HEALTH ZONE *Vaccines*

Superheroes in a Syringe

BY DR. CHRISTY CORP-MINAMIJI

If you weren't felled by polio, your children missed the measles, your barn dodged a flu outbreak, and you've never seen a horse tormented by tetanus, you probably can thank vaccination. Superheroes in syringes, vaccines the world over battle forces of evil—or at least those of disease-causing pathogens.

Whether in a human or horse, a vaccine works by stimulating the individual's own immune system to fight specific agents. The vaccine dons a disease agent (pathogen) disguise and stages a pretend invasion of the body. This drill prepares the body's immune system to repel real bacterial or viral invaders.

A behind-the-scenes look at how your horse's immune system is best primed for battle

"The basic concept behind any vaccine is that it stimulates the immune system in a manner similar to the normal infectious disease process without causing disease," said Dr. David Horohov, professor and William Robert Mills Chair in Equine Immunology in the Department of Veterinary Science at the University of Kentucky's Gluck Equine Research Center. The ideal vaccine, he said, rallies forces from two sides of the immune response, stimulating a systemic (antibody) response as well as a more local cell-mediated response.

How Heroes Emerge

Like every good superhero, vaccines have their origin stories. You have your Batman-style vaccines, tried-and-true stalwarts providing protection without mutant superpowers; and then you have your flashy newcomers, products of genetic technology and still learning their strengths and limitations.

Killed virus or bacteria vaccines are the immunology equivalent of 1930s superheroes. Horohov describes "a killed agent that contains necessary proteins that the immune system recognizes" as the fundamental goal of vaccine development. However, the original killed vaccines couldn't always get the job done; for some diseases, said Horohov, it isn't enough to merely stimulate an antibody response in the blood. The body also needs to respond at the cellular level to effectively fight the disease.

"So, sometimes killed vaccines let us down, especially 10 to 20 years ago," he said.

The problem? First of all, the adjuvants. Manufacturers typically formulate killed vaccines using these chemical agents, which, like trusty sidekicks, help the superheroes do their jobs. Adjuvants help "energize the immune system," explained Dr. Wendy Vaala, senior equine technical services specialist at Merck Animal Health, essentially accentuating its response to the antigen.

However, Horohov said these early adjuvants didn't stimulate cell-mediated immunity.

"The other problem with early vaccines was the method of inactivation," he added.

Heat and certain chemical reactions can denature and break down proteins, the features that allow the immune system to recognize a pathogen. So, the same technology that killed the virus or bacterium, making the vaccine safe for the animal, also destroyed the protein structures, making it so "the antibodies that would recognize that structure had no structure to recognize."

He said this circumstance led researchers to look for ways to mimic natural processes better.

Scientists learned it was possible to select and grow mutant relatives of disease-causing bacteria or viruses under lab conditions that reduce their virulence (ability to make the animal sick) while still preserving their immune-stimulating capacities. Vaala said this modified-live vaccine (MLV) technology safely tricks the immune system into thinking it's responding to natural disease, which veterinarians hope leads to longer duration of immunity.

But even with the wide availability of these special MLV products, Vaala said 90% of the vaccines available in the

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horse world are still killed or inactivated. Why so?

First of all, MLV technology does have its limitations, said Horohov, including cost to develop, risk of vaccinated animals shedding virus that could infect immunocompromised individuals, and storage and handling issues.

Also, similar to how it only takes the wrong sort of radiation to turn comic book superheroes to the dark side, "it is a bit more art than science to isolate mutants that would cause immunogenicity (provocation of an appropriate immune response) without causing disease," said Horohov. Fortunately, both art and science are always progressing.

As researchers have worked with MLV technology, they have gained "better recognition of mutants that work," Horohov said. This knowledge, coupled with the explosive advances in genetic science, has allowed researchers to isolate the specific genes or proteins that stimulate the immune system to recognize a pathogen.

Think of this approach as a more fine-tuned, less messy solution to the vaccine problem—say, Superman's targeted heat vision vs. Hulk's smash-and-destroy approach.

These subunit vaccines, which use just the proteins immune systems recognize (antigenic proteins), prime the immune system without risking illness. But the proteins require special additions, called co-factors, to respond properly, according to Horohov.

Recombinant or vector technology answers this need.

With vector vaccines, "you take a nonpathogenic organism (usually an agent that doesn't cause disease in horses or humans, such as canarypox) and add genes from the pathogenic one, so that you expose the immune system to the agent," Horohov explained.

In this way, the horse gets exposed to the triggers needed to fight disease—the shell of the canarypox containing the pathogenic cousin—but not the disease itself. Vaala called these vaccines "the wave of the future," explaining that they give a "broader immune response but in a very safe method."

Vaccines to the Rescue! (Or Not?)

When the meteor is hurtling toward Metropolis, you really just want the superhero to swoop in and save the day. But think of the collateral damage if a whole slew of superheroes and superheroines got called in for every municipal crime. Likewise, with vaccines, need and timing are critical.

A horse that never leaves his home state has no need for vaccination against diseases prevalent in other regions, said Vaala. On the other hand, she said, it's imperative to use core vaccines such as rabies, which is present across all 48 continental states. While an owner might rationalize skipping a flu vaccine for his or her horse because in most cases the consequences of influenza virus infection are more along the lines of missed days of work than death, Vaala called the potential fallout of a rabies infection to both the horse (fatal) and exposed humans (prophylactic vaccination to avoid fatal infection) "pretty striking."

When determining vaccination needs, Vaala suggested working with your veterinarian to answer the following questions:

- What is the consequence of infection? (Consider the rabies vs. flu example.)
- What is my horse's likelihood of disease exposure? Certain diseases, such as PHF, are restricted to specific regions.

Others, like equine herpesvirus, influenza, and strangles, are more likely to turn up in show or barn environments with horses coming and going than in a closed or an isolated herd. Mosquitoes are responsible for spreading some diseases, such as Eastern or Western equine encephalitis and West Nile virus, and they can infect a lone backyard horse just as easily as one in a busy stable. In some cases geography influences exposure in subtle ways. A horse in Michigan might only be exposed to mosquito-borne diseases for a few months of the year, while a horse in Florida will have nearly year-round exposure.

- What is my horse's risk of becoming sick if he is exposed to the disease? Susceptibility varies with age and immune function.

After deciding what vaccinations your horse needs, look at when and how often to vaccinate. Timing is everything. Superman is no help if he shows up after the death-ray has destroyed the White House, and a half-suited Iron Man can't offer much aid.

In most cases vaccination is the equivalent of showing the immune system a wanted poster. The body then needs several initial doses to figure out how to respond when it sees the pathogen in question.

Vaala said it's "critical to read what each manufacturer recommends for the initial vaccine series."

For horses that have never been vaccinated against a particular disease (e.g., foals, import horses, rescues with unknown histories), multiple vaccine doses at specific intervals stimulate the immune system's memory cells. In this way, said Vaala, "the immune response produces antibodies much more quickly than if it had never been primed."

Most equine vaccines require the initial series, though a few, such as a modified-live intranasal flu vaccine, require only one dose.

It is particularly important to consider vaccination timing in terms of likely exposure if a horse has never been vaccinated against a disease. For most vaccines, the immune system requires an average of two weeks after the last dose of an initial series or booster dose to mount a complete response, said Vaala. This means that if a horse is due to travel from California to Maryland, giving him a PHF vaccine a day or two before he gets on the trailer isn't likely to do much good.

Vaccination frequency is a common concern in the horse world. After all, humans get booster shots every 10 years or so, and many cats and dogs receive vaccinations every three years rather than yearly. So why do we vaccinate horses so often?

The main factor is the high prevalence of killed vaccines in the equine world.

"It's hard to get long-lasting immunity with current killed vaccines," said Vaala. "But, as with many things in the equine industry, (using killed vaccines) is what we're used to."

When it comes to vaccination interval and duration of immunity, another question, said Horohov, is "are horses different (from humans or dogs/cats), or are horses' vaccines and diseases different?" He points out that we know about 14 viruses that affect horses. Some 60 viruses are known to infect humans. So, when we see what looks like flu in a horse that received an influenza vaccine last year, has the immunity from the vaccine worn off, or is the horse sick from a virus that we haven't yet identified? We can't be sure.

First of all, according to Horohov, we just don't know horses' duration of immunity.

Couldn't we just test a horse to see if he's still immune to a disease rather than revaccinating? Horohov said this poses some logistical concerns.

Ideally, he said, "If you have a reliable measure of immunity, you could test the horse prior to vaccination and ask what is its level of immunity."

With diseases such as influenza, for which researchers know what antibody level is protective, this theory could work. However, for diseases such as equine herpesvirus we don't yet have a routine screening test for immunity. Another problem with testing immune function vs. revaccination is time and expense. Current antibody tests take several days to return results and are usually more expensive than a booster dose of vaccine.

Take-Home Message

Vaala pointed to weighing disease risk and severity against the cost or inconvenience of vaccination. "That's where owners need to enlist a veterinarian," she said, "to make determinations on the environment, the patients, exposure, etc."

Every superhero needs a strategy, and together veterinarians and owners can work to give vaccinations the best chance in their battle against the forces of disease. BH

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