Although a range of plasma-based products (e.g., cryoprecipitate, albumin, platelet-rich plasma, individual coagulation factors) are available to human physicians, equine veterinarians are largely restricted to using whole blood, frozen plasma, and fresh frozen plasma for transfusions. The indications for frozen or fresh frozen plasma in human medicine are relatively limited, and there is little evidence supporting the efficacy of these products in many cases. Furthermore, many human physicians have concerns regarding disease transmission and anaphylactic reactions after administration of any plasma product. In equine medicine, plasma products have been used (1) to treat failure of passive transfer (FPT); sepsis; and coagulopathies; (2) as "antiendotoxin" agents; and (3) to provide colloidal support. The use of plasma should be carefully considered before administration because of potential (although rare) adverse reactions as well as expense. In addition, the benefits are uncertain in some equine patients.

Production of Fresh Frozen Plasma and Derivatives

Fresh frozen plasma may be collected by either centrifugation of whole blood or plasmapheresis and is frozen within 8 hours of collection. Fresh frozen plasma is used mainly to provide plasma proteins and coagulation factors, but it also contains anticoagulants (e.g., antithrombin, protein C) and may have a relatively high sodium concentration. The storage conditions of plasma products determine the degree of decrease in the activity of hemostatic proteins (particularly factor VIII) within a product; for example, fresh frozen plasma stored at –70°F will retain clinically useful hemostatic activity for at least 12 months. To reduce costs, some hospitals prepare plasma on site by gravity sedimentation of refrigerated whole blood for 48 hours, followed by decantation of the plasma.1 A study of plasma produced in this manner found that activity of factors VII, VIII, IX, XI, and XII and antithrombin was preserved, but factor X activity decreased below the reference range.1

Hyperimmune Plasma

Hyperimmune plasma is harvested from donor animals with high concentrations of circulating antibodies against a specific antigen and is usually frozen shortly after collection (i.e., fresh frozen). In horses, hyperimmune plasma has been used for treating West Nile virus encephalitis and Clostridium botulinum infection and for preventing Rhodococcus equi pneumonia in foals.2,3

Antiendotoxin Plasma

Lipopolysaccharide (LPS, endotoxin) is an intrinsic structural component of the outer membrane of gram-negative bacteria and is essential for bacterial viability. LPS is composed of the following domains:

- A hydrophilic region of polysaccharides that project into the extracellular environment
- The hydrophilic lipid A region buried within the bacterial outer membrane
- A core region connecting the lipid A and the outer polysaccharide domains

The outer polysaccharide domain is highly variable, but the lipid A and core domains are well conserved between bacterial strains. “Antiendotoxin” plasma contains antibodies directed against the conserved portions of LPS and theoretically binds LPS released from gram-negative bacteria, preventing its interaction with cellular receptors.

Indications for Plasma Product Administration

Administration of Plasma to Neonatal Foals With Failure of Passive Transfer

The phagocytic cells of a newborn foal’s immune system are functionally mature, but their functionality appears to be limited by reduced concentrations of serum opsonins, primarily IgG and complement factor. Therefore, neonatal foals depend on the ingestion of maternal immunoglobulins from colostrum (i.e., passive transfer) until they start manufacturing sufficient immunoglobulins of their own.5–8 Complete FPT is usually defined as an IgG concentration <400 mg/dL at 24 hours of age. Partial FPT is defined as an IgG concentration between 400 and 800 mg/dL at 24 hours of age; an IgG concentration >800 mg/dL is considered to be adequate.

Plasma should always be administered through a blood administration set with a 150- to 260-µm filter.

Key Points

- Complete failure of passive transfer (FPT) in foals is usually defined as an IgG concentration <400 mg/dL at 24 hours of age. Partial FPT is defined as an IgG concentration between 400 and 800 mg/dL at 24 hours of age; an IgG concentration >800 mg/dL is considered to be adequate.

- Plasma should always be administered through a blood administration set with a 150- to 260-µm filter.
be adequate. Neonatal foals with FPT have a significantly reduced opsonization capacity, putting them at increased risk of infection and sepsis.

When a neonatal foal is older than 18 to 24 hours, immunoglobulins (and other molecules) within colostrum are no longer absorbed across the intestinal wall; for optimal absorption of IgG, foals need high-quality colostrum within 12 hours of birth. Therefore, intravenous administration of hyperimmune plasma harvested from donors vaccinated against pathogens that cause neonatal sepsis is recommended to treat FPT in foals older than 12 hours, along with other treatments (e.g., antimicrobials), if necessary. It has been recommended that plasma be administered in volumes sufficient to increase the IgG concentration to >800 mg/dL. This typically requires 1 to 3 L of plasma, depending on (1) the IgG concentration of the plasma (a minimum IgG concentration between 1500 and 2500 mg/dL is usually guaranteed by the manufacturer), (2) the size of the foal, and (3) concurrent disease processes. After plasma transfusion, the IgG concentration should be reassessed within a few hours to determine whether additional units are required. Immunoglobulin concentrations in critically ill neonatal foals may decrease rapidly as a result of opsonization of bacteria, loss of serum proteins (including immunoglobulins) across leaky vasculature, or catabolism of proteins (including immunoglobulins) due to a negative energy balance.

Plasma transfusion to neonatal foals with partial or complete FPT is considered to be the standard of care and can be expected to increase serum opsonizing capacity and to support or enhance neutrophil phagocytosis. Administration of hyperimmune plasma to septic foals was associated with a short-term (although statistically insignificant) improvement in neutrophil phagocytic function in one study and was thought to sustain opsonization capacity in another. The effect of plasma administration on neutrophil oxidative burst activity in septic foals is less clear, although it was transiently decreased immediately after transfusion in one study. The trend toward improved phagocytic function was evident only at 12 and 24 hours after treatment, supporting the suggestion that multiple transfusions may be required. The benefits of plasma administration to healthy foals are less certain; in one study, plasma transfusion to healthy foals (n = 9) to treat partial or complete FPT caused a slight (statistically insignificant) reduction in neutrophil phagocytic activity, although oxidative burst activity (an indicator of intracellular killing capacity) was not affected. The clinical relevance of these latter findings is unclear and warrants further investigation.

Administration of Plasma to Critically Ill Adult Horses and Foals for Colloidal Support and Treatment of Sepsis, Endotoxemia, and Coagulopathies

Administration of a colloid is recommended in critically ill horses (e.g., those with colitis or large colon volvulus) when the total protein (TP) concentration is <4.0 g/dL, the albumin concentration is <2.0 g/dL, or the colloid oncotic pressure is <12 mm Hg. In human medicine, plasma products are not routinely used for colloidal support because of the risk of disease transmission and anaphylaxis and the higher cost compared with that of synthetic colloids. The amount of plasma required to increase a patient’s plasma protein concentration can be estimated as follows:

Volume (L) = ((TP_{target} – TP_{Patient}) × 0.05 × Bodyweight [kg]) ÷ TP_{Donor}

Four to 5 L of plasma is typically required to increase the plasma protein concentration of an average-size horse by 1 g/dL; however, the actual increase in protein concentration is almost always disappointing. In my opinion, colloidal support for adult horses is usually better and more economical with boluses or (even better) continuous infusion of a synthetic colloid. Using plasma as a colloid in foals may be economically feasible because their small body size reduces the amount of plasma required to increase colloid oncotic pressure. Some authorities have expressed concern that administration of plasma to patients with increased capillary permeability may exacerbate edema as albumin escapes the vascular space and moves into the interstitium. Care is required to avoid volume overload in hypoproteinemic but euvolemic foals.

In human medicine, the current recommendation is to administer fresh frozen plasma only to patients with sepsis to correct a documented coagulation factor deficiency (increased prothrombin or partial thromboplastin time) in the presence of active bleeding or before a surgical or invasive procedure. However, this recommendation is not strongly supported by clinical trials. There is some evidence that intravenous immunoglobulin therapy (administration of solutions containing high IgG concentrations) may be beneficial for treating adult and neonatal sepsis. However, these products are not routinely available to equine practitioners. No large human trials have shown any benefit of administering plasma containing antibodies against LPS to patients with sepsis. There is conflicting evidence for administering serum or plasma containing antiendotoxin antibodies to foals and adult horses: administration has been beneficial in some studies, had no benefit in others, and had deleterious effects in another. Given the mechanism of action of LPS and the cascade nature of cellular activation, it is surprising when there is a positive effect. Nevertheless, several studies in horses have shown a positive effect, so this treatment warrants further investigation in well-controlled trials.

Disseminated intravascular coagulation (DIC) occurs secondary to severe systemic inflammation and represents a loss of balance between the procoagulant and fibrinolytic systems. Initial hypercoagulability is followed by hemorrhagic diathesis subsequent to procoagulant factor consumption and hyperactivity of the fibrinolytic pathways. Liver disease is associated with a range of coagulopathies as a result of decreased procoagulant factor synthesis. Coagulopathy may also occur after massive hemorrhage as a consequence of shock; hypothermia; and activation, consumption, and dilution of coagulation factors. For all of these conditions, plasma transfusion has been suggested for replacing multiple coagulation factors.

Although plasma transfusion may have a role in managing massive hemorrhage in humans, plasma transfusion is currently not recommended in humans with DIC or liver failure based on laboratory results indicating coagulopathy alone. Plasma therapy
is indicated in humans with DIC or liver failure who have active bleeding or are scheduled for an invasive procedure; however, there is no evidence for the prophylactic use of fresh frozen plasma in DIC or liver failure.11,16 There is little information regarding the appropriate volume of fresh frozen plasma to administer to human patients with DIC or liver failure, although large volumes are typically required to correct coagulation defects. In 43 horses with histologically confirmed liver disease, there was no difference in the incidence of complications after liver biopsy in subjects with an abnormal clotting profile (n = 25) compared with subjects with a normal clotting profile (n = 18).17 In both groups, complications were rare and mild, and there is likely little benefit in the prophylactic administration of fresh frozen plasma to horses before biopsy.17 Coagulopathies are common in critically ill neonatal foals18 and horses with severe gastrointestinal disease (e.g., colitis, volvulus of the large colon)19,20; however, there is little or no evidence to support (or refute) the administration of fresh frozen plasma to these patients.

**Acute Volume Resuscitation**

For decades, human critical care specialists have debated the benefits of colloids versus crystalloids for acute volume resuscitation; however, numerous trials have not demonstrated a significant difference between the two fluid types.21 Because there is no evidence-based support in horses for using one fluid type instead of the other and because crystalloids are less expensive than colloids, the continued use of crystalloids as a resuscitation fluid is most appropriate for equine patients. However, resuscitation with crystalloids rather than colloids requires administration of more volume to achieve the same hemodynamic results because crystalloids are not restricted to the intravascular space; therefore, edema may result.

**Intravenous Immunoglobulin Therapy**

Administration of 5% or 10% solutions of IgG at doses of 500 to 1000 mg/kg appears beneficial for treating immune-mediated and inflammatory diseases in people22 and has been used in small animal medicine to treat immune-mediated hemolytic anemia.23 Immunomodulation appears to occur through (1) nonspecific effects mediated through the constant regions (Fc portion) of immunoglobulin and (2) specific effects that involve binding of the Fab portion of immunoglobulins to exogenous or host antigens. Although there may be some indications for using intravenous immunoglobulin therapy in horses, its cost will likely preclude its use in large animal medicine.

**Practical Aspects of Plasma Administration**

Fresh frozen plasma should be warmed in a warm-water bath and should probably not be warmed to >98°F to 100°F (>36.7°C to 37.8°C).24 Once thawed, plasma should be administered as soon as possible, although it may be safely refrigerated for at least 24 hours, and probably longer if sterility is maintained.25 Plasma should always be administered through a blood administration set with a 150- to 260-μm filter. The initial 50 to 100 mL of plasma should be administered very slowly over 10 to 20 minutes, and the patient should be observed closely for adverse reactions (e.g., tachycardia, tachypnea, fever, piloerection, urticaria, muscle tremors). If there are no adverse reactions, the administration rate may be increased; experience suggests that 1 L of plasma may be safely administered over 20 to 30 minutes, but slower rates (e.g., 20 mL/kg/h) are recommended for septic foals that have received multiple transfusions. If a reaction (e.g., acute fever; increasing body temperature, if fever is already present; tachycardia; tachypnea) occurs at any time, the transfusion should be slowed or stopped. Plasma reactions become more likely in patients receiving multiple units over several days.

**References**


