CASE I – NADC SCO 01 (AFIP 2787418).

**Signalment:** Female, 3-year-old bison, 7-10 days prior to estimated parturition.

**History:** This bison cow was anorexic for 5 days and became progressively weaker. The weakness progressed to complete recumbency at which time the animal was euthanized. Blood for analysis was collected immediately. Blood from six “normal” periparturient bison was also collected for comparison.

**Gross Pathology:** The liver was diffusely firm, pale, and yellow, with rounded edges. Sections collected for microscopic analysis floated in formalin. The pleural surface of the lungs was covered with a fibrinopurulent exudate with multiple fibrinous adhesions to the costal pleura. There were multifocal necrosuppurative lesions of variable size within the right and left cranial lung lobes. There was abundant perirenal and intra-abdominal fat.

<table>
<thead>
<tr>
<th>Laboratory Results:</th>
<th>“Normal” Bison</th>
<th>Affected Bison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>Range 139-147</td>
<td>Mean±SD 143.2 ± 2.9</td>
</tr>
<tr>
<td>K</td>
<td>3.3-4.4</td>
<td>3.92 ± 0.37</td>
</tr>
<tr>
<td>Cl</td>
<td>99-106</td>
<td>102 ± 2.5</td>
</tr>
<tr>
<td>TCO2</td>
<td>18.7-26.2</td>
<td>21.6 ± 2.7</td>
</tr>
<tr>
<td>Ca</td>
<td>8.2-9.5</td>
<td>8.7 ± 0.4</td>
</tr>
<tr>
<td>Phos</td>
<td>5.3-7.5</td>
<td>6.4 ± 0.7</td>
</tr>
<tr>
<td>Mg</td>
<td>1.54-2.71</td>
<td>1.81 ± 0.45</td>
</tr>
<tr>
<td>Creat</td>
<td>2.3-5.2</td>
<td>3.4 ± 1.0</td>
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</table>
**Histopathologic Description:** Diffusely hepatocytes are filled with numerous small vacuoles of variable size and smoothly contoured borders. Hepatocytes in all zones are affected. There are also multifocal small aggregates of neutrophils randomly scattered throughout the parenchyma.

**Contributor’s Morphologic Diagnoses:** 1. Liver: Hepatocellular vacuolar change, diffuse, severe, with mild, multifocal, suppurative hepatitis.

2. Lung (not submitted): Bronchopneumonia, fibrinopurulent with necrosis, multifocal, moderate, with fibrinopurulent pleuritis.

**Contributor’s Comment:** Hepatic lipidosis is a morphologic change characterized by the accumulation of lipid vacuoles within hepatocytes. In cattle, miniature horses, cats, sheep and others, this condition develops in response to a negative energy balance (i.e. energy requirements are not matched by energy intake from feed). Hepatic lipidosis is a common lesion of “fatty liver syndrome” or “fat cow syndrome” described in dairy cattle, and arising as a result of improper feeding during late lactation and the dry period. The syndrome occurs particularly in high yielding dairy cows when overfeeding during the dry period results in overfat cows at calving. A negative energy balance may result from parturition, high milk production, or anorexia from other disease states such as mastitis, displaced abomasum, ketosis, etc. As a result, excessive fat is mobilized from body reservoirs and fatty acids are transported to various organs such as the liver, kidney, and muscle. The ability of the liver to process triglycerides for export as lipoproteins is limited; therefore, the excess is deposited as intracellular droplets of triglycerides.

The elevated GGT, Alk Phos, with decreased TCO$_2$ and glucose are consistent with that seen in cattle with hepatic lipidosis.
A disease syndrome associated with fat mobilization and hepatic lipidosis has not been identified in bison. The previous year on the same site, 3 bison died in a similar fashion with histories of anorexia of 7-12 days duration at approximately 180 days gestation. Similar gross and microscopic lesions were seen in the livers of all 3 bison. In the current case, the overconditioned nature of the cow, a period of anorexia (likely from the pneumonia) resulting in a state of negative energy balance, and the resulting lesions, suggest that bison are also susceptible to such a syndrome.

**AFIP Diagnosis:** Liver: Hepatocellular microvacuolar change, lipid-type, diffuse, severe, bison, bovine.

**Conference Comment:** There are several different mechanisms by which triglycerides can accumulate in the liver. Free fatty acids mobilized from adipose tissue or ingested food are normally transported to the liver where they are esterified to triglycerides, converted into cholesterol or phospholipids, or oxidized to ketone bodies. Triglycerides are complexed with apoproteins forming lipoproteins that are transported out of the liver into plasma. Defects in any of the steps from fatty acid entry to lipoprotein exit results in excess accumulation of triglycerides in hepatocytes.4,5

In addition to the “fat cow syndrome” described by the contributor that occurs in dairy cattle and bison, deficiencies of vitamin B12 and cobalt have been associated with fatty liver in sheep (ovine white-liver disease) and goats.6,7 Hepatocellular lipidosis associated with a negative energy balance secondary to ketosis also occurs in sheep and guinea pigs (pregnancy toxemia).6,8 Feline fatty liver syndrome is an idiopathic hepatocellular lipidosis that occurs when obese cats are stressed and become anorectic resulting in a negative energy balance and mobilization of fat stores. Affected cats often develop hepatic failure, icterus, and hepatic encephalopathy.6,7 ALP activity typically increases to a greater magnitude than GGT activity in feline hepatic lipidosis.9 The hepatic lipidosis that occurs in ponies, miniature and donkeys usually occurs in overweight, pregnant, or lactating mares and is associated with stress and/or anorexia. Shetland ponies are predisposed. Affected ponies are hyperlipemic with lipidosis extending to the heart, skeletal muscle, kidneys, and adrenal cortex. Hepatic rupture, renal failure, hepatic encephalopathy, and/or terminal DIC may occur.6,7 A fatal fasting syndrome of obese macaques has also been described. The syndrome is characterized by acute rapid weight loss in obese macaques which is often attributed to the social stressors following recaging, leading to fatty change in the liver and kidneys. Affected monkeys die unexpectedly or after a very short illness. Interestingly, the syndrome is not associated with liver dysfunction and blood chemistry profiles of affected monkeys do not suggest liver failure. The most common clinical
Pathologic finding is azotemia.\textsuperscript{10,11} Metabolic fatty liver syndromes also occur in chickens and turkeys.\textsuperscript{12,13} Hepatic lipidosis can also occur with diabetes mellitus, hypothyroidism, acute pancreatitis (cats), and hepatotoxicity.\textsuperscript{6,9}

Conference attendees discussed the clinical pathologic findings associated with the case. The increased anion gap was most likely due to a titration (organic acid excess) acidosis due to ketoacidosis resulting in loss of HCO\textsubscript{3} (decreased TCO\textsubscript{2}) by titration. The increased GGT and ALP indicate cholestasis that occurs secondary to hepatocellular swelling due to lipid accumulation and subsequent compression of bile canaliculi.\textsuperscript{9} The total protein was slightly increased with normal albumin levels indicating that the increase was due to increased globulins which can be seen in chronic infections in ruminants. It is unusual that the CK activity was decreased as this value is usually elevated in downer cows. However, the reference range established by blood samples collected from six “normal” periparturient bison was extremely wide.

In some sections of liver, there was a multifocal, mild, neutrophilic portal hepatitis.

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\textbf{References:}
2. Rukkwamsuk T, Kruip TAM, Wensing T: Relationship between overfeeding and overconditioning in the dry period and the problems of high producing dairy cows during the postparturient period. Vet Quart 21:71-77, 1999
CASE II – 06-61-2 (AFIP 3006324).

**Signalment:** 9-year-old, neutered male, German Shepherd Dog, canine.

**History:** A conjunctival mass was removed from the dog’s left eye two months before referral and was diagnosed as a melanocytic neoplasm. Thoracic radiographs were taken to check for metastasis. A large thoracic mass was identified radiographically in all views. On the lateral view, the mass was located in the cranioventral thorax and was approximately the size of the cardiac silhouette. On ventrodorsal view, the entire cranial thorax was radiopaque and normal architecture obscured. Ultrasound-guided percutaneous fine needle aspirate was performed. A cavernous, mixed echogenicity mass was located around rib 3-4 and copious amounts of mucoid, viscous serosanguineous fluid was aspirated. The dog was clinically normal at this time. The dog was referred for further work-up and possible surgical intervention. Additional imaging and a repeat fine-needle aspirate were performed along with a needle biopsy of the mass. Surgical resection of the mass was deemed impractical. The dog was euthanized and a necropsy performed.

**Gross Pathology:** At necropsy, an approximately 15 cm diameter, irregularly round, firm, multilobular mass was identified in the right cranial lung lobe. (digital images) The mass is white to tan on cross section with a cavitated center. The right middle lung lobe is multifocally atelectatic. The tracheobronchial lymph nodes are moderately enlarged, firm and mottled red on cross section. There is approximately 5-10 ml of clear fluid in the pericardial sac. The heart is mildly rounded with a flaccid left ventricle. The spleen is enlarged and oozes blood on cross section (congestion). There is a 1 cm soft tan mass in the subcutis of the left flank.
(lipoma, confirmed with histopathology). Physiological atrophy of prostate is noted (neutered male).

**Laboratory Results:** FNA cytology of thoracic mass: Multiple slides are examined and are moderately cellular with a prominent, dense, eosinophilic, stippled background and windrowing of erythrocytes with occasional aggregates of amorphous basophilic material suggestive of protein. A moderate amount of blood is also present. Nucleated cells are predominantly a population of polygonal to spindle cells that exhibit moderate anisocytosis and anisokaryosis. Cells are medium to occasionally large with a moderate amount of deeply basophilic cytoplasm and frequent intracytoplasmic vacuoles. Occasional cells contain intracytoplasmic, homogenous, eosinophilic material. Nuclei are round to oval with stippled chromatin and prominent nucleoli. A rare mitotic figure is observed.

**Contributor’s Morphologic Diagnoses:** Lung: Chondrosarcoma, German Shepherd Dog, canine.

**Contributor’s Comment:** This appears to be a primary chondrosarcoma of the lung due to the size of the lung mass and failure to identify any primary bony lesion clinically or during gross necropsy. During histological examination of tissues collected at necropsy, a microscopic focus of apparent metastasis of the pulmonary chondrosarcoma was found in extradural fibro-adipose tissue at the lumbar level of the spinal column. No compression of the spinal cord at this level was noted. The tracheobronchial lymph nodes, noted to be enlarged during gross necropsy, did not show evidence of metastasis, but did exhibit draining hemorrhage and edema.

Primary lung tumors in dogs are rare and usually originate from epithelial tissue. Primary chondrosarcomas are extremely rare in both dogs and humans, but have been occasionally reported. Chondrosarcomas can arise from existing normal cartilage and perichondrium. In dogs, more common sites of occurrence are the pelvis, nasal cavity, sternum and ribs and less commonly in long bones. Chondrosarcomas are less likely to metastasize and do so later in the course of disease than osteosarcomas. Chondrosarcomas tend to occur in older large breed dogs and are the most frequent bone tumor in sheep.

Cytology findings typical of a chondrosarcoma include oval to fusiform or spindle shaped cells with abundant basophilic cytoplasm that often contains vacuoles and eosinophilic granules. Often lakes of eosinophilic smooth to slightly granular material may be present in the background and occasionally cells are noted to be embedded. This material is thought to represent matrix material or “chondroid”. Cells generally exfoliate in lower numbers (compared to epithelial lesions) as individual cells or small aggregates. These finding are not always specific for a chondrosarcoma. Other sarcomas including osteosarcoma, myxosarcoma, and
fibrosarcomas can have similar cytological appearances. Definitive diagnosis of sarcomas often requires histopathological examination of tissues. A staining procedure using alkaline phosphatase on cytological specimens has been recently described to help differentiate osteosarcomas from other Vimentin-positive tumors in animals.

AFIP Diagnoses: Lung: Chondrosarcoma, German Shepherd Dog, canine.

Conference Comment: The contributor provides an excellent synopsis of chondrosarcomas in the dog as well as the typical cytological findings associated with the neoplasm.

Primary lung tumors are uncommon to extremely rare in domestic animals depending on the species. One exception is ovine pulmonary carcinoma (pulmonary adenomatosis), a transmissible, Type B/D retrovirus-induced neoplasia of ovine lungs. Neoplastic cuboidal to columnar epithelial cells tend to infiltrate the cranioventral lung lobes and line airways and alveoli forming papillary or acinar structures. The neoplasm is considered a bronchioalveolar carcinoma since neoplastic cells originate from type II pneumocytes and Clara cells. Granular cell tumors are the most frequently reported primary tumor of horses and usually present as a unilateral, firm, coarsely nodular, whitish mass causing obstruction of a major airway or several major airways. The neoplasm occurs most frequently in the right lung lobe. Histologically, neoplastic cells are round to polygonal with abundant, coarsely granular, eosinophilic cytoplasm. The cytoplasmic granules are PAS positive and diastase resistant. Ultrastructurally, the cells contain packed lysosomes and phagosomes (myelin bodies). The granular cells are thought to be derived from Schwann cells. Primary lung tumors, largely carcinomas, occur most frequently in aged dogs and cats.

Secondary neoplasms in the lung are relatively common compared to primary neoplasms and can be of epithelial or mesenchymal origin as well. Common metastatic neoplasms of epithelial origin include mammary, thyroid, and uterine carcinomas. Metastatic neoplasms of mesenchymal origin include osteosarcoma, hemangiosarcoma, melanoma (dogs), lymphoma (cows, pigs, dogs, cats), and vaccine associated fibrosarcomas (cats).

The gross and microscopic appearance of metastatic tumors can be difficult or impossible to distinguish from those of a primary tumor. Therefore, a thorough attempt to exclude the possibility of metastasis from a distant site must be made prior to diagnosing a primary lung tumor.
The most common types of benign and malignant pulmonary neoplasms in domestic animals are listed in the table below from Pathologic Basis of Veterinary Disease:  

**Classification of Pulmonary Neoplasms**

<table>
<thead>
<tr>
<th>PRIMARY EPITHELIAL ORIGIN</th>
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<tbody>
<tr>
<td><strong>Benign</strong></td>
<td></td>
</tr>
<tr>
<td>Papillary adenoma</td>
<td></td>
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<tr>
<td>Bronchiolar-alveolar adenoma</td>
<td></td>
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<tr>
<td><strong>Malignant</strong></td>
<td></td>
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<tr>
<td>Adenocarcinoma (acinar or papillar)</td>
<td></td>
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<tr>
<td>Squamous cell carcinoma</td>
<td></td>
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<tr>
<td>Adenosquamous carcinoma</td>
<td></td>
</tr>
<tr>
<td>Bronchiolar-alveolar carcinoma</td>
<td></td>
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<tr>
<td>Small cell and large cell carcinomas</td>
<td></td>
</tr>
<tr>
<td>Anaplastic (undifferentiated) carcinoma</td>
<td></td>
</tr>
<tr>
<td>Carcinoid tumor (neuroendocrine)</td>
<td></td>
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<tr>
<td>Ovine (retroviral) pulmonary carcinoma</td>
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<table>
<thead>
<tr>
<th>PRIMARY MESENCHYMAL ORIGIN</th>
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<tbody>
<tr>
<td><strong>Benign</strong></td>
<td></td>
</tr>
<tr>
<td>Hemangioma</td>
<td></td>
</tr>
<tr>
<td><strong>Malignant</strong></td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma, chondrosarcoma</td>
<td></td>
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<tr>
<td>Hemangiosarcoma</td>
<td></td>
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<tr>
<td>Malignant histiocytosis</td>
<td></td>
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<tr>
<td>Lymphomatoid granulomatosis</td>
<td></td>
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<tr>
<td>Granular cell tumor</td>
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<tr>
<td>Mesothelioma</td>
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<table>
<thead>
<tr>
<th>SECONDARY (METASTATIC) LUNG TUMORS</th>
<th></th>
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<tbody>
<tr>
<td>Any malignant tumor metastatic from another body location (e.g., osteosarcoma in dogs, uterine carcinoma in cows, malignant melanoma in horses)</td>
<td></td>
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</tbody>
</table>

**Contributor:** Comparative Pathology, AFRL/HEDV, 2509 Kennedy Circle, Brooks AFB, TX

**References:**

CASE III – Case 2  (AFIP 3026267).

Signalment:  8-month-old, intact male, domestic short-haired cat (*Felis catus*).

History:  (From referring veterinarian) Patient is from a multiple (7) cat household. Two of the seven cats exhibited acute onset lethargy, vomiting and pyrexia. No response to antibiotics. Both patients died.

Gross Pathology:  An intact male gray cat with white paws weighing 10 pounds 6 ounces is presented for necropsy. There are moderate numbers of fleas present on the carcass with a few ticks identified. Oral and scleral mucous membranes are yellow in color with some edema. Bilaterally, lungs are overinflated, dark red to dark pink in color with thin clear fluid and foam exuding out of airways on cut surface. Multifocal hemorrhages are noted on the epicardial surface. The spleen is enlarged. The stomach is empty, and the small intestine contains minimal yellow content and some tapeworms.
**Histopathologic Description:** Spleen and lung: The red pulp of the spleen contains a disseminated population of large schizonts-laden macrophages. Similarly, numerous schizonts-laden macrophages partially or completely occlude trabecular vessels. The white pulp is moderately atrophied. The open alveolar architecture of the lung is extensively obscured secondary to alveolar filling by hemorrhage, edema and scattered fibrin deposition. Alveoli contain numerous large foamy macrophages, some exhibiting erythrophagocytosis and others expanded by schizonts. Alveolar septa are expanded by edema. The septal capillaries along with large pulmonary vessels (both arteries and veins) are partially to completely occluded by numerous schizonts-laden macrophages.

**Contributor’s Morphologic Diagnoses:** 1. Lung: Severe, regionally extensive, pulmonary hemorrhage and edema with intralveolar and intravascular, intrahistiocytic schizonts consistent with *Cytauxzoon felis*. 2. Spleen: Intravascular and intrahistiocytic (red pulp) schizonts consistent with *Cytauxzoon felis* and mild to moderate, diffuse, lymphoid atrophy.

**Contributor’s Comment:** *Cytauxzoon felis* is a protozoan hemoparasite associated with severe clinical disease and high mortality in domestic cats. Organisms in the genus *Cytauxzoon* are closely related to the genera *Babesia* and *Theileria*. Moreover, piroplasms of small *Babesia* species are morphologically indistinguishable from *C. felis*.

The reservoir for *C. felis* appears to be the bobcat, where *Cytauxzoon* infection is usually asymptomatic but results in a long-lasting erythroparasitemia. The parasite is transferred form the wild bobcat to domesticated cats by tick vectors. Research has shown *Dermacentor variabilis* to be a competent vector. Whereas the intraerythrocytic piroplasms seem to do little harm, the schizogonous phase of the organism is responsible for the marked clinical signs of disease. Schizont-laden macrophages become greatly enlarged and are typically found within the lumen of blood vessels that become nearly or totally occluded. Vascular obstruction and damage is thought to be one of the major pathophysiologic mechanisms in this disease. Concomitantly, gross lesions of infection are associated with vascular lesions and include: marked pulmonary congestion and edema, widespread petechial and ecchymotic hemorrhages, abdominal vein distension, and body cavity effusions. Figure 2 highlights gross lesions of Cytauxzoonosis including pulmonary congestion/edema, pulmonary hemorrhages and pleural effusions.

Diagnosis of Cytauxzoonosis is usually made by identification of the organism in blood smears. Since the schizogonous phase is responsible for clinical disease, and since this phase precedes detectable erythroparasitemia, some cats may not have circulating piroplasms at the time of initial presentation. Therefore, negative smears should be temporally repeated if clinical suspicion of disease remains strong. On the other hand, false diagnosis of Cytauxzoonosis is not uncommon.
secondary to misidentification of stain precipitates and Howell-Jolly bodies (Figure 1) as true organisms.1

Lastly, cats infected with *Cytauxzoon felis* have invariably been given a grave prognosis. However, recently, there have been some reports of cats surviving natural infection without treatment.4 The current hypothesis is that recovery is linked to the existence of a less virulent strain of *C. felis*.4

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**AFIP Diagnosis:** 1. Lung, vessels: Intrahistiocytic schizonts, myriad, with diffuse hemorrhage and edema, domestic short hair, feline.

2. Spleen, vessels and red pulp: Intrahistiocytic schizonts, myriad.


**Conference Comment:** The contributor provides an excellent synopsis of Cytauxzoonosis.

As pointed out by the contributor, the signet ring-shaped erythrocytic piroplasms of *C. felis* closely resemble the small form of *Babesia* and some *Theileria* organisms. In contrast to *C. felis* with an erythrocytic phase and a schizogenous phase in macrophages, *Babesia* only infects erythrocytes. *Theileria* organisms also have erythrocytic and non-erythrocytic phases; however, the schizogenous phase occurs in lymphocytes rather than in macrophages.1

In addition to the 3 intracellular protozoal parasites mentioned above, intracellular rickettsial organisms (*Anaplasma*) and epicellular mycoplasma organisms (*Mycoplasma haemofelis, M. suis*) are known to occur in or on erythrocytes. All of these erythrocyte infectious agents cause mild to severe hemolytic anemia depending on the pathogenicity of the organism and host susceptibility. Additionally, distemper virus inclusions may be seen in canine erythrocytes.5

Many species of *Babesia* infect animals worldwide and vary markedly in size from large and easy to visualize (*B. canis*) to small and difficult to see (*B. gibsoni, B. felis*). Large babesial species typically occur in pairs and are pear-shaped whereas small babesial organisms are more round.5

Theilerial organisms appear similar to babesial organisms on stained blood films. The theilerial organisms present in the United States are usually nonpathogenic and are most commonly observed in deer blood.5
*Anaplasma* organisms are round to oval basophilic inclusions in ruminant erythrocytes and must be differentiated from Howell-Jolly bodies. *Anaplasma* organisms are generally not perfect spheres and are smaller than Howell-Jolly bodies.\(^5\)

*Mycoplasma haemofelis* (formerly *Haemobartonella felis*) appears as small blue-staining, variably sized (0.5 – 1.5 um in diameter) cocci, rings, or rods on feline erythrocytes. *M. haemofelis* occurs in cyclic parasitemias and is not always visible in blood smears. *M. haemocanis* (formerly *Haemobartonella canis*) forms chains of organisms on the surface of erythrocytes. *Mycoplasma suis* (formerly *Eperythrozoon suis*) species appear as small delicate basophilic rings on or between erythrocytes in sheep, pigs, cattle, and llamas. While mycoplasma infections can cause significant anemia in pigs and sheep (especially young animals), they usually do not in cattle and llamas.\(^5\) Additionally, most hemotropic mycoplasma subspecies cause disease in immunocompromised animals or animals with concurrent disease. The exception is *M. haemofelis* which causes acute hemolytic anemia in immunocompetent cats.\(^6\)

Although *Bartonella henselae* infects erythrocytes, this small Gram-negative bacteria is rarely seen in blood films.\(^5\)

Distemper viral inclusions appear as variably sized, round, oval, or irregular, blue-gray inclusions that most often occur in polychromatophilic cells during the viremic phase of infection. If the Diff-Quik stain is used, distemper inclusions typically stain red.\(^5\)

Common avian blood parasites include *Hemoproteus*, *Plasmodium*, and *Leukocytozoon*. Only the gametocytes of *Hemoproteus* are found in peripheral blood and vary in size from small, developing ring forms to elongate, crescent-shaped, mature gametocytes that partially encircle the erythrocyte nucleus. *Hemoproteus* gametocytes contain refractile, yellow to brown pigment granules (iron pigment). In contrast to *Hemoproteus*, schizonts and trophozoites as well as gametocytes can be found in erythrocytes, thrombocytes, and leukocytes in infections with *Plasmodium*. The gametocytes of *Plasmodium* also contain iron pigment granules. Like *Hemoproteus*, only the gametocytes of *Leukocytozoon* are seen in peripheral blood. The gametocytes are large and grossly distort infected cells making cell identification difficult. Some parasitologists believe that erythrocytes rather than leukocytes serve as the host cell for *Leukocytozoon*. The gametocytes of *Leukocytozoon* do not contain refractile pigment granules.\(^7\)

Hemogregarines are the most common reptilian hemoparasites and include *Hemogregarina*, *Hepatozoon*, and *Karyolysus*. The sausage-shaped gametocytes are found within the cytoplasm of erythrocytes. Typically only one gametocyte is
found per erythrocyte; however, in heavy infections up to two gametocytes may be found in erythrocytes.  

Erythrocyte parasites must be differentiated from precipitated stains, refractile drying or fixation artifacts, poorly staining Howell-Jolly bodies, basophilic stippling, and platelets overlying erythrocytes.

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**References:**

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**CASE IV – 06-12133** (AFIP 3027434).
**Signalment:** 8-year-old, 41.5kg (91lb), spayed female, Dalmatian dog (*Canis familiaris*).

**History:** Approximately two weeks prior to necropsy, the dog presented to the referring veterinarian after falling down the stairs. The dog was slightly lame in the hind limbs and treated with Adequan® (polysulfated glycosaminoglycan) injections and pain management and sent home. Over a week and a half later the dog presented to the University of Illinois Veterinary Teaching Hospital for acute lameness and swelling of the left hind limb. On physical examination the left hind limb was cool to the touch with cyanotic nail beds. Proprioceptive and nociceptive deficits were also detected. Evaluation of the right limb also revealed similar, but less severe findings. A complete blood cell count, serum chemistry and urinalysis were performed. Abdominal ultrasonography with Doppler evaluation revealed minimal flow in the distal aorta. The dog was subsequently euthanized due to progressive clinical signs.

**Gross Pathology:** On gross examination the dog was obese with plentiful subcutaneous and visceral adipose tissue stores (Figure A). The abdominal aorta distal to the renal arteries was completely occluded by a column of a dark red to tan dull and friable material that was tenuously adhered to the vascular endothelium (thrombus). The thrombus extended through the external iliac arteries into the femoral arteries occluding the lumina along the entire length of the vessels (Figures B and C). The endothelial surface adjacent to the ostia of major branches of the aorta was often thickened, firm, roughened and slightly raised by irregular plaques composed of a dull yellow tan grumous to granular core with a pale yellow to white firm fibrous cap.

The coronary arteries were also segmentally affected by similar plaques (Figures D and E).

The thyroid glands were symmetrically shrunken measuring approximately 0.3 x 0.3 x 1 cm and diffusely pale tan.

**Laboratory Results:** The CBC revealed a mild anemia with a hematocrit of 31.1% (35-52%), red blood cell count of 4.36x10⁶/µl (5.50 to 8.50x10⁶/µl) and a hemoglobin concentration of 11.1 g/dl (12.0 to 18.0). The dog also had a moderate leukocytosis with a white blood cell count of 29.1x10³/µl (6.00 to 17.00x10³/µl) and a mature neutrophilia 27.7x10³/µl (3.00 to 11.50x10³/µl) and mild lymphopenia 0.819x10³/µl (1.00 to 4.80x10³/µl).

Serum chemistry revealed minimal to mild elevations in serum calcium 12.0mg/dl (7.9 to 11.5mg/dl), alkaline phosphatase 178 U/l (12 to 110 U/l), and corticosteroid induced alkaline phosphatase (cALP) 87 U/l (0 to 40 U/l). Serum triglyceride levels
were moderately increased at 235 mg/dL (25 to 145 mg/dL) and total serum cholesterol was severely increased at 1416 mg/dl (109 to 315 mg/dl). Bicarbonate levels (TCO2) were also moderately decreased at 13.3 mmol/l (17.0 to 29.0 mmol/l) with a normal anion gap.

The urinalysis was unremarkable with a specific gravity of 1.025.

A thyroid profile revealed a severely decreased total T4 of less than 6.4 nmol/L (15.0 to 48.0 nmol/L), a severely decreased free T4 of 1 pmol/L (6 to 42 pmol/L) and a markedly increased thyroxin stimulating hormone (TSH) concentration of 2 ng/ml (0.03ng to 1.00 ng/ml).

**Histopathologic Description:** The tunica intima and media are eccentrically thickened, moderately to markedly expanded and partially effaced by variable amounts of foamy vacuolated macrophages (foam cells) admixed with lipid droplets and acicular clear spaces (cholesterol clefts) that separate the smooth muscle myofibers. In affected areas the myofibers are occasionally fragmented and degenerative with foamy pale eosinophilic cytoplasm and pyknotic or karyorrhectic nuclei. The tunica media is occasionally mildly infiltrated by lymphocytes and plasma cells admixed with an amorphous to granular deeply basophilic material (mineral). The internal elastic lamina and endothelium are segmentally disrupted and confluent with a fibrillar to amorphous pale eosinophilic material (fibrin) that fills and occludes the lumen entrapping numerous leukocytes, erythrocytes, hematoidin crystals and much cellular debris in vaguely laminated sheets (lines of Zhan).

**Contributor’s Morphologic Diagnosis:** Marked chronic atherosclerosis with severe acute thrombosis, femoral artery, dog

**Contributor’s Comment:** Atherosclerosis, while a leading cause of morbidity and mortality in man, is uncommon in domestic species. Atherosclerosis is characterized by intimal thickening due to lipid accumulation with variable amounts of inflammatory infiltrate (macrophages, lymphocytes and plasma cells), fibrosis, proteoglycan matrix and mineralization. These aggregates form atheromatous plaques that protrude into the lumen and weaken the tunica media. Elastic arteries are often affected and serious sequel include thrombosis and aneurism; however canine atherosclerosis is uncommonly associated with thrombosis and extensive atheromatous plaque formation. In this case segmental disruption of the internal elastic lamina is visualized using Verhoeff’s Elastic stain (Figure F). In man atherosclerosis is currently considered to be a chronic inflammatory response to endothelial injury. Unlike the disease in man, the role of chronic inflammation in the development of canine atherosclerosis remains unclear.
In the dog a predisposition for spontaneous atherosclerosis has been associated with hypothyroidism. In concordance with this observation, atherosclerosis can be experimentally induced in thyroidectomized dogs fed large quantities of cholesterol or cholic acids. Hypothyroidism is a commonly diagnosed condition of canines with idiopathic thymic atrophy or lymphocytic thyroiditis as the leading causes of this disorder. An immune mediated pathogenesis for lymphocytic thyroiditis has been postulated due to the similarities to Hashimoto’s thyroiditis in man, however a definitive molecular pathogenesis has yet to be determined. Current research has demonstrated an association between a rare DLA class II haplotype and lymphocytic thyroiditis in Doberman Pinschers and several other breeds.

In this case, the thyroid gland was evaluated histologically and was found to be almost entirely effaced by a lymphoplasmacytic infiltrate that surrounded, separated and individualized the few remaining follicles (Figures G and H). The remaining follicles were often small shrunken with a pale amphophilic finely stippled colloid. The microscopic findings in the thyroid were consistent with lymphocytic thyroiditis.

AFIP Diagnosis: Large muscular artery: Atherosclerosis, chronic, multifocally extensive, severe, with thrombosis.

Conference Comment: The contributor provides a nice summary of the components of a classic atherosclerotic lesion, possible sequela, and its association with hypothyroidism in the dog.

Conference attendees began by discussing the thyroid profile. A normal total T4 generally rules out hypothyroidism. Although the presence of anti-T4 autoantibodies in 10% of cases of hypothyroidism may increase the total T4 concentration into or above the reference interval, and hypothyroidism will not be detected. A decreased total T4 alone does not confirm hypothyroidism. Nonthyroidal illness may decrease the serum total T4 concentration (euthyroid sick syndrome). Hypothyroidism should be confirmed or excluded by determining TSH and fT4 concentrations. The direct dialysis fT4 assay has the highest single-test diagnostic sensitivity, specificity, and accuracy in detecting thyroid disease. Measurement of endogenous TSH concentration detects a lack of negative feedback on the pituitary gland and hypothalamus. Serum TSH levels are increased in approximately 75% of dogs with primary hypothyroidism.

Generalized vascular degenerative diseases in animals are classified into three different groups: atherosclerosis, arteriosclerosis, and arterial medial calcification. Pigs, rabbits, and chickens develop atherosclerosis when fed high-cholesterol diets,
whereas dogs, cats, cows, goats, and rats are resistant. Atherosclerosis naturally develops in aged pigs and birds, and also occurs in dogs with hypothyroidism or diabetes mellitus. Atherosclerosis is infrequently seen in dogs with hypothyroidism. When it is seen, it is most likely associated with an increased proportion of cholesterol-rich VLDL. Grossly, arteries of the heart, mesentery, and kidney are prominent, yellow-white, and cordlike. Arteriosclerosis literally means hardening of the arteries and is further defined as “chronic arterial change consisting of hardening, loss of elasticity, and luminal narrowing resulting usually from proliferative and degenerative, rather than inflammatory, changes of the media and intima” in Pathology of Domestic Animals. Arteriosclerosis occurs commonly in many aged animal species and rarely causes clinical signs. The aorta is most frequently affected, but other elastic and muscular arteries may be involved. Grossly, the lesions appear as raised, firm, white plaques. Histologically, the intima is thickened by accumulation of mucopolysaccharides, proliferation of smooth muscle cells in the tunica media, and fibrous tissue infiltration into the intima. Additionally, the internal elastic lamina is frequently split and fragmented. Arterial medical calcification involves muscular and elastic arteries and is commonly seen in animals with concurrent endocardial mineralization. Causes of arterial medial calcification include vitamin D toxicosis, renal insufficiency, calcinogenic plant toxicosis, and severe debilitation (Johe’s disease). Spontaneous medial calcification occurs in rabbits, aged guinea pigs, and rats with chronic renal disease. Grossly, affected arteries appear as solid, dense, pipelike structures with multiple white mineralized foci in the tunica intima and media. Histologically, prominent basophilic granular mineral deposits to complete rings of mineralization are visible in the tunica media.

Other lesions associated with hypothyroidism in the dog include hepatomegaly, glomerular and corneal lipidosis, bilaterally symmetrical alopecia, hyperkeratosis, hyperpigmentation, and myxedema.

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