ABSTRACT: Many congenital and acquired bone marrow disorders have been described in dogs. Major categories include infectious diseases, immune-mediated bone marrow destruction, toxic marrow injury, congenital and acquired myelodysplastic syndromes, acute and chronic myeloproliferative and lymphoproliferative disorders, primary polycythemia, primary and secondary myelofibrosis, malignant histiocytosis, hemophagocytic syndromes, and aplastic pancytopenia. Because choice of therapy and prognosis for these disorders vary markedly, establishing a definitive diagnosis is essential.

Bone marrow aspiration and core biopsy techniques are important diagnostic tools for evaluating hematologic disorders in dogs. Sample collection and initial assessment of the adequacy of bone marrow aspiration smears can readily be done in a practice setting, but detailed evaluation of aspiration smears and core biopsy samples are best done by veterinary clinical laboratories. The greatest challenge for clinicians is interpreting bone marrow reports in terms of diagnosis, prognosis, and treatment approaches. Results of bone marrow cytology must be interpreted in light of history and physical findings, changes in peripheral blood, and concurrent disease conditions. In this review, we concisely discuss canine bone marrow disorders and focus on how results are integrated with the case history and peripheral blood alterations to reach a diagnosis. We group these disorders in general categories, including hematologic disorders associated with poorly regenerative anemias, neutropenia, multiple cytopenias, and neoplastic conditions.

HEMATOPOIETIC DISORDERS ASSOCIATED WITH POORLY REGENERATIVE ANEMIAS

Disorders associated with poorly regenerative anemias include the following:

- **Erythroid hypoplasia** denotes a decrease in erythroid elements in bone marrow.
- **Erythroid aplasia** denotes a marked decrease or absence of erythroid elements in bone marrow.
- **Erythroid maturation arrest** refers to a condition in which normal or
increased numbers of immature erythroid cells are present in bone marrow but later stages are decreased or absent.

- **Dyserythropoiesis** indicates the presence of atypical (i.e., dysplastic) features in erythroid cells. These dysplastic features include fragmented nuclei, binucleation, megaloblasts, asynchronous maturation, and sideroblasts (i.e., nucleated erythroid cells containing granular deposits of iron).

### Secondary Anemias

Secondary anemias are mild (packed cell volume [PCV], 25% to 35%) and associated with systemic diseases, including inflammatory disease, neoplasia, chronic renal and hepatic diseases, hypothyroidism, and hypoadrenocorticism (Table 1). Although persistent, these types of anemia do not become severe. Terms used to describe them include anemia of inflammatory disease, anemia of chronic disorders, anemia of chronic renal disease, and anemia of malignancy. Although erythropoiesis is mildly suppressed, the bone marrow may appear normal or have mild erythroid hypoplasia. Hemosiderin is usually increased.

Bone marrow examination is usually not indicated for evaluation of secondary anemias unless leukemia is suspected. Clinical evaluation should be focused on discovering the associated disease condition. Resolution of the primary disease condition results in return of the PCV to the normal range. Treatment of secondary anemias is usually not necessary. However, anemia associated with chronic renal failure can become severe and is commonly treated with erythropoietin.

### Pure Red Cell Aplasia

Pure red cell aplasia is characterized by insidious onset of severe nonregenerative anemia (PCV, 4% to 18%) in middle-aged dogs (Table 1). Bone marrow is characterized by erythroid aplasia (i.e., myeloid:erythroid ratio [M:E] > 75:1). Granulocytes and platelets in blood...
and bone marrow are normal or increased. Plasma cells are usually increased in bone marrow. Most cases of pure red cell aplasia are caused by immune-mediated destruction of early erythroid precursor cells in bone marrow. Therefore, pure red cell aplasia is a type of immune-mediated anemia. Pure red cell aplasia is treated with steroidal and nonsteroidal immunosuppressive drugs, similar to the way immune-mediated hemolytic anemia is treated. Pure red cell aplasia responds as well as or better than immune-mediated hemolytic anemia, with greater than 75% of patients surviving long term. Because of the chronic nature of the anemia, clinical signs are less prominent than expected. However, a whole blood or packed red blood cell (RBC) transfusion is recommended if PCV is less than 10% or the patient is clinically compromised at rest.

**Nonregenerative Immune-Mediated Anemia**

Nonregenerative immune-mediated anemia is characterized by a severe anemia (PCV, 5% to 22%) in middle-aged dogs in middle-aged dogs (Table 1). As with pure red cell aplasia, granulocytes and platelets in blood are normal or increased. This disorder differs from pure red cell aplasia in that erythroid cells in bone marrow are present in low (M:E < 75:1), normal, or increased numbers. In some animals, erythroid maturation is arrested at the rubricyte or metarubricyte stage (Figure 1). Several factors may be involved in the anemia. Antibody-mediated destruction of late-stage erythroid cells (i.e., rubricytes and metarubricytes) may explain the dogs in which maturation arrest is identified. Other dogs have concurrent myelofibrosis, myelodysplastic syndrome, secondary hemophagocytic syndrome, or bone marrow necrosis.

Because this is a form of immune-mediated anemia, affected dogs are treated with steroidal and nonsteroidal immunosuppressive drugs. Response to treatment is similar to regenerative forms of immune-mediated hemolytic anemia, with complete or partial response in 73% of cases. Even dogs with myelofibrosis may respond to treatment, and myelofibrosis may resolve.

**Congenital Myelodysplastic Syndromes**

Congenital causes of myelodysplastic syndromes include congenital dyserythropoiesis, polymyopathy, and cardiac disease in English springer spaniels; vitamin B<sub>12</sub> malabsorption in giant schnauzers; and poodle macrocytosis. Congenital dyserythropoiesis, polymyopathy, and cardiac disease in English springer spaniels is characterized by moderate anemia with spherocytes, schizocytes, dacryocytes, codocytes, and vacuolated RBCs seen in blood smears (Table 1). Bone marrow is characterized by erythroid hyperplasia with dyserythropoiesis (i.e., binucleation and abnormal mitotic figures). Vitamin B<sub>12</sub> malabsorption in giant schnauzers is an autosomal recessive disorder characterized by chronic nonregenerative anemia and neutropenia (Table 1). Dysplastic features in the blood include microcytes, macrocytes, schizocytes, acanthocytes, elliptocytes, keratocytes, hypersegmented neutrophils, and giant platelets. Dysplastic features in bone marrow include giant band neutrophils and asynchronous maturation in the erythroid series. Clinical signs resolve with parenteral administration of vitamin B<sub>12</sub>. Poodle macrocytosis occurs in toy and miniature poodles and is characterized by macrocytosis in the blood and marked dyserythropoiesis in bone marrow (Table 1). Dysplastic features in bone marrow are characterized by megaloblasts, binuclear erythroid cells, nuclear fragmentation, and atypical mitotic figures. Despite these features, affected dogs are not anemic and have no associated clinical signs.
Primary Myelodysplastic Syndrome with Refractory Anemia

Primary myelodysplastic syndrome with refractory anemia probably results from genetic mutations in hematopoietic stem cells. It is characterized by moderate normocytic normochromic nonregenerative anemia with hypercellular bone marrow (Table 1). Dysplastic features are usually limited to the erythroid series. Among the limited number of cases of myelodysplastic syndrome with refractory anemia described, the anemia appears to respond well to erythropoietin therapy and affected dogs have prolonged survival.

Hematologic Disorders Associated with Neutropenias

Transient acute neutropenias have been associated with rapid movement of neutrophils from the blood into inflamed tissues due to bacterial infection or endotoxemia, parvovirus infection, ehrlichiosis, cyclic hematopoiesis in gray collies, and drug toxicities. Poorly defined chronic neutropenias are occasionally observed. Causes include immune-mediated neutrophil destruction; congenital neutropenia in Border collies; breed-related leukopenia in Belgian Terriers; myelodysplastic syndromes; and leukemias/lymphomas.

Immune-Mediated Neutropenia

Immune-mediated neutropenia has been infrequently reported in dogs. As with immune-mediated hemolytic anemia, most cases of immune-mediated neutropenia have myeloid hyperplasia in bone marrow. However, if the antibody destroys precursor cells, pure white cell hypoplasia/aplasia may occur. Some cases respond to steroidal immunosuppressive therapy. If neutrophil counts drop below 1000/µl, broad-spectrum antibiotic therapy is necessary to prevent bacterial infection.

Cyclic Hematopoiesis

Cyclic hematopoiesis is a congenital abnormality of bone marrow stem cells in gray collies characterized by cyclic variation in production of all bone marrow cells. The length of the cycle is approximately 11 days.
short circulation time of neutrophils (i.e., 4 to 8 hours) results in severe neutropenia and variable thrombocytopenia in blood associated with panhypoplasia of bone marrow. Many affected puppies die within the first few days of life. Dogs that survive the neonatal period die as a result of repeated infection. Dogs treated with antibiotics develop chronic arthritis, anemia, glomerulonephritis, or amyloidosis and die by 2 years of age.

**Leukopenia in Belgian Tervurens**

Many healthy adult Belgian Tervurens have total leukocyte counts less than 6000/µl. The incidence increases with age; few dogs younger than 2 years of age are leukopenic, and 65% of dogs older than 4 years of age are leukopenic. The condition does not appear to be of clinical significance because affected dogs appear to be healthy.

**HEMATOLOGIC DISORDERS ASSOCIATED WITH MULTIPLE CYTOPENIAS**

**Toxic Injuries**

A variety of toxic insults can result in destruction of hematopoietic cells (Table 2). Causes of marrow degeneration include therapeutic drugs, infectious agents, systemic lupus erythematosus, leukemias, and disseminated intravascular coagulopathy. Pathologic changes that may occur with toxic marrow injury include cellular degeneration, necrosis, fibrosis, macrophage proliferation, and myelodysplasia (Figure 2).

**Infectious Agents**

Nonbacterial causes of hematologic dyscrasias include ehrlichiosis, histoplasmosis, and parvovirus infection. Thrombocytopenia is consistently seen in dogs with acute granulocytic and monocytic ehrlichiosis. Thrombocytopenia appears to be the result of immune-mediated platelet destruction; thus bone marrow is relatively unaffected. Treatment with doxycycline frequently results in prompt resolution of thrombocytopenia. In the chronic form of monocytic ehrlichiosis, however, the marrow may be hypocellular, with pancytopenia resulting from decreased hematopoiesis. The cytopenias may not respond to doxycycline therapy.

Parvovirus infection directly destroys rapidly proliferating bone marrow cells. Marrow injury due to secondary endotoxemia, septicemia, or both can also occur. The bone marrow is characterized by degenerative changes in hemic cells, areas of necrosis, and increased numbers of phagocytic macrophages. Treatment involves broad-spectrum antibiotics to control secondary infections. Recombinant granulocyte colony-stimulating factor can be given to accelerate granulo- lopoiesis, thereby reducing the period of neutropenia.

Septicemia and endotoxemia can induce neutropenia as a result of a rapid migration of neutrophils into inflamed tissues, overwhelming the capacity of the bone marrow to replace them. However, septicemia and endotoxemia can also cause bone marrow disorders. Bone marrow may be hypocellular, normocellular, or hypercellular. Mechanisms that lead to bone marrow injury are complex and include endotoxin-induced destruction of bone marrow precursor cells, toxic or hypoxic bone marrow necrosis, inflammation associated with bacterial invasion of marrow, and inflammatory cytokine-induced suppression of hematopoiesis. Recovery of neutrophil numbers in blood usually occurs within a few days after clinical recovery.

**Drugs**

Many drugs have been reported to induce hematologic alterations in dogs (Table 3). Dogs often become ill within 10 to 14 days after treatment is initiated. Canine bone marrow is highly susceptible to estrogen-induced suppression of hematopoietic stem cells. Estradiol cypionate, administered to induce abortion or treat prostatic hyperplasia, circuminal gland tumors, or urinary incontinence, is the most frequent drug incriminated in hematologic dyscrasias. Diethylstilbestrol appears to be less toxic. Endogenous sources of estrogen include cystic ovarian follicles, ovarian granulosa cell tumors, retained testicles, and testicular Sertoli cell tumors. Recovery from estrogen-induced aplastic pancytopenia is prolonged and uncertain.

<table>
<thead>
<tr>
<th>Causative Agent</th>
<th>Amount of Cases</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen</td>
<td>Many</td>
<td>Irreversible</td>
</tr>
<tr>
<td>Chemotherapeutic drugs</td>
<td>Many</td>
<td>Reversible</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>Many</td>
<td>Irreversible</td>
</tr>
<tr>
<td>Meclomenamic acid</td>
<td>One</td>
<td>Irreversible</td>
</tr>
<tr>
<td>Trimethoprim–sulfa diazine</td>
<td>Many</td>
<td>Reversible</td>
</tr>
<tr>
<td>Albendazole</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Thiacetarsamide</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Two</td>
<td>Reversible</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Captopril</td>
<td>One</td>
<td>Reversible</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Pheno barbital</td>
<td>Few</td>
<td>Reversible</td>
</tr>
<tr>
<td>Primidone</td>
<td>Few</td>
<td>Reversible</td>
</tr>
</tbody>
</table>

Table 3. Drug-Associated Hematologic Disorders in Dogs
Phenylbutazone-associated neutropenia or pancytopenia occurs sporadically in dogs. These adverse reactions are not dose dependent and may occur within 2 weeks after starting treatment or after months or years of treatment. Neutropenias that occur shortly after starting treatment may be immune mediated, and affected dogs frequently recover promptly after discontinuation of treatment. Pancytopenia that occurs after months or years of treatment is frequently the result of bone marrow stem cell destruction, and the prognosis for recovery is poor.

For other drugs, hematologic dyscrasias are typically reversible. Onset of cytopenias in the blood usually occurs within 2 weeks of initiating treatment, and neutropenia and thrombocytopenia are prominent features. Hematologic recovery typically occurs within 2 weeks after the drug is discontinued. Treatment of drug-induced bone marrow disorders includes discontinuation of the drug, broad-spectrum antibiotics if neutropenia is present, platelet transfusions if thrombocytopenia is present, and RBC transfusions if severe anemia is present. Use of recombinant hematopoietic cytokines, including granulocyte colony-stimulating factor, erythropoietin, and thrombopoietin for treating drug-induced hematologic dyscrasias, has not been extensively investigated.

Secondary Myelofibrosis

Secondary myelofibrosis may result from toxic marrow injury or chronic overproduction of erythropoietin or thrombopoietin (Table 2). Therefore, myelofibrosis tends to be associated with immune-mediated hemolytic anemia; immune-mediated thrombocytopenia; and congenital hemolytic anemias, such as congenital pyruvate kinase deficiency. Secondary myelofibrosis has also been associated with marrow necrosis and long-term drug treatment (e.g., phenobarbital, phenytoin, phenylbutazone). Approximately half of the cases of secondary myelofibrosis associated with immune-mediated anemia resolve after treatment with immunosuppressive drugs.

Hemophagocytic Syndrome

Several nonmalignant proliferative disorders of macrophages have been described. Hemophagocytic syndromes are characterized by proliferation of hemophagocytic macrophages in bone marrow and other tissues (Table 2). Hemophagocytic syndromes can be idiopathic; but most cases occur secondary to other diseases, including immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, myelodysplastic syndromes, infectious diseases, and neoplasia (e.g., lymphosarcoma, mast cell tumors, carcinomas, sarcomas). Tests to detect underlying diseases should include the direct Coombs test; antinuclear antibody test; radiology and/or ultrasonography for detecting tumors; and serology for infectious agents (e.g., Ehrlichia spp, Rickettsia rickettsii, Borrelia burgdorferi, Histoplasma, Blastomyces). The outcome of hemophagocytic syndromes depends on the underlying disease condition.

Aplastic Pancytopenia

Aplastic pancytopenia (also called aplastic anemia) is pancytopenia associated with marked hypocellularity of bone marrow in which the hematopoietic space is replaced by adipose tissue (Table 2). Causes include chronic ehrlichiosis, drug toxicities (e.g., estrogen, phenylbutazone, chemotherapeutic agents, sulfadiazine), and idiopathic aplastic pancytopenia. Unlike the human version of the disease, idiopathic aplastic pancytopenia in dogs is rare, and not all potential causes were ruled out in the reported cases. Clinical evaluation of dogs with aplastic pancytopenia should include evaluating for immune-mediated and infectious diseases (e.g., parvovirus and Ehrlichia spp infections) and the case history for drug or toxin exposure.

Primary-Acquired Myelodysplastic Syndrome with Excess Blasts

Primary-acquired myelodysplastic syndromes probably result from genetic mutations in hematopoietic stem cells. Myelodysplastic syndrome with excess myeloblasts is characterized by pancytopenia in the blood; hypercellular bone marrow with dysplastic features in the myeloid, erythroid, and megakaryocytic cell lines; and 5% to 30% myeloblasts (Table 2, Figure 3). Dysplastic features of erythroid, myeloid, and megakaryocytic cells are as follows:
Table 4. Hematologic Disorders Resulting from Neoplastic Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Blood</th>
<th>Cellularity</th>
<th>M:E</th>
<th>Blast Cells</th>
<th>Maturation Arrest</th>
<th>Pathologic Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myeloproliferative disease</td>
<td>Variable</td>
<td>Increased</td>
<td>Increased</td>
<td>&gt;30% myeloblasts</td>
<td>Myeloid</td>
<td>Atypical myeloblasts</td>
</tr>
<tr>
<td>Acute lymphoproliferative disease</td>
<td>Variable</td>
<td>Increased</td>
<td>Increased</td>
<td>&gt;30% lymphoblasts</td>
<td>Lymphoid</td>
<td>Many lymphoblasts</td>
</tr>
<tr>
<td>Chronic myeloproliferative disease</td>
<td>Leukocytosis</td>
<td>Increased</td>
<td>Increased</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Primary erythrocytosis</td>
<td>Polycythemia</td>
<td>Increased</td>
<td>Normal</td>
<td>&lt;5% total</td>
<td>No</td>
<td>Normal</td>
</tr>
<tr>
<td>Primary myelofibrosis</td>
<td>Anemia; poikilocytosis</td>
<td>Decreased</td>
<td>Variable</td>
<td>&lt;5% total</td>
<td>Variable</td>
<td>Megakaryocyte hyperplasia; dysmegakaryopoiesis</td>
</tr>
<tr>
<td>Malignant histiocytosis</td>
<td>Pancytopenia</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
<td>Atypical macrophages</td>
</tr>
</tbody>
</table>

Features of **dyserythropoiesis** include fragmented nuclei, binucleation, megaloblasts, asynchronous maturation, and sideroblasts (i.e., nucleated erythroid cells containing granular deposits of iron).

Features of **dysmyelopoiesis** include giant band and segmented neutrophils, hypersegmented neutrophils, asynchronous maturation, and small myeloblasts and myelocytes.

Features of **dysmegakaryopoiesis** include large and small size, asynchronous maturation, and dispersed nuclei.

Bone marrow is usually normocellular or hypercellular and has dysplastic features in two or more cell lines. Myelodysplastic syndrome with excess blasts may progress to acute myelogenous leukemia. The condition responds poorly to treatment, and survival is usually short.

**Secondary Myelodysplastic Syndrome**

Secondary myelodysplastic syndromes have been associated with malignant lymphoma, myelofibrosis, immune-mediated thrombocytopenia, immune-mediated hemolytic anemia, multiple myeloma, and treatment with a variety of drugs. (Table 2). Dysplastic features
may be present in one or more cell lines. Drugs associated with myelodysplasia include vincristine, chloramphenicol, melphalan, cyclophosphamide, chlorambucil, and cephalosporins. Secondary myelodysplastic syndromes usually resolve if the underlying cause is eliminated.

HEMATOLOGIC DISORDERS ASSOCIATED WITH NEOPLASTIC DISORDERS

As with myelodysplastic syndromes, leukemias arise from genetic defects in hematopoietic stem cells. Leukemias are divided into myeloproliferative and lymphoproliferative disorders and are subclassified by the cell type and degree of differentiation. In acute leukemias, malignant cells are immature blast-type cells, whereas in chronic leukemias, malignant cells are relatively mature. If blast cells in marrow exceed 30% of all nucleated cells, a diagnosis of acute leukemia is made. If blast cells in marrow are less than 30% of all nucleated cells, chronic leukemia or myelodysplastic syndromes may be present. Chronic myelogenous leukemias can be differentiated from myelodysplastic syndromes by minimal to no dysplastic features in bone marrow and leukocytosis in the blood. Alternatively, in myelodysplastic syndromes, dysplastic features are prominent and cytopenias are present in the blood.

Acute myeloproliferative disorders are classified by name and a notation system (i.e., M1 through M7). Specific types are as follows:

- **M1 or M2**—Acute undifferentiated leukemia, acute myelogenous leukemia
- **M2B**—Acute myelogenous leukemia with basophilic differentiation
- **M4**—Acute myelomonocytic leukemia
- **M5a or M5b**—Acute monocytic leukemia
- **M6**—Erythroleukemia
- **M6Er**—Erythroleukemia with erythroid predominance
- **M7**—Acute megakaryoblastic leukemia

Chronic myeloproliferative disorders include chronic myelogenous leukemia, eosinophilic leukemia, basophilic leukemia, chronic myelomonocytic leukemia, primary erythrocytosis, essential thrombocytemia, and primary myelofibrosis. Primary erythrocytosis (also called polycythemia vera) is a primary proliferation of erythroid cells resulting in high PCV and RBC counts in blood.

**PRIMARY MYELOFIBROSIS**

Primary (idiopathic) myelofibrosis is a chronic myeloproliferative disorder of erythroid, myeloid, and megakaryocytic cell lines. Fibroblast proliferation appears as a result of the release of growth factors from abnormal megakaryocytes or platelets. Primary myelofibrosis is differentiated from secondary myelofibrosis by the presence of large numbers of atypical megakaryocytes in bone marrow and marked extramedullary hematopoiesis in the spleen and liver. Dysplastic features are frequently present in all hematopoietic cell lines.

**Malignant Histiocytosis**

Malignant histiocytosis is an aggressive malignancy of macrophages characterized by pancytopenia and proliferation of atypical macrophages in the liver, spleen, lymph nodes, lungs, or bone marrow. Malignant histiocytosis occurs sporadically in several canine breeds and has been described in 11 related Bernese mountain dogs. Bone marrow from affected dogs may be hypocellular, normocellular, or hypercellular. Cytologically, malignant histiocytosis cannot always be differentiated from benign hemophagocytic syndromes. A diagnosis of malignant histiocytosis is based on finding features of malignancy, the presence of multinucleated macrophages, or greater than 20% macrophages in bone marrow.

Pancytopenia is the most frequent finding in the peripheral blood in malignant histiocytosis. These cytopenias may result from phagocytosis of blood cells by the malignant macrophages or from suppression of hematopoiesis. Affected dogs respond poorly to treatment with chemotherapeutic drugs, and survival is usually short.
REFERENCES

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logic features in four dogs and a cat with hemophagocytic syn-

### ARTICLE #3 CE TEST

The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. Choose the **best answer** to each of the following questions; then mark your answers on the postage-paid envelope inserted in *Compendium*.

1. Which of the following is not considered an immune-mediated hematologic disorder?
   a. pure red cell aplasia
   b. nonregenerative immune-mediated anemia
   c. immune-mediated hemolytic anemia
   d. pure white cell aplasia
   e. cyclic hematoipoiesis

2. Which of the following hematologic disorders has the **best prognosis**?
   a. myelodysplastic syndrome with refractory anemia
   b. myelodysplastic syndrome with excess myeloblasts
   c. acute myelogenous leukemia
   d. malignant histiocytosis
   e. acute lymphocytic leukemia

3. Which drug has an associated toxicity with the poorest prognosis?
   a. sulfadiazine
   b. quinidine
   c. amiodarone
   d. phenylbutazone
   e. albendazole
4. Which is the best parameter for differentiating malignant histiocytosis from hemophagocytic syndromes?
   a. percentage of macrophages in bone marrow
   b. direct Coombs test
   c. cytophagia
   d. nonregenerative anemia
   e. bone marrow cellularity

5. Which statement regarding secondary myelofibrosis is incorrect?
   a. It may resolve with treatment of the primary condition.
   b. It is associated with immune-mediated diseases.
   c. It occurs secondary to marrow necrosis.
   d. It is a form of chronic myeloproliferative disease.
   e. It may be caused by chronic overproduction of erythropoietin.

6. What is the best diagnosis for a dog with bone marrow characterized by increased cellularity, an M:E of 38:1, normal maturation in the erythroid series, myeloid series shifted toward immaturity, and 53% blast cells?
   a. chronic granulocytic leukemia
   b. myelodysplastic syndrome with refractory anemia
   c. acute myelogenous leukemia
   d. erythroleukemia
   e. myelodysplastic syndrome with excess blasts

7. What is the most likely diagnosis based on the following hematologic data obtained from a 6-year-old spayed dog with a history of decreased exercise tolerance? Complete blood cell count (CBC) was characterized by severe nonregenerative anemia and normal total leukocyte and platelet counts.

   Bone marrow
   Cellularity     Normal
   Megakaryocytes  Normal number
   M:E             106:1
   Maturation      Normal
   Morphology     Normal

   a. nonregenerative immune-mediated anemia
   b. myelodysplastic syndrome with refractory anemia
   c. secondary anemia
   d. pure red cell aplasia
   e. myelodysplastic syndrome with excess blasts

8. What is the most likely diagnosis based on the following hematologic data obtained from a 12-year-old neutered dog with a history of polyuria and polydipsia? CBC was characterized by moderate nonregenerative anemia and normal total leukocyte and platelet counts.

   Bone marrow
   Cellularity     Normal
   Megakaryocytes  Normal number
   M:E             3.2:1
   Maturation      Normal
   Morphology     Normal

   a. nonregenerative immune-mediated anemia
   b. myelodysplastic syndrome with refractory anemia
   c. secondary anemia
   d. pure red cell aplasia
   e. myelodysplastic syndrome with excess blasts

9. What is the most likely diagnosis based on the following hematologic data obtained from a 7-year-old neutered dog with a history of anorexia and weight loss? CBC was characterized by severe anemia and neutropenia and moderate thrombocytopenia.

   Bone marrow
   Cellularity     Increased
   Megakaryocytes  Normal number
   M:E             10.3:1
   Maturation      Myeloid series shifted toward immaturity
   Morphology     Giant bands and segmenters; small myeloblasts; asynchronous maturation in erythroid cells; 10.2% blast cells

   a. nonregenerative immune-mediated anemia
   b. myelodysplastic syndrome with refractory anemia
   c. secondary anemia
   d. pure red cell aplasia
   e. myelodysplastic syndrome with excess blasts

10. What is the most likely diagnosis based on the following hematologic data obtained from a 9-year-old spayed dog with a history of anorexia and vomiting? CBC was characterized by severe poorly regenerative anemia and normal total leukocyte and platelet counts.

    Bone marrow
    Cellularity     Increased
    Megakaryocytes  Normal number
    M:E             1:6.3
    Maturation      Normal
    Morphology     Asynchronous maturation in erythroid series; megaloblasts

    a. nonregenerative immune-mediated anemia
    b. myelodysplastic syndrome with refractory anemia
    c. secondary anemia
    d. pure red cell aplasia
    e. myelodysplastic syndrome with excess blasts