to disease, and are the major source of infection for other kittens. Adult cats, though they often carry many pathogenic microorganisms, rarely shed them in large numbers. The magnitude of environmental contamination is greatly magnified by infection of kittens. These infected kit-

tens shed many times more organisms than adult carriers.

Segregation of Litters: A fourth rule is to segregate each litter until the kittens are at least 12 weeks of age. Following weaning, the mother should be removed and the litter kept together in separate quarters. The greatest mistake made by cattery owners is to put all of the kittens from all litters together in a common area following weaning. Because various litters are seldom born at the same time, newly weaned kittens often are mixed with kittens of a wide age range.

Adult carrier cats (usually cats less than 2-4 years of age) are the source of many infectious agents, but infection is usually amplified in kittens. For instance, most kittens have maternal immunity to many organisms enzootic to the cattery. This maternal immunity can be overcome at a young age (6-10 weeks of age) if exposure is great enough. If exposure is mild, however, they may not become infected until their maternal immunity has waned (12-16 weeks of age). The first litter born is not exposed to other kittens, but rather to the adult cats. Because exposure is minimal, maternal immunity may not be overcome until the kittens are 12 weeks of age or older. The resultant disease is likely to be mild because of the small exposure dose and the age resistance. Though they do not show signs of illness, the older kittens may nonetheless shed far more of the pathogenic organisms than the adults that started the cycle.

If a second litter is then placed in the same quarters, these kittens are exposed much more severely than the first litter. They will likely show clinical signs of illness and shed even more of the pathogenic microbes than the previous litter. A third litter will be exposed to even greater numbers of organisms than the second, etc. If the exposure is severe enough, the maternal immunity may be overcome at a progressively younger age (6-10 weeks of age). Because younger kittens are much less immunocompetent, they become much sicker and may die.

To break this cycle, kittens should not be directly exposed to older kittens until they are at an age when their resistance is well developed, usually at about 12 weeks of age.

It might be inferred from this discussion that it is acceptable to put kittens of the same age together. This is also unwise because each litter of kittens and each individual in the litter develop differing levels of maternal immunity. One litter of kittens may still have considerable maternal immunity at 10 weeks of age, while another can be totally susceptible by 6 weeks of age.

Sanitation

Cleanliness is an absolute requirement for good health in catteries. Secretions, excretions and exfoliations must be removed from the environment to minimize the levels of potentially pathogenic organisms where the animals are kept. The term "potentially pathogenic" is used rather strictly. Many pathogenic organisms do not cause disease unless they are present in certain minimum levels. For instance, pathogenic doses of enteric bacteria may not be achieved until there are several million organisms per square foot of cattery surface. Levels below this are insufficient to cause problems. The object of cleanliness is to keep the levels of potentially pathogenic organisms below this threshold and not necessarily to eliminate them altogether. Complete elimination of organisms from the environment is practically impossible and potentially hazardous.

Note that an environment that is very neat and well organized can still harbor pathogenic accumulations of microorganisms, while less neat areas may be devoid of such accumulations. Organisms tend to reside in permeable surfaces, litter boxes, food, water, dishes, crevices, air conditioning ducts and other such areas. The objectives of good sanitation are to reduce the amount of microbes that enter the cattery and to limit the accumulation of potentially pathogenic microorganisms.

The amount of secretions, excretions and exfoliations that enter the environment can be limited by keeping the numbers and density of animals as low as possible. Removal of waste material from the environment is facilitated by frequent removal of litter, sweeping and vacuuming to remove gross and microscopic debris, and judicious use of hot soap and water to loosen adherent debris and wash it away.

Litter should be changed every 1-2 days to prevent the accumulation of microorganisms and spread of contamination from pans to floors, perches, food dishes and other pens. Cattery owners often use commercial types of litter that decrease odor and absorb a great amount of moisture. This type of litter, though most effective, has several limitations. First, the fact that it absorbs odor and moisture and is expensive means that it is less likely to be changed every day or so. Also, the absorptive particles can accumulate large numbers of microorganisms that can be readily tracked around the environment. Finally, odor-retaining litter tends to mask ammoniacal odors that indicate urine accumulation. Dust-free pine shavings, peat moss, redwood mulch, diatomaceous earth, vermiculite and other such material are inexpensive alternatives to clay-type litter. Many of these have the advantage of being biodegradable and useful for mulching. Their main disadvantage is that they can be easily tracked around the pens.

Litter pans should be as deep as possible to prevent spread of litter around the room. Litter pans with covers have been developed for such situations, though some cats avoid such covered boxes. Special covered litter pans are also available for cats that spray urine inside of the pan (Fig 7). Instead of the top's fitting over the bottom, the top fits inside the bottom. Urine then runs into the pan and not down the sides and to the outside. Litter pans should also not be overly filled. Less litter and more frequent changes are preferable to more litter and less frequent changes.

Urine spraying by male and female cats can be a major source of odor and contamination within a cattery or multiple-cat household. Spraying is defined as urination not in the litter box. It is usually directed at walls, windows and objects around the home. Spraying is usually brought about by psychological maladjustments (see chapter on behavior). Spraying by queens is often associated with estrus. It may also be caused by such stresses as overcrowding or sudden changes in their normal routine. Spraying in toms is particularly irritating, due mainly to the greater odor of tomcat urine. Toms begin spraying for various reasons. Toms housed in runs in view of queens or other toms are often more prone to this behavior than toms that are visually isolated. It is important to take this into account when designing the cattery and assigning space. However, toms of some breeds, such as Persians, Manx and Siamese, may be content when kept in isolation but tend to become "hyper" when placed in view of other toms at shows.

Urine spraying by both toms and queens in catteries can be minimized by proper construction of the cattery. Queens should not be overcrowded and toms should not be kept in runs with a view of other cats. That is not to say that toms and queens need to be provided with their own private quarters. Many toms can be kept together without many problems with spraying or fighting, especially if they are raised with each other. The same is true for queens.

Owners may find that grouping certain cats together results in continual social problems. If 2 cats in the same run cannot establish a dominant-submissive "pecking order," the result may be constant tension among the entire group of animals. Cattery owners are usually knowledgeable and observant enough to control the problem before it gets out of hand. No matter how much effort is made in designing a cattery, some spraying is bound to occur. If the cattery is well designed, however, the urine is easily cleaned up. Cleaning sprayed urine and eliminating urine odors are virtually impossible if cats are kept in homes. This is yet another reason to provide the cats with their own quarters.

Defecation out of the litter box is more of a response to overcrowding and social stress than to sexual factors. If the litter boxes become too contaminated with excrement, there is more of a tendency to defecate on the floor. This situation is worsened by spilling of litter outside the box. Cats are more apt to defecate on the floors when some free litter is scattered about than if the floors are relatively litter free. Some breeds and some bloodlines within breeds may have more problems with improper litter box training than others. This suggests that genetics may also play a role in this type of behavior.

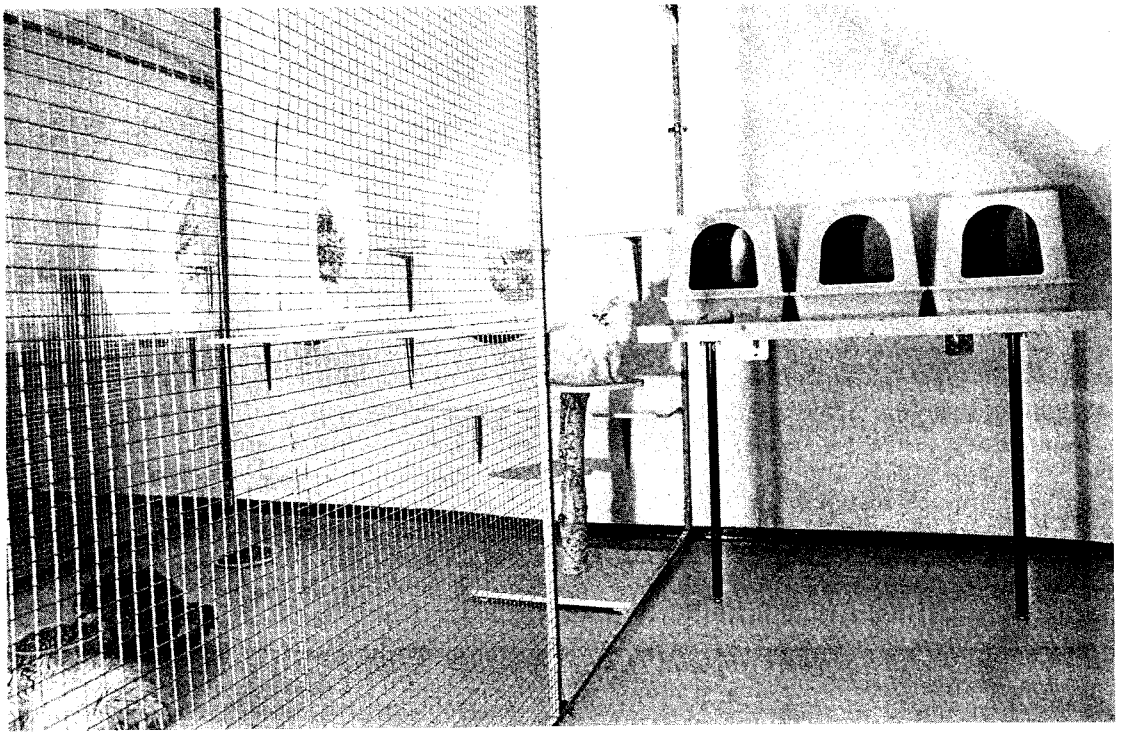
Cattery floors and perches should be cleaned daily if possible. The frequency of

cleaning depends on the size of the facility and number of animals. Every few days, depending on the density of animals, the cattery walls, perches and floors should be washed with hot water and a dilute mild soap solution. This can only be accomplished if the runs are impermeable to water and adequate drainage is provided. Mopping is much less efficient than hosing, though it is still preferable to vacuuming and sweeping only. Impermeable surfaces also prevent accumulation of microscopic debris in porous surfaces.

Cleaning of well-constructed facilities can be relatively simple and rapid (Fig 7). Litter pans are usually emptied into a waste container and placed outside of the unit. Food and water pans can then be placed on the perches. A garage or shop-type vacuum is used to clean any loose litter, excreta and hair within the unit. The cats usually move to higher perches to watch the operation, so there is usually no need to move the animals to different quarters during cleaning. Once or twice weekly the floors and walls should be hosed down with a hot, dilute, low-sudsing, soap and water solution applied with a high-pressure nozzle. High-pressure cleaning apparatuses used to wash cars are useful for this. The floors and walls can usually be rubbed with a rubber squeegee to remove puddled water. If gutters and drains are not part of the design, a shop vacuum with a noncorrosive plastic waste container can also be used for this purpose.

After the unit is cleaned, litter pans are hosed out to remove adherent material and refilled with clean litter. Washing down the unit with dilute soap and water is crucial for cattery health, especially if relatively large numbers of animals are kept in cramped quarters. Frequent removal of dirty litter and cleaning of floors, walls and

Figure 7. The litter boxes in this cattery are placed on tables to facilitate cleaning. Note that the top cover of the litter boxes fits inside the litter pan, so that any urine sprayed inside the box runs down the sides and back into the pan. (Courtesy of Elke and Norbert Deutschmann, Essen, West Germany)



perches prevent accumulation of microorganisms and parasites.

If the surfaces are permeable to excreta and water, cleaning is not nearly as effective. One of the greatest disadvantages of using human homes for catteries is that it is virtually impossible to keep them properly clean. Vacuuming may give the appearance of cleanliness, but the myriad pores in floors, carpets and wood cages provide innumerable places for accumulation of microorganisms.

Disinfection

Disinfection is employed when sanitation measures have failed. It is, therefore, not a substitute for proper cattery design or management, but rather an attempt to remedy poor cattery practices. If not coupled with sound management practices, disinfection has minimal impact on cattery disease problems, can be a waste of time and money, and may be potentially hazardous to the health of animals.

The principles of disinfection have been discussed elsewhere.[9] The term "disinfect" usually applies to destruction of pathogenic microorganisms by chemical or physical means. Disinfection is applied only to inanimate objects; one does not "disinfect" a cat, but rather a pen, floor or litter pan.

Disinfection is not synonymous with sterilization, though such an assumption is often made. Disinfection usually reduces rather than eliminates (sterilization) microorganisms from the environment.

Various factors determine the effectiveness of disinfection. The pathogenic microbes in the environment vary greatly in their susceptibility to disinfectants in general and to different disinfectants in particular. Generally speaking, viruses are much more susceptible to disinfectants than bacteria. Enveloped viruses are more susceptible to disinfectants than nonenveloped viruses, and RNA viruses more susceptible than DNA viruses. Fungi are more difficult to destroy by disinfection than other types of microbes. The spore forms of bacteria and fungi are the most resistant of all to disinfectants. The concentration of disinfectant needed to destroy microbes also varies greatly, depending on the microbe and the disinfectant. If the microbe is hidden in organic matter, such as excretions, secretions or exfoliations, it is protected from the effects of the disinfectant. This is why it is essential to precede all disinfection with thorough vacuuming, followed by washing with soap and water to remove as much gross material as possible. Care must be taken, however, to remove as much of the soap residue as possible, as this may inhibit the effect of some types of disinfectant. Special solutions are available for use before application of disinfectant. They are less likely to interfere with the disinfectants.

Heat, especially if applied in the form of steam, is the most potent disinfectant. Steam applied under pressure requires special equipment, however, and surfaces must be resistant to such treatment.

Non-ionizing radiation, usually generated by ultraviolet lamps, is another form of disinfection. The ionizing radiation in sunlight also has a similar disinfectant property. Though ultraviolent lamps are popular among cattery owners, there is no evidence that they have a significant disinfectant effect. Radiation produced by these units decreases with the square of the distance from the source (the amount of radiation 4 inches from the lamp is only one-fourth as great as that at 2 inches, and the amount at 8 inches is only one-sixteenth). Microbes must be brought into close proximity to the lamps before they are killed. This requires proper positioning of the units as well as proper air flow patterns. Even then, the low power of most units, coupled with the short time that microbes are exposed directly to the radiation, provides only minimal disinfection.

Chemical disinfectants are the mainstay of disinfection in most catteries. For reasons of practicality, effectiveness and lack of toxicity, only a few are routinely recommended for catteries. The most popular are the cationic surfactants or quaternary ammonium compounds. They are more effective when used in warm than cold water but are inactivated by soap residues, hard water and large amounts of organic matter. Quaternary ammonium compounds are effective against bacteria, enveloped viruses and fungi, but not bacterial spores. Household bleach, containing about 5.25% sodium hypochlorite in water, is a commonly used disinfectant. Household bleach, when diluted 1:32 in water, is effective against

many viruses, bacteria and fungi. Chlorine solutions are inactivated by organic matter but are not affected by hard water. Phenolic compounds, and many other types of common household disinfectants, are not recommended for use in catteries due to their toxicity. The potential for toxicity is increased by cats' grooming habits. Residues of the disinfectant get onto the cat's hair and are concentrated in the mouth by grooming. Disinfectant toxicosis is usually manifested by sloughing of the membranes on the tip of the tongue, roof of the mouth, and esophagus (see chapter on toxicology). Severe sloughing of tissue can be fatal.

Nutrition

Specific aspects of nutrition are covered in another chapter. General aspects of cattery nutrition are discussed here.

Cattery owners should be meticulous about the care and storage of food. Dried food should be left in the original bags, and the bag placed into vermin-proof containers. When the sack is empty, it should be discarded and replaced with a freshly opened bag of food. Dried food should not be poured from the bags into containers. Such a practice encourages the retention of residual amounts of old food in the cans, which in turn encourages mold growth in the food. Moldy food can be very toxic for cats and may lead to chronic ill health and liver degeneration. Dried food should be purchased in small lots so that it will be used up within a few days or weeks of its expiration date. Once bags are unsealed, they should be used up in a few days.

Food and water pans must be kept free of fecal contamination by being carefully positioned in the pen. They should also be cleaned out every week or so and disinfected. The amount of fecal contamination of the food is directly proportional to the amount of litter contamination. Cats carry litter on their feet after using the litterbox and often transfer it to their food and water dishes. If the litter is dusty, air-borne litter also settles into the water and food dishes. Cats often use food bowls and litter trays for sleeping, which further contaminates the food. Baby pig feeders can be used to circumvent this problem.

Kitten Production and Rearing

Production of kittens is the paramount goal of catteries. Paradoxically, kitten production is the most difficult aspect of cattery management. If done poorly, it is the most important factor responsible for cattery failure. Though the main cattery goal is to raise kittens, the numbers of kittens should be kept to a minimum. Kittens are both the greatest source and greatest target of disease. Limiting kitten numbers tends to minimize cattery disease.

Kitten production is also the greatest cause for cattery overpopulation. That is because a single queen can have as many as 8 or more kittens a year. It is important, therefore, to rear only as many kittens as necessary to accomplish the goals of the cattery for show and sale. A few exceptionally healthy kittens of outstanding quality do more for cattery reputation and economic health than many kittens of poor quality and ill health. Good-quality, robust kittens can only be obtained by carefully planned breeding of animals that are themselves healthy and robust, and have a history of weaning most of their kittens.

The final measurement of breeding soundness should be conception rate, average litter size at birth, average litter size at weaning, and average litter size at the time of maturity. Having a high average litter size at birth, but a high mortality between birth and adulthood, is not synonymous with good breeding performance.

Controlled Breeding: Breeding within a colony of cats is not as easily controlled as it may seem. Cats are seasonally polyestrous, which means that they come into heat repeatedly over a several-month period. In the northern hemisphere, the period ranges from early spring to late fall (under natural lighting). If the cat is not bred at one of the estrous cycles during this period, it eventually goes out of heat until the next spring. Ovulation is stimulated by coitus, and not by actual insemination. The cycle of rapid, repeated estrus can be broken, therefore, by inducing the cat to ovulate. Under normal breeding conditions, this is accomplished by breeding the cat. It can also be induced by mimicking coitus with a smooth, blunt probe that is thrust into the vagina. Such a procedure is not easily mastered, however,

and is often not effective. The penis of the cat has backward pointing barbs that irritate the vaginal wall during retraction. This vaginal stimulation is important in inducing ovulation and is not easily mimicked by smoother implements. Some breeders prefer to use vasectomized male cats to stimulate ovulation. Toms castrated later in life sometimes continue to breed out of habit, though this is uncommon. If treated with testosterone, they may regain libido. Cryptorchid toms may also prove useful. If only the scrotal testicle is removed, the cat is sterile due to atrophy of the seminiferous tubules of the retained testicle. It still has normal libido, however.

Estrous cycles can be stopped with injectable or oral medications containing progestins (see chapter on reproduction). Megestrol acetate is particularly popular for this purpose, as are some repository (long-acting) injectable forms of synthetic progesterones still used in human medicine. Drug-induced cessation of estrus carries some risk, however. Pyometra occurs more frequently in animals treated with such drugs. Preventing normal conception during each estrus period can also have a deleterious effect on overall fertility. Cats not kept in continual breeding may have lower conception rates and smaller litters at subsequent estrous periods. The problems with controlling conception, however, are not usually great enough to outweigh the benefits in population control.

Selection of Breeding Stock: Breeding stock should be selected by more than just good show conformation. Queens and toms should have good temperaments and be free of chronic or intermittent disease. High-strung and easily frightened animals are more susceptible to cattery stress, and thus to disease. This trait is highly heritable and is passed on to many of the kittens. Likewise, cats that are overly aggressive and introverted should not be used for breeding. Such animals detract from the breed's or bloodline's reputation.

Mating: Mating should commence only after careful study and planning.

Queens selected for breeding should be fully mature. Cats are usually mated in either of two ways. Most breeders prefer to place the tom and queen together for 2 hours or so. If breeding does not take place, the animals are separated for several hours and the process is repeated. Reintroducing the tom results in more frequent ovulation and larger kitten sizes.

Alternatively, queens in estrus can be placed with toms and they left together until pregnancy is confirmed. The latter procedure may work better with toms that lack libido and are overly stressed by having people always present. It is also advantageous in limiting the numbers of rooms required in the cattery. We have found that more than one queen can be housed with the tom using the latter approach.

It should also be remembered that inexperienced queens often require experienced toms for successful breeding. Some queens are also very particular, and rebuff all but selected or very aggressive suitors. Likewise, some toms show little interest in certain queens. Careful records should be kept of the date, duration and intensity of estrus, and times when breeding is observed. The gestation period of individual queens is usually the same at each pregnancy. However, gestation periods can vary among different cats by several days. Such information is essential for evaluation of reproductive problems (see chapter on reproduction). Pregnancy can usually be detected by palpation between the third or fourth weeks of gestation. Fetuses at this time feel like ping-pong balls in the caudal abdomen.

Parturition: Queens should be isolated to individual quarters as soon as their pregnancy is confirmed, usually before 40 days of gestation. A cardboard box with a newspaper-lined bottom is usually placed into the pen about 1-2 weeks before the estimated due date. Some breeders prefer special delivery cages. These are much more expensive and seldom necessary if the queen is allowed time to adjust to her maternity quarters. During very cold weather, heat lamps can be hung several feet above the box. The temperature at the bottom of the box should be adjusted to 75-85 F by varying the distance of the lamp from the top of the box. Heating pads on low heat can be wrapped in a towel and placed beneath the box. Part of the box can be left off of the heating pad so that kittens may move to a cooler area if they feel overheated.

Towels can also be placed in the bottom of the box, though newspapers are more than adequate. Electric cords should be positioned so they cannot be chewed or urinated upon.

As parturition nears, the mammary glands of the queen begin to rapidly enlarge and milk can be expressed a day or so before delivery. The queen also begins spending more time in the box, and a day or so before parturition she may begin to claw and chew the newspapers lining the box. Parturition should be allowed to proceed with as little human interruption or assistance as possible. Though most kittens are born within a 12-hour period, the entire litter may be born over 24-48 hours. In rare cases, the last kitten may suddenly appear 3 or more days after the next to the last one.

Neonatal Care: Kittens should be quietly and quickly examined after birth. Young queens may not always chew off the umbilical cord and consume the placenta, as is normally expected for cats. If the umbilical cord is dried and placenta is still attached, the cord should be severed no closer than 1 1/2 inches from the abdominal wall and the placenta discarded. An intertwined mass of placentas, umbilical cords and kittens often develops if the queen does not sever the cords at birth. Under such conditions, the limbs of the kittens are often entangled by the dried and twisted umbilical cords. If the blood supply is compromised too long before the leg is freed, the limbs can develop dry gangrene over the next several days and slough off. Tangling of the umbilical cords can also lead to massive umbilical hernias and abdominal evisceration. Such lesions result from the kittens' pulling on the umbilical cord attachment.

Overattention of the queen to the umbilical cord can be equally damaging. Some queens chew off the umbilical cord at the abdominal wall. This leads to formation of a microabscess just inside the body wall due to infection of the umbilical stump by bacteria from the queen's mouth. If the umbilicus is chewed off further from the body wall, which is usually the case, it dries up and the remaining stump acts as an impermeable barrier for bacterial migration. Microabscesses in the intraabdominal part of the umbilical vein are often not detected from the outside. They usually spread bacteria directly into the bloodstream of the kitten. If the umbilical cord is chewed off too short, the kitten should immediately be given an injection of long-acting benzanthine penicillin. Failure to treat the infection before it becomes established leads to high kitten mortality.

Routine care of the umbilical cord is not usually required. Some cattery owners cut and tie the umbilical cord as the kittens are born and treat it with an antiseptic solution. This is only necessary if the queen fails to cut the cord. If the cord is cut too short by the queen, antiseptic solution applied to the stump may be helpful. This should not replace prophylactic treatment with penicillin, however. By the time the problem is noticed, bacteria from the cut edge of the cord have often reached the intraabdominal portion of the umbilical vein. Bacteria at this site cannot be eliminated by locally applied antiseptics.

The care that the queen gives to the kittens at the time of birth is crucial to the kittens' survival and a topic of some controversy among breeders. Most queens are very attentive to their kittens as each is born. They cut the umbilical cord, consume the placenta, and clean the kittens of fetal membranes and fluids. They lick the kittens' perineum to encourage them to pass meconium (digested amniotic fluid swallowed during fetal life). If strong and vigorous, the kittens immediately seek a nipple on which to nurse. Nursing is encouraged by the queen.

The time from birth to nursing varies greatly with different queens. Some spend endless hours with their newborn kittens, while others clean their kittens very quickly and then leave the box to roam about the cage. If the kittens are quiet and their abdomens distended, the queen has obviously done her duty. If, however, the queen fails to cut the placenta and clean the kittens following birth, or if the kittens are restless and crying with gaunt abdomens, the queen is not paying proper attention to her litter. Failure of the queen to properly care for her kittens at the time of birth is more common in primiparous (first-time) mothers. Some queens, if given a day or so, develop good maternal behavior. Such queens often need

some assistance in their maternal duties for the first day or so. Other queens, however, abandon their kittens entirely. These kittens must be quickly fostered onto other queens, or hand reared.

Periodic weighing of kittens for the first few weeks of life can help detect diseases before they become severe (Fig 8). Slow weight gain or loss of weight often is the first indication of disease. A thorough examination at the time weight loss is detected may allow treatment while the disease is in the early stages.

Care of Abandoned or Orphaned Kittens: Fostering abandoned kittens to another queen is the best way to handle abandonment. If the age disparity between the fostered kittens and those of the foster queen is more than 14 days, the foster mother may not accept the new kittens. Further, foster mothers often are not available for every abandoned litter. In such circumstances, there is no alternative to hand rearing. Fostering is preferable to hand rearing because it circumvents bottle or eyedropper feeding and the associated risk of under- and overfeeding and aspiration pneumonia. Cat's milk is more nutritive than milk substitutes, and also provides passive systemic immunity and passive local immunity.

Kittens acquire passive systemic immunity by drinking colostrum during the first 12 hours of life. Passive systemic immunity helps destroy pathogenic microorganisms entering the bloodstream and is essential for survival. Colostrum is the antibody-rich milk produced by the mammary glands during the first 24-72 hours after parturition. The intestinal tract of the kittens can absorb most ingested proteins during the first 12-24 hours of life. It is during this period that most colostral antibodies enter the kitten's bloodstream. The intestinal lining cannot absorb ingested proteins after this time, so antibodies from colostrum are no longer absorbed into the blood. Failure to ingest colostrum during the first few hours of life leaves the kitten without blood antibodies. These kittens are very susceptible to infections that enter the blood via the skin or mucous membranes of the respiratory, digestive or genitourinary tract.

Passive local immunity persists for as long as the kittens are nursing. Even after the queen no longer produces colostrum, her milk still contains an appreciable level of antibodies. Though these antibodies are no longer absorbed into the kitten's bloodstream, they act locally within the oropharynx, esophagus, stomach and intestines to prevent local invasion by microorganisms ingested with the food. Therefore, passive local immunity is the first line of defense against infection. If infection broaches this initial barrier and enters the blood, the second line of defense is passive systemic immunity. Passive local and systemic immunity are both essential for survival of newborn kittens. They protect the kitten during the first 6-12 weeks of life when the kitten's own immune system is developing.

By understanding passive local and systemic immunity, it is possible to prevent some of the undesirable consequences of fostering or hand rearing kittens. If a kitten is abandoned before it nurses its mother and is hand reared for more than 1 day before being fostered, it does not absorb antibodies from the foster mother's milk into its bloodstream. It receives passive local immunity as long as it nurses, but it is deficient in passive systemic immunity. If a kitten is abandoned before it nurses and is hand reared entirely, it will be deficient in both passive and systemic immunity. If a kitten is abandoned after having nursed for 12-24 hours and is hand reared thereafter,

Figure 8. Periodic weighing of kittens helps detect weight loss that may indicate disease.

it develops passive systemic immunity but is deficient in passive local immunity. Kittens that have received neither passive systemic nor passive local immunity are highly susceptible to overwhelming infections. Kittens that receive one or the other form of immunity are more prone to infection than normal kittens, but their chances for survival are fair to good.

If kittens are abandoned before nursing and cannot be fostered onto a queen in the colostral phase of lactation (first 72 hours after parturition), they should be artificially provided with systemic antibodies and kept away from other cats until after they are weaned. Passive systemic immunity can be artificially provided by inoculating each kitten subcutaneously with 2-5 ml of sterile serum derived from blood collected from the queen or other adult cats in the cattery. Care should be taken that the blood donor is not carrying blood-borne viruses, such as feline leukemia, immunodeficiency or syncytium-forming viruses. The same treatment would be beneficial to newborn kittens fostered onto queens not secreting colostrum.

Hand rearing kittens requires a great deal of time and patience. In addition to providing passive systemic immunity, one must provide appropriate nutrition. This is usually accomplished with commercially prepared canine or feline milk substitutes. These usually mimic the higher protein and fat content of cat's milk (Table 3).[11] Substitutes should be given frequently, slowly and in small amounts during the first week of life. Eyedroppers are vastly superior to small bottles, plastic nipples and stomach tubes. Stomach tubing should be done only when the kitten is too weak to swallow.

Feedings are given faster, less frequently and in larger amounts during each subsequent week of life. Care should be taken when feeding milk substitutes by bottle, eyedropper or stomach tube to avoid feeding too rapidly. Rapid feeding may allow aspiration of milk into the lungs, which can cause severe and potentially fatal pneumonia. Care in feeding is particularly essential in weak kittens with a poor suckling response.

The estimated daily caloric intake for kittens increases progressively from 0.20 Kcal/g (5.7 Kcal/oz) of body weight in week 1 to 0.29 Kcal/g (8.2 Kcal/oz) of body weight in week 4.[5] Commercial milk substitutes should be used in preference to whole cow's milk. If sufficient calories are provided, the diet can be balanced for all other essential nutrients. Kittens should obtain a substantial proportion of their dietary needs from regular foods by the fourth week of life and do not require complete milk supplementation after this time.

Medical Care of Kittens

After birth, the next most critical time in the life of kittens is the period between birth and 2 weeks of age. This time is referred to as the neonatal period, and kittens in this period are referred to as "neonates." The neonatal period is when diseases acquired either *in utero* or during birth are manifested. (The section on common cattery diseases contains a discussion of neonatal diseases.)

Since infectious diseases are inextricably linked with cattery design and management, excessive neonatal kitten losses can be related in turn to problems with cattery

Table 3. The composition of various milk sources for hand rearing kittens.

Source of Milk	Kcal/ml	% Solids	% Fat	% Protein	% Carbohydrate
Cat	0.9	19.2	25.0	42.2	26.1
Cow (whole)	0.7	12.0	30.0	25.6	38.5
Esbilac powder (1:3 water)	1.0	98.4	44.1	33.2	15.8
Esbilac liquid (4:1 water)	0.9	15.3	44.1	33.2	15.8
KMR	0.9	18.2	25.0	42.2	26.1

husbandry. Unfortunately, kittens that die at birth or during the first few weeks of life are seldom necropsied and the real cause of their death is seldom determined. Without such information, it is impossible to determine the main causes of kitten mortality and the steps needed to eliminate them. Catteries with a high incidence of neonatal kitten mortality should seek the services of veterinarians willing to do thorough necropsies. Tissues should also be sent to a diagnostic laboratory for microbiologic and pathologic analysis.

Diseases that occur in kittens from 2 weeks of age to adolescence (6-8 months of age) are the most amenable to prevention by good cattery design and management. One of the most important steps in limiting disease during this period is to keep litters segregated from each other (see previous section). This is the most effective mechanism for limiting infectious diseases within the cattery. Segregation limits exposure of the kittens to microorganisms carried only by the queen. Since immunity acquired from colostrum is most effective against organisms carried by the mother, the kittens are well protected.

Cattery owners frequently must provide basic health care for their animals. Indeed, may catteries are well stocked with vaccines and commonly used drugs. However, overreliance on home medical treatment can have repercussions that outweigh benefits. Treating animals improperly can enhance disease problems within a cattery rather than help resolve them. Use of antibiotics when they are not needed also encourages emergence of antibiotic-resistant organisms. It is important, therefore, for cattery owners to learn as much as possible about the common diseases they are likely to be faced with and to understand the rationale for treatment of these conditions. A large number of different disease problems can plague catteries, but fortunately only a few account for most of the problems (see section on common cattery diseases).

Home therapy, like hospital treatment, can be supportive or specific. Supportive care involves encouraging the cat to eat, keeping sick animals warm, dry and comfortable, and giving fluids to correct dehydration and electrolyte (salt) imbalances. Specific care usually is limited to administration of specific drugs, such as antibiotics.

Encouraging sick cats to eat can be very difficult (see chapter on nutrition). As cats become ill, they progressively lose their appetite for various foods. If the disease is mild, a simple change of commercial food brands or flavors may keep the animal eating. As the illness becomes more severe, ill cats only eat their most favorite foods, often only in small amounts. They quickly lose their appetite for even these special foods, and must be constantly tempted with new and different foods. Generally speaking, cats with a poor appetite are more likely to eat foods of high palatability (flavor, aroma, texture), especially animal meats. Raw liver is especially palatable to many sick animals. Once the cat has completely lost its appetite, the owner must become more forceful about placing food in the cat's mouth, making liquid slurries of the food to be fed by syringe or eyedropper. If this is not possible, a stomach tube may have to be used. The final resort is placement of a gastrostomy or pharyngostomy tube.

The importance of keeping convalescing animals in warm, dry, stress-free quarters cannot be overemphasized. Sick cats should not be kept with healthy ones. They should be left alone as much as possible, being handled only when they are medicated and their condition reevaluated.

Many cattery owners are trained by their veterinarians to give fluid and electrolyte solutions subcutaneously with a large syringe and needle. Subcutaneous fluid therapy is only of benefit, however, if it is absorbed into the bloodstream. If the cat is not in shock, fluids are transported within minutes from the subcutaneous spaces to the blood. If the initial fluid bleb is still present hours later, or has shifted from the dorsum to the ventrum of the animal, it is not being absorbed and has no therapeutic benefit. Failure to absorb subcutaneous fluid is common in cats with a subnormal rectal temperature, shivering, and muddy, bluish-tinged oral membranes. Animals in shock have constricted blood vessels in the subcutaneous tissues to divert peripheral blood to internal organs. This peripheral constriction of blood vessels prevents absorption of subcutaneous fluids. Cats that are dehy-

drated and in shock must be given fluids intravenously.

Dehydration is usually manifested by a lack of elasticity of the skin. If the skin over the back is pinched up or tented, and falls back into place within a fraction of a second, the animal is not dehydrated. If the tented skin retains its shape for some seconds, then the animal is dehydrated. Dehydration is often associated with sunken eyes, shivering, subnormal temperature, and other shock-like signs. Dehydration cannot be measured accurately by skin elasticity, however, in badly emaciated animals. Emaciation causes a change in the normal skin structure and elasticity.

Specific drug therapy is the most abused aspect of home medical care. Many cattery owners believe that antibiotics can cure anything, and that all diseases are caused by microbes that are antibiotic sensitive. In truth, very few cattery diseases can be treated specifically by antibiotics. Injudicious use of antibiotics has a number of serious complications. First, antibiotics, especially if given to kittens, often depress the appetite, cause gastrointestinal upsets, such as diarrhea, and can be stressful. Second, some antibiotics cause serious side effects. For instance, some eye and ear preparations can also induce reactions in the ears and eyes that may mimic the very disease against which they are first used. Severe and potentially fatal reactions may occur in animals that have become sensitized to continued use of certain drugs. Finally, indiscriminate use of antibiotics encourages development of antibiotic-resistant strains of organisms within the cattery. Later, when an antibiotic is really needed, the offending organism may be highly resistant to therapy.

Weaning Kittens

Purebred kittens are usually sold when they are 12-16 weeks of age. This is because most breeders want the first 2 vaccinations completed before the kitten is sold. They also believe that older kittens adjust better to people in their new homes and that their immune systems are better developed. At 3-5 weeks of age, kittens are usually out of their nest boxes. Between 6-8 weeks, kittens tend to socialize mostly with each other and do not like as much human attention. Kittens over 8 weeks of age are more apt to socialize with people. Breeders also keep kittens for a longer time so they can observe them for developing show characteristics.

Weaning time varies with different breeds but is usually at 8-9 weeks of age. This is on the average 2 weeks or more later than domestic kittens. It tends to be longer than this with such breeds as Abyssinians and shorter for such breeds as Persians. Therefore, these are kept in the cattery for an additional 4-7 weeks until they reach sale age.

Litter Box Training

Litter box training, like potty training of human infants, normally takes its own course. When the kittens are ready, usually at 5-7 weeks of age, they follow the example of their mother. Litter box training before this is futile. Moreover, the queen usually ingests most of the waste material during the first few days or weeks of life while the kittens are still confined to the birthing box.

It is important that kittens be trained with litter materials likely to be used by their new owners. Breeders of long- and thick-coated cats may prefer to use shredded newspapers for litter to prevent matting of litter and excreta on the perineum. Kittens litter trained to paper may be especially prone to improper litter box use when placed in their new homes. It is always disheartening to a cat breeder when one of their kittens is returned because of poor litter box use. The breeder may be reluctant to place this kitten in a second home, and equally reluctant to have it destroyed. Often these kittens become another unneeded member of the cattery population.

Teaching Proper Nail Scratching

Nail scratching is an early habit that can be minimized if it is not allowed in kittens. When the kittens come out of the box at 3-5 weeks of age, the tips of their claws should be clipped. This should be continued once a week until 4-5 months of age, when it can be done every 2-4 weeks. Also, there should not be any attractive scratching surfaces in the kitten area, such as posts or mats. Hav-

ing such objects around encourages the kittens to scratch. When the kittens begin coming into the household or play area at about 9 weeks of age, they are less inclined to scratch, even when they see adults do this. Scratching surfaces should be provided for adults who have developed this habit, or cats who scratch in spite of all efforts to teach them otherwise.

Showing of Kittens

Showing kittens after weaning is fraught with many problems. The earliest time that kittens are allowed in the show ring is 4 months of age. Most are 4-8 months old. Kittens, especially those closest to 4 months of age, are often in the immediate postrecovery stage of common infectious diseases, such as herpesvirus infection, chlamydiosis, mycoplasmosis and enteric infections. Though they may appear relatively normal, the internal recovery process is often incomplete, and they still carry and shed a great number of pathogenic organisms.

The stress of showing at this young age can reactivate the original disease, prolong the natural recovery period, or increase the number of organisms shed. If the kittens have not been infected before with these organisms, taking them to a show with kittens from many different areas may lead to initial exposure. Kittens coming back from shows are often replaced immediately into areas containing other young animals. If the other cats in the cattery have never been exposed to that organism, an outbreak of disease may follow return of young animals from shows.

Preventing Disease at Shows

A number of precautions must be taken at shows to limit spread of disease. Touching of cats by people other than the owners is usually not allowed. Cats showing signs of disease or parasitism usually are ejected. These steps help reduce some disease problems. The biggest improvement at shows to protect the health of cats was made several years ago in the US, when routine veterinary check-in examinations were abolished by most cat associations. Paradoxically, veterinarians would often use ungloved hands (or did not use new examination gloves for each animal) to examine the animals. The examination often involved opening the cat's mouth and examining the teeth, palate, oropharynx and tonsils for abnormalities. Since many infectious agents are carried in the mouth and are transmitted primarily by the oral route, veterinarians would unknowingly transmit disease organisms from one animal to the next. In the case of ringworm, contaminated hairs were also transmitted from cat to cat on the sleeves of examination gowns and tables.

The practice of show judges' "disinfecting" their hands between handling each cat in the ring is not just symbolic. It is mainly done to eliminate odors on the judging tables, hands and holding cages so that the cats do not become upset and hard to handle. It is also done to keep the table and cages clean. An important part of disinfection comes from the friction of wiping. This friction tends to remove larger adherent pieces of material that can harbor infectious organisms. These principles underlie the ritualized hand and table disinfection done by show judges.

Because sneezing cats or other animals with obvious signs of disease are easily recognized and reported, the greatest danger to show cats may be from ectoparasites, such as fleas or mites. These types of organisms are resistant to disinfectants and can move some distance from the animal. As a further precaution, therefore, experienced exhibitors usually spray the benching tables and floor with an appropriate insecticide before putting down the benching cage. They often use dilute chlorine bleach (1:32 parts water or less) to wipe down the benching cage, particularly the front and top, which are not covered with fabric. They often spend extra money to purchase or construct a "double" cage, providing a buffer space between their cage and adjacent cages. Some take a "grooming space" adjacent to the benching cage; this further increases the space between cages.

People that show cats are careful not to leave their animals unattended, never share grooming tools or surfaces, and prevent visitors from putting their hands in the cage to touch cats. Some people put up a sign telling visitors why the cats should not be touched without permission. They also wipe their hands with dilute chlorine bleach before handling anyone else's cats and let

some time elapse before touching other animals.

Show rules require that any cats showing signs of illness be reported to the show manager. These cats are examined by a veterinarian and may be required to leave the show hall. Show cats should also be kept away from other cats when returning home, and all clothes and show fabrics washed before reuse.

Procurement and Sale of Animals

Critical to the success of cat breeding is the ability to start with the highest-quality cats available from the selected breed. Ideally, original stock should come from a breeder with a well-established and successful breeding program, a reputation for honest kitten quality evaluation, excellent cattery conditions and consistent production of healthy, well-mannered cats that are fine examples of the breed.

Unfortunately, it is almost impossible for a novice breeder to buy from such a person. In most breeds there is a high demand for "top show" quality and "breeding" quality cats from experienced and reputable breeders. The cost of such kittens is likely to be very high, therefore. These breeders also tend to be highly particular in their kitten evaluation and often consider as few as 1 in every 10 kittens from the best of pedigrees as "show quality." They also have stringent criteria for sale of breeding stock and place their cats only to people who are dedicated to improvement of the breed and who will properly care for the cats. In addition, waiting lists of 1-2 years are not unusual for kittens from a respected cattery. All of this makes it difficult, therefore, for an unproven person to be considered as a potential owner of top-quality cats.

Many well-meaning but impatient people begin their breeding experience by being badly burned through dealings with less than reputable sellers of kittens and stud service. As they start to learn, they find that their first purchases are often of poor quality and sometimes carrying disease or parasites as well. Another discouragement faced by novice breeders is the reluctance of established people to accept mediocre females for stud service to their quality tomcats. Breeders more interested in stud fees than breed improvement may easily take advantage of those not familiar with stud service procedures and contracts. It is no wonder that newcomers sometimes give up after a few expensive and frustrating years.

Few people plan initially to become serious breeders and to develop a bloodline of cats within a breed. They are attracted to a breed and think it would be fun to have 1-2 litters of kittens or perhaps show a top cat. Since there is no plan and often the poorest of starts, it is only through hindsight that they learn. In spite of these drawbacks, the enjoyment and challenge of working with purebred cats help to overcome the setbacks of the first years for persistent cat lovers, and many novices develop into respected breeders.

Though it takes time, the best way to start is by careful study. Novices should read about their selected breed, analyze the show standard, go to cat shows and watch the judging, and talk with breeders and veterinarians about the good and bad qualities of the breed. Most breeds have local and/or national breed clubs with regular meetings or informative newsletters. The usual membership requirement is to be the owner of at least one registered cat of the breed. Various cat books and magazines offer information for new cat breeders. Breeders from different countries also need to consider magazines and books written for their specific geographic areas.

Such preparation leads to the second step in the learning process. Breed club membership, as well as showing a cat, helps determine if the breed and its breeding is an activity suited to the person's financial means and lifestyle. It is not difficult to obtain a show-quality male kitten for showing in the "Premiership" class, which is for altered animals. Breeders sell few of their male cats as studs, no matter how good their quality. They also do not keep many studs because of urine spraying and the problem of finding confinement space. It is possible, therefore, to buy a good-quality male, provided the new owner signs a written agreement that the cat will be neutered and be kept only as a pet.

Veterinarians are good sources of names of local breeders. They often have at least one client who is a well-respected breeder.

This person will, in turn, have the names of other reputable breeders. Attending a cat show is another excellent way to locate an experienced breeder with a suitable kitten. Breeders are anxious to have their fine neutered males exhibited, and can provide invaluable grooming and show conditioning tips. Knowledge about bloodlines and refinements of the breed standard can be absorbed better through listening and watching at shows and meetings than through reading.

Buying for the First Time: When the time finally comes to obtain the first breeding cats, the experience of showing and the contacts made are valuable assets. Most important, the new breeder is no longer considered a novice and reputable breeders are much more willing to provide them with the "perfect cat." It also is more evident to the "seasoned novice" that the perfect cat of any breed is an illusive creature. The seasoned novice is also less likely to purchase too many cats.

The initial cats purchased should be the best quality females possible from 2 top but diverse bloodlines and strong linebred pedigrees. Sound health and good personalities must be the highest priorities because these cats will provide the foundation for the desired kittens to come. The inevitable flaws of each female should be offset by the strengths of the other. If these cats could be molded together, an ideal example of the breed would be the result. Quality females in any breed are expensive, however. Part of the cost is for the seller's general assistance and guidance in selecting proper mates.

A wise way to start is to buy at least one proven female. Because she is mature, her qualities and flaws are apparent and her show achievements are known. There is assurance that she can produce and raise kittens. All of the unknowns of buying a kitten are then avoided. Occasionally it is possible to lease a top female for one litter, or co-own the cat with the seller. This may be a cat from a breeder who would like to reduce the number of litters born in their premises.

A new female kitten destined to be the basis of the breeding stock should be approximately 5 months old, and preferably already a show winner. In this way the chances of disqualifying faults, either currently going unrecognized or those developing later, are minimized.

For the beginner, use of an outside stud cat is preferable to owning one. Because the ability to pass on desired genetic characteristics seems to be stronger in male than female cats, stud cats are the heart of the cattery breeding program. There are considerable risks in buying a young unproven male kitten. Finding an available top-quality adult stud, as well as the stress of introducing him to new quarters, is also trying. By mating the foundation females with different males, it is usually possible to determine the compatibility of bloodlines. This method gives greater flexibility for future breedings and allows eventual mixing of the foundation bloodlines without close inbreeding. Use of outside stud services usually involves a contractual agreement between both parties (see Appendix for sample agreement).

Purchase, Leasing, Co-ownership and Sale of Cats: Purchase, lease or co-ownership of breeding cats, as well as arrangements for stud service, must involve written agreements to avoid misunderstanding (see Appendix for sample agreements). In addition, the greatest of care must be taken when sending cats for breeding to avoid exposing them to diseases and parasites. Sending out cats for breeding and introducing new cats are among the greatest health dangers for a cattery.

All agreements should include provisions requiring that the cats are examined by a veterinarian and certified free of any evidence of contagious disease or parasites, and tested for feline leukemia virus. As an additional precaution, it is good practice to isolate a cat accepted into a new cattery for at least 2 weeks to watch for signs of ill health. Females arriving in heat for breeding should be exposed only to the selected stud cat. Many breeders have "closed catteries," which means they do not offer stud service at all. They do this to protect the health of their males. Others allow stud service only to females belonging to a few people with whom they are very familiar.

With good planning and cattery management, eventually there are litters of healthy kittens to sell. Integral to the sale of

kittens is an understanding of breeder ethics, which helps build a cattery's reputation and generates referrals and repeat customers. One of the most important considerations is honest and objective kitten evaluation. The main purpose of breeding purebred cats is to preserve the distinguishing features and history of the breeds, and to strive for continuous breed improvement. Only the finest animals should be kept or sold for breeding.

Most of the litters, because of various faults defined by the breed standards, are sold as pets with a "Conditional Sales Agreement" (see Appendix for sample sales agreements). This ensures that the kittens will be altered when mature and not used for breeding. Ethical breeders are conscious of their responsibility to protect their breed, deter exploitation of purebred cats, control overproduction of pet kittens, and prevent use of their cats in mixed-breed matings. Registration papers are provided to the new owner, if desired, only after receipt of a certificate of altering from a licensed veterinarian. Most breed clubs have a written code of ethics that lists these restrictions and prohibits breeding to non- registered cats.

Kittens displaying potential for breeding and/or show should be retained until they are 4-6 months of age or older, depending on the breed. It is unfortunate for a seller to misrepresent a kitten as show quality, when later it is disqualified for a fault that was either overlooked or not apparent because of immaturity at the time of sale. Kittens determined to be "breeder quality" are usually those with overall good conformation and without serious faults. They may carry several weaknesses, however, that hinder show competitiveness. Breeder-quality cats can be valuable in a breeding program if they excel in some feature that is needed by the breed or a bloodline. They do best when used by experts who know how to select complementing mates and have the contacts necessary to locate and use such animals.

"Show-quality" kittens are those exceptional few who can stand up to the high competition of today's cat shows. A "top show" kitten is one that can become a grand champion and is a consistent finalist. Ethical breeders do not guarantee potential wins of a kitten. Show success depends partially on the new owner's ability to keep the cat in proper weight and condition. Estrous cycles in females and maturity in studs affect show cats in unpredictable ways, both in condition and show hall temperament.

In all kitten sales, breeders have an obligation to provide proof of testing for feline leukemia virus infection, accurate registration and health records, and to advise a new owner of any known problems that may affect future breeding use. Previous health conditions that could be reactivated should also be disclosed. Probably the most common problem that breeders must deal with is the kitten that appears healthy on the day of sale but becomes ill within a few days or weeks. Ringworm, enteric and upper respiratory diseases and ectoparasites, such as ear mites, are the most usual conditions that affect newly purchased kittens. Often these are recurrences of earlier infections brought on by stress of adjusting to a new home, or former illnesses thought to have been cured.

Sometimes a disease originating from the original cattery can occur months or years after sale. Feline infectious peritonitis, feline leukemia virus (FeLV) infection, or anomalies of genetic origin are examples. Though some infectious diseases can be troublesome, they may be eventually overcome. Serious but inapparent conditions are potentially devastating to a new owner. With the availability of accurate tests for FeLV, there is no excuse for this disease to exist in a cattery and for infected kittens to be sold. However, there still are careless breeders who allow the disease to enter their cattery. Feline infectious peritonitis (FIP) is the most troublesome chronic disease of cattery cats. Though infection occurs within the first few weeks of life, clinical manifestations of disease may not always occur until many months later. By this time the cat often has been exposed to numerous other cats, so that the source of the infection is not always traceable. To complicate matters, the disease may originate in catteries that have never had clinical cases of FIP in their resident animals.

Disorders of genetic origin, including amyloidosis, intraventricular septal defects, hip dysplasia and patellar luxation, may also be manifested months later. Because

many of these problems become widespread throughout an entire breed, it is difficult for an individual breeder to feel assured that any kittens they sell will remain disease free. The mode of inheritance of some genetic disorders is not entirely understood. The severity and time required for clinical manifestation may also vary greatly from one affected individual to another.

Though a breeder must be forthright about known problems, it is unrealistic for a breeder to be expected to offer guarantees for the overall quality or the future health of a kitten except at the time of sale. Many breeders allow a kitten to be returned within a few days or a week if the buyer is not satisfied for any reason. If a buyer insists on special long-term assurances, these should be outlined in a written agreement. However, even when there is no specific agreement, many breeders compensate the new owner in various ways for a later development that affects the health or breeding capability of a cat. This could include a partial refund of money, a replacement kitten or free stud service. Return of an unhealthy kitten is rarely possible, except within the first few days following a sale. Breeders often allow return of kittens with behavior problems. When a mature cat or stud is sold for breeding, it is usually with a guarantee for reproduction, and its return is allowed only through mutually agreed terms in a written contract.

Alternatives to Catteries

As a breeding program expands, it is important for a cattery owner to constantly reevaluate whether or not the home cattery is adequate. After a few years of breeding, the cats usually require some confinement because of estrual behavior, spraying and health considerations. With determination and imagination, a breeder can easily improve his or her home, with respect to cattery management, at minimal expense. Extra bedrooms can be subdivided by temporary solid and wire partitions to create containment units for kitten delivery and rearing. Many homes have screened porch areas or decks for exercise space. Large prefabricated bird aviaries equipped with trees, plants and platforms make excellent garden structures suitable for cats during the day. It is not difficult to leash train some cats, especially when young, and this offers an expanded world for a stud cat in areas free of fleas.

Before a home cattery becomes unmanageable, steps should be taken to prepare for building a separate structure to accommodate the optimal number of cats necessary for a planned breeding program. In some cases this is not feasible due to space, time or financial constraints. However, several methods can be used to continue breeding without overcrowding and jeopardizing the health of the cats.

Co-ownership of Studs

Breeders in America are beginning to follow the example of those in Europe, where housing is often not as spacious, by sharing ownership of a stud cat among 2-3 people. The male lives with one person who can provide good facilities. All of the partners have exclusive breeding rights, provide compensation for the cat's care, and by mutual agreement decide on all matters concerning the cat's use for outside stud service and sale of his kittens. Sometimes a co-owned stud lives for 6 months with each owner. Not all males are content to be moved from their home, so this solution should be undertaken only after consideration is given to the well-being of the cat.

Cattery Partnerships

It is not unusual for 2-3 people to work together as partners on all cattery aspects. One person's primary contribution may be travel to shows, another may be responsible for raising litters, while a third may keep several stud cats, maintain cattery records and handle correspondence, advertising, kitten sales and contracts. Though there is a certain degree of cat exchange, it is among a closed group, and this minimizes introduction of disease. This method has worked well even for breeders living in different parts of the country.

Cooperative Breeding

Sometimes several separate small catteries have a loose cooperative arrangement in which they all exchange breeding cats to increase their ability to outcross without having to buy more cats. The group has similar goals and the assurance that all partici-

pants have clean and well-managed catteries, and they never add a new member or exchange cats with outsiders without everyone's approval.

Obviously, aside from an ability to work well with each other on a long-term basis, people entering into any cooperative cattery arrangement must be willing to abide by rules set up in a written contract. Their dedication to improving the chosen breed also must take priority over the desire for individual recognition, since all bloodline and show achievements are shared.

Leasing or Co-ownership of Queens

An individual cattery owner has a few alternatives that allow adding new bloodlines without increasing numbers of cats kept. Leasing a proven queen to another breeder eliminates rearing of one or more litters, and may help provide new genes for the other breeder's line or make it possible for a novice breeder to get started. At the same time, this arrangement enables the queen's owner to receive the pick or second pick of the litter and bring in some new qualities.

Special care should be taken to ensure proper care of the female while in the other cattery. Any queen to be sent away for an extended time must have superior vigor and an adaptable temperament.

By selling a female on a co-ownership basis, the original owner gains access to the best of her kittens without having the cat as a cattery resident. The cat has the advantage of being permanently settled in a new home. Usually the buyer pays a reduced price and either returns a kitten from each litter or has ownership of every other litter. Selection of studs for the breedings is mutually decided. Often full ownership is transferred to the buyer at a later date.

When co-ownership or leasing is with a novice breeder, the seller usually has full control in selection of the stud, evaluation of kittens, and kitten sale decisions until the time of ownership transfer.

As in any other enterprise, it is very important to have contractual agreements between participating individuals (see Appendix for sample agreement). Written contracts help prevent misunderstandings on the conditions of the agreement.

Pet Cats as Breeders

A few breeders have found that placing queens in the homes of relatives and friends who enjoy them as pets helps prevent cattery overpopulation and provides the breeding females a pampered life. According to one breeder, who is also a veterinarian, "Our foster program is designed so that cats live in the home as pets. I provide stud service for the females, take care of all veterinary costs, and vaccinate the kittens and cats as needed. In exchange for keeping and loving the queen and caring for the kittens until they are 9 weeks old, the foster owners get half of any money from sale of the litter, minus the pick of the litter, which is ours to keep or sell as we see fit. At 9 weeks, the kittens move into my house. This gives me a better chance to evaluate the litter on a day-to-day basis, and the kittens learn to adjust to environmental and social changes, thus making the move into other homes at 12-13 weeks much smoother."[11,12]

Such a program avoids many of the health problems associated with a large cattery; however, it must be undertaken with some caution. Often pet owners are not accustomed to females in estrus and do not understand the extra care needed to prevent the queen from escaping the house while in heat. The new owner must also have the expertise and time to assist delivery of kittens in case of problems, and the ability to feed a queen and her litter 3-4 times daily.

It seems inevitable in cat breeding that the numbers of cats will be extended to the limit no matter what the circumstances, especially during when breeders are trying to establish a reputation through show wins. Sometimes the very limitations of space, time and money, which force a breeder to be highly selective, may actually benefit the health of the cats as well as the goals of purebred cat breeding.

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Index

C

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W, X, Y, Z

Appendix

Written agreements are often required for a number of cattery functions. The following agreements are samples of those most frequently used. They are intended for use only as guides to make breeders aware of considerations involved in cattery transactions. Certain clauses may be illegal in some states. Individual situations may also require unique agreements. To avoid legal problems, all written agreements should be reviewed by competent legal counsel before signing. Contractual agreements should not be undertaken without a thorough understanding of what is being agreed upon and the legal implication at the time of signing and in the future.

The first agreement is an all-purpose contract for sale of an adult cat or kitten for either pet, breeding or show (courtesy of Luane Fleming and *Cat Tracks Magazine*). The second agreement is for sale of kittens for nonbreeding purposes and is used by one of the authors (J. Wastlhuber). Additional sample agreements are for conditional sale of breeding males and females, stud service, co-ownership of breeding females, and lease of breeding females.

Cat or Kitten Contract

Breed _____ Color _____ Sex _____

Name (if applicable _____

Birth Date _____ Litter Reg # or Reg # _____

Sire _____

Dam _____

Sold to _____ Telephone _____

Address _____

Sold to _____ Telephone _____

For the following price or terms _____

_____ Date Paid _____

Purchaser agrees to the following:

1. Under no circumstances will this cat or kitten be sold, leased or given away, or sold to any pet shop, research laboratory or similar facility.
2. This cat or kitten will be kept indoors and not be allowed to roam freely outside.
3. This cat or kitten is purchased for Pet _____ Breeding _____ Show _____.
4. If purchased as a pet, Purchaser agrees to castrate or spay this cat between the ages of 6 months and 1 year, or within 30 days after purchase if this is an adult cat, and agrees and guarantees that this cat or kitten WILL NOT be used for stud or breeding.
5. If this cat or kitten is found to be neglected or mistreated, Purchaser will surrender said cat or kitten to Seller, unconditionally.
6. Seller agrees to provide pedigree and registration papers for this cat or kitten upon presentation of a veterinarian's certificate of castrating or spaying. Yes _____ No _____
7. This cat or kitten cannot be shown without written permission of the Seller.
8. No cash refunds.
9. If this cat is purchased as a breeder male, Purchaser agrees not to use this cat for outside stud service, except as follows: _____

_____

10. If this cat is purchased as a breeder male, Purchaser agrees not to resell the cat for stud to anyone unless approved by the Seller.
11. Vaccinated _____

Vaccine used _____ Needs revaccination _____

12. Purchaser has three working days to have blood test on this cat or kitten for feline leukemia virus.
13. Seller makes no guarantees as to the health or show quality of this cat or kitten, except as follows: _____

_____

14. This cat or kitten is being fed _____
15. Other conditions of sale are as follows: _____

_____

_____

Purchaser's signature indicates full agreement of all above conditions.

Signature of Purchaser _____ Date _____

Signature of Seller _____ Date _____

Conditional Sales Agreement

Kitten Born _____

Name _____

Description _____

Sire _____

Dam _____

Show Approval _____

Purchase Price _____

The above kitten is sold to _____

on _____ with the understanding that he / she is not to be used for breeding purposes. The kitten must be castrated / spayed between 6 and 9 months of age.

Upon receipt of a licensed veterinarian's written certification, showing that an altering operation has been performed, the above kitten's pedigree and registration application will be forwarded if requested. If altering certification has not been received by _____, the undersigned Buyer agrees that the Breeder has the right to reclaim the above kitten without refund of the purchase price. Reasonable legal fees incurred in so doing will be paid by the Buyer.

Medical Record

Signed _____

Buyer

_____

_____

_____

Address

_____

Telephone

_____

Breeder

Conditional Sales Agreement

Breeding Female

This Agreement concerns _____ , CFA Registration Number _____ and is between _____Seller_____ and _____Buyer_____.

General Conditions

The female, _____ , will be sold to _____ for $ _____. She will be sent with a veterinarian's certificate showing her to be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will also be provided, as well as proof of FeLV negative status of all cats residing in the Seller's cattery. The Buyer shall provide the Seller with proof of FeLV negative status of all cats residing in the Buyer's cattery.

_____ may be returned to the Seller within 10 days if the Buyer is not satisfied for any reason. There are no guarantees given on future health, show achievements or reproductive capability, except as follows: _____

_____.

Should the Buyer at any time in the future decide to sell _____ , the Seller will be given first opportunity to buy her at $ _____. Should the Seller not be able to take _____ at that time, she may be offered for sale as an intact (unspayed) cat to another party only with the Seller's written approval of the new potential owner before final sales arrangements.

Option for Kitten

The Seller will have the option to buy the first show/breeding quality female or the first show/breeding quality male kitten the Buyer offers for sale from the first litter produced by _____.

The price for this kitten will be $ _____. The time of selection will be after the kittens reach 4 months of age but before 6 months. Kittens displaying show faults, as defined in the breed standard, may be sold as pets earlier.

Should the Seller choose not to exercise this option, there will be no further obligation on the part of the Buyer to offer a kitten from future litters.

	_____	_____
Agreed	Seller	Buyer
	_____	_____
	Date	Date

Conditional Sales Agreement

Breeding Male

This Agreement concerns _____ , CFA Registration Number _____ , and is between _____Seller_____ and _____Buyer_____.

General Conditions

The male, _____ , will be sold to _____ for $ _____. He will be sent with a veterinarian's certificate showing him to be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will also be provided, as well as proof of FeLV negative status of all cats residing in the Seller's cattery. The Buyer shall provide the Seller with proof of FeLV negative status of all cats residing in the Buyer's cattery.

_____ may be returned to the Seller within 10 days if the Buyer is not satisfied for any reason. There are no guarantees given on future health, show achievements or reproductive capability, except as follows: _____

_____.

Should the Buyer at any time in the future decide to sell _____ , the Seller will be given first opportunity to buy him at $ _____. About 6 months' notice is to be given of intent to alter or sell him. Should the Seller not be able to take _____ , then he may not be sold except as a neutered pet.

It is understood that _____ is to be generally not available as an open stud. Should an exceptional stud service be desired by the Buyer, then the Seller's written approval shall be obtained before any arrangements are concluded.

Breeding Rights

The Seller will have the right to send no more than one female per year for breeding to _____ , commencing with the CFA Transfer of Ownership. The Stud Fee will be $ _____. Any female sent to be bred shall be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will be provided. Intention to send a female shall be made known to the Buyer at least 2 months before the planned mating. A recent FeLV negative certificate for the stud, _____ , will be sent to the Seller as soon as possible thereafter. If the queen does not conceive, resorbs or aborts her litter, or does not deliver at least two live kittens surviving to the age of 8 weeks, she may be returned, after satisfactory veterinary examination, for rebreeding with no additional stud fee.

Agreed

_____	_____
Seller	Buyer
_____	_____
Date	Date

Stud Service Agreement

This Agreement concerns the stud cat, _____ , CFA Registration Number _____ , owned by _____Party 1_____ , and the queen, _____ , CFA Registration Number _____ , owned by _____Party 2_____.

Stud Service Conditions

The queen, _____ , will be sent to Party 1 with a veterinarian's certificate showing her to be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will also be provided, as well as proof of FeLV negative status of all cats residing in the cattery of Party 2. Party 1 shall provide Party 2 with proof of FeLV negative status of the stud cat, _____.

Party 2 will pay all expenses for shipping the queen, including health certificates. Party 1 will be responsible for the good health and well-being of the queen while she is visiting; however, total liability shall not exceed the amount of the stud fee.

The stud fee will be $ _____ , payable at the time the queen is sent to Party 1. If the queen does not conceive, resorbs or aborts her litter, or does not deliver at least two live kittens surviving to the age of 8 weeks, she may be returned, after satisfactory veterinary examination, for rebreeding with no additional stud fee. If for any reason the stud cat, _____ , is not available for rebreeding at that time (sold or altered, etc), another stud owned by Party 1 will be offered. Party 2 may instead have half of the paid stud fee reimbursed and this Agreement is terminated.

Party 1 has the first option to purchase one kitten from any available for sale from this breeding for the price of $ _____. The selection of a kitten for purchase by Party 1 must be made within one month after Party 2 has notified Party 1 that one or more kittens are available for sale.

All offspring produced by the above breeding may be sold, leased or loaned for breeding and championship show purposes only to individuals who have been approved in writing by both Party 1 and Party 2. All kittens sold as pets or for premiership (altered) show purposes must go with a written Agreement requiring castrating or spaying.

Should any cat resulting from the above breeding be offered for sale at a future time by either party, the other will have first option to buy the cat for a price established at that time. This price will not be higher than that subsequently offered to any other party.

Agreed

_____	_____
Party 1	Party 2
_____	_____
Date	Date

Co-Ownership Agreement

Breeding Female

This Agreement concerns _____, CFA Registration Number _____, and is between _____Party 1_____ and _____Party 2_____.

Co-Ownership Conditions

Party 2 will pay Party 1 the sum of $_____.

_____ will be bred to the stud cat, _____, owned by Party 1, with no stud fee.

_____ will be sent with a veterinarian's certificate showing her to be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will also be provided, as well as proof of FeLV negative status of all cats residing in the cattery of Party 1. Party 2 shall provide Party 1 with proof of FeLV negative status of all cats residing in the cattery of Party 2.

When _____ arrives in the cattery of Party 2, all subsequent veterinary or other costs for care will be provided by Party 2.

Should _____ not conceive, abort her litter, or should all kittens die, she will be returned for rebreeding after being certified in good health by a veterinarian. Should she fail again to produce a live litter, she may be spayed or returned to Party 1. If she is returned, Party 1 will reimburse Party 2 $_____.

Party 1 will have first pick of the litter and Party 2 will have second pick of the litter. The time of selection will be after the kittens reach 4 months of age but before 6 months. Kittens displaying show faults, as defined in the breed standard, may be sold earlier by Party 2 as pets to be altered. If only one kitten is born, this kitten will belong to Party 1 and if sold will be first offered to Party 2.

Proceeds from the sale of any kittens in the litter, aside from first and second pick, will be split between the two parties.

The litter will be registered with CFA, with Party 1 listed as Breeder, and all kitten registrations will bear the cattery prefix of Party 1.

In the case of loss of _____ for any reason, Party 2 will not be held liable and Party 1 will not reimburse the initial sum paid for her.

Transfer of Ownership

Following satisfaction of the above conditions and upon Party 1's taking possession of pick of the litter kitten, the CFA registration certificate of _____ will be signed over to allow Party 2 to apply for transfer of ownership and obtain full ownership of _____.

Should either party in the future decide to sell their pick kitten, the other party will have first option to buy. Should the other not elect to take this kitten, it may be sold to another party only with written approval of Party 1 and Party 2. This shall not be unreasonably withheld.

Agreed

_____	_____
Party 1	Party 1
_____	_____
Date	Date

Other co-ownership alternatives to consider:

- The Agreement is extended to allow for two or more litters before transfer of ownership.
- Party 1 has ownership of all kittens in the first litter and Party 2 has ownership of all kittens in the second.
- Pick and second pick of the litter could be reversed between parties.

Lease Agreement

Breeding Female

This Agreement concerns _____, CFA Registration Number _____, and is between _____Lessor_____ and _____Lessee_____.

General Conditions

The female, _____, will be leased to the Lessee for one litter. The litter will be registered with CFA, with a copy of this signed Agreement as proof of lease, showing the Lessee listed as "Owner" and bearing the cattery prefix of the Lessee.

_____ will be sent with a veterinarian's certificate showing her to be in good health and free of any contagious condition, illness or parasites. A recent FeLV negative test certificate will also be provided, as well as proof of FeLV negative status of all cats residing in the Lessor's cattery. The Lessee shall provide the Lessor with proof of FeLV negative status of all cats residing in the Lessee's cattery.

The Lessee will pay all expenses for shipping the queen, including health certificates, and will also be responsible for the good health and well-being of the female while she is in his care and will pay for any necessary veterinary expense. In case of loss, the total liability will not exceed $_____.

_____ will be bred to a stud selected by the Lessor, with the stud fee paid by the Lessee. If the stud selected is owned by the Lessor, there will be no stud fee charged and _____ will be sent to the Lessee after palpation at 3 weeks to determine pregnancy. Should _____ abort her litter or deliver only one kitten surviving to the age of 8 weeks, the Lessee will have the right to enter into another Lease Agreement for this or another female owned by the Lessor.

As compensation for lease of _____, the Lessor will have the pick of the litter. This kitten will be selected after the kittens reach 4 months of age but before 6 months. Kittens displaying show faults, as defined in the breed standard, may be sold as pets by the Lessee earlier and must go with a written Agreement requiring castrating or spaying.

All offspring produced in this litter may be sold, leased or loaned for breeding and championship show purposes only with approval of the Lessor and only to individuals who have been approved in writing by the Lessor. If the Lessor cannot evaluate the litter in person, he has the right to have an experienced breeder or judge do this in his place.

_____ must be returned to the Lessor when her kittens are between 12 and 16 weeks old. She will be returned in good health.

	_____	_____
Agreed	Lessor	Lessee
	_____	_____
	Date	Date