IMMUNITY - Part 1

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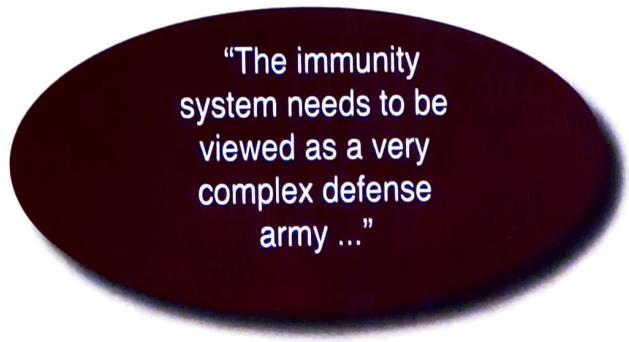
Why do some horses easily catch a cold and others don't? Why do we need to vaccinate and is it actually so important to respect the intervals at which repeat vaccinations need to be performed? Why make such a fuss about that? Do we, as horse owners, really have any impact on the immune capacity of our horses or is it just a matter of genetics? Are some horses vulnerable; while others aren't?

To better understand these important questions, let's take a closer view at what "the immune system" of the horse is.

Just like humans, horses have their own defense system against diseases. It's called "the immune system". Actually the scientific knowledge about this system is quite young. When you compare what is currently known with what was known let's say 30 years ago, the progress in knowledge that has been realized is overwhelming. Researchers have a clear view now on how the immune system interacts with "unwanted invaders" that attack your horse's body.

Actually our own and the equine body has two important lines of defense against unwanted invaders such as bacteria, parasites and viruses, let's call them microbes for reasons of simplicity. First of all the body contains physical and chemical barriers to infection such as our skin, mucous membranes and the acid environment in the stomach. This strong acid within the stomach destroys many pathogens that are swallowed with food. All the aforementioned physical and chemical barriers form a first protection against invasions by unwanted guests. Also the digestive and respiratory tracts—both portals of entry for a number of microbes—also have their own levels of protection through certain barriers such as specialized epithelial cells that line the surface of these tracts, and mucus that is produced to function as a kind of protecting "coating". Secondly, besides these physical barriers there is the immune system. The immune system has two important subsets: the innate immunity and the adaptive immunity. Later on the meaning and function of both important subsets of the immune system will become clear.

The immune system basically does two things: first it is responsible for fighting off all new infections; and secondly it remembers the past infection (like memory) so it can effectively kill off the infection faster the next time it occurs. The latter aspect of the immune system is used when you vaccinate a horse. The immune system is not only capable of fighting off infection; it also has the ability to distinguish between "your cells" and "foreign cells". This is a very important function as otherwise your own immune system would gain the ability to attack yourself. In some cases the immune system is not able to distinguish between "own" and "foreign" cells. In that case it attacks its own body, which is seen in auto-immune diseases. Another problem occurs when the immune system overreacts. In which case allergies and arthritis can manifest themselves.



The immune system needs to be viewed as a very complex defense army that is stationed throughout the entire body. It contains many different types of soldiers and weapons, and if needed it can even construct tactical weapons to specifically attack certain invaders. So, in essence you have soldiers that can attack anything and this is called "aspecific immunity". These are immune cells that are sent as front line defense

towards unwanted invaders of any kind. Examples of immune cells that are part of the aspecific immunity are neutrophils and eosinophils Once these cells have received an alarm signal, they undergo tactical changes and begin to produce powerful chemicals. These substances attrack other immune cells, they enable immune cells to regulate their own growth and behavior and direct new recruits to trouble spots. Actually, this army of soldiers that can be sent as first line defence towards any type of threat is called "innate immunity". "Innate Immunity" is that subset of the immune system that is naturally present and is not there due to prior sensitization of the body to a certain microbe. Since it is not stimulated by specific microbes, innate immunity is generally nonspecific. In addition, the immune system can produce very specific weapons, called antibodies, to specifically attack unwanted invaders. This is called "specific" or "acquired immunity".

When an unwanted invader infects your horse, certain symptoms will appear. In the case of a respiratory infection, coughing and a runny nose are symptoms that horse owners see quite often and the seriousness of these symptoms depends on the cause. Causes of coughing and a runny nose are diverse: most often this can either be a viral or bacterial infection. In any case, the immune system of such a horse is working full force in order to kill off the infection. However, when the symptoms shown by the horse get worse, it means that the immune system of the horse is unable to cope with the infection. At that point, a check-up by a veterinarian is mandatory, because interventions are needed to give the immune system a helping hand.

To make things even more complex, not all horses have an evenly vigorous immune system. This can be a continuous situation due to genetics. For example, it is well known that animal populations with a high degree of inbreeding have an immune system that is more vulnerable when compared with animal populations that have a rich genetic background. On the other hand, within the same horse, the robustness of the immune system can vary depending on age or certain conditions such as pregnancy, stress or ongoing disease. Young horses, elderly horses and pregnant mares are known to be ~~more~~ especially at risk to develop infections, because their immune system is less vigorous and robust. The immune system of young horses is still 'in training' and has to learn how to cope with infections. In elderly horses, the immune system fails to fulfill all its functions, which makes these horses vulnerable for pathogens. Pregnant mares are also more at risk for developing diseases since they have a suppressed immune system during pregnancy. Mother nature does this to prevent the immune system of the mother from attacking the growing fetus, which obviously not only contains genetic material of the mother, but also of the father. The latter could function as a "red alert" for the immune system of the mother. Gastro-intestinal parasites can also take advantage of the suppression of the immune system that occurs in pregnant mares, young and old horses. That's the very reason why these three categories of horses are known to be at risk for severe parasitic burdens and thus can maintain parasitic infections within a horse population of medium age that otherwise would be able to naturally fight off these infections. Within these horse populations, the young, old and pregnant mares serve as a reservoir, a "home camp" of sorts, from which the parasites can keep bothering medium aged horses, which tend to have a robust immune system.

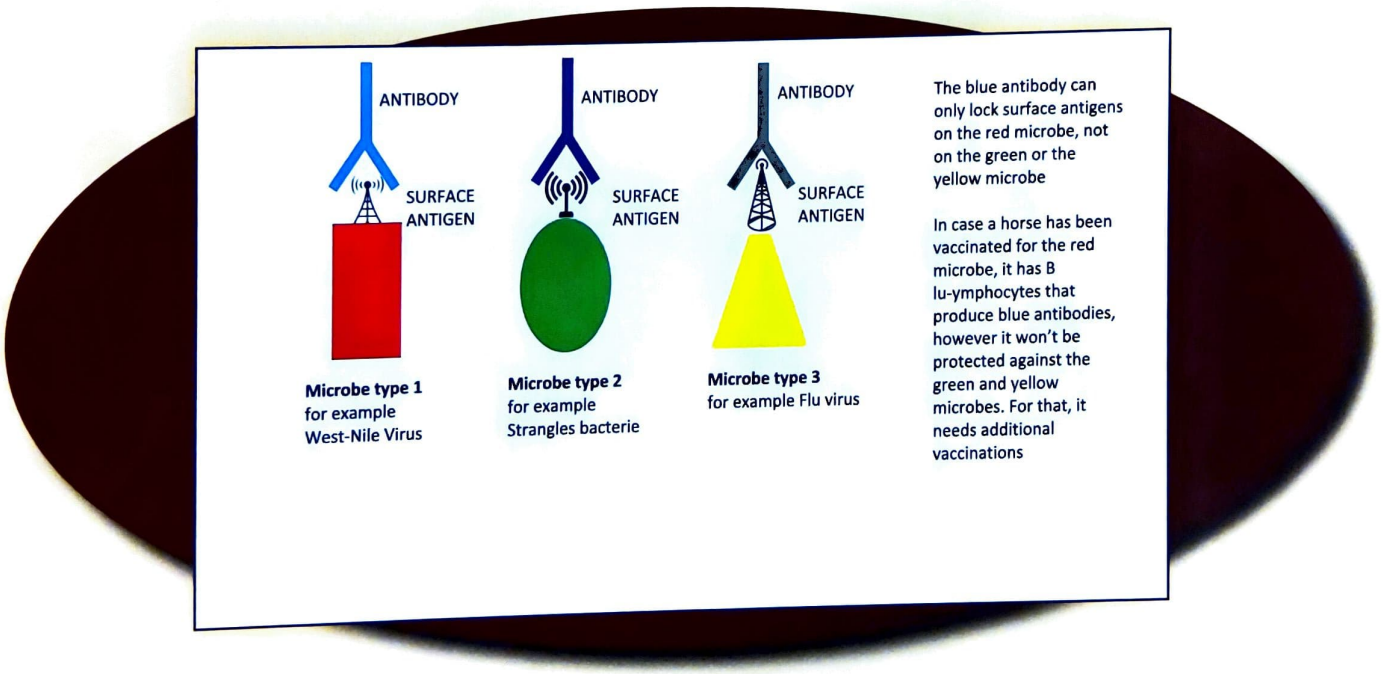
Auto-immune mediated hair loss - the immune system of this horse attacks its own hair follicles.

The Structure of the Immune System

The organs of the immune system are positioned throughout the body. They are called *lymphoid organs* because they are home to *lymphocytes*, small white blood cells that are the key players in the immune system. There are essentially four important "homelands" for the cells of the immune system: first of all the lymph nodes, which tend to swell when infection occurs in the region of the body of which they drain lymphoid fluid. "Strangles" is a great example of such swelling and is caused by a streptococcal bacteria. Once the bacteria have invaded the throat of the horse, extreme swelling of the lymph

nodes occurs below and behind the jaws. Secondly there is the bone marrow as "homeland". The bone marrow can be found in the hollow center of bones throughout the body. Here the immune cells are produced out of germinal cell lines that quickly start dividing in answer to infection. Thirdly there is the thymus. This organ is located inside the thoracic cavity of the horse. It functions as The Central Training Center for lymphocytes in young horses. Last but not least there is the spleen. The spleen is a flattened oval shaped large organ that lays against the left abdominal wall inside the abdominal cavity of the horse. Like the lymph nodes, the spleen contains specialized compartments where immune cells gather and work, and it serves as a meeting point where immune defenses confront invaders.

Of course, immune cells need to be able to travel towards the location inside the body that's being invaded. Immune cells, like lymphocytes can travel throughout the body using the blood vessels. The cells can also travel through a system of lymphatic vessels that closely parallels the body's veins and arteries. Cells and fluids are exchanged between blood and lymphatic vessels, therefore the lymphatic system with its lymphatic vessels and lymph nodes can monitor the entire body for invading microbes.



But what actually happens when a microbe starts entering your horse's body? In other words: How is an immune response mounted?

To understand how your horse's body starts up an immune response, it is important to understand the term "antigen" and "antibody". Anything that can trigger an immune response is called an antigen. An antigen can be a microbe or a virus, or even a part of a microbe. The immune system recognizes these antigens because they carry certain "foreign" molecules at their surface. This is the very reason why transplanted organs can be rejected because the cells of these organs carry surface molecules that are foreign to the immune system of the patient that receives the transplantation. As soon as the immune system encounters cells or organisms carrying markers that say "foreign," they quickly launch an attack. As mentioned previously, in abnormal situations, the immune system can mistake "self" for "non-self" and launch an attack against the body's own cells or tissues. The result is called an autoimmune disease. Unlike in humans, autoimmune diseases are quite rare in horses. In other cases, the immune system responds to a seemingly harmless foreign substance such as dust and pollen. The result is dust and pollen allergy in horses, and this kind of antigen is called an *allergen*. Allergy needs to be viewed as an overreaction of the immune system.

Antibodies are proteins that are produced by a subset of lymphocytes, namely B-lymphocytes. As mentioned previously, because the equine body provides an ideal environment for many microbes, they try to break in. It is the immune system's job to keep them out. Once microbes have past the physical barriers such as the skin, and the first line defense (aspecific immunity), they need to be "tracked and traced" by the immune system and destroyed by means of antibodies (specific or acquired immunity). These antibodies are part of the family of the immunoglobulins and have a unique molecular build-up. They contain a region that is "antigen specific" and therefore only that specific antigen can be locked into the structure of the antibody, like a certain key only fits into a certain lock. This means that there is for example a subset of B-lymphocytes that produce antibodies that can lock antigens that are specifically owned by viruses that cause "a cold" in horses. Still others produce antibodies that specifically catch and lock surface antigens on tetanus bacteria, for example. Each of these B-lymphocyte cell lines need to be viewed as factories that produce a specific subset of

antibodies. Let's consider a horse that has never encountered a certain microbe in its life, for example West Nile virus, and that horse is confronted with that disease. This horse doesn't have the factory inside its body to produce the proper type of antibodies, with devastating results as a consequence. When you vaccinate a horse, you mimic disease contact in a safe way. When you vaccinate for West Nile, for example, you inject either "pieces" of the West Nile virus into the horse or you inject whole virus particles, which have been killed in the lab. These virus pieces or killed virus particles can't harm the horse, but the immune system of the horse will be trained to recognize the antigens which are typical for West Nile virus and a vaccinated horse will have its own B-lymphocyte cell line that produces protective antibodies, without ever being infected by the real naturally occurring virus. It is mportant to realize that these B-lymphocyte cell lines have their own memory: they have their own "hard disk" so to say. Every time you repeat the vaccination or every time the horse comes into contact with the real virus, the hard disk is refreshed and the memory is updated. For some microbes these hard disk updates need to be executed more frequently than for others in order to keep the B-lymphocyte cell lines capable of producing protective antibodies. This explains why some vaccinations need to be repeated more frequently than others. It also shows how important it is to comply with the manufacturer's recommendations for repeat intervals for vaccination. It's like an anti-virus program update on your computer. If you don't allow for regular updates, your computer won't be protected anymore against certain viruses.

To make things even more complex, some microbes are very smart. The influenza virus is one such microbe. These viruses can mutate, and they do so every once in a while. When they mutate, they fool around with the immune system. They change their surface antigens all of a sudden, in which case, ~~again~~ there is no effective antibody producing B-lymphocyte cell line available anymore. The B lymphocyte cell lines inside that horse will produce anti-influenza antibodies, but they won't be protective against "the mutant influenza virus". It all sounds very spacy and futuristic. But that's how it is. This is the reason why human flu vaccines are reformulated every year. Researchers need to figure out upfront what types of mutants will circulate that specific year. Sometimes researchers wrongly forecast the cocktail, which explains how people who are vaccinated against the flu can still become sick despite being vaccinated. These mutations are described in horses, though with a less pronounced frequency.

It's also important to realize that antibodies don't penetrate and kill microbes. They need to be viewed as the key asset of the immune system to perform intelligent warfare. Once specific antibodies are locked on their specific antigen on the surface of a certain microbe, it's like a huge spot light that is turned on in the dark and the soldiers of the immune system move towards these spotlights to attack them. You need to view it like surgical bombardments.