

How to perform the diagnosis in a case with anemia ?
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INTRODUCTION

Anaemia is a common clinical sign in horses and is characterized by decreased red blood cell count, decreased packed cell volume (PCV), and, except in cases of hemolysis, decreased hemoglobin below the lower end of the reference range. It can be classified in 3 categories according to its origin: (1) anaemia due to blood loss (hemorrhage), (2) anaemia due to hemolysis (those 2 first categories being of regenerative nature) and (3) anaemia due to an inappropriate erythropoiesis, the latter being of non regenerative nature. In horses, it is not possible to distinguish between regenerative and non regenerative anaemia on the basis of haematology. Only a bone marrow aspiration allows differentiating between those 2 kinds of anaemia. Recognition of clinical signs associated with different types of anaemia is thus essential to identify the cause of anaemia if appropriate management is to be instituted. The most common causes of anemia in horses are shown in Table 1.

In this conference, the diagnosis and treatment of the most common causes of anaemia in horses will be reviewed. Therefore, this approach will be applied on clinical cases on an interactive basis.

ANAEMIA DUE TO BLOOD LOSS (HEMORRHAGE)

Acute hemorrhage

The most common cause of acute hemorrhage is a vascular damage that can be iatrogenic (surgery), traumatic or secondary to a neoplastic, infectious or parasitic disease.

Less commonly, it can be associated with a congenital or acquired coagulopathy, a disseminated intravascular coagulation (DIC) or a thrombocytopenia.

Clinical signs suggestive of an acute hemorrhage include tachycardia, tachypnea, mucous membrane pallor, weakness, cardiovascular collapse, prolonged capillary refill time, decreased jugular filling, oliguria, ileus, reduced peripheral temperature, and symmetric edema. Those signs are obvious only if there is a rapid loss of more than 30 % of the blood volume (i.e. ± 11 L for a 450 kg horse). If blood loss is associated to a coagulopathy, petechiae and ecchymotic hemorrhage, hematoma formation, prolonged bleeding, or frank bleeding can be seen. In cases of external hemorrhage, the blood loss is in most of the cases

easily detected. On the contrary, in cases of internal hemorrhage, the localization of the hemorrhage is more difficult and should be based on a complete clinical examination (including auscultation and percussion) and ultrasonography. In those latter cases, icterus or signs specific of the localization of the hemorrhage (colic, dyspnea, lameness, etc.) can be present.

Within the first 12 to 24 hours after the hemorrhage, its severity can only be evaluated on the basis of the clinical signs or on the volume of the lost blood, because the falls in red blood cell count and in PCV are delayed.

When the hemorrhage is external, after 24 hours all the blood components are lost and there is a redistribution of the blood from the interstitial compartment. The blood analysis shows an anemia and a decrease in the total protein content. When the blood loss is internal (hemothorax or hemoperitoneum), two third of the lost red blood cells return into the circulation within 24 to 72 hours. The last third is phagocytosed or destructed, and the iron and proteins are reused.

To treat an acute hemorrhage, its source should first be controlled and hypovolemia corrected with isotonic electrolyte solution administered massively and rapidly (40 to 80 ml/kg IV). If the bleeding is controlled, small volumes of a hypertonic solution can be used (4ml/kg NaCl 7%). Blood transfusion is recommended if the PCV decreases to less than 12 % over 24 to 48 hours, if there is uncontrolled bleeding, or if there is a poor clinical response to the crystalloid therapy.

Chronic hemorrhage

Chronic hemorrhages can affect all the body systems, but the most commonly affected are the digestive (parasitism, gastrointestinal ulcerations, large intestine infiltrative diseases, neoplasm) and the respiratory (guttural pouch mycosis, ethmoid hematoma, pulmonary abscess, exercise-induced pulmonary hemorrhage, neoplasm) systems. It also sometimes occur secondary to a coagulopathy.

With chronic hemorrhages, anemia is slow to develop because of the simultaneous regenerative response by the bone marrow. Clinical signs are more obscure and appear only when the PCV is lower than 12-15%. Pallor of the mucous membranes, exercise intolerance, and signs of depression are common. Vital signs (heart and respiratory rate) are often normal at rest, but dramatically increase when the horse is submitted to stress. The clinical signs of the disease responsible for the anemia can also be detected.

The therapeutic approach will consist of identifying and treating the underlying cause.

If the horse developed an iron deficiency secondary to the red blood cell loss, iron sulfate can be given 2 mg/kg/j PO.

ANAEMIA DUE TO HEMOLYSIS

It occurs when there is a destruction of the erythrocytes, and when this destruction exceeds the capacity of the bone marrow to compensate this destruction. Clinical signs are icterus, fever, hemoglobinemia and hemoglobinuria. In those cases, the anemia is not associated with a decrease in the total protein content, but is rather associated to an increase in the indirect bilirubin.

Hemolytic anemia most often is the result of an immune-mediated process (equine infectious anemia, neonatal isoerythrolysis, a primary or secondary auto-immune hemolytic anemia), oxidative injury, a parasitic hemolytic anemia, or a microangiopathic anemia (including DIC and acute hepatitis). Some snake's bite and exotoxins (by instance exotoxins produced by some *clostridium*), leptospirosis or the administration hypotonic fluids or of DMSO can also induce a hemolytic anemia.

Equine infectious anemia: induces fever, depression, edema, icterus, petechia, weight loss, anemia and thrombocytopenia. The Coggin's test (a radial immunodiffusion test) is used for diagnosis.

Neonatal isoerythrolysis: The affected foals are normal at birth. Clinical signs appear after 12 to 24 h and include lethargy, decreased suckling reflex, tachycardia, and icterus. The treatment is the following: stop the colostrum if the foal is younger than 36 hours, give preventive antibiotics, nurse the foal, and perform a blood transfusion if necessary (i.e. when PCV<12%)

Primary or secondary auto-immune hemolytic anemia: Primary auto-immune hemolytic anemia is rare. Secondary auto-immune hemolytic anemia is more frequent and can be due to sensitization against a drug (penicillin, phenylbutazone), an infectious agent (virus, bacteria, parasites...) or a neoplasm. The diagnosis is done on the basis of the Coombs' test (however difficult to perform into field practice). If an immune-induced process is suspected, any given drug should be stopped and replaced by other drugs. Corticoids should be given at immune-suppressive doses (by instance dexamethazone 0,05 to 0,2 mg/kg SID to BID), and then progressively reduced depending on the clinical evolution.

Oxydative hemolytic anemia: some oxydative agents (phenothiazine, wild onions, red maple leaves) are able to deteriorate hemoglobin that aggregate and form the Heinz bodies near the

cellular margin of erythrocytes. Severe oxidative damage to the erythrocytes is further characterized by methemoglobinemia, resulting in grey-brown mucous membranes, and chocolate-brown colored blood.

The treatment consists of removing the cause and increasing the diuresis.

Parasitic hemolytic anemia: include by instance babesiosis, theleiriosis and ehrlichiosis.

ANAEMIA DUE TO AN INAPPROPRIATE ERYTHROPOIESIS

It is a non regenerative anemia. Its development is slow because of the long live span of the red blood cells (155 days).

The most common cause is an underlying chronic disease that can be of infectious, inflammatory, or neoplastic origin. The more commonly affected systems are again the respiratory (pneumonia, pleuresia, abscess, neoplasm) and the digestive (peritonitis, abscess, neoplasm) system. Chronic renal insufficiency is rare in the equine species, but when it occurs, it is often associated with an aplastic anemia. Other causes of inappropriate erythropoiesis include a nutritional deficiency, a medullar aplasia, or a medullar disease.

Clinical signs of non regenerative anemia are obscure because the development of the anemia is slow, and the compensatory mechanisms have time to install. They include pallor of the mucous membranes, lethargy and exercise intolerance. There is neither edema nor icterus, excepted if the underlying disease induces those signs.

The treatment should be directed to the primary disease. Palliative transfusion can be considered in the short term to control bleeding episodes.

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Table 1 : Causes of anemia in horses

ANAEMIA DUE TO BLOOD LOSS (HEMORRHAGE)

- Surgery, trauma
- Hemothorax
- Hemoperitoneum
- Epistaxis (guttural pouch mycosis, ethmoid hematoma, pulmonary abscess, exercise-induced pulmonary hemorrhage, neoplasm)
- Intestinal parasitism (strongylosis)
- Ectoparasites
- Gastrointestinal ulcerations
- Neoplasm
- coagulopathy : DIC, thrombocytopenia, vasculitis

ANAEMIA DUE TO HEMOLYSIS

- Immune-mediated : equine infectious anemia, neonatal isoerythrolysis, auto-immune hemolytic anemia, incompatible transfusion
- Exotoxins : Clostridium
- Oxydative agents (phenothiazine, wild onions, red maple leaves)
- *Parasitic hemolytic anemia*: babesiosis, theleiriosis, ehrlichiosis.

ANAEMIA DUE TO AN INAPPROPRIATE ERYTHROPOIESIS

- Chronic infectious, inflammatory or neoplastic disease (pneumonia, pleuresia, peritonitis, abscess, neoplasm, etc.)
- Nutritional deficiency
- Chronic renal insufficiency
- Medullar aplasia
- Medullar disease