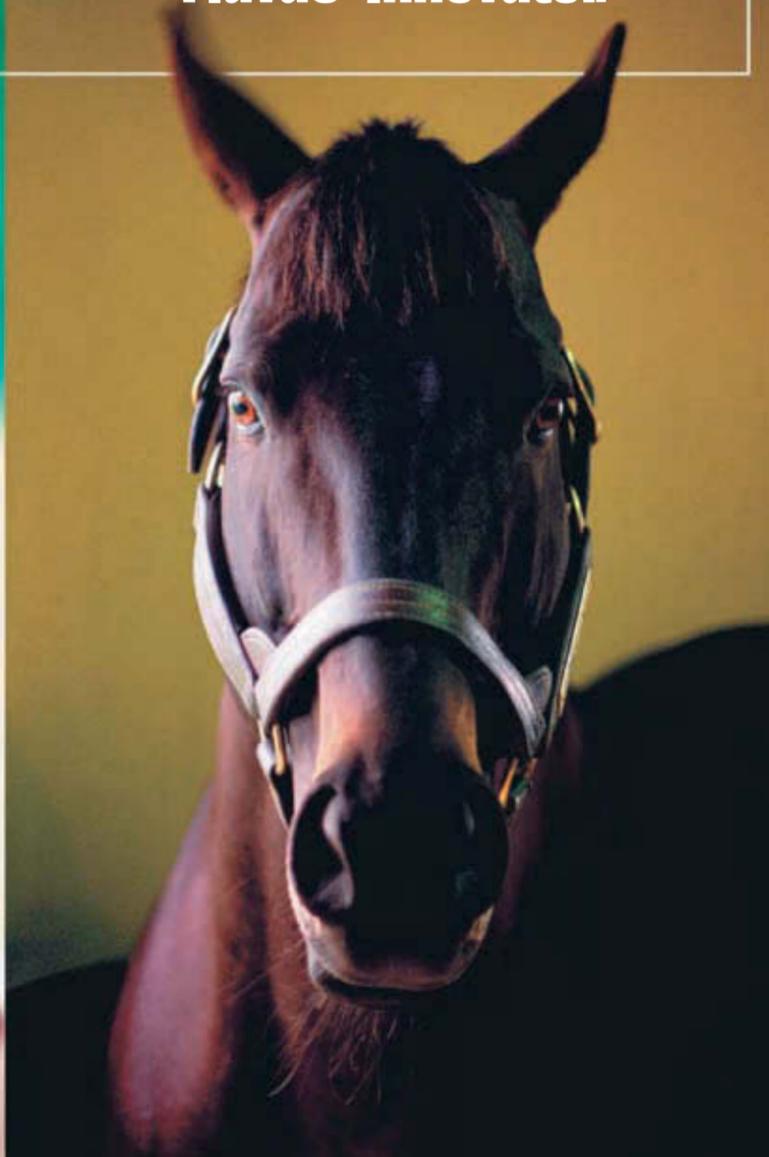


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# INFLUENZA



BY HEATHER SMITH THOMAS

**E**quine 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

*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.*



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.

LEE THOMAS

## VACCINATIONS

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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



COURTESY DR. DAVID POWELL

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

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response, he says. "The influenza virus-specific B cells make antibodies that will recognize that virus," Horohov explains.

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

## 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."

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



ANNE EBERHARDT

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

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.

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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 BERHARDT

**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



JANIS TREMPER

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

"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."

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](http://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.