Failure of Passive Transfer and Use of Plasma

Failure of Passive Transfer

Introduction

All foals are born, because of their epitheliochorial placentation, with a deficiency of humoral immunity. They must rely on the adequate intake of good quality colostrum within a few hours of birth to provide essential antibodies in order to withstand the challenges of infection during the first few weeks of life. Unfortunately, this transfer of antibodies from dam to foal does not always occur successfully and failure of passive transfer (FPT) may result. FPT is defined as an absence of IgG in serum at 7 days of age or a level less than 50 mg/dl. FPT affects the foal’s ability to resist disease and is associated with increased incidence of enteric disease, respiratory disease, and/or sepsis. In: Sixth Annu. ACVIM Proc., 145, 1988.


Adverse Reactions

As with any biological (or pharmaceutical) product, reactions can occur. Fortunately, the incidence with commercially produced plasma is very rare. Over almost twenty years we have not had to recall the product on the basis of adverse reactions reported in the literature. As reactions caused by not using a filter, are easily avoidable. There are potentially several types of adverse reactions:

1. Anaphylaxis – there are two types:
   a. Type I: an immediate reaction, occurring usually within a few minutes of administration of the plasma. Symptoms may include rapid dilation of the pupil, apnea and sudden death. It is likely that a fibrin clump enters the cardiac circulation causing myocardial ischemia.
   b. Type II: a delayed reaction occurring usually within 1-2 hours of administration of the plasma.

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   b. Type II: a delayed reaction occurring usually within 1-2 hours of administration of the plasma.

All these problems are easily avoided by using properly harvested plasma from screened donors. The only occasion which might cause an unexpected problem is when a foal is transfused that was born to a mare with unknown hypersensitivity from a previous foaling.

Plasma is shipped frozen in insulated containers by express Delivery. On arrival, the plasma should be stored at -20°C and thawed in a water bath kept at 37°C before use.


The EQUINE NEONATE

Plasma is shipped frozen in insulated containers by express Delivery. On arrival, the plasma should be stored at -20°C and thawed in a water bath kept at 37°C before use. Occasionally some formalin are present and these are blended out by the administration set. Plasma should be given USING A BLOOD ADMINISTRATION SET WITH APPROPRIATE FILTER (40 – 180 microns). It should be used straight from the bag with nothing added. Occasionally, some fibrin strands are present and these are filtered out by the administration set. One liter of plasma can be safely administered to a 50-Kg foal in 15-20 minutes.

It is important to note that more than 15 years older have colostrum of low IgG concentrations. This is a rapid semi-quantitative test for equine whole blood or serum. It can be used in the field to determine if the colostrum contains sufficient colostral IgG (20-80 mg/dl) to be of benefit or not. Testing is performed by making a half dilution of the sample with a 1:1 mixture of saline and serum. A 0.5 ml plasma sample is added to 4.5 ml of this mixture and the mixture is gently shaken and allowed to stand at room temperature. After 30 minutes, 0.5 ml of the mixture is added to a tube containing 4 ml of 1:1 mixture of saline and anti-rabbit IgG, and the tube is shaken again. After 30 minutes the tube is centrifuged at 1000 x g for 30 minutes. The absorbance of the supernatant at 490 nm is measured with a spectrophotometer. The absorbance is compared to the absorbance of a standard curve which is prepared with a series of 1:10 dilutions of a 5 mg/ml standard colostral IgG. IgG concentrations are calculated based on the absorbance of the sample and the standard curve. The concentration of IgG should be equal to or greater than 15 mg/ml. If the concentration is less than 15 mg/ml, the plasma should not be used for administration. The test is performed in less than 1 hour.

The EQUINE RID test is an accurate and easy way of determining equine IgG in serum or plasma using a radial immunodiffusion method. Each kit comprises a plate containing agar gel pre-stained in a ring (0-400 μg/ml IgG). After incubation at 37°C for 24 hours, the diameter of the ring, the higher the IgG concentration in the sample. For more details see the EQUINE RID technical bulletin.


The GAMMA-CHECK-E test: This is a rapid, semi-quantitative test to determine if there is an adequate gamma globulin level in colostrum. The test can be performed at foaling or prior to nursing, or to evaluate colostrum prior to nursing or after nursing to evaluate immunity. The test uses a mini-column test strip. A 0.5 ml sample is mixed with 1 ml of anti-human IgG. Then 0.5 ml of the mixture is added to the test strip and incubated for 10 minutes. The test is performed in less than 1 hour. The presence of sufficient colostral IgG is indicated by a positive test strip. In a 1:1 mixture of saline and serum. A 0.5 ml plasma sample is added to 4.5 ml of this mixture and the mixture is gently shaken and allowed to stand at room temperature. After 30 minutes, 0.5 ml of the mixture is added to a tube containing 4 ml of 1:1 mixture of saline and anti-rabbit IgG, and the tube is shaken again. After 30 minutes the tube is centrifuged at 1000 x g for 30 minutes. The absorbance of the supernatant at 490 nm is measured with a spectrophotometer. The absorbance is compared to the absorbance of a standard curve which is prepared with a series of 1:10 dilutions of a 5 mg/ml standard colostral IgG. IgG concentrations are calculated based on the absorbance of the sample and the standard curve. The concentration of IgG should be equal to or greater than 15 mg/ml. If the concentration is less than 15 mg/ml, the plasma should not be used for administration. The test is performed in less than 1 hour.
Specific Antibodies

Plasvacc USA Inc. produces plasma with high levels of antibodies. The product is used as an aid in the management and control of respiratory disease associated with other organisms and be present in sufficient quantity to neutralize the agent. The gut is still able to absorb antibodies. Colostrum (or possibly oral plasma) should be given. The person in charge of foaling (foal night watchman) to test the

Foals under 18 hours old:

Independent studies have shown that foals in a totally deprived environment foals can survive with very small amounts of maternally derived antibodies. However, these antibodies may not be present in plasma at all.

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Plasvacc USA Inc. produces Plasma containing gram negative core antibodies by using a specific vaccination protocol. This protocol has been developed in a double blind study by University of California, Davis, California.

Other sources of IgG are now being made available. Serum products suffer from the frequent problem of being inadequate in terms of antibody concentration and prevention of bacterial endotoxins. Reactions are rare. With sophisticated vaccine delivery systems, prevention of bacterial endotoxins is now possible.

As well as specifically increasing resistance to infection by pathogens are present in the plasma, even though it might be produced 2000 miles from where the mare and foal are. As endotoxemia is a serious problem in horses of all ages and, whilst its treatment is a controversial topic, we produce plasma containing gram negative core antibodies by using a specific vaccination protocol.

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Specific Antibodies

Plasvacc USA Inc. produces plasma with high levels of antibodies against Rhodococcus equi. The product is used as an aid in the management and control of respiratory disease associated with Rhodococcus equi under 6 months of age. Colostrom (or milk) from colostrum in a timely manner will have high (over 1000mg/dl) IgG levels by about 6 hours of age. Because the GAMMA-CHECK-E test is easy to economical and gives the results in 10 to 15 minutes, it can be used to initiated plasma therapy in foals under 24 hours of age. Plasma is not as effective as colostrum, but it can be used in the face of rapid IgG consumption having, therefore, a very short half-life. (Plasma proteins provided by transfusion normally have a half-life of 40 minutes to 2 hours.) In young foals, plasma may be required every few days to keep IgG levels up in the face of rapid consumption, severely compromised foals can require many liters over a few days.

Colostrum is the best source of antibodies and it is included in the treatment of foals with FPT. Cheque  (specifically IgG), a special vaccination protocol is utilized. Accurate IgG measurements are done on each batch using a standardised radial immunodiffusion test. The level of IgG is determined at levels of 40 and 80 mg/dl, the total protein is measured during the production stage by refractometer and ranges from 50 g/L to 68 g/L. For a positive IgG level is needed to have the IgG level checked in the first few hours of life. The plasma donors with the Equine rotavirus vaccine. Plasma with a high rotavirus titer has been used for a number of years in Europe both orally and IV to treat severely ill and dehydrated foals.

Colostrometer™

A positive (+) result indicates adequate levels of antibody. The interpretation of (+) is left to the practitioner for some of the tests. Foals may be reared with 400 mg/dl of antibodies and they can also be used in the treatment of FPT. The screening test “GAMMA-CHECK-E” has a cut off of 800 mg/dl using whole blood or serum.

EQUINE PLASMA (POLYMUNE® AND POLYMUNE-PLUS®)

Research has shown that the amount of IgG absorbed is directly dependent on the time of administration. Close to 100% could be absorbed if the plasma is given within the first 10 minutes after birth, 80% within the first hour, 40% at 2 hours, and less than 10% after 4 hours. The most convenient means is to place the bag into warm water with a temperature of about 40°C (this will feel like a warm shower – hot). Thawing in water too hot will denature certain proteins. Foals have a small gut and cannot absorb IgG directly from the plasma. Therefore, colostrum IgG is over 60g and this will be supplied by about two liters of POLYMUNE-PLUS® (see Treatment of FPT, page 3).

Oral:

In young foals, plasma has been implicated in as a source of colostrom. Some of the plasma donors with the Equine rotavirus vaccine. Plasma with a high rotavirus titer has been used for a number of years in Europe both orally and IV to treat severely ill and dehydrated foals.

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Plasvacc USA Inc. produces plasma with high levels of antibodies against Rhodococcus equi. The product is used as an aid in the management and control of respiratory disease associated with Rhodococcus equi under 6 months of age.
Specific Antibodies

The product is used as an aid in the management and control of respiratory disease associated with Rhodococcus equi in foals under 6 months of age. If it is not possible to test the foal before 18-24 hours of age, then the GAMMA-CHECK-E test is still of considerable help as a screening test. In a sick foal, occasionally a positive test result with GAMMA-CHECK-E is used to help as a screening test in sick foals, occasionally a positive test result with GAMMA-CHECK-E is used. Such foals are usually raised with high-birthweight foals. If this is the case, a more quantitative test of foal IgG is recommended and we strongly recommend checking every foal with this test. A positive test result may be expected in some newborn foals and in foals with diseases characterized by low IgG levels.

Plasma treatment is of choice and has been for many years. The available plasma will be perfectly effective and safe. Resistance factors are rare. With sophisticated vaccine strategies and the use of common newborn pathogen preparations are present in the plasma, even though it might be produced 2000 miles from where the mare and foal are located. Other sources of IgG are now being made available. Serum products differ from the perspective of being classified as blood plasma compared with the blood metabolites of the source animal. As such, the better the quality of the colostrum and blood plasma, the more desirable will be the results for the newborn foal. In the absence of other indications, current plasma preparations will be the first choice.

Endotoxemia is a serious problem in horses of all ages, and, whilst its treatment is a controversial topic, we produce plasma containing gram negative core antibodies by using a process that prevents the presence of antibodies to endotoxins in plasma. The gram-negative core antibodies are the antibodies that protect against endotoxins and endotoxin shock. Research has shown that the amount of IgG absorbed is directly dependent on the time of administration. Close to 100% could be absorbed if the plasma is given within the first 24 hours. However, if the plasma is given later than 24 hours, the amount absorbed will be less. Typically, a 50 Kg foal has a blood volume of approximately 5 liters. The following formula can be used to estimate the amount of IgG that will be absorbed:

\[ \text{Absorbed IgG (mg)} = \frac{\text{Blood Volume (liters)} \times \text{IgG Concentration (mg/dl)}}{1000} \]

A positive (+) result indicates adequate levels of antibody. The interpretation of (+) is left to the practitioner for some of the tests. It is not possible to compare 400 mg/dl of antibody in whole blood or serum or 800 mg/dl in whole blood or serum.

EQUINE PLASMA

EQUINE PLASMA (POLYMUNE™)

Equine Plasma is indicated where a foal that is 24 hours old or more has been diagnosed as having inadequate circulating immunoglobulin G levels. The definition of "inadequate" is open to some degree of interpretation and dependant on several factors. In one recent study, 85% of foals showed a response to plasma when given within the first 24 hours.

Other studies have shown that in the right environment, plasma cannot be used to correct entirely malnourished antibody levels. The "right" environment might be the addition of fresh colostrum, as well as a warm environment (providing at least 20°C with only its dams to share the load. Conversely, a coronary infection or situation where the foal is suffering from diarrhea and share the field with other colostrum. The "right" environment is used to correct entirely malnourished antibody levels.
such foals do so year after year and if a transfusion is essential in a subsequent foal, intradermal skin testing could be performed with the plasma prior to transfusion.

B – If using plasma from a donor not screened for red cell antibodies, then agglutination and/or hemolysis might occur. Signs include hyperventilation, but not profound bubbling. This is not a problem with commercial plasma from screened donors.

3. Fibrin entering the system – by not using a filter. Symptoms include rapid dilation of the pupil, apnea and sudden death. It is likely that a fibrin clump enters the cardiac circulation causing myocardial ischemia.

All these problems are easily avoided by using properly screened plasma, not heated, not used in a syringe containing mercury, and at the appropriate rate.

1. Jeffcott, L.B.: Diagnosis and management of immune system failures in foals. By allowing plasma to warm to about body temperature, this precipitate will dissolve and the blood will become clotting deficient. If plasma is warmed to body temperature, it is easily to understand how volume overload might occur. A healthy foal is able to handle the transfusion of 1 liter of plasma in about 15-20 minutes but 2 liters should be given over a minimum of 8 hours. A sick and compromised foal will require more time for the administration of the same volume. Signs of volume overload include hypertension, tachycardia and sweating. The rate of administration should be slowed down if these signs appear and stopped completely if these signs are not quickly abated.

Anaphylaxis – there are two types:

A – This usually occurs when the foal is in some way sensitized to the plasma being transfused. In the neonate, the likely cause of this is by receiving sensitizing antibodies through the colostrum. We are aware of several instances where this appears to have occurred in mares with previous histories of dystocia. It is clear that in these instances, the colostrum plasma (IGG) antigens and then producing antibodies to these antigens. This sensitization is probably promoted by antigenic material not normally encountered by the young foal and may be responsible for the injuries also thought to be due to antibodies against the fetal membranes.

B – This form of anaphylaxis may be due to the intravenous transfusion of non-compatible plasma affecting the kidneys, lungs, myocardium, or other vital organs. Drugs should be administered. Forced ventilation, thiamine injection and oxygen might be needed. Plasma producing such foils do so year after year and if a transfusion is essential in a subsequent foal, intradermal skin testing could be performed with the plasma prior to transfusion.

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4. Anaphylaxis – there are two types:
   - This usually occurs when the foal is in some way sensitized, e.g. by receiving sensitizing antibodies through the colostrum. In this case, the likelihood of an anaphylactic reaction is greater than with any other type of reaction. The severity of the reaction can be varied depending on the amount of antibody present in the plasma being transfused. In the neonate, the likely cause of this is by receiving sensitizing antibodies through the colostrum. We are aware of several instances where this has occurred with severe consequences. In these instances, the foal was born to a mare with a history of allergic reactions to certain plasma components. These reactions are typically characterized by a rapid onset of respiratory distress, bronchospasm, and hypotension. In some cases, the onset of symptoms may be delayed for several hours after the plasma transfusion. The severity of these reactions can vary from mild to fatal.

_delivery, intravenous administration

_Antigenic stimulation causes production of immune antibodies, which may cause excessive production of certain plasma proteins. These antibodies may then react with the foreign proteins in the plasma being transfused, leading to hypersensitivity reactions. The symptoms of an allergic reaction may include fever, chills, vomiting, diarrhea, and anaphylaxis. It is important to monitor the foal closely for any signs of an allergic reaction and to administer appropriate treatment if necessary.

_Antibodies to plasma proteins may cause hemolysis, leading to the destruction of red blood cells. This can result in anemia and a decrease in the foal’s oxygen-carrying capacity. In some cases, the hemolysis may be severe enough to cause hemoglobinuria, leading to the excretion of hemoglobin in the urine. It is important to monitor the foal’s urine for signs of hemoglobinuria and to administer appropriate treatment if necessary.

_Antibodies to red blood cells may cause hemolytic anemia, leading to the destruction of red blood cells and a decrease in the foal’s oxygen-carrying capacity. In some cases, this can be a life-threatening condition. It is important to monitor the foal’s red blood cell count and to administer appropriate treatment if necessary.

_Antibodies to fetal antigens may cause immunization of the foal against certain plasma components. This can lead to the foal developing antibodies against the plasma proteins being transfused, leading to a rejection of the transfused plasma. This can result in the foal developing a plasma transfusion reaction, which can be life-threatening.

_Antibodies to plasma proteins may cause a reduction in the foal’s platelet count, leading to a decrease in the foal’s ability to form clots and a potential for excessive bleeding. It is important to monitor the foal’s platelet count and to administer appropriate treatment if necessary.

_Antibodies to plasma proteins may cause a reduction in the foal’s white blood cell count, leading to an increased risk of infection. It is important to monitor the foal’s white blood cell count and to administer appropriate treatment if necessary.

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