Anesthetic and medical management of acute hemorrhage during surgery

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One of the biggest challenges faced by anesthetists is the patient that suffers massive perioperative hemorrhage. Many surgeries such as excision of large tumors, maxillectomies and mandibulectomies, limb amputations, and nasal or sinus operations entail a risk of substantial blood loss. By foreseeing this risk, preparing appropriately, and knowing how to react in the actual crisis, the anesthetist may be able to not only protect the patient from life-threatening harm, but also to minimize stress incurred by the personnel involved in the procedure, while the surgeon works to control the hemorrhage.

Animals scheduled for surgery in which the potential for substantial hemorrhage exists should have an IV catheter (or 2) placed and secured, to facilitate fluid or blood replacement, as well as administration of emergency drugs. It is helpful to use the largest-diameter catheter appropriate for the animal, so that if large volumes of fluid must be given, the flow rate will be as great as possible.1 Whenever possible, arterial blood pressure should be monitored, preferably directly and moment-to-moment via an indwelling arterial catheter and pressure transducer or anaeroid manometer, or alternatively, indirectly (noninvasively) by use of an ultrasonic or oscillometric device. Although palpation of the peripheral pulse may be helpful, it is not an accurate or reliable blood pressure measurement technique, because pulse pressure is the difference between systolic and diastolic blood pressure.

Oxygen delivery to tissues depends on arterial oxygen content, which depends on blood hemoglobin concentration (proportional to hematocrit or PCV) and degree of saturation of hemoglobin with oxygen; and cardiac output, the amount of blood per minute pumped by 1 ventricle. As blood volume decreases, compensatory vasoconstriction helps maintain venous return to the heart and cardiac output, and a gradual shift of interstitial fluid into the vascular compartment attempts to restore blood volume. As hemoglobin concentration and arterial oxygen content decrease during hemorrhage, oxygen delivery is maintained as much as possible through compensatory increases in heart rate and stroke volume that enhance cardiac output.

Severe hemorrhage in conscious animals causes decreases in arterial blood pressure, central venous pressure, and cardiac output, and increased heart rate and systemic vascular resistance.2-4 Signs that indicate substantial blood loss in an anesthetized animal include arterial and central venous hypotension; peripheral vasoconstriction, resulting in pale mucous membranes and prolonged capillary refill time; and apparent increased anesthetic depth (decreased responsiveness), without a change in anesthetic administration. Anesthetized animals do not always respond to hemorrhage with an increase in heart rate.5

Assessing Blood Loss
The first step in managing intraoperative hemorrhage is to quantify or estimate the actual volume of blood that the animal has lost. In all situations, communication between the anesthetist and the surgeon is critical. The surgeon may be able to provide an estimate of blood loss, as well as status reports concerning the rate of ongoing hemorrhage and the prognosis for controlling it. Estimating volumes of puddles of blood on surgical drapes or on the floor is often difficult. A pool of blood covering a 12 X 12-in floor tile is approximately 100 ml. For small animals, in which losses of < 100 ml may be important, counting blood-soaked gauze sponges (4 X 4 in), each of which may contain approximately 5 to 10 ml of blood, depending on their degree of saturation, is helpful. Laparotomy sponges (12 X 12 in, or 30 cm²), moistened with physiologic saline solution before use, may absorb approximately 50 ml of blood, depending on their degree of saturation. An alternative to counting individual sponges is to collect all blood-soaked sponges in a separate trash bag and weigh them. Considering the negligible weight of dry sponges, the weight of the wet sponges may be considered to represent the weight of lost blood, with 1 g approximately equal to 1 ml of blood.

When a suction apparatus is used to aspirate blood and fluids from the surgical site, the fluid in the suction container should be monitored. If the

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Table 1—Reference ranges for blood values used to assess need for treatment of hemorrhage

<table>
<thead>
<tr>
<th>Species</th>
<th>Blood volume* (% of body weight)</th>
<th>PCV* (%)</th>
<th>Plasma total protein* (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine</td>
<td>9</td>
<td>37 to 55</td>
<td>6.0 to 8.0</td>
</tr>
<tr>
<td>Feline</td>
<td>5.6 to 6.7</td>
<td>24 to 45</td>
<td>6.0 to 8.0</td>
</tr>
<tr>
<td>Equine</td>
<td>5.8 to 6.7</td>
<td>32 to 44</td>
<td>NA</td>
</tr>
<tr>
<td>Draft horse</td>
<td>6</td>
<td>24 to 44</td>
<td>NA</td>
</tr>
<tr>
<td>Thoroughbred</td>
<td>10</td>
<td>32 to 42</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Can be calculated as (% of body weight for species) (10 mL/kg) × body weight in kg. NA = not available.

Fusion much earlier. Although surgical control of hemorrhage is paramount, some of the medical means available to treat perioperative hemorrhage are outlined in the following text.

**Treatment with Isotonic Crystalloid Fluids**

After blood loss has been estimated, initial treatment should be directed toward replacing the volume lost from the vascular system. This can be accomplished by administering a balanced electrolyte solution, such as lactated Ringer’s solution, which is similar in ionic composition and osmolarity to extracellular fluid (ECF). Caution is advised when administering fluids with a greater concentration of potassium than in ECF (3 to 5 mEq/L), because potassium has notable effects on cardiac conduction that may be deleterious, especially if potassium is administered rapidly (> 0.5 mEq/kg of body weight·h). A balanced electrolyte solution is given at a dose of 2 to 4 (usually 3) times the blood volume lost, because crystalloid fluids do not contain protein and therefore, rapidly redistribute throughout the entire ECF space. The ECF varies somewhat in different species, but generally comprises about 20 to 30% of the body weight, and includes blood as well as interstitial fluid and body cavity fluids. Because blood normally is approximately 8% of body weight, blood represents about a third of the ECF. Therefore, when crystalloid fluid is administered IV, only about a third of it will remain within the vascular system, while two-thirds will redistribute to other areas of the ECF, usually within about 30 minutes. To offset the loss of 100 ml of blood, approximately 300 ml of isotonic crystalloid fluid must be administered IV. It has been suggested that isotonic fluids can be administered at rates up to 60 to 90 ml/kg·h in the first hour of resuscitation from hypovolemic shock; after one hour, the rate is decreased to 20 ml/kg·h until the animal is stabilized.

Because crystalloid fluid contains neither protein nor cells, hemodilution will result from fluid treatment. Hemodilution means that the blood has an increased fluid content, and consequently contains fewer RBC (and thus a lower oxygen content) and less protein per unit volume. Despite hemodilution, delivery of oxygen to the tissues may be maintained or even enhanced, because of an increase in stroke volume and cardiac output and a decrease in vascular resistance that accompanies the decreased viscosity of diluted blood. As long as the PCV remains at 20% or greater and cardiac output and cardiovascular function are adequate, tissue oxygenation can be maintained.

Dilution of proteins in the blood also must be considered. Albumin is the serum protein most responsible for the oncotic pressure that holds fluid in the vascular system. Insufficient albumin concentration (< 1.5 g/dl) may lead to development of edema, specifically pulmonary edema. Because, in the clinical setting, albumin is more difficult to assay than serum total protein (TP), TP is usually

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Determined How Much Blood an Animal Can Afford to Lose

Two of the primary problems that develop with acute blood loss are loss of the volume necessary to maintain adequate venous return, cardiac output, and tissue perfusion; and loss of hemoglobin necessary for transport of oxygen to tissues. Having some concept of how much blood volume loss can be tolerated by an animal is important, so that if a critical volume of loss is approached, appropriate steps can be initiated. The animal’s normal or expected blood volume should be calculated (Table 1). Blood volume, PCV, and serum total protein concentration vary with species, age, and breed; for instance, Thoroughbred or hot-blooded horses tend to have larger blood volumes and greater PCV than cold-blooded or draft horses have.

Clinical experience suggests that most healthy, anesthetized, adult animals can tolerate loss of 10% of their total blood volume, without any treatment, with minimal effects. A previously healthy, young adult animal, with good cardiovascular function and a normal PCV and serum protein concentration prior to hemorrhage, may be able to tolerate loss of 40 to 50% of its blood, as long as adequate volume replacement is achieved with crystalloid fluids. However, many surgical patients are not healthy and, particularly if anemic or hypoproteinemic, may require special treatment such as blood trans-

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monitored instead. In healthy young adults, albumin usually composes about half of serum proteins, so a TP of at least 3.5 g/dl is considered to provide enough albumin to maintain adequate oncotic pressure.19 However, animals with a low albumin: globulin ratio may be hypoalbuminemic even when TP > 3.5 g/dl. To avoid excessive hemodilution, PCV and TP should be monitored regularly during any intensive fluid treatment.

**Treatment with Hypertonic Saline Solution**

Isotonic crystalloid solutions have an osmolality similar to that of blood plasma, approximately 300 mOsm/kg. Normal isotonic saline solution is 0.9% sodium chloride. In recent years, much information has been published about hypertonic solutions, usually 7 or 7.5% sodium chloride, which have an osmolality of about 2,400 mOsm/kg, or 8 times the osmolality of plasma.20-24 Small doses (4 ml/kg, usually administered over 3 to 5 minutes) of hypertonic saline solutions have been used to resuscitate animals in severe hemorrhagic shock.20 Hypertonic saline solutions temporarily restore mean arterial blood pressure, cardiac output, acid base equilibrium, and mean circulatory filling pressure, partly through an increase in plasma volume by an osmotic fluid shift into the vascular compartment, but also through enhanced myocardial contractility that is possibly mediated by a pulmonary-vagal reflex.21-24 The benefits of hypertonic saline treatment wane after about an hour,24 so further treatment, in the form of more isotonic fluids or blood products, is required in most cases to prevent deterioration of the animal’s hemodynamic function.

The advantages of hypertonic saline over isotonic fluid treatment are that the smaller volume of hypertonic saline solution can be administered more quickly and easily than the larger volume of isotonic fluid can, severe hemodilution is less likely, and cardiovascular function is augmented. In acute intraoperative hemorrhage, hypertonic saline treatment may conveniently be used to provide immediate support, or to bridge the time gap between hemorrhage and later transfusion (eg, when blood for transfusion is not immediately available or when blood cross-matching test results are not yet complete). However, hypertonic saline treatment is only a temporary adjunct to more specific treatment for severe hemorrhage and additional treatment is required. Contraindications for the use of hypertonic saline solutions include hypernatremic hypovolemia (severe dehydration), hypokalemia, and renal shutdown.25

**Indications for Blood Products**

If the extent of blood loss is such that volume replacement with crystalloid fluids will result in excessive hemodilution (PCV < 20% or TP < 3.5 g/dl), treatment with whole blood or blood components may be indicated. Thus, whole blood may be necessary not only for the previously healthy animal that loses 40% of its blood volume acutely during surgery, but also for the anemic and hypoproteinemic animal with a preoperative PCV of 21% and TP of 3.5 g/dl, even though the latter loses only 10% of its blood volume during surgery. Administration of whole blood will help restore oxygen-carrying capacity and oncotic pressure. Return to a normal PCV is usually unnecessary; an optimal PCV for critically ill patients may be 30%.26 and as previously reported, a PCV of 20% will suffice for tissue oxygenation if cardiovascular function is adequate.16,17 Thus, attaining a PCV of approximately 25% is a reasonable goal in most situations. In addition to augmenting oxygen-carrying capacity, fresh whole blood can help supply other essential components such as coagulation factors or platelets. Stored whole blood is a convenient alternative to fresh blood, but has several limitations: stored blood retains less 2,3-diphosphoglycerate, an enzyme that stabilizes deoxyhemoglobin, resulting in decreased release of oxygen to tissues; platelets become essentially nonfunctional after 2 to 3 days of blood storage; and some coagulation factors deteriorate with storage.19 The concentration of 2,3-diphosphoglycerate is restored within hours after blood is transfused into an animal, so when the need for blood can be predicted, transfusion several hours or the day before surgery, to maximize oxygen delivery during the surgical procedure, may be advisable.19

In animals in which PCV < 20% but TP is adequate (after restoration of normovolemia), packed RBC may be used to restore oxygen-carrying capacity. Conversely, if PCV is adequate but TP < 3.5 g/dl, blood plasma may be used to restore blood proteins and intravascular oncotic pressure. If plasma is not available, dextran or hetastarch, synthetic high-molecular-weight substances, may be administered to help temporarily restore intravascular oncotic pressure. The advantages and disadvantages of these substances have been discussed in several reports.19,27-29 Other reports have addressed the specific concerns of blood transfusion, blood component treatment, and transfusion reactions in various species.30-35 Canine36 and feline blood and blood products are commercially available, as is plasma for horses and llamas.37

To calculate the volume of whole blood needed to attain a desired PCV in an animal, either of 2 formulas may be used:

\[
2.2 \text{ ml of whole blood}^* \text{ /kg of body weight} \times \frac{\text{Desired PCV} - \text{Actual PCV}}{\text{Donor blood PCV}} = \text{Recipient blood volume (ml)}
\]

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Animal Blood Bank, PO Box 6211, Vacaville, Calif.
Veterinary Dynamics Inc, PO Box 2406, Chino, Calif.

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A similar formula can be used to determine the volume of plasma required to attain a target TP:

\[
\text{Amount of donor plasma needed (ml)} = \frac{\text{Desired TP} - \text{Actual TP}}{\text{Recipient plasma volume}} \times \frac{\text{Donor TP}}{\text{ml}}
\]

Normal plasma volume is approximately 50 to 60% of total blood volume, or about 5% of body weight.

Blood and its components should be given through a blood administration set with a filter that captures clots and other fragments before they reach the animal. If blood is to be given through a line that has been used to administer a calcium-containing fluid such as lactated Ringer’s solution, flushing the line and catheter with physiologic saline solution before starting blood administration is a good idea, because calcium can initiate coagulation process and cause blood in the line to clot. Hypotonic fluids (5% dextrose in water) or hypertonic fluids (5% dextrose in lactated Ringer’s solution) should not be combined with whole blood or packed RBC, because they may osmotically damage the RBC. Under circumstances of massive intraoperative hemorrhage, in which cardiovascular function is severely compromised and the animal’s life is at stake, the risk of an adverse reaction to transfused blood must sometimes be taken and blood may be administered as rapidly as possible by use of gravity, a pressure bag, a pump, or a large syringe. Blood administration rates up to 22 ml/kg/h in dogs and up to 40 ml/kg/h in cats have been recommended. In less critical situations, it is normally recommended that blood products initially be administered slowly (0.2 ml/kg for the first 30 minutes, then 10 ml/kg/h, until the desired PCV or TP has been achieved), while watching the animal for potential transfusion-related problems such as hypotension, tachycardia, fever, hemolysis, or bleeding diathesis. Urticaria is sometimes seen in response to foreign proteins in transfused blood, but if not accompanied by hypotension or other signs of anaphylaxis, does not necessarily warrant terminating the transfusion.

Besides the risk of transfusion reactions, other complications may arise from rapid administration of stored blood or blood products. These include hypothermia, acidosis, and hypocalcemia that may compromise cardiovascular function or coagulation. Stored refrigerated blood can be warmed before administration, but care should be taken not to exceed body temperature (maximum, 42°C) to avoid damaging cells and proteins. Acidosis can be minimized by using the anticoagulant citrate phosphatex dextrose, instead of acid citrate dextrose; the former is also considered to preserve blood better than does the latter. In animals in which massive blood transfusion is performed (> 50 ml/kg), the negative inotropic and anticoagulant effects of citrates can be counteracted by administering calcium chloride to the animal through a different IV access than that used for blood administration. The suggested dose is 6 ml of 10% calcium chloride per unit of transfused blood,19 1 unit being 450 to 500 ml of blood.

**Other Management of Surgical Patients with Hemorrhage**

Providing a high inspired concentration of oxygen (50 to 100%) to the animal during and after a hemorrhagic crisis is advisable. Saturation of hemoglobin with oxygen depends on the partial pressure of oxygen in arterial blood, and many anesthetized animals or those recovering from anesthesia (especially large animals,40 and in our experience, small animals during and after thoracotomies), have substantial ventilation/perfusion imbalance, which results in lower than expected arterial oxygen tension. Supplemental oxygen will help maximize hemoglobin saturation and therefore, may improve arterial oxygen content and oxygen delivery to tissues. The use of nitrous oxide, which necessitates a decrease in inspired oxygen concentration, is discouraged. In many inhalation anesthetic regimes, essentially 100% oxygen is used as the carrier gas, but the anesthetist should not forget that animals anesthetized with injectable drugs also will benefit from oxygen insufflation. Oxygen supplementation should be continued into the recovery period if the animal is still severely anemic or has cardiovascular compromise.

An important consideration that is often overlooked in the crisis of massive intraoperative hemorrhage is that the animal’s anesthetic depth should be frequently reassessed. With hemorrhage, as vascular volume decreases, cardiac output decreases, resulting in less inhalation anesthetic being removed from the alveoli into the bloodstream; thus, at the same inspired anesthetic concentration, the alveolar anesthetic concentration increases. The brain receives a higher proportion of the reduced cardiac output, so anesthetic depth deepens.41 Because inhalation anesthetics are potent and dose-dependent myocardial depressants, vasodilators, and hypotensive agents,42 reducing the depth of inhalation anesthesia may enable the animal to better tolerate a severe hemorrhagic crisis. Therefore, if an animal hemorrhages severely while under inhalation anesthesia, the vaporizer setting should be decreased or even turned off.

If decreasing anesthetic depth results in the animal responding to surgical stimulation, maintaining surgical anesthesia with alternative, less-depressant drugs should be considered. Some injectable drugs, such as opioids,43 ketamine,44 and neuromuscular blocking agents such as atracurium, are generally less detrimental to cardiovascular function than are inhalation anesthetics. Therefore, many animals may benefit from balanced anesthesia techniques involving minimal amounts of inhalation anesthetics, in combination with opioids or ketamine to supplement analgesia. Neuromuscular blocking drugs may be used to en-
hance relaxation, but they do not provide analgesia. Whatever drugs are given, doses should be minimized, because severe hemorrhage may decrease a given drug’s volume of distribution, and therefore drug concentration in the blood may be increased, resulting in enhanced effects.47

The use of inotropic drugs during a hemorrhagic crisis is controversial; some clinicians think that the potential increase in cardiac output and blood pressure will cause bleeding to worsen. Certainly, the primary treatment for volume depletion should be directed toward controlling the source of hemorrhage and restoring vascular volume with crystalloid fluids, blood or blood components, or a combination of these. However, large-volume fluid replacement is time-consuming, so while replacement is ongoing or if the animal has not responded as expected to the administered fluids, inotropic support is indicated. Dobutamine and epinephrine have each been shown to augment cardiovascular function in halothane- and isoflurane-anesthetized dogs,48,49 even after removal of 40% of the dogs’ circulating blood volume. After hemorrhage, larger dosages of the drugs were needed to effect the desired increases in cardiac output and blood pressure: dobutamine at 5 to 10 \( \mu g/\text{kg-min} \) and epinephrine at 0.3 to 0.5 \( \mu g/\text{kg-min} \). Heart rate was not significantly affected by epinephrine or dobutamine. An ancillary benefit of certain inotropic drugs, such as dobutamine50,51 and ephedrine (dosage, 0.25 mg/kg in dogs),51 may be their ability to induce splenic contraction, with a consequent increase in circulating PCV and therefore, oxygen-carrying capacity. In normovolemic anesthetized horses, dobutamine and dopamine,52 as well as ephedrine,53 have been shown to improve cardiac output and blood pressure, and these drugs also may be beneficial in horses after hemorrhage.

Hypothermia, which tends to reduce metabolic rate and therefore, reduce oxygen requirement, helps protect vital organs from hypoxic damage during periods of reduced oxygen delivery. Children undergoing major cancer surgery are sometimes allowed to cool to a body temperature of 32 \( ^\circ \text{C} \), which decreases their oxygen consumption to about 60% of normal, to better tolerate severe perioperative hemodilution.54 In veterinary patients in which severe intraoperative hemorrhage is not always anticipated, the technique of deliberate hypothermia may not be advisable or even possible, but the tendency of most patients to lose a degree or 2 in body temperature during anesthesia and surgery may be fortuitous. From 37 to 30 \( ^\circ \text{C} \), metabolic oxygen requirement decreases by about 7% per degree \( ^\circ \text{C} \).55 Excessive heat loss should be avoided, however, because ventricular fibrillation and asystole may occur at body temperatures of 21 to 28 \( ^\circ \text{C} \).56

Assessing Response to Treatment

Whatever therapeutic measures are used in a severe hemorrhagic crisis, the response to treatment should be assessed. Periodic analyses of PCV and TP should be performed, and fluid or blood administration should be adjusted as necessary to keep them at or greater than the minimal values of 20% and 3.5 g/dL, respectively. Systemic arterial blood pressure should be monitored, with a goal of maintaining a mean arterial pressure of at least 60 mm of Hg through volume replacement, as well as through inotropic treatment, when indicated. Below this mean pressure, vital organs such as the brain and kidneys cannot autoregulate their blood supply,51 and the frequency of postanesthetic myopathies in horses increases.57,58 When practicable, monitoring of central venous pressure, via a jugular catheter and water manometer, will assist in judging adequacy of volume replacement, with a central venous pressure of 6 to 10 cm of H\(_2\)O indicating sufficient replacement.59 Urine production of at least 2 mL/kg·h indicates that the kidneys are being sufficiently perfused. When available, arterial blood gas analysis also is helpful in determining how well tissues are being supplied with blood; inadequate tissue oxygenation leads to anaerobic metabolism, with resulting metabolic acidosis (decreased pH and bicarbonate concentration and increased base deficit).

Conclusions

Whereas control of perioperative hemorrhage is the surgeon’s domain, vigilance on the part of the anesthetist may prevent a life-threatening hemorrhagic crisis from becoming a life-ending one. This vigilance entails preoperative preparation; assessing blood losses as accurately as possible; appropriate volume replacement with crystalloid fluids or blood components; implementation of other compensatory techniques such as oxygen supplementation, reduction of anesthetic depth, and inotropic treatment; and continual reassessment of the animal’s status throughout anesthesia and into the recovery period.

References

7. Schalm OW, Jain NC, Jain AH, et al. Veterinary hema-


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