Colloid Replacement in the ICU

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Colloids are fluids containing large molecular weight molecules that do not readily cross the capillary membrane. Colloid replacement is becoming increasingly more common in the equine intensive care unit. Advantages of colloid therapy include improved oncotic pressure, rapid intravascular volume replacement, and improved microvascular perfusion. Edema formation is minimized through the use of colloids, rather than crystalloids, in the volume resuscitation of hypoproteinemic animals. Available colloids include both natural (biologic) and synthetic formulations. Plasma is the most common biologic colloid utilized in horses, and offers the advantage of providing a broad range of proteins in addition to its principle colloid, albumin. These additional proteins include coagulation factors, antithrombin, and immunoglobulins. The most widely used synthetic colloid in horses is hydroxyethyl starch (hetastarch). Side effects of hetastarch include dose-dependent effects on coagulation, primarily because of decreases in factor VIII and von Willebrand factor concentrations. Other synthetic or semisynthetic colloids include pentastarch, dextrans, and a polymerized ultrapurified bovine hemoglobin product. Monitoring of patients receiving colloid therapy should include direct colloid osmometry. Indirect estimates of colloid osmotic pressure are not reliable in critically ill patients and in those receiving synthetic colloids. Total protein measurements do not account for the oncotic contribution of synthetic colloids.

Key Words: Colloids, volume replacement, horses, equine, plasma, hetastarch

Colloid replacement in the equine intensive care unit (ICU) setting has made recent advances and the use of colloids is increasing.[1-4] An improved understanding of colloid osmotic pressure (COP), or oncotic pressure, allows for more effective control over fluid balance in critically ill patients. Better fluid balance translates to improved hemodynamics, enhanced oxygen delivery to end organs, and reduction of edema. Therefore, the goal of colloid therapy is more than simply replacing lost plasma proteins, but rather to improve the circulatory status in patients with compromised Starling's forces.

Starling's equation defines fluid movement across capillary membranes (Fig 1). In simplified terms, fluid flux across the capillary is dependent on higher capillary than interstitial hydrostatic pressure, which drives fluid out of the vessel, and higher oncotic pressure within the capillary lumen than the interstitial fluid, which counteracts hydrostatic pressure. Colloid osmotic pressure, therefore, opposes the drive of fluid out of the capillary. Other variables in Starling's equation that affect fluid movement include the filtration coefficient (K), which is the product of hydraulic conductivity (water permeability) and capillary surface area available for fluid exchange. The last component of the equation is the osmotic reflection coefficient (σ), which relates to membrane pore size. Aside from capillary hydrostatic pressure, oncotic pressure, filtration properties of the capillary membrane, and capillary permeability, the final determinant of edema formation is lymphatic flow. It is important clinically to determine which of these factors is contributing to edema.

Colloid osmotic pressure is generated by two properties: (1) The presence of plasma proteins, particularly albumin, that are not freely diffusible across capillary membranes (ie, a large component of COP is the osmotic pressure generated by dissolved proteins), and (2) The Gibbs–Donnan equilibrium. The latter relates to the redistribution of ions induced by negatively charged proteins in plasma; these anions attract cations that would otherwise diffuse freely across the capillary. Water is osmotically retained with these cations, thereby increasing the amount of intravascular volume.

Plasma COP is also opposed by the oncotic pressure of the interstitium; the difference between plasma and interstitial COP is what opposes hydrostatic pressure in determining net fluid flow across the capillary. Interstitial COP is substantially lower than that of plasma COP, but is highly variable among tissues. For example, interstitial COP within the myocardium is 70 to 80% of plasma COP.[5] Pulmonary, cutaneous, skeletal muscle, gastrointestinal, renal, and hepatic interstitial COP values are also relatively high.[5] Oncotic pressure is largely (60 to 80%) determined by albumin, although fibrinogen and globulin proteins also contribute.[6] Alterations in the A:G ratio can thus alter COP. Albumin is the primary determinant of plasma COP because of its relatively high concentration, small size, and highly negative charge (Gibbs–Donnan effect).[7] As can be seen in the Starling equation, the COP gradient can be modified by the osmotic reflection coefficient (σ). The value of σ varies between 0 and 1, with 0 representing free permeability to proteins. A value of 1 is associated with complete impermeability. The more permeable the capillary membrane is, the less osmotic pressure that can be generated intraluminally. The clinical significance of this phenomenon is that capillary leak states, such as systemic inflammatory response syndrome (SIRS), lead to an increase in endothelial permeability to proteins and water. Sepsis and endotoxemia can thus lead to alterations in the reflection coefficient.

As hypoproteinemia develops, filtration is favored as the predominating determinant of capillary fluid flux. Edema develops when compensatory mechanisms become overwhelmed. These compensatory processes that prevent edema formation include an increase in lymphatic flow and in interstitial hydro-

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$$J_v = K_f [(P_c - P_i) - \sigma(\pi_p - \pi_i)]$$

J_v = net capillary (microvascular) filtration rate
K_f = capillary filtration coefficient
Where $K_f = L_p A$
L_p = hydraulic conductivity (water permeability)
A = capillary surface area
P_c = capillary hydrostatic pressure
P_i = interstitial hydrostatic pressure
σ = osmotic reflection coefficient
π_p = plasma colloid osmotic pressure
π_i = interstitial colloid osmotic pressure

Fig 1. The Starling-Landis equation for determination of capillary filtration.

static pressure that develop as fluid moves into the interstitium. This counteracts the effects of capillary hydrostatic pressure and causes a dilutional decrease in interstitial COP. These counter-balance mechanisms are what prevent clinically significant edema, even when hypoproteinemia is severe. It is this delicate balance that should not be disturbed by clinical intervention. For example, overzealous crystalloid administration in a hypoproteinemic animal will cause overt edema by increasing hydrostatic pressure.

The clinical significance of edema formation (Fig 2) extends beyond dependent subcutaneous edema. Organ and tissue edema may be more clinically important as they reduce the efficiency of oxygen delivery by increasing oxygen diffusion distance.

How to Measure COP in Horses: Normal Values and Direct and Indirect Methods of Measurement

Oncotic pressure reported for normal adult horses and ponies ranges from 19.2 to 31.3 mm Hg, with the average COP in most studies being approximately 21 to 25 mm Hg.[1,2,4,8,9] Both direct and indirect methods can be used to measure COP. Direct colloid osmometry is performed by means of a colloid osmometer. Figure 3 depicts the Wescor 4420 colloid osmometer (Wescor Inc, Logan, UT) which is the most common osmometer used in clinical practice. This device utilizes a semipermeable membrane to separate a reference chamber (filled with saline) from a test chamber into which the sample, consisting of whole blood, plasma, or serum, is injected.[10,11] The reference chamber mimics the Gibbs–Donnan effect. As the pressure changes with fluid flow, the electrical impedance is altered, and a pressure transducer measures the pressure gradient created by the migration of water into the test chamber from the reference chamber. This movement of water is in response to oncotic pressure exerted by the test sample, and results in a negative pressure gradient within the reference chamber. Maintenance of this type of osmometer is fairly simple and requires that both the test and reference chambers be flushed daily with saline. Calibration should also be performed daily

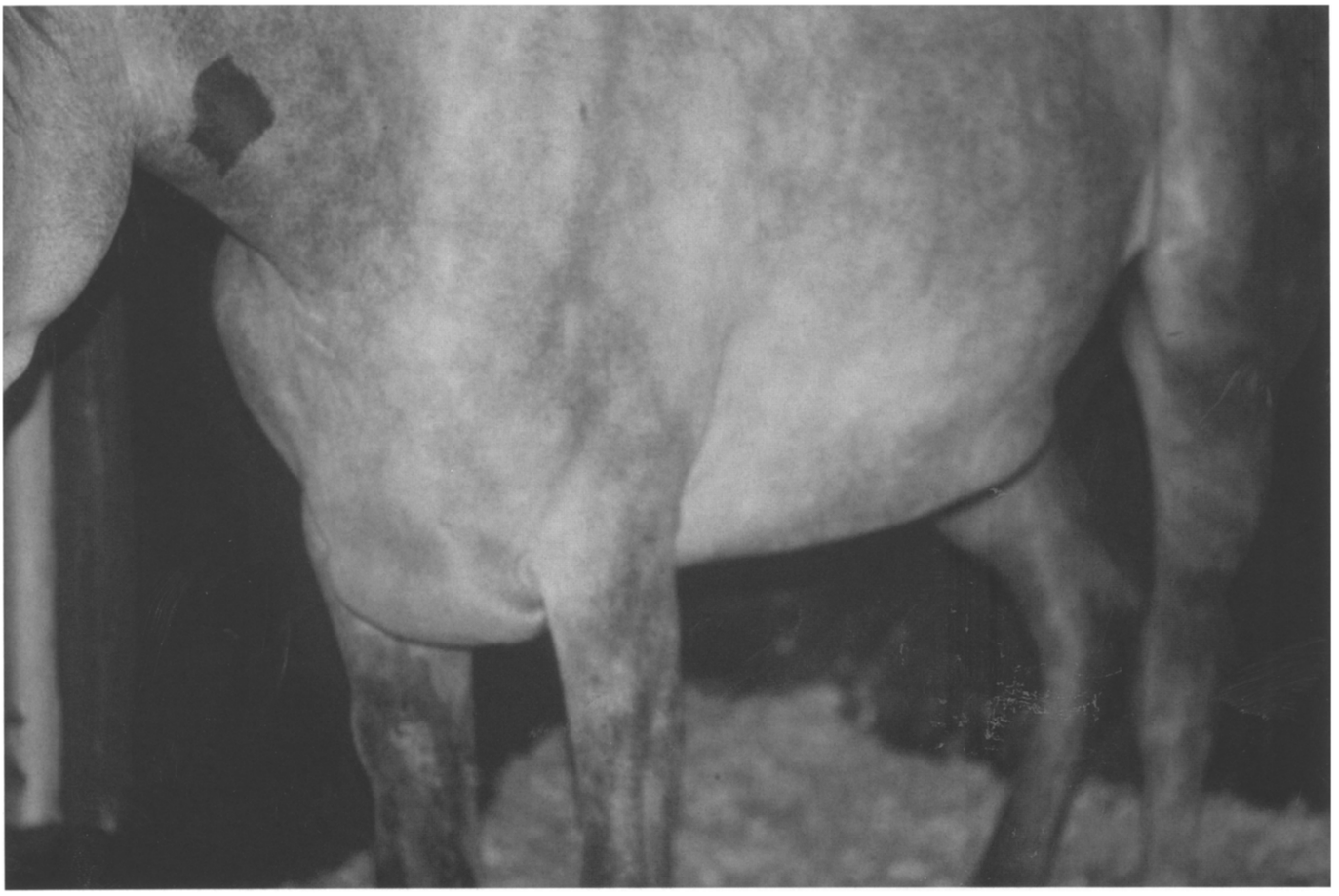

Fig 2. Ventral edema in a horse with hypoproteinemia associated with colitis.

Fig 3. The Wescor 4420 colloid osmometer.

with standard solutions of albumin. In addition, the instrument should be calibrated to zero with saline before and after each use. Continuous measurements of COP can be made with the use of a needle-type colloid osmometer, although indications for continuous monitoring in clinical practice are few.[10,12]

Indirect estimates of COP are calculated based on serum total protein or albumin and globulin concentrations. Indirect calculations are not as accurate in clinically ill animals, and should not replace the use of direct measurements in these patients.[8] A number of calculations have been developed to determine indirect COP values using total protein or albumin and globulin concentrations.[8,9,13] The Landis-Pappenheimer (L-P) equation is utilized in human medicine, and has been shown to be a good estimate of measured COP in healthy foals:[4,13,14]

$$COP = 2.1TP + (0.16TP^2) + (0.009TP^3)$$

However, the L-P equation did not provide reliable results for plasma samples in adult horses in one study, and consistently underestimated COP.[9] Equations for estimating COP have been developed for use in *healthy* adult horses, and have high correlation coefficients with actual COP values (r^2 = 0.987 to 0.999):[9]

$$COP = 0.986 + 2.029A + 0.175A^2$$

$$COP = -0.059 + 0.618G + 0.028G^2$$

$$COP = 0.028 + 1.542P + 0.219P^2$$

$$COP = -1.989 + 1.068Pr + 0.176(Pr)^2$$

Another formula was developed for horses using both albumin and globulin concentrations (r^2 = 0.961 in healthy animals; r^2 = 0.876 in hospitalized horses):[8]

$$COP = -4.384 + 5.501A + 2.475G$$

A = albumin
G = globulin
P = total protein as measured using the biuret method
Pr = total protein as determined by refractometry

Although indirect estimates of COP are reasonable predictors of actual COP in healthy animals, they are less reliable in critically ill patients.[8,15] A number of factors may modify the relationship between total protein and COP. The albumin:globulin (A:G) ratio may be altered with critical illness. Relative hypoalbuminemia or hyperglobulinemia, both potential sequelae to sepsis or SIRS, result in a lower oncotic pressure at equivalent total protein concentrations.[9] Other factors that may affect the relationship between total protein and COP include alterations in pH and sodium concentrations which affect the Gibbs–Donnan relationship.[10] Indirect measurements do not detect changes in COP produced by synthetic colloids, and direct osmometry is the only means of monitoring and directing synthetic colloid therapy. One study comparing measured and calculated values for COP in hospitalized horses found that the equation using both albumin and globulin was the most accurate indirect estimate of COP. However, there was still considerable variation between direct and indirect values, with up to

as much as 5 mm Hg difference for some samples. The predictive equations for COP were least reliable in horses with altered A:G ratios, particularly for equations that used total protein values.[8] Because albumin is the primary determinant of COP, indirect calculations of COP based on total protein will underestimate actual COP in horses with high A:G ratios and overestimate them in horses with low A:G ratios. Although an equation utilizing albumin and globulin concentrations strengthened the estimation, it yielded results that were more than 10% different from actual values in 44.3% of horses.[8] Based on these findings, direct measurements cannot be replaced in the monitoring of COP in critically ill patients in the ICU.[1,8]

Colloid solutions are fluids that contain large, osmotically active molecules that are retained within the vasculature. By increasing COP, they serve to promote fluid retention within the intravascular compartment. Different colloids provide oncotic pressure that is relative to the number and molecular weight of the contained colloid particles. The size of colloid molecules can be described by both weight average molecular weight and number average molecular weight (MW).[16] The weight average molecular weight is determined by the scattering of light and is not as accurate as the number average molecular weight. It assigns higher statistical weight to larger molecules and is associated with viscosity. The number average MW is the arithmetic mean of the range of molecular weights in the solution and assigns equal weight to all molecules regardless of size. As the weight average MW becomes equal to the number average MW in colloid solutions, the distribution of molecular weights of the colloid becomes narrow. In most cases, however, the weight average MW is greater than the number average MW because of the varying distribution of actual molecular weights in most solutions. Albumin has a molecular weight of 69,000 D.

Crystalloids or Colloids, Which Is Better?

The ideal fluid choice for volume replacement in the ICU is equivocal. There is a great deal of controversy in human critical care medicine as to whether crystalloids, colloids, or a combination of the two should be used during the acute resuscitation phase of hypovolemia in patients. Concrete evidence favoring one over the other is lacking, however. Current clinical philosophy recognizes the advantages of both crystalloids and colloids, and the concurrent or sequential administration of each likely represents the optimal approach to fluid therapy. Insensible and isotonic fluid losses should be replaced with crystalloids and free water sources. Crystalloids distribute among the extracellular fluid space, with approximately 75% distributing to the interstitium. Therefore, crystalloids allow for greater interstitial expansion compared with colloids, which may be disadvantageous when edema formation is pending. In hypovolemic patients, expanding volume with crystalloids results in a decrease in plasma protein concentrations and thus COP. Colloids, on the other hand, are restricted to the intravascular space, and are particularly indicated in hypovolemic shock.[17] Though colloids replace intravascular losses more rapidly than crystalloids, colloids alone will not effectively replenish interstitial fluid losses. In people, colloids are associated with a plasma volume expansion between 100 and 200% of the infused volume.[18-20] Cardiac output is better maintained with lower volumes of fluid administration when colloids are utilized. However, sepsis and other SIRS conditions may reduce the capillary reflection coefficient, thereby reducing the effectiveness of colloids. Marked alterations of the reflection coefficient, as is associated with some forms of acute respiratory distress syndromes, may be contraindications to the administration of colloids.

The concurrent use of both crystalloids and colloids obviates the need for administration of large volumes of crystalloids, minimizes the risk of interstitial edema, and may restore blood volume rapidly. A 'blending' of crystalloids and colloids should be considered if colloids are not contraindicated.

Types of Colloids

Biologic Colloid Solutions

Plasma. Albumin is the primary determinant of plasma oncotic pressure, providing approximately 65 to 75% of total COP.[16] The COP of plasma is approximately 20 to 25 mm Hg. Because albumin distributes throughout the extracellular fluid compartment, approximately 60% may ultimately move to the interstitium. Rarely is plasma used as the sole source of colloid support because of cost-limitations and the large volume required to effectively increase oncotic pressure. In addition to providing oncotic pressure, albumin is an important carrier protein for hormones, drugs, and toxins. Other advantages of plasma include the provision of globulin, fibronectin, clotting factors, and anticoagulants (eg, antithrombin). Both stable and labile clotting factors are provided by fresh (administered to the patient within 6 hours of collection) and fresh frozen plasma (frozen within 6 hours of collection without being refrigerated; stored for less than 1 year). Stored plasma (frozen for longer than one year) will provide only stable factors, including factors II, VII, IX, and X. Refrigeration destroys labile coagulation factors (V, VIII, vWf). Platelet rich plasma is the only source capable of replacing platelets. Controversy exists as to the role of hyperimmune plasma products (eg, antiserum) in endotoxemic animals.[21,22] Because of the fact that plasma has the oncotic pressure of normal horses, and because 60% or more of albumin may distribute extravascularly, it is often not cost effective as the sole colloid. In the author's experience, it is best combined with synthetic colloids. Concentrated albumin is available for use as a colloid in human and small animal medicine, and has been used to a limited extent in horses when equine sources were available.[23] Horses receiving plasma transfusions should be monitored for signs of hypersensitivity reactions, including pyrexia, tachycardia, tachypnea, muscle tremors, colic, urticaria, and anaphylaxis. Plasma should be administered through a blood administration set containing filtration devices (Fig 4).

Whole blood. Whole blood may be indicated as the colloid of choice in cases of hemorrhagic shock. Complications of blood transfusions include reactions associated with incompatible red blood cells, and/or plasma antibodies, as well as those associated with transfer of leukocytes. Citrate toxicity and hypocalcemia are other potential side effects. Donor animals should be screened for blood-borne diseases. Autotransfusion of fresh blood from body cavities can be performed if it is sterile. This source of blood does not contain active platelets or clotting factors. Coagulopathies from red blood cell fragmentation are

Fig 4. Plasma administration set.

potential complications. The blood collected for autotransfusion should be anticoagulated and filtered. Whole blood is not a concentrated source of colloid, thereby requiring potentially large volumes when used primarily for colloid support. Red blood cells do not exert oncotic pressure, and therefore packed red blood cells do not offer an advantage over whole blood from a colloid standpoint. Whole blood should not be administered through the same lines as calcium containing fluids, and fluids such as Normosol-R (Abbott Laboratories, North Chicago, IL) or Plasma-Lyte 148 (Baxter Health care Corporation, Deerfield, IL) should be used instead.

Synthetic Colloids

Hydroxyethyl starch (hetastarch). Hetastarch is the most commonly used colloid in adult horses. It is produced by chemical modification of the starch amylopectin, through hydrolysis and hydroxyethyl substitution, and is a modified branched-chain glucose polymer. It is available as a 6% aqueous solution in saline (Abbott Laboratories, North Chicago, IL) or lactated electrolyte solution (Hextend, Abbott Laboratories). The weight average MW of hetastarch is 450,000 to 480,000, with 80% of molecules having a MW between 30,000 and 2,000,000 Dalton. The number average MW is 69,000. Sixty to seventy percent of the starch molecules in hetastarch are substituted with a hydroxyethyl group. The COP of hetastarch is 30 mm Hg, making it a more cost-effective colloid than plasma. The primary side effect associated with hetastarch administration is an induction of coagulopathies associated with reductions in factor VIII and von Willebrand's factor. Hypersensitivity reactions are rarely reported. Unlike dextrans, hetastarch does not interfere with blood typing or cross matching. Hetastarch molecules smaller than 72,000 Dalton (renal threshold) are excreted unchanged in the urine.[3] Larger molecules are hydrolyzed by plasma and tissue α-amylases or are metabolized by the reticuloendothelial (RE) system. Those molecules that escape into the interstitium are absorbed into lymph. The elimination of hetastarch thus has two phases, the first being associated with plasma loss through urinary excretion and redistribution to the interstitium, and the second consisting of degradation by the RE cells over days to weeks.[3]

The kinetics of hetastarch have been described in horses.[3] The oncotic, hemodilutional, and hemostatic effects of hetastarch in clinically normal ponies have also been reported.[1] Ponies were administered 10 mL/kg or 20 mL/kg hetastarch. Hetastarch exhibited dose-dependent hemodilutional and hemostatic effects. Colloid osmotic pressure was increased above baseline for up to 5 days postadministration. A trend toward prolongation of bleeding time was noted in the ponies receiving 20 mL/kg of hetastarch, leading to a fourfold increase over baseline values at 48 hour postinfusion.[1] Plasma factor VIII activity was reduced for up to 72 hour and 120 hour after infusion in the groups administered 10 and 20 mL/kg of hetastarch, respectively. Activity of von Willebrand factor (vWf) antigen was decreased for up to 120 hours. Platelet counts decreased for 48 hours in the 20 mL/kg group, and this was speculated to result from hemodilution similar to what occurs in dogs and people. Coagulation times (PT and PTT) were not prolonged. The exact mechanism of von Willebrand factor decrease is unknown, but the reductions are greater than that expected from hemodilution. It is speculated that hetastarch may bind to von Willebrand factor and factor VIII:C. Some of the reduction of factor VIII may also be related to the role of vWf as a carrier protein. In this study of healthy ponies, hetastarch induced a dose-dependent drop of PCV and total protein concentrations. This drop in hematocrit was consistent with another study, where values were below baseline for up to 24 hour after administration.[3] This decrease in hematocrit results from the volume expanding effects of hetastarch. Fibrinogen concentrations also decrease.[2] A second study found a significant prolongation of PTT 1-hour post infusion of 15 mL/kg, but not after 10 mL/kg of hetastarch in normal horses.[24] Partial thromboplastin times (PTT) were also prolonged in normovolemic anemic ponies that were administered 15 mL/kg

of hetastarch.[24] A dose of 8 mL/kg did not alter PT or PTT in another group of normal horses.[3] Based on these findings, a dose of 10 mL/kg/d should not be exceeded to avoid iatrogenic coagulopathies. In human patients, hetastarch reduces clot strength because of impaired fibrinogen polymerization.[25] Desmopressin (DDAVP) reverses the decrease of factor VIII:C associated with hetastarch administration in human patients, although this remains to be studied in horses.[26] In general, hetastarch is considered safer than dextrans, with fewer anaphylactoid, bleeding, and renal side effects.[27]

In a study evaluating the effects of hydroxyethyl starch in hypoproteinemic horses with gastrointestinal disease, hetastarch (8 to 10 mL/kg) resulted in an increase in COP for 24 hour after administration.[1,2] Oncotic pressure was elevated above baseline for approximately 6 hours, but was raised in the face of decreasing total protein and albumin above expected COP (as calculated using albumin and globulin concentrations) for up to 24 hours.[1]

Recommended doses of hetastarch based on these studies are 8 to 10 mL/kg/d.[1,3] This volume can be administered as a bolus in hypovolemic animals, or alternatively as a slow infusion for colloid support in hypooncotic animals. Until further research is available, larger doses of hetastarch should be used with caution, particularly in animals undergoing surgery.

Pentastarch. Pentastarch (DuPont Critical Care, McGaw, IL) is a narrow-range, medium molecular weight derivative of hetastarch. It may become available for veterinary use in the future. It is an analog of hetastarch with less hydroxyethyl substitution (40 to 50% of its starch molecules). Pentastarch has a more rapid and predictable excretion pattern than hetastarch. The COP of pentastarch is 40 mm Hg. Its weight average MW is lower than that of hetastarch, being 264,000 to 280,000 D. The number average MW of pentastarch is higher than hetastarch, however (120,000 D). This makes it more homogenous than hetastarch in terms of size, excluding very small or large molecules. Advantages over hetastarch include fewer side effects on the coagulation and RE systems.[27,28] Because of its molecular weight range, pentastarch may be indicated for use in patients with increased capillary permeability associated with the syndrome of multiple organ failure. Pentastarch shows promise for use in capillary leak syndromes, as it should be retained within the circulation to a greater extent than hetastarch and may aid in plugging leaky capillaries.[29] Fractions of colloids with molecular weights between 100 and 1000 kd may represent the ideal size for sealing of widened endothelial cell gap junctions. Smaller MW molecules may potentiate third space accumulation of fluid, while larger molecules may interfere with sealing.[30] Another advantage of pentastarch is its potential for larger volume expansion as compared with hetastarch.

Dextrans. Dextrans are long glucose polymers produced from sucrose by the bacterium *Leuconostoc mesenteroides*. The average MW of dextran 70 is approximately 70,000, with 80% of the molecules falling between 20,000 and 200,000 D. The number average molecular weight is approximately 39,000. Dextran 70 is available as a 6% solution (6% Gentran 70, Baxter Health care Corp., Deerfield, IL) with a COP near 60 mm Hg. The higher colloid oncotic pressure of dextran 70 compared with hetastarch is because of a greater number of smaller molecular weight molecules. This number can be misleading, as smaller molecules are more rapidly eliminated, and thus, the initially greater blood volume increase is short-lived and not clinically significant. It is the number of larger molecules remaining that ultimately determines the sustained volume expansion effect of colloids, and this is very similar for both dextran 70 and hetastarch. In fact, hetastarch has a larger molecular size and may have a slightly longer duration of action than dextran 70.

Dextran 70 is associated with a higher rate of complications than hetastarch. Allergic reactions and coagulation disturbances appear to be more common.[27] As with hetastarch, the coagulopathy associated with the use of dextrans is dose-related. This has been attributed to the coating of platelets, inhibition of platelet, neutrophil and erythrocyte aggregation, clotting factor dilution, and decreased von Willebrand's factor and factor VIII activity. Template bleeding times may increase. These effects on bleeding are greater than those caused by hetastarch. Dextrans also cause a greater reduction in viscosity, making them better antithrombotic agents, but less useful in hypocoagulable patients. Dextrans interfere with crossmatching of blood products because of adherence to red cell membranes and clumping of erythrocytes.

Dextran molecules smaller than 20,000 D are renally excreted, while larger particles are degraded by reticuloendothelial cells. As with hetastarch, this occupation of RE cells may reduce the ability of that system to remove other toxic particles from the bloodstream. Dextran 40 should be used with caution, as its colloids have a shorter duration of action and it is associated with renal failure in other species. Dextrans should be used with caution in pregnant mares, as rare fetal deaths have occurred when used in pregnant women.[27]

Dextran 70 has been conjugated to polymyxin for prolongation of the half-life and limitation of the side effects associated with polymyxin administration in horses.[31] Side effects of this combination product included transient tachypnea, sweating, and increased plasma TXB_2 concentrations, all of which were prevented by prior administration of ketoprofen.[31] In this study, control horses received 6.6 g of dextran 70/kg (approximately 11 mL/kg of 6% dextran 70) with no mention of side effects in this group. Dextran 70 has also been combined with hypertonic saline (25%) for use as a volume expander in horses experimentally.[32] Side effects in this study included severe hemolysis and hemoglobinuria in 3/7 horses, likely associated with the marked hyperosmolarity induced by the product.[32] In vitro experimentation confirmed dextran 70-induced inhibition of equine platelet aggregation in response to platelet-activating factor.[33] Early clinical reports of the use of dextran 70 in horses included treatment of suspected verminous arteritis and diarrhea. It was used as an antithrombotic agent in these papers. Side effects included muscle fasciculations, swaying of the hind quarters, tachycardia and collapse in 8/64 horses.[34,35] Doses used in these reports were 1 to 3 mL/kg of dextran 70 (6% dextran 70 in 5% dextrose).

Hemoglobin-based products. Oxyglobin (Biopure, Cambridge, MA) contains polymerized bovine hemoglobin and is labeled for use in dogs. The hemoglobin in this product is sterile and ultrapurified, and the polymerization prolongs its half-life by slowing renal excretion. Transfusion reactions are unlikely because it is stroma-free and lacks erythrocyte membranes, and therefore, does not require cross matching or blood typing. It provides for oxygen carrying capacity in plasma, an advantage for treating anemia and hemorrhagic shock. It decreases blood viscosity that also aids in improving tissue perfusion. Oxyglobin also provides a colloid effect (42.6 ± 0.9 mm

Hg).[36] The shelf life of the product is 3 years at room temperature. Oxyglobin (15 mL/kg) was administered to normovolemic anemic ponies. Compared to hetastarch administered to control ponies, oxyglobin resulted in improved hemodynamic parameters, including heart rate and cardiac indices.[37] In this study, one pony (of 6) developed an anaphylactoid reaction, characterized by pruritus, tachycardia, and tachypnea, which resolved with discontinuation of the infusion. Disadvantages of Oxygoblin include discoloration of mucous membranes and body fluids. It also interferes with several biochemical analyses and may diminish the usefulness of monitoring hematocrit or erythrocyte count. Scavenging of nitric oxide by Oxyglobin may result in regional tissue vasoconstriction, a disadvantage that may counteract some of its oxygen carrying benefits. The rate of conversion to methemoglobin in horses also needs further study. Finally, the administration of additional iron to patients with pro-oxidant states may increase the production of reactive oxygen metabolites. Its ability to provide oxygen carrying capacity to plasma is an advantage in low flow and ischemic tissues.

Because of cost, Oxyglobin has received primary clinical use in neonatal foals. Anecdotal reports suggest that a dose of 5 to 7.5 mL/kg may be of benefit to foals with neonatal isoerythrolysis (NI) while awaiting blood transfusion. One case report described the administration of 22 mL/kg of polymerized hemoglobin to a foal with NI.[38] The Oxyglobin treatment maintained oxygen delivery for up to 18 hours before washed red blood cells were administered. Polymerized hemoglobin has been used in a miniature horse with ovarian hemorrhage and in a miniature horse and pony with presumed red maple toxicosis.[39,40] In the latter report 16 and 11 mL/kg of Oxyglobin were administered.

Clinical Applications of Colloid Therapy

Colloids provide several advantages for volume resuscitation of patients experiencing a systemic inflammatory response syndrome (SIRS). They are effective at replacing intravascular deficits rapidly. Small volumes and shorter infusion times are required for volume resuscitation as compared with crystalloids. Other indications for colloids include hypoproteinemia, especially if coupled to hypovolemia. The author attempts to maintain COP above 14 mm Hg when restoring intravascular volume in horses with acute hypoproteinemia.

The author prefers to use a combination of crystalloids and colloids in treating horses with fluid deficits. A combination of plasma and hetastarch offers the advantages of each. Plasma is often administered at a dose of 4 to 8 mL/kg. Hetastarch should be added for additional colloid support at a dose of 10 mL/kg, and can be administered as a bolus (10 mL/kg/h) for volume expanding effects or as a continuous rate infusion of 0.5 to 1 mL/kg/h for continuous colloid support until desired volumes are given. Horses potentially undergoing major surgery (ie, surgical colic) and those with hypocoagulable states (such as von Willebrand's syndrome or thrombocytopenia) should not be administered hetastarch. However, horses with hypercoagulable syndromes, such as disseminated intravascular coagulation, may benefit from hetastarch administration. Caution should be utilized when using colloids in horses with severe capillary leak states, such as acute respiratory distress syndromes, because colloids could exacerbate edema if they cross compromised endothelial barriers. Judicious use is also prudent in animals at risk for volume overload or elevations in central venous pressure, including horses in heart failure and anuric renal failure.

In general, volume deficits could be replaced with one-third colloid and two-thirds crystalloid to provide for both rapid volume expansion as well as interstitial rehydration. Monitoring of horses on colloid therapy should include measurement of direct COP whenever possible. Though measurement of total protein is useful in monitoring plasma therapy, refractometric readings of total solids will underestimate increases in COP caused by synthetic colloids.[41] (Refractometer reading of total solids in Hetastarch is 3.8 g/dl.) COP will be even further underestimated if chemistry values for total protein are used. Other techniques that aid in monitoring fluid balance should be employed, including measurements of body weight changes, hematocrit, albumin, serum BUN and creatinine, urine output and specific gravity, arterial blood pressure, plasma osmolarity, CVP, blood lactate concentration, thoracic radiography, and echocardiography.

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