Defending Against DISEASE

A vaccine is merely one tool in the control of infectious disease, not a panacea. Just as crucial as vaccination are sound management practices. Your veterinarian can help you decide what vaccination and management protocols are best for your horse(s).

DOUG PRATHER

Vaccines have changed the way we manage our horses, and how long they can live

BY KAREN BRIGGS

Of all the medical advances in the past couple of centuries, the one that might be the most remarkable is also the one we're most likely to take for granted. The simple pinprick of an intramuscular injection taking less than 10 seconds protects our families, our pets, our horses, and ourselves from diseases that once meant certain death. In a flash, there are no more worries about the horrors of diphtheria, rabies, tetanus, or equine encephalomyelitis. All from a few ccs of vaccine.

Perhaps we are so casual about vaccination because it's so familiar. In grade school, most of us learned the story of Edward Jenner, who in 1796 deduced that milkmaids exposed to cowpox, a relatively benign disease, seemed to be immune to the far more virulent smallpox. Jenner might in fact have been borrowing knowledge from more ancient sources—there is some indication that medical practitioners in the Middle East had known for centuries how to immunize patients against smallpox with a small amount of pus from a cowpox vesicle.

Smallpox, which had wreaked untold misery on the human race for millennia, became the first disease against which humans were immunized—and in the 20th Century, the first disease to be officially eradicated from the face of the earth.

A century after Jenner, Louis Pasteur advanced our knowledge of vaccines another giant leap by discovering, quite by accident, that viruses that had been killed or altered by exposure to heat or chemicals might still confer lasting immunity. He injected chickens with a preparation of fowl cholera that had been left out on the lab bench overnight and had dried out. Not only did the chickens not develop the disease from the injections, but when exposed to infected birds, they remained healthy. Pasteur eventually followed up on this revelation by creating groundbreaking vaccines against anthrax and rabies.

By the end of the 19th Century, humanity had gained protective immunization against plague; diphtheria, pertussis (whooping cough), and tuberculosis vaccines followed in the early 1900s.

It wasn't long after vaccination started to become accepted in human medicine that researchers started applying that knowledge

Editor's Note

This is the first installment in a 12-part series of articles on vaccinations of horses.

to horses. A team of researchers at the University of Kentucky were likely the first. In 1914, they came up with an equine vaccine against a form of contagious abortion after isolating salmonella bacteria from aborted fetuses. Although it wasn't a very safe or effective vaccine, it was notable as a first try.

The same team followed that up in 1917 with a far more successful equine antitoxin against botulism, based on antitoxin research that had been developed just a few years earlier by a team investigating human diphtheria. The same process also yielded a tetanus antitoxin in 1928.

With the development of a new tetanus toxoid for humans in the 1930s (a breakthrough that saved thousands of lives in World War II), vaccine research blew wide open. While products for equines have always lagged a little behind their human counterparts, the pharmaceutical industry has remained reasonably progressive. Today we consider it routine to vaccinate against a vast array of life-threatening diseases, including rabies; tetanus; botulism; Eastern, Western, and Venezuelan encephalomyelitis; West Nile virus; and Potomac horse fever. We also vaccinate against some diseases that are not usually life-threatening, but might take valuable recovery time away from our horses (such as influenza, equine herpesvirus strains I and IV, strangles, and rotavirus).

Since the science was first sorted out, horses have been inextricably linked to vaccine development. Early on they were the natural choice for researchers studying the effects of experimental vaccines, and large enough to produce quantities of antitoxin, when their immune systems were properly stimulated, for human vaccines against diphtheria during the first World War. Recently, horses have actually enjoyed priority over humans in terms of the development of vaccines against West Nile virus, and the innovative technologies used to formulate those fast-tracked equine vaccines will undoubtedly benefit humans.

Targeting Disease

Vaccines confer disease resistance by the same process that occurs every time an antigen (a foreign protein, or part of a protein) enters the body's tissues. The immune system reacts to all sorts of antigens, from living pathogens (bacteria, viruses, protozoa, and fungi) to pollens and particles in the air. The immune response is a vastly complex mechanism with multiple defenses, and its share of weaknesses, much like any modern-day army. But the familiar goal is to vanquish the invader and maintain (or return the horse to) good health.

As a fringe benefit, once the immune system recognizes an invader, it is much better prepared to defend itself against any further incursions by that invader, thereby (usually) giving the horse some degree of immunity (sometimes long-term, sometimes only for weeks or months, depending on the disease and the vaccine formulation).

The idea of a vaccine is to get the immune system to mount a response against a pathogenic invader while saving the horse from suffering disease symptoms that at best are uncomfortable and inconvenient, and at worst are fatal. In essence, vaccines give the immune system a heads-up about a possible future invader, and they give it time to design the best possible defense with the minimum deleterious effects on the horse.

The goal of vaccine developers is the same now as it was 100 years ago: To isolate the disease-causing organism, grow it in a laboratory situation, render it non-infective, purify it, mix it with carriers called "adjuvants" that enhance its immune-stimulating properties while causing as few side effects as possible, and make it available in an easy-to-administer format. Injectable vaccines are the ones we're most familiar with, but there are also oral vaccines and formulations that are sprayed on the inner surfaces of the respiratory passages.

LEARNING MORE ABOUT VACCINATIONS

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VACCINATIONS

PART 1

Defensive Mechanisms

Two types of immune responses are called into play when a vaccine enters the horse's system. First, there's the humoral response, in which antibody levels in the blood increase. There's also a cell-mediated response, in which disease-fighting white blood cells, or phagocytes, are summoned to destroy foreign agents. It's the humoral response that is generally most important in the fight against re-infection, but with some diseases, cell-mediated response is also key.

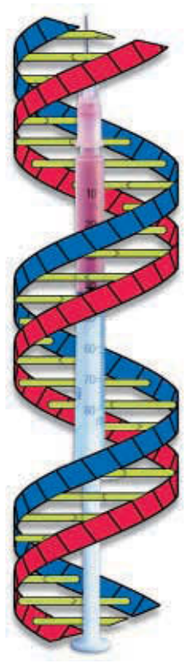
In order to understand how vaccines manipulate disease-causing products, it's helpful to be able to picture the enemy. Viruses and bacteria come in a wide variety of shapes, each with its own immune challenges, but all have an outer coat studded with surface proteins (parts of which stimulate the immune response) and an inner core of genetic material. The aim of a vaccine is to get the horse's immune system to recognize the pathogen's unique surface proteins as "foreign" and mount an attack response, without allowing the inner genetic material to trigger disease or multiply inside the host.

Achieving a balance between safety and effectiveness has always been the main challenge in vaccine formulation. Over the last couple of hundred years, there have been several improvements in strategy that have made vaccines far more dependable than they once were. The evolution goes something like this:

Attenuated "Live" Vaccines—Early vaccines often conferred immunity at a price. Because they contained virus or bacteria that were weakened, but alive, they provoked an excellent, long-lasting immune response. But sometimes they triggered the disease itself—a mild case if you were lucky, a full-fledged case if you were not. Vaccines for canine distemper in dogs and red measles in humans were originally of this type, but "attenuated live" vaccines are rarely used in the Western hemisphere today for either horses or humans if there is an alternative available. (One exception is the oral polio virus vaccine for humans, which because of its ease of administration is especially suited to mass immunization programs.)

Toxoids—A variation on the attenuated live vaccine is the toxoid, which is formulated not with live pathogens, but with their toxic by-products. Tetanus and botulism, for example, tend to kill because the bacteria responsible for the disease release highly toxic compounds into the animal's system. Rendered non-toxic by chemical processes, these toxoids, when introduced to the body, can trigger an immune response similar to that seen with attenuated live viruses. One of the earliest discoveries in vaccine research, toxoids are still routinely used to protect against tetanus, botulism, and other clostridial infections.

Killed Pathogens—A vaccine made with killed organisms is far safer than the attenuated live version, but it must be delivered by injection. Antigenic proteins on the surface of the dead pathogens are still able to launch the process of immunity, but the invaders are completely inactivated and pose no danger to the recipient. The down side? The immune response provoked by a killed vaccine is sometimes less complete—or shorter-lasting—than that stimulated by an attenuated vaccine. So these preparations generally depend on the addition of an adjuvant to enhance the long-term immunostimulating effects of the killed virus, and recruit additional immune-cell armies to create a more thorough response.



Vaccine researchers have recently found that introducing only the genetic nucleic acids (the components of DNA or RNA) of the pathogen can sometimes confer immunity. "The Centers for Disease Control believes that 'naked DNA' will be the basis of most vaccines in the future," says Kevin Hankins, DVM, MBA, an assistant professor at Kansas State University and field veterinary consultant for Fort Dodge Animal Health.

Adjuvants have much to do with a vaccine's effectiveness, and pharmaceutical companies often closely guard their "recipes" for adjuvants. Some of the ingredients that might be present are mineral or vegetable oils, mineral salts, and saponins (emulsifiers that break oil-based solutions into droplets and give the vaccine a time-release quality).

Recombinant Vaccines—One 21st Century approach to immunization is the recombinant vaccine, so named because it's based on advances in gene manipulation techniques. Recombinant vaccines might feature only surface proteins of a disease-causing virus or bacterium—fragments just complete enough for the immune system to recognize and attack the invader.

Others are gene-deleted vaccines, in which the pathogen has been tampered with to eliminate the genes that cause disease, but retain the ones that trigger the immune response.

Then there are viral vector vaccines, which use recombinant technology to piggyback an immunity-provoking gene onto an harmless virus, so that it masquerades as a pathogen. (A very successful oral rabies vaccine for wildlife, used in bait drops in rabies-infested areas like Texas, Oklahoma, and Ontario, is created this way.)

The advantage of a recombinant vaccine is that it doesn't contain any intact copies of the pathogen—alive or dead—so it's extremely safe, and it can still stimulate good immunity. Merial Limited's Recombitek West Nile virus vaccine is the first formulation of this kind to be made commercially available for horses.

Naked DNA Vaccines—Vaccine researchers have recently found that introducing only the genetic nucleic acids (the components of DNA or RNA) of the pathogen can sometimes confer immunity. This was something of a surprise because these nucleic acids are not generally recognized by the immune system as foreign. But, when strange DNA is introduced to the body, it's taken up by cells that make proteins encoded by that DNA. The immune system then responds to the cells with the foreign proteins by rallying the troops, which confers immunity to the horse.

"The Centers for Disease Control believes that 'naked DNA' will be the basis of most vaccines in the future," says Kevin Hankins, DVM, MBA, an assistant professor at Kansas State University and field veterinary consultant for Fort Dodge Animal Health. "They see it as a better technology, with some significant advantages. There's no vector with a naked DNA vaccine, so there's no risk of infection."

Safety is just one of the advantages of a DNA vaccine. Scientists acknowledge that DNA can be highly purified and does not seem to trigger autoimmune reactions (when the body recognizes its own cells as "not self" and initiates an immune response to destroy them). Furthermore, it's easy to handle, with a long shelf life and no requirement for refrigeration (a major plus for Third World situations). And because DNA is easy to manipulate, vaccines could be easily and inexpensively modified to keep up with mutations and make it to the market faster than the current crop of killed vaccines.

DAVID YOUNG

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Finally, according to Hankins, "The CDC is hoping it might be effective against diseases we haven't had much success fighting with conventional vaccines."

If the idea of injecting foreign DNA and encouraging its uptake into your horse's cells sounds alarming at first, Hankins offers reassurance. "The DNA in the host cells isn't going to replicate because what's being used is not the whole DNA strand. It just stimulates immunity to those specific antigens, and the cells get destroyed in that process. It's important that people realize this is not the same as genetic engineering. It's not even in the same ballpark."

One of the challenges with DNA vaccines is finding the best method of delivery. The goal is to promote the uptake of the DNA material into cells—and while intramuscular injections have been used, researchers are exploring other avenues, including spraying the vaccine on mucous membranes, or even firing microscopic gold pellets coated with nucleic acids into the skin via a "gene gun." Ultimately, we might be able to inject a string of genes from different organisms and protect against a whole series of diseases all at once.

There are currently no naked DNA vaccines on the market for horses, but it's no secret that they are in development and coming soon to a veterinarian near you.

Reminding the Immune System

DNA vaccines might be the wave of the future, but for now, most of the vaccines we use for horses are the killed-organism type. When a horse is vaccinated against a disease for the first time with an inactivated (killed) virus product, his antibody titer—the level of antibody against that particular virus in the bloodstream—keeps rising for several weeks afterward. The practice of giving a "booster shot," a repeat dose two to four weeks after the original injection (while the titer is still on its way up), ensures the maximum number of immune cells with "memory" are jolted into action for the best possible humoral immune response.

Immunity doesn't last forever. It tends to diminish over time if the horse has no further exposure to the pathogen. So, it's necessary to "remind" the immune system of the danger periodically. The majority of equine vaccines are given on a yearly basis to ensure the antibody titer stays high. Some need to be administered more often; vaccines for influenza, for example, might be repeated every three months. Immunity dissipates more quickly with killed vaccines; those made with attenuated live organisms tend to confer longer-lasting protection.

It's suspected that many equine vaccines might actually confer immunity for longer than a year, but most pharmaceutical companies don't do duration-of-immunity studies—it's both expensive and difficult to measure what qualifies as sufficient immunity. Researchers have yet to answer the thorny question: How much response is enough?

Admittedly, pharmaceutical companies are motivated to sell vaccine, and thus are not likely to investigate whether dosages can be given less often, but the yearly booster does have a less mercenary rationale: It helps you establish a routine and keep track of which boosters are needed. Longer intervals might mean boosters are forgotten. (For example, human vaccinations for tetanus are administered at least every 10 years. Do *you* remember when you had your last tetanus shot?)

Some vaccines are more effective than others. Those protecting against influenza, equine herpesvirus (rhinopneumonitis, or "rhino"), strangles, and Potomac horse fever are among those that confer something less than 100% immunity, or have to be administered more frequently (often four to six times a year) to provide protection.

The reason? Viruses are sneaky critters with a talent for mutation, and sometimes the mutations change the surface proteins to the point where an immunized body no longer recognizes them as the enemy.

Flu viruses are notorious mutants (although less so for horses than for humans), and even the most up-to-date vaccine cannot possibly protect against all the various strains in the environment. Your horse might be fully protected against several flu strains and still fall victim to one not included in the vaccine formulation. Or he could contract another respiratory virus, like EHV, and exhibit identical symptoms, leading you to blame his symptoms on a failed flu vaccine. You often don't know which disease you're really dealing with.

Furthermore, the vaccines might be conferring as much immunity as they can; most researchers feel that the natural immunity a horse might acquire from contracting and overcoming an infection lasts no longer than the immunity he acquires through vaccination.

Finally, the realities of the pharmaceutical industry mean that by the time a vaccine hits the market, its formulation might already be outdated. Because horses make up a relatively small chunk of the veterinary drug market, it's less profitable for companies to formulate new versions of equine vaccines than to research new ones for cattle or swine. And even when a new formulation for horses is designed, it must still go through years of testing, followed by a long wait in line for licensing, before it lands in your veterinarian's hands.

That's not to say research isn't continuing at a relatively vigorous pace. Companies are continually working on new methods of

ANNE EBERHARDT

In an age where most of us have never witnessed a case of rabies, tetanus, or EEE, it can become easy to see the prevention as worse than the disease, but one only has to read the descriptions of these diseases from a few scant decades ago to be reminded of just what we don't want our horses to suffer.

growing and purifying vaccines to lessen the risk of side effects. Older vaccines, for example, often contained virus grown in chicken eggs. The resulting formulations sometimes contained proteins that triggered allergic responses. Today, viruses are usually grown in purified cell culture media in the lab. Adjuvants are also more highly purified than in the past, and as a result they are more effective and less irritating to the horse.

Taking a Hard Look

Vaccination isn't a perfect process, but it's a lot better than the alternative, say most experts. Over the past couple of centuries, vaccines have saved countless lives and have had incalculable economic impact the world over. Improved sanitation and hygiene have also contributed to the improved health and life spans of humans and horses, of course, but not all disease declined with the advent of indoor plumbing.

Polio is one example of a disease that increased in frequency and virulence when improved sanitation began to allow more people to crowd into urban areas. (Since the virus is shed in fecal material, it's even thought by some researchers that high-tech flush toilets spread polio through the air!) Although less than 1% of children exposed to the virus contracted the paralyzing form of polio, it was still enough to put tens of thousands of North Americans in wheelchairs and iron lungs in the first half of the 20th Century. When Jonas Salk finally came up with an effective vaccine in the early 1960s, it was considered a revolution. (As a direct result of the Salk and Sabin vaccines, polio outbreaks now occur in only a few isolated pockets of the world, and it has been almost completely eradicated in industrialized nations.)

Are we, as some have claimed, weakening the horse's immune system by bombarding it with boosters? The jury is still out on this question, but there is little hard evidence to suggest we are over-vaccinating and doing harm. (More on this debate later in our series.) Rarely do horses suffer localized or systemic allergic responses to vaccines with repeated exposure, but the reaction often comes from the adjuvant rather than the virus itself. A change of brand often takes care of the problem.

Even more rarely, they might experience life-threatening anaphylactic reactions. Is the incidence of allergic response on the rise? Most researchers say not. Those horses who do suffer them are generally older individuals with long exposure to the vaccine—horses which, in another time without that vaccine, might not have survived long enough to exhibit an allergic response.

Severe reactions to vaccines are extremely unusual, largely because attenuated live vaccines are almost never used in horses today. Recombinant or DNA vaccines, the direction the industry is taking, have a particularly wide safety margin. Researchers and veterinarians agree that the danger posed by exposure to deadly diseases such as tetanus, encephalomyelitis, or botulism is far greater than the risk of a vaccine reaction. These are, after all, products that are used safely in millions of horses every year.

We might be circumventing the natural course of evolution by vaccinating our horses, but that's of course true of almost all of our equine management practices. Would it be better to allow our horses to be exposed to, and overcome, disease as nature intended? This theory might be valid if all equine diseases were nothing but a nuisance. But several of them can be deadly; some, like rabies, have no other possible outcome. And some of the safest and most effective vaccines are those that protect against the most horrific disease. To fail to protect your horse against such scourges is not only to risk personal heartbreak, it could put your neighbor's horses at risk as well. That's not to mention the fact that some equine diseases are transmittable to other species, including humans.

In an age where most of us have never witnessed a case of rabies, tetanus, or EEE, it can become easy to see the prevention as worse than the disease, but one only has to read the descriptions of these diseases from a few scant decades ago to be reminded of just what we don't want our horses to suffer.

Perhaps the most dangerous thing about vaccines is that we sometimes expect them to work miracles. It's important to remember that they are merely a tool in the control of infectious disease, not a panacea. Just as crucial as vaccination are sound management practices such as controlling exposure and spread of disease.

Over the next 11 months, we'll bring you much more information about equine vaccines, their pros and cons, risks and realities, with the help of a panel of experts from both academia and industry. Stay tuned for all the vaccine vital statistics.

ABOUT THE AUTHOR

Karen Briggs *writes for more than 20 equine magazines in Canada, the United States, and Great Britain. Based in Ontario, she also is a Canadian certified riding coach, an equine nutritionist, and an active preliminary-level three-day eventer. Briggs authored* Understanding Equine Nutrition *and* Understanding The Pony, *published by Eclipse Press and available at www.ExclusivelyEquine.com or by calling 800/582-5604.*

Vaccination Essentials:

Tetanus, Rabies, and Botulism

BY KAREN BRIGGS

Ask veterinarians anywhere in North America and they'll likely agree: If you vaccinate for nothing else, at the very least vaccinate for tetanus and rabies. The two diseases have much in common. They're endemic—meaning your horse could be exposed to the causative organisms at any time, anywhere in his environment. They're exquisitely painful, have no cure, and are almost certainly fatal. And it's completely unnecessary for your horse to suffer from these diseases since the vaccines available to protect against them are inexpensive, extremely effective, and are part of every veterinarian's arsenal.

There's a third disease—botulism—that is caused by an organism closely related to the one that causes tetanus. It shares many of the same characteristics (it's painful, has a high mortality rate, and horses are exposed to the organism daily). But at the moment, it's not routinely vaccinated against except in parts of North America where incidence is high (Kentucky and Ohio, for example). Yet, given some of the risk factors for the disease, vaccinating against botulism ought to be as much a part of our yearly health care routine for our horses as protecting them against tetanus and rabies.

Let's look at each disease in more detail.

Terrible Tetanus

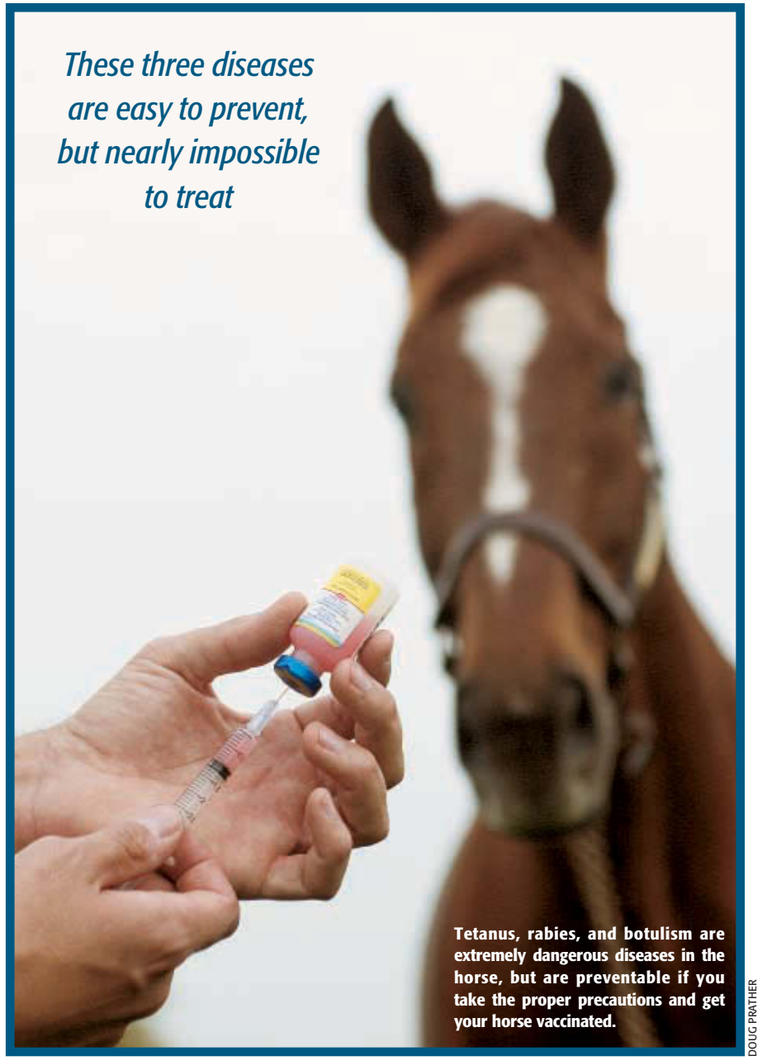
Once upon a time it was called lockjaw, and even 200 years ago horse owners knew it was a terrible way for a horse to die.

Clostridium tetani, the organism that causes tetanus, is an anaerobic bacterium

Editor's Note

This is the second in a 12-part series of articles on vaccinations for horses.

These three diseases are easy to prevent, but nearly impossible to treat



Tetanus, rabies, and botulism are extremely dangerous diseases in the horse, but are preventable if you take the proper precautions and get your horse vaccinated.

DOUG PRATHER

VACCINATIONS

PART 2

found in soil and fecal material. Ordinarily it's harmless because it dies on exposure to the air—but if it finds a hospitable, moist, airless environment in which to live, it flourishes and gives off one of the most potent natural toxins known to man. Its preference? A puncture wound, sometimes one so small you might not notice it on your horse, as such wounds tend to bleed very little and close over quickly. *C. tetani* can also infect unvaccinated stallions following castration, and it can infect foals with failure of passive transfer via the umbilical stalk (hence the practice of dipping a newborn's umbilical stalk with antiseptic).

Tetanus can incubate for one to three weeks before signs start appearing. Once the toxin begins to work, it impairs the inhibition of excitatory signals to the nerves—meaning that muscles, once contracted, will tend to stay contracted and not be able to relax. A horse with tetanus will show a classic "startled" expression and a straddled, "sawhorse" stance, might have ears pulled permanently forward or back and down, retracted lips, flared nostrils, and difficulty opening jaws (lockjaw). He might also seem colicky.

Within 24 hours of the appearance of the initial symptoms, he'll experience spasms of his third eyelid, a retraction of the eyeball into the socket (which makes the eyes look sunken), and he'll be over-reactive to any sudden noises, going into spasms or seizures. His temperature might rise to 110°F, and eventually he'll go down, lying on his side with his legs extended rigidly and his neck stretched awkwardly upward. Death follows soon afterward.

Horses that contract tetanus have an 80% mortality rate, and few treatment options apart from emergency administration of tetanus anti-toxin (more on this in a moment) and supportive therapies. He might need to be fed intravenously because he'll be unable to relax his jaw. Even if your horse does recover, he'll need more than six weeks to get anywhere near back to normal, and his experience will not grant him long-lasting immunity from further tetanus infections.

Equine tetanus anti-toxin is a treatment, not a vaccine; it confers passive immunity to an unvaccinated horse that might have been exposed to *C. tetani*. Stephanie Thompson, DVM, manager of technical services for Merial pharmaceutical company, describes it like this: "Instead of stimulating an immune response, an anti-toxin *provides* the animal with the short-term immune response. The antibodies contained in an anti-toxin are meant only as help in a crisis."

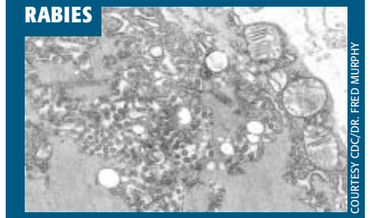
Anti-toxins are expensive, not always readily available, and can only do so much. They can bind to circulating toxins in the horse's bloodstream, but once the toxin binds to the nerve cells, anti-toxins have no way to dislodge it. Thus, early administration is crucial if you think you have an unvaccinated horse that is at risk for tetanus. But apart from exceptional circumstances—say, you rescue a neglected horse at auction who has a visible puncture wound and no medical history—you should never find yourself in the position of having to get your veterinarian to administer anti-toxin

TETANUS

COURTESY CDC

Clostridium tetani **is the organism that causes the disease tetanus. It is an anaerobic bacterium found in soil and fecal material.**

RABIES



COURTESY CDC/DR. FRED MURPHY

The rabies virus is introduced to the horse's system by the bite of an infected animal. It enters nerve cells at the wound site and travels to the brain.

BOTULISM

COURTESY CDC/LARRY STAUFFER, OREGON STATE PUBLIC HEALTH LIBRARY

Clostridium botulinum **produces a neurotoxin that causes botulism. Horses can contract botulism from ingestion of the toxin through contaminated feed or water, or through the entrance of** ***C. botulinum*** **from the soil into a puncture wound.**

because your horses should be routinely protected against tetanus through vaccination. It's a no-brainer, says Thompson.

"Because the exposure risk is so high in horses—and all farm animals—there really is no reason *not* to vaccinate against tetanus," she says. "Tetanus vaccine is readily available (usually along with other vaccines in a combined injection), and it's extremely effective in protecting (horses) from the disease." Furthermore, there's very little danger of reaction, and no risk whatsoever of contracting the disease from receiving the injection because the tetanus vaccine is a toxoid, formulated from proteins in the toxin rather than from the bacteria itself. Since there are no live components in the formulation, and only selected proteins from the toxin (enough to stimulate the immune system to recognize it as "foreign" and attack it, but not enough to cause disease), the vaccine is one of the safest available, with a track record decades long.

Why a toxoid instead of a killed-bacteria vaccine? Thompson explains that with tetanus, the bacteria tend to stay in the wound where they initially take hold; it's the toxin that circulates in the horse's system. Therefore, it's the toxin the immune system needs to recognize and attack, particularly because it can linger in the system even after you kill the organism itself.

Incidentally, although the disease is not transmissible between humans and horses, our two species are considered among the most vulnerable to its effects, so if you work around a barn, you should make sure your own tetanus protection is up-to-date as well as your horse's! Consult your physician for a human-approved vaccine.

Rabies: No Way for a Friend to Die!

If tetanus sounds like a horrific disease, it might just be surpassed by rabies, a true nightmare with no hope of a happy ending.

Historically one of man's most feared diseases, rabies was described by the ancient Greeks as lyssa, meaning "frenzy." The Romans gave us its present name by adapting their Latin word meaning "to rage." It's a form of viral encephalitis that

Vaccination Schedules for Tetanus, Rabies, and Botulism

DISEASE/VACCINE	FOALS/WEANLINGS	YEARLINGS	PERFORMANCE HORSES	PLEASURE HORSES	BROODMARES	COMMENTS
TETANUS TOXOID	Foals from nonvaccinated mares: First dose given at 3-4 months, second dose given at 4-5 months	Annual	Annual	Annual	Annual, 4-6 weeks before foaling	Booster at time of penetrating injury or surgery if the last dose was not administered within six months
	Foals from vaccinated mares: First dose given at 6 months, second dose given at 7 months, third dose given at 8-9 months	Annual	Annual	Annual		
RABIES	Foals born to nonvaccinated mares: First dose given at 3-4 months, second dose given at 12 months	Annual	Annual	Annual	Annual, before breeding	Vaccination recommended in endemic areas. Do not use modified-live virus vaccines in horses.
	Foals born to vaccinated mares: First dose given at 6 months, second dose given at 7 months, third dose given at 12 months	Annual	Annual	Annual		
BOTULISM	Foals from nonvaccinated mares: See comments	Consult your veterinarian	Consult your veterinarian	Consult your veterinarian	Initial 3-dose series at 30-day intervals with last dose 4 to 6 weeks before foaling; annually thereafter, 4-6 weeks before foaling	Only in endemic areas. A third dose administered 4-6 weeks after the second dose may improve the response of foals to primary immunization. Foals from non-vaccinated mares may benefit from toxoid at 2, 4, and 8 weeks of age; transfusion of plasma from vaccinated horse; or antitoxin. Efficacy needs further study.
	Foals from vaccinated mares: Three-dose series of toxoid at 30-day intervals starting at 2-3 months of age	Consult your veterinarian	Consult your veterinarian	Consult your veterinarian		

SOURCE: AAEP GUIDELINES FOR VACCINATION OF HORSES

is transmitted by the saliva of infected animals, meaning that in almost all cases you must be bitten to contract it. Rabies exists in populations of all sorts of wildlife with which horses might come into contact—skunks, raccoons, bats, foxes, coyotes, groundhogs, and feral cats and dogs, to name only a few—and the disease is considered endemic in most parts of North America.

The rabies virus, once introduced to the system by the bite of an infected animal, takes aim at the cells of the central nervous system. It enters nerve cells at the wound site and travels to the brain, then follows nerve pathways to the muscles and organs, wreaking havoc in the process.

The virus concentrates in salivary glands, which explains why it is usually spread by bites, but it also invades the muscles used for drinking and swallowing, causing extreme pain when the animal tries to swallow liquids. The result is that although the animal might be desperately thirsty, the pain on trying to drink induces a fear response to the mere sight of water—hence one of the other historical names for rabies: Hydrophobia (fear of water).


COURTESY DR. EARL GAUGHAN

A puncture wound, such as this one caused by a nail, can open a route into the horse that could result in tetanus.

The incubation period for rabies is usually two to six weeks (according to an extension publication from the University of Kentucky), depending on the site of the bite from the rabid animal. A bite on the muzzle means the virus hasn't got far to travel to reach the brain, while a chomp on a hind leg presents the virus with a longer journey and a longer incubation time.

Broadly described, there are two ways rabies is expressed: The "furious" form and the "dumb" form. In the furious form, animals become abnormally aggressive, even vicious, as well as super-sensitive to stimuli, especially touch. Horses usually, but not always, exhibit the dumb form, which is less dramatic. The animal becomes lethargic and weak, and he soon is unable to raise his head or vocalize because the throat and neck muscles are paralyzed. He might show photophobia (an aversion to light), develop a high fever, become colicky, or go temporarily or permanently blind. Excessive salivation, heart arrhythmias, even seizures can all be present. It's often said that the only thing typical about rabies is that it's atypical.

As the virus spreads, it destroys the brain matter, with symptoms depending on what parts of the brain are targeted. By the time any symptoms are evident, one thing is for sure: Death is three to five days away, and there is no treatment. Rabies is 100% fatal!

Rabies also has the distinction of being a "zoonose"—a disease transmissible between animals and humans. That makes it extremely dangerous for horse owners, especially since, as Thompson explains, "The dumb form in horses can be mistaken for choking—so owners might stick their hands in these horses' mouths trying to locate a blockage."

There have been rare cases of horses with the furious form as well; in one shocking case in Ontario a few years ago, a rabid Belgian horse savaged and killed his owner.

As with tetanus, Thompson emphasizes the value of vaccination. "Rabies is a horrible, horrible disease, and the vaccine is extremely safe and virtually 100% effective," she says. "It's surprising how many people don't routinely give rabies vaccinations to their horses, saying there isn't much of it in their area. It's the law to vaccinate for rabies in most places for dogs, and even for cats, but there's no such legislation for horses.

"I think part of the reason people don't vaccinate is that they don't truly understand the risk, because they've never *seen* a case of rabies," continues Thompson.[4] "If you see it, you will never, ever forget it. Vaccinating is so inexpensive and has such a low reaction rate…the disease risk far outweighs any risk inherent in vaccination."

The rabies vaccine used for horses in North America is a killed-virus formulation with an adjuvant (a substance added to a vaccine to boost the immune response). This means there is no risk of live organisms in the solution, so it's extremely safe.

If your horse does react to the injection, he's probably reacting to the adjuvant. Since each manufacturer has its own proprietary adjuvant formula, choosing a vaccine from another manufacturer next time will generally take care of the problem.

The AAEP Guidelines state: "None of the licensed vaccines are labeled for administration to pregnant mares; therefore, it is recommended that mares be vaccinated before breeding. However, it should be recognized that some veterinarians administer the killed-virus vaccine to pregnant mares without reports of adversity. Modified live rabies vaccines are not licensed for horses and should not be used."

It's reassuring to know that although there are several different strains of rabies (you might have heard of "skunk rabies" or "bat rabies," for example), there are enough common proteins in the various strains that the commercially available rabies vaccines will protect against all of them.

Beware of Botulism

The dark horse in our trio of deadly diseases is botulism, which is still not considered a common disease in horses. That, unfortunately, is changing.

Botulism is caused by a neurotoxin produced by the anaerobic bacterium *Clostridium botulinum*, first identified in 1897 in Belgium during an outbreak of food poisoning. It's closely related to *C. tetani*, the bacterium that causes tetanus, and like *C. tetani*, produces one of the most potent poisons known to man. Horses are particularly sensitive to botulinum toxin; untreated foals can suffer up to 90% mortality. Mortality is also high in untreated adults.

Eight toxin types, each produced by a different bacterial strain, have been identified: Types A, B, C1, C2, D, E, F, and G. Each type is unique in its geographic distribution and species susceptibility. Type B accounts for more than 80% of equine cases, with Types A and C making up the rest.

The clinical signs of botulism can easily be confused with other conditions such as rabies, equine protozoal myelitis (EPM), tetanus, and azoturia (tying-up). Unlike most of these, however, botulism can strike very swiftly. The toxin works by inhibiting the release of acetylcholine (a neurotransmitter) at the neuromuscular junction, the point at which nerve endings meet muscle fibers. Without acetylcholine, muscles are not stimulated to contract, and become progressively weaker and finally paralyzed. Affected horses lose the ability to swallow


WIND RIVER PHOTOGRAPHY

One way a horse can contract botulism is ingestion of the toxin through contaminated feed or water.

food or water, dribbling grain and saliva from their lips; move in a shuffling fashion or drag their toes; and can suffer other signs such as depression, muscle tremors, a protruding tongue, dilated pupils, constipation, colic, shortness of breath, and violent spasms or seizures. Physical activity may worsen clinical signs.

In as little as 48 hours, horses affected with botulism are recumbent and unable to rise, typically with their chins resting on the ground. Respiratory paralysis usually forces euthanasia. The severity of symptoms, however, is largely dependent on the amount of toxin, and less severely affected horses might decline slowly—a characteristic that can confuse diagnosis.

Horses can get botulism in three ways. The most common is ingestion of the toxin (not the bacterial spores themselves) in contaminated feed or water. Decomposing carcasses of rodents or birds in baled hay are often blamed, but it is far more common for hay or silage to be contaminated through improper storage or poor fermentation. The risk increases markedly when horses are fed large round bales, especially the wrapped silage type, which can become infected with *C. botulinum* when their plastic wrapping is compromised. Outbreaks of botulism in several horses on a farm are almost always due to this type of feed.

More rarely, horses can contract botulism through the entrance of *C. botulinum* from the soil into a puncture wound. In young foals, botulism can be contracted by the entrance of the organism through the tissue of the umbilical stump. The result is called "shaker foal syndrome" because the foal develops violent muscle tremors, a stilted walk, and an inability to swallow (milk dribbling from a foal's mouth and nose is a classic sign of botulism). Death usually occurs within 72 hours.

As with tetanus, the vaccine is an inactivated toxoid, which is extremely effective. There is also a botulism anti-toxin for treating horses and foals with suspected botulism, but it's prohibitively expensive for most, difficult to get, and must be specific to the type of toxin causing the disease (which is a challenge with lab results often taking several days to determine this).

Currently, the only botulism toxoid readily available in North America protects only against the B strain, which luckily is the serotype most commonly associated with forage contamination. Although vaccinating for botulism might not be as widely recommended as for tetanus and rabies, any farm considering feeding cost-effective haylage or silage products, or round hay bales, should consider protecting their animals from this disease, especially broodmares, who can pass their antibodies on to their nursing foals and thus protect them from shaker foal syndrome.

It can also be useful to test your forage for pH (acidity) before you feed. *C. botulinum* is very pH-sensitive and thrives at levels over 4.5. Feedstuffs that test at a pH level below 4.5 are probably acidic enough not to be contaminated with the toxin.

In sum, there's virtually nothing to lose and everything to gain by vaccinating all horses against tetanus and rabies. Botulism guidelines are fuzzier, but your veterinarian can help you decide whether you should vaccinate against this often fatal disease.

ABOUT THE AUTHOR

Karen Briggs *writes for more than 20 equine magazines in Canada, the United States, and Great Britain. Based in Ontario, she also is a Canadian certified riding coach, an equine nutritionist, and an active preliminary-level three-day eventer. Briggs authored* Understanding Equine Nutrition *and* Understanding The Pony, *published by Eclipse Press and available at www.ExclusivelyEquine.com or by calling 800/582-5604.*

West Nile Virus: Threat and Response

BY KAREN BRIGGS

Management beyond vaccination is important

For a graphic demonstration of the value of vaccination, look no further than West Nile virus (WNV). When it roared onto the Eastern shore of the United States in 1999 (most likely thanks to a European or African bird), WNV struck fear into the hearts of horse owners when it quickly became clear that equines were more vulnerable to the virus than humans. Appearing more virulent than it had ever been on the other side of the Atlantic (where it had been recognized since the 1930s), WNV took full advantage of the naïve immune systems of North American horses. One in three equines that contracted the disease died, and many survivors were left with lasting neurological problems.

Editor's Note

This is the third in a 12-part series of articles on vaccinations for horses.

DOUG PRATHER

The virus also showed an alarming ability to spread with its avian carriers—a wide variety of birds from blue jays to crows. Mosquitoes that feasted on infected avian blood, then punctured horses with their next bite, spread WNV from species to species. From 25 equine cases documented by APHIS (Animal and Plant Health Inspection Service of the United States Department of Agriculture) in 1999, all on the Eastern seaboard, the incidence of WNV in horses more than doubled to 60 (in New England, New York, and Pennsylvania) in 2000, then skyrocketed to 738 in 2001 as West Nile virus infiltrated the warm, humid, mosquito-friendly southern states of South Carolina, Georgia, and Florida.

From there it continued its rapid spread westward, reaching Montana and New Mexico in 2002 and devastating horse populations in the central states of Texas, Oklahoma, Nebraska, Iowa, Missouri, Illinois, and Minnesota, each of which reported in excess of 800 equine cases that year (see maps on page 102). All told, there were more than 15,000 cases of WNV in horses in the United States in 2002, and the westward spread was mirrored in Canada as the virus hit Manitoba, a province that suddenly saw great irony in its claim that the mosquito is the "provincial bird." Of the 336 reported cases of equine WNV in Canada in 2002, 236 came from Manitoba, with the remainder in Ontario, Quebec, and Saskatchewan.

By 2004, WNV had been reported in every American state except Alaska, Hawaii, and Washington state, and it had progressed as far west as Alberta in Canada. But the overall number of cases had dropped significantly, especially in the east. In the continental United States, there were 5,181 reported cases of equine WNV in 2003, and the 2004 tally was just 1,341. Canada's numbers showed a similar trend—445 horses in 2003, and only 13 in 2004.

What caused the turnaround? Researchers speculate that climatic conditions had a major impact; cooler, drier conditions in many parts of North America in the past two years just didn't favor a burgeoning mosquito population and could have affected bird migration patterns. Control measures—such as spraying and increased vigilance about cleaning up standing water where mosquitoes breed—helped too. But perhaps the most pivotal factor was the introduction of a vaccine protecting horses against WNV in August of 2001. Fast-tracked to the market on a conditional license, Fort Dodge Animal Health's West Nile Innovator, a killed virus vaccine, was instantly embraced by veterinarians and owners alike.

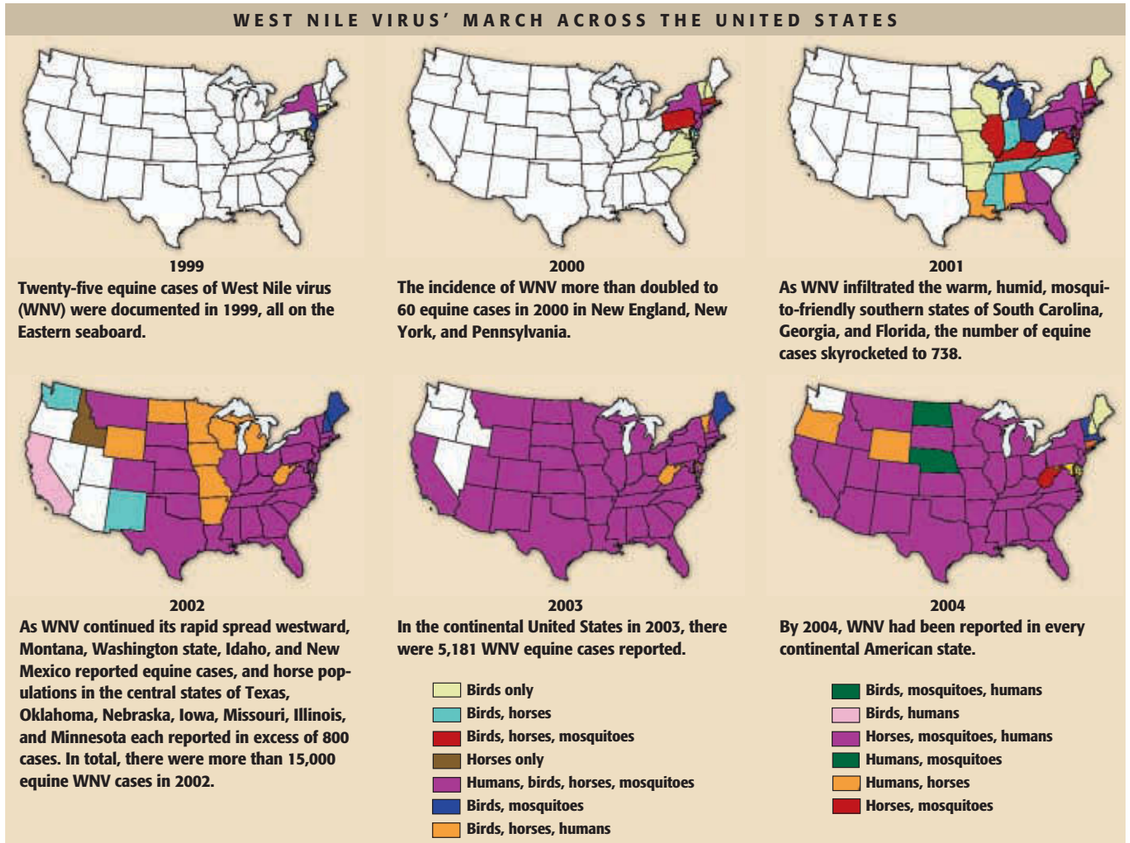
Protection from WNV

Fort Dodge's vaccine is, in fact, the rarest of creatures—a vaccine for horses that hit the commercial market before a comparable vaccine was available for humans. Ordinarily, it's the other way around, with developments in the veterinary pharmaceutical market lagging months or years behind treatments and preventions for people. Fort Dodge was able to launch its record-time response to the crisis through the use of a conditional license based on early challenge studies. By 2003, with millions of horses having received the vaccine and a strong record of safety and efficacy, it was granted full approval by the USDA.

W. David Wilson, BVMS, MS, professor of equine internal medicine and associate director of the large animal clinic in the Veterinary Medical Teaching Hospital at the University of California, Davis, explains, "In order to get a conditional license for a vaccine, you have to demonstrate (that the disease is) an imminent threat, and you have to demonstrate a reasonable expectation of efficacy and safety. Because West Nile virus is similar in many ways to the viruses for Eastern and Western equine encephalitis (EEE and WEE), formulating a vaccine for WNV wasn't much different than formulating those vaccines. Basically they killed the (causative) bug, added the adjuvant, and the vaccine was ready for testing, with expectations that it would perform similarly to those EEE and WEE vaccines, which had already been proven very successful."

DOUG PRATHER

Even if vaccination has vastly reduced the incidence of WNV in horses, remember that the infection rate in mosquitoes is still high.



At the time researchers at Fort Dodge began their investigation into creating an equine West Nile vaccine, the disease had affected fewer than 100 horses in the United States. "You have to applaud them for taking the gamble," says Wilson. "When West Nile first showed up here, many predicted it was going to be no big deal as it generally is on the other side of the Atlantic. Few expected it would sweep across the continent the way it did or be so virulent. Fort Dodge thought otherwise, and their fast action certainly has paid off. I don't think there's anyone who's not grateful for the availability of that vaccine."

Kevin Hankins, DVM, MBA, assistant professor at Kansas State University and field veterinary consultant for Fort Dodge Animal Health, notes, "The demand (for West Nile Innovator) was greater than we anticipated in 2001, but fortunately we were able to keep up. By 2002, it was in widespread use in the United States and had also been approved in Canada. By 2003, we saw cases of West Nile in horses drop dramatically. That's pretty good evidence of efficacy, along with our challenge studies that demonstrated a 96% protection rate (against viremia), so it was relatively easy to get full approval for the vaccine in 2003."

There was, however, a blip on the radar that never had an impact on the USDA, but did temporarily make some horse owners hesitant to use the Fort Dodge vaccine. In 2003, a few individuals calling themselves the "Lost Foals Group" alleged that administering the West Nile virus vaccine to their broodmares had caused them to abort or have deformed foals. The accusation got some mainstream media attention in the Denver *Post*, and nervous horse owners started to question their veterinarians about the safety of the vaccine. Many reputable veterinarians spoke up in support of the safety and efficacy of Innovator, while closer examination of the circumstances of the admittedly unlucky breeders of the Lost Foals Group revealed no substantiation for their claims.

"It was a lot of noise for a while there," says Hankins, "and it didn't really have an effect on sales because vets didn't buy into it. But it did make the USDA and APHIS do something they normally don't do: They posted messages on their web sites supporting the use of Innovator in horses and emphasizing the importance of vaccination against West Nile."

A recently completed retrospective study from Texas A&M University examining the vaccination history of 595 broodmares now confirms that there is no link between the Innovator WNV vaccine and reproductive problems, although like many vaccines, West Nile Innovator is not specifically labeled for use in pregnant mares.

"Use it at your veterinarian's discretion," says Hankins.

More discretion is needed regarding vaccination frequency. West Nile Innovator is labeled for a one-year duration of immunity to help prevent viremia, but many veterinarians recommend giving it more often where mosquitoes are active year-round.

"It's very important to communicate with your veterinarian to develop a protocol for your individual horses and your individual circumstances," Hankins emphasizes, while suggesting that there's no known risk in

NEW FOR 2005

First West Nile Virus DNA Vaccine for Mammals on the Way

A new vaccine to protect horses against West Nile Virus (WNV) has been developed and submitted for USDA review. If approved, it would be the first commercially available DNA vaccine for any mammalian or animal species.

Steve Chu, DVM, PhD, senior vice president of Global Research and Development at Fort Dodge Animal Health, explained the conceptual DNA vaccine to *The Horse*. The vaccine has two major components—one is a piece of DNA that codes for two West Nile viral proteins (the membrane protein and the envelope protein), and an adjuvant, which helps stimulate immune response.

In a conventional killed-virus vaccine, "We prepare the viral proteins in the manufacturing plants and put them in the final product as the antigen," said Chu. "Host animals that have received conventional WNV vaccines will create an immune response to the protein antigens and become protected."

Chu explained the novel DNA vaccine: "DNA is the genetic code of life. Once it's given to a host animal in a vaccine, it will be taken up by the host's cells. The DNA (of the disease you want to protect against) molecules need to get inside an animal's cells—in this case they could be picked up by the muscle cells and they can then, inside the muscle cells, go through further life cycle changes and be processed, or transcribed, into RNA. That RNA then can be translated into proteins. The proteins can be used to stimulate antibodies and a lymphocyte (white blood cell) immune response," thus protecting the horse from disease.

This WNV DNA vaccine technology also differs from another vaccine that has been on the market about a year. That canarypox vectored vaccine (by Merial) is a recombinant viral vaccine, not a DNA vaccine. Canarypox is used to carry West Nile virus genes into the horse's cells to stimulate immunity.

DNA vaccines are relatively new to science—the very first DNA vaccine concept was presented in 1992, while conventional vaccine concepts were presented over 100 years ago. The Food and Drug Administration approved the first DNA vaccine protocol for use in human trials in 1995. While thousands of DNA vaccine research papers have been published, no vaccine has been approved for commercial use in humans or any other animal species, to Chu's knowledge.

All commercial animal vaccines must be independently approved by the USDA for purity, potency, efficacy, and safety. "Certainly significant protection and safety would need to be demonstrated to make it acceptable to the USDA—safety to the horses, handlers, and the environment," he said.

The WNV DNA vaccine will be administered much like the other WNV vaccines available—two initial doses given approximately three to four weeks apart.

"We don't expect the use of this product will be fundamentally different than how people are used to protecting their horses," said Chu.

According to Chu, Fort Dodge's DNA vaccine is in the late stages of the USDA approval process, and he hopes it will become available during 2005. Detailed efficacy and safety information will be available for the public until that time.

"This certainly represents an additional new technology that could be made available for disease protection," Chu concluded.

—Stephanie L. Church

vaccinating more often.

"It's an extremely smooth vaccine with less than a 0.01% incidence of reactions reported in our challenge trials," he adds.

With WNV the new disease focus for many horse owners, virologists noticed an unsettling phenomenon in 2004: A spike in the incidence of EEE in unvaccinated horses in the eastern United States. Researchers speculate that many owners might have forgotten to vaccinate for this long-standing, very dangerous disease, which has double the mortality rate of WNV. So, it's timely that Fort Dodge now formulates the West Nile Innovator vaccine in various combinations. Depending on your location and the recommendations of your veterinarian, you can now give a single injection to protect against other encephalitides such as WEE, VEE, and/or EEE, in addition to West Nile virus.

"We call it the mosquito shot," says Hankins. There's also a combination vaccine that includes tetanus.

Any horse receiving a West Nile Innovator vaccine for the first time should get two injections three to six weeks apart. Thereafter, a single booster yearly (ideally administered a couple of weeks before mosquito activity begins) should provide good protection. Naïve horses that receive only one West Nile Innovator shot can launch enough of an immune response to protect them to some degree—in studies, such horses sometimes contracted the disease on exposure, but experienced milder symptoms. But if you administer the first shot and miss that three- to six-week window, Hankins recommends you "start over" with a course of two shots in order to ensure the best protection for your horse.

Something Old, Something New

Fort Dodge had no competitor in the marketplace with regard to WNV vaccines until January of 2004. That's when Merial Ltd. launched, with full FDA approval, a new WNV vaccine called RECOMBITEK. It's now available in the United States and Canada.

The difference between the Fort Dodge and Merial vaccines is that RECOMBITEK is a recombinant vaccine that piggybacks a couple of antigenic proteins from WNV on a canarypox vector. The WNV proteins are just enough to stimulate immunity with no danger of provoking disease symptoms in the horse. As for the canarypox, Stephanie Thompson, DVM, manager of technical services for Merial, explains, "Canarypox is like a shuttle bus, carrying the information the horse needs to stimulate his immune response. The canarypox is alive, but it's completely benign to horses. It attempts to replicate in the horse's cells, but it can't complete the process and it dies. So, the horse will not develop a neutralizing immune response against the canarypox, meaning there'll be no problem using the vaccine over and over in the same animal."

Fort Dodge's vaccine is the rarest of creatures—a vaccine for horses that hit the commercial market before a comparable vaccine was available for humans.

ANNE EBERHARDT

A study from Texas A&M University examining the vaccination history of 595 broodmares now confirms that there is no link between the West Nile Innovator vaccine and reproductive problems, although like many vaccines, it is not specifically labeled for use in pregnant mares.

Although RECOMBITEK represents the first use in North America of a recombinant canarypox vaccine for horses, it's not the first one based on canarypox in Merial's arsenal. Merial markets an equine influenza vaccine based on the same technology in Europe, and it has several canarypox vaccines available for small animals on this continent. There's even a canarypox-vector distemper vaccine for ferrets, and a very well-received one used in zoos for giant pandas, which are vulnerable to distemper.

"Canarypox is an extremely safe and effective vector," Thompson says. "It's very specific to canaries and their close relatives. One of the most unique things about recombinant technology is that you stimulate both the humoral immunity (when B lymphocytes are activated by the presence of an antigen, they transform into plasma cells that produce antibodies against the antigen) that a killed vaccine would stimulate, and cell-mediated immunity (the part of the immune system that produces "killer" cells that directly attack foreign invaders), so you get a more complete immune response. And they also seem to give a more rapid onset of immunity than you'd see with a killed vaccine.

"According to our trials," she continues, "West Nile protection starts in most naïve horses after you give the first shot. We do recommend that horses new to the RECOMBITEK vaccine get two boosters initially, but in our challenge studies, eight out of nine horses that had received only the first injection were protected (against viremia) 26 days later (Bowen et al, *American Journal of Veterinary Research* 2004). That's good news for people who might live in a region where West Nile suddenly sweeps in, who want to give their horses rapid-onset protection." (For more information, see page 18).

Furthermore, two separate Merial studies indicate that horses previously vaccinated with the killed WNV vaccine demonstrated an excellent antibody response two to four weeks after being injected with a single dose of RECOMBITEK. Thompson says this indicates that horse owners who want to switch from one to the other can do so with confidence. "It makes sense that they'd react similarly to the recombinant vaccine—they've been exposed to the same proteins previously," she explains.

The Merial WNV vaccine, like its Fort Dodge counterpart, is labeled for a one-year duration of immunity (aid in reduction of viremia), but Thompson says that in mosquito-endemic areas, veterinarians might recommend using it more frequently. There have been no reported safety concerns with frequent use. RECOMBITEK will likely be available in combination vaccines sometime in 2005.

Merial's vaccine against West Nile virus piggybacks a couple of antigenic proteins from the WNV on a canarypox vector; the proteins are just enough to stimulate immunity with no danger of provoking disease symptoms in the horse.

What's Next for WNV?

Those watching WNV's progress across the North American continent could be excused for hoping its westward march might just take it straight out to sea in 2005, never to be heard from again. Unfortunately, say experts, that's not likely. WNV has been considered an endemic disease in the United States since late 2002, lurking in bird and mosquito populations and causing occasional outbreaks in unvaccinated horses, as does EEE.

"It'll take us another few years to really be able to predict what it's going to do, though," says Thompson. "We're still trying to put together models that work."

"Anyone who makes predictions about (the behavior of) West Nile virus is foolhardy!" says Wilson. "The only thing I can say for sure is that I believe it's here to stay.

"It depends so much on the climate, which affects bird migratory pathways, populations of mosquitoes, and the amount of contact between birds and mosquitoes," Wilson continues. "Even if vaccination has vastly reduced the incidence of West Nile in horses, we have to remember that the infection rate in mosquitoes is still high, so the virus remains active in the reservoir population. It's just not spilling over into horses as much now."

So much about the behavior of WNV remains unexplained—including how it got to North America in the first place, why it spread so quickly, and why it's so much more virulent here than in its place of origin. Hankins speculates, "It might have a lot to do with the species of mosquitoes that carry it here, and with the migration patterns of the birds that spread it."

"What I'd hate to see happen is people deciding West Nile is no longer a problem, so they stop vaccinating for it," says Thompson. "All in all, vaccines are pretty cheap insurance."

ABOUT THE AUTHOR

Karen Briggs *writes for more than 20 equine magazines in Canada, the United States, and Great Britain. Based in Ontario, she also is a Canadian certified riding coach, an equine nutritionist, and an active preliminary-level three-day eventer. Briggs authored* Understanding Equine Nutrition *and* Understanding The Pony, *published by Eclipse Press and available at www.ExclusivelyEquine.com or by calling 800/582-5604.*

The Ever-Present THREAT

BY KAREN BRIGGS

West Nile virus (WNV) might be the new kid on the block, the one gaining all the media attention, but unfortunately, it is not the only mosquito-borne disease to which your horse is vulnerable. Long before WNV ever reached North American shores, there were two other forms of viral encephalitis (literally, inflammation of the brain) for horse owners to worry about, as well as an occasional invader from South America. You probably know them as EEE, WEE, and VEE—Eastern, Western, and Venezuelan equine encephalitis (the encephalitides). Or you might be familiar with the older, more general term "sleeping sickness." Either way, these viruses are as dangerous today as they were decades ago.

Eastern, Western, and Venezuelean equine encephalitis are known killers, but vaccination can help stave off these diseases

Editor's Note

This is the fourth in a 12-part series of articles on vaccinations for horses.

The main reservoir for Eastern, Western, and Venezuelan equine encephalitis is various migratory birds. Because multiple species are involved, from blue jays and chickadees to cardinals and catbirds, the distribution of encephalitides is widespread. Rodents can also harbor the viruses.

ANNE EBERHARDT

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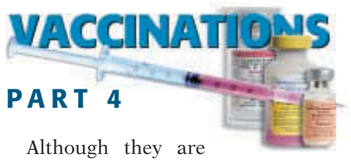
The progression of EEE is swift and ugly. Affected horses will struggle with muscle tremors, weakness, and staggering gaits, and might circle aimlessly or tilt their heads at odd angles.



PART 4

Although they are three separate diseases with three separate vaccines, EEE, WEE, and VEE have several qualities in common:

- All three viruses are found in North, Central, and South America, with WEE being the most widely distributed. They have not been noted in Europe, Asia, or Africa.
- The main reservoirs for each disease are various migratory birds. Because multiple species are involved, from blue jays and chickadees to cardinals and catbirds, the distribution of encephalitides is widespread. Rodents can also harbor the viruses.
- Each is transmitted from birds to horses via mosquitoes that first bite an infected bird, then a healthy horse.
- Humans can also contract all of the equine forms of encephalitis, although the diseases are not generally considered transmissible from humans to horses or vice versa (dead-end hosts). The one possible exception to this is VEE, which in horses can develop high enough viremia (levels of virus in the bloodstream) for it to be picked up by mosquitoes and passed on to other species. VEE virus can be detected in the blood, saliva, and nasal discharge of an infected horse (potentially zoonotic). Horses also develop viremia with WEE and EEE infection, but not at high enough levels to pass it on to other horses or other species.
- The incidence of each disease is tied to the mosquito season. When mosquitoes aren't active, the risk is low; when mosquito populations are high, the risk is very real.
- All three diseases are extremely difficult to treat. There are no known anti-viral drugs that can tackle equine encephalitides, so veterinarians can only help an affected horse by treating the clinical signs (primarily with fluid therapy, anti-inflammatory drugs to help reduce fever and inflammation of the brain and spinal cord, and possibly anticonvulsants).
- Horses that survive a bout of WEE, EEE, or VEE often suffer from lasting neurological deficits. Essentially, they're brain-damaged, sometimes so much so that they're dangerous to ride or handle.
- The causative viruses for EEE, WEE, and VEE all belong to the family called alphaviruses. (By contrast, WNV, which behaves similarly in many ways, comes from a viral family called flaviviruses.)
- EEE, WEE, and VEE all attack the horse's central nervous system (brain and spinal cord). Although diagnosis can sometimes be made by isolating the virus in blood samples of acutely affected horses, the best confirmation is by post-mortem analysis of brain tissue.
- Cases of EEE, WEE, and VEE in the United States are all monitored by the Centers for Disease Control in Fort Collins, Colo., because horses are considered sentinels for possible outbreaks in the human population.

Differentiating WEE, EEE, and VEE

So what separates the three viruses? First and foremost, distribution.

EEE is usually found along the Eastern seaboard, from the Canadian maritime provinces down to Florida, and only rarely in the Midwest or points farther toward the Pacific. WEE, in contrast, is generally found west of the Mississippi. VEE, which was first diagnosed in Venezuela in 1936 after a major outbreak, generally stays south of the equator, but it is responsible for occasional outbreaks in horse populations in Central America (it was diagnosed in Mexico as recently as 2000, and Belize in December 2004). In 1971, VEE caused widespread alarm in the southern United States when it crossed the border and invaded parts of Texas. While it is a rare invader, it's not a disease to be dismissed lightly, as we'll see in a minute.

What else differentiates EEE, WEE, and VEE? Here's a rundown.

EEE: High Mortality, High Risk

With a fatality rate of 75-90%, EEE is the most deadly of the encephalitis trio. It's also one of the most opportunistic, as it's found in multiple species of birds with all kinds of migratory patterns. Several kinds of small mammals and reptiles are also possible reservoirs. EEE is considered endemic in the United States, eastern Canada, the Caribbean, and Central America; there was also a horse diagnosed with EEE in Venezuela in 2004.

Because it can also affect humans and other species, EEE is designated as a reportable disease in the United States (any positive diagnosis must be reported to federal authorities).

The progression of EEE is swift and ugly. The clinical signs usually appear abruptly and can kill a horse in as little as two to three days. It starts with a fever, which is sometimes accompanied by no other clinical signs and is easy to miss if the horse is turned out. The fever might break, only to rise again, this time accompanied by depression, loss of appetite, and a "sleepy" appearance. Soon, neurological symptoms begin to appear. Affected horses will struggle with muscle tremors, weakness, and staggering gaits, and might circle aimlessly or tilt their heads at odd angles. Within 24 hours, the clinical signs can progress to include a characteristic behavior called head pressing (the horse presses his face against walls or other solid objects, as if he's trying to hide), convulsions, and sometimes blindness. These clinical signs can be followed by recumbency; when a horse lies down, death from respiratory arrest often occurs within two to three days.

DUSTY PERIN

Use bug spray to keep mosquitos off your horse, and reduce mosquito breeding grounds at your farm. Outbreaks of WEE occur at the end of mosquito season when birds migrate out of the area for the winter and mosquitos turn to horses for the food supply.

Horses that survive EEE have been described as "disabled" and often have lingering vision problems.

WEE: Widespread, But Less Virulent

Although its mortality rate (20-50%) is far lower than EEE, WEE is nothing to sneeze at. Sparrows and house finches seem to be the main reservoir hosts of the virus, and one species of mosquito, *Culex tarsalis*, is responsible for spreading WEE across the western U.S. and Canada, with occasional outbreaks in the eastern United States as well as in Central and South America.

Outbreaks of WEE tend to occur toward the latter part of the mosquito season. That's because *Culex tarsalis* normally prefers to feed on birds, but as birds start to migrate out of an area for the winter, the insects have to turn to other food sources. That's when they're most likely to bite mammals, including horses, and spread the virus.

It might take a horse one to three weeks of incubation time after he is bitten by an infected mosquito to show signs of WEE. Many of the clinical signs are similar to those seen in EEE, but with the Western form, some horses become agitated or excitable rather than sleepy. Every stimulus has the potential to send them into a frenzy. With a fever as high as 105ºF in the acute stage, it's not surprising that restlessness is also a clinical sign of WEE. With this disease, the first 24-48 hours will tell the tale; if the horse's immune system is able to beat the virus, it will usually do so in that initial window. If not, the central nervous system will come under attack as the virus replicates in lymph nodes and muscle and spreads to highly vascularized (supplied with lots of blood vessels) areas such as the liver, spleen, and the lining of the heart. By this time, the horse will exhibit severe depression, tremors in the head and shoulders, difficulty swallowing, loss of coordination, and circling or walking blindly into walls. These clinical signs might come on gradually over a couple of weeks. If the horse is able to remain on his feet, he still has good odds for recovery, but most veterinarians agree the prognosis is poor if he goes down or muscle paralysis sets in.

VEE: Somewhere in Between

VEE might be a rare disease in North America, but epizoologists keep a close eye on it nonetheless. With a mortality rate of 40-80%, VEE is an extremely dangerous and unpredictable disease. It's more variable than either EEE or WEE, with the ability to progress quickly or slowly, and be mild or extremely virulent. It's possible that's because VEE in horses can be caused by more than one variant of the virus.

Horses that contract VEE generally exhibit clinical signs similar to the Eastern and Western varieties of encephalitis, although the incubation period is shorter than WEE (usually only one to two days). Loss of appetite, excitability, an increased heart rate, and a fever of up to 105ºF are common. Severely affected animals might

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later suffer weakness, muscle spasms, depression, loss of coordination, diarrhea or colic signs, and might circle aimlessly or press their heads against solid objects. If the disease progresses to convulsions, the prognosis is usually grim.

Unlike WEE and EEE, which generally don't result in detectable viremia, the VEE virus can be detected in the blood, saliva, and nasal discharge of an infected horse. Although it's never been documented with absolute certainty, epizoologists believe that this gives VEE the potential to be spread directly from horses to humans who might come into contact with that saliva or discharge from the nostrils or eyes. This makes VEE a true zoonotic disease.

ANNE EBERHARDT

Talk to your veterinarian about the best vaccination program for your horse to protect him from encephalitides.

Shooting Down Encephalitis

As with rabies, tetanus, and WNV, by far the best strategy for avoiding encephalitis is to protect your horses with vaccines.

D. Craig Barnett, DVM, senior equine technical services veterinarian for Intervet pharmaceutical company, points out, "In 2003, there was a serious outbreak of Eastern equine encephalitis in the southeastern United States, thanks to some very wet weather and flooding, which resulted in high mosquito populations. There were a significant number of deaths spread over a number of states, and the horses that died were those that had not been properly vaccinated." Some of the horses were overdue for a booster vaccination or didn't receive the recommended number of doses for primary immunization.

In fact, there was a 690% increase in the total number of cases of EEE in Alabama, Florida, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia in 2003 compared to 2002. Says Barnett, "We have a concern that at the time everyone was so focused on West Nile that they might have neglected to vaccinate for EEE. West Nile gets a lot of press, but we have to remember that EEE has twice the mortality rate. It's by far the deadlier disease."

Barnett cites an earlier example of encephalitic virulence that should be enough to give all of us pause. "In 1931, there was an outbreak of WEE in California, which then spread eastward to the Midwest. Between 1931 and 1938, 180,000 horses died—which shows just how devastating these diseases can be.

"It's so important to remember that EEE and WEE are endemic in a lot of areas, and because it stays viable in bird populations, we're never going to eradicate it," he warns. "It's not going away, so vaccination, because it's so safe and so effective, should be a no-brainer."

The vaccines available for EEE, WEE, and VEE have been around since the diseases were first isolated in the 1930s. They're simple killed-virus vaccines, which are almost invariably packaged in a polyvalent form. In other words, a single vaccine will combine protection against EEE and WEE simultaneously, or EEE, WEE, and VEE, or even EEE, WEE, and WNV. Sometimes protection against rabies and tetanus is rolled in there, too, to simplify the routine for horse owners. There are even vaccines that can protect against all of these *plus* equine herpesvirus and influenza. The consistent part is that protection for EEE and WEE are almost always provided together.

"The main reason you get protection against both EEE and WEE in one formulation is that so many horses are transported across wide distances now that it just makes sense to protect them from the full spectrum," says Barnett. "It's also more economical for the company to combine them."

Whether you decide to protect your horse against VEE in addition to EEE and WEE will have mostly or South America, or in a state bordering Mexico (or you expect to be shipping to these regions), you'll want to add a VEE vaccine to your regimen. Interestingly, "(Horses) tend to respond better to the VEE antigen when the EEE and WEE antigens are also in (the same vaccine)," Barnett says.

Equine encephalitis vaccines are widely available from most pharmaceutical companies that make equine vaccines. The difference in the formulations is generally confined to the adjuvants (chemical carriers that enhance the formulation's immune-stimulating properties). Regardless of the brand name, equine encephalitis vaccines have all been demonstrated by decades of use to be extremely safe and nearly 100% effective. "The cases (of encephalitis) we do see are almost always in unvaccinated animals or improperly immunized ones, such as very young horses who might have received the first immunization but not the second," says Barnett.

It's important, he emphasizes, to stimulate a naïve horse's (one who has never been exposed to the vaccine or virus before) immune system properly by giving two doses of an encephalitis vaccine a month apart. In foals, a three-dose regimen is often done beginning at three or four months of age, but your veterinarian might recommend that you hold off until the foal is four to six months old (depending on the area's EEE risk) if his dam received an encephalitis booster four to six weeks before foaling. This is because foals can acquire maternal antibodies through nursing, the effect of which can protect them from the diseases for the first few months. Maternal antibodies can also have what Barnett calls "a blocking effect on immunization," so it's best to wait until their influence starts to wane before administering any vaccine or else any vaccinations you give the foal will have an unpredicatable response (the foal might not be adequately protected against the disease).

The choice of when to begin vaccinating foals will also have to do with mosquito activity at the time. "It doesn't make a lot of sense to begin providing protection when the vector (mosquito) is non-existent," Barnett says. "In the southern states, where mosquitoes are active year-round, it's a good idea to get that foal protected even if it's October or November, but in the north, you might want to wait till about a month before mosquitoes are due to appear in the spring."

No vaccine confers instant protection. In naïve horses, full immunity to encephalitides doesn't develop for about four weeks after the final injection, Barnett says, and even in horses who have previously been exposed to the vaccine, you should expect the process to take 14-28 days.

So think pre-emptive strike and ask your veterinarian to administer the vaccine(s) at least a month before bug season is due to start in previously vaccinated horses. In areas where mosquitoes are only active for part of the year, one yearly booster might be all that's needed, since the vaccines confer good protection for about six months. In the south, you'll be more likely to booster two, three, or four times a year, depending on the climate and mosquito populations. Consult with your veterinarian to design the best program for your conditions and your horses.

DOROTHY WOODWARD

If a horse goes down from a case of Western equine encephalitis (WEE) or Venezuelan equine encephalitis (VEE) and muscle paralysis sets in, veterinarians agree the prognosis is poor for that horse to recover.

ABOUT THE AUTHOR

Karen Briggs *writes for more than 20 equine magazines in Canada, the United States, and Great Britain. Based in Ontario, she also is a Canadian certified riding coach, an equine nutritionist, and an active preliminary-level three-day eventer. Briggs authored* Understanding Equine Nutrition *and* Understanding The Pony, *published by Eclipse Press and available at www.ExclusivelyEquine.com or by calling 800/582-5604.*

INFLUENZA

BY HEATHER SMITH THOMAS

There is more than one way to protect your horses against flu, but diligent management and proper vaccination schedules are musts

Editor's Note

This is the fifth in a 12-part series of articles on vaccinations for horses.

Equine influenza is a common respiratory infection. While it affects many horses, it has a low mortality rate; horses generally recover. However, flu can cause your horse physical distress, it's highly contagious, and it can keep your horse out of training and competition for weeks or months for recovery. There are vaccinations against equine flu, but are all vaccines created equally? For the latest news from researchers on equine influenza, read on.

David Horohov, PhD, an immunologist at the University of Kentucky's Gluck Equine Research Center, says the virus is very similar to that of human influenza. "There are differences that restrict equine influenza to horses and human flu to humans," he explains. "The vaccination approach, however, is the same because the protective immune response is the same.

"To prevent infection from occurring, we need antibodies against the viral proteins, and in particular, antibodies against the hemagglutinin, which is the major surface protein of the virus," Horohov explains. "If you have an antibody against that, you can prevent the virus from actually infecting the host. The inactivated vaccines (injected intramuscularly) for both human and equine influenza target the hemagglutinin proteins."

Killed Virus Vaccines

There are two types of vaccines currently available. The first is the inactivated vaccine, in which the virus is inactivated by using formaldehyde

LEE THOMAS

Influenza isn't likely to kill your horse, but it can cause him physical distress, it's highly contagious, and it can keep him out of training and competition for weeks or months for recovery. Vaccination can prevent or minimize infection.

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or some other chemical reagent, Horohov says. When inactivated, the virus is not particularly immunogenic (causing disease), so to help the host create an antibody response, it is mixed with an adjuvant to help boost the animal's response to the "killed" virus.

Once injected in the muscle, the adjuvant helps the virus remain there. "One of the most common vaccine reactions is swelling and inflammation at the site," says Horohov. "Actually this is a good thing; it's telling you that the immune system has recognized the antigen and an immune response is being generated."

Lymphocytes (T cells and B cells) that recognize the virus move in and out of the injection site, circulate in the blood, and ultimately provide the horse protection in the form of an antibody response, he says. "The influenza virus-specific B cells make antibodies that will recognize that virus," Horohov explains.

COURTESY DR. DAVID POWELL

Testing nasal swabs from infected horses can demonstrate which respiratory viruses and strains are affecting them.

The limitation of influenza vaccines is that they generate an immune response only against that particular strain of influenza, and that particular form of hemagglutinin contained within the virus, he continues.

"The problem with influenza is that the virus mutates and changes," states Horohov. "If you vaccinate against one form of the virus and there's a mutation in the hemagglutinin, then the antibodies generated against that vaccine may not be cross protective against the new circulating virus, and your horse may still get influenza. Thus, it is necessary to update the vaccine periodically."

In human vaccines, this updating is done annually. The World Health Organization, Centers for Disease Control and Prevention, and vaccine manufacturers get together before human flu season begins to determine which circulating strains of human flu virus will be out there that year, and what needs to be in the vaccine. It is vitally important that the vaccine match circulating strains of the virus to be protective.

"In horses, the good news is that the virus doesn't change as much," says Horohov. "It mutates the same as the human virus, but doesn't spread as rapidly. There are not as many horses as there are people, and not as much contact. We do bring horses in from overseas and send them overseas. We've moved influenza virus around that way."

But there is a quarantine period for horses traveling internationally, as well as a vaccination requirement (which is not the case for humans). This helps limit the spread of new strains of the virus in horses. But the virus still mutates and the vaccines have to be updated.

Tom Chambers, PhD, also of the Gluck Equine Research Center, says the equine flu vaccine can sometimes go five to seven years before it must be changed. He is part of a team of researchers monitoring the equine flu virus; veterinarians send swabs from infected horses to his lab. Chambers is head of the Office International des Epizooties (OIE) International Reference Laboratory for Equine Influenza.

"The only way we know whether the vaccines need to be updated is by getting our hands on swabs from sick horses and isolating the virus," Chambers explains. "If vaccinated horses come down with flu, this also tells us the vaccine doesn't work anymore." (For Chambers' thoughts on flu vaccine formulation, see page 146).

Horohov says, "The killed vaccine has been used for dozens of years because it will induce a protective immune response to whatever strain is in the vaccine, but one of its limitations is that this protection is restricted only to the strain that's in the vaccine; it often gives very little cross-reactive response. Also, since it's an inactivated vaccine and the virus isn't very immunogenic, it doesn't give a very good response in terms of the total antibodies produced following the vaccination."

Thus it is often necessary to vaccinate horses frequently.

Horohov says how often you vaccinate (how many times per year) will depend on the amount of exposure the horse gets. An animal frequently brought into contact with other horses and potentially exposed to the virus needs the highest level of protection. This might mean vaccinating with the killed vaccine every 90 days or so. An animal that doesn't have much contact with other horses might need vaccination only once or twice a year.

"The problem is that the inactivated vaccine isn't good at inducing longer-lived immunity or the kind of cross-protective immune response we'd like against other strains of the virus," Horohov reiterates. "Even if you vaccinate a horse, if it comes in contact with another strain of the virus, the horse will still get sick."

Modified Live Virus Vaccine

The latest weapon in the fight against flu is a modified live virus vaccine. The best part about this, Horohov explains, is that it protects against a wider range of flu strains than a killed vaccine. This is because the immune response isn't directed against just the hemagglutinin molecule on the surface. It is directed against all proteins in the virus, including internal proteins. This is important, because in addition to stimulating antibody production, the modified live virus vaccine also causes the horse's

ANNE EBERHARDT

There are several options for vaccinating horses against influenza: Killed virus and modified live types, and intranasal or injectible delivery.

FOAL VACCINATION

Protecting Foals from Influenza

A live virus vaccine for influenza is given by the intranasal route (into the respiratory system). If a horse already has antibodies against flu, the antibodies inactivate that vaccine virus and prevent it from being effective in creating immunity. In the average animal this is not a problem, because if a horse is already protected, that's fine.

"Where it's a problem is in foals, if they have maternal antibodies from colostrum," notes David Horohov, PhD, an immunologist at the University of Kentucky's Gluck Equine Research Center. "Vaccination of foals, particularly with a live vaccine, should not be done until the maternal antibodies are absolutely gone."

This time frame might vary from foal to foal. "So we tend to make a broad recommendation, telling horse owners to wait until the foal is nine months old before vaccinating for influenza," he says. "Live virus vaccines are very susceptible to being inactivated by maternal antibodies (thus not stimulating the foal's own immune system). The vaccine is only good if it's infectious. If it is inactivated by a pre-existing antibody response in a young foal, it won't work (for long-term protection); you might think the foal is protected, but he's not."

Tom Chambers, PhD, also of the Gluck Equine Research Center, adds, "Our data says it doesn't hurt him, but it doesn't help. There is a disagreement in the literature about this, but we've found it's not harmful." He also notes that flu is seldom seen in foals younger than six months old, except in foals that fail to get adequate colostrum. "The other exception is if there has been a mutation in the virus and the dam is just as vulnerable as the foal," he says. "We often see herpesvirus in foals, but not flu. Based on the surveillance we've done, usually a horse's first experience with flu is as a yearling or 2-year-old."

ANNE EBERHARDT

The broad recommendation for vaccinating foals for influenza is to wait until they are nine months old.

Horohov says, "The rule of thumb is to vaccinate the mare so she passes antibodies to the foal to protect him for a certain period of time. We vaccinate the foal later, so his immune system can pick up from there."

Vaccination decisions must be made on a case-by-case basis, weighing the age of the foal, the risk (if there's an outbreak of flu), etc. "If you are really concerned about a foal's immunity at a young age, use one of the killed products and later give the foal the live

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body to generate a cell-mediated immune response, which is what recognizes those internal proteins in the virus.

"The cell-mediated immune response is cross-reactive with different influenza strains," he stresses. "So, even if there is a modification of the hemagglutinin this year, the horse will still be protected because the proteins that the cell-mediated response recognizes are inside the virus—and those proteins don't change as much. So getting a precise match between the vaccine and the circulating virus is not as critical as in the case of the inactivated vaccine."

Horohov explains, "This (modified live vaccine) is a strain of influenza virus grown in the laboratory and specifically modified so it has a restricted replication in the horse's respiratory tract (upper portion only). This virus is a temperature-sensitive mutant. It doesn't grow at normal body temperature of the horse; it prefers a slightly cooler temperature. Therefore it grows well in the upper portion of the tract, but will not go deep down into the lungs."

When this vaccine is administered, it causes very slight or no clinical signs.

Another difference between modified live and killed virus vaccines is that the live virus vaccine is given via the respiratory tract. You are actually stimulating the immune system in the area of the body most likely to encounter the virus. When you give the vaccine in the muscle, the protection in the respiratory tract must come via the bloodstream.

"The intramuscular vaccination isn't as good as we'd like it to be, because we don't know how to target it to enhance the respiratory immune response," says Horohov. "By giving a horse the virus a natural way—the route it's typically encountered—there is better stimulation of the local immune system that plays a greater role in terms of protection."

Chambers says the respiratory tract has a mucosal immune system like the GI tract. "These are parts of the body that get exposure to the outside world from food (GI tract) or inhaled particles (respiratory tract)," he says. "The mucosal immune system interacts with the systemic immune system; they are all part of the body's immune system, but their responses to vaccine are a bit different. If you are targeting the mucosal immune system, you should not expect to see the same result as if you were targeting the systemic immune system.

"We think the intranasal vaccines are stimulating immune cells residing in the respiratory tract," Chambers continues. "Some of them make antibodies, and some of the antibodies will get into the systemic circulation, but many will stay in the respiratory tract. There are also helper cells and killer cells that are stimulated in the respiratory tract. Some of those will get into the systemic circulation, but many stay in the respiratory tract."

VACCINE EFFICACY

Will My Horse Respond To Vaccination?

A number of factors are involved in whether or not a horse develops good immunity from vaccination. One factor is getting the vaccination (or initial series of vaccinations) into the horse ahead of exposure to the disease so an adequate immune response is mounted to protect him. This is probably the most vital thing; don't wait until horses are coughing in the barn before you vaccinate.

The second factor affecting response is the status of the animal. "You often hear that you should not vaccinate sick animals," says David Horohov, PhD, an immunologist at the University of Kentucky's Gluck Equine Research Center. "It's not that the vaccine will make them any sicker; it won't. But they won't respond very well to the vaccine if the immune system is stressed. The rule of thumb is to not vaccinate a sick animal until after recovery."

This also applies to health status in general—whether the horse is undernourished, compromised by parasites, stressed by weaning, etc. A stressed animal cannot make a good immune response.

Thirdly, "We can't control the genetics of the animal," says Horohov. "Some individuals just don't respond to vaccines. This is why live virus vaccines will ultimately be better than killed vaccines since you are replicating the whole infectious process; there is more opportunity for even the low responder animals to generate a response."—*Heather Smith Thomas*

ANNE EBERHARDT

Once you've given a horse the primary course of flu vaccines, you should give a booster every six to 12 months for older horses that are not at risk for constant exposure. If it's a horse going to shows or races, you might want to vaccinate every three to four months.

If you are only looking at serology (blood tests) for serum antibodies, you won't see the whole picture of what is going on in the respiratory tract. "When we were doing the initial studies on Flu-Avert (the equine intranasal vaccine), we could give a dose of vaccine up the nose and not see any serum antibodies, or only very low levels, yet the horses would be protected for three months or more from this single dose. Thus our test of effectiveness became whether or not the animal was protected from disease (when exposed to flu) rather than looking at serum antibodies."

The live virus vaccine for flu is a recent development; it became available for horses in the United States in the late 1990s. There is some resistance among horse owners to use live virus vaccines instead of inactivated vaccine, however. Horohov says one of the myths with a live virus vaccine is that it might suddenly revert back to being virulent and cause the disease.

"In the case of flu vaccine, there has been no evidence of any kind of reversion to virulence (ability to cause disease signs) in any of the horses vaccinated with the live virus vaccine," says Horohov. "It's been proven safe not only in healthy horses, but also in horses that are stressed. We've given it to very young horses, very old horses, horses with compromised immune systems, and sick horses, and we have seen good protection. At this point in time, we see no evidence for concern with this vaccine."

The main problem with a live virus vaccine is that it is only effective when it's live. Horohov says it is easy to accidentally "inactivate" the modified live virus. "You must keep it out of the sunshine, keep it cool, and make sure it's not out of date," he stresses. "If it's become inactivated, it's useless."

JANIS TREMPER

Discuss influenza with your veterinarian to design an ideal program for your horses and your farm.

Some people think it would still work, like a killed virus vaccine, but this is not the case. There is very little active virus in it to begin with, and no adjuvant in the vaccine, so if it becomes inactivated by heat or sunlight, it won't work.

The vaccine is freeze dried and must be rehydrated before use, and must be used soon after rehydration. "You can't mix it and put it in the refrigerator for later," he says. "It must be fresh. That's the drawback to any live virus vaccine; it's only good if the viruses are still alive. If you do anything to compromise that, the vaccine becomes useless."

The modified live virus vaccine must be given intranasally, and some people don't like doing that. "You also must make sure you get it in the right spot and don't accidentally stick it in the false nostril," says Horohov. "You have to make sure the full amount gets discharged, otherwise you may not get complete protection. Veterinarians who have some experience with this don't have any problems, but many equine vets are more used to giving injections. Once they start doing it, however, they find it's not a problem."

How Often Should I Vaccinate?

Vaccination frequency need not be as often with the live virus product as with the killed one. "When the live virus vaccine was developed, we thought it might provide protection for more than a year," says Horohov. When a horse or human is infected with influenza, there usually is a good immunity once recovery is complete. This natural immunity might last a number of years.

"We hoped the live virus vaccine would do this, but it turns out that the protection may be for considerably shorter periods of time and we're not sure why," says Horohov. "My guess is that when we make an attenuated vaccine we have to remove some of the aspects of the virus that cause disease—or it would just be giving them flu. By doing that, we are probably weakening it in some way so it doesn't stimulate the immune system as well, either."

The degree of protection might be high, but not as high as that conferred by the disease itself. Immunity lasts about nine months. So, most veterinarians recommend twice-a-year vaccination for optimum protection with a live virus vaccine for horses at high risk for exposure.

In contrast, the inactivated vaccine must be given more often. Chambers says the problem with serum antibodies (in the bloodstream) in the horse is that their lifetime is relatively short. "After a month the titers are only half of what they were at their peak," he says. "If you vaccinate and boost and get a good, high serum antibody response today, a month from now it will be only half of that. And a month after that it will be half again. After a few months, you need to give another booster shot."

Ten years ago these vaccines were not as potent as they are today, and some people were vaccinating their horses every two months. "The current recommendation is that once you've given a horse the primary course (of inactivated vaccine), you should give a booster every six to 12 months for older horses that are not at risk for constant exposure. If it's a horse going to shows or races, you might want to vaccinate every three to four months," says Chambers.

How Quick is the Response?

If faced with an outbreak, how long will it be before vaccinated horses are protected? And does it hurt to vaccinate an exposed horse that might be coming down with flu?

"The answer to how long it takes to mount an immunity depends on whether the horse has been vaccinated before or has residual immunity from early vaccination or exposure," says Horohov. "If horses are three or four years old or older, chances are they've been vaccinated or have had the flu. When you vaccinate these animals, it's a rapid return to immunity. Within a few days the immune system will snap to, and you'll get good levels of protection very quickly. If they are naïve animals and have not seen the vaccine or the disease at all, it will take much longer, since they require a booster shot.

"In the face of an outbreak, one of the great disappointments in vaccines is that it takes so long to get the protective immune response; it may be too late," he continues. "The horse may get sick (despite vaccination). There's no evidence that there's any harm in vaccinating a sick horse. It won't make it worse, but it won't make it better. It's just too late."

Take-Home Message

There are several ways to help reduce the incidence of flu in your horses, and one of the best is with a good vaccination program. Whether you use a killed or modified live virus vaccine, the key is making sure you use it properly and in a timetable suited to your horses' potential exposure. Discuss options with your veterinarian, and don't forget your own flu shot!

ABOUT THE AUTHOR

Heather Smith Thomas *ranches with her husband near Salmon, Idaho, raising cattle and a few horses. She has raised and trained horses for 45 years, and as a freelance writer has published 13 books (including the recently released* Care and Management of Horses, *available at www.ExclusivelyEquine.com) and more than 5,400 articles for horse and livestock publications. She is a member of American Horse Publications, American Agricultural Editors Association, and Livestock Publications Council.*

EHV 1&4

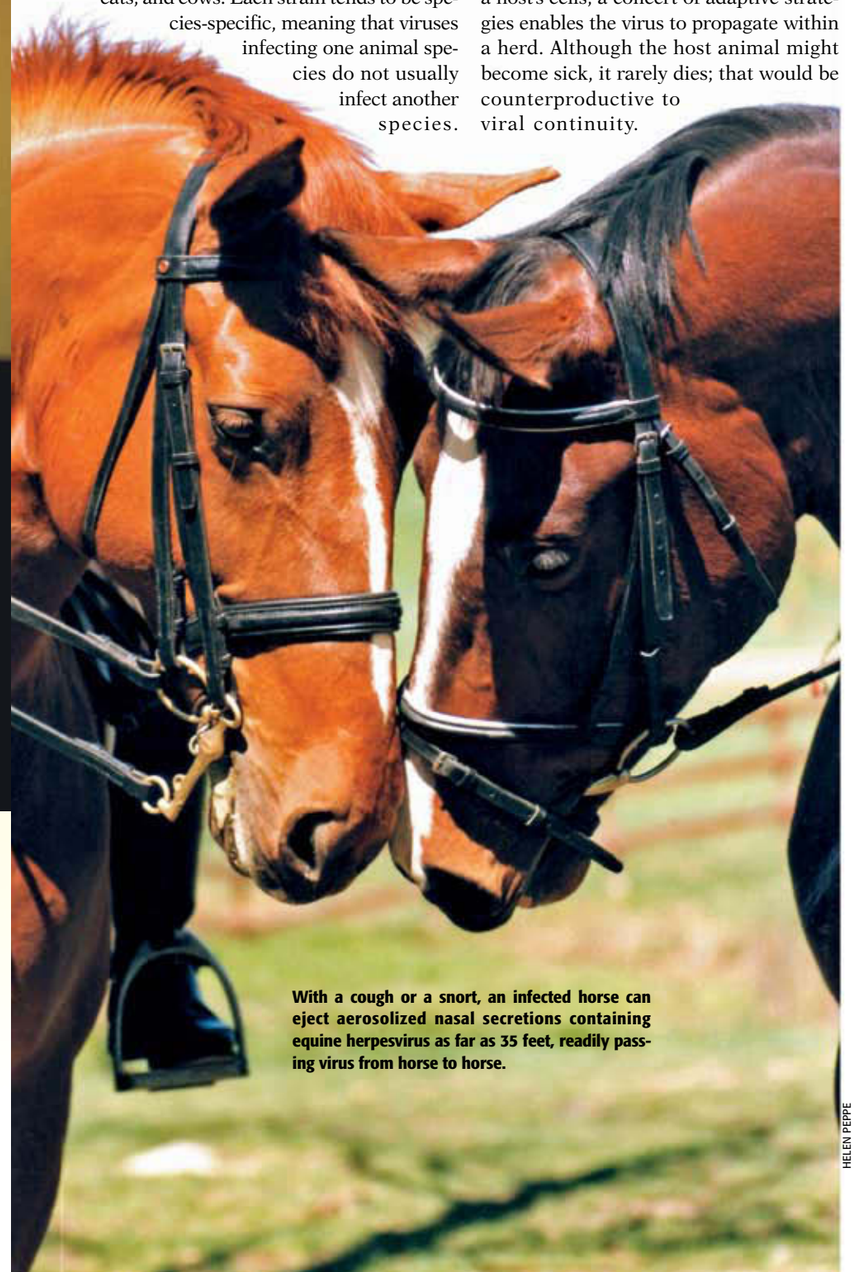
BY NANCY S. LOVING, DVM

Herpesvirus is a particularly well-evolved virus that occurs in many mammals, such as humans, horses, cats, and cows. Each strain tends to be species-specific, meaning that viruses infecting one animal species do not usually infect another species.

In the world of microbes, viruses are specialized in their ability to infect and survive within a host. After a virus inserts itself into a host's cells, a concert of adaptive strategies enables the virus to propagate within a herd. Although the host animal might become sick, it rarely dies; that would be counterproductive to viral continuity. Instead, an infected animal serves as a reservoir for viral infection.

Viruses are masters at the game of hide-and-seek. Some, like influenza virus, mutate to elude recognition by a host's immune response. Others, like equine infectious anemia, debilitate a host's immune system so it cannot counteract the virus.

Herpesvirus has developed its own adaptation: It maintains itself within its host by evading detection by the host's immune system. And herpesvirus is unique in its ability to persist in the host in a latent form, recurring at intermittent periods that correspond with stress events.



With a cough or a snort, an infected horse can eject aerosolized nasal secretions containing equine herpesvirus as far as 35 feet, readily passing virus from horse to horse.

HELEN PEPPE

Respiratory disease, abortion, and neurologic disease are all caused by herpesviruses

In humans, we are most familiar with herpesvirus in the form of recurrent cold sores. In the horse, equine herpesvirus (EHV) is classified into five different strains: EHV-1, EHV-2, EHV-3, EHV-4, and EHV-5. Of these, EHV-1 and EHV-4 are the strains associated with viral respiratory disease. EHV-1 is the most prevalent concern in horse populations not only because its respiratory disease is more virulent than that caused by EHV-4, but also because it is incriminated in causing viral abortion or neurologic disease (myeloencephalopathy).

Spread of Infection

With a cough or a snort, an infected horse can eject aerosolized nasal secretions containing equine herpesvirus as

Editor's Note

This is the sixth in a 12-part series of articles on vaccinations for horses.

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far as 35 feet, readily passing virus from horse to horse. Yet this virus is best transmitted through direct contact rather than aerosol transmission. Direct nose-to-nose contact passes copious quantities of viral material from one horse to another, as do shared water sources that are contaminated with nasal secretions. Infected organic material clings to feed, water tanks, stalls, horse trailers, tack, equipment, wheelbarrows, rakes, muck buckets, shoes, and clothing with the potential to move across a farm. Direct contact with an aborted fetus or placental tissue readily spreads infection due to the high concentration of virus within aborted tissues.

Of key importance in transmission of this virus is exposure by carrier horses that are incubating disease and not yet showing clinical signs, or from horses that silently shed virus when a latent infection is reactivated by stress or illness.

Latent Infection

What makes herpesvirus peculiarly unique is its ability to persist in a latent state, reappearing at intervals through an animal's life. Herpesvirus might be present in as many as 50% of adult horses, maintaining its presence in its hideout place within the trigeminal nerve of the face or within specialized white blood cells of the lymphatic system. It is clever in its ability to evade a host's immune recognition. While virus rests in a dormant state within latently infected cells, it does not turn on its machinery to replicate itself. Instead, it lurks and waits. During this stealth period while it is not expressing antigenic proteins that might alert the host to its presence, it is "silent" to the immune system, effectively escaping detection and destruction by the horse.

During stressful periods associated with training, competition, transport, management changes, or illness, high levels of circulating corticosteroids suppress a host's normal defense mechanisms. Poor nutrition, a heavy parasite load, overcrowding, and rigorous climatic events are other stressors that adversely affect a horse's immune defenses. It is during stress periods that latent virus is reactivated and shed into the nasal secretions. A horse might appear clinically normal, yet he serves as a silent shedder. This increases the potential to spread virus within a herd to individuals whose immune systems have not been previously challenged by herpesvirus.

George Allen, PhD, of the University of Kentucky's Gluck Equine Research Center, is an authority on equine herpesvirus. He suggests that transmission maintains itself within a horse population in several ways:

- Passage from a latently infected mare to her foal;
- Persistence of infection in a latently infected youngster into adult life; and
- Reactivation of latent virus to pass from horse to horse of any age.

Invasion of the Host

To understand the dynamics of effective vaccine control, it is helpful to understand how herpesvirus infects a horse. Its primary attack assaults the respiratory tract within 48 hours of exposure. Virus entering there attempts to attach to and penetrate epithelial cells lining the airways. At that site in the respiratory lining, a horse's immune response has its first opportunity to neutralize the virus. It can do this through protective antibodies that prevent cellular invasion, and by rallying specialized white blood cells contained within the clearance apparatus (mucociliary system) of the respiratory tract. It is there a viral vaccine has the best effect by priming the system to induce antibodies, which recognize specific foreign proteins on herpesvirus particles before they invade the host's cells.


DUSTY PERIN

Direct nose-to-nose contact passes copious quantities of viral material from one horse to another, as do shared water sources that are contaminated with nasal secretions.

To mount an effective immune response, it is important for the respiratory lining to remain healthy and in optimal working condition. Poor air quality, dust, allergic airway disease, and other viruses create conditions that detract mightily from a host's defensive immune function in the upper airways.

If herpesvirus breaches the defenses of the upper respiratory tract, it then follows two routes: In 48 hours it makes its way to the trigeminal nerve of the face, where it will remain as a latent infection as described previously. The other route is dissemination within 72 hours to the lymphatic and blood circulatory systems. Once virus infects a white blood cell, it is able to circulate through the bloodstream without interference from the host immune system even in the presence of high antibody titers.

Researching herpesvirus immunity is the special focus of Cormac Breathnach, PhD, who earned his doctorate under the mentorship of Allen at the Gluck Center. Breathnach observes, "The virus evades the host antibody response by remaining intracellular (within a host cell) at virtually all stages of its movement throughout the body. This is a critical strategy by which it circumvents anti-EHV antibodies, which are the primary response induced by most vaccines."

Effective immune defense then relies on cell-mediated mechanisms whereby white blood cells engulf virus-infected cells. During the phase when virus is circulating throughout the body (viremia), herpesvirus further interferes with normal defensive response mechanisms of cytotoxic T-lymphocytes that are meant to eliminate virus-infected cells.

The viremic phase lasts from seven to 21 days, and during that time virus-infected cells can spread to other organs, such as a pregnant uterus and fetus to cause abortion, the central nervous system to elicit myeloencephalitis, or the eye to induce ocular disease like chorioretinitis. Typically, a horse that develops viral abortion or viral neurologic disease will have mild respiratory disease and/or fever in the two weeks preceding clinical evidence of reproductive or neurologic disease, albeit the signs might be so subtle as to be unnoticed.


COURTESY DR. DAVID POWELL

Direct contact with aborted fetus or placental tissue readily spreads infection due to the high concentration of virus within aborted tissues.

Clinical Signs

Although equine herpesvirus is most prevalent in horses younger than two years of age, it can infect horses of any age. Initially, infection with herpesvirus produces mild respiratory signs of watery nasal discharge, mild fever, and cough. There might be pinpoint hemorrhages (petechiations) on the mucous membranes. Some horses also develop edema (fluid swelling) of the limbs or abdomen. After several days, the clear nasal discharge turns progressively thicker, leaving a crust around the nostrils. Less than a week into the illness, this turns into an obvious yellowish, snotty discharge due to bacterial invasion of damaged cells lining the respiratory tract.

Once the infection moves to the lymph nodes in those first few days, it can reach a pregnant uterus or the central nervous system through blood circulation. Direct damage to the lining of the blood vessels adversely affects these organs. Abortion results from malnourishment of the fetus related to blood vessel damage within the uterus.

Breathnach explains the process leading to abortion: "Farm owners and breeders often note that mares appeared 'perfectly normal' prior to aborting virus-positive fetuses. One of two things can have happened. Either the infecting virus successfully reached the draining lymph nodes despite only causing an inapparent subclinical infection and established sufficient viremia for abortion (or neurologic disease) to occur, or the mare was latently infected with the virus, which became reactivated through stress, and the abortive infection 'occurred from within.'


PAULA DA SILVA

The recommended protocol for protecting pregnant mares against viral abortion is to administer herpesvirus vaccine prior to breeding, then at five, seven, and nine months of gestation.

"Reactivated virus emerging from lymphocytes or from the central nervous system can establish viremia in the absence of clinical disease in the upper respiratory tract," he continues. "Once viremia is established, all bets are off. This is one of the important features of EHV-1 that makes it so difficult to control. A mare that never showed a fever or runny nose can abort an EHV-1-laden fetus, and this can lead to an abortion storm."

A mare infected with equine herpesvirus might abort in the latter months of gestation, or an infected foal might be stillborn or born very weak and unlikely to survive due to viral pneumonia.

Allen comments, "For the last 25 years (following the commencement of widespread vaccination in 1980), the abortion incidence due to EHV-1 has remained relatively constant, between 2 and 2.5 abortions per 1,000 pregnant mares." An abortion storm can occur at any time, sweeping through an entire farm with disastrous results.

Similarly within the central nervous system, blood vessel damage results in cellular death of neurons, with variable neurologic deficits related to specific areas of damage. An affected horse is overtaken suddenly with ascending paralysis that usually peaks to its worst state within two to three days of onset. Telltale signs of paralytic

rhinopneumonitis are poor tail tone along with fecal incontinence and urinary leakage due to partial or complete bladder paralysis. The hind limbs become weak or hind limb coordination falters (ataxia), usually in a symmetrical fashion. Many horses afflicted with paralytic rhinopneumonitis go down and remain recumbent with the effects of the infection lasting for three weeks or more.

Breathnach notes, "The incidence of EHV-1 neurologic disease in the field is presumably low, even allowing for the fact that many neurologic cases may be mild and self-limiting. Again, however, some strains can apparently induce severe neurological deficits in a very high percentage of exposed animals. How do they arise? What confers this enhanced virulence? This is a hot-button issue in EHV-1 research."

As research strives to answer these questions, the impact of EHV-1 in a neurologic storm remains a current concern to the horse industry, particularly as more cases arise in locations of congregated horses, such as training barns and racetracks. As an example of the havoc this EHV-1 viral manifestation can cause, we need only turn to the 2003 herpesvirus outbreak in Findlay, Ohio. Of 138 horses in the herd, 124 developed fever and a nasal discharge. Of those, 30 developed neurologic signs and 12 had to be euthanatized. This kind of epidemic outbreak occurs because a horse that is incubating and shedding disease might not demonstrate any clinical signs until it is too late to isolate him.

This virus is highly contagious, it spreads like wildfire in a herd, and it spreads to others elsewhere if a sick horse is moved to another location (such as a veterinary hospital). If an exposed horse does not develop clinical signs within three weeks, the good news is that he probably is not going to become ill.

Vaccination Quandaries

Currently, vaccines are labeled for activity against the respiratory and abortigenic forms of equine herpesvirus, but none are available to counter the neurologic form. Allen, in collaboration with Nicholas Davis-Poynter, PhD, head of equine infectious diseases at the Animal Health Trust in Newmarket, England, has made a recent discovery: "Neuropathogenic isolates of EHV-1 possess a mutation that offers a possible explanation for many of the unique properties of these neurologic strains. For example, it explains the basis for the increased vigor of such isolates to replicate, their ability to cause amplified magnitudes of viremia following infection, their greater capacity to infect cells lining the blood vessels (endothelium), and the relative inefficacy of all current vaccines for preventing infection by such aggressive strains of EHV-1. The core question, as yet without an answer, is whether such neuropathogenic mutants of EHV-1 arise anew with each disease outbreak or whether there exists a subpopulation of horses that carry the mutant strains as latent virus with the potential for initiating new outbreaks of paralytic disease. Such a gene mutation of EHV-1 renders current vaccines ineffective against it."

In addition, no vaccine can protect against latent infection because the virus does not present itself to the horse's immune system when it persists in this silent form. Breathnach's assessment on EHV-1 vaccines is revealing: "In general, the vaccines for EHV-1 are suboptimal. Most of them are inactivated vaccines, which typically induce only circulating antibodies, but do little or nothing to induce cytotoxic T-cell (CTL) activity. EHV-1 gets into the bloodstream and circulates by hiding in lymphocytes and monocytes. It is therefore largely inaccessible to serum antibodies. The virus can then pass directly from infected lymphocytes to vascular endothelial cells lining the blood vessels of the pregnant uterus or central nervous system, further avoiding antibody intervention. If serum antibodies are the only source of immunity in the infected horse, they cannot effectively control spread of the virus to the blood vessel lining (endothelium)."

He elaborates about future research possibilities: "What we need are vaccines that induce CTL responses that will kill virus-infected circulating lymphocytes. Use of such vaccines could be expected to reduce the burden of virus in the bloodstream and decrease the risk of spread of virus to vulnerable endothelial cells."

Of available vaccines worldwide, there are killed or "inactivated" forms and "modified live" (MLV) forms. When given intramuscularly, inactivated vaccines stimulate circulating antibodies in the bloodstream, but are not designed to effectively elicit responses at the level of the respiratory lining or within white blood cells of the cell-mediated arm of immune defense. When given intramuscularly, MLV vaccines stimulate circulating antibodies along with a cell-mediated response from white blood cells, but whether immunity is developed in the respiratory lining is debatable.

Breathnach speculates on improvements in vaccine availability in the future: "While vaccination with the currently available products is important, it is clear

BLM FILE PHOTO

Poor nutrition, a heavy parasite load, overcrowding, and rigorous climatic events are just some of the stressors that adversely affect a horse's immune defenses.

COURTESY DR. DAVID POWELL

After several days of infection with equine herpesvirus, the clear nasal discharge turns progressively thicker, leaving a crust around the nostrils. Less than a week into the illness, this turns into a yellowish, snotty discharge due to bacterial invasion of damaged cells lining the repiratory tract.

that improved vaccines are desirable. One thing to keep in mind is that even live virus infection of horses results in relatively short-term protective immunity. Typically a young horse that has had limited exposure to the virus can become sick, recover, then be vulnerable to re-infection within six months. With this in mind, it becomes very difficult to design vaccines that emulate this protective immunity, let alone exceed it. Most likely, the best we can hope for in vaccine design is to create one that is as protective as a live virus infection. To do so, we would have to create a vaccine that stimulates the various arms of the immune response that are activated by live virus infection (far more than just serum antibodies). With inactivated vaccines this is virtually impossible. Our best hope remains MLV vaccines, or recombinant subunit vaccines (where a small component of the virus is inserted into a live—but innocuous—carrier virus for vaccination). However, development of such subunit vaccines has its own caveats. You first have to identify the "immunodominant" (most relevant) protein(s) in the virus for inclusion in the vaccine. In the case of EHV-1, there are about 70 proteins, many of which are good candidates for immunogenicity. Furthermore, there is no guarantee that any single protein will suffice; it might take two or more."

Some horse owners have dug in their heels and won't use herpesvirus vaccines, basing their objection on hearsay about the possibility of MLV vaccination inducing paralytic rhinopneumonitis. Allen puts this outdated concern to rest, saying the following: "The only MLV for EHV-1 currently marketed in the USA is a product that is prepared from a non-neuropathogenic strain of EHV-1 and has been used for many years without any indication of causing either paralysis, abortion, or even respiratory disease. The concern about MLV and paralysis probably is a holdover from the use of a neuropathogenic mutant in the 1970s, which did result in a large number of paralytic cases in vaccinates."

Breathnach concurs, saying, "Given my experiences, the potential of the currently available MLV herpesvirus vaccine to induce secondary complications like neurological disease is infinitesimally small."

To Vaccinate, and With What?

The argument over equine herpesvirus vaccination is controversial. Some maintain that since at least half of the horse population has already been exposed to equine herpesvirus, then vaccination cannot prevent disease, so why bother?

Even with vaccines for EHV-1 that are currently available, there are sound reasons to implement a vaccination protocol. Foremost is to diminish the level of viremia for horses that have not been previously exposed or in those in which latent infection is reactivated. Both at the time of initial exposure and during reactivation of a latent infection, the presence of local immunity within the respiratory lining determines the outcome: If a horse had previous exposure and infection, or if the horse had received vaccination, then his body will have mounted some sort of immune response. Subsequently, sufficient antibody could be present within the lining of the respiratory surface to neutralize reactivated virus. Then, the infective process would be stopped in its tracks before nasal secretions could shed virus to others within a herd.

Breathnach states, "One of the main functions of vaccination and serum antibody elevation is that it may reduce the amount and/or duration of virus shedding. So, increasing herd immunity by vaccination is a valid attempt to restrict the virus burden in the environment."

The role of vaccination is not to eliminate latent infections, but rather to stimulate immunity to a state of readiness to neutralize reactivated virus. This keeps herd health at its best.

The objective in stimulating immunity is to eliminate virus before it can enter the cells or restrict the spread of virus thereafter. Currently, the most effective control of respiratory infection lies at its site of entry—the upper respiratory lining. Based on this strategy, intranasal inoculation is particularly beneficial to limit viral respiratory disease. Immunity provided by intranasal vaccine lasts from three to six months.

When to Vaccinate?

The recommended protocol for protecting pregnant mares against equine herpesvirus abortion is to administer herpesvirus vaccine prior to breeding, then at five, seven, and nine months of gestation. For this purpose, it is best to use those herpesvirus vaccines labeled specifically for pregnant mares. Currently, these are inactivated vaccine products, given as an intramuscular injection.

Most initial cases of herpesvirus infection occur from weaning age to 12 months, and it is speculated that 80-90% of young horses will have been infected by two years of age. If a young horse encounters herpesvirus for the first time when he's over a year of age, he is likely to develop a serious bout of infection. In light of these facts, the best immunization strategy is based on vaccination of young horses. Up until three to five months of age, a foal is unlikely to respond to vaccination due to blockage from maternally derived antibodies of passive transfer that came from a mare's colostrum, particularly if she was vaccinated prior to foaling.

Allen says that vaccination titers are highest when a foal receives its first immunization at five months of age or older. A series of three immunizations should be administered to start a young horse on a herpesvirus vaccine program. For the best effect, all horses (young and old) within a herd should be properly immunized. Many vaccines target both EHV-1 and EHV-4. An adult horse should receive boosters at three- to six-month intervals; the frequency is dependent on the risk of exposure and the risk of stress-related travel and competition. In all cases, immunize according to manufacturer's labels.

ABOUT THE AUTHOR

Nancy S. Loving, DVM, *owns Loving Equine Clinic in Boulder, Colo., and has a special interest in managing the care of sport horses. An enthusiastic endurance rider, Loving is also a veterinary judge for the American Endurance Ride Conference and for FEI (international) endurance events. She authored the books* Go the Distance: The Complete Resource for Endurance Horses, Conformation and Performance *(both available at www.ExclusivelyEquine.com or by calling 800/582-5604), and* Veterinary Manual for the Performance Horse.

STRANGLES

Many horses with strangles develop a creamy discharge from one or both nostrils.

Streptococcus equi *bacteria cause strangles, a highly contagious disease that affects lymph nodes and potentially other organs in the horse*

BY NANCY S. LOVING, DVM

Strangles is hardly a new disease, having been recognized as a contagious bacterial problem in horses for centuries. Yet it still remains a troublesome and persistent issue, and it is identified worldwide. Research has been directed toward developing effective vaccines to control its spread through the horse population, but management strategies are even more important in limiting its presence.

What is Strangles?

Strangles is the colloquial name given to an infection caused by the bacterial organism *Streptococcus equi*. This bacterial infection invades the respiratory tract of horses, donkeys, and mules and causes swelling of the lymph nodes around the head and neck. In some cases, the swelling around the pharynx might become so severe as to obstruct the airway; the audible respiratory effort and potential for suffocation spawned the name "strangles."

Fortunately, most cases of strangles do not become this extreme. Very few strangles cases result in death today. An affected horse might stand listlessly in the paddock and be off his feed; he feels poorly due to fever and discomfort. Many horses sick with this disease eventually develop a creamy nasal discharge from one or both nostrils. If a cough develops, it is usually mild. The lymph nodes under the jaw (submandibular) and/or the throatlatch (retropharyngeal) swell to varying degrees. There might be some edema (fluid swelling) around the face, and breathing might be labored.

At the onset, the lymph nodes can feel firm, yet the horse resents your touch on them long before they soften and break open with a creamy drainage. Typically, lymph node abscesses rupture within a couple of weeks after a horse shows initial signs of infection.

In only half the cases do draining lymph

Editor's Note

This is the seventh in a 12-part series of articles on vaccinations for horses.

nodes culture positive for *Streptococcus equi* since following rupture, the bacteria are quickly cleared and cultures become negative. Identification of the disease is based on clinical signs and probabilities since few other illnesses infect the lymph nodes, but bacterial culture swabs and a blood test for antibody titers help confirm the diagnosis.

Who Is At Risk?

Horses of any age can be affected by strangles, but it is the very young ones that usually suffer the worst. John Timoney, MVB, MRCvS, MS, PhD, DSc, Keeneland Association Chair in Equine Science, is a leading authority on equine strangles, basing his research out of the Gluck Equine Research Center at the University of Kentucky in Lexington. His experience finds that the most susceptible horses are those at the weanling through yearling ages; these young horses might not have yet developed sufficient immunity through natural exposure in their short lives.

Incubation takes from three days to two weeks from the time a horse is exposed until he shows clinical signs of infection. Not all infected horses develop obvious signs of disease; asymptomatic individuals can serve as carriers and shed the organism through their respiratory secretions and saliva to spread it to susceptible horses. Older horses might show nothing more than nasal discharge, but they could be more likely to harbor *S. equi* infection in the guttural pouches. The immune system of a geriatric horse might not be working properly due to age-related decline, and there might be age-related scar tissue around the openings to the guttural pouches, which could inhibit drainage and facilitate disease.

Strangles is a highly contagious disease, particularly in conditions of stress. This includes situations where horses are housed in crowded areas, or with poor hygiene, or with inadequate nutrition. Transmission occurs by direct contact with nasal secretions or saliva. Flies also spread the disease, as do contaminated vectors (fomites) such as feed buckets, rakes, and human hands and clothing.

Timoney remarks, "A water source is the main culprit for temporary persistence in the environment. The bacteria survive for three to four weeks in water in tanks contaminated by discharges. Soil contamination does not seem to be a factor in persistence in the environment since soil bacteria appear to kill off *S. equi*. However, in wintertime, pus and contaminated discharges that freeze can persist to infect others when the ground thaws."

COURTESY DR. JOHN TIMONEY

This bacterial infection invades the respiratory tract of horses, donkeys, and mules, and it causes swelling and abscessation (seen above) of the lymph nodes around the head and neck.

Once the bacteria are established on a property, another outbreak can occur on that farm a year or two later. A strangles infection can keep cycling through a herd to become a persistent, frustrating management issue. Once a horse has been infected with strangles, he might continue to shed the organism intermittently for months through nasal secretions. In a small percentage of horses, the bacteria remain resident in the guttural pouch for prolonged periods, with the potential to carry the infection to others despite the horse appearing to be fully recovered. However, most horses stop shedding within about three weeks.

Timoney notes, "Carriers only shed intermittently. Even though the carrier state occurs and is a problem from time to time, the disease does not persist on most farms. Young horses are less likely to be chronic carriers than older horses."

In suspected carriers, nasal washes or culture swabs of nasopharyngeal or guttural pouch contents help identify inapparent shedders of *S. equi* organisms. Reports from one study found that the average period of shedding from carriers was 9.2 months, with one horse shedding for 42 months. Shedding persisted in 68% of horses for at least four weeks following resolution of clinical signs.

Timoney noted that 75% of horses that recover from strangles develop immunity for at least two years and possibly as long as five years.

Treatment

This disease is labor-intensive, requiring supportive nursing care. The disease must run its course, but hot packs applied to the swollen glands can help an abscess come to a "point" for drainage. Surgical lancing of affected lymph nodes hastens drainage and speeds a horse to recovery. An opened abscess should be irrigated daily with an antiseptic solution made by mixing 10-30 mL of povidone iodine per liter of salt water. Supportive care is essential: The horse should be encouraged to eat by providing pelleted gruels, and food and water should be accessible where he can reach comfortably.

Timoney has advice that is pertinent to both treatment and prevention: "It is important to feed in a head-down position. The act of feeding and swallowing adds pressure to open up the guttural pouches to facilitate drainage."

Non-steroidal anti-inflammatory medications improve comfort, help control swelling and fever, and encourage eating and drinking by reducing pain and inflammation.

The use of antibiotics has sparked much controversy. Antibiotics can, in fact, be counter-productive. Timoney notes, "Antibiotics suppress bacteria for a time, but infection may flare up when the antibiotics are discontinued." Treated horses might become re-infected because they do not develop protective immunity.

He continues, "Once an abscess forms in the lymph nodes, antibiotics won't penetrate to reach the organism, so when antibiotics are withdrawn, there is recrudescence (reappearance) of disease."

Antibiotic therapy might be indicated when an affected horse remains persistently off feed and is depressed despite other supportive care, or if the fever remains elevated (greater than 104°F), or if the

JANIS TREMPER

Rectal temperatures of new farm arrivals should be checked twice daily. If strangles is suspected, a bacterial culture should be taken to identify a potentially sick horse.

airway is obstructed by lymph node swelling (contributing to difficulty in breathing). In these cases, bacterial culture and antibiotic sensitivity can be determined in the lab to help choose antimicrobial therapy.

Complications

Besides the frustration experienced in dealing with horses affected by acute disease, strangles is not without its set of complications that arise subsequent to infection. About 20% of horses infected with strangles develop problems other than the basic upper respiratory signs. Some of the complications might be life-threatening, so an infected horse should be monitored closely following initial clinical signs. As an example, a *Streptococcal* organism can seed itself within lung tissues and cause bacterial pneumonia.

One of the complications that is difficult to identify is called bastard strangles. In these horses, bacteria spread to other internal lymph nodes (particularly those of the gastrointestinal tract) or to organs such as the spleen, liver, kidney, lungs, or even the brain. A horse with bastard strangles might appear relatively normal until infection wears him down. His hair coat appears dull and ragged, he might lose weight in the presence of ample food and good dental care, his performance might suffer, and his listless demeanor suggests an underlying problem that cannot be explained by an obvious cause.

Lab results of a complete blood count and fibrinogen level might identify a systemic infection. A rectal exam, an abdominal ultrasound exam, or an abdominal tap might identify the location of an internal abscess. These are hard cases to treat, requiring long-term antibiotic therapy.

Another complication that isn't immediately apparent is infection of the guttural pouch with the development of empyema (accumulation of pus) or chondroids (hardened concretions of pus). This can be a life-threatening problem if the infection erodes through large blood vessels that course through the guttural pouches. Major nerve branches can also be affected in this area, creating neurologic problems. Pus debris that accumulates within the laden guttural pouch is often swallowed as it drains into the pharynx, but it is sometimes visible as a nasal discharge from one or both nostrils.

An endoscopic exam and radiographs of the head are useful diagnostic tools to detect this problem. Most asymptomatic carrier horses harbor *S. equi* within their guttural pouches.

The *Streptococcus* bacteria can also create an immune-mediated syndrome known as purpura hemorrhagica, which leads to hives and edema in the abdomen, limbs, head, and scrotum. This is an emergency situation; contact your veterinarian if you see these signs. Protein antigens of the bacterial organism combine with antibodies to set up an allergic response in the horse, causing vasculitis (leakage of blood vessels). This occurs in less than 1% of infected horses, but it is noted that this condition has been reported after a second natural exposure or following vaccination of animals that previously had strangles.

A horse that had a case of strangles might seem to be well on the mend, only

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to suffer a severe setback one to four weeks following strangles infection. Gravity-dependent areas (such as the legs, abdomen, and head) will swell. The horse is depressed, off feed, and pinpoint blood spots (petechiations) are present on the mucous membranes of the gums, conjunctiva, and nasal lining.

Pronounced limb edema often causes serum leakage and skin sloughing from swollen limbs. If a similar event occurs in internal organs, the horse might demonstrate colic, respiratory disease, or muscle problems. Since this syndrome arises due to an immune-mediated complex stimulated by components of the bacteria, aggressive treatment requires corticosteroids and systemic antibiotics for a lengthy period of time.

Myositis (muscle inflammation) is another potentially fatal complication of infection with *S. equi* that might involve an immune-mediated process.

Prevention and Control

It is good management to isolate newcomers to a farm for two to three weeks in case they are carrying a bacterial infection or virus to which resident horses have not been previously exposed. This allows new horses to incubate and break with disease before they've had a chance to mingle with and infect other horses on the farm. The cause of the infection is identified and controlled before too much damage is done. This strategy is especially important for foals, weanlings, and yearlings.

Rectal temperatures of new arrivals should be checked twice daily. If *S. equi* is suspected or is a concern based on a horse's past history or exposure, Timoney suggests that bacterial culture of nasopharyngeal washes or guttural pouch swabs be done; this is the gold standard to identify a sick or carrier horse. Ideally, a horse is considered not to be a carrier if it has three negative nasopharyngeal swabs for *S. equi* over a two- to three-week period.

Nasopharyngeal bacterial cultures detect 60% of carrier horses. Combining this test with PCR (polymerase chain reaction) blood testing increases detection of carriers to 90%. The PCR test detects DNA from both living and dead *S. equi* bacteria and is as much as three times more sensitive than bacterial culture. Active infection should be confirmed by bacterial culture of the swab. If either test shows a positive result, endoscopic exam of the guttural pouches might be used to screen for carriers. Samples taken from the guttural pouches can be tested with PCR and cultured for final confirmation.

NHI PHOTOGRAPHY

John Timoney, MVB, MRCVS, MS, PhD, DSc, of Gluck Equine Research Center in Lexington, Ky., says it is important to feed horses with strangles in a head-down position to open up the guttural pouches to facilitate drainage.

Once a horse is identified as having a fever, it should be isolated until shedding has ceased. Timoney remarks, "Shedding of the organism does not begin until 24-48 hours following onset of a fever, thereby giving time to separate sick horses from well ones. It would be nice to have a stall-side diagnostic test to give immediate confirmation that the fever is related to *S. equi* infection. However, during an outbreak, a horse with a fever is presumed to have strangles."

Excellent sanitation and good common sense are important to control spread of the disease. Fly control measures are important. Contaminated bedding should be composted beneath a layer of plastic so flies cannot access the bedding. Use separate halters, water and feed buckets, cleaning utensils, wheelbarrows, and brushes to manage sick horses. Always handle a sick horse last, taking care of the healthy horses first. Change clothing after contacting any sick horses, wash your hands with antiseptic soaps, and wear boots that can be immersed in a footbath to decontaminate the soles of your shoes.

Also, scrub down fences, stall walls, and anything that might have been contaminated by respiratory secretions, using materials known to kill the *Streptococcal* organisms. These include phenolic products, iodophors, chlorhexidine, or glutaraldehyde disinfectants. Contaminated pastures should be kept free of horses for at least a month. And, Timoney encourages, "Clean and disinfect water tanks daily."

In the face of an outbreak, it has been demonstrated that vaccinating healthy animals might aid in the prevention of disease. However, this strategy can have limited usefulness in horses that have never before been vaccinated against strangles since in order to ensure the maximum protective effect, healthy horses need to receive the full protocol of two vaccines spaced two to three weeks apart at least four weeks before exposure. Discuss the risks and rewards of vaccinating during an outbreak with your veterinarian.

Corinne Sweeney, DVM, Dipl. ACVIM, professor of medicine at the University of Pennsylvania veterinary school, has devoted her efforts to studying the epidemiology of strangles infections. She comments, "Vaccination during an outbreak is of no value to horses already infected. During an outbreak, only horses with no known direct contact with strangles cases or the exudates from these cases should be promptly vaccinated. It is known that following vaccination, immunity will take a minimum of two to four weeks and the highest titers are usually obtained by eight weeks. Thus during an outbreak, if a horse is vaccinated and is then exposed to the infected horses before he has developed adequate immunity, he may contract strangles."

Horses that have been on a previous strangles vaccine program can be "boosted" with one dose of vaccine, and this should stimulate some immunity to limit the severity of the infection. However, keep in mind that it might be difficult to determine which horses in a herd are incubating disease, and which have not yet been infected.

Timoney expresses concern that it might be inappropriate to handle and immunize horses that haven't shown clinical signs in a herd during an outbreak for fear of spreading disease from those that are shedding bacteria to those not yet exposed.

With regard to the intranasal vaccine, Timoney says, "There is risk in administering a live attenuated organism in a horse which may already be incubating disease. If disease develops, there can be confusion as to whether it is caused by a natural infection or by the vaccine strain."

The risk of developing a serious complication such as purpura hemorrhagica is more likely when using intramuscular products in horses that already have high antibody titers. Horses that have existing high antibody titers from a previous infection or vaccination need not be immunized again.

Sweeney comments, "Because of some of these issues associated with vaccination, it seems inappropriate that boarding stables should require horses housed in their facilities to be vaccinated for strangles. In fact, there are some instances when vaccinating a horse is contraindicated. When? If a horse's natural antibody titer is high (a titer of 1:1,600 or greater in the ELISA test), that horse should not be vaccinated. This has less to do with the disease strangles and more to do with the disease purpura hemorrhagica. The risk of your horse developing immune-mediated purpura hemorrhagica will increase if the horse already has good immunity (as determined by the ELISA test) to *Streptococcus equi* and then is subsequently vaccinated. Should your horse have a high titer, you may need to have your veterinarian notify the farm manager that it is ill advised to vaccinate your horse and that your horse should be allowed to be stabled without vaccination. Because of these many issues with the strangles vaccine, it is best that the farm does not require vaccination prior to boarding."

Vaccination

About 75% of horses that recover from a strangles infection will be immune from exposure for up to five years. However, strangles infections are not always definitively diagnosed in a mildly sick animal. As a consequence, many barns with large numbers of mobile horses give strangles vaccinations as a matter of course.

In earlier years, all vaccination strategies against strangles relied on intramuscular injections (extract vaccines) that elicited a systemic immune response. Those vaccines have had limited efficacy, only curtailing disease in 60-70% of those horses challenged by the organism. They do not prevent infection. In addition, intramuscular injections often create sore muscles, malaise, and fever, with adverse reactions lasting as long as a week.

Although those complications occur in only a small percentage of horses, many horse owners weighed the risks and concluded that the intramuscular vaccine was not for their horses. For that reason, horse owners have practiced limited use of the strangles vaccine until the advent of the intranasal form.

Timoney notes, "Protective immunity is expressed in the tonsil, so we need to get the tonsil to respond. It may need an intranasal presentation to achieve that."

However, despite "protection" derived from the available intranasal vaccine (Pinnacle I.N. by Fort Dodge), some vaccinated horses challenged with the organism still develop clinical signs of disease, although at a much lower rate than unvaccinated horses. Extent of illness is decreased in vaccinated horses, and of those that do get sick, clinical signs are reduced by 65% compared to unvaccinated horses.

Just as with the intramuscular vaccines, no horse can receive complete protection from the strangles organism when he is challenged. Timoney wonders if perhaps the intranasal vaccine attenuated organism does not completely penetrate into the tonsils, thereby resulting in incomplete efficacy. Nonetheless, the intranasal vaccine might reduce the number of horses affected and the severity of an infection if it occurs.

NHI PHOTOGRAPHY

***Streptococcus equi* bacteria can survive for three to four weeks in water in tanks that are contaminated by discharges.**

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The intranasal strangles vaccine is given as a series of two doses spaced two to three weeks apart. After an initial series of two immunizations, a horse should receive a booster annually. Pregnant mares should be vaccinated with approved products about a month prior to foaling so a newborn foal will receive protective antibodies in the colostrum.

The material in the intranasal vaccine is a live, avirulent *S. equi* organism that is freeze-dried and reconstituted with sterile water just prior to administration. The 2-mL dose is squirted through a nasal canula into a nostril to reach the upper nasal cavity. This provides the best protective response since it stimulates local production of antibodies at the site of invasion in the upper respiratory tract. The objective is to prevent attachment of "wild" *S. equi* to tonsil receptors, and thereby prevent invasion.

There is some concern that an attenuated live *S. equi* organism could pass from vaccinated individuals to those that have not been vaccinated. Safety studies indicate that slight shedding occurs only during the first day. However, it is recommended that the intranasal strangles vaccine be administered with care after immunizing a horse with other intramuscular products during routine inoculations. Ideally, it should not be administered on the same day as other injections are given. This strategy helps prevent inadvertent contamination of intramuscular inoculation sites with the live vaccine.

Timoney concludes, "Bacteria are a lot more complicated than viruses. Although we have made progress, vaccine efficacy is not easily improved. Why is this so difficult? First, the genomic sequence of *S. equi* has revealed an extensive set of new proteins involved in the horse's immune response and in virulence. Only a few of these proteins stimulate protective immune responses, and these must be identified by experiment in the horse. Furthermore, we need to understand which combinations, and which aspects of the immune system, must be stimulated. Do they need to be presented to the respiratory tract by intranasal administration or systemically via intramuscular injection? The research potentially will improve vaccine efficacy and safety."

Even with vaccines, no horse can receive complete protection from the strangles organism when challenged.

Take-Home Message

Management techniques are key in preventing a strangles outbreak on your farm, or in curtailing the number of horses that become ill during a strangles outbreak. Recognize that some horses show no clinical signs, but shed the *S. equi* organism, especially during times of stress. Young horses are most susceptible. Quarantining new arrivals is the first step. Vaccination can help prevent or reduce the number of horses that become ill and can reduce the severity of clinical signs in horses that do become ill. Thorough disinfection and good horse management during an outbreak can help break the cycle of contamination.

Treatment with antibiotics isn't always advised, so seek the advice of a veterinarian. Above all, don't try to "hide" cases of strangles from boarders, neighbors, or those at competitions or trail rides. Even though strangles isn't a reportable disease in a legal sense, horse owners owe it to one another to be honest about a disease outbreak.

ABOUT THE AUTHOR

Nancy S. Loving, DVM, *owns Loving Equine Clinic in Boulder, Colo., and has a special interest in managing the care of sport horses. An enthusiastic endurance rider, Loving is also a veterinary judge for the American Endurance Ride Conference and for FEI (international) endurance events. She authored the books* Go the Distance: The Complete Resource for Endurance Horses, Conformation and Performance *(both available at www.ExclusivelyEquine.com or by calling 800/582-5604), and* Veterinary Manual for the Performance Horse.

ONE COMPLICATION OF STRANGLES—PURPURA HEMORRHAGICA


COURTESY DR. JOHN TIMONEY

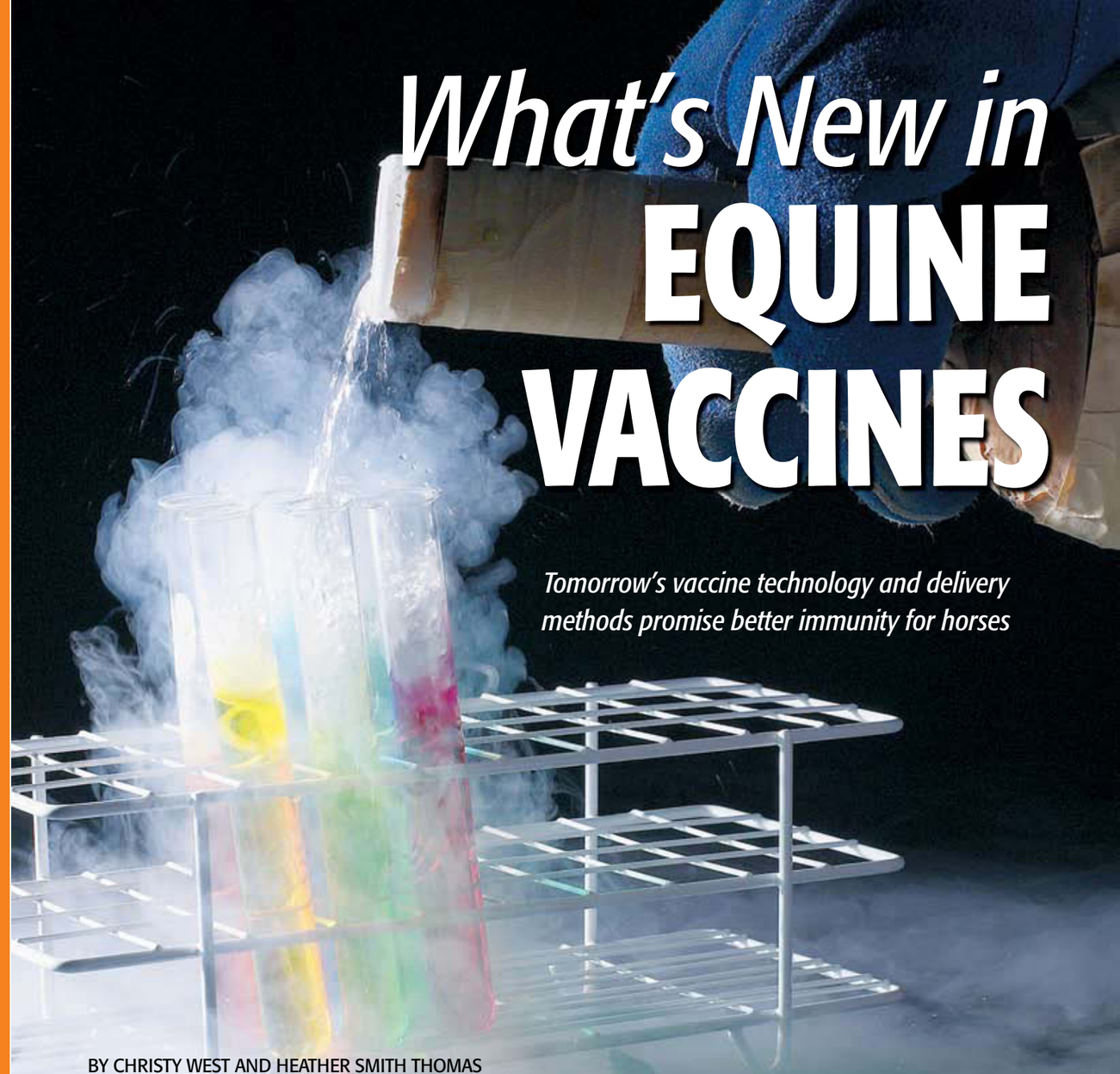

COURTESY DR. MARIANNE SLOET


STAFF PHOTO

Strangles can also create an immune-mediated syndrome known as purpura hemmorrhagica that leads to edema in the abdomen, limb, head, and scrotum, as seen in the photos above.

What's New in EQUINE VACCINES

Tomorrow's vaccine technology and delivery methods promise better immunity for horses



BY CHRISTY WEST AND HEATHER SMITH THOMAS

For most of us, equine vaccines seem pretty simple and boring—halter and restrain horse, pop in a needle and release contents, then a short time later the horse will be protected against that disease. But it's a lot more complicated than that, and the various factors affecting immunity and vaccination provide seemingly limitless possibilities for new technologies and ways to get vaccines into horses.

Lately we've heard a lot about the new vectored vaccines (such as Merial's canarypox-vectored West Nile virus, or WNV, vaccine) and DNA vaccines (such as Fort Dodge's, or FDAH, DNA WNV vaccine). And there are more possibilities on the way, such as transdermal vaccines (currently used in cats), subunit vaccines, orally delivered vaccines, and several ways to improve currently available vaccines. More on these in a moment.

"People are looking for alternatives to traditional approaches to get the best immunity possible," says Robert Holland, DVM, PhD, senior technical services veterinarian at Pfizer Animal Health. "Scientists are looking at improving less effective vaccines and exploring new vaccine technologies. We've also learned a lot about nutrition, exercise, stress, etc., while trying to find the best way to safely boost immunity (with management techniques, not just vaccines)."

Whether a particular vaccine is new or improved, one thing is for sure: The companies that develop and manufacture vaccines aren't making products and

Editor's Note

This is the eighth in a 12-part series of articles on vaccinations for horses.

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forgetting about them.

Research to better understand the equine immune system and how to optimize it is spread across several countries and countless institutions, all with the goal of keeping more horses healthy in the face of new, old, and mutating disease challenges.

DNA Technology

Fort Dodge's equine DNA vaccine for WNV is awaiting USDA approval and might become available in 2005, making it the first commercially available DNA vaccine for any species, including humans.

"This is a naked DNA vaccine—not recombined with anything," says Kevin Hankins, DVM, MBA, a field veterinary consultant at FDAH. "It's just the DNA of the virus and an adjuvant (which boosts the immune response), unlike current vectored vaccines that require a vector agent. There's no antigen for the horse to react to, so it's basically a reaction-free vaccine, and it also gives very rapid protection."

Steve Chu, DVM, PhD, of Global Research and Development at FDAH, explains that when a virus' DNA is given to an animal in a vaccine, it is taken up by the body cells to be processed into RNA. The RNA can then be translated into proteins that stimulate antibodies and white blood cell immune response, protecting the vaccinated animal from that disease.

Hankins says, "The minute the DNA starts entering cells, it starts the RNA replicating, so the protection is much more rapid than with vaccines available today. With a DNA vaccine, you can also vaccinate foals at a younger age."

With traditional vaccines, there has always been a problem with maternal antibodies from colostrum interfering with the foal's ability to mount an immune response to the vaccine. But naked DNA vaccination is attractive for immunizing foals because it contains no antigens for the maternal antibodies (from colostrum) to block; the maternal antibodies target proteins on the pathogen and DNA is not a protein. "This way the vaccine 'flies under the radar' of the maternal antibodies," explains Hankins.

Once in the foal's cells, the DNA directs them to make immunogens, which teach the immune system to recognize the pathogen and destroy it. Also, studies in humans and some animal species have shown that when given early in the course of disease, a DNA vaccine can act therapeutically to reduce disease signs and severity, he notes.

DNA vaccines were first presented in 1992. The FDA approved the first DNA vaccines for human trials in 1995, but none have been approved for commercial use. If FDAH's equine WNV vaccine is approved, this will open the way for other veterinary and human uses for this technology.

DNA vaccines are also being developed to enhance cancer immunotherapy for injection into tumors (such as melanoma), activating the body's immune system so it can recognize tumor cells. The immune response creates tumor-killing T-cells that can spread to other tumors in the body; injection into a single tumor can thus treat multiple tumors, Hankins explains.

> *The goals of improving vaccines include better immune response, more relevant strains, and fewer adverse reactions.*

Another DNA vaccine is being developed to fight lymphoma, he adds. This vaccine targets tumors with much more specificity than traditional killed tumor cell vaccines, and it is much cheaper to produce.

Naked DNA has an advantage over whole virus in creating a vaccine, since DNA is more stable. DNA vaccines might not require refrigeration, and they rarely produce any adverse reactions.

DNA vaccines can be made quickly once a new virus is isolated, which is very handy when faced with a new disease outbreak or epidemic. "If a new disease appears, we can rapidly develop a vaccine just by getting the DNA from the virus and growing it in a culture," explains Hankins. "It goes through a washing process to purify it, then an adjuvant is added, and that's your vaccine."

For instance, in both the WNV outbreak in North America and the SARS (severe acquired respiratory syndrome) in China, the DNA components for use in clinical testing became available four to six months after the antigen gene sequences were discovered. By contrast, traditional vaccines usually take two to three years to safely develop, Hankins notes.

The WNV equine vaccine, if approved, will be given intramuscularly in two initial doses three to four weeks apart, with an annual booster thereafter, he says. If this vaccine is approved for use in horses, a human WNV vaccine will probably be approved in the next few years.

Another DNA-based vaccine generating a lot of discussion in the equine immunology research world is Merial's therapeutic melanoma vaccine for dogs. "Many in the equine world are interested in trying this with gray horses, so this will be clearly under experimental consideration for this important disease," says Bob Nordgren, PhD, head of research, development, and technology acquisitions at Merial.

Vectored Vaccines

"Vectored vaccines are another hot area," says David Horohov, PhD, William Robert Mills Chair of Equine Infectious Diseases at the University of Kentucky's Gluck Equine Research Center. With a vectored vaccine, a specific piece of DNA from the pathogen against which you want immunity is carried into the animal's cells by a carrier or vector that does not cause disease itself.

Along with the canarypox-vectored WNV vaccine (Recombitek) Merial already markets, Merial also has a canarypox-vectored influenza vaccine based on the same technology in use in Europe. This product is in field testing for U.S. approval, says Nordgren. At the field testing stage of the approval process, he says, a product is usually about six months away from approval.

"We have wonderful data with this product in Europe, with a publication (*The Veterinary Record,* 156 (12)) reporting short-onset protection with a single shot application and a one-year duration of immunity with three shots, with broad-spectrum protection against strains that have broken through conventional products," says Julius Minke, DVM, PhD, director of equine research and development at Merial.

COURTESY MERIAL

Merial's Vet Jet system is currently used for vaccinating cats transdermally (into the skin). While no commercial transdermal equine vaccines currently exist, researchers say they hold great promise.

New Delivery Methods

Transdermal (through/into the skin)— "There is lots of potential for immunity via skin; the potential for generating response there is very exciting," says Horohov. "Any kind of IM immunization is painful, there's no getting around that. You're introducing things into the muscle body, where there is damage, inflammation, pain, and soreness due just to the method. Transdermal delivery avoids this issue."

Merial is currently marketing a transdermal vaccine against feline leukemia, which is delivered with their Vet Jet system. The device pushes liquid medication through small punctures in the skin that are about the diameter of a human hair.

"We're really excited about how transdermal vaccines are working in companion animals, although horse applications are currently in the research stages," says Nordgren. "One thing we've found is extraordinarily important with transdermal vaccines is adjusting the application for each species. We're trying to derive optimal immune response for the host and antigen in question, limit dose volume, and improve safety."

Intradermal administration puts the antigen where the dendritic cells are, which Nordgren says are "what everyone has decided are the key immune cells, and they're really rich in the intradermal space. They orchestrate the whole immune response, initiating the appropriate immune cascade (to best combat a particular pathogen, which might be a cell-mediated or antibody response, etc.)

"We have nothing pending approval now, but it certainly holds great promise, particularly for DNA-based vaccines," he says.

Oral delivery— "One of the things that's always interesting to me is that in humans, there has been great interest in orals to avoid sticking small children. But veterinary medicine is just the opposite—it's easier to just stick an animal than to get him to swallow it!" notes Horohov. "The problem with oral vaccines is this—are you sure they got enough? Did they swallow or spit it out?

"I think for some (vaccine) applications, oral would be the best delivery method, such as for *Salmonella* or other intestinal parasites," he adds. "There's lots of interest in using attenuated *Salmonella* as a vector, including in the horse. The thing about it is that it's an invasive organism in the intestinal tract, which could be very useful (to gain access to the bloodstream). But you'd have to use strains that aren't as pathogenic (disease-causing); then they might not be as effective (at stimulating an immune response).

"There's a real possibility of orals with horses and other species in the future; viral/bacterial/yeast-mediated delivery are all possibilities," he adds.

Subunit Vaccines

Subunit vaccines are those including only a part of the pathogen being vaccinated against, such as a particular protein or group of proteins. Subunit vaccines are being researched for several pathogens, particularly against those for which serologic testing can be confounding (such as equine infectious anemia, EIA, or equine protozoal myeloencephalitis), says Horohov.

"The question has always been 'How do you vaccinate populations when that could make them positive on serologic testing?' This is what you're trying to avoid," he explains. "Can one derive a subunit type vaccine to differentiate horses that are infected from those that are vaccinated?"

The difference between the naturally encountered pathogen and the version in the vaccine might just be a single protein. This could be deleting a protein, changing it, or adding one for marker purposes.

"This is primarily of interest for surveillance purposes or if someone buys a horse (without knowing his history) and wants to know if he's been exposed or vaccinated," Horohov says. "Over the years, the most interest has been with EIA. African horse-sickness was another one that generated a lot of interest in Europe at one time."

Genes to Maximize Response

We're always looking for ways to help vaccines boost a horse's immune system. One approach that could possibly help horses (and is currently being researched in mice and cattle) is adding cytokine genes to vaccines to increase the body's production of natural immunostimulants.

"You use a cytokine gene to push the immune system in the direction you want it to go," explains Horohov. "It's sort of like a fancy adjuvant, which boosts all over res-

ponse; this is more like a specific adjuvant (to stimulate a particular part of the immune system, such as antibodies only if that is the most effective action against the pathogen in question, or cell-mediated immunity only).

"This is still very much in the research stage," he adds. "On paper, it looks like it should work, but reality is often a far different thing."

Improving Current Vaccines

Often we think that when a vaccine lands on the shelf, the company that produced it is done with it, but that's not the case—constant improvement of vaccine products is more a rule than an exception. The goals of improving a vaccine include better immune response, more relevant strains, and fewer adverse reactions.

"The companies don't get enough credit—they continue to monitor and modify vaccines and work with people like me to see what can be done to make them even better," opines Horohov. "These are costly things to do, and it's an ongoing effort. This is why we have better vaccines than we did 10-15 years ago. They're still working to improve their products, and that's important. (Improving modified live vaccines) is probably our most active area (of immunology at Gluck and elsewhere) right now."

What is involved in improving a vaccine? "We're looking at modifying vaccines by mixing new strains in or using things that are modified in different ways," he explains. "The big problem is that it's a lot like Goldilocks and the three bears—it can't be too hot or cold, but just right. That's the trick with modified lives, that they do what you want them to do without the disadvantages of real infection." The pathogen in the vaccine must be robust enough to replicate in the animal and thus stimulate the immune system to act against it, but weak enough that it doesn't make the animal sick.

Traditionally, Horohov explains, a modified live vaccine is created by culturing the virus in the lab under various conditions and testing what survives. "When you do that a number of times and the virus mutates, you're selecting for viruses that grow well in culture," Horohov explains. "They often don't do quite as well going back into the natural host. It's more of an art than science approach, because it's really difficult to know what modifications were made (throughout the packaging and mutation process).

"What we'd like to do is look at the pathogen and know what proteins are involved in pathogenesis (disease-causing ability), so we can limit pathogenesis, but still stimulate full immunity," he says. "Ultimately what it comes down to is genetic mapping of an agent to determine where the susceptible genes are to lead to a less pathogenic organism."

Another approach is to adapt the pathogen to a different environment. An example that is already in use in horses, and might have future uses, is cold-adapted pathogens (Flu-Avert by Intervet is one). These are well suited for respiratory applications, in which a pathogen might be adapted so it can't survive in normal equine body temperatures, but can live and replicate in the cooler environment of the upper respiratory tract. Thus, it stimulates local immunity in the respiratory tract—the first line of defense for these pathogens—without causing disease elsewhere in the body.


HELEN PEPPE

Oral vaccines present challenges with dosing in animals, but could be effective against some problems, such as gastrointestinal pathogens.

"For something like WNV, this has no use, because (WNV) is injected in or near the bloodstream (where it would enter the body with natural infection from a mosquito bite) where it will be at the core body temperature," says Horohov. "It wouldn't replicate at all, and would be essentially inactivated—then it wouldn't stimulate good immunity. I think, for the most part, cold-adapted pathogens will always be developed with an eye towards respiratory applications. An interesting one might be equine herpesvirus; since EHV is typically spread as a respiratory disease, (an effective cold-adapted vaccine) would be a very attractive vaccine indeed."

Take-Home Message

With so many available and upcoming options available to maximize immunity, we can expect tomorrow's horses to have better protection against disease than many might have thought possible. New and mutating pathogens will continue to attack, but vaccine manufacturers and researchers are meeting the challenge.

ABOUT THE AUTHOR

Heather Smith Thomas *ranches with her husband near Salmon, Idaho, raising cattle and a few horses. She has raised and trained horses for 45 years, and as a freelance writer has published 13 books (including the recently released* Care and Management of Horses, *available at www.ExclusivelyEquine.com) and more than 5,400 articles for horse and livestock publications. She is a member of American Horse Publications, American Agricultural Editors Association, and Livestock Publications Council.* ***Christy West*** *is the managing editor of* The Horse; *she grew up riding Saddlebreds and various other breeds and is an avid skydiver.*

Strategies to ENHANCE VACCINE EFFICIENCY

BY NANCY S. LOVING, DVM

When it comes to protection from infectious diseases, the best defense is a good offense. Not only is a strategic vaccination program important, but the housing and handling of horses on a farm can enhance vaccination efficacy. A successful outcome (no disease) is best accomplished by applying intelligent management strategies for individual horses and proper herd health principles. Immunizations are available for many diseases, not all of them communicable from horse to horse. Some infectious microbes that have a huge impact on herd health include respiratory diseases like equine influenza, equine herpesvirus, and strangles.

In the following article, we'll give you tips and strategies on protecting your horses from infectious and contagious diseases with proper management strategies.

Vaccine efficacy is dependent not only on the vaccine, but also on how you manage your horses and their levels of exposure to infectious agents

Health Exam Prior to Entry

The best defensive strategy stops communicable diseases before they enter a property. This is accomplished by requiring health certificates on any horse coming to your farm, whether the horse

ANNE EBERHARDT

Stop communicable diseases before they enter a property; check horse health certificates on any horse coming to your farm.

Editor's Note

This is the ninth in a 12-part series of articles on vaccinations for horses.

remains indefinitely or is just passing through. When possible, every incoming horse should be examined thoroughly close to the time of entry to your facility. Many infectious diseases have an incubation period of up to 21 days. The standard requirement for a health certificate for interstate travel requires an exam to be conducted within 30 days of travel, although some states require a shorter, 10-day window prior to movement.

Consider that at 30 days out, it is difficult to identify those horses that might be incubating disease, or those that have not yet been exposed, but could be exposed within that 30-day window. There are also problems identifying horses that are spreading disease as inapparent carriers; they show no signs of clinical illness. This is particularly true for carrier horses with equine herpesvirus (EHV-1) and strangles.

John Timoney, MVB, PhD, DSc, MRCVS, is a leading authority on equine strangles, basing his research out of the Gluck Equine Research Center at the University of Kentucky. He has some sound advice to identify risky horses coming to a farm: "It is important to ask questions about a horse's history: Where did he come from, had there previously been a disease outbreak, an unexplained cough, a unilateral nasal discharge, or asymmetrical swelling behind the jaw?"

Quarantine

In addition to requiring a preliminary health exam prior to entry on a farm, a newcomer should be quarantined in an isolated area for two to three weeks to allow monitoring for clinical signs associated with a health concern. Quarantine of new horses on a farm implies that there is no opportunity for these horses to touch each other, share food or water, or to co-mingle in any way. George Allen, PhD, from the Gluck Center, suggests, "The greatest danger for infectious disease dissemination within a herd lies in the introduction of new horses into already established groups, especially those with recent opportunities for exposure to large, intermingled assemblages of horses from diverse sources such as sales, shows, boarding stables, racetracks, competitions, and training centers."

Many organisms are passed through respiratory secretions and aerosolized droplets thereof, so it's important to house new horses far enough away from resident herd members. The new horses should be fed and handled, and their paddocks and stalls mucked, only *after* caring for the needs of the resident horses. All personnel, including visitors, farriers, and veterinarians who interact with horses on a farm, should respect quarantine principles.

The likelihood of a horse developing an infection is not only related to the immune system of each individual, but it is often related to the dose of virus or bacteria that a horse receives. By minimizing the amount of microbes that are shed from an infected individual, you can greatly reduce the number of other horses that get sick, and/or the degree of sickness that develops on a farm. With this in mind, stalls and the insides of horse trailers should be scrubbed with disinfectant, especially in the face of an outbreak. Water tanks should be cleaned daily.

Many infectious diseases cause a fever, so rectal temperature should be taken at least daily on quarantined horses.

KIM AND KARI BAKER

Good-quality hay maximizes inner health and the immune system, thus helping the horse avoid airway disease.

(A normal, adult horse has a rectal temperature ranging from 97 to 101.5°F, while a temperature of 102°F is considered to be within normal limits for a foal, provided he is acting normally.) The presence of any nasal or eye discharge or coughing should be noted. The horse's appetite should be monitored closely. If a horse appears "out of sorts" in any way, a veterinary examination should be performed and possibly a blood sample submitted to the lab for a complete blood count to screen for systemic infection.

Before being released into a resident group, a horse should be examined by your veterinarian. This should include monitoring all vital signs, listening to the lungs with a stethoscope, and palpating the external lymph nodes. Other screening tests may be warranted if the quarantined horse has come from a premises known to have infectious disease.

Daily Practices

Implementing strategic management practices on a farm all the time is a sensible strategy. Allen advocates segregation of horses on the premises into small groups. Each group should be maintained as an isolated unit for purposes of stabling, pasture turnout, watering, and feeding. Allen elaborates on how to do this: "For maximal effectiveness, group size should be as small as the physical facilities will reasonably allow, with each group kept under conditions that limit the transmission of disease between established groups. Horses should be segregated into groups that are similar in age, gestation status, use, and frequency of removal of individual animals. Restrictions should be placed on movement of horses into and out of each established group, and contact with transient horses in particular should be avoided."

He qualifies the idea of quarantine even further: "The addition of any new horse into a closed group should be preceded by a 21-day period of isolation. A horse temporarily removed from a group for purposes that may involve prolonged transport or contact with other horses (e.g., breeding, showing, training, veterinary care, or sales) should also undergo a 21-day period in isolation and evaluation for signs of infection before returning to its resident group."

While these strategies are applicable to containment of any infectious disease, Cormac Breathnach, PhD, of the Gluck Center, relates the value of immunization and management in reducing abortion or

JANIS TREMPER

When possible, every incoming horse should be examined thoroughly by a veterinarian close to the time of entry to your facility. This can help identify diseases before they become widespread.

VACCINATIONS

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neurologic storms caused by equine herpesvirus infection (EHV-1): "Part of the reason for the reduction in storms was herd immunity arising from vaccination. But a large part was improved awareness and diligence of farm managers who more effectively quarantined and segregated sick or aborting mares. This remains a key to prevention of EHV-1 abortion or neurologic disease outbreaks. With major outbreaks of either (such as the EHV outbreak that occurred in Findlay, Ohio, in 2003), it seems you can always track the spread of the virus from the index case by retracing the movement of animals around that time. All of these large outbreaks that spread across premises appear to arise from cases where horses were not effectively quarantined or were discharged from quarantine too early. This is when an already serious problem becomes disastrous."

Scrubbing contaminated areas with disinfectant can help reduce the number of microbes that are shed from an infected horse, which can minimize the chances of other horses getting sick.

Optimizing a Healthy Environment

Critically important as a management strategy is the reduction of stress to individuals within a herd. Allen says, "It is important to minimize stress caused to horses by crowding, poor nutritional state, heavy parasite infestation, lengthy transport, disruption of established social groups, inclement weather, *en masse* weaning, and other disease states."

Common sense dictates that to obtain the best in health and performance, it is best to develop the most nurturing environment for every horse. Daily turnout is important for mental health as well as the positive effects it has on improving circulation and muscle tone. Horses should be turned out with, or stabled beside, compatible members of the herd. While this encourages horses to eat comfortably and to maintain good body condition, herd compatibility also minimizes fighting and the risk of injury. Good-quality hay maximizes inner health and the immune system, thus helping the horse avoid allergic airway disease that adversely affects respiratory tract immunity. Run-in sheds and other shelters shield horses from stress created by adverse weather.

ANNE EBERHARDT PHOTOS

It is important to check at least daily for wounds, and to administer first-aid care immediately; this will dramatically reduce the risk of a horse developing tetanus.

Strategies that promote clean air have significant favorable effects on immune responses of a horse's respiratory tract. Dust from hay should be kept to a minimum by not storing hay over the stalls and by moving hay storage to a different barn from where horses are housed. Hay should be covered to protect it from mold-producing moisture. Arena dust can be managed by periodic watering. Stalls should be bedded well with mats and/or shavings to eliminate aerosolized dust generated by kicking and stomping at flies.

Stabling should have adequate drainage for urine, and feces and urine-soaked materials should be removed regularly from stalls and paddocks. Decomposing bedding should be stored away from the stabling area to minimize exposure to proliferating mold spores or ammonia fumes. This will also help keep away flies that can carry disease. Ample ventilation within a barn minimizes ammonia fumes in the stalls while promoting air exchange to remove infectious organisms and to decrease humidity that favors formation of aerosolized microbe-containing droplets.

Craig Barnett, DVM, a technical service veterinarian for Intervet, notes that any stressor to a horse's system can depress the immune system. For example, he comments about stress-induced viral abortion related to transport: "Unless absolutely necessary, I recommend avoiding long-distance hauling of mares during their last trimester, as hauling is known to stress horses and has a negative effect on the immune system. I know of late-term pregnant, vaccinated mares that have been hauled long distances only to abort herpesvirus-positive foals. In these situations the hauling had an immunocompromising effect on the mares, the latent virus reactivated, and the mares aborted. Even though they were vaccinated, the vaccine could not overcome the immunocompromising effects of the stress and hauling and the reactivation of the latent infection."

Studies have also proven that stress induced by transport has significant adverse effects on a horse's immune system. Horse trailers should be purchased with the comfort of the horse in mind to minimize the stresses related to hauling. Attention to individual quirkiness about drinking and eating on the road also maximizes a horse's comfort en route and upon arrival. Many destinations are fraught with stimulation, anxious horses, and stressful energy. Fear is communicable from one horse to another, so efforts to remove a nervous horse from the presence of other excitable animals can go a long way toward creating a calm environment.

Managing Non-Communicable Diseases

Some diseases can be mostly prevented through vaccination, but management has a large role to play in minimizing risk. For example, although a horse that contracts tetanus is not contagious to any others, he still suffers a gruesome sickness, which is often fatal. Even the smallest puncture wound has the potential to create tetanus. Also, a program should be in place to immunize annually with tetanus toxoid, so it is important to check at least daily for wounds, and to administer first-aid care immediately; this will dramatically reduce the risk of a horse developing tetanus.

Other neurologic diseases, such as equine encephalitis viruses (Eastern, Western, and Venezuelan encephalitis, and West Nile virus), are transmitted by infected mosquitoes. Prevention relies on immunization against these viruses at least once or twice a year following an initial primary series of two injections. But management strategies, such as eliminating breeding sites for virus-transmitting mosquitoes, have a significant effect on reducing exposure.

Mosquitoes can hatch in stagnant water that is there only four days; to limit such reservoirs, remove containers that might fill with even small amounts of water. Some items are not so obvious, such as flower pots, bird baths, rain gutters, wading pools, wheelbarrows, stock tanks, clogged roof gutters, discarded tires, swimming pool covers, boat covers, discarded cans, or paint buckets. Open containers should be turned facedown so water cannot accumulate, or holes should be drilled in container bottoms for water to drain through. More obvious sites of water collection include ditches, creeks, or ponds. Chlorine in swimming pools kills the larvae, but a swimming pool cover and other sites of freestanding water should be cleaned regularly. Stock tanks should be cleaned at least weekly to remove algae and debris. Ornamental pools can be aerated or stocked with fish that eat insect larvae to avoid developing mosquito breeding grounds.

On properties with bodies of freestanding or slow-moving water, additional strategies will need to be applied to each horse. Fly sheets and leg nets limit the surface area of a horse's body that's exposed to mosquito bites, but cannot cover an entire horse. Insect repellents are somewhat useful, and efforts should be made to apply them to all body parts. Permethrin-containing repellents are safe for use in horses and offer some protection against mosquitoes. However, repellents retain only a limited duration of protection, and rain or sweat or rolling in the dirt removes them from a horse's coat. Screened barns protect horses from mosquitoes during their feeding times.

Different species of mosquitoes transmit viruses, with each displaying a different feeding habit: Some feed during the daytime, while others feed only at dawn or dusk. This makes it difficult to predict which part of the day horses should be left in the barn. Mosquitoes also lurk in corners and cracks in the barn, so spray these areas with insecticides. The use of fans to keep air moving in the stalls is helpful to prevent mosquitoes from landing on and biting horses (mosquitoes don't fly well in moving air).

Botulism is yet another neurologic disease that can infect one or many horses in a herd, although it is not communicable from horse to horse. Besides vaccination against botulism type B in high-risk areas, careful monitoring of the feed is essential for prevention. Horse feed can be a source of botulism toxin if it's contaminated by a decomposing animal, such as a rodent or bird, that was inadvertently bound in the baler. Decomposing plant matter (including hay or grain) is also a possible source of the organism and subsequent production of toxin. Round bales are commonly implicated as sources of botulism. Conditions that favor growth of mold in feed also create an environment that is favorable for botulism. This applies not only to baled hay or grain, but especially to silage or feed bagged in plastic.

CHARLES MANN

Management strategies such as eliminating breeding sites for mosquitoes (like this stagnant tank) can significantly reduce disease exposure.

Getting the Most from Vaccines

Keeping accurate records and a calendar plan ensures that an effective vaccine schedule is followed to provide optimal protection. Viral vaccines should be up-to-date to protect against current strains of disease. Vaccines should be stored to manufacturer's recommendations and administered to those specifications. Timing immunization prior to the highest likelihood of exposure is a key factor in minimizing the incidence or severity of infection. As an example, a horse that is frequently exposed to large congregations of horses should be immunized against respiratory viral vaccines approximately three to four times per year. And immunizing against mosquito-borne viruses should coincide with the period just prior to mosquito season.

To gain the best effect from vaccine boosters, they should be administered at least two weeks prior to expected exposure to give the immune system time to develop protective antibodies against a specific disease. Similarly, if vaccinating a horse for the first time against a pathogen, the two- or three-dose regimen should be completed one to two weeks prior to the beginning of the period when a horse will be at greatest risk of exposure to that pathogen. These offensive strategies give your horse the best defense against disease.

Take-Home Message

Vaccines are an important part of managing the health of your horse. However, vaccinations alone are not enough. Good management practices can considerably lower the risk of disease in your horses, and can mitigate outbreaks if they do occur. Consult with your veterinarian and develop a plan to manage your horses to avoid disease.

ABOUT THE AUTHOR

Nancy S. Loving, DVM, *owns Loving Equine Clinic in Boulder, Colo., and has a special interest in managing the care of sport horses. An enthusiastic endurance rider, Loving is also a veterinary judge for the American Endurance Ride Conference and for FEI (international) endurance events. She authored the books* Go the Distance: The Complete Resource for Endurance Horses, Conformation and Performance *(both available at www.ExclusivelyEquine.com or by calling 800/582-5604), and* Veterinary Manual for the Performance Horse.

CROSSING BOUNDARIES

Vaccinating pregnant mares protects both mares and unborn foals

BY RALLIE MCALLISTER, MD

Vaccination of broodmares is just one part of a complete disease prevention program, but its importance should not be underestimated. Immunization is one of the least expensive, and most effective, strategies horse breeders can use to protect broodmares and their foals from disease, and even death.

"When you vaccinate broodmares, you're not just protecting the mares, you're protecting their foals as well," says Tulio Prado, DVM, MS, Dipl. ACT, professor of theriogenology at the University of Tennessee's College of Veterinary Medicine. Foal protection comes in the form of passive immunity foals acquire as they absorb antibodies from the mare's colostrum. "The antibodies produced by the mare don't cross the placenta during pregnancy," Prado explains. "They are transferred from mother to foal only after birth through the colostrum, in the first 12 to 24 hours of life. This is why it is essential to maintain current vaccination of broodmares."

Editor's Note

This is the 10th in a 12-part series of articles on vaccinations for horses.

"Have a veterinarian check the foal's blood at 12-24 hours of age to make sure he got the colostrum and its valuable antibodies," urges Robert Holland, DVM, PhD, senior technical services veterinarian at Pfizer Animal Health. "It's some of the best money you can spend on your foal's health. If he didn't get the colostrum, none of the vaccines matter to the foal."

According to Laurel Gershwin, DVM, PhD, professor of immunology at the University of California, Davis, School of Veterinary Medicine, "One of the most important things to remember about vaccinating pregnant animals is that it is necessary to use the inactivated—or killed—form of the vaccine. If you give a live vaccine to

BARBARA LIVINGSTON

pregnant mares, there's a risk of abortion or fetal abnormality."

(Editor's note: There is a modified live EHV vaccine labeled for use in pregnant mares.)

Since there isn't a one-size-fits-all vaccination protocol for every broodmare or breeding operation, owners should work closely with veterinarians to design a plan that fits the needs of individual mares, as well as the entire herd. Factors to consider are the age and health of each horse, the geographic location of the farm, and any unique circumstances that heighten horses' risks of getting various diseases, including exposure to outside horses or to wildlife.

"You have to think about all the diseases that you need to vaccinate against," says Gershwin, "and consider whether or not each vaccine is really necessary."

According to Judy Marteniuk, DVM, MS, equine medicine/extension veterinarian at Michigan State University's College of Veterinary Medicine, "What you vaccinate broodmares against depends on which

JANIS TREMPER

Since there isn't a one-size-fits all vaccination protocol for every broodmare or breeding operation, horse owners should work closely with their veterinarians to design a plan that fits the needs of individual mares, as well as the entire herd.

diseases are prevalent in your area. On the other hand, some vaccines are essential for all horses, especially for diseases that are mosquito-borne, because they exist in the environment. Every horse in the U.S. will be exposed to these diseases, even if it's a solitary horse on an isolated farm."

Eastern Equine Encephalitis

One of the deadliest mosquito-borne diseases is Eastern equine encephalitis (EEE), a viral illness that attacks the central nervous system of its host and is almost always fatal. Although the virus is most prevalent in the southeastern United States, it is found near wetland habitats along the eastern seaboard from New England to Florida.

Closely related to EEE are Western equine encephalitis (WEE) and Venezuelan equine encephalitis (VEE). WEE occurs mainly in the plains regions of the western and central United States, while VEE is endemic in South and Central America. For protection against EEE and WEE, horses require an initial two-shot series with inactivated vaccine, administered two to four weeks apart, followed by an annual or semi-annual booster.

"In endemic areas, semi-annual boosters are recommended," says Marteniuk. "In non-endemic areas, mares may require only one booster, given four to six weeks prior to foaling, if their foaling dates coincide with the onset of mosquito season. For mares that will foal earlier in the year, two boosters may be necessary. One is given four to six weeks prior to foaling for the protection of the foal, while the other is given four to six weeks prior to the onset of mosquito season to protect the mare."

"Vaccination for EEE and WEE is recommended for all broodmares," says Gershwin, "but in the absence of an outbreak, the VEE vaccine isn't routinely given to horses in the U.S. Vaccination against VEE should be considered if there is a threat of exposure with international travel."

VEE vaccination is sometimes recommended by veterinarians in U.S. southern border states and Mexico.

West Nile Virus

Like EEE and WEE, West Nile virus (WNV) is spread by infected mosquitoes, and it can cause encephalitis and death. Although most horses exposed to WNV don't get sick, the disease is fatal in a third of infected horses that develop neurologic signs. For most breeders, odds like these make vaccination against WNV worthwhile. After the initial two shots given three to six weeks apart, semi-annual revaccination with the inactivated vaccine is recommended in warm, wet climates where mosquitoes live year-round. In non-endemic areas, mares may require only one annual booster, as long as it can be administered four to six weeks prior to the onset of both the mosquito season and the foaling date.

"The West Nile virus vaccine is usually given twice yearly," says Gershwin. "Administration of the vaccine should be avoided during the first 60 days of gestation, if possible. The first vaccine is given to mares before they're bred, and the booster is given four to six weeks before foaling. This way, the mares are protected, and the foals are protected through the colostrum."

ANNE EBERHRARDT

Influenza immunization is always a good idea if your broodmares will be exposed to other horses at horse shows, events, or breeding farms.

Tetanus

Tetanus is a non-contagious disease caused by *Clostridium tetani*. Its spores, which are present in soil worldwide, can contaminate wounds and surgical incisions, and the umbilici of foals. In the body, *Clostridium tetani* produces a powerful neurotoxin that blocks transmission of nerve impulses, resulting in a type of muscle spasm known as tetany. If untreated, infection is usually fatal.

"Every broodmare should receive an inactivated tetanus toxoid booster annually four to six weeks prior to foaling, to ensure colostral protection for her foal," recommends Gershwin.

Rhinopneumonitis (Equine Herpesvirus)

Equine herpesvirus (EHV) is an organism transmitted from horse to horse via body fluids. Infection with EHV causes rhinopneumonitis, which is a highly contagious disease that can lead to respiratory infection, abortion, paralysis, and even death. Although there are several strains of EHV, EHV-1 is the strain responsible for causing equine abortion, generally in the last three months of gestation.

Because the EHV ("rhino") vaccines offer short-term immunity, boosters every two to three months are recommended. "As the old saying goes, herpes is forever, so giving the rhinopneumonitis vaccine is very important for all broodmares," says Marteniuk. "At the very least, you should give it according to the manufacturer's recommendation, at five, seven, and nine months of gestation. On farms that have had several abortions, I recommend giving the vaccine at three, five, seven, and nine months."

Up to 90% of horses carry equine herpesvirus by the time they are two years old—some without showing clinical signs (latent carriers), writes George Allen, PhD, of the Gluck Equine Research Center in *Equine Respiratory Diseases*. Stress can reactivate infection, causing clinical signs. Vaccination of carriers helps boost the immune response to keep the organism under control, since it currently can't be eradicated.

According to Gershwin, "The vaccine is available as a combination of EHV-1 and EHV-4. When you give the mare her annual booster before breeding, use a combination of EHV-1 and EHV-4. During gestation, you should give the inactivated EHV-1 vaccine alone."

Atwood Asbury, DVM, Dipl. ACT, professor emeritus at the University of Florida and a retired dean of that veterinary school, says, "Many veterinarians give a combination vaccine with both EHV-1 and -4 to mares four to six weeks before foaling to make sure the foal is protected against both forms via colostrum. Discuss options with your veterinarian."

The AAEP guidelines also state: "Vaccines containing EHV-1 appear to offer some protection against EHV-4."

Vaccines for At-Risk Mares

For some mares, vaccination against certain diseases might be added to the core requirements, depending on the environment of that horse and the herd. Discuss these options with your veterinarian.

Rabies—"Whether or not to give your mares the rabies vaccine depends on where you live," says Gershwin. "If you live in an area where rabies is endemic, and there is a significant risk of exposure to wildlife vectors, you should definitely give the vaccine. If you live in an area where rabies is rare, you can probably skip this one."

Rabies is caused by a rhabdovirus that affects the nervous system, and since there is no effective treatment, the disease is considered to be 100% fatal. Unvaccinated horses can contract the disease from the bites of infected animals. Although skunks, foxes, raccoons, and bats are most likely to transmit the virus, the bite of an infected dog or cat can also cause infection. According to Gershwin, "If you're going to vaccinate for rabies, you should do it annually, before you breed the mare, because you're going to be giving her enough other vaccines during the pregnancy."

Vaccination guidelines endorsed by the American Association of Equine Practitioners state: "None of the licensed (rabies) vaccines are labeled for administration to pregnant mares…Some veterinarians administer the killed (rabies) vaccine to pregnant mares without reports of adversity."

(More information: See page 18.)

Equine influenza—This viral respiratory disease most often affects young horses between one and five years old. "Influenza immunization is always a good idea if broodmares will be exposed to other horses," says Marteniuk. "It should be a core vaccine for mares having contact with other horses at shows, events, and breeding farms."

While vaccination doesn't guarantee complete protection against influenza, the disease in vaccinated horses is less severe than in non-immunized horses. Broodmares should get an annual vaccine before breeding, as well as a pre-parturition booster.

"One can give the intranasal modified live virus annually before breeding," says Marteniuk, "but the booster should be an inactivated, injectable flu vaccine, given four to six weeks prior to the birth of the foal."

Strangles—This highly contagious disease is caused by the bacterium *Streptococcus equi*. Infection most often occurs in groups of horses younger than five years of age, es-

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pecially weanlings and yearlings. It is characterized by severe inflammation of the mucosa of the head and throat that can lead to rupture of lymph nodes under the jaw and death by asphyxiation. Intramuscular vaccines contain a protein from the strangles-causing organism and are considered safe for gestating mares. A modified live intranasal vaccine is also available.

"If you have a breeding farm that has had a lot of strangles, it is important to vaccinate the brood string to ensure that foals get colostral protection," says Gershwin. "If broodmares will come in contact with outside horses, they should be vaccinated prior to breeding, with a booster vaccine administered four to six weeks before foaling."

According to Marteniuk, "The strangles vaccine is quite controversial. If the protection is intended for the foal, an inactivated intramuscular vaccine should be given to the broodmare four to six weeks prior to foaling. If the protection is for the mare only, you can give her the intranasal live vaccine before she's bred."

Special Circumstances Vaccines

Some vaccines are given to broodmares only when dictated by special circumstances. Specific management practices, environmental risks, and your veterinarian's recommendations will help you decide if these vaccines are necessary.

Equine viral arteritis (EVA)—This disease causes inflammation of blood vessels that can lead to hive-like reactions, limb swelling, and abortion. It can become established as a carrier state, with shedding of virus via semen from some infected stallions. According to Marteniuk, "If you're getting a mare ready to be bred to an EVA-infected stallion, give her the EVA vaccine about a month or so beforehand. If you don't, she won't settle, because the infection typically causes early embryonic death."

Botulism—This neuroparalytic disease is caused by *Clostridium botulinum*, an organism found in decaying plant material. Hay and hay silage can be contaminated with the bacteria during raking and baling. Infection of adult horses typically occurs when pre-formed toxins are eaten, leading to a paralysis that affects the head, limbs, and tail. The inactivated vaccine should be administered to broodmares that are fed hay silage, and to those that live in endemic areas. Mares should receive an initial three-dose series at 30-day intervals, with the last dose given four to six weeks before foaling. Thereafter, the vaccine is given annually, four to six weeks before parturition.

"Typically, you're giving the botulism vaccine to broodmares to protect the foals from shaker foal syndrome," says Gershwin. This syndrome, which usually strikes foals between the ages of two weeks and eight months, is caused by a gastrointestinal infection with *Clostridium botulinum*.

Potomac horse fever (PHF)—Caused by the bacterium *Neorickettsia risticii*, horses get PHF through accidental ingestion of infected aquatic insects, including mayflies and caddis flies. The disease causes diarrhea, colic, and occasionally abortion. The development of severe dehydration, electrolyte imbalances, or laminitis can lead to death or might necessitate euthanasia.

"Vaccination may be considered in areas where the disease is endemic, but I don't recommend this vaccine, since it doesn't offer complete protection," says Marteniuk. While at least six strains of PHF are thought to exist, the vaccine is made from a single strain. Vaccination in at-risk areas consists of an initial two-shot series, followed by an annual booster.

Rotavirus—"Vaccination of mares for rotavirus should be considered on farms where risk of infection is high," says Marteniuk. "Passive transfer of colostral antibodies helps prevent rotaviral diarrhea in foals.

"Rotavirus is a vaccine you'll want to give your mares if they're going to be exposed to other horses, or if they live on endemic farms," she adds. "To protect the foals, the rotavirus vaccine is given to broodmares at eight, nine, and 10 months of gestation."

Your Veterinarian: The Key to Disease Management

Although a thorough understanding of immunization principles and practices is important for all horse owners, a veterinarian's input is critical to the success of the vaccination program.

"Your local veterinarian knows which diseases are prevalent in your area, and which vaccines are necessary for your broodmares," says Prado.

ABOUT THE AUTHOR

***Rallie McAllister, MD**, is a horse enthusiast who practices corporate medicine in Lexington, Ky.*

VACCINATIONS *for Youngsters*

It starts with the dam's immunity, but it doesn't stop there

BY MARCIA KING

Protecting tender immune systems against disease is the surest way to ensure the young horse doesn't fall victim to either temporarily uncomfortable or life-ending infections.

Even though foals receive some immunity by drinking colostrum within the first 12-24 hours of life, lack of exposure and the naiveté of the immune system sooner or later leave them susceptible to various disease-causing agents. Fortunately, many of these deficits can be addressed through vaccination.

The question is, against which diseases should you vaccinate the foal and at what age do you start?

Before the Beginning

Even before the foal hits the ground, newborn health can and should be assisted by vaccinating the broodmare, from whom protective antibodies pass to the newborn. Says Rebecca S. McConnico, DVM, PhD, Dipl. ACVIM, associate professor of equine medicine in the Equine Health Studies Program at Louisiana State University, "Broodmares should have booster vaccinations for tetanus, the encephalitis viruses (EEE, WEE, and WNV), equine herpesvirus 1 and 4, and equine influenza 1 and 2 about one month prior to foaling to ensure adequate antibody levels in the mare's colostrum." (To help protect against abortion, broodmares should be vaccinated against EHV 1 during the fifth, seventh, and ninth months of gestation as well.)

As those maternal antibodies wane in the growing foal, vaccinations are called upon to step in and continue the protection. Unfortunately, it's not exactly known when maternal antibody levels drop to a point where they cease to provide protection. Adding to the unknown, small amounts of maternal antibodies (even those below protective levels) can interfere with vaccines, leaving a window of opportunity for infectious disease. Given too soon, the vaccine is rendered ineffective; given too late, the foal is left exposed.

That's one reason why foal vaccinations are boostered at least once during the first year—vaccine potency. All vaccines need a second administration several weeks later

Protecting young horses begins with his dam's immunity, but as those antibodies wane in the growing foal, vaccinations of the foal must continue the protection.

ANNE EBERHARDT

Editor's Note

This is the 11th in a 12-part series of articles on vaccinations for horses.

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in order to stimulate an adequate immune response.

There is some disagreement concerning timing of foal vaccinations. "Foals should have the first set of vaccinations between three and six months of age," McConnico states. "However, it is thought that even very low amounts of (maternal) passive IgG (colostral immunity required for healthy foal survival) remaining in the foal between three and five months of age may actually interfere some with the foal's ability to mount an immune response following vaccination. Therefore, booster vaccinations are necessary every four to eight weeks until one year of age."

McConnico notes that in some areas of the world such as Great Britain, veterinarians recommend waiting until the foal is six months of age to begin vaccination. "Timing of vaccinations for foals is still under intense investigation," she says.

JANIS TREMPER

A veterinarian should be present when vaccines are given because an allergic reaction is always possible; a vet might be able to counteract the reaction.

Philip J. Johnson BVSc (Hons), MS, Dipl. ACVIM, MRCVS, professor of internal medicine and equine medicine and surgery at the University of Missouri, Columbia, recommends waiting until the foal is six months old, warning, "If vaccines are given much sooner than six months of age, their effectiveness might be inhibited by maternally derived antibodies (from colostrum) and the net result of the vaccine might not be so predictable. Simply said, giving a vaccine too early might cause nothing to happen, good or bad. Therefore, owners should not rely on early vaccines as they might for vaccines given to older horses.

"Also, foals don't have a well-developed immune responsiveness compared with adults," Johnson says. "Some have suggested that foals are, for several weeks or months following birth, under the influence of mare-derived signals that work in the mare (during pregnancy) to reduce immunity (in order that the mare can 'tolerate' the developing fetus—which is technically an immunologically 'foreign' object)."

Regardless of when the first shots are given to a young horse, Johnson strongly recommends that vaccinations be performed by veterinarians. "Vaccine failures can often be attributed to vaccine that hasn't been properly stored, is over-date, and so forth. Additionally, there is the very rare risk of an allergic reaction; if a horse does develop a reaction to the vaccine given by a horse owner, the horse might die from the reaction." A veterinarian at the scene could counteract that potential tragedy.

"It is also important to note that 'active' vaccines (those that provoke the host to develop a helpful immune response) must be allowed time to work," Johnson says. "Giving a 'shot' does not confer instant immunity." Even without interference from maternal antibodies, it can take two to three weeks before the initial vaccination and its booster can achieve maximum protection.

Choose Your Weapons

Vaccination recommendations for young horses are fairly uniform, with some variance according to degree of risk. For all youngsters, both Johnson and McConnico recommend protection against tetanus, influenza, Eastern equine encephalomyelitis (EEE), Western equine encephalomyelitis (WEE), West Nile virus (WNV), rhinopneumonitis, and rabies.

"Young horses, especially those exposed to new horses, should also be vaccinated for respiratory tract diseases, especially equine influenza (flu) and equine herpesvirus," McConnico says. Vaccinate several weeks prior to introduction to other young horses of different (and uncertain) viral exposure backgrounds, Johnson suggests, to ensure the maximum immune response.

Johnson points out that much current thinking suggests that the influenza vaccines should not include equine type-1 (A1) influenza. "The current recommendations by the Influenza International Surveillance Panel from April 2005 recommend the current vaccines contain updated strains (A/eq/South Africa/4/03 or A/eq/Ohio/03, and A/eq/Newmarket/2/93, A/eq/Suffolk/89, or A/eq/Borlange/91)," he says.

He also notes that the neurologic form of EHV-1 seems to be on the rise: "There have been several epidemics of the neurologic form of EHV-1 (encephalomyelopathy) in the past couple of years."

Recent research suggests that the modified live EHV vaccine, although it isn't labeled against neurologic disease, might offer better protection against the neurologic form of EHV-1 than killed preparations.

Additionally, McConnico reports that vaccination against equine protozoal myelitis (EPM) should be considered. "This potentially debilitating and fatal disease occurs more commonly in young horses in training," she says.

Vaccinating foals intended to be breeding stallions against equine viral arteritis is also a good idea, Johnson says.

Protection against botulism and Venezuelan equine encephalomyelitis (VEE) is generally recommended only in areas where there's a threat. "I recommend vaccinating against type B botulism on those farms that have experienced botulism, which is not very common in many parts of the U.S.," states Johnson.

The strangles vaccine, used to protect against infection from *Streptococcus equi*, remains controversial. Explains McConnico, "Although effective in stimulating a protective immune response, this vaccine carries the possibility of complications including fever, anorexia, muscle pain, and abscess formation. This vaccination is often considered for young horses, since they are more likely to become infected with moderate to severe forms of the disease. However, the American College of Veterinary Internal Medicine does not recommend strangles vaccination in horses that have had recent exposure (in the face of an outbreak)."

Although vaccines exist to protect horses against Potomac horse fever (PHF), endotoxins, equine viral arteritis, and anthrax, they aren't routinely recommended. "Vaccination against these diseases may be useful in areas where these diseases pose a threat," says McConnico.

However, Johnson adds, "I've been unimpressed with published data regarding efficacy for the PHF vaccine; it appears that there are several immunologically different strains of the causative organism and the vaccine only contains one strain. That said, we do not have high incidence of this disease on which to make a judgment regarding the effectiveness of the vaccine based on field use. There's a lack of evidence that providing vaccination against endotoxin is helpful for horses (and humans) that are affected with endotoxin diseases. Anthrax fortunately remains a *very* rare disease in horses."

Johnson reminds horse owners that it is important that vaccines be given in a manner that appropriately follows the manufacturers' administration recommendations. Doing so provides the best protection for any horse, with a minimum of risk.

Common Diseases Affecting Young Horses

Tetanus	This severe disease progresses very quickly. Affected horses experience stiffness, rigidness, overreaction to noise and stimuli, inability to open the mouth, difficulty breathing, and recumbency. Fatal if untreated and sometimes despite early, aggressive treatment. Usually occurs consequent to a wound in a non-vaccinated horse.
Encephalomyelitis (EEE, WEE, WNV, VEE)	Spread by mosquitoes, these viruses affect the brain and spinal cord. Infected horses have severe depression, weakness, incoordination, ataxia, stiffness, fever, difficulty eating, and abnormal behavior.
	WEE is fatal in about 25% of cases. EEE is nearly always fatal. WNV fatalities are relatively rare (about 30% of horses with neurological signs of WNV infection will die) although recovered horses might or might not retain neurologic deficits. VEE is often fatal.
Rhinopneumonitis (Equine Herpesvirus I and IV)	This virus is extremely well dispersed. Type 1 is commonly associated with respiratory disease, weak foals, and abortion (and rarely neurologic disease); type 4 is primarily associated with respiratory disease (and rarely weak foals and abortion). The neurologic form of the disease (EHV-1) appears to be on the rise recently; it causes horses (sometimes in groups) to lose control of their hind legs and bladder (and other things). There have been several epidemics of the neurologic form in the past couple of years; vaccination is likely not protective against the neurologic form.
Influenza	Influenza is usually not life-threatening, but it increases vulnerability to other diseases, including pneumonia. Clinical signs include fever, lethargy, cough, nasal discharge, muscle aches, and inappetence.
Rabies	Clinical signs include weakness in the limbs, loss of neurologic control of limbs, loss of ability to swallow, profound depression, or furious states where the animal aggressively attacks objects or people. Always fatal.
Potomac Horse Fever	This disease can cause severe diarrhea, severe laminitis or founder, and abortion.
Equine Protozoal Myeloencephalitis (EPM)	Clinical signs can include weakness, lameness, incoordination, inability to move correctly (especially in the hindquarters) or to stand up, seizures, weight loss, blindness, loss of balance, disuse of a single limb, and/or inappropriate sweating. Lack of treatment can lead to permanent nerve damage and death.
Strangles	Easily transmitted by other horses and by intermediaries such as people, buckets, and tack. Early clinical signs include nasal discharge, cough, inappetence, and fever. Later, the horse often develops swellings in the throat, between the jaws, and/or under the ears. Occasionally, abscesses affect other parts of the body, causing colic or signs of neurological disease.

Information provided by Philip J. Johnson, BVSc (Hons), MS, Dipl. ACVIM, MRCVS, professor of internal medicine and equine medicine and surgery at the University of Missouri, Columbia.

ABOUT THE AUTHOR

Marcia King *is a free-lance writer based in Ohio. She specializes in articles on equine and pet health, care, training, and behavior.*

Vaccination Schedules for ADULT HORSES

DOUG PRATHER

There are many vaccines out there, but which are necessary for your horse?

BY MARCIA KING

As desirable as it would be to have a national (or even regional) one-size-fits-all protocol for vaccinating adult horses, vaccination recommendations are best tailored to individual circumstances. These primarily include the areas of the country the horse lives in or travels to (the specific disease risks that abide in said area) and whether a horse is exposed to transient populations.

"Some vaccines are given based on specific geographical factors, a good example of which is the widespread advocacy for vaccination against West Nile encephalitis for horses in the USA during the past few years," explains Philip J. Johnson, BVSc (Hons), MS, Dipl. ACVIM, MRCVS, professor of internal medicine in the Equine Medicine and Surgery department at the University of Missouri, Columbia.

When West Nile virus (WNV) first hit the United States, it was considered to be a regional problem, thus after the development of the WNV vaccine, recommendations were to vaccinate horses only in endemic areas. Since then, WNV has spread throughout North America, as have recommendations for protective measures against the disease.

Vaccination protocols for mature horses vary from area to area, and can be different among farms in the same area

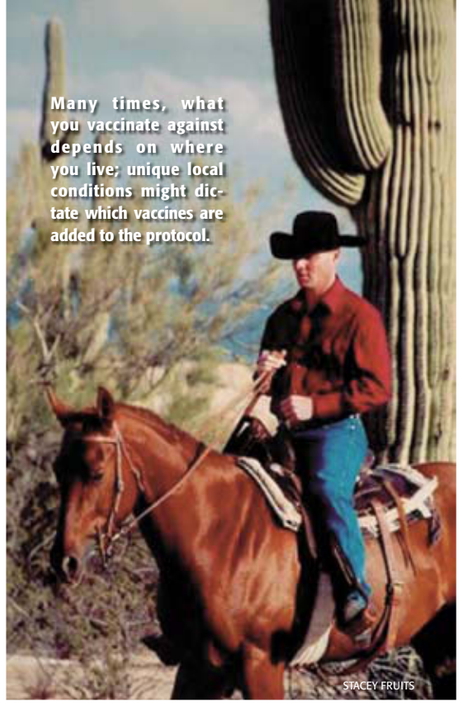
Sometimes unique local conditions dictate which vaccinations are added to a protocol. "Horses in Kentucky tend to be vaccinated against botulism to a far greater extent than horses in many other parts of the country," Johnson continues, "because botulism has been recognized as a common and important condition in parts of Kentucky. Moreover, there exists a vaccine for type B botulism—the type that tends to occur in that part of the country."

Botulism strikes quickly, mortality is high in untreated adults, foals can become extremely ill, and treatment is expensive. This means if you are shipping a mare to Kentucky to be bred, you should have your veterinarian vaccinate her prior to shipping. The same is true for endemic diseases in other parts of the country.

Local climate influences not only *what* you vaccinate against, but *when*. "In those parts of the USA for which there exists a 'vector' (mosquito) season, vaccines against the mosquito-borne encephalitis viruses tend to be given a month or so before the insects are anticipated," states Johnson. "This seasonal approach to 'strategic' vaccination is important for Eastern equine encephalitis (EEE), Western equine encephalitis (WEE), and West Nile encephalitis. For horses living in parts of the country (such as Florida) in which the

Editor's Note

This is the 12th in a 12-part series of articles on vaccinations for horses.


Many times, what you vaccinate against depends on where you live; unique local conditions might dictate which vaccines are added to the protocol.

STACEY FRUITS

mosquito-borne encephalitis viruses are a risk year-round, the vaccines against these diseases are given more frequently."

These encephalitic diseases are difficult to treat, can leave neurologic deficits in survivors, and, in the case of EEE, carry a high mortality rate.

Besides geographic recommendations based on risk, protocols should consider individual situations. Pregnant mares, for example, are routinely vaccinated against equine herpesvirus type 1 (EHV-1) to reduce the risk of abortion.

Another example is that stay-at-home horses isolated from transient populations are at less risk for strangles, influenza, and rhinopneumonitis, so there would not be as much indication for protection against those diseases. In contrast, horses that show or stay-at-home horses exposed to other horses that come and go are more likely candidates for rhino, flu, and strangles inoculations.

Protocols

Your veterinarian is the best resource for helping determine which diseases you should vaccinate against, how often, and at what time of the year.

Nevertheless, there are some diseases for which vaccination is routinely recommended, regardless of geographic location, Johnson states. "Perhaps the most important one of these is tetanus—a globally important disease for horses which, as a species, are particularly prone!"

Tetanus carries a high mortality rate, and treatment is costly and complicated.

"The tetanus toxoid vaccine is safe, affordable, and very effective; tetanus is rarely seen these days because horses tend to be well-protected by this vaccine," Johnson adds.

Rebecca S. McConnico, DVM, PhD, Dipl. ACVIM, associate professor of equine medicine in the Equine Health Studies Program at Louisiana State University, adds, "Tetanus toxoid should be given at the same time as the other vaccinations and is usually provided commercially in combination with the flu or encephalitis vaccine."

Vaccinations against the encephalitis viruses—EEE, WEE, and WNV—are also widely recommended. But for these mosquito-vectored diseases, timing varies.

"In the Southeast states, horses should be vaccinated at least twice a year for encephalitis viruses; timing should be one or two months prior to peak periods of exposure (early spring and mid- to late summer)," says McConnico. "In states with four distinct seasons (several weeks or months of below-freezing temperatures), vaccination against encephalitis viruses should occur three to four weeks prior to mosquito season."

Rabies is a relatively uncommon disease, but it is always fatal, thus it often makes the must-have list, decidedly so in endemic areas. Timing doesn't matter; it's usually administered annually along with other vaccinations.

McConnico says that equine protozoal myeloencephalitis (EPM), a potentially debilitating, difficult-to-treat, and sometimes fatal disease, is another infection that some people consider worth protecting against.

Individual circumstances tend to dictate whether other vaccines should be considered. These include:

Travel—"Horses that travel or are exposed to any new horses should be vaccinated for respiratory tract diseases, especially equine influenza and equine herpesvirus 1 and 4 (rhino)," McConnico says. While flu has a high morbidity (illness) rate and can keep a horse out of competition and training for several weeks, it has a low mortality rate. Equine herpesvirus type 1 can cause respiratory disease, abortion, or fetal damage (and rarely neurologic disease); type 4 can cause respiratory disease (and rarely weak foals and abortion), says Johnson.

New data suggests that the intranasal flu vaccine might give a better immune stimulus than most of the intramuscular preparations, Johnson says.

"Vaccination against respiratory diseases should be given at least three to four weeks prior to travel/show/race activities," McConnico advises. "Horses traveling to other states, regions, or internationally may need to be vaccinated for additional diseases. Owners should contact their local or state veterinarians for specific requirements or recommendations (for example, horses living in or traveling to states bordering Mexico should be vaccinated for Venezuelan equine encephalitis)."

Pregnant mares—Pregnant mares should be vaccinated during the fifth, seventh, and ninth months of pregnancy with equine herpesvirus type 1 vaccine to protect against abortion, McConnico says. "Broodmares should have booster vaccinations for tetanus, the encephalitis viruses, and equine influenza about one month prior to foaling to ensure adequate antibody levels in the mare's colostrum."

Johnson states that influenza vaccines should not include type 1 influenza. "The current recommendations by the Influenza International Surveillance Panel from April 2005 recommend the current vaccines contain updated strains (A/eq/South Africa/4/03 or A/eq/Ohio/03, and A/eq/Newmarket/2/93, A/eq/Suffolk/89, or A/eq/


JANIS TREMPER

Equine protozoal myeloencephalitis can be a devastating neurological disease; some people might now consider vaccinating against it.

Vaccination Roundup

We hope you've enjoyed our 12-part series on equine vaccinations; if you want to enjoy it even more, all 12 articles will be available for free download at www.TheHorse.com/emag.aspx?id=6313 after Dec. 1. Below is a list of the article titles:

- January: Defending Against Disease
- February: Vaccination Essentials: Tetanus, Rabies, and Botulism
- March: West Nile Virus: Threat and Response
- April: Encephalitides: The Ever-Present Threat
- May: Controlling Influenza
- June: Equine Herpesviruses 1&4
- July: Strangles
- August: What's New in Equine Vaccines?
- September: Strategies to Enhance Vaccine Efficiency
- October: Crossing Boundaries: Broodmare Vaccination
- November: Shots for Youngsters
- December: Vaccinations for Adult Horses

VACCINE SAFETY AND EFFICACY

Questions Remain

Despite a long history of vaccination use, questions and concerns still remain regarding the efficacy and safety of these products.

Says Philip J. Johnson, BVSc (Hons), MS, Dipl. ACVIM, MRCVS, professor of internal medicine in the department of Equine Medicine and Surgery at the University of Missouri, Columbia, "Many horse owners may be surprised to know that vaccine manufacturers do *not* have to show that their vaccines are effective at preventing the disease in order to sell the product. They do have to show that the vaccine product is safe, contains substances that are supposed to be in a vaccine, and has a logical basis (that the vaccine can stimulate antibody production, for example, which does not mean it will stop the disease)."

Probably even less known, although vaccine manufacturers are supposed to be tailoring influenza vaccines based on the current/circulating influenza viral strains, is that many influenza vaccine products for horses continue to incorporate the type-1 strain of the virus that hasn't been reported worldwide since the early 1980s, Johnson reports. "I am curious as to why they persist with this policy," he says.

There is also a lot of current interest, Johnson says, in whether or not vaccination should be recommended for protection against equine herpesvirus type 1 (EHV-1) encephalomyelopathy (the neurological form of herpesvirus infection).

Johnson states that there's a "fair bit of discussion about the fact that veterinarians might be over-vaccinating animals. I am uncertain that this is the case for the important horse diseases such as tetanus. However, older, solitary horses that do not travel so often or mix with younger horses probably do not need to be vaccinated as often against influenza, etc."

In contrast, under-vaccinating could be an issue in some situations. "Many veterinarians administer annual shots as a routine," Johnson says. "Probably for younger horses, there might be value in administering influenza vaccine more often (every three to four months); I would make a similar comment for EHV-1 when it's being used to prevent the respiratory form of the disease (rhinopneumonitis). However, I do not think that once-a-year shots against EHV-1 are likely very effective."—*Marcia King*

VACCINATIONS

PART 12

Borlange/91)," says Johnson.

For more information on vaccinating broodmares, see "Crossing Boundaries" in the October issue, www.TheHorse.com/emag.aspx?id=6266.

Stallions—Vaccinating breeding stallions against equine viral artertis is a good idea, Johnson says. Vaccinating open mares before breeding to positive stallions might be recommended; discuss options with your veterinarian.

Maybe, Maybe Not

Both the intranasal and intramuscular strangles vaccines (for protection against *Streptococcus equi*) can cause concern among veterinarians. "Although effective in stimulating a protective immune response, this vaccine carries the possibility of complications including fever, anorexia, muscle pain, and abscess formation," McConnico reports. The vaccine does not offer long-lasting protection, she says. While it might reduce severity of clinical signs, its efficacy isn't stellar. She says some veterinarians prefer to let the disease strike, run its course (under veterinary supervision), and produce natural immunities.

"The strangles vaccination is not usually necessary for horses older than three who are not exposed to young horses," says McConnico. "The intranasal strangles vaccine must be administered by a veterinarian after all other injections have been administered (it's recommended to give it on a separate day)."

Adds Johnson, "There's not much argument that both the intranasal and injectable vaccines have some risks—the intramuscular vaccine can cause muscle abscesses if it is either inappropriately or inadvertently injected (usually by owners), or the intranasal can cause problems if the contents of the vaccine accidentally contaminate the hands of the person giving subsequent intramuscular injections."

The *AAEP Guidelines for Vaccination of Horses* lists strangles as "optional," suggesting semi-annual vaccinations for adult horses when endemic conditions exist or the risk is high.

There are vaccines against Potomac horse fever and endotoxins, but recommendations for their use varies, in part because there aren't yet a lot of cases to study.

Horses that travel or are exposed to other horses should be vaccinated for upper respiratory tract diseases.

JANIS TREMPER

Do It Right

When it's time for your horse to get its vaccinations, it's best to let your veterinarian administer the vaccines. Explains Johnson, "There is the very rare risk of an allergic reaction; if a horse does develop a reaction to the vaccine given by a horse owner, the horse might die from the reaction." A veterinarian at the scene is better equipped to deal with any adverse reactions.

Be sure to vaccinate the whole herd, not just select horses. "If you just immunize one horse in a group," says Johnson, "the other horses that are not immunized could generate the virus as they get sick to the extent that the virus will overcome the effects of the vaccine in the protected horse. Vaccines represent a *part* of an overall disease prevention program; broad use of vaccines is intended to decrease disease incidence in a population as a whole (owners are often under the impression that the vaccine is mainly for the individual)."

Take-Home Message

Vaccines are easily obtained today by horse owners, but they shouldn't be taken lightly. They're still pharmaceuticals that can cause unwanted reactions if handled unwisely. Also, the need for protection against various diseases differs among locales, and even between farms in the same location. Discuss your vaccination needs with your veterinarian.

ABOUT THE AUTHOR

Marcia King *is a free-lance writer based in Ohio. She specializes in articles on equine and pet health, care, training, and behavior.*