Key Points

- Horses that have acutely lost at least 30% of total blood volume require an emergency resuscitation and blood transfusion.
- Percentage blood loss can be estimated based on physical exam parameters.
- In an emergency situation, blood flow from the affected internal carotid artery (ICA) can be reduced by ligation of the ICA or bilateral occlusion of the common carotid artery (CCA).

Guttural pouch mycosis can lead to life-threatening hemorrhage from the ICA, external carotid artery (ECA) or maxillary artery (MA). Definitive treatment consists of arterial occlusion or embolization both distal and proximal to the site of bleeding. However, when there is active, severe hemorrhage, emergency stabilization and resuscitation must be accomplished prior to general anesthesia and surgery.

Assessment of blood loss

One advantage of assessing hemorrhage in cases of guttural pouch mycosis is that the bleeding is seen externally and can therefore (in theory) be estimated. However, there are major limitations to visual estimation of blood loss. In simulated blood loss scenarios, human EMS personnel underestimated blood loss, with only 8% of estimates within 20% of the actual volume. Conversely, emergency department patients significantly overestimated blood loss 70% of the time. Because estimates of blood loss can be inaccurate, shock categories are quite useful for estimating percent blood loss (Table 1). Since the goal of resuscitation is to maintain oxygen delivery above the critical level, animals in Stage III or Stage IV of hemorrhage are in need of immediate resuscitation (Fig 1).

Initial resuscitation

Traditional protocols for treatment of hemorrhagic shock involved large boluses of crystalloid fluids (90ml/kg). When hemorrhage can be readily controlled (e.g. ligation of a lacerated digital artery), large volume fluid resuscitation can be very effective. In cases of uncontrolled hemorrhage (e.g. guttural pouch ICA bleed), large volume resuscitation may have several disadvantages. First, the sudden increase in blood pressure may dislodge the clot, resulting in further bleeding. Second, dilution of blood with crystalloid fluids can produce a coagulopathy due to reduced platelets and clotting factors. Additional concerns include a reduction in plasma viscosity (which may lead to peripheral vasoconstriction and decreased tissue perfusion) and an increase in tissue edema.

Alternative fluid therapy strategies are low-volume resuscitation, delayed resuscitation, permissive hypotension, and resuscitation with larger volumes of blood products. These methods of resuscitation have been investigated in experimental animal models as well as in human clinical trials. Low-volume resuscitation can be performed using hypertonic saline or a hypertonic saline-colloid mixture. This strategy has the advantage of limiting tissue edema, but may still have the risk of dislodging the clot, similar to high-volume crystalloid administration.
From a practical standpoint, hypertonic saline is a mainstay of resuscitation in horses, simply because the smaller volume (2-4 ml/kg bolus) can be delivered quickly. Delayed resuscitation means that the patient is not fluid-resuscitated until hospital admission and definitive treatment. This strategy can be used in patients with a palpable pulse and conscious mentation, and has been shown in some human studies to result in higher survival rates. Hypotensive resuscitation or permissive hypotension involves resuscitating the patient to a mean arterial pressure of approximately 50 mmHg or systolic pressure of 80-90 mmHg rather than aiming for normal blood pressure values. In the short term, this strategy can be successful in maintaining perfusion while not worsening the blood loss.

Experimental and clinical evidence do not point to an ideal resuscitation protocol. Furthermore, controlled clinical trials have not been performed in actively bleeding horses, so the choice of resuscitation plan must be made based on good clinical judgment. For the equine patient with uncontrolled hemorrhage, a reasonable strategy would be to delay resuscitation until hospital admission, and then to employ hypotensive resuscitation until the bleed can be controlled. In experimental models, it has been shown that mild to moderate active hemorrhage may be worsened by aggressive fluid resuscitation. In cases of massive hemorrhage, however, aggressive resuscitation may be life-saving.

**Blood transfusion and response to therapy**

Whole blood transfusion should be considered for any severely bleeding horse that does not respond to initial fluid resuscitation, and for any horse that has acutely lost 30% or more of total blood volume. In addition to the physical exam parameters, laboratory values such as oxygen extraction ratio (OER) and blood lactate concentration may be used to guide the decision to transfuse. Blood lactate concentration, along with central venous pressure, appear to be useful early indicators of hypovolemia. An OER $\geq 50\%$ or a blood lactate $\geq 4$ mmol/L indicate a need for greater oxygen-carrying capacity. In an emergency, a blood transfusion can be given without crossmatching, as long as the patient has not had a previous blood transfusion and has not had a foal. Some horses will have RBC antibodies even without prior history of transfusion, so the transfusion should be given slowly for the first 15 minutes, and the patient should be monitored carefully.

The goal of resuscitation and blood transfusion is to maintain adequate tissue oxygenation. Normalization or improvement of physical exam parameters (heart rate, respiratory rate, mucus membrane appearance, temperature of extremities) indicates a positive response to treatment. In cases of acute hemorrhage, the PCV may not increase in response to blood transfusion since fluid redistributed from the interstitial and intracellular spaces will cause a decrease in PCV. A decrease in blood lactate concentration and a decrease in the oxygen extraction ration are good laboratory indicators of positive response to blood transfusion. Although authors of earlier studies had concluded that the RBC half-life from allogeneic transfusion was only 2-4 days, more recent data based on biotin-labeled RBCs indicates that compatible blood has a half-life of approximately 20 days.

**How do you stop the bleeding in an emergency?**

Retrospective data indicates that the most likely source of a guttural pouch bleed is the ICA; however, bleeding from the ECA/MA only may occur a smaller number of cases, and in some cases, both the ICA and ECA may be affected. Based on the experimental work by Woodie et al, ligation of the ipsilateral CCA will actually increase blood flow (via retrograde
flow) to the ICA. Therefore, ligation of the ICA on the affected side, or ligation of both CCAs is recommended to reduce blood flow through the ICA.

It is not always possible to determine the source of the bleed because the guttural pouch is filled with blood during active hemorrhage. In these cases, temporary occlusion of both CCAs is recommended to slow the bleeding, and hopefully allow a clot to form until further diagnostics can be performed. It is useful to make at least a brief assessment of cranial nerve function, both during the physical exam, and by questioning the owner about signs of dysphagia. Although cranial nerve involvement does not alter the need for surgical embolization of the bleeding vessel, it does change the prognosis and cost of treatment.

Adjunctive medications

There are several medications that can be used to help stabilize the clot or slow bleeding. These medications, which include aminocaproic acid, transexamic acid, formalin, conjugated estrogens, and naloxone, have been reviewed in detail elsewhere. In brief, aminocaproic acid and transexamic acid are synthetic derivatives of lysine and inhibit fibrinolysis by inhibiting plasminogen activation. These medications will not stimulate coagulation, but may help to stabilize the clot once it has formed. The author commonly uses aminocaproic acid at a dose of 40 mg/kg intravenous bolus, followed by 10-20 mg/kg q6 hours.

Formalin has not been shown to alter coagulation in healthy horses, but it is proposed that it may enhance platelet activation in bleeding animals. Conjugated estrogens have been used in human patients, and while the mechanism of action is unknown, it is proposed that these medications decrease antithrombin activity. Naloxone has been used in horses with experimentally-induced hemorrhagic shock, attenuating the decrease in heart rate and blood pressure, likely by antagonizing the effects of endogenous opioids during shock.

References

Table 1: Estimated blood loss (adapted from American College of Surgeons Advance Trauma Life Support (ATLS) Shock Categories)

<table>
<thead>
<tr>
<th>Shock Category</th>
<th>% Blood Loss</th>
<th>Heart Rate</th>
<th>Respiratory Rate</th>
<th>Capillary Refill Time</th>
<th>Blood Pressure</th>
<th>Urine Output</th>
<th>Other Physical Exam Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Up to 15%</td>
<td>Normal to minimal increase</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Possible mild anxiety</td>
</tr>
<tr>
<td>Stage II</td>
<td>15-30%</td>
<td>Increased</td>
<td>Increased</td>
<td>Mildly prolonged</td>
<td>Normal</td>
<td>Mildly decreased</td>
<td>Mild anxiety</td>
</tr>
<tr>
<td>Stage III</td>
<td>30-40%</td>
<td>Moderate to severely increased</td>
<td>Increased</td>
<td>Prolonged</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Altered mentation; cool extremities</td>
</tr>
<tr>
<td>Stage IV</td>
<td>&gt;40%</td>
<td>Severely increased</td>
<td>Increased</td>
<td>Absent, very pale mucous membranes</td>
<td>Severe hypotension</td>
<td>Negligible</td>
<td>Obtunded; cool extremities</td>
</tr>
</tbody>
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Fig 1: The hypothetical relationship of oxygen delivery/consumption with stages of hemorrhage. From Gutierrez et al, 2004.11