

Foal IgG (Antibody)

We will start this story on foal IgG with a more general discussion of the immunoproteins, or "Igs," in an effort to give a better understanding of what these terms stand for and the importance of what they do. The term IgG stands for "immunoglobulin type G, sometimes referred to as gamma globulin G. The immunoglobulins, also known as antibodies, are a family of proteins that exist in the plasma component of the blood and other body fluids. Plasma is the clear, yellowish liquid component of the blood that can be observed when the red blood cells are removed.

The immunoglobulin family includes immunoglobulin "A" (IgA), immunoglobulin "G" (IgG), immunoglobulin "M" (IgM), and immunoglobulin "E" (IgE). All of the immunoglobulins play a role in the immune system's defense mechanisms or, in the case of IgE, allergic reactions. Immunoglobulin "A" is present in high concentrations in secretions on mucosal surfaces and plays a role in the first line of defense from foreign invaders gaining access to the body via these surfaces. Immunoglobulins "G" and "M" are present in plasma and other body fluids and function in main line defense against foreign invaders of the body. Immunoglobulin "E" also is present in the plasma and other body fluids and plays a role in allergic reactions.

The immune system manufactures the immunoglobulins in response to exposure to a foreign invader. After exposure to a foreign invader, such as a specific virus, bacteria, or toxin produced by an organism, a certain type of lymphocyte (a type of white blood cell) produces the immunoglobulins. There actually are "sets" of immunoglobulins produced that recognize certain characteristics of the specific foreign invader. These specific immunoglobulins then bind to the foreign invader and in essence "mark" it for destruction by other components of the immune system. If the body has been exposed to that particular foreign invader previously, the immune system already has the specific immunoglobulins floating around in the body. In addition, the immune system already has been programmed to provide defenses against that particular invader and can more rapidly produce additional immunoglobulins and other defensive mechanisms.

It is this system that is the basis for vaccine protection.

For example, a vaccine, such as the equine influenza vaccine, contains the foreign invader. In most vaccines, the virus or bacteria has been deactivated or changed in such a way that it can no longer cause the disease, but retains the ability to activate the immune system to produce immunoglobulins specifically directed against that foreign invader. This process does two things: 1) stimulates the production of the immunoglobulins effective against that particular invader, which places the body in a defensive posture with respect to that disease, and 2) primes the immune system so that a second exposure to the invader (either by natural infection or booster vaccination) will evoke a quicker and more powerful production of more immunoglobulins specific for that invader.

The immunoglobulins can be measured in the blood. This measurement often is referred to as a "titer." The titer can be useful in determining exposure or infection of an individual horse to a variety of organisms causing equine disease. With most of the diseases, a single blood sample is of limited value as the number or "titer" obtained could be related to vaccination or general exposure to the organism in question, but not necessarily indicate infection. A second blood sample should be analyzed several weeks after the first, and the "titer" again determined. If the titer has risen (generally two to three times greater than the original sample), it is a general indication of active infection and related to the production of immunoglobulins by the body in response to that particular infection.

Foal IgG

So, how does all of the aforementioned information about immunoglobulins relate to foal IgG?

The foal is born with a functional immune system (if all is normal), but has a general absence of immunoglobulins to aid in the defense against infection. The foal acquires his initial immunoglobulin protection from the mare's first milk, which contains the vital component called colostrum. One of the first acts by a newborn foal that ensures the vital consumption of colostrum is nursing. With that said, we will start with a discussion of that important first act.

Nursing

Once the foal is up, he will begin to search for milk, often making suckling noises and nursing his tongue. Although at first the foal will suckle everything but the mare's nipple, (mare's shoulder, mare's flank, or stall boards), the foal should be nursing from the mare within two to three hours after birth. A helping hand to guide the foal to the udder can help him find the milk wagon, but some mares and foals prefer to be alone. If your mare becomes restless with people in the stall or the foal becomes irritated, leave them alone. You can monitor from stall side, and if there is no nursing by two hours, call your veterinarian.

Once the foal has found out where the milk is, he will drink maybe only a few swallows the first time, then rest. This is normal. Foals will normally drink from the mare, then lie down to rest/sleep in frequent intervals. The other way to check to make sure a foal is nursing normally is to monitor the mare's udder. If the udder is deflated, but easily produces a stream of milk, then the foal most likely is nursing just fine and getting enough milk. If however, the foal is sleeping too much and the mare is streaming milk with an engorged udder, there is a problem!

It is not normal for a foal to lie down and stay down for an hour or more--this indicates a problem and you should summon your veterinarian. Furthermore, if you find the foal to be standing and butting the udder repeatedly, the mare most likely is not producing enough milk to keep the foal happy. Check the udder, and if you can only get a few drops or a fine stream of milk, or if you have any questions, you should call your veterinarian.

Suckle Reflex

If the foal does not stand and nurse within three hours, or stands but shows no suckle reflex and/or little interest in the mare, call your veterinarian immediately to examine the foal. The veterinarian will check for musculoskeletal problems that might be preventing the foal from standing, such as contracted tendons or angular or flexural deformities that can make standing nearly impossible.

Foals which are born with septicemia can be very weak and do not have the energy to stand. Foals suffering from neonatal maladjustment syndrome, also known as "dummy foals," might not be able to stand, or can stand, but will wander the stall with little interest in the mare. These foals usually are born normally, then lose interest in the mare after 24 hours. These foals will not have a suckle reflex--you can check this reflex by placing clean fingers within the foal's mouth to stimulate it to suck on your fingers. If there is no reflex, then the foal should be evaluated by your veterinarian. Make sure you wash your hands thoroughly before checking the suckle reflex or you could be giving your foal a dose of bacteria before he receives the colostrum.

Colostrum or "First Milk"

The colostrum is the "first milk" that a mare produces. It will be thick, yellow, and sticky, much different from regular milk, which is thin and white. The colostrum is loaded with immunoglobulins (antibodies) that not only nourish the foal, but protect him from infection. (Remember, foals are not able to obtain antibodies from their dams before birth due to their unique placenta.) Although the foal is born with a working immune system, before the foal ingests colostrum, it essentially is lacking in antibodies to fight infection. The antibodies used to fight off infection for the first four to eight weeks of life will be available in colostrum, provided the foal ingests colostrum from the mare and the colostrum is of good quality. This is why it is so imperative for a newborn to nurse promptly.

Foals must receive colostrum within six to eight hours of birth as their gastrointestinal system can only absorb the immunoglobulins (antibodies) present within the colostrum during a short window of time--usually not longer than 12 hours after birth.

The mare produces colostrum by concentrating antibodies otherwise known as immunoglobulins within the mammary gland shortly before she gives birth. The mare will secrete the colostrum for 12-24 hours after birth, then produce "normal" milk. The foal also has specialized cells within the small intestine that allow for absorption of the larger immunoglobulin molecule. These special cells only function maximally for eight to 12 hours after birth. Therefore, the foal only has this short window of time to absorb the immunoglobulins from the colostrum.

Remember, foals are born with virtually no ability to fight off infection other than the antibodies they absorb from the colostrum. Without adequate colostrum, a foal can rapidly succumb to overwhelming infection from a variety of sources.

Foals also need the colostrum as nutrition to prevent hypoglycemia (low blood sugar). Foals have little or no fat stores and need frequent meals. Going several hours without colostrum or milk can leave a newborn foal very weak and unable to stand.

Some mares lose their colostrum before the foal is born because they drip milk for several days to weeks before delivering. It is extremely important to monitor the mare carefully in the days prior to foaling for the loss of milk; any mare which is leaking milk prior to foaling could create a situation where the foal receives inadequate colostrum. If that happens, the foal will need colostrum from another source.

Colostrum also is needed when a mare dies from complications of the birth process. If the mare suffers from lack of normal milk production (agalactia), there also will be a lack of normal colostrum production. The condition often is associated with a mold (endophyte) produced on fescue grass. It can cause a decrease in milk production, or a complete absence of milk production. For those of you who might be seeding a pasture, there are commercially available fescue grass seeds that are resistant to the mold that causes this condition. The endophyte-resistant fescue can help prevent this condition. Again, careful monitoring of the mare prior to foaling and a knowledge of the type of hay or pasture grass being fed can prevent many foal tragedies related to this condition.

Many equine hospitals and large breeding farms stock colostrum and freeze it for just such emergencies. If you need colostrum, try these places as a source.

Colostrum can be banked from healthy mares. The milk can be frozen and kept for nearly two years. Mares with healthy foals by their sides are thought to be able to spare around 200 ccs of colostrum. It can be placed in plastic bottles or freezer bags for later use. If you have a source of frozen colostrum, remember to thaw the colostrum in a warm water bath. Microwaving the colostrum will destroy the beneficial immunoglobulins within the milk.

I always thaw colostrum in a warm water bath, it takes more time (up to an hour), but it is safe and I am assured that the colostrum will do its job.

In addition, there are commercial products available to supplement IgG in newborn foals orally. One such product (Seramune, Sera, Inc.) was reported on by Sally Vivrette, DVM, PhD, Dip. ACVIM, North Carolina State University, College of Veterinary Medicine, at the 1998 American Association of Equine Practitioners Convention in Baltimore, Md. It was demonstrated that when used at the manufacturer's recommended dosage, the oral administration of Seramune did not raise the foal's IgG to the target concentration of 800 milligrams per deciliter of blood, but did appear to help minimize neonatal infections. It appears that the use of such oral immunoglobulin supplements can be beneficial, but more research will be required to evaluate fully the extent of these benefits and to establish adequate administration requirements. These products demonstrate some promise in preventing neonatal infections related to failure of passive transfer.

IgG (Antibody) Determination

The main immunoglobulin (antibody) produced in the colostrum is gamma globulin (IgG). There are others, of course, but they are produced in smaller quantities. Veterinarians have developed tests to measure the amount of gamma globulins within the foal's bloodstream to estimate if an "adequate" quantity of immunoglobulins has been ingested and absorbed by the foal. These tests measure the gamma globulin concentrations within the bloodstream. The tests often are not performed until the foal is at least 12-18 hours old, although the peak level of absorption is at 24 hours. Waiting until 24 hours allows the foal to nurse and absorb as many immunoglobulins as possible.

However, some veterinarians like to perform the test when the foal is 12 hours of age, and if there is a low level of immunoglobulin, then there still is time to administer more colostrum. At 24 hours of age, if the level of immunoglobulins is low, then the only alternative is intravenous therapy with plasma, which has high levels of immunoglobulins, to help protect against infection.

There are many different types of tests that can estimate the concentration of immunoglobulins within the bloodstream. Some of the tests can be performed at the farm; others must be run within a laboratory. There are several different tests that have a fairly high accuracy level and can be performed on the farm. These tests are an important part of the physical examination of the newborn, as low concentrations of immunoglobulins can mean that the foal is at risk of developing infection.

Examples of some common test names are the CITE test, FoalCheck, zinc sulfate turbidity test, etc. A more accurate test (RID), which is highly specific for gamma globulins, can be performed; however, the results take 18-24 hours. If the concentration of immunoglobulins is low, depending on the age of the foal at the time of the examination, then added colostrum or oral immunoglobulins can be administered. If the foal no longer is able to absorb the immunoglobulins through the gastrointestinal tract, then the foal must receive intravenous immunoglobulins through the administration of plasma or whole blood.

Failure of Passive Transfer

Failure of passive transfer is a syndrome that occurs when foals fail to absorb adequate colostrum. This can result from the following causes: 1) the foal fails to ingest an adequate quantity of colostrum; 2) the mare produces colostrum that is lacking in adequate immunoglobulin levels; 3) the mare produces normal colostrum, but prematurely lactates and thus loses the colostrum; or 4) the mare fails to produce any colostrum or milk of any kind (agalactia).

Regardless of the cause, this syndrome is thought to be the most common predisposing factor of infection in neonates. This syndrome can be classified as complete failure or (more commonly) partial failure of passive transfer. The latter occurs when some degree of immunoglobulins was transferred from the mare to the foal, but not enough to protect the foal from infection. If the foal is found to have a low concentration of immunoglobulins, then your veterinarian will recommend that the foal be supplemented with plasma, if available. Whole blood can be used, but is not as desirable since you must give red cells, which are not needed except in cases where the foal is anemic. Whole blood that contains the red cells also can lead to transfusion reactions.

Plasma can be purchased commercially, and although a bit expensive (about \$150 for one liter), its contents can be lifesaving.

Just because a foal is found to have a low immunoglobulin concentration does not mean that the foal will develop septicemia. However, the chances are greater for the "low" foal to develop problems than for a foal with a "normal" amount of immunoglobulins.

No one knows what level of immunoglobulins is necessary to protect a foal from septicemia. We only have guidelines for what we think are high enough concentrations. It is not uncommon for a foal to be tested at 24 hours of age and found to have a high concentration of immunoglobulins, then succumb to infection within the first two weeks of life.

If the bacterial challenge(number of bacteria) is high, the foal is more likely to develop septicemia. This is why a clean and healthy environment is so important for foals. Keep the stalls and paddocks clean and free of manure as much as possible, and keep all sick horses separated from the foals. This will help reduce bacterial numbers and contribute to reducing infection rates on your farm.

Careful monitoring of the neonate for any signs of illness (weakness, loss of interest in nursing, swollen joints, etc.) is of great importance. Foals developing illness can deteriorate very rapidly, so early detection of illness and prompt evaluation by your veterinarian can make a significant difference. An important note here is that a swollen or puffy joint is typically a sign of infection--it might be tempting to explain this by the foal's having been stepped on by a clumsy mare, but this usually is not the case. A swollen or puffy joint should be assumed to be infected until proven otherwise, and prompt veterinary evaluation is imperative.

WHAT IS MATERNAL ANTIBODY INTERFERENCE?

Most people vaccinate their young foals for equine influenza. Why, then, do some of my young horses still catch influenza as yearlings? We think we have the answer. New evidence suggests that antibodies given to the foals through colostrum actually are interfering with the vaccines that are given to foals.

The whole purpose of a flu vaccination program is to make an animal produce antibodies against several flu strains. A high enough level of antibodies ought to protect the animal from the disease caused by those strains. I've noticed that foals themselves almost never get influenza. The reason is that the first time the newborn foal suckles its mother's milk, it ingests a large amount of antibodies contained in that first milk (or the colostrum). These are the "maternal antibodies," the newborn's first line of defense against germs. The maternal antibodies gradually wear out. When they do, the foal needs to replace them by making its own protective antibodies.

As a part of my doctoral work on the University of Kentucky Gluck Equine Research Center influenza team headed by Dr. Tom Chambers, we now have new data to suggest that maternal antibodies actually interfere with commercial inactivated influenza vaccines in foals. There appears to be a problem that arises when you vaccinate the foals when they have maternal antibodies. The first vaccination should be done by the time these protective maternal antibodies are gone. So the important question is this: Just when is the right age to vaccinate foals for influenza?

The influenza team set out to determine which foal vaccination schedules produced the strongest antibody response to influenza. We analyzed blood samples from a total of 210 foals which were vaccinated at different ages (two months, three months, etc.) to determine which schedules caused foals to produce the highest level of antibodies against equine influenza. Initially, we thought that by the fourth month, there would be no maternal antibodies left to interfere with vaccination. Then foals should be able to produce their own antibodies. But to our surprise, using the recommended two or three doses of vaccine for equine influenza, we were still unable to get a good antibody response from foals even when they were eight months old.

Why were these foals not responding to their initial flu vaccinations? Could the vaccines themselves be faulty or were there maternal antibodies interfering? To test whether or

not the vaccines were any good, we vaccinated two- to three-month old foals from unvaccinated mares which had no antibodies to equine flu. To everybody's surprise these foals did have a good antibody response. This experiment proved that a young foal can respond to the inactivated vaccines and that the maternal antibodies actually do interfere with foal vaccinations for flu.

We now are working on figuring out how to overcome the problem of maternal antibody interference in foal vaccinations. Until that time, our findings indicate that foals from vaccinated mares should be eight to nine months of age before vaccinating for equine influenza. We also recommend that these foals receive one primary dose of vaccine followed by two boosters one month apart. To date, the mechanism of how the maternal antibodies interfere with inactivated vaccines in foals is unknown. The hope is that by understand how these maternal antibodies interfere with the foal's immune response to inactivated vaccines, we might be able to design a more effective influenza vaccine program for foals. The vaccination situation for other diseases might be different, and this needs to be tested.

Our research team would like to express our sincere appreciation to the American Quarter Horse Association for its support of this vital research at the University of Kentucky.--*By Robert E. Holland Jr., DVM*

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Michael A. Ball, DVM, completed an internship in medicine and surgery and an internship in anesthesia at the University of Georgia in 1994, a residency in internal medicine, and graduate work in pharmacology at Cornell University in 1997, and was on staff at Cornell before starting Early Winter Equine Medicine & Surgery located in Ithaca, N.Y. He is also an FEI veterinarian and works internationally with the United States Equestrian Team.