Acute hemorrhage, a form of hypovolemic shock, can result from external or internal blood loss. Distinguishing between these two types of hemorrhage is important to rendering proper therapy because cases of controllable hemorrhage must be treated differently than cases of uncontrollable hemorrhage.

**PATHOPHYSIOLOGY OF HEMORRHAGIC SHOCK**

Acute hemorrhage results in hypovolemia and a reduction in oxygen-carrying capacity (hemoglobin). A blood volume loss of 15% to 20% is clinically detectable, while life-threatening circulatory failure occurs with a blood volume loss of 30% to 40%. Compensatory physiologic mechanisms include vasoconstriction, increased cardiac contractility, and tachycardia (activation of the sympathetic nervous system). In addition, the drop in hydrostatic pressure due to hypovolemia causes filtration fraction to diminish and lymphatic flow to increase as a result of sympathetic activation and a reduction in central venous pressure (CVP). These changes result in a net movement of interstitial fluid into the vascular space. Simultaneously, the renin–angiotensin–aldosterone system is activated, resulting in a decreased glomerular filtration rate, decreased urine production and enhanced renal sodium resorption, increased thirst, and vasoconstriction. Vasopressin contributes to vasoconstriction and thirst. These compensatory mechanisms can maintain circulation in cases of mild blood loss (up to a volume loss of 15%). Losses exceeding this amount require volume replacement and are beyond physiologic compensation. If the patient’s condition is left unchecked, shock results from persistent hypoperfusion, leading to cell dysfunction and, ultimately, apoptosis and necrosis.

**CLINICAL SIGNS OF HEMORRHAGIC SHOCK**

Vital signs can be misleading as to the degree of hemorrhage, particularly in young and healthy animals; therefore, monitoring tools are critical in evaluating the bleeding patient. Because of compensatory vasoconstriction and contractility, the heart rate may not reflect the severity of blood loss.

In general, the signs of blood loss reflect hypovolemia, including pale mucous membranes, prolonged capillary refill time, progressive deterioration of mental status, tachypnea, hypothermia, poor pulse quality (narrow pulse pressure), and cool extremities. Tachycardia often does not develop until severe loss has occurred. Colic, sweating, and ileus may also occur in horses with significant blood loss.

**MONITORING TOOLS**

Because a physical examination can underestimate the quantity of blood lost, monitoring tools should be used to enhance the sensitivity of detecting clinically significant hemorrhage. The hematocrit and total protein concentration are poorly correlated with blood volume deficits in acute hemorrhage because it takes several hours (>8 to 12) for fluid redistribution to occur and for the renin–angiotensin–aldosterone system to affect
the hematocrit. Decreased systolic blood pressure (<100 mm Hg in adult horses) and fluid responsiveness are consistent with hypovolemia due to blood loss. Laboratory data can be particularly useful as well. Markers of significant blood loss include decreased blood pH, increased base deficit, increased lactate, and decreased mixed venous (or estimated by central venous) oxygen tension. Coagulopathies with increased prothrombin time and partial thromboplastin time can develop. In humans, the combination of progressive metabolic acidosis, coagulopathy, and hypothermia are considered “the lethal triad,” which precedes circulatory failure in patients with blood loss. With currently available diagnostic tests, most of this monitoring can be performed stall-side. Indirect blood pressure and portable blood gas analyzers (e.g., i-STAT handheld clinical analyzer [Heska, Loveland, CO]) are practical means of obtaining these data (see the box on this page).

In an experimental model of modest blood loss in horses, CVP decreased and blood lactate concentration increased significantly before the heart rate changed. Normal CVP in adult horses is 5 to 15 cm H$_2$O, and after 16 ml/kg of blood loss, CVP values decreased to ~4 to 5 cm H$_2$O. Lactate increased from 0.7 ± 0.2 mmol/L (range: 0.4 to 1.1) to 2.2 ± 1 mmol/L (0.5 to 6.7).

**TREATMENT**

Therapy for hemorrhage consists of the following:

- Providing hemostasis when possible
- Increasing cardiac output with fluid resuscitation
- Increasing oxygen-carrying capacity by providing hemoglobin in the form of blood products

**Hemostasis**

Controllable hemorrhage can be stopped by ligation of vessels, cautery, pressure bandages, manual pressure, the application of topical procoagulants (“fibrin sealants” [e.g., thrombin, fibrin]), or a combination of these therapies. After cessation of bleeding, fluid resuscitation is the primary aim in treating affected horses.

**Fluid Resuscitation Strategy**

Therapy of acute blood loss depends on the form of hemorrhage. The treatment goals for uncontrolled hemorrhage (e.g., intraabdominal, uterine arterial, or pulmonary hemorrhage) are very different than those for controllable hemorrhage. Whereas normalizing blood pressure (through increasing cardiac output) is the goal in treating controlled hemorrhage, hypotensive resuscitation is the approach used when managing uncontrolled hemorrhage. With hypotensive resuscitation, the goal is to maintain a minimal mean arterial blood pressure to ensure end-organ perfusion without potentiating blood loss. Normalization of blood pressure should be avoided to prevent worsening of hemorrhage. The optimal blood pressure target for this type of resuscitation is unknown in horses; however, a mean blood pressure of 60 mm Hg is a reasonable goal. On the other hand, controlled (ligated or stopped) hemorrhage is treated more aggressively with fluids, with the goal of normalizing perfusion (see the box on page 82).

Several types of resuscitation fluid used to treat acute hemorrhagic shock, including isotonic crystalloids, synthetic and natural colloids, and blood products, are discussed in the following sections.

**Fluid Management of Controlled Hemorrhage**

Acute blood loss results in loss of cardiac output and hemoglobin—two components in the oxygen uptake and delivery equations (see the box on page 84). Each of these is corrected using distinct strategies. The consequences of a low cardiac output are more life-threatening than those of anemia; therefore, the primary initial aim in treating controlled hemorrhage is rapid restoration of cardiac output through increasing preload.
Fluid Choices Available for Controlled Versus Uncontrolled Hemorrhage

**Goal in treating controlled hemorrhage**
Rapid normalization of blood pressure and cardiac output

**Fluid choices**
- Early in the course of hemorrhage (during hypovolemic shock) for rapid administration of fluids
  - Isotonic crystalloids
  - Hypertonic saline
  - Colloids
- Later in the course of hemorrhage (after volume has been replaced)
  - Isotonic crystalloids
  - Plasma for correction of hypoproteinemia or clotting factor deficiency
  - Whole blood for correction of anemia or thrombocytopenia
  - Packed RBCs for correction of anemia

**Goal in treating uncontrolled hemorrhage**
Maintenance of organ perfusion with a minimal mean arterial pressure of approximately 60 mm Hg (or maintenance of urine output) through slow administration of fluids

**Fluid choices**
- Whole blood
- Packed RBCs plus plasma or isotonic crystalloids
- Plasma (slow administration, not bolus)
- Isotonic crystalloids

with fluid administration. Because of the viscosity effects of erythrocytes, blood products (whole blood, packed red blood cells [RBCs]) may not be the preferred fluids for early volume resuscitation in acute blood loss when rapid augmentation of cardiac output is the goal. Erythrocyte-containing fluids are the only resuscitation fluids with a viscosity higher than that of water; therefore, whole blood flows less rapidly than cell-free fluids, and packed RBCs have the slowest infusion rate of any fluid. Therefore, these blood products are used only after the initial volume expansion in order to achieve the second goal in treating acute hemorrhage: increases in hemoglobin concentration and oxygen-carrying capacity. With definite control of hemorrhage, the goals of resuscitation can be achieved by titrated administration of fluids until the following parameters are met: normalization of vital signs and restoration of microcirculation as indicated by normalization of blood pH (7.4), lactate (<2 mmol/L), mixed (or estimated from central) venous oxygen tension (normal partial pressure of central venous oxygen [PcvO₂] in horses is 32.3 ± 1.2 mm Hg [range: 27.4 to 36.2]), and urine output. Urine output can be measured through the use of indwelling urinary catheters. Mares are easily instrumented with a 24- to 28-Fr Foley catheter, while males can either be catheterized with a stallion urinary catheter or have a collection harness placed (with the collection bucket near the sheath). Alternatively, urine output can be estimated through urination frequency and spot checks of urine volume with intermittent collection of urine into a bucket. Cardiac output can also be measured directly in horses in advanced monitoring settings through the use of lithium dilution or placement of a pulmonary arterial catheter. Once initial volume has been restored, blood products should be administered until the hematocrit is greater than 15% to 20% and the platelet count is greater than 50,000/µl.

**Fluid Management of Uncontrolled Hemorrhage**

Fluid therapy should be conservative when hemorrhage is ongoing and uncontrollable. This approach is called hypotensive resuscitation. Vigorous fluid administration can increase the rate of bleeding from damaged vessels and counter local vasoconstriction. It can also dilute clotting factors and platelets and exert pressure on fragile clots. In these cases, as might occur with intraabdominal or intrathoracic hemorrhage, rapid plasma expanders, such as artificial colloids and hypertonic saline, should be used judiciously or avoided altogether. Instead, whole blood, plasma, or isotonic crystalloids should be administered at a conservative rate that is individualized to the patient to maintain organ perfusion. Adequate minimal organ perfusion is indicated by the production of urine and prevention of rises in serum creatinine concentration. A starting point for administration of crystalloids should be between 1 and 1.5 times maintenance requirements (the maintenance fluid requirement for adult horses is 1.5 to 3 ml/kg/hr). Goals for hypotensive resuscitation include a mean arterial pressure of 60 mm Hg, blood lactate concentration less than 4 mmol/L, blood pH greater than 7.25, and maintenance of urine production (see preceding section). Serial monitoring of plasma creatinine is important in these patients.
Types of Fluids

Crystalloids: The importance of isotonicity when using crystalloid fluids in treating shock lies in the physiology of fluid distribution. Isotonic fluid distribution is limited to the extracellular fluid (ECF) compartment. Because acute hemorrhage primarily results in losses from the ECF compartment, isotonic fluids are desirable to reverse signs of shock. Fluids that are isotonic in vivo, including Normosol R (Abbott Laboratories, North Chicago, IL), PlasmaLyte 148 and PlasmaLyte A (Baxter Healthcare Corporation, Deerfield, IL), lactated Ringer’s solution, and 0.9% saline, are preferable because they are more effective blood and interstitial volume expanders. Hypotonic fluids, including Normosol M (Abbott Laboratories, North Chicago, IL), PlasmaLyte 56 (Baxter Healthcare Corporation, Deerfield, IL), and fluids that are hypotonic in vivo (0.45% saline/2.5% dextrose and 5% dextrose in water), distribute to all fluid compartments, including the intracellular fluid compartment, and are, therefore, inappropriate.

A potential advantage of using isotonic fluids is rehydration of the interstitial volume, including the transcellular space, because replacement crystalloids distribute according to volume among the subcompartments of the ECF, plasma volume, and interstitium as governed by Starling’s forces. Therefore, approximately three-fourths or more of the fluid volume of isotonic fluids is distributed to the interstitium, and only the balance (20% to 25%) remains in the plasma within 60 minutes after administration. This is also a potential drawback because approximately three to four times the volume of lost blood must be infused as crystalloid fluid to restore plasma volume.

Colloids are solutions containing large molecular weight compounds, such as proteins and polysaccharides, that are not freely diffusible across the endothelium under normal circumstances, in contrast to crystalloids. Natural colloids include plasma and blood products (see “Blood and plasma products,” p. 86), and synthetics include hetastarch and dextran products. A potential advantage of colloids is that they are more efficient plasma volume expanders and are, therefore, more effective than whole blood or crystalloid fluids for increasing cardiac output. Synthetic colloids are the most effective plasma expanders on a volume-to-volume basis. Theoretically, the blood volume expansion is greater than the volume infused because the rise in colloid osmotic pressure produced causes additional fluid to move into the vascular space from the interstitium. In reality, approximately 50% to 75% of the infused volume of synthetic colloids increases the blood volume, which is significantly more than that attainable by using crystalloids. A potential inherent disadvantage of using colloids, in contrast to using isotonic crystalloids, is that interstitial losses are not replaced. These potential advantages and disadvantages highlight the complementary nature of crystalloids and colloids and explain why they are commonly used together.

The volume of synthetic colloids that can be administered is limited by side effects, including coagulopathies and hypersensitivity reactions, which are more common with the use of dextrans than with hetastarch products. Therefore, hetastarch products (6% Hetastarch [Abbott Laboratories, North Chicago, IL; hetastarch in normal saline] or 6% Hextend [Abbott Laboratories, North Chicago, IL; hetastarch in a lactated electrolyte solution]) are recommended. To avoid hemostatic complications, the safe upper limit of the dose is 10 ml/kg/day.

Goals in Treating Acute Blood Loss

\[ \text{VO}_2 = Q \times \text{Hb} \times 13.4 \times (\text{SaO}_2 – \text{SvO}_2) \]

• Cardiac output (Q) is increased by optimizing preload through fluid volume loading.
  — For controlled hemorrhage, this should occur rapidly through aggressive fluid administration.
  — For uncontrolled hemorrhage, this process should occur more slowly, with increasing cardiac output to the point that arterial blood pressure can be maintained at approximately 60 mm Hg or that blood pressure maintains organ perfusion as indicated by urine output.

• The hemoglobin (Hb) concentration is increased by providing blood products.
  — For controlled hemorrhage, this should occur after the initial rapid bolus of crystalloids is given to immediately increase cardiac output.
  — For uncontrolled hemorrhage, blood products can be used as the initial administered fluid (slower administration should be used, with the goal of maintaining lower but organ-perfusing blood pressure).
Hypertonic saline is commonly administered as a 7% to 7.5% solution. It has many advantages in treating acute hemorrhagic shock patients with controlled hemorrhage, but its use in horses with uncontrolled hemorrhage is limited due to its rapid volume-expanding effects. Hypertonic saline has additional hemodynamic and immunomodulatory effects: it reduces endothelial and erythrocyte edema, results in vasodilation, and has positive inotropic, anti-inflammatory, antioxidant, and antiapoptotic properties. Like the colloids, it rapidly expands plasma volume (by two to three times the volume infused) as it osmotically draws water into the intravascular space from the interstitium and, ultimately, the intracellular fluid; however, this effect is short lived and limited. The dose of hypertonic saline is 2 to 4 mL/kg once.

**Blood and plasma products:** Plasma transfusions have the advantages of synthetic colloid administration (as discussed above) as well as provide albumin and clotting factors; however, the oncotic pressure of plasma is less than that of synthetic colloids. Fresh plasma contains platelets in addition to clotting factors. Fresh-frozen plasma (collected and frozen without refrigeration and within 6 hours of harvesting) that is used within 1 year of freezing contains all the clotting factors. Frozen, stored plasma (>1 year) contains stable clotting factors, including factors II, VII, IX, and X; proteins S and C; and antithrombin. Labile factors (factors V and VIII as well as von Willebrand’s factor) are lost over time with storage.

When erythrocytes are required to increase oxygen-carrying capacity, whole blood or packed erythrocytes should be administered. Packed erythrocytes are indicated when the need for erythrocytes outweighs the requirement for large volumes of fluids, as in patients with uncontrolled hemorrhage. In patients with controlled or stopped bleeding, whole blood offers the advantage of replacing lost proteins and platelets (if plastic containers are used rather than glass).

Whole blood and packed erythrocytes are relatively ineffective in promoting cardiac output because of increased viscosity due to the presence of cells; therefore, because augmentation of cardiac output is the first priority in the management of acute controlled hemorrhage, blood is not the fluid of choice for early volume resuscitation in acute blood loss. However, these fluids are ideal in treating anemia or hemostatic abnormalities in the later stages (once initial volume resuscitation is complete) of controlled hemorrhage as well as in treating uncontrolled hemorrhage when modest hypotension is the goal.

Polymerized bovine hemoglobin (Oxyglobin, Biopure [Cambridge, MA]) was an oxygen-carrying product that was labeled for use in dogs. It was described in a few case reports as a treatment for acute blood loss in horses; however, it is no longer commercially available.

After volume deficits are replaced and cardiac output is restored in a patient with controlled hemorrhage, correction of deficits in the oxygen-carrying capacity of blood is addressed through blood administration. For a patient with ongoing blood loss (uncontrolled hemorrhage), whole blood can be used for concurrent slower correction of cardiac output and oxygen-carrying capacity.

### Key Points

- The two distinct goals in treating acute blood loss are (1) correct cardiac output and (2) replace hemoglobin.
- Acute blood loss is treated slightly differently, depending on whether the hemorrhage is controllable or uncontrolled (ongoing).
- For controlled hemorrhage, the goals of therapy are, first, to increase cardiac output through the rapid administration of fluids, with a secondary goal of restoring hemoglobin concentrations through the use of blood products, such as whole blood or packed red blood cells.
- For uncontrolled hemorrhage, the goals are maintenance of organ perfusion without complete normalization of blood pressure to avoid potentiation of ongoing hemorrhage.
- For controlled hemorrhage, the initial fluid bolus should consist of isotonic or hypertonic crystalloids and/or colloids, with concurrent or subsequent administration of whole blood or packed red blood cells for restoration of oxygen-carrying capacity.
- For uncontrolled hemorrhage, cardiac output is restored more slowly, through the administration of whole blood and/or isotonic crystalloids. Boluses of hypertonic saline or colloids should be avoided to prevent rapid rises in blood pressure and further potentiation of bleeding.

### Blood Transfusions

Deciding the need for blood transfusion can be difficult in horses, and there are currently no consensus guidelines as to transfusion triggers in this species. In humans, these triggers include hematocrit, lactate, and oxygen-extraction ratio:

\[
\text{Oxygen extraction} (\%) = \frac{(\text{Arterial oxygen saturation} - \text{Central venous oxygen saturation})}{\text{Arterial oxygen saturation}} \times \frac{\text{ScvO}_2}{\text{SaO}_2}
\]
SaO₂ can be monitored with a pulse oximeter or with arterial blood gas analysis, whereas ScvO₂ is measured with central venous blood gas analysis. Central venous samples can easily be obtained by using 20- to 30-cm jugular catheters in foals or 50-cm catheters in adult horses.

An oxygen-extraction ratio of 50% is used as an indication for blood transfusion because it represents the maximum extraction compensation for a decrease in oxygen delivery. In the volume-resuscitated patient, an oxygen-extraction ratio of 50% or greater indicates tissue dysoxia or a state of oxygen-limited energy production (a normal oxygen-extraction ratio is approximately 25%). Hematocrit has lost favor as a trigger because of the pitfalls of using it in acute periods of hemorrhage. In addition, even in a normovolemic patient, hematocrit gives no information about the adequacy of tissue oxygenation. However, a hematocrit under 12% is below a critical level of oxygen-carrying capacity and warrants blood administration.

In horses, some suggested but not definitive guidelines for transfusion triggers include a hematocrit less than 12%, an acute blood volume loss of 30% to 40%, a lactate concentration greater than 4 mmol/L (or >2 mmol/L in the presence of fluid resuscitation), persistent hypotension despite adequate fluid loading, and uncontrolled hemorrhage.

How to perform blood transfusions: Donor horses should be blood typed and tested for antierythrocyte antibodies. The best donors to maintain in practice are geldings that are Aa and Qa negative and that lack antierythrocyte antibodies. In addition, they should be free of blood-borne pathogens, such as equine viral arteritis and equine infectious anemia. Up to 15 to 18 ml/kg of blood (20% of blood volume) can be safely harvested each time from the blood donor; although generally safe, this degree of volume loss is clinically detectable in terms of mild tachycardia and agitation and warrants administration of 5 to 10 L of isotonic crystalloid to the blood donor if these signs are present. Crossmatching (both major and minor) should be performed when possible. However, initial transfusions in horses are rarely associated with reactions because naturally occurring antibodies are rare. If a transfusion is incompatible, antibodies against foreign erythrocytes will develop within 5 to 14 days.

To prevent inactivation of platelets, blood should be collected into plastic blood collection bags rather than glass bottles. The optimal anticoagulant for blood storage may be citrate phosphate dextrose adenine, although acid citrate dextrose and heparin may also be used, particularly when using fresh, whole blood in an emergency setting where storage is not an issue. The amount of whole blood administered to horses with blood loss is often 30% to 40% of the estimated volume of lost blood because this is adequate in most cases when used in conjunction with isotonic fluids. The amount of lost blood can be estimated from the following formula (packed cell volume [PCV] can be used in this formula once blood volume is reestablished with fluid administration or after 8 to 12 hours of compensation):

\[
\text{Liters of blood lost} = \frac{\text{Normal PCV} - \text{Patient PCV}}{\text{Normal PCV}} \times 0.08 \times \frac{\text{Weight (kg)}}{}
\]

As a rule of thumb, if a PCV of 40% is assumed for the donor, 2.2 ml of whole blood per kilogram of patient weight will increase the PCV by approximately 1% in most horses. For example, 1,100 ml of whole blood will raise the PCV from 15% to 16% in a 500-kg (1,100-lb) horse. The rate of administration of blood varies with the patient’s clinical status. For horses with severe hypotension and hemorrhage, blood can be administered as a rapid bolus along with (but not in place of) crystalloids and colloids because the benefits outweigh the risks of reactions. More often, crystalloids and colloids are given as boluses first and then followed with blood administration. When possible, it is advisable to initially administer blood slowly (approximately 0.1 ml/kg over 10 to 15 minutes) to ensure tolerance. After that period, rates of up to 20 to 30 ml/kg/hr can be used. To remove fibrin and debris, plasma filtration sets should be used for blood administration.

Horses with uncontrolled, ongoing hemorrhage benefit most from the administration of fresh, whole blood because it provides not only erythrocytes but also platelets, if the use of glass containers has been avoided. Whole blood can be used as the maintenance fluid for these horses. Once transfused, equine donor cells can survive in the short term (≤4 days in adults; half life of 5.2 ± 1.1 days in foals).

Packed erythrocytes (70% PCV) can be used in horses in which volume restriction is necessary and provision of erythrocytes is the most required component. Packed erythrocytes are prepared from spinning whole blood and removing the plasma supernatant. Physiologic saline is added to achieve a PCV of approximately 70%.

Side effects of blood transfusions include hypersensitive-
Hemostatic Agents

Prophylactic hemostatic agents used in humans include the antifibrinolytic lysine analogues amino-caproic acid and tranexamic acid, aprotinin (a bovine-origin protease inhibitor and direct inhibitor of plasmin), and desmopressin (a synthetic analogue of vasopressin that raises plasma concentrations of factor VIII and von Willebrand’s factor). Recombinant activated factor VII is used prophylactically and therapeutically for severe hemorrhage in humans. Thrombotic complications are potential side effects of these drugs.

Of these hemostatic agents, only aminocaproic acid has been evaluated in horses. One of these studies suggested the use of a loading dose of 3.5 mg/kg/min IV over 15 minutes, followed by a constant-rate infusion of 0.25 mg/kg/min for 4 to 6 hours based on computer simulation of the pharmacokinetics. The safety and efficacy of this medication have not been established in horses. Formalin has been advocated by some clinicians as an adjunctive treatment for uncontrolled hemorrhage. A study of healthy horses showed that doses of formalin that do not induce adverse reactions did not have a detectable effect on measured hemostatic variables. Infusion of higher doses of formaldehyde resulted in muscle fasciculations, tachycardia, tachypnea, ocular and nasal discharge, agitation, and restlessness. Conjugated estrogens have been used by equine clinicians to promote coagulation in hemorrhaging horses; however, I am not aware of controlled studies of their efficacy for this purpose in horses.

CONCLUSION

Current treatment of acute, severe hemorrhage includes rapid and definitive control of hemorrhage, if possible; restoration of tissue perfusion and hemostasis; and maintenance of blood composition. Treatment should depend on early evidence of tissue malperfusion, including a high lactate concentration, low blood pH, and high base deficit, rather than solely on physical examination findings. Horses with controlled hemorrhage should have cardiac output corrected as a priority through the use of rapid administration of crystalloids and colloids. Anemia can be corrected afterward through the use of blood products. Animals with uncontrolled hemorrhage are administered whole blood and fluids at a slower rate—just enough to maintain organ function.

REFERENCES