May, 1990

Differential Diagnosis of Anemias in Llamas

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DIFFERENTIAL DIAGNOSIS OF ANEMIAS IN LLAMAS

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The llama has numerous unique characteristics of red blood cells and hemopoietic responses. They are well adapted to high altitudes with lower atmospheric oxygen concentrations. The PCV tends to be lower normally than most domestic species but the hemoglobin is normally significantly greater than one-third of the PCV value. The MCHC (39-46 gm/dl) is, therefore higher than other domestic species. The MCV (22-29.5 fl) is much lower than most species.

Llama RBCs are small and oval. The erythrocytes of most domestic animals have MCVs close to the human range and can therefore be accurately counted on most cell counters. Llama, goat and sheep erythrocytes will often be smaller than the lower size threshold of most human-oriented cell counters. These instruments will often grossly underestimate erythrocyte counts in these species. Falsely decreased erythrocyte counts will in turn cause inaccurate MCV and MCH determinations. Coordination with laboratory personnel is essential to obtain accurate measurements.

Reticulocytes are often rare or absent in healthy adult llama hemograms. Reticulocytes are released during responding anemias and can be used as an indicator of regeneration. Though the mature erythrocyte is oval in shape, reticulocytes are typically round. Reticulocytes and nucleated erythrocytes are observed more frequently in neonates than in adult blood films.

These characteristics need to be considered during the evaluation of the anemias in llamas. The PCV is normally low especially in neonates. The PCV may increase slowly in response to anemia. Depending on the cause of the anemia, even with correction of contributing factors, it may still take several weeks for the PCV to return to normal. Evaluation of bone marrow is warranted when other parameters are inconclusive. The morphology of bone marrow aspirates appears similar to other domestic species during health.

Although we are still documenting diseases and pathophysiologic processes in llamas, a number of causes of anemias have been reported. A recent finding in llamas has been eperythrozoonosis. The source of this rickettsia is yet to be elucidated. Gastrointestinal parasites affecting llamas include Haemonchus, Ostertagia, Trichostrongylus, Nematodirus, Oesophagostomum, Cooperia, Bunostomum and Coccidia. Fascioliasis, sucking lice and possibly ticks can cause sufficient blood loss to result in anemia. Chronic parasitism may lead to iron deficiency anemia. Llama erytrocytes display pallor with iron deficiency. The pallor can be central, at either end or fairly diffuse.

Copper toxicity, with a hemolytic crisis, has been reported in the llama. Iron deficiency anemia, anemia of chronic disease, copper deficiency and vitamin B_{12} deficiency have been mentioned. Braken fern toxicity, renal disease and hypothyroidism can suppress the bone marrow. Clostridial enteritis and salmonellosis can potentially cause enough damage to the intestine to precipitate a blood loss anemia.

I. Evaluation of Anemia in Domestic Animals - (decrease in red cell mass)

A. Physical Examination
1. Pale mucous membranes
2. Weakness
3. Exercise intolerance

B. Hemogram
1. PCV best primary indicator of anemia
a. must evaluate hydration
b. effect of splenic contraction
2. Reticulocyte count is best indicator of response
3. Red cell count and hemoglobin concentration used to calculate indices

II. Responsive or regenerative anemia (indicates the bone marrow is responding)

A. Indicators of response
1. Reticulocytosis - must correct for decrease in PCV as reticulocytes are counted as a percent of erythrocytes, neonatal llamas normally have a higher reticulocyte count than adults.
2. Erythrocyte morphology - anisocytosis and polychromasia - reticulocytes are round in llamas
3. Red cell indices - macrocytic normochromic
4. Metarubricytosis
5. Hypercellular marrow with decreased M/E ratio (bone marrow evaluation is warranted when other indicators are inconclusive).

B. Causes of responsive anemias
1. Hemorrhage
2. Hemolysis

C. Erythropoietin production increases
1. Main function of red cell is to carry oxygen to tissues
2. During anemia, oxygen carrying capacity is diminished due to decreased blood hemoglobin concentration
3. Tissues become hypoxic causing erythropoietin release from kidney
4. Erythropoietin is a glycoprotein hormone, largely renal in origin
5. Effects of erythropoietin:
a. stimulates stem cells to divide and amplify erythropoiesis
b. facilitates release of reticulocytes one day early
c. shortens time between mitotic divisions in developing erythroid cells
d. increases the rate of hemoglobin synthesis by each cell
e. In healthy animals, development from unipotential stem cell to reticulocyte is 5 days. Under the influence of increased concentrations of erythropoietin, reticulocytes may be released in 2-3 days.
f. Erythrocyte production may be amplified 6-8 times, if the marrow is healthy and nutrients are adequate.

D. Causes of acute blood loss
1. Trauma
2. Surgery
3. Gastrointestinal hemorrhages
4. Clotting defects

E. Dynamics of acute blood loss from traumatic wounds:
   1. During the first few minutes the PCV remains normal as both plasma and erythrocytes are lost.
   2. Within seconds to minutes, splenic contraction empties high PCV blood into circulation causes a transient rise in PCV.
   3. In 2-3 hours, the tissue fluid moves into the vasculature. Fluid dilutes out erythrocytes causing decreased PCV, Hb, RBC and plasma protein.
   4. In 2-3 days reticulocytosis begins (anisocytosis, polychromasia) reaching a maximum by 7 days.
   5. In 1-2 weeks the hemogram returns to normal from a one time bleeding episode.
   6. If the anemia and reticulocytosis persist for longer than 3 weeks look for continuing hemorrhage.
   7. Red cell production can increase 6-8 times in hemolytic anemia because iron is available.
   8. Red cell production can only increase 4-5 times in blood loss anemia if iron is lost.
   9. Blood loss due to hemorrhage into a body cavity is not as severe as blood lost to external hemorrhage because 2/3 of the erythrocytes may be recovered intact by the lymphatic system. The iron of the rest of the erythrocytes is conserved by the RES.

F. Causes of chronic blood loss:
   1. Internal parasites
   2. External parasites
   3. Small gastrointestinal ulcers
   4. Hematuria
   5. Platelet defects
   6. Clotting defects
   7. Neoplasia

G. Dynamics of chronic blood loss:
   1. Anemia is slow to develop
   2. Clinical signs are slow to develop. Generally clinical signs are noticed at a lower PCV than acute blood loss due to adaptation.
   3. Initially the anemia is responsive.
   4. With time, iron stores are depleted (faster with neonate) and anemia becomes less and less responsive.
   5. Long term hemorrhage with iron deficiency causes a microcytic hypochronic, nonregenerative anemia.
   6. Thrombocytosis often also develops.

H. Hemolytic anemias
   1. Accelerated extravascular hemolysis
      a. caused by erythrocyte parasites, immune mediated disease, oxidative drugs or chemicals, erythrocyte metabolic defects or fragmented erythrocytes
      b. these conditions generally make the erythrocyte less deformable, and more susceptible to phagocytosis by splenic macrophages
      c. these conditions are often low grade, slow onset
      d. do not see hemoglobinemia or hemoglobinuria. Occasionally may see hyperbilirubinemia

2. Accelerated intravascular hemolysis
   a. caused by bacterial toxins, erythrocyte parasites, oxidative drugs or chemicals, immune mediated disease, or osmotic lysis
   b. often acute onset
   c. results in hemoglobinemia and hemoglobinuria. May see hyperbilirubinemia
3. Both intravascular and extravascular hemolytic anemias are generally highly regenerative as iron is not lost.

III. Nonresponsive Anemia

A. Corrected reticulocyte count is approximately 1%.
B. Anemias are usually normocytic normochromic.
C. Nonresponsive (nonregenerative) anemias are either primary or secondary problems of bone marrow erythropoiesis.
D. Types of nonregenerative anemias:
   1. erythropoietin deficiency
      a. chronic renal disease
      b. endocrine disorders - hypothyroidism, hypoadrenocorticism
   2. anemia of chronic disease (inflammatory, neoplastic)
      anemia resolves when primary disease is cured
   3. marrow damage
      a. damage to stem cells (radiation, chemicals, drugs) causes aplastic anemia and pancytopenia
      b. damage to erythrocytes only - pure red cell aplasia - rare
   4. myelophthisic anemia - myelophthisis
      a. normal hematopoietic bone marrow cells are crowded out by neoplastic or inflammatory cells
      b. tumor may originate in marrow or metastasize there
   5. anemia caused by infectious agents
   6. chronic blood loss anemia - eventually depletes iron stores, becomes microcytic and hypochronic

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