Vaccinations: Immunization Needs or a Shot in the Dark?

Dr. Susan A. Mende, DVM, Dipl. ABVP

Your equine partner brings you joy, and you repay that debt by providing the very best care. That care includes comprehensive vaccinations . . . probably a more complete regimen of immunizations than you receive yourself! With contemporary vaccines rendering many diseases uncommon, it is easy to forget how awful those diseases can be, and tempting to forget that no disease is ever truly stamped out. Horse owners must respect and remain aware of the dangers of these diseases. Few things will protect your horse as easily and effectively as immunizations. The specific immunization needs of a particular horse depend upon several factors, such as environment, age, use, exposure risk, value, geographic location, and general management.

Vaccinations are a vital part of proper equine management, and keeping up with the evolution of the available vaccines is paramount. Each year new discoveries are made not only to address specific pathogens, but also to formulate new methods for stimulating or enhancing immunity. When incorporated into a program that includes regular deworming, an ample supply of clean water, a good nutrition program, and a safe environment, you and your horse will be set to enjoy many happy, healthy, productive years together. Of course volumes could be written regarding each individual condition; we are providing instead a brief rationale regarding the choices we have made on your behalf to help protect your horse.

Tetanus: Tetanus is a distressing and often fatal disease caused by three protein exotoxins liberated by the bacterium *Clostridium tetani* (Radostits 1994). The tetanus bacterium is a commensal of the GI tract of man and domestic animals and its spores are highly resistant to environmental changes, acid and alkali, and may persist in the soils for many years. The organism generally gains entry to the body via wounds or lacerations with suitable anaerobic conditions (Cullinane 1999). Although not contagious from horse to horse, tetanus poses a constant threat to horses and humans alike. Tetanus occurs worldwide and is considered a problem in warmer, developing countries where vaccination programs for both man and equids are not established. Annually, approximately 800,000 human infant tetanus cases occur worldwide (Abrutyn 1991). Horses as a species are especially sensitive to tetanus toxins, exceeded only by the chicken in level of sensitivity. Sometimes called "lockjaw," symptoms include muscle rigidity, flared nostrils, hypersensitivity to sounds, and the legs stiffly held in a 'sawhorse' stance. As the disease progresses, the muscles of the jaw stiffen, preventing the horse from eating and drinking. More than 80% of affected horses die. According to a recent comparative study, ***Encephalovac***^{TM} (manufactured by Boehringer-Ingelheim), provided the greatest protection against the tetanus organism (Townsend 2008). This is the product used at our practice.

West Nile Virus: This virus which can cause encephalitis (inflammation of the brain) in animals and humans has been found in Africa, Western Asia, the Middle East, the Mediterranean region of Europe, and most recently in the United States. We are now more familiar with this strange tropical virus that mysteriously landed on our shores in 1999. By 2002, it had spread to all 48 of the continental United States and reported cases increased from 25 to more than 15,000 horses (Long 2002). West Nile Virus (WNV) made its first appearance in the Western Hemisphere when an outbreak was discovered in New York. While it has not been possible to confirm the source of WNV or how the pathogen spread to the US in the first place, the prevailing opinion is that the virus was introduced through the illegal importation of an infected bird. WNV is transmitted by the bite of an infected mosquito and spread nationwide by bird migration. WNV has been shown to "over winter" in mosquitoes, although the risk of infection decreases during the first hard frost then reappears each summer. WNV has also been found in other species - bats, squirrels, chipmunks and skunks - indicating that WNV may be a significant wildlife issue as well.
The most common signs in the horse are stumbling or incoordination, weakness of limbs, partial paralysis, muscle twitching, and death. Thanks in part to vaccination, the incidence of WNV has dropped to 468 reported cases nationwide in 2007. But that doesn't mean the threat is over; WNV is still deadly.

A study conducted by Colorado State University showed some alarming statistics. Of the horses where information was available, 50.2% of the equine population has still not been vaccinated against WNV. Horses that were not vaccinated were 2.1 times as likely to die as compared to horses that were vaccinated. In the study, 28.4% of infected horses died or were euthanized, 80% of horses that survived fully recovered but 20% of survivors developed complications to the disease.

The first vaccine available was a killed vaccine created from the whole organism. This vaccine (*Innovator West Nile*^{TM}, manufactured by Ft Dodge) withstood the ultimate challenge of preventing disease in the face of a national outbreak. We used this vaccine exclusively until 2008. However, a new vaccine has recently emerged that offers superior protection. ***Vetera***^{TM} (manufactured by Boehringer Ingelheim) is the first WNV licensed with claims to prevent viremia and aid in the prevention of diseases caused by WNV. Research in yearlings and older horses vaccinated with a single dose of *Vetera*^{TM} showed its protection lasted a full 12 months (in some cases 16 months), so there's no need for a fall booster. It is safe in foals and pregnant mares in all trimesters, but foals do require a second-dose booster to establish immunity. We now use this vaccine, available exclusively through veterinarians.

Equine Encephalomyelitis: Also known as "sleeping sickness," this extremely dangerous viral disease is caused by the Western (WEE), Eastern (EEE) or Venezuelan (VEE) viral strains. Equine encephalomyelitis is transmitted by mosquitoes. Humans can also become infected if bitten by an infected mosquito that acquired the virus from a bird or rodent. Although VEE has been eradicated from the United States, a recent outbreak did occur in Mexico. The WEE and EEE strains are not geographically restricted; all horses should be vaccinated against both. Health agencies reported a record number of EEE-affected horses in 2003 in the Southeastern US, especially Louisiana and southern Texas. The number of cases rose 8000% in some flooded areas. The disease, which has existed in the US for decades, kills nearly all unvaccinated horses. Although it would seem that the flurry of media and industry attention surrounding WNV might overshadow the awareness and knowledge of EEE, the opposite is true. Concern over WNV and improved detection methods for WNV may have led to better detection of EEE. WNV has raised national awareness of mosquito-borne viruses and diseases. They are from different viral families (WNV – flavivirus, EEE – alphavirus) thus, there is no cross protection for WNV by vaccinating against EEE or vice versa. They have similar clinical signs and can be mistaken for each other. WNV prefers to infect the hindbrain and spinal cord, whereas EEE has an affinity for forebrain and cerebral cortex. Early signs can include fever, depression, and loss of appetite. Later, the horse may begin to stagger, often leading to paralysis. WNV encephalitis has about a 25-30% fatality rate for horses, whereas the mortality rate from EEE ranges 75-90%. Unlike WNV, nonfatal EEE can cause permanent neurologic damage and lasting effects from myocardial damage.

There are several companies that manufacture encephalomyelitis vaccines and they are all protective. However, in a comparative study, ***Encephalovac***^{TM} demonstrated superior protection (Townsend 2008). This is the vaccine we use.

Rabies: While the incidence of rabies in the horse is low, the disease is invariably fatal and has considerable public health significance. Unfortunately, it takes only one rabid horse to threaten thousands of horses and people. A sobering reminder of the importance of rabies vaccination was given to 150,000 people in attendance at the Tennessee Walking Horse National Celebration in August of 2006. All were at risk of coming into contact with the saliva of a gelding stabled there, which was later confirmed rabid and euthanized, according to the Centers for Disease Control and Prevention (Center Disease Control, 2007). Despite the availability of vaccine protection, the incidence of rabies in horses has not decreased proportionately and reported cases of equine rabies in 2006 increased by more than 12% compared with 2005 (Blanton 2007, Blanton 2006). Our neighbor states Pennsylvania, Virginia, and New York were among the highest reported states in 2006. Because rabies is highly contagious, there is no room for compromise when protecting horses in your care. Horses contract rabies most often through exposure to infected wildlife. The most common carriers of rabies include skunks, raccoons, foxes, and stray dogs and cats. The rabies virus is carried in the salivary glands of infected animals then transmitted to the

horse via a bite wound often on the muzzle, face, or lower limbs. Foals and young horses are more likely to be bitten than older horses, due to their inquisitive nature. The incubation period for rabies in the horse may range from 1-2 months, with death after onset in 3-10 days. There is no diagnostic test for rabies in the live animal and there is no treatment for rabies infection. According to the new January 2008 AAEP guidelines, it is recommended that rabies vaccine be a core vaccine for all horses, along with encephalomyelitis, tetanus, and West Nile vaccines. Fortunately, although some differences exist between manufacturers, all available vaccines are highly protective. Rabies vaccine should be administered by a licensed veterinarian.

Influenza: This is one of the most common and highly contagious viral diseases in the horse. The virus is spread from horse to horse by an aerosol (from snorting or coughing) with droplets traveling distances as far as 50 yards. Symptoms are similar to the human "flu," e.g., cough, nasal discharge, fever, depression and loss of appetite. With proper care, most horses recover in about 10 days. Some, however, may have symptoms for weeks, especially if put back into work too soon. Influenza is not only uncomfortable for your horse, but can also be expensive to treat, resulting in 'down time' and indirect financial loss. Vaccination should be considered a must for horses that are in contact with other horses. Challenge studies proved that original ***Calvenza***™ (manufactured by Boehringer Ingelheim) produces significantly higher influenza titers and challenge results were statistically superior (Townsend 2003). Duration of immunity proved to be 6-12 months (Animal Health Trust). We have used this vaccine for several years. Since the influenza virus is constantly changing in an effort to bypass the horse's immune system, new strains continue to emerge. Experts who survey equine influenza outbreaks worldwide and make recommendations have suggested that North American influenza vaccines should include the South Africa/2003 strain or equivalent. ***Calvenza 03***™ meets this specific requirement, containing both North American and Eurasian strains, and we use this vaccine too!

The issue of when to vaccinate foals against equine influenza has been a topic of debate since the mid-90s, when a number of publications reported that a high percentage of foals from well-vaccinated mares failed to respond to inactivated vaccines when administered at less than 6 months of age. The presence of colostral antibodies appeared to reduce or eliminate the ability to produce protective levels in foals. Worse, it was reported by some researchers that foals vaccinated in the presence of maternal protection had developed an immunotolerance as they failed to respond to as many as 6 doses of vaccine administered over the next year (Morley 1999). An excellent study in 1999 concluded that foals could be vaccinated at 6 months for influenza, even from well vaccinated mares, because the antibodies' half-life was merely 38 days (Wilson 1999). Studies with *Calvenza*™ in 2002 demonstrated seroconversion in 6 month weanlings and showed that foals were protected following severe challenge at 1, 6 and 12 months after the last of three vaccination boosters (Mumford 2002). Another study was undertaken in 2006 where mares with good vaccination history (all different vaccines) received a booster vaccine with *Calvenza*™ 4-8 weeks prior to foaling. The foals were followed through weaning age. It was demonstrated that 95% of weanlings had no detectable protection from influenza at 6 months of age, but responded well to two vaccinations with *Calvenza*™ at 6 and 7 months of age (Sallaway 2006). This suggests that the current AAEP recommendation to delay vaccination of foals from well vaccinated mares until 9 months of age is excessively conservative, as it leaves foals fully susceptible for at least three additional high risk months.

This new generation of equine influenza vaccine offers a solution for more effective control and prevention of clinical influenza. *Calvenza 03*™ even guarantees that your horse won't become sick if vaccinated appropriately with this product (*Calvenza 03*™ Breathe Easy Vaccination Guarantee, Boehringer Ingelheim)

Rhinopneumonitis: Another highly contagious disease, rhinopneumonitis is spread by aerosol or by direct contact with secretions. Two distinct strains of the herpes-virus cause different disease syndromes which are all known as rhinopneumonitis. Both equine herpes-virus type 1 (EHV-1) and type 4 (EHV-4) cause respiratory tract problems, but EHV-1 may also cause abortion storms (many mares losing their unborn foals at the same time), foal death, and paralysis. Published reports of failure of vaccinated animals to mount an adequate immune response and clinical disease occurring in vaccinated animals led to concerns regarding the efficacy of EHV vaccines that were available at that time (Morley 1999, Morley 2001). A harsh publication in 2000 stated that "based on current, published information, there is no clear need to vaccinate horses against EHV respiratory disease. We do not have the data to show that this disease is of widespread clinical or economic importance. In addition, there is no convincing data to show that we can prevent acute or latent infections with vaccination" (Townsend 2000). Based on this statement, many equine veterinarians lost faith in rhino vaccines, and some stopped using them altogether. This coupled with a correlation drawn between overly vigilant vaccination schedules and neurologic outbreaks at famous farms and venues (Jones, 2004) made the use of rhino vaccine a controversy indeed.

However, it was misleading to suggest that even the older vaccines had been totally ineffective; the incidence of abortion in Kentucky declined by 75% over a 20 year period after the introduction of intensive vaccination programs against rhinopneumonitis and additional herd management procedures (Vickers, 2001; Powell, 1993). And more facts have been revealed . A study presented at the 2003 AAEP Convention showed that the response of naïve horses to tetanus, influenza, and equine herpesvirus antigen varied markedly among vaccines registered in the United States (Townsend 2003). ***Calvenza***™, manufactured by Boehringer Ingelheim, came out on top. In additional studies, *Calvenza*™ stimulated the highest level of viral neutralizing antibodies in experimental horses (Wilson 2007) and demonstrated a profound rise in virus neutralizing titers to both EHV-1 and EHV-4, with effective cross protection against EHV-4 (Summit research Inc).

Calvenza™ can be administered intranasally, which produced strong mucosal immunity, thus strengthening the first wall of defenses against EHV. *Calvenza*™ can also be given as an injection, thus strengthening the circulating antibodies (humoral immunity), which form the second line of defense to prevent EHV. Recently, a study designed to determine if nasal swabbing of EHV-1 infected horses was as diagnostic as a nasopharyngeal swab (which horses really resent) came to some startling conclusions (Pusterla 2007). Neurologic horses in the study showed low viral loads in blood and up to 1,000,000-fold higher viral loads in nasal secretions. In addition, viral loads in nasal secretions of neurological horses were significantly higher than those of either febrile or subclinically infected horses. These findings are in contrast with the previous, erroneous assumption that neurological horses infected with EHV-1 were no longer shedding virus. The contagiousness of neurologically affected horses has finally been proven. And now more than ever, it's important to administer a vaccine clients can rely on. We use *Calvenza 03*™, by both intranasal and intramuscular routes, and this year we are recommending that high-risk horses be inoculated every 90 days against EHV-1.

Strangles: This highly contagious equine scourge was first described by veterinarians of ancient Rome (Pelagonius 1980). Also known as distemper, strangles is a highly contagious bacterial respiratory infection. Infected horses develop high fevers with large swollen glands under the jaws which make eating and drinking difficult. The bacteria that causes strangles is transmitted by contact with the nasal discharge of an infected animal, or contaminated troughs, feed bunks, pastures, stalls, trailers, tack, or grooming equipment. Overall complication rates can be as high as 20%, with case fatality rates up to 8% (Sweeney 2005). Strangles has all the hallmarks of an infection that should and could be eradicated, but because it is not reportable, its presence may fail to be disclosed for economic or other reasons. Therefore the disease may be introduced unknowingly. An important aspect of strangles is that most outbreaks are initiated by introduction of horses incubating the disease or recently recovered, that most animals become immune following infection, and that persistent carriers are few. The disease therefore dies out in most infected herds as herd immunity develops. A crucial advance was the recognition that the carrier state is

usually associated with persistence of infection in the auditory tube diverticulum (guttural pouch). Guttural pouch empyema and chondroids are observed by endoscopy in most persistent carriers (Newton 1997, 2000). These carriers can be identified by bacteriologic culture or by PCR assay and treated successfully (Newton 2000). The chronically infected guttural pouch carrier is possibly the main reservoir of *S. equi* but accounts for as few as 0.3% (6/1850) of animals following strangles outbreaks (Newton 1997). It must be stressed, however, that transmission by carrier horses to susceptible animals has rarely been authenticated.

Older vaccines created from whole cell extracts were famous for causing local reactions at the site of injection and systemic signs such as fever and depression, and possible abscess at the injection site. With the complete genome sequence decoded, modern vaccines utilize the purification of the M-protein antigen from the cell wall. The modified-live intranasal vaccine, ***Pinnacle***™ (Ft Dodge), stimulates mucosal immunity, which is the first line of defense against strangles and is highly protective, even in the face of an outbreak. A killed, injectable vaccine, ***Strepvax II***™ (manufactured by Boehringer Ingelheim), is much safer, as it is free of the sensitizing elements of whole wall bacterins, and is said to stimulate both mucosal and cell-mediated immunity. We use both vaccines, choosing the killed, injectable product for pregnant mares and horses that <u>really</u> resent intranasal medications.

A notation here for anyone who has heard that the strangles vaccine can have harmful side effects. It is true that a few horses have become very sick after vaccination. This can occur when a horse is over-stimulated by antigen (e.g. vaccinate a horse who has recently recovered from strangles and has high circulating antibodies). We choose to handle this vaccine carefully; if vaccination history is unknown, it may be worthwhile to measure circulating antibodies (a titer) before administering anything.

Potomac Horse Fever: Potomac Horse Fever (PHF) has been recognized as a serious equine disease for more than 20 years. While it was named after the river where it was discovered, it has now been detected in at least 43 of the continental United States and 3 Canadian provinces (Madigan, 2005). It is usually found near bodies of water, but has also been found in nontraditional areas as remote as northern Wyoming, often deduced to occur due to flooding and standing water in these locations (Hamende, 2002). Changing weather patterns and improved diagnostics suggest that PHF may be widespread. It is a potentially life-threatening intestinal disease characterized by fever, depression, loss of appetite, lameness, colic, abortion, and profuse watery diarrhea. It is fatal in approximately 50% of all cases and survivors may be left permanently lame. *Neorichettsia risticii* has been identified as the agent involved in PHF, also known as Equine Ehrlichial Colitis. In recent years, more has been learned about the complex life cycle of this pathogen, involving flukes, freshwater snails, and aquatic insects. It may also involve the consumption of these insects by bats and birds. Horses become infected when they consume infected adult insects (caddisflies, mayflies, dragonflies) or ingest the flukes directly in contaminated water (Madigan 2005). Aquatic insects often hatch in peak numbers during mid-to-late summer and into early fall, so management, monitoring, and vaccinating initiatives should be timed accordingly. Is PHF making a deadly comeback or just finally getting our attention? Vaccination against PHF is recommended in areas where the disease has been positively diagnosed; for horses housed near streams, rivers, and ponds; or for horses traveling to such areas. Newer vaccines ***Potomavac***™ (manufactured by Merial) offer wider protection and better efficacy, with 86% protection from clinical disease and 100% protection from death. We have used this vaccine since it became available.

Botulism: Known as "shaker foal syndrome" in young horses and "forage poisoning" in adult horses, botulism is caused by potent toxins produced by the soil-borne, spore-forming bacterium *Clostridium botulinum*. The botulism toxin is the most potent biological toxin known. Forage poisoning occurs when an animal ingests pre-formed toxin produced by decaying plant material or animal carcasses present in feed. Feeding round-bale hay (where a small animal can be crimped and rolled during hay preparation) or access to ponds or streams (where the water cannot be freshened if something dies in or near it) are the risk factors for forage poisoning in adult horses. Foals are the toddlers of the horse world, putting everything in their mouths, which is how toxins are ingested that cause shaker foal syndrome. The toxin

acts by blocking nerve impulses at the motor end plate which results in weakness that progresses to paralysis, an inability, to swallow, and often death. Of the eight different toxins produced, types B and C are associated with most botulism outbreaks.

A toxoid vaccine directed against *C. botulinum* type B (***BotVax B***™, manufactured by Neogen) is licensed for use in horses in the US. Its primary indication is the prevention of shaker foal syndrome. Foals are protected by immunizing mares to provide passive-derived colostral antibodies. Foals are protected for approximately 12 weeks, then they should be inoculated at 3 months of age. For adult horses, a three-booster priming series is necessary, followed by an annual booster thereafter. This vaccine is only available through licensed veterinarians, and it becomes unavailable to us on occasions of heightened terrorism activity (as it could be used as a biological weapon). And do not try to use this for wrinkles, as seven people died in California after injecting it into their foreheads!

Rotavirus: Equine rotavirus is one of the prominent causes of infectious diarrhea in foals during the first few weeks of life and the virus often causes outbreaks involving most of the foal crop on the farm. Equine rotavirus is transmitted through fecal-oral contamination and causes diarrhea by damaging the tips of villi in the small intestine, resulting in cell damage, maldigestion and malabsorption. Most equine rotavirus isolates are of the P12 genotype and the G3 serotype with 2 subtypes. An inactivated rotavirus vaccine (***Rotavirus***™, manufactured by Ft Dodge) containing G3 serotype in an oil-in-water emulsion is licensed for use in the US. The vaccine is only sold to veterinarians. The vaccine is indicated for administration to pregnant mares in endemic areas as an aid to preventing diarrhea in foals. Much like botulism vaccine, it has a three-booster priming series in the last trimester of pregnancy followed by annual boosters to the mares.

Studies of the immunoglobulin isotype responses of mares and of antibodies passively transferred to their foals after vaccination of the mares with rotavirus vaccine indicate that this approach was unlikely to provide foals with intestinal mucosal protection in the form of IgA antibodies. Consequently, it is not surprising that current protocols do not provide complete protection. In addition, because the vaccine only contains the serotype G3 subtype A, it cannot be expected to protect against infection with all field strains. We do use this vaccine occasionally for Thoroughbred mares traveling to large farms to have their foals. Many of these large farms do have troubles with rotaviral infections and the protection the vaccine provides is better than none at all.

Equine Protozoal Myeloencephalitis: A vaccine comprised of killed cultured whole organisms in a proprietary adjuvant (***S. Neurona Vaccine***™, manufactured by Ft Dodge) is of unknown efficacy because EPM cannot reliably be produced experimentally in the horse. The vaccine has been shown to induce both protozoacidal antibodies and specific cell-mediated responses in experimental horses. The vaccine is safe but may cause spurious positive immunoblot results, especially when the vaccine is given to horses that are already positive in serum. Experiments were conducted where the vaccine was administered to horses affected with EPM, in hopes that boosted immunity would render a better recovery, but those experiments were inconclusive. The vaccine was recently pulled from manufacture due to lack of demand, and is currently unavailable.

Equine Viral Arteritis: EVA is a contagious disease found throughout the world. It is a special concern because the virus can cause abortion in pregnant mares, death in young foals, and establish a long-term carrier state in stallions. Outbreaks of EVA occur infrequently and can be difficult to diagnose because of their clinical similarity to several other diseases: fever, anorexia, depression, edematous swelling of eyelids, face, limbs, conjunctivitis, and nasal discharge. A venereal disease in horses, transmission is usually via semen from infected carrier stallions. Vaccination of non-pregnant mares and non-infected stallions before breeding season is only recommended under special circumstances. Seroconversion induced by vaccination cannot be distinguished from natural infection, therefore vaccination may complicate testing of horses for export. Although only a few countries currently restrict the importation of horses that test positive for neutralizing antibodies against EVA, several countries

restrict entry of seropositive stallions because of the likelihood that they are chronically infected and may shed the virus in semen. A blood sample should be collected for serologic testing before the first dose of vaccine is administered. Coordinating vaccination with state or federal regulatory officials (or both) and providing evidence (in the form of negative test results) before vaccination may help resolve disputes, but even these measures do not guarantee entry into foreign countries or onto breeding farms. We do not carry this vaccine, as federal veterinarians are required to administer it.

Anthrax: Anthrax is a serious, rapidly fatal, septicemic disease that develops when the vegetative form of the bacterium *Bacillus anthracis* enters the body, proliferates and spreads. *B. anthracis* is acquired through ingestion or contamination of wounds by soil-borne spores of the organism. The disease is encountered only in limited geographic areas, where alkaline soil conditions favor survival of the organism. A non-encapsulated live spore vaccine (Sterne 34F2 strain, manufactured by Colorado Serum Company) has been used to vaccinate horses. Little objective information is available on use of this vaccine in horses. Because the vaccine is a live bacterial product, appropriate caution should be used in storing, handling, and administering. Details on use of the vaccine should be coordinated through the State Veterinarian Office**.**

Lymes Vaccine: Currently, no equine vaccine against Lyme disease is available, but there is one for dogs. The canine vaccine has an unusual mechanism for preventing infection. The vaccine stimulates the production of antibodies that travel from the host (i.e. dog) into the body of the tick when it starts sucking blood, thus attacking and disabling the bacteria before it has a chance to enter the host's body through the tick bite. Cornell University researchers have investigated the use of a similar vaccine in test ponies. Ponies have been protected by vaccination with an OspA vaccine, but a vaccine approved for use in horses is not commercially available. Efficacy of administration of the canine vaccine in the horse is unknown.

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