Microbe Hunters of the 21st Century: Reinventing Epidemiologists

Dyar Lecture Series – Davis, CA
May 30, 2001
Lonnie J. King

Introduction

The environment in which humans and animals evolved and developed their basic defenses against disease remained relatively stable for thousands of years. However, during the past century, the earth's physical, social and economic environment has changed with unprecedented rapidity. Humans have altered between one-third to one-half of all landmasses, our water supplies have been contaminated, the climate has destabilized, the human population is expanding at a rate of 80-100 million per year, and our public health infrastructure has deteriorated.

Concurrently, there has been a significant increase in human tourism, migration, and trade which has allowed microbes access to large populations. Ecosystems have changed dramatically and the juxtaposition of human and animal populations have greatly increased the likelihood of new zoonotic, emerging disease outbreaks. Indeed, there is a huge biological mixing bowl that is planet-wide. Earth is nothing but a crazy quilt of microbial sources scattered all over its 196,938,800 square-mile surface. Their forces are overwhelming and they evolve, adapt, and draw from their vast mobile genetic lending library constantly accessible in their environment.

Historically, diseases and microbes have altered the fate of nations and even the rise and fall of civilizations. Even today, there is a growing concern about the implications of the global infectious disease threat in terms of health, economics, foreign policy, and national security.[1]

Human ecology and behavior, along with the constantly changing nature of pathogens, are factors that have greatly altered the incidence and patterns of disease. Epidemiology is the study of patterns of disease in populations and the factors that determine their occurrence; epidemiologists connect the many seemingly unrelated events and factors to better understand and alter the course of diseases.[2]

As we begin the 21st century, epidemiologists better appreciate the fact that conditions other than diseases caused by infectious agents profoundly impact our health. Yet, at the same time, microbes too have entered a new era and the challenges to public health have never been greater. Today's mingling of people, animals and microbes in completely different environments has no historical precedent. The world really is becoming just one large village. And surely as Laurie Garrett suggests, we do await the coming plague.[3] Certainly, the scope and complexity of epidemiologic principles characterize the 21st century and will lead to the reinvention of microbe hunters. The following discussion highlights the new perspective, scientific advances, environmental and social changes, and a new emphasis on zoonoses that will be the context for reinvention and represent the challenges of the new microbe hunters of tomorrow.

Microbe hunters were popularized by the writings of Berton Roueché in a series for the *New Yorker* magazine and later put together in a collection, *The Annals of Epidemiology*, 1967. Roueché's stories were influenced by the adventures of Sherlock Holmes. The tales were often complicated stories with blind alleys, red herrings, and heroic investigators. Much of the romanticism of the stories and protagonists centered around the epidemiologists associated with the Centers for Disease Control and Prevention's (CDC) Epidemic Intelligence Service (EIS) under the U.S. Public Health Service. Interestingly, the EIS began in 1951 under the leadership of its first director Dr. Alex Langmuir, and was a congressional mandate at the time as a result of fears of biological warfare during the time of the Korean War.[4]

The historical references to the great plagues of early Egypt, the Black Death of the mid-14th century, the great epidemics of rinderpest in the cattle population of Europe and the Spaniards introducing smallpox and measles to the western world, retrospectively, added to the interest of microbe hunters and epidemiologists.

The World Divided in 2025

The world of human hosts, demographics and future trends suggest that epidemiologists will be especially challenged in the 21^{st} century when considering potential public health scenarios.

By 2025, there will be approximately 8.4 billion people on earth. Thus, between 80-90 million people will be added to the world population each year over the next few decades. World population will divide into three tiers:[5] at the top, World 1, made up of advanced nations and the world's middle classes living in prosperity (e.g., U.S., Japan, Germany); and in the middle, World 2, a vast range of people living comfortably but not extravagantly in the context of their culture; and, World 3, people living in destitution and poverty. There is estimated to be 450 cities in the world that have populations of at least 10 million. This massive urbanization will also experience failure of sanitation systems, unhealthy water supply and further degradation of the environment.

These three populations will have distinct disease challenges and because of social and economic forces will interact in numerous ways producing new environments for the spread and dissemination of diseases. Epidemiologists will continue to investigate infectious diseases that were problems in the 18^{th} and 19^{th} centuries – tuberculosis, cholera, typhus and plague. Yet, at the same time, populations in the World 1 categories will benefit from the fruits of genetic research and technological advances in human and veterinary medicine. Steady socioeconomic progress will not be soon to overcome the abject poverty in a number of developing countries. Because of these countries' incomplete transition to health, a heavy infectious disease burden will be prolonged and the least developed countries will sustain their role as reservoirs of infection for the rest of the world.

While 19^{th} century epidemiologists were using the power of observation to offer theories of disease, 21^{st} century epidemiologists will take on the role of information arbitrage experts. Health, more and more, is not defined by the absence of disease; rather, it will be defined by enhanced conditions of one's quality of life and productivity.

Global Contradictions

Humanity seems to be left with a disturbing, contradictory picture of the new medicine. On the one hand, true miracles are ahead. On the other, a grim, global, social context challenged all optimism.

The 20th century began with a medical revolution sparked by the microscope opening people's eyes to agents of disease. Epidemiologists were driven by the Germ Theory, the discovery of diseases and the advent of prevention and control strategies. With the discovery of DNA in 1953 and the beginning of genetic engineering techniques, medicine entered the Genome Era. Single gene diseases will be eliminated and many diseases that occur today because of genetic predisposition will also be eradicated. Vectors of disease will be altered to eliminate their pathogen-carrying capacity and molecular processes and implanted sensors will feed data into individual smart cards that already have our entire genetic map available. Medicine will then shift to another context of family medicine – based on a family's genes. In considering the future and role of epidemiologists Dr. Richard Klausner, the Director of the National Cancer Institute, in a recent speech suggests that there are three key areas of scientific innovation: human genetics, protein chemistry, and nanotechnology. Without question, medicine will focus on the prevention of chronic diseases – cancer, strokes, diabetes, Alzheimer's, and dozens of others – through interventions either at the genetic or protein level. In the future, we will be able to inject microscopic detectors and these "nanoprobes" will seek out cancers and eventually destroy cancer cells.

While the 20th century began by focusing on the germs, it ended with a genome era. At the dawn of the 21st century, the genome era will soon be passing its baton to the "Age of Proteomics," promising an upheaval in pharmaceuticals and medicine that many believe will be every bit as dramatic as is the discovery of rabies and TB by Pasteur and Koch. There could likely be a new protein-based preventive medicine for the 21st century.

We have entered into a renaissance in microbiology and genomics. Our ability to define genomes affords us great opportunities for comparative analyses. Genetic analyses of pathogens are leading to new insights as we reconstruct the origins and evolution of disease and infections. The ability to retrospectively understand the ecology of pathogens and diseases gives us clues as to the future changes and ecological variations of pathogens. The 21st century epidemiologist will have an impressive array of new tools and will have computational biologists, biocomplexity experts, paleopathologists, and bioinformatic specialists as associates and co-workers.

However, all of these seemingly wonderful changes will not take place without unintended and potentially serious consequences. 21st century epidemiologists, who also need to understand the role of microbes, will now also be asked to evaluate and analyze new healthcare alternatives and new interventions supposedly leading to enhanced health.

Transforming Life

Enriquez and Goldberg predict that advances in genetics and proteomics will also help create an entirely new life science industry that will be characterized by the convergence of agriculture, pharmaceuticals, health care, and computing.[6] Goldberg has estimated that this new life science conglomerate may be a $15 trillion business that will reshape vast sectors of the world economy in the next 25 years.

This transformation will likely change the future of food. Instead of food being just a necessary staple of our existence, food will become an essential component of our health, quality of life, and enhanced productivity. Food will be combined with medicine, vaccines, and nutraceuticals to produce new foods to meet special health needs and improve our health status and medical well-being.

Many of these remarkable possibilities will become our reality, yet as we learned with the advent of biotechnology and genetically modified foods, a constant and long-term monitoring and evaluation of these products and their consequences will be necessary. This is a perfect role for 21st century epidemiologists. They will need to bring objectivity and advanced tools to this opportunity. Albert Schweitzer said that "Man can hardly recognize the devils of his own creation." Although these wonderful scientific breakthroughs will improve our lives, there is a social acceptance and trust that will also need to be gained. Can epidemiologists broker this special challenge?

Origins of Human Diseases from Animal Diseases

Jared Diamond views the world history as an onion, of which our modern world constitutes only the outer surface and whose layers are peeled back in the search for historical understanding as we seek to grasp our past lessons for our future.

The author makes a case that animal origins of human disease lie behind the broader pattern of human history, and behind some of the most important issues in human health today. Diamond discussed two types of diseases: (1) individual diseases characteristically found in small isolated populations which are the oldest diseases of humanity; and (2) crowd diseases which followed the buildup of large, dense populations. This buildup, according to Diamond, began with the rise of agriculture about 10,000 years ago and then greatly accelerated with the rise of cities starting several centuries ago.[7]

Agriculture sustains much higher human population densities than the hunting-gathering lifestyle – on the average 10 to 100 times higher. The rise of farming was then a benefit to the world of microbes. Diamond's other premise is that these pathogens were not part of the microbial ecology of small isolated populations. Rather, they evolved as a result of humans choosing interactions with animals and livestock. Evolutionary microbiologists and molecular epidemiologists can now identify the closest relatives of our disease-causing microbes of today. He believes that animal and livestock diseases were also diseases of crowding that caused various epidemics. Hence these diseases were transferred to people and continued to adapt and survive in today's society. Diamond described the deadly gifts from our animal friends as measles (from rinderpest), tuberculosis (from *M. bovis*), smallpox (from cattle pox), flu (from avian and porcine influenzas), and malaria (from pigs, dogs, and birds).

Diamond's theories are interesting considering the context of our current era of emerging and re-emerging diseases. Given our proximity to our pets and livestock and closer interfaces with wildlife and their vectors of disease, we seemingly are continuing to prove Diamond's premises. Almost 70% of emerging diseases of the last few decades are zoonotic in nature.

Ensuring Safe Food

Dramatic changes in our food supply including the restructuring of food-animal agriculture into large, concentrated production units have contributed to recent outbreaks of infectious food-borne illnesses and toxic agents. It would appear that our livestock and poultry populations are not finished in passing on more deadly gifts to mankind.

At least five trends contribute to food-borne diseases in the U.S.: changes in diet, the increasing use of commercial food services, new methods of producing and distributing food, new or re-emerging infectious foodborne agents, and the growing numbers of people at risk for severe or fatal foodborne diseases.[8]

E. coli 0157:H7, Cyclospora, Cryptosporidium, salmonella enteritidis, and *S. typhimurium* DT104 are examples of food-borne pathogens that have caused significant disease. *S. typhimurium* DT104 has been referred to by some as the "super bug" because of its emergence as a multiple drug-resistant organism and rapid distribution around the world.

Changes in Host Susceptibility

The 21st century will create another interesting epidemiologic phenomenon. There will be an unprecedented number of elderly people in the global population. In 1998, there were 580 million over-sixty-year-olds, including more than 355 million residing in the poorest countries. The WHO predicts that by 2020, there will be a billion elders on earth of which 700 million will be living in developing countries.[9]

Veterinarians understand the concept of herd immunity from our experiences in observing herds and flocks of animals and gauging their vaccination and immunity levels. A critical threshold of immunity is needed to protect a herd (or community), but the threshold is less than 100%. What can be expected in the 21st century with decaying immune systems of huge numbers of the elderly? In the U.S., with the aging Baby Boomer generation, we can anticipate that 30% of our population will be considered part of our elderly population. There have been no precedents from which to derive predictions, except perhaps from our recent experience with HIV and AIDS. Will childhood diseases again emerge but this time the senior population and the elderly who are progressively immunocompromised?

Rapid Movements of Pathogens

In 1346 a particular set of circumstances occurred, in a strange sequence, that produced the first truly global epidemic—Black Death. With epidemics, timing is everything. *Yersinia pestis* had been infecting fleas and rodents for centuries before 1346 with only an occasional human victim. Then a new globalization emerged: the "silk route" brought caravans of goods across Asia, and sailing ships began dispersing people and products among countries. At the same time, almost 20% of the population was crowded into cities, ports, and trading posts. This early globalization also created new opportunities for *Yersinia pestis*. Probably weather conditions were also propitious and the population of fleas, rats, and pathogens expanded and spread across continents. Within 18 months, millions of people were dead of bubonic plague.

In the 16th century, global travelers were few and slow. By the 17th century, European nations were amassing wealth through global conquest and trade. Today, our world that was once globalized for kings and queens, is accessible to the masses – millions on the move, billions of humans on earth, trillions of tons of cargo, crops, and animals. New global risks have grown exponentially. The new globalization is pushing communities against one another.

Thus, a remarkable milieu of new risks and opportunities for pathogens from all parts of the world has been created. René Dubos in the mid-twentieth century stated that we should "think globally, and act locally." As we begin the 21st century, the reverse is true. Global public health and emerging infectious diseases will be critical to future exposure experiences of literally billions of people.

A good example is tuberculosis. In the 1970s, TB was widely assumed to be waning into insignificance and the elimination of human TB seemed to some, to be imminent. Yet today the disease burden of TB defies exaggeration. Incredibly, at the beginning of this millennium, one-third of all people alive are thought to be infected with *M. tuberculosis.* Approximately 10% of TB infections will actually develop into active, "open" cases. Thus, 200 million people alive at the start of the 21st century will eventually develop clinical TB, which far exceeds the total estimated number of TB cases that occurred over the course of the entire 19th century. This year, more people will die with TB worldwide than in any previous year in our history (2-3 million). Multidrug-resistant strains of TB render past treatment regimes useless. We probably did a better job of controlling TB by social factors at the time Robert Koch discovered the pathogen than through contributions more than a century later.[10]

Since 1800, the average distance and speed that people travel has increased one thousand-fold, while there has been no change in the incubation periods of the pathogens. Today more than 1.4 billion people travel by air annually and a half billion of these travel international. At any given moment there is a veritable city of 61,000 people in flights over North America. Fifty million passengers now arrive in the U.S. from overseas each year on some 500,000 flights at some 102 international airports.

In addition to transporting all types of diseases and pathogens, vectors and antibiotic-resistant organisms will also hitchhike along to add to the potential risk for U.S. citizens. The risk is further heightened by the movement of products and foods of plant and animal origin. For example, Cyclospora was transported to the U.S. with raspberries from Guatemala in 1996 and caused several major outbreaks. Before 1996, this protozoan was merely a medical curiosity in the U.S.

Another mechanism for the transportation of pathogens is in ballast water from ocean-going ships, which release ballast tanks of water at ports. Epidemic cholera is the most recent case. Genetic analysis of *Vibrio cholera* bacteria in South America has linked their epidemics to the transportation of the pathogens from Asia to the coastal fisheries and ports of Peru. In addition to pathogens, ballast water often contains aquatic organisms that are releases into new marine ecosystems thousands of miles away. Zebra mussels found their way into the Great Lakes of the U.S. in this manner.

The Livestock Revolution of 2020

At the same time that the world's population grows and interacts, agriculture may be engaging in a new revolution – the livestock revolution that many believe will be an unprecedented event in agriculture.[11] This revolution will have profound implications for our health, livelihoods and environment. Population growth, urbanization, and income growth in developing countries, especially those considered in the World 2 category, are fueling a massive global increase in the demand for food of animal origin. The resulting demand comes from changes in the diets of billions of people. Animal agriculture is already restructuring into fewer but considerably large production units and issues of sustainability are being questioned. Developing countries will be especially challenged as they attempt to keep up with the demand for animal protein sources for their growing populations.

This revolution will, of course, have some negative implications such as stress on new resources, waste management, and the concentration of large numbers of animals in urban environments close to the closer populations of people and the potential for increases in zoonotic diseases and new emerging disease situations. In addition, the “westernization” of diets that result in an over-consumption of animal foods raises other public health concerns. The livestock revolution will be one of the largest structural shifts to ever affect food markets in developing countries, and will lead to issues of food security, environmental sustainability, food safety and public health. Based on our understanding and appreciation of the new foodborne and waterborne pathogens of the late 20th century, the next two decades may greatly expand the scope and complexity of new zoonotic pathogens.

Multihost Pathogens

Perhaps of special interest to veterinarians are pathogens capable of infecting more than one host species. This includes 60% of human pathogen species that are zoonotic, causing diseases of major public health concern, such as influenza, sleeping sickness, Lyme disease, food poisoning, and variant CJD. It also includes more than 80% of pathogens of domestic animals, notably those causing 57 of the 70 livestock diseases of greatest international importance, such as rinderpest, foot-and-mouth disease, and bluetongue.[12]

Many of these pathogens that infect multiple hosts are also transmitted by multiple hosts and can be regarded as ecological generalists rather than specialists.

Scientists and population biologists are now attempting to better understand selection pressures, crossing species barriers, transmission mechanisms, and the changes in pathogenicity that produce outbreaks and epidemics. These issues are of increasing importance in the context of emerging diseases.

Comparing Epidemics at the Close of the 19th and 20th Centuries

One of the most productive times in the history of biomedical research occurred from 1880-1885 when the pathogens of five globally important infectious diseases were discovered: leprosy, malaria, tuberculosis, cholera, and typhoid fever. Field research was the key to these discoveries as 19th century epidemiologists worked on both the cause and transmission of these diseases.

In comparison, the major epidemics at the close of the 20th century were Hanta virus, Bovine Spongiform Encephalopathy, influenza (Hong Kong 1998), Nipah virus, and most recently, West Nile virus. While field research is still part of the investigative process, epidemiologists have a new appreciation of the complex dynamics of the emergence and transmission of diseases. It is also of interest to note that these latest epidemics are all zoonotic diseases.

Modern microbe hunters today may even identify potential pathogens before they find new susceptible hosts, i.e. agents looking for disease. Over a century ago, the opposite was true. For example, recent field research conducted in Australia disclosed that fruit bats carry a number of viruses that could be deadly in other hosts. Hendra virus, Menangle virus, and Australian Bat Lyssavirus have all been isolated recently from fruit bats. These bats have a wide distribution globally and one can certainly expect that viruses related to these Australian viruses exist and will likely produce human diseases. Thus, there are two types or patterns of vectorborne zoonotic diseases involving viruses: (1) increases in known diseases through higher incidence or geographic spread; and (2) novel diseases that have not been previously recognized emerging as disease pathogens as they infect new hosts and cross species lines.[13]

Chronic Diseases may be Result of Infectious Agents

The balance of evidence suggests that the major infectious plagues are not emerging from the African jungle. They are already here, embedded in every society and, in fact, have been here for centuries. While not manifested as epidemics, they are nevertheless slow-motion plagues that have spread more insidiously and slowly. The major uncertainty is just how many infectious plagues are smoldering. A substantial portion of pain and suffering that is occurring at the dawn of this new century will be recognized as the result of long-standing, slow-burning plagues that are infectious, but were not generally accepted as being infectious in the year 2000.[14]

Challenges to the microbe hunters of the 21st century are no longer easy-to-recognize acute infectious diseases. Rather, they are the stealth infections that insidiously generate a cancer or neurological damage or a lesion in an artery wall. They kill in slow and less apparent ways and not due to obvious infections. What should a modern day microbe hunter do? Investigate the chronic diseases that most experts do not think are caused by infection, and figure out how to control them; this may be as productive and with positive effects on human health as the challenges met by those who applied the germ theory to acute infectious diseases years ago.

Influenza – A Complex Zoonosis

Influenza pandemics are typically characterized by the rapid spread of a novel type of influenza virus around the world, resulting in high numbers of illnesses and deaths for about 2-3 years. Such pandemics occurred in 1918, 1957, and 1968. The famous influenza epidemic of 1918 resulted in at least 20 million deaths.

Molecular analysis of viral nucleic acid supports the hypothesis that animals, in particular birds and hogs, were probably the source and reservoir of key genes found in the pandemics of the past.[15] Because of the different seasonality of influenza in northern and southern China and the close contact among humans and hogs and birds raised for food, most new strains of the virus are products of the reassortments that occur in this favorable ecological milieu. The World Health Organization is stressing the need for better animal surveillance in order to better evaluate and predict the status of influenza outbreaks and epidemics. The new microbe hunters will need to do more work with evaluating and analyzing the dynamics of diseases among species and across species lines.

Global Warming

Today there is a consensus of scientists that agree that the atmosphere is warming. Recent computer models predict that global warming, and other climate alterations it induces, will expand the incidence and distribution of many serious medical disorders.[16]

Vectorborne diseases, especially those transmitted by mosquitoes such as malaria, dengue, yellow fever and several encephalitises, are of greatest concern with global warming. Some computer models predict that by the end of the 21st century, ongoing warming will have enlarged the zone of potential malaria transmission from an area containing 45 percent of the world's population to an area containing about 60 percent.

In addition, warming is causing shifting patterns of rains, storms and floods. Floods often favor the dissemination of waterborne problems like cholera and cryptosporidia. The heating of the atmosphere can also produce variable climactic conditions often conducive to the overwintering of vectors. Thus, St. Louis encephalitis, West Nile virus, and other infections that cycle among birds, urban mosquitoes and humans will have favorable conditions to spread.

West Nile Virus: An Emerging Global Zoonosis

West Nile Virus (WNV) was first identified as a pathogen in the West Nile region of Uganda in 1937. The first known human and avian cases occurred in New York in August of 1999. The spatial and temporal juxtaposition of avian and human infections and eventually equine, in this instance and historically, has led many epidemiologists to conclude that the birds act as introductory hosts and ornithophilic mosquitoes in turn infect other hosts, including humans.[17] This has been the case for both Eastern and Western Equine Encephalomyelitis viruses which are ecological relatives of the West Nile virus.

Subsequently, New York City recorded 62 human cases with 7 deaths and literally thousands of birds dead in the same area. At this point it is only conjecture regarding the entry of WNV into the U.S. Certainly, an infected mosquito “hitchhiking” on an international flight could have been the culprit. Yet, just as likely is the possibility of migratory birds or displaced birds harboring the infection brought the WNV to the U.S.

There are a series of 4 major bird migration routes that pass through New York City. In addition, a few birds, particularly seabirds, are carried by tropical storms across the Atlantic each summer from their native environs near the coast of West Africa. WNV is now seemingly well on its way to spreading across the temperate climates of the U.S. Epidemiologists are now determining the viremic potential of North American bird species in order to understand and predict the future of this virus and its dissemination in the U.S.

Threats to Biodiversity

Because we live in a world of great mobility and population expansion, novel interactions and new exposures of pathogens within pristine populations are more likely to occur. The introduction of pathogens, termed pathogen pollution, is increasingly recognized as a significant threat to global biodiversity and forms an integral part of human history.

While this epidemiologic phenomenon has been well recognized in human and domestic animal epidemics, there is now new evidence that suggests the emerging infectious diseases are increasingly found to be the cause of death in free-living wild animals found in both terrestrial and marine habitats.

Global declines in amphibian populations are perhaps one of the most pressing and enigmatic environmental problems of today. While some declines are clearly due to habitat destruction and toxins and chemicals in our environment, emerging infectious diseases in these wildlife species are clearly playing an increasing role in that significant population decline.[18]

A good example is the finding of chytridiomycosis, a fungal pathogen, in Australia and Central America. The pattern of amphibian deaths and population declines associated with chytridiomycosis is characteristic of a newly introduced virulent pathogen dispersing through a naïve population. This example of pathogen pollution threatens the survival of several wildlife species. However, these effects of introduced wildlife pathogens may be more far-reaching and subtle with ripple effects permeating through the entire ecosystem and significant impacts on other population species.

The Flow of Biota in the Atmosphere

As we consider the influence of environment and ecosystems on the patterns of disease, it is important to understand the aerial flow of biota. Aerobiology is the study of factors and processes that influence the movement of biota in the atmosphere. The diversity of the types of biota that move in the atmosphere is immense. Aerobiota include plant and animal viruses, fungi, bacteria, pollen and seeds, soil, nematodes, arthropods, and birds.

The temporal and spatial scales which are relevant for organisms that move in the atmosphere range from weeks to seconds and from continents to leaf parts. Biota can flow from one geographic place through the atmosphere to colonize an entirely different habitat.

The importance of long-distance aerial movements of organisms and vectors as a fundamental component of the dynamics and epidemiology of populations in North America have been recognized in both plants and animals. For example, the spread of western equine encephalitis virus in 1981 took place in the North American corridor through migrating waterfowl and/or windborne mosquitoes. The mosquito vectors, *culex tarsalis,* which overwinter along the U.S. Gulf coast, may have traveled between 1,200-1,300 km over 18-24 hour periods in the atmosphere and were washed out periodically by precipitation associated with recurring cold fronts.[19]

The Ocean as a Conduit of Disease

The ocean can act as a conduit for a number of human diseases. The distribution of viral, bacterial, and protozoal agents and algae toxins in marine habitats depends on the interplay of currents, tides, and human activities.

Coastal and estuarine circulation patterns influence the frequency and geographic pattern of harmful algae blooms. Pathogens from human or animal waste contaminate coastal and estuarine areas through freshwater runoff from sewers, rivers, and streams. Viruses such as hepatitis A and poliovirus and bacteria such as *E. coli* and *Salmonella* of fecal origin become concentrated in filter-feeding shellfish such as oysters and clams. Marine pathogenic bacteria like *Vibrio cholera* can invade new areas through the transport of ballast water of ships. Thus, shipping activities can introduce a disease from one part of the world into a new location causing ecological, economic, and human health problems. Finally, international trade transmits toxins and pathogens through commerce in seafood.[20]

Conclusion

Laurie Garrett, the author of *The Coming Plague*, is concerned that human and veterinary medical colleges and graduate schools are no longer producing public health experts with the interests and skills to recognize and understand the perturbations of our microecology and microbial threats. Thus, we are being lulled into a complacency born of proud discoveries and medical triumphs, but unprepared for the coming plague.[21] We must not forget that one of the responsibilities and obligations of veterinary medicine is our involvement with improving the public’s health and wellbeing.

I hope today that you have a better picture and understanding of the role of epidemiologists in the 21st century. We live in an exciting time full of remarkable opportunities; yet, at the same time, we also live in a new era of emerging diseases impacting human, animal and plant diseases individually and collectively.

William McNeill, in his landmark book *Plagues and Peoples* (1976), stated: "Ingenuity, knowledge, and organization alter but cannot cancel humanity's vulnerability to invasion by parasitic forms of life. Infectious disease which antedated the emergence of humankind will last as long as humanity itself, and will surely remain, as it has been hitherto, one of the fundamental parameters and determinants of human history”.[22]

The dynamics and interactions of hosts, pathogens and environment are like the changes seen as we rotate the cylinders of a kaleidoscope and produce totally new pictures of our world that will continue to alter human history. I hope that there will be several new 21^{st} century microbe hunters emerge from this group of students. You will certainly be involved in an exciting career that stretches both your intellect and ingenuity. You will make great contributions and make a real difference while improving both human and animal health.

References

[1] National Academy Press. *Infectious Disease in an Age of Change*. B. Roisman, Editor. N.A.S., Washington, D.C., 1995.

[2] Thrushfield, Michael. *Veterinary Epidemiology.* Butterworth and Co., London, England, 1986.

[3] Garrett, Laurie. *The Coming Plague*. Penguin Books, New York, NY, 1996.

[4] American Museum of Natural History. *Epidemic! The World of Infectious Disease.* Rob DeSalle, Ed., New Press, Washington, D.C., 1999.

[5] Coates, J.F., Mahaffie, J.B. and Hines, A. *2025.* Oakhill Press, Greensboro, NC, 1997.

[6] Enriquez, J. and Goldberg, R. *Transforming Life, Transforming Business: The Life Science Revolution.* Harvard Business Review, March-April, 2000: 96-104.

[7] Diamond, Jared. *Guns, Germs, and Steel*. W.W. Norton and Co., New York, NY, 1999.

[8] Institute of Medicine, National Research Council. *Ensuring Safe Food.* National Academy Press, Washington, D.C., 1998: 51-52.

[9] Garrett, Laurie. *Betrayal of Trust.* Hyperion, New York, NY, 2000.

[10] Eberhart-Phillips, J. *Outbreak Alert.* New Harbinger Publications, Inc., Oakland, CA, 2000: 76-78.

[11] Delgado, C., et al. *Livestock to 2020: The Next Food Revolution.* International Food Policy Research Institute, 1998.

[12] Woolhouse, M.E., et al. *Population Biology of Multihost Pathogens. Science,* Vol. 292, No. 5519, May 11, 2001: 1109-1112.

[13] Brown, C. and Bolin, C. *Emerging Diseases of Animals.* ASM Press, Washington, D.C., 2000: 7-8.

[14] Ewald, Paul. *Plague Time.* The Free Press, New York, NY, 2000: 164-166.

[15] Snacker, Rene, et al. *The Next Influenza Epidemic: Lessons from Hong Kong.* Journal of Emerging Infectious Diseases, CDC, Vol. 5, No. 2, March-April 1999.

[16] Epstein, Paul. *Is Global Warming Harmful to Health?* Scientific American, August 2000: 50-57.

[17] Rappole, John, et al. *Migratory Birds and Spread of West Nile Virus in the Western Hemisphere.* Journal of Emerging Infectious Diseases, CDC, Vol. 6, No. 4, July-August 2000.

[18] Daszak, Peter, et al. *Emerging Infectious Diseases and Amphibian Population Declines.* Journal of Emerging Infectious Diseases, CDC, Vol. 5, No. 6, November-December 2000.

[19] Isard and Gage. *Flow of Life in the Atmosphere.* Michigan State University Press, East Lansing, MI, 2001.

[20] National Academy Press. *From Monsoons to Microbes.* Washington, D.C., 1999.

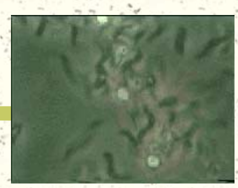
[21] Garrett, Laurie. *The Coming Plague*. Penguin Books, New York, NY, 1996.

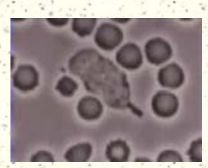
[22] McNeill, William. *Plagues and People.* Doubleday and Co., Inc., New York, NY, 1977.

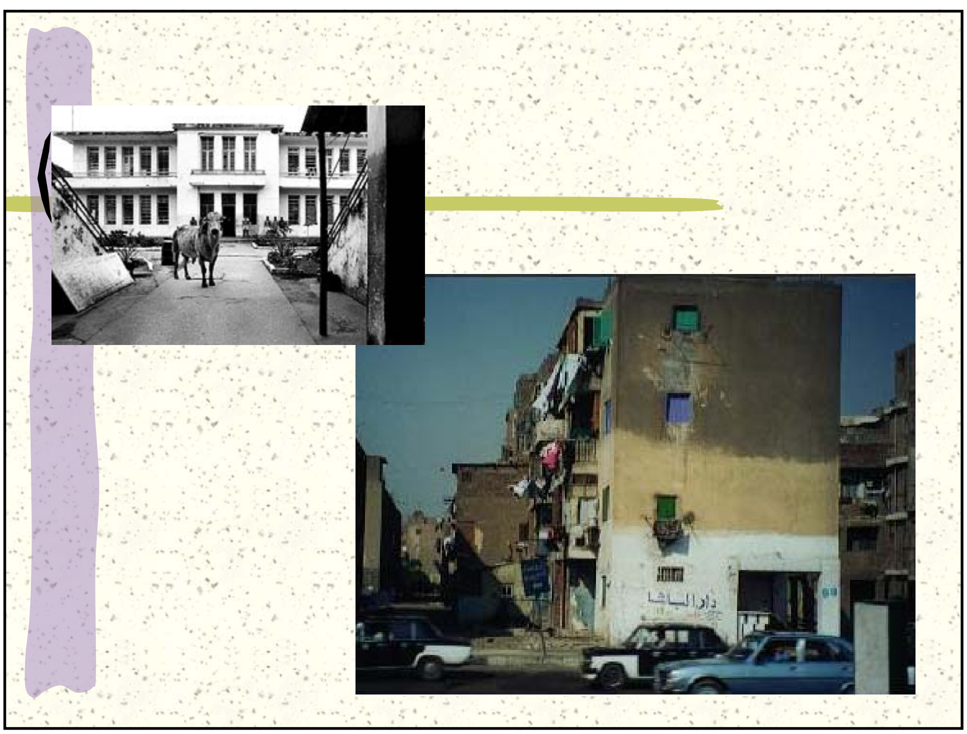
Microbe Hunters of the 21st Century:

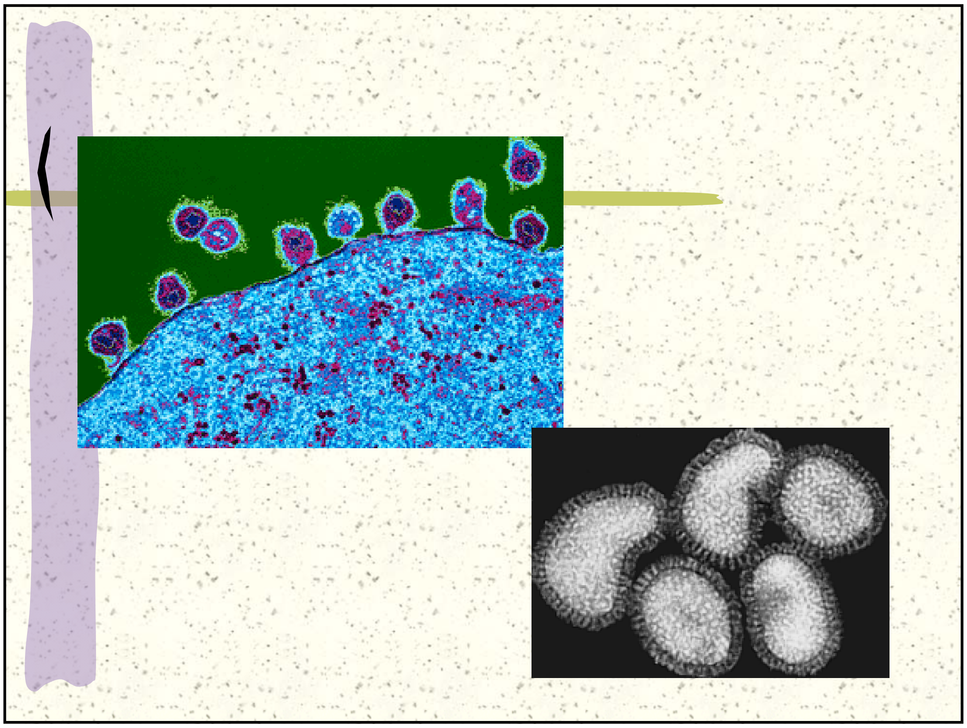
Reinventing Epidemiologists

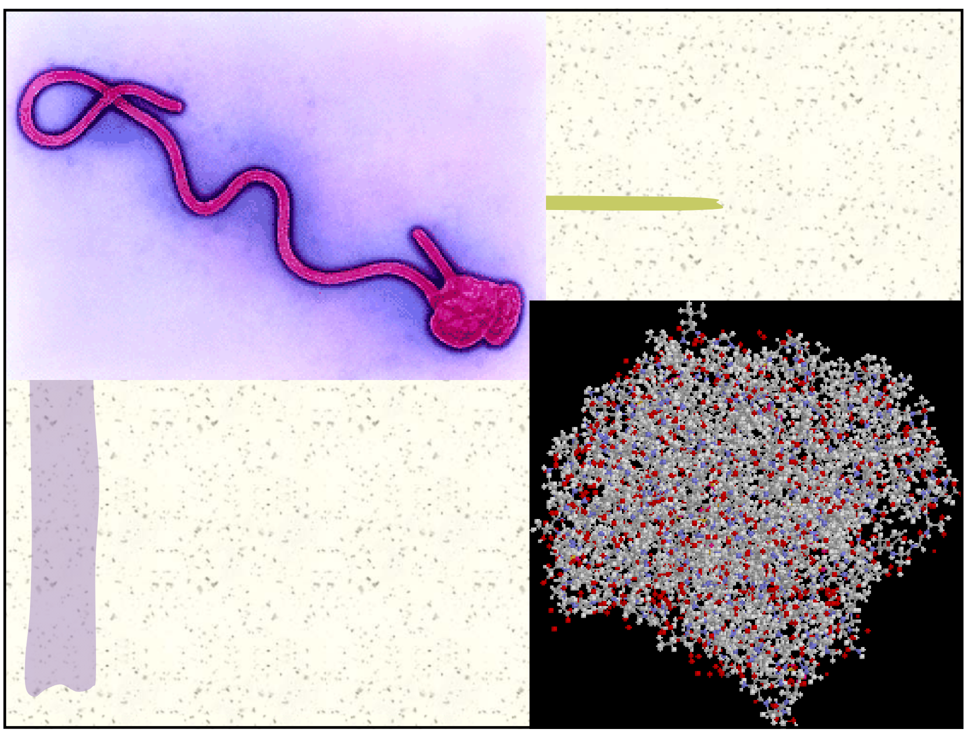
Microbes











The Year 2025

- 8.4 billion people on earth
- 450 cities larger than 10 million people each
- 3 populations
  - World 1 – Advanced Countries
  - World 2 – Comfortable
  - World 3 – Destitution and poverty

The Year 2025 continued

- Epidemiologists function in multiple worlds simultaneously and from 18th century to the 21st century

The 21st Century: A Brave New World for Microbe Hunters

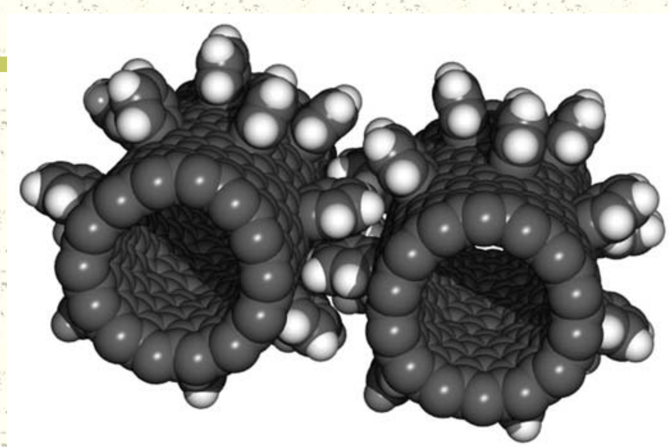
- Miracles of medicine vs pessimism
- Globalization
- Scientific revolution unevenly distributed

21st Century – Next Great Epidemic

- Millions on the move
- Billions inhabiting earth
- Trillions of tons of cargo, crops, animals

Key 21st Century Areas for Epidemiologists

- Genetics
- Proteins
- Nanotechnology



"Agriceuticals" = convergence of agriculture, pharmaceutical, healthcare and computing

- A $15 trillion enterprise in 2025
- Transformation of food – sustenance to health promotion
- New role for 21st century epidemiologists - assessment

"Animal Origins of human disease lie behind the broader pattern of human history."

Jared Diamond

- Rise of agriculture 10,000 years ago
- Start of cities
- Pathogens shifted from animals to humans
- Examples: measles, TB, smallpox, flu and malaria

Food Safety

- Major emerging diseases of animal origin
- Restructured agriculture favors epidemics
- New susceptibles: poor, elderly, immuno-compromised
- Example: S. typhimurium DT-104 – "Super Bug"

A New Population of Susceptibles in the 21st Century

- Growth in the cohort of elderly
- 580 million – over 60 year olds in 1998
- "Herd immunity" revisited

The Black Death
Epidemic of Plague 1346

- Silk route
- Crowding
- Proper set of conditions

The Four Horsemen of the Apocalypse

Albrect Durer

Think globally, act locally

-Rene Dubos

- Now the reverse is also true

Tuberculosis

- The true “millennium bug”
- 1/3 of the world’s population infected
- Multiple-drugs resistance
- 2-3 million TB deaths this year
- 21st century environment favorable to TB
- TB in fish in Chesapeake Bay

Movement of Interactions of People and Commerce

- Distance and speed of travel increased 1000 fold since 1800
- 1.4 billion air travelers/year
- 50 million foreign visitors, to US year through, 102 sites
- Antibiotic resistance
- Global trade of food, animals and plants

Livestock 2020 – The Next Food Revolution

- Global increase and demand for protein and food of animal origin
- Shift from poverty of 1-2 billion people to middle class
- "Westernization" of Asia and Latin America
- Concerns with sustainability
- Increases in emerging zoonoses through the concentration of people and animals

Multihost Pathogens

- 60% of all human pathogens are zoonotic
- 80% of animal pathogens
- Ecological generalists

Comparison of Microbe Hunters

1880-1885	1995-2000
Leprosy	Hantavirus
Malaria	BSE
TB	Influenza
Cholera	Nipah virus
Typhoid Fever	West Nile virus

Fruit bats

Emerging Disease Patterns

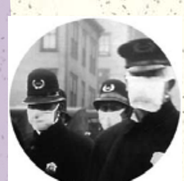
- Increased incidence and wider geographic spread
- Novel pathogens "looking for diseases"

- Major infections plagues are not emerging from the African jungle – they are already here

- 21st century microbe hunters will need to focus on chronic diseases that are likely to have their origins in acute infectious diseases

Influenza Epidemics

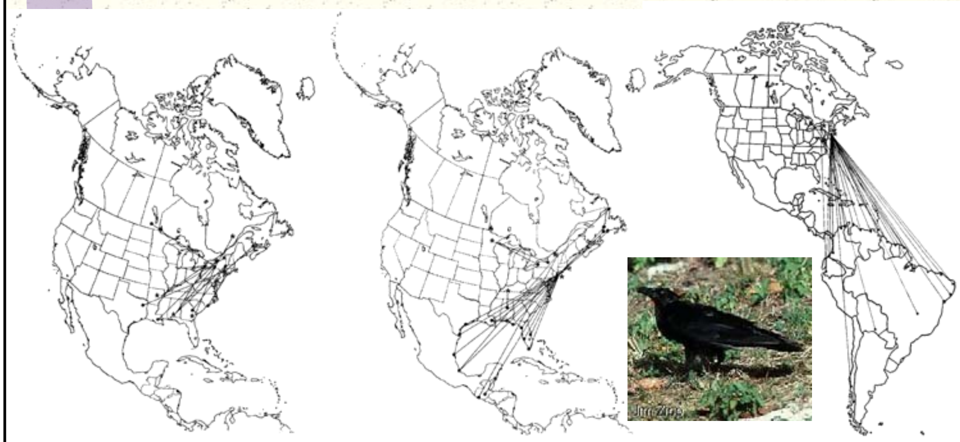
- Pandemics – 1918, 1957 and 1968
- China – the great bird-hog-people mixing pot of viral nucleic acids and genes



Flu Outbreak 1918

Global Warming

- Shifting and enlarging the incidence and distribution of disease
- Malaria zone 45% of population to 60%
- Habitat change and disruption via weather changes



Migratory Birds and Spread of West Nile Virus in the Western Hemisphere

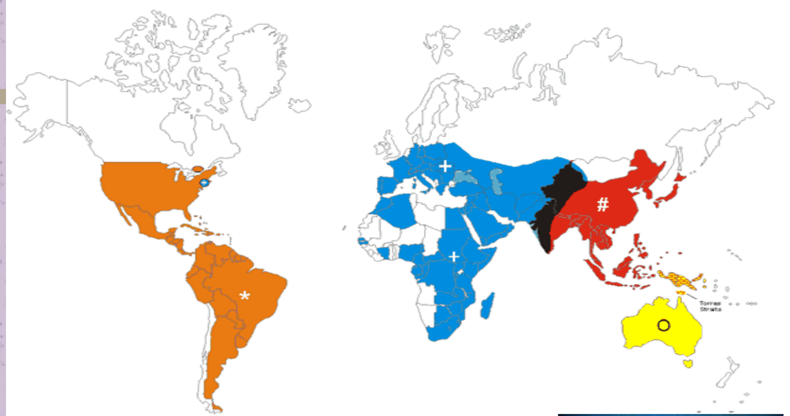
1

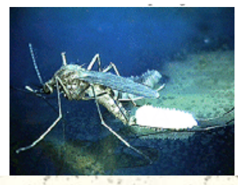
2

3

Malaria invading blood cell

The Geographic Distribution of the Japanese Encephalitis Serocomplex of the Family Flaviridae, 2000.





West Nile Virus- Microbe Hunters on Alert

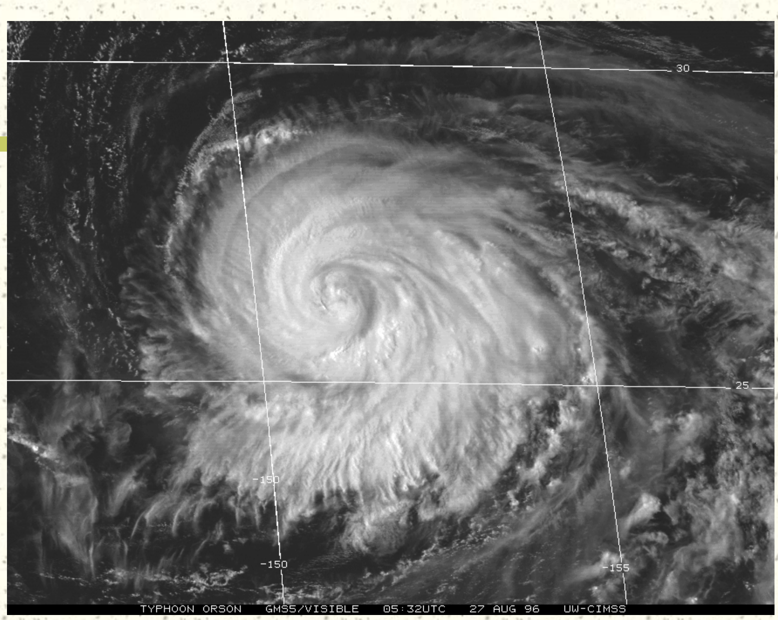
- New York – August 1999
- Spatial and temporal juxtaposition of avian-human-equine hosts
- Ornithophilic mosquitoes
- Bird migration patterns

Pathogen Pollution

- Human and domestic animal populations
- Free-living wild animals
- Example: global decline in amphibian populations due to chytridiomycosis
- Concern with adverse effects on biodiversity

Atmospheric Flow of Biota

- Aerobiota defined
- Temporal and spatial changes
- Transportation of vectors – mosquitoes and encephalitis
- Migrating birds
- Plants and insects



Monsoons to Microbes

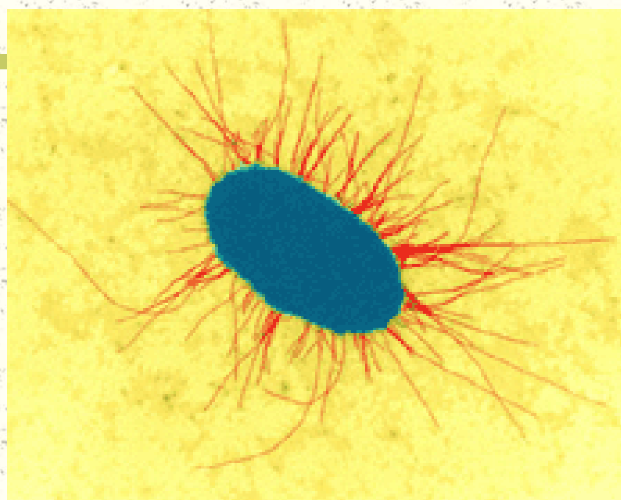
- Interplay of currents, tides and human activities
- Coastal and estuarine environments
- Hepatitis A, poliovirus
- Ballast water from ships - cholera

The Coming Plague

- Complacency and lack of expertise
- A quiltwork of microbes
- Global Village

- "Ingenuity, knowledge, and organization alter but cannot cancel humanity's vulnerability to invasion by parasitic forms of life. Infectious disease which antedated the emergence of humankind will last as long as humanity itself, and will surely remain, as it has been hitherto, one of the fundamental parameters and determinants of human history."

William McNeill
Plagues and People (1976)



Microbes