Anemia is defined as a reduction in Hct, RBC count, or Hb. Hb is perhaps the best measurement because Hct is affected by RBC size and RBC counts are less precise than Hb measurements. It is a common problem in cats, in part because of the reduced erythroid mass and short RBC lifespan (73 days vs. 104 days for most dog breeds). This is compensated for by the lower affinity of feline Hb for oxygen, promoting the release of oxygen to needy tissues, thereby allowing cats to better tolerate anemia.

Anemia may be classified pathophysiologically as being due to hemolysis, hemorrhage, [erythroid] hypoplasia, or hemodilution (4 H’s). Hemolytic and hemorrhagic anemias are most often regenerative, while hypoplastic anemia is, by definition, nonregenerative. Anemia may also be classified by duration as acute or chronic, but there is a spectrum in between the two. Acute anemias may be caused by either hemolysis or hemorrhage. Chronic anemias may be caused by hemolysis, hemorrhage or hypoplasia. Hemodilution will also cause a drop in Hct, Hb, and RBCs, but does not cause a true anemia in that there is no decrease in red cell mass. Dilutional pseudoanemia may occur with crystalloid and colloid fluid therapy, as well as physiologic states that cause plasma volume expansion.

Regeneration
Following an episode of RBC loss, regeneration occurs, beginning as erythroid hyperplasia in the bone marrow. In the last stage of maturation in the marrow, metarubricytes express their nuclei becoming reticulocytes. The latter are normally held in the marrow for 1-2 days before release. Once released, reticulocytes are in their aggregate form, and remain so for about 1 day. Aggregate reticulocytes have larger clusters (aggregates) of endoplasmic reticulum when stained with new methylene blue. These are roughly equivalent to the polychromatophils seen with a routine hematology stain, and what are typically reported when a reticulocyte count is performed for a cat. The intensity of regeneration is typically less than for a dog. After a day the reticulocytes continue to mature into punctate reticulocytes with small clusters of endoplasmic reticulum (resulting in a punctate appearance), detectable 5 days after RBC loss. These reticulocytes mature into a normal RBC over several weeks. An increase in aggregate reticulocytes is best to document regeneration in the presence of a moderate-to-severe anemia, but a short episode of regeneration may be missed. An increase in punctate reticulocytes is best to document low-grade regeneration, but there are no counting standards.

Nucleated red cells (nRBCs) are normally released from the marrow in small numbers. An increase in nRBCs occurs with regeneration, numerous disorders affecting bone marrow stroma, erythremic myelosis and in extra-medullary hematopoiesis. The key question to ask is whether or not the presence of nRBCs is appropriate for the degree of reticulocytosis. If it is not, then a cause of inappropriate rubricytosis should be sought.

Guidelines to judge adequacy of peak regeneration (4 – 7 days) following an episode of acute RBC loss are:

<table>
<thead>
<tr>
<th>Degree of anemia</th>
<th>PCV(%)</th>
<th>Polychromasia (/oil field)</th>
<th>Reticulocytes (/μL), (x 10⁹/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref range</td>
<td>28 – 49</td>
<td>0 – 1</td>
<td>&lt; 40,000</td>
</tr>
<tr>
<td>Mild</td>
<td>21 – 27</td>
<td>1 – 2</td>
<td>50,000</td>
</tr>
<tr>
<td>Moderate</td>
<td>12 – 20</td>
<td>3 – 4</td>
<td>100,000</td>
</tr>
<tr>
<td>Marked</td>
<td>≤ 11</td>
<td>&gt; 4</td>
<td>200,000</td>
</tr>
</tbody>
</table>

Peak punctate reticulocyte numbers are seen at 10 days post-RBC loss.

Clinical signs of anemia
Signs of anemia are related to severity and duration. Cats with moderate-to-marked acute anemia will be weak and inappetent. Many nonregenerative anemias are chronic and cats may be minimally weak and inappetent because of mechanisms that alleviate tissue hypoxia to compensate for decreased Hb. These mechanisms are hemodynamic and non-hemodynamic. The main non-hemodynamic mechanism in dogs (increased DPG synthesis) is not present in cats. The main hemodynamic compensatory mechanism is increased cardiac output, due to decreased afterload, increased preload, increased contractility, and increased heart rate. Decreased afterload is due to lower blood viscosity and nitric oxide-mediated vasodilation, because Hb, which is low, is a potent binder of nitric oxide. Increased preload is due to salt and water retention, due to low systemic vascular resistance. Anemic cats appear to be at increased risk for acute and chronic volume overload (which causes eccentric cardiac hypertrophy) compared to other species, and this may reflect more exuberant hemodynamic compensation because of no mechanism to decrease Hb affinity to oxygen. Sympathetic nervous system activation causes increased heart rate and contractility. In acutely anemic cats, these changes are manifested as tachycardia and increased pulse strength. As anemia becomes more chronic, heart rate and pulse strength normalize. Acute and chronic anemia may cause pica characterized by eating cat litter and licking concrete or ceramics.
Causes of regenerative anemia (hemolysis/hemorrhage, following DAMNPIT scheme)

Hemolytic anemias

1. Degenerative – None
2. Anomalous – Hereditary RBC Defects
3. Metabolic – Hypophosphatemia

Hypophosphatemia may occur during treatment of DKA. Phosphorus is shifted out of cells during acidosis and insulin deficiency, and lost in the urine because of polyuria, resulting in a depletion of phosphorus. When insulin is given and acidosis corrected, phosphorus is shifted back into cells. There is insufficient phosphorus for RBCs ATP production, which is needed to maintain membrane integrity (Na-K ATPase). This is most likely to occur on the 2nd or 3rd day of therapy. The author prefers to begin phosphate (using KPO₄), 0.01 – 0.03 mmol/kg/h for 6 hours, if a serum phosphorus level of < 1 mg/dl (0.32 mmol/L) is measured or anticipated. Occasionally higher doses, up to 0.12 mmol/kg/h for 24 hours, are needed. This requires the use of NaPO₄ to avoid hyperkalemia, which is more expensive and not as readily available.

Hypophosphatemia may also occur as a result of severe malnutrition, typically associated with liver disease. It is most likely to occur during a “refeeding syndrome” when nutritional support is started. Total body phosphorus is low, insulin release is stimulated by feeding, and hypophosphatemia results. Hemolysis is uncommon, but monitoring serum phosphorus is recommended for the first 3 days after starting enteral feeding. Hypophosphatemia has also been reported as a complication of renal transplantation.

4. Neoplasia – Disseminated Histiocytic Sarcoma

Disseminated histiocytic sarcoma (malignant histiocytosis) is a rare neoplasm of macrophages, presumed to be arising from the bone marrow, spleen or liver. A feature may be hemophagocytosis, where extravascular hemolysis by malignant macrophages causes a regenerative anemia (nonregenerative anemia may also occur). Thrombocytopenia is common. Historical signs are nonspecific. Hepatosplenomegaly is common. As with hemophagocytic histiocytic sarcoma in dogs, the initial clinical and hematologic picture may be identical to idiopathic IMHA. The presence of thrombocytopenia, splenic masses on ultrasound, or poor response to immunosuppression should prompt fine needle biopsy of the spleen. Treatment of HS is poorly defined, but treatment with prednisone, lomustine, or liposomal clodronate is recommended.

5. Physical – None

6. Infectious – Hemoplasmas, ehrlichiosis, *Cytauxzoon felis* babesiosis, FeLV
  a. Immune – Autoimmune (IMHA) and Alloimmune Hemolytic Anemia

IMHA in dogs is most often characterized by an acute anemia and strong regenerative response. Regeneration is stronger than hemorrhagic anemia because iron is not lost and readily available for reuse. Consistent with the overall lower prevalence of immune-mediated diseases in cats than in dogs, IMHA is less common in cats. Compared to dogs, nonregenerative forms of IMHA are more common, fulminant disease and intravascular hemolysis are rare, and icterus is less common (reflecting the more subacute nature of hemolysis). Diagnosis of IMHA is based on acute-to-subacute anemia, ruling-out hemorrhage, and the presence of agglutination. Cats are more likely to form rouleaux than dogs, and caution must be taken in identifying agglutination. (Note: EDTA-induced agglutination may occur, and should be ruled-out by re-examining the blood in citrate if a cat is not anemic.) A Coomb’s test is usually positive in regenerative IMHA (and becomes less often positive the “deeper” IMHA becomes). Increased osmotic fragility may also be used to support the diagnosis, but is not routinely performed. Spherocytes are difficult to identify in cats, and, given less intense regeneration, anisocytosis (and RDW) are less pronounced compared to dogs. Secondary IMHA is considered to be more common than primary, although there appears to be increasing recognition of primary idiopathic IMHA. Regardless, investigation for underlying diseases is recommended. A minimum investigation includes probing for history of drug therapy (especially antithyroid drugs), FeLV/FIV tests, and PCR for hemoplasmas. More extended investigation includes abdominal ultrasound examination, fine needle aspiration of the spleen (which may be enlarged in cats with IMHA as with dogs) and other lesions, thoracic radiographs, bone marrow biopsy (especially if nonregenerative), ANA, and testing for infectious diseases for which the cat is considered at risk.

Treatment is as for IMHA in the dog, except that routine thromboprophylaxis is not given. Thromboembolic disease appears to be rare, which is perhaps unexpected because cats have more reactive platelets and faster clotting times than dogs, and likely reflects the less acute nature of the disease in cats. The need for immunosuppression beyond prednisone in cats is controversial as it is in the dog. Most cats have initially responded to prednisone alone, but there is strong anecdotal evidence that the chronic nonregenerative forms need more intense immunosuppression. The author prefers to start with prednisone alone if there is strong regeneration and/or an acute history, and use more intense treatment the “deeper” and more chronic the problem is. However, if there is no response within 1-2 weeks, the addition of cyclophosphamide (50 mg/cat PO q2weeks), chlorambucil (2 mg/cat PO q2-3 days) or cyclosporine (5 mg/kg PO q12h) should be considered. Routine doxycycline or marbofloxacin is also recommended while awaiting hemoplasma PCR, or if cost restraints prohibit theses tests. The prognosis is better than with IMHA in dogs, with a long-term survival rate >75%, perhaps reflecting the less acute nature of the disease. A recurrence of 30% has been reported, therefore the possibility of long-term therapy
should be discussed with owners, and is definitely recommended following relapse. Cats can become cushingoid with long-term steroid use necessitating the use of other immunosuppressive drugs.

Alloimmune hemolytic anemias result from blood-type incompatibilities. Transfusion reactions occur because cats have naturally occurring anti-RBC alloantibodies. Severity of reaction is related to antibody titer and type (IgM worse than IgG). In the unlikely event that a type A cat is given type B or AB blood, weak (probably IgG) anti-B titers will result in subacute extravascular hemolysis (delayed transfusion reaction/premature RBC loss), which is manifested as the transfusion not lasting as long as expected. If a type B cat is given type A blood, a typically high IgM anti-B antibody titer will result in peracute intravascular hemolysis, of which the salient finding is severe hypotension. Hemoglobinemia/uria may not be seen because the reaction occurs after very few RBCs are transfused. Some type B cats have lower IgM titers and IgG antibodies, resulting in a spectrum of less severe reactions of intravascular and extravascular hemolysis. Blood-typing is easy to perform in cats, so A-B transfusion reactions should not occur. However, another blood group, Mik, has been reported, where natural antibodies may result in an acute hemolytic reaction. In addition, other crossmatch incompatibilities have been seen and some type A cats that have received multiple transfusions have developed delayed hemolysis, suggesting sensitization to other blood groups. Ideally all cats should be crossmatched as well as blood-typed prior to transfusion.

Neonatal isoerythrolysis occurs when type A kittens are born to a type B queen (from mating with a type A tom). Anti-A antibodies in the queen’s colostrum will attack the kittens type A RBCs resulting in acute death, fading, transient weakness, or delayed tail-tip necrosis. This can be prevented by removing all kittens (or blood-typing and removing type A kittens) from the queen and hand-rearing for 24 hours if the blood type of the tom is A or not known. In the event of a first time presentation of a queen and fading kittens, part of the investigation should be blood-typing of the queen and kittens. Fading kittens should be transfused.

Hemorrhagic Anemias

Depending on severity, hemorrhage may result in sudden death, depression with preredenerative anemia, or later presentation with regenerative anemia. Hemorrhage should be considered in any regenerative anemia without evidence of agglutination (and negative Coomb’s test), and the cat closely examined and imaged for evidence of trauma, and intrathoracic and abdominal hemorrhage, and tested for hemostatic defects.

1. Degenerative – None
2. Anomalous

Rare inherited platelet function defects. Hemophilia and vitamin K responsive coagulopathy in the Devon Rex. Peliosis hepatitis may result in spontaneous hemoabdomen.

3. Metabolic

Hepatic lipidosis, EPI, and severe IBD may cause vitamin K deficiency. The liver is friable with lipidosis and more likely to bleed post-biopsy.

4. Neoplasia

Hepatic or splenic lymphoma, mast cell tumor and hemangiosarcoma (rare) may cause spontaneous hemoabdomen.

5. Physical – None
6. Infectious

Severe thrombocytopenia sufficient to cause hemorrhage has been seen with pancytopenia due to FeLV, FIV and histoplasmosis.

a. Immune/inflammatory

Immune-mediated thrombocytopenia is similar to the disease in dogs, although much less common. It may also be a feature of immune-mediated pancytopenia. A circulating anticoagulant may rarely cause a bleeding tendency. Hepatic amyloidosis and hepatic necrosis may cause spontaneous hemoabdomen.

7. Toxic

Cats are not as frequently poisoned with vitamin-K antagonist rodenticides as are dogs, but poisoning does occur, and may be secondary. The clinical picture is similar to dogs, and presenting clinical signs include unexplained depression, re-bleeding from wounds, internal bleeding, and widespread cutaneous hemorrhages. Hemostasis should be assessed if bleeding is excessive for any injuries. Treatment is as for dogs. Toxins and drugs may cause pancytopenia. Snake bite envenomation may cause bleeding.

8. Trauma

A cat presented with anemia should be examined for external signs of trauma such as shorn nails, road burns, soiled fur, dried nasal bleeding, blood in the ear canals and oral bruising. Cats suffering motor vehicle and other major trauma are most likely to present with pneumothorax, signs due to head trauma, and fractures. Anemia, if present, is preredenerative. Occasionally major intrabdominal bleeding from trauma occurs, and if a cat is presented several days later, a regenerative anemia may be present.
References & suggested reading


Josephine Deubler Genetic Disease Testing Laboratory, University of Pennsylvania; Veterinary Genetics Laboratory, University of California, Davis; Langford Veterinary Diagnostics, University of Bristol, UK.


Silvestre-Ferreira AC, Pastor J. Feline neonatal isoerythrolysis and the importance of feline blood types. Vet Med International 2010, Article ID 753726.

