VACCINATION: AN AID TO INFECTIOUS DISEASE PREVENTION

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Introduction

Vaccination constitutes an important component of infectious disease prevention and control programs for horses; however, vaccination alone cannot be expected prevent infectious disease. Management practices designed to minimize the risk of introducing and spreading diseases are also of critical importance. The decision to use a particular vaccine depends on the risk of acquiring infection and on the medical and economic consequences of infection, balanced against the anticipated effectiveness, cost, and potential adverse effects of the vaccine. Factors to consider when evaluating the risk of exposure to specific diseases include the age, type, gender, number, use, and stocking density of horses; season; environmental conditions; and the operation's facilities, management practices, and geographic location. For these reasons, **there is no "standard" vaccination program** that can be recommended for all horses; each situation must be evaluated individually. Estimates of cost should include expenses incurred and money lost during the time horses are out of competition, labor and medication expenses for horses that develop clinical disease and require treatment, and the expenses in time, labor and vaccines required for proper immunization. The expectations of the horse owner must be realistic, taking into account the following realities:

- Vaccination reduces the risk of infection but does not prevent disease in all circumstances – no vaccine gives a 100% guarantee of protection.
- Not all horses respond to vaccination in the same manner; therefore, horses in a particular population will not all be protected to an equal extent or for the same duration after vaccination.
- It typically takes several weeks or months after administration of the first dose of a vaccine to induce protection, particularly when inactivated vaccines are used. Optimal protection generally is not achieved until 2 to 3 weeks after completion of the primary series, or 1 or more weeks after administration of a booster dose to a previously vaccinated horse.
- The effectiveness of vaccines directed against different diseases varies considerably. There is also variation between manufacturers with regard to efficacy of vaccines directed against a particular disease and no one manufacturer has the "best" vaccines against all diseases.
- Whenever possible, all horses in a herd should be vaccinated on the same schedule; this simplifies record keeping, minimizes replication and transmission of infectious agents in the herd, and optimizes herd immunity.

Only federally licensed vaccines should be used, and strict attention must be paid to the manufacturer's recommendations for storage, handling, and routes of administration to maximize the product's

effectiveness and safety. However, research or clinical experience may support alternate protocols for vaccination that will improve the vaccine's effectiveness without increasing adverse effects. For instance, inactivated (killed) vaccines administered intramuscularly generally induce a greater response when an initial series of three doses is administered rather than the two-dose series recommended by most vaccine manufacturers.

Available Vaccines

Fully licensed vaccines are available in North America as aids to protection of horses against the following infectious diseases: Tetanus, Western and Eastern equine encephalomyelitis (WEE, EEE; Sleeping sickness), West Nile Virus (WNV) infection, Rabies, Equine influenza, Equine herpesvirus types 1 and 4 infection (EHV-1, EHV-4, rhinopneumonitis), Strangles *(Streptococcus equi* infection), Equine viral arteritis (EVA), Venezuelan equine encephalomyelitis (VEE), Equine monocytic ehrlichiosis (Potomac horse fever), Toxicoinfectious botulism (type B), and Anthrax. In addition, **conditionally licensed** vaccines directed against Rotaviral diarrhea and Equine protozoal myeloencephalopathy (EPM) are also available. The equine veterinarian is in the best position to provide advice regarding which vaccines to use, and protocols for their use, under the unique circumstances that exist on individual premises.

Diseases for inclusion in Vaccination Programs

A. "Core" diseases against which **all horses in Northern America** should be vaccinated:

- Tetanus
- Western and Eastern equine encephalomyelitis (WEE, EEE; Sleeping sickness)
- West Nile Virus (WNV) infection

B. Frequent additions to the "core"

For the many horses that have potential exposure to wildlife vectors of rabies (skunks, raccoons, foxes and bats), it is prudent to add:

- Rabies

For horses that come into contact with other horses at shows, sales, competitions, and on breeding farms, the following vaccines are typically added to the core to help prevent contagious respiratory disease:

- Equine influenza
- Equine herpesvirus types 1 and 4 (EHV-1 and EHV-4 or rhinopneumonitis). All pregnant mares should be vaccinated against EHV-1, regardless of where they reside. The efficacy of EHV-4 vaccines for preventing respiratory disease in weanlings remains controversial.

C. Additions to the "core" only under special circumstances

On premises where the risk of exposure is high (typically breeding farms or training barns experiencing outbreaks), it may be prudent to add:

- Strangles

The following vaccines may be indicated under special circumstances in which the regional or local risk is high:

- Equine viral arteritis (EVA)
- Toxicoinfectious botulism (Shaker Foal syndrome, type B Botulism)
- Rotaviral diarrhea
- Venezuelan equine encephalomyelitis (VEE)

D. Rarely recommended

Vaccines against the following diseases are rarely recommended either because of questionable efficacy, low risk of infection, or both:

- Equine monocytic ehrlichiosis (Potomac horse fever)
- Equine protozoal myeloencephalopathy (EPM)
- Anthrax

Table 1 presents typical vaccination schedules for use of the above vaccines when their use is indicated.

Special Considerations for Broodmares

Whereas vaccination programs for pleasure, show, and performance horses typically focus on prevention of diseases that threaten the health of the individual horse and it's herd mates, vaccination recommendations for broodmares must also consider protection of the unborn fetus and pregnancy, protection of the foal during the first few months after birth, the potential impact of pregnancy on the response of the pregnant mare to vaccination, and safety of vaccines to the mare and fetus.

Most available equine vaccines are considered to be safe for use during pregnancy; however, few vaccines actually carry specific label recommendations for use in pregnant mares. In addition to the two available EHV-1 vaccines (Pneumabort-K®+1b, Fort Dodge, and Prodigy®, Intervet) marketed for use in pregnant mares as an aid to prevention of EHV-1 abortion, only the Calvenza line of influenza and EHV vaccines marketed by Boehringer Ingelheim, the BotVax®B vaccine (Neogen) for prevention of

Type B botulism in foals and the conditionally licensed vaccine (Equine Rotavirus Vaccine, Fort Dodge) for prevention of rotavirus infection in foals, carry label recommendations for use in pregnant mares. While not specifically labeled for administration during pregnancy, widespread use in practice over many years has failed to document that any of the inactivated vaccines currently marketed for use in horses pose an unacceptable risk to pregnant mares. Therefore, pregnant mares are routinely vaccinated with inactivated vaccines directed against tetanus, EEE, WEE, WNV, influenza, EHV-4, strangles and, to a lesser extent, PHF, rabies, and VEE. Similarly, adverse impacts on pregnancy have not been documented for modified live intranasally administered strangles and influenza vaccines or the modified live parenterally administered EHV-1 vaccine (Rhinomune®, Pfizer) In addition, safety of the recombinant WNV vaccine (Recombitek®, Merial) should not be a significant concern because the modified live canarypox vector lacks the ability to infect mammalian cells. In contrast, modified live virus EVA and VEE vaccines and live anthrax spore vaccines should not be used in pregnant mares. Protection of mares against the potential abortigenic effects of EVA infection is, therefore, best accomplished by completing the primary immunization series before the mare enters the broodmare band and by administering subsequent boosters during the open period before rebreeding. Because formation of fetal organs occurs early in gestation and this period is also characterized by substantial embryonic loss, even in normal mares, it is sound practice to avoid administering vaccines to mares during the first 60 days of gestation unless conditions of imminent risk prevail.

The practice of booster vaccinating mares against multiple diseases to maximize colostral transfer of antibodies to the foal, and the fact that mares in broodmare bands are generally middle aged or older, results in the typical broodmare receiving multiple doses of many vaccine antigens and adjuvants during her lifetime. In addition to stimulating high levels of antibody against a range of antigens, this practice may also predispose these mares to a higher rate of local and systemic adverse reactions, an issue that may force horse owners and veterinarians to carefully consider strategies for revaccination of individual horses. Simultaneous administration of multiple vaccines to mares late in gestation is a common practice that may increase the risk of an adverse reaction. In addition, the possibility that “competition” between multiple antigens will compromise the response to some or all of the administered antigens should be considered. When administration of multiple vaccines late in gestation is indicated, it is good practice to administer no more than 4 or 5 antigens at one time and to allow an interval of 3 to 4 weeks between administration of different vaccines.

It is widely assumed that pregnant mares are fully capable of mounting appropriate immune responses to vaccines; however, this issue has received little research attention. Mares that have received their primary series of vaccines before breeding appear to mount appropriate booster (anamnestic) responses when revaccinated during pregnancy. However, we have recently found that pregnancy may

dampen responses to some vaccines (including inactivated WNV and rabies vaccines) if these vaccines are administered for the first time while the mare is pregnant, resulting in failure of vaccinated mares to passively transfer specific antibodies to the foal via colostrum. Thus we strongly recommend that primary vaccination against important diseases should be completed before the mare is bred.

Mares that will be shipped short distances for breeding can be transported during estrus and returned to the farm on the same day to reduce the risk of the mare and her foal acquiring infection. Foaling mares that are to be sent to a distant farm for breeding should be transported at least 6 to 8 weeks before foaling to allow the mare's immune system sufficient time to produce antibodies against the bacteria, viruses, and other infectious agents present on the breeding farm. During the last few weeks of pregnancy, the mare concentrates these antibodies in the colostrum (first milk) that she produces in her udder. A normal foal will nurse the mare within an hour after birth and will ingest this antibody-rich colostrum in the process. The intestinal lining of the newborn foal contains specialized cells that allow these colostral antibodies to be absorbed intact into the foal's bloodstream rather than being broken down and digested as would happen in a foal more than 24 hours of age or in an adult horse. This phenomenon, termed **passive transfer of maternal antibodies**, allows the foal to acquire antibodies against many disease-causing agents at a level similar to that found in the blood of the mare at the time of foaling. These maternal antibodies are crucial to the health of the foal because they provide passive protection against many infectious diseases during the first few weeks and months of life.

Capitalizing on the protective effect of maternal antibodies constitutes a major focus of vaccination programs for broodmares. This goal is typically accomplished by administering booster doses of vaccines to mares between 30 and 60 days before foaling in order to maximize levels of specific colostral antibodies. Maintaining consistent vaccination protocols for mares will maximize the likelihood that a uniformly high level of colostral antibody transfer and passive protection will be achieved within the foal crop. Whereas intranasally administered vaccines, such as those used to prevent influenza and strangles, may be used to protect the mare, they are typically less effective than inactivated vaccines administered by intramuscular (IM) injection in stimulating high levels of circulating antibodies of the type (IgG) that are passively transferred to the foal in high concentration. Injectable vaccines are, therefore, preferred for booster vaccination of mares during late gestation.

Pre-foaling boosters for pregnant mares should include the "core" diseases (tetanus, WEE, EEE, WNV) and influenza. In addition, all pregnant mares should be vaccinated against EHV-1 three times during pregnancy (during the 5^{th}, 7^{th}, and 9^{th} months of gestation) to reduce their risk of experiencing EHV-1 induced abortion. This series of three EHV-1 vaccines typically induces high levels of EHV-1 antibody for passive transfer to the foal. Mares in rabies-endemic areas should be vaccinated against rabies. The inactivated rabies vaccines licensed for use in horses are very potent and typically induce

rabies antibodies that persist at high levels for a prolonged period. Therefore, the annual rabies booster can be administered before breeding and will still provide passive protection to the foal born 11 months later.

In addition to the "core" diseases outlined above, your veterinarian may recommend inclusion of other diseases such as strangles in the vaccination program for broodmares if he or she judges the risk of infection to be sufficiently high on the farm where the mare will foal or be re-bred. Rotavirus infection causes sporadic outbreaks of diarrhea in foals and can pose substantial problems on certain farms in certain years. Vaccination of the mare during pregnancy with 3 doses of a conditionally licensed inactivated rotavirus vaccine may help reduce the risk to the foal. Similarly, foals in central Kentucky and some other eastern states are at risk for developing botulism (Shaker foal syndrome) caused by *Clostridium botulinum* type B. Although vaccination against botulism is not typically indicated for mares residing in California, it is frequently recommended for mares that will foal in Kentucky and other endemic areas in order to protect their foals. Equine viral arteritis (EVA) is a venereal disease that is transmitted from asymptomatic carrier stallions to mares during natural cover or artificial insemination. Infected mares then shed the virus in their respiratory secretions and may, in turn, infect other horses, including pregnant mares. These mares may then experience fetal loss, abortion, or the birth of an infected live but severely compromised foal. An EVA vaccine is available to prevent mares from becoming infected and may be recommended by your veterinarian. This modified live vaccine must be administered before the mare is bred.

Considerations for use of vaccines in foals and weanlings

Few vaccines carry label directions for primary immunization of foals. Of those that do, the range of recommended minimum ages is wide and includes the following: 3 months for several inactivated rabies vaccines; 6 months for inactivated influenza and EHV-1 vaccines from one company (Calvenza™ EIV, EHV, and EIV/EHV, Boehringer Ingelheim); 9 months for a modified live intranasal strangles vaccine (Pinnacle® I.N., Fort Dodge); and 11 months for a modified live intranasal influenza vaccine (Flu-Avert™ I.N., Intervet). Considering that foals are at risk for acquiring many of the diseases against which we vaccinate horses, and the fact that the period before weaning is regarded by many horse owners and veterinarians as a convenient time to vaccinate, it became common practice during the 1970's and 80's, to start primary vaccination of foals at 3 to 4 months of age so that the primary immunization series for multiple antigens could be completed before weaning.

Research performed at UC Davis and elsewhere during the 1990's and 2000's has shown that the same maternal antibodies that are so important for protection of foals against infection during the first

few months of life, may also dampen or completely block the normal immune response of the foal to antigens contained in vaccines, a phenomenon, termed **maternal antibody interference.** The duration of the inhibitory effect of maternal antibodies varies by antigen and vaccine type, and is also influenced by the level of antibodies in the mare's blood and colostrum at the time of foaling and the efficiency of maternal antibody transfer via colostrum. Maternal antibody interference appears to persist for up to 6 months for antigens contained in many inactivated vaccines, including tetanus, EEE, WEE, EHV-1, EHV-4, and rabies, and up to 9 months or longer for inactivated influenza vaccines and perhaps others. Consequently, most inactivated vaccines administered before 6 months of age are ineffective, a finding that has prompted the AAEP to recommend that primary vaccination of foals with most inactivated vaccines should commence later (typically 6 months of age or older) than has been the case in the past. The West Nile virus vaccines are important exceptions, in that foals as young as 3 months of age respond well to both the inactivated (West Nile Innovator™, Fort Dodge Animal Health) and the canarypox-vectored recombinant (Recombitek®, Merial) WNV vaccines. For all inactivated vaccines other than rabies vaccine, a much better response is obtained if 3 doses of vaccine are included in the primary series rather the 2 doses routinely recommended by vaccine manufacturers. Typically, the 3rd dose stimulates a serologic response of greater magnitude and durability than 2 doses and may also induce a higher "set-point" for the response to subsequent booster doses. The interval between the 1st and 2nd doses of vaccine is typically 3 to 4 weeks, while the 2nd and 3rd doses should be separated by 8 to 12 weeks.

Adverse reactions to vaccines

Some horses experience local muscle swelling and soreness or transient, self-limiting systemic signs, including fever, reduced appetite, and lethargy after receiving vaccines. For this reason, administration of vaccines within 2 weeks of a show, performance event, sale or domestic shipment should be avoided if possible. Multi-component "combination" vaccines containing multiple antigens tend to cause local reactions more of often than do single-component vaccines. For horses that react repeatedly to a particular combination vaccine, it is advisable to administer the antigens separately as single-component vaccines. If the horse then experiences an adverse reaction to one of the component vaccines, several options are available: 1. Use a different brand of vaccine containing a different adjuvant, 2. Premedicate the horse with an NSAID such as Banamine® or phenylbutazone before administering the vaccine and allow free exercise afterwards, and 3. Carefully consider whether it is necessary to administer the vaccine component in question or whether the interval between vaccines can be extended. When the risk from administering the vaccine outweighs the risk from the disease, you should reconsider your vaccination protocol, in consultation with your veterinarian.

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