CASE I – C-33738-06 (AFIP 3083594).

**Signalment:** Adult, spayed, female Chihuahua

**History:** This dog developed vomiting, diarrhea and anorexia one day following routine vaccinations and was treated symptomatically with fluids and antibiotics. However, the patient continued to deteriorate with evidence of a progressively worsening liver disorder and was euthanized eight days following the vaccinations.

**Gross Pathology:** The submitting veterinarian did a necropsy on the patient but did not report abnormal findings. Fixed specimens of spleen, kidney and liver were received from the referring veterinarian for histopathology.

**Histopathologic Description:** The section of liver is characterized by marked centrilobular and midzonal hepatic necrosis (Fig. 1-1) with sparing of hepatocytes located adjacent to portal triads. Canalicular plugging with bile is frequently observed between surviving hepatocytes (Fig. 1-2). In the necrotic tissue, ghost-like remnants of necrotic hepatocytes and the accompanying sinusoids can generally be visualized (coagulative necrosis). Inflammatory cell activity is minimal in all areas.

**Contributor’s Morphologic Diagnosis:** Marked acute hepatic necrosis with periportal sparing and periportal cholestasis, Chihuahua, canine.

**Contributor’s Comment:** Upon further investigation, the referring veterinarian discovered that the patient had inadvertently been vaccinated by injection with an intranasal trivalent *Bordetella bronchiseptica*–canine parainfluenza-canine adenovirus-2 vaccine product due to an error in vaccine preparation by a newly hired technician. The product package insert warns that subcutaneous or intramuscular administration of the intranasal product may result in icterus or death from liver failure, but we were unable to find any information in the scientific literature to explain the mechanism of hepatic injury or which component in the vaccine might be responsible for the injury. There is one published report of acute hepatic necrosis associated with subcutaneous administration of an intranasal canine *B. bronchiseptica*-canine parainfluenza vaccine, but the authors did not speculate as to pathogenesis. The patient survived and hepatocellular disease was still present two months later based on hepatic biopsy and serum bile acid concentrations. Equine serum hepatitis, sometimes known as Theiler’s disease, occurs subsequent to vaccine nation with biologics that contain equine serum and has a similar pattern of marked hepatic necrosis with periportal sparing. However, after nearly one hundred years since equine serum hepatitis was first reported, the pathogenesis of the disorder remains elu...
Ordinarily, massive hepatic necrosis in dogs suggests a toxic etiology. Although many drugs, toxins and chemicals have been shown to cause hepatic injury in dogs, it is difficult to find a comprehensive list of substances in which the toxicosis in dogs is predominately manifested by acute, severe hepatic necrosis. In our laboratory, ingestion of fly litol, cycad palm, poisonous mushrooms (particularly *Amanita* sp.), or water containing blue-green algae are our first considerations as causes of marked hepatic necrosis when there has been no known exposure to drugs or chemicals.

**AFIP Diagnosis:** Liver: Hepatocellular necrosis, acute, submassive to massive, diffuse, with hemorrhage and canalicular cholestasis, Chihuahua (*Canis familiaris*), canine.

**Conference Comment:** Massive hepatic necrosis is defined as necrosis of entire acini. In the sections examined at the conference, there are acini that are entirely necrotic as well as acini that are largely necrotic with a rim of surviving hepatocytes around the portal areas. Massive necrosis leads to collapse of the remaining stroma, impaired regeneration and postnecrotic scarring. It is usually, but not always, caused by toxins. Hepatosis dietetica is a nutritionally induced form of massive hepatic necrosis.

Hepatotoxic agents can be divided into two broad categories based on their predicted activity. Predictable hepatotoxins are those that produce a generally consistent activity in the majority of the animals that are exposed. The extent of injury produced in an individual animal by a predictable hepatotoxin may differ depending on various factors including age, sex, diet, and endocrine function. Idiosyncratic drug reactions are caused by those agents that produce an effect in a small minority of the animals exposed, such as carprofen occasionally causing acute hepatic necrosis in Labrador retrievers and diazepam causing acute fatal hepatic injury in some, but not all, cats.

Hepatotoxic agents can be classified into six different categories based on their cellular target:

1. Production of toxic metabolites by the cytochrome p450 system is the most common form of hepatocellular injury. The enzymes of this system are located in the high-concentration of central lobular hepatocytes. They function to metabolize lipid-soluble chemicals into water-soluble compounds for excretion.
2. Drugs and cellular enzymes may combine together to form neoantigens. When transported to the cell surface and presented as antigens, these neoantigens may stimulate both cellular and humoral immune responses resulting in either direct cellular cytotoxicity or an antibody-dependent cellular cytotoxicity. (halothane)
3. Some toxins may directly initiate apoptosis by stimulating proapoptotic pathways within hepatocytes. (hydrophobic bile acids)
4. Certain toxins may directly damage cellular membranes disabling calcium homeostasis and resulting in cell death. (carbon tetrachloride)
5. There are chemicals that will bind and disrupt the cellular membranes.

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1-1. Liver, Chihuahua. Diffuse coagulative necrosis of the hepatic cords. (HE 40X).
1-2. Liver, Chihuahua. Multifocally, hepatocytes of the limiting plate are often degenerate characterized by swollen, pale, vacuolated cytoplasm (arrowhead) and/or contain green-brown intracanalicular bile plugs (cholestasis). (HE 400X).
Selected hepatotoxins extracted from Cullen

<table>
<thead>
<tr>
<th>Category</th>
<th>Members</th>
<th>Mechanism of action</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue-green algae</td>
<td>Anabaena, Aphanizomenon, Microcystis</td>
<td>Microcystin LR (cyclic heptapeptide)</td>
<td>More closely related to bacteria</td>
</tr>
<tr>
<td>Pyrrolizidine alkaloids</td>
<td>Senecio, Cynoglossum, Crotalaria, Heliotropium</td>
<td>Ingested alkaloids converted to pyrrolic esters by cytochrome p450 enzymes</td>
<td>Esters are alkylation agents that act on cytosolic and nuclear proteins. Megalocytes due to antimitotic effect.</td>
</tr>
<tr>
<td>Aflatoxin</td>
<td>Aspergillus flavus Aflatoxin in B1 (toxic intermediates produced by cytochrome p450 enzymes)</td>
<td>Toxin and carcinogen. Sheep more resistant.</td>
<td></td>
</tr>
<tr>
<td>Sporidesmin</td>
<td>Pithomyces chartarum (fungus growing on dead rye grass)</td>
<td>Necrosis of the epithelium of large intrahepatic and extrahepatic biliary ducts</td>
<td>Results in cholestasis with failure to excrete phylloerythrin leading to photosensitization</td>
</tr>
<tr>
<td>Mushroom</td>
<td>Amanita sp.</td>
<td>Toxic cyclopeptides</td>
<td>Inhibition of RNA polymerase II function disrupting DNA and RNA transcription Disruption of intracellular actin filaments</td>
</tr>
</tbody>
</table>

Nalicular pumps that normally secrete bile into the ca naliculari. Thi disruption results in cholestasis. (estrogen, erythromycin) 6. Direct damage to mitochondria decreases production of adenosine triphosphate as well as resuting in the release of cytochrome-c leading to cytoptosis or necrosis (antiviral nucleosides, intravenous tetracycline)

Certain toxic compounds may affect cells of the biliary epithelium may be caused by trimethoprim-sulfa or sporidesmin, while damage to Kupffer cells can be caused by endotoxin. Arsenicals damage endothelial cells of the liver, and vitamin A excess causes activation of hepatic stellate cells.

Equine serum hepatitis is an idioopathic condition most closely associated with administration of equine-origin biologics. It is generally reported 41-60 days following administration of a biologic product, and is characterized by acute hepatic centrilobular necrosis.1

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References:
5. Toshack K, Jackson MW, Dubielzig RR: Hepatocellular necrosis associated with the subcutaneous injection of...

CASE II – S61/07 (AFIP 3063785).

Signalment: Two and a half-year-old, male beagle, canine.

History: The dog died with multiple bite wounds inflicted by other dogs kept in the same kennel.

Gross Pathology: At necropsy the animal displayed multifocal, severe epidermal ulcers and excoriations of the skin of the neck, thorax and both hind limbs associated with multifocal subcutaneous and intramuscular hemorrhages. The mandibular and retropharyngeal lymph nodes were enlarged and severely hyperemic. The endocardium had multiple petechial hemorrhages and the atrioventricular valves had mild nodular endocardiosis. The liver and lung were moderately congested. In addition, the lung had mild alveolar edema and emphysema.

Histopathologic Description: Within the kidney there was multifocal vacuolation, degeneration and necrosis with sloughing and loss of tubular epithelial cells. Epithelial degeneration and necrosis were frequently associated with small cytoplasmic granular deposition of a brown-greenish pigment. Tubuli were multifocally moderately dilated and contained hyaline or coarsely granular eosinophilic to brown-greenish casts (Fig 2 -1). The Bowman’s capsule and e vacuoles contained abundant eosinophilic, proteinaceous material. Interstitial and glomerular blood vessels were moderately congested with multifocal prominent dilation of cortical veins.

A Turnbull blue stain identified iron in the tubular casts, the brush border and in cytoplasmic granular deposits of the tubular epithelium, consistent with chromoproteinuria.

Contributor’s Morphologic Diagnosis: Kidney: Tubular degeneration and necrosis (Fig. 2-2), acute, moderate, multifocal with cytoplasmic pigment deposition and intratubular chromoprotein casts.

Contributor’s Comment: The lesions are consistent with acute tubular necrosis following traumatic rhabdomyolysis and chromoproteinuria. Myoglobinuria as a consequence of elevated myoglobin serum concentration can be seen in metabolic dysfunction (e.g. exercise, rhabdomyolysis, tying up), stress (e.g. capture myopathy) or severe direct trauma to muscles. In cases of traumatic injury, animals commonly also have renal hypoperfusion due to hypovolemic shock. The proposed mechanisms involved in myoglobinuria-induced renal injury include renal and arteriolar obstructive, intraluminal cast formation and direct intracellular toxicity of myoglobin.

It has been argued that renal vasconstriction is due to extravasation of fluid in areas of damaged muscle tissue leading to intravascular volume depletion. Furthermore, activation of cytokine cascades and scavenging of nitric oxide as an important endogenous vasodilator by heme protein contribute to renal hypoperfusion.

In contrast to earlier views, it has been shown that the intraluminal cast formation does not increase toxicity of hemoglobin by its accumulation and uptake and not by intratubular obstruction. Additionally, hypovolemia, renal vasconstriction and loss of myoglobin solubility in acidic urine facilitate the formation of casts.

The exact mechanisms of direct myoglobin toxicity are still under investigation. It has been hypothesized that by heme protein endocytosis, tubular plasma membranes become more vulnerable to the effects of phospholipase A2. Furthermore, iron dependent mechanisms of cellular damage including formation of free radicals, subsequent oxidative stress and lipid peroxidation have been proposed.

Acute tubular necrosis is the most common reason for acute renal failure. Early degenerative lesions commonly seen with acute renal failure in clude loss of brush borders, flattening of the epithelium, atrophy of cells, disruption of tubular basement membranes, formation of intratubular casts, and dilation of the lumen. These changes are observed predominantly in proximal tubules, but injury can also be demonstrated in the distal nephron and may progress to signs of necrosis like hypereosinophilia and loss of cellular detail. The distal casts appear to be secondarily damaged by obstruction with degenerated cells, cellular debris, hemoglobin, myoglobin, and other plasma proteins. Tubular regeneration, represented by flattened and elongated epithelial cells with hyperchromatic nuclei and mitosis can be seen after about three days. With 2-3 weeks after toxin exposure, recovery of normal renal structure may be completed.

Other conditions damaging renal tubular epithelium may result in morphologic changes similar to the lesions described...
scribed here. However, the pigment deposition seen in this case is regarded as specific for hemoglobinuria, myoglobinuria or bilirubinuria. Other common nephrotoxins producing specific acute tubular necrosis in domestic animals include heavy metals (e.g. mercury, lead, arsenic), antibiotics, antifungal agents, anti-inflammatory drugs, and fungal, bacterial and plant toxins.

AFIP Diagnosis: 1. Kidney: Degeneration and necrosis, tubular, acute, multifocal, moderate, with orange-red-brown casts, Beagle (Canis familiaris), canine.
2. Kidney: Anisotropic green-brown crystals, intratubular, multifocal (Fig. 2-3).

Conference Comment: The contributor gives an excellent overview of myoglobinuric nephrosis. Hemoglobin and myoglobin are chromoproteins that have been associated with hemoglobinuric nephrosis or myoglobinuric nephrosis respectively. Hemoglobin is normally bound to the carrier protein haptoglobin, which is too large to be filtered by the glomerulus. Therefore, hemoglobin is not excreted in the urine unless supplies of the carrier molecule are depleted. Hemoglobin and myoglobin have little nephrotoxicity by themselves, but when associated with renal ischemia, acidic urine, and decreased glomerular filtration rate, they contribute to acute renal failure.

It is generally accepted that vasoconstriction, lipid peroxidation, and acidification of the urine all play roles in acute tubular necrosis. Cast formation is thought to result from decreased urine flow associated with decreased GFR. In vitro studies of myoglobin toxicity in Fischer 344 rats suggest primary mechanisms of damage result from diminished pyruvate-stimulated gluconeogenesis, decreased total glutathione levels and induction of lipid peroxidation. The exact mechanisms for these actions and their effect in vivo are not fully known.

Hematuria, hemoglobinuria, and myoglobinuria will all generate a positive occult blood test. They can be differentiated by various diagnostic tests. Centrifugation will cause sedimentation of erythrocytes leaving a clear supernatant with hematuria. Red-brown urine that does not clear upon centrifugation may be either hemoglobinuria or myoglobinuria. These may be differentiated by adding saturated ammonium sulfate solution, which will precipi-

2-1. Kidney, Beagle. Numerous ectatic tubules and ducts contain moderate amounts of red-orange granular casts. Often these tubules are lined by attenuated epithelium. (HE 400X).
2-2. Kidney, Beagle. There is multifocal tubular epithelial necrosis characterized by hypereosinophilic, shrunken epithelial cells with pyknotic nuclei (arrowhead). Multifocally within the interstitium there is mild hemorrhage. (HE 400X).
Pigmentary changes in the kidney, extracted from Maxie et al.\textsuperscript{4} and Newman et al.\textsuperscript{6}

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pigment</th>
<th>Gross lesion</th>
<th>Histologic lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobinuric nephrosis (acute hemolytic crisis)</td>
<td>Hemoglobin</td>
<td>Dark red-brown to blue-black with radial streaks</td>
<td>Fine red granular speckling within epithelial cells or granular casts</td>
</tr>
<tr>
<td>Myoglobinuric nephrosis (acute rhabdomyolysis)</td>
<td>Myoglobin</td>
<td>Dark red-brown to blue-black with radial streaks</td>
<td>Fine red granular speckling within epithelial cells or granular casts</td>
</tr>
<tr>
<td>Hemosiderosis (chronic hemolytic anemia)</td>
<td>Hemosiderin</td>
<td>Brown discoloration of cortex</td>
<td>Pigment within the epithelial cells of proximal tubules</td>
</tr>
<tr>
<td>Cloisonné kidney (non-clinical condition)</td>
<td>Ferritin and hemosiderin</td>
<td>Brown to black renal cortices</td>
<td>Brown pigmentation of basement membrane, convoluted portions of proximal tubules</td>
</tr>
<tr>
<td>Lipofuscinosis Brown</td>
<td>iron-free pigments</td>
<td>Radial dark lines on the cut surface of cortex, sparing the medulla</td>
<td>Fine brown granules in epithelial cells of convoluted tubules</td>
</tr>
</tbody>
</table>

Hematoglobin. A clear supernatant following ammonium sulfate addition is indicative of hemoglobinuria, while a red-brown color indicates myoglobinuria.

The green-brown intratubular crystals were identified by scanning electron microscopy with energy dispersive x-ray analysis (SEM-EDX) and infrared spectroscopy (IR) as consistent with calcium oxalate monohydrate. The calcium oxalate crystals in this case are unusual in appearance because of the green-brown color in H&E. The crystals stained positive for Von Kossa and negative for Alizarin red. It is possible that protein and iron deposition within the crystals could account for their abnormal appearance. We would like to thank the AFIP Department of Environmental and Toxicologic Pathology for their assistance in evaluating this case.

Contributor: Department of Veterinary Pathology, Freie Universität Berlin, Germany
http://www.vetmed.fu-berlin.de/einrichtungen/institute/we12/index.html

References:

CASE III – CAS 2 (AFIP 2991412).

Signalement: 1-year-old, male, Beagle dog.

History: This dog was part of a 10-day oral toxicological study and was euthanized at the end of the study. There were no relevant clinical signs.

Gross Pathology: An abnormal shape of the cecum was the only relevant macroscopic finding.

Histopathologic Description: There is invagination of
the tip of the cecum within its lumen. All parts of the cecum wall are diffusely, moderately thickened (about twice normal thickness). The muscularis mucosa, the submucosa, some parts of the muscular layers (particularly the longitudinal layer), and the serosa are replaced by a poorly demarcated tissue, primarily in the same location as the myenteric (Auerbach’s) and submucosal (Meissner’s) plexuses (Fig. 3-1). The tissue is composed of irregularly-arranged wavy fascicles of nerve fibers with round and spindle cells, and some clusters of enlarged ganglion cells (Fig. 3-2). The mucosa is moderately hyperplastic, with multifocal to coalescing hemorrhages in the lamina propria, and multifocal minimal degeneration of some glands. Scattered in the submucosa and the proliferative neural tissue are some cells containing large pigmented brown granules (hemosiderin).

**Contributor’s Morphologic Diagnoses:** Cecum: Transmural ganglioneuromatosis, locally extensive, with intussusception.

**Contributor’s Comment:** Intestinal ganglioneuromatosis refers to a hyperplastic proliferation of ganglion cells, nerve fibers, and supporting cells of the enteric nervous system. In humans, in testinal ganglioneuromatosis is most often part of multiple tumor syndromes, particularly the multiple endocrine neoplasia (MEN) 2B syndrome. In MEN-2B is inherited in an autosomal dominant fashion and is caused by a single mutation in the RET proto-oncogene. This heritable endocrine disorder is characterized by medullary thyroid carcinoma, pheochromocytoma, multiple mucosal neuromas, gastrointestinal ganglioneuromatosis, cor neal nerve thickening and skeletal abnormalities. Gastrointestinal symptoms are common in patients with MEN-2B, and are secondarily due to pseudo-obstruction caused by the ganglioneuromatosis. The pathogenesis of ganglioneuromatosis is not well understood, but some studies in humans indicate that it may be related to overproduction of nerve growth factors.

Immunohistochemically, some cases of intestinal ganglioneuromatosis were shown to be a complex hyperplasia of several peptidergic, cholinergic, and probably adrenergic nerve fibers instead of a selective overgrowth of one type of nerve fibers.

Some rare cases of intestinal ganglioneuromatosis or ganglioneuromas have been reported, most often in young animals: in a horse, a steer, a cat, and 3 dogs. In all cases, there were clinical signs (e.g. colic, impaction, anorexia, vomiting, diarrhea, rectal prolapse) that led to surgical resection of the masses. Masses were located in the small intestine (3 cases), colon (1 case), and the rectum (2 cases) or Vater’s papilla (1 case). These masses were first reported in the first part of the small intestine from the pyloric end of the duodenum in the region of the pyloric sphincter.

**AFIP Diagnosis:** Cecum (per contributor): Ganglioneuromatosis, with intussusception, Beagle (Canis familiaris), canine.

**Conference Comment:** Ganglioneuromas are composed of mature autonomic ganglion cells, satellite cells, un-
Intussusceptions are described as having three layers: (1) outer wall of the receiving segment, (2) middle returning segment of invaginated bowel, and (3) inner entering segment. The intussusception seen in this lesion is unusual in that it contains only two of the three layers, a feature that will occur only through the invagination of a blind pouch (in this case, the tip of the cecum). Cecal inversion is another term for such a lesion (Fig. 3-3). Various causes of intussusception may include: foreign bodies, heavy parasitism, previous intestinal surgery, enteritis, and transmural lesions. It may also develop as a terminal, agonal or postmortem event. We appreciate the assistance from the Departments of Gastrointestinal Pathology, Neuropathology, and Soft Tissue Pathology at the Armed Forces Institute of Pathology in consultation on this case.

Fig 3-3. A. Intussusception of tubular section of bowel consisting of three layers: (1) outer wall of the receiving segment, (2) middle returning, segment of invaginated bowel, and (3) inner entering segment. B. Intussusception of a blind pouch consisting of two layers: (1) outer wall of the receiving segment, and (2) the middle returning, segment of invaginated bowel.

Gastrointestinal Pathology, Neuropathology, and Soft Tissue Pathology at the Armed Forces Institute of Pathology in consultation on this case.

Contributing Institution: Pfizer PGRD, Department of Pathology, Z.I. Pocé-sur-Cisse, B.P. 159, 37401 Amboise Cedex, France

References:
**CASE IV - 07-45 (AFIP 3074806).**

**Signalment:** Seven-month-old, female, Golden Retriever mixed breed, *Canis familiaris*, dog

**History:** The dog was presented with chronic conjunctivitis, gingival lesions, and respiratory disease. The clinical signs had begun at 4.5 weeks of age and had progressed. Pruritus, diagnosis including conjunctival biopsies, cytology, and bacterial culture of conjunctival swabs, canine distemper serology, virus isolation, and routine bloodwork failed to establish a diagnosis. On presentation, there were multifocal, raised, pink, fleshy, mucosal lesions of the conjunctiva, throughout the oral cavity, and nasopharynx, and an ulcer on the soft palate. Thoracic auscultation revealed harsh referred upper airway sounds. A repeat biopsy of the ocular conjunctiva identified a profuse accumulation of fibrin in areas of ulceration and under-running the epithelium. A diagnosis of ligneous conjunctivitis was made. Based on this diagnosis and involvement of other mucosal surfaces, a presumptive diagnosis of plasminogen deficiency was made. This was confirmed by a low plasminogen functional activity assay of 3.5% (compared to a normal age-matched control of 111% and pooled samples from normal dogs of 118%). The conjunctival lesions recurred after the excisional biopsy. A 2-week round of topical and intravenous treatment with fresh frozen plasma diminished the conjunctival lesions; however, four weeks later the dog had a lower plasminogen activity assay (1.0%), weight loss, anorexia, and lethargy. The owners requested euthanasia.

**Gross Pathology:** Multifocal to coalescing.

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4-1. **Oral cavity. Golden retriever mix, canine.** Raised, white to gray, granular, plaques decorate the glossal, buccal and gingival surfaces.

4-2. **Esophagus. Golden retriever mix, canine.** 0.5 cm to 1 cm diameter gray plaques on the esophageal mucosa.

**Histopathologic Description:** The sections of esophageal mucosa submitted have focal erosion to ulceration of locally hyperplastic epithelium covered by an exophytic coagulum of fibrin and cellular debris (Fig. 4-3). Gray to yellow, granular, fibrinous plaques were disseminated over the length of the tracheal mucosa. Multifocally slightly elevated plaques covered the epicardium of the right and left ventricles. Additionally, there was mild hydrocephalus, rare intestinal mucosal hemorrhages, and a mild fibrinous perihepatitis.
eral conjunctival lesions. The clinical diagnosis of ligneous conjunctivitis was made based on the histologic appearance of the conjunctival biopsy and functional plasminogen activity assay. This form of conjunctivitis is so named because of the wood-like consistency of the membranes. Reports of this condition in canines are rare, predominantly in the Doberman Pinscher breed. It is more commonly reported in females in both the veterinary and human literature. The condition is linked to a type I plasminogen deficiency and an autosomal-recessive genetic mutation has been identified as a common cause of this functional deficiency. The pathogenesis of the lesions in the conjunctiva and other mucosal sites involves the coagulation of fibrin following minor mechanical

Contributor’s Morphologic Diagnosis: Severe, chronic, ulcerative and proliferative, fibrinomembranous esophagitis

Contributor’s Comment: This patient was initially presented to the Ophthalmology service because of bilateral conjunctival lesions. The clinical diagnosis of ligneous conjunctivitis was made based on the histologic appearance of the conjunctival biopsy and functional plasminogen activity assay. This form of conjunctivitis is so named because of the wood-like consistency of the membranes. Reports of this condition in canines are rare, predominantly in the Doberman Pinscher breed. It is more commonly reported in females in both the veterinary and human literature. The condition is linked to a type I plasminogen deficiency and an autosomal-recessive genetic mutation has been identified as a common cause of this functional deficiency. The pathogenesis of the lesions in the conjunctiva and other mucosal sites involves the coagulation of fibrin following minor mechanical
AFIP Diagnosis: Esophagus: Esophagitis, proliferative, fibrinous, n eutrophilic and lymphoplasmacytic, multifocal, marked, with ulceration, ac antholysis, granulation tissue an d multifocal subepithelial fibrin, Golden retriever mix (Canis familiaris), canine.

Conference Comment: The contributor gives an excellent overview of plasminogen deficiency associated with ligneous conjunctivitis. Conference participants are encouraged to review the article on this case published by Johnstone McLean et al. Plasminogen plays a vital role in intravascular and extravascular fibrinolysis, wound healing, cell migration, tissue remodelling, angiogenesis, and embryogenesis. Plasminogen may be converted to plasmin by cleavage with either tissue-type plasminogen activator (tPA) leading to lysis of fibrin clots in the blood stream or u rokinase-type plasminogen activator (uPA) associated with wound healing and tissue remodelling.

It is interesting to note that in humans and animals diagnosed with type I plasminogen deficiency, there is little to no increase in the risk of developing intravascular thrombosis, which implies the existence of an alternative pathway for intravascular fibrinolysis.

The pseudomembranous deposits on mucous membranes occurs primarily in areas of previous damage. The hyaline material may contain scattered neutrophils, e osinophils, T -lymphocytes, plasma cell ls, mast cell ls and/ or foreign material. Immunohistochemistry may be positive for fibrin, albumin and immunoglobulins (IgG, IgA).
Contributor: The University of Tennessee, College of Veterinary Medicine, 2407 River Dr., Knoxville, TN, 37996

References:
1. Bugge TH, Flick MJ, Danton MJ, Daugherty CC, Roman J, Dano K, Carmeliet P, Co Ilen D, Deg en JL: Urokinase-type plasminogen activator is effective in fibrin clearance in the absence of its receptor or tissue-type plasminogen activator. Proc Natl Acad Sci USA 93:5899-5904, 1996