The Armed Forces Institute of Pathology
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Conference Moderator: Dr. Denzil Frost, DVM, Diplomate ACVP
Covance Laboratories, Inc.
9200 Leesburg Pike
Vienna, VA 22182

CASE I – 05-625 (AFIP 3026821).

Signalment: 1.5-year-old Tennessee Walking Horse gelding.

History: This horse was recumbent and unable to rise three days after introduction of a new feed mix. Three of the group of five horses refused the feed. The two horses that ate it (including this one) were "wobbly" on their feet for two days. This horse ate double rations and progressed from recumbency to a moribund state. Treatment was unsuccessful and the horse was euthanized.

Gross Pathology: There were 720ml of serosanguinous pericardial effusion. The heart weighed 2.37kg (0.7% of body weight). There were multifocal to coalescing irregular areas of myocardial pallor. The myocardium of the apex, subendocardium, and papillary muscles were most severely affected.

Laboratory Results: Feed samples were positive for monensin at 396 ppm.

Histopathologic Description: Heart (left ventricular free wall): There are multifocal to coalescing patchy areas of necrosis characterized by loss of striations, granular pale eosinophilic cytoplasm, and mineralization. There are increased numbers of plump nuclei in the interstitium (fibroblasts, macrophages, and hypertrophic endothelial cells).

Contributor's Morphologic Diagnosis: Subacute multifocal to coalescing myocardial necrosis

Contributor's Comment: Ionophores such as monensin, salinomycin, lasalocid, laidlomycin, and narasin are used as growth promoters in ruminants and

coccidiostats in poultry. In this case, monensin was introduced into equine sweet feed in a mixing error at a local feed mill. Several horses on multiple different farms died or showed clinical signs. Exposed horses were evaluated by bloodwork, electrocardiogram (ECG), and echocardiogram. Numerous horses had elevated creatine kinase (CK), the cardiac isoform of CK (CK-MB), and/or aspartate transaminase (AST). Horses are exquisitely susceptible to monensin toxicity. This is thought to be due to the low catalytic activity of equine hepatic cytochrome P450.[1] The species susceptibilities are as follows:[2]

Species	Monensin LD50 (mg/kg)
Horses	2-3
Dogs	5-8
Pigs	5-8
Sheep and Goats	10-12
Cattle	20-34
Poultry	90-200

Ionophores inhibit sodium and potassium ion transport across mitochondrial and other cell membranes. This leads to mitochondrial failure, depletion of ATP, failure of calcium transport out of cell, and persistent contraction. Highly metabolically active cells, such as papillary muscle myocardiocytes, are most severely affected. In some cases skeletal muscles are also affected, while in others there are no gross or microscopic lesions.[1] Although skeletal muscles were affected in this horse, the lesions only involved the large pelvic limb adductors, and this was presumed to be due to recumbency.

AFIP Diagnoses: Heart, myocardium: Degeneration and necrosis, multifocal, moderate, with mineralization, Tennessee Walking Horse, equine.

Conference Comment: The contributor provides a concise summary of ionophores, differences in species susceptibility, and the pathogenesis involved in ionophore toxicity.

Gross lesions associated with monensin toxicity vary depending on dose and duration of exposure and may not be detectable in acute cases. Ill-defined pale streaks may be visible in cardiac and skeletal muscle. As the disease progresses, these areas of pallor become more prominent and affected skeletal muscles atrophy. Myocardial lesions in monensin toxicity are irreparable, especially in growing animals, and the probability of lasting cardiac malfunction is high.[2]

Ultrastructural characteristics include marked swelling and disintegration of mitochondria, multifocal necrosis with type 1 fiber preference, vacuolization of sarcoplasmic reticulum, lipid accumulation, and formation of myeloid bodies.[2,3]

Differential diagnoses for the cardiac muscle lesions in this horse include ionophore (monensin) toxicity, vitamin E/selenium deficiency, exertional rhabdomyolysis, and ingestion of *Cassia* sp. plants. Because the histologic lesions in monensin toxicity differ very little from nutritional or exertional myopathy, clinical history and feed analysis are critical for definitive diagnosis. Simultaneous onset of pronounced clinical signs in multiple, especially adult, animals suggests exposure to a toxic agent. Vitamin E/selenium deficiency most often occurs in young foals and commonly involves the masticatory muscles and tongue, and concurrent steatitis is often present. Nutritional myopathy occurs sporadically in older horses, and steatitis is usually absent. Myocardial lesions may be present in foals and adult horses with nutritional myopathy. The myocardium is infrequently involved in exertional rhabdomyolysis, and there is usually significant damage to the renal proximal convoluted tubules secondary to myoglobinuric nephrosis and ischemia. The myocardium is also not extensively involved in cases of *Cassia* sp. toxicity and necrosis of pancreatic acinar cells also occurs.[2,4]

Readers are encouraged to review WSC 4 Case 1 2006-2007 to compare and contrast this case with a case of capture (exertional) myopathy.

Contributor: University of Tennessee College of Veterinary Medicine, Department of Pathobiology, 2407 River Drive, Knoxville, TN 37996-4542
http://www.vet.utk.edu/departments/path/

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CASE II – 03-11548 (AFIP 3027582).

Signalment: 1-year-old, female German Shorthair Pointer.

History: The dog was bitten by a rattlesnake while hiking with its owners. It was treated with steroids by a local veterinarian but died the next day.

Gross Pathology: The subcutis of the muzzle, lips and intermandibular space were severely expanded by thin, red-tinged fluid, especially on the left side. Within the oral cavity, on the ventral buccal mucosa of the left side were a pair of 2mm, round, red puncture wounds that were 1.3 cm apart (presumptive snake bite wound). The right ventricular myocardium had numerous, pale, linear streaks.

Other gross lesions included pansystemic petechiation, serosanguinous pleural effusion, suffusive pulmonary hemorrhage and severe melena. The kidneys were grossly normal.

Histopathologic Description: Within a single section of kidney, many glomerular capillaries contain fibrin thrombi. In several glomeruli, capillaries are widely dilated and distended by fibrin and red blood cells (microaneurysm formation). PTAH stain confirmed fibrin within dilated glomerular capillaries. Occasionally, microaneurysms obliterate glomerular structures. Hyaline casts and bright red, granular casts are present within proximal convoluted tubules and within collecting ducts. Renal tubular epithelium is degenerate and necrotic in these areas. Rare basement membranes are mineralized.

Other histologic lesions seen in this case were 1) Skeletal muscle hemorrhage and necrosis (associated with the snake bite), 2) Pulmonary hemorrhage and edema and 3) Acute, severe, multifocal myocardial degeneration and necrosis with mineralization

Contributor's Morphologic Diagnoses:
1. Diffuse, acute, moderate hemoglobin nephrosis
2. Mesangiolysis with glomerular capillary thrombosis and microaneurysm formation

Contributor's Comment: Pit vipers are the largest group of venomous snakes in the United States, and account for the vast majority of venomous snake bites in the US.[1] The common pit vipers of the western US are rattlesnakes (*Crotalus* and *Sistrurus* spp.); in the location where this bite took place, the most likely species was the Northern Pacific rattle snake (*C. viridis oreganus*). Pit viper venom does not vary in toxicity throughout the year, although snakes produce more venom in

the hot, summer months and adults within a species can have higher levels of toxic components.[1] Individual snakes can also control the amount of venom delivered in each strike; initial defensive strikes may be non-envenomating, whereas agonal bites often deliver the entire venom load. Beside these snake-related factors, severity of envenomation is also affected by host factors, including body mass, location of the bite, post bite excitability and premedications such as NSAIDS that can predispose the victim to more severe clotting defects.

Pit viper venom is composed of several enzymatic and non-enzymatic components that affect the variable clinical signs of pain, swelling, ecchymoses, weakness, nausea, shock and grossly visible tissue necrosis. Trypsin-like enzymes can mediate tissue destruction, while hyaluronidase, also called "spreading factor", decreases connective tissue viscosity, allowing penetration of other toxic components. Phospholipases A and B mediate membrane breakdown and release of a variety of endogenous proinflammatory products. Systemic hemorrhage may be mediated by venom components that either inhibit platelet aggregation or platelet-collagen interactions, inducing fibrinogenolysis through plasminogen activation or by direct toxic action on blood vessels. Thrombin-like enzymes can mediate increased clotting; this action, along with venom-induced thrombocytopenia and fibrinogenolysis often results in a syndrome resembling disseminated intravascular coagulation. In addition, direct cardiotoxic effects have been attributed to snake venom. Some venoms have primarily neurotoxic effects; in these cases, life-threatening envenomation can occur with little local tissue reaction.

Toxic glomerular vasculopathy associated with snake envenomation has been called mesangiolysis, capillary ballooning or glomerular microaneurysm formation. Mesangiolysis refers to direct injury to mesangial cells and matrix, reducing support for glomerular capillaries and leading to capillary dilation. Eventually endothelial damage occurs leading to coalescence of capillary lumina and microaneurysm formation.[2] Direct injury to mesangial cells by snake venom has been demonstrated experimentally using venom from the pit viper *Bothrops moojeni*.[3] Phospholipase A and other proteolytic enzymes are likely responsible for severe mesangiolysis seen in some snake bite cases. It is unclear whether glomerular fibrin deposits are secondary to abnormal vascular flow through the dilated glomerular capillaries, or are secondary to clotting abnormalities. Experimental renal lesions of envenomation are transitory and mesangiolysis is considered to be a reversible change, or the lesion may resolve to proliferative glomerulonephritis or glomerulosclerosis.

Although snake bite cases are most often not fatal, the bite in the oral cavity from a snake likely in its death throes probably delivered a large amount of venom into the systemic circulation of this dog. The cause of death was considered to be a

combination of acute myocardial necrosis, acute renal failure and a DIC type syndrome associated with snake envenomation.

AFIP Diagnosis: Kidney: Glomerular aneurysms and fibrin thrombi, multifocal, with moderate, acute tubular degeneration and necrosis, and cellular and granular casts, German Shorthair Pointer, canine.

Conference Comment: The contributor provides a thorough overview of snake envenomation to include snake and host related factors affecting the severity of envenomation, the components of pit viper venom, the typical light microscopic findings associated with toxic glomerular vasculopathy, and the pathogenesis involved in the development of the clinical signs associated with snake bite envenomation.

Clinical pathological findings may include the following: echinocytosis, leukocytosis, hemolytic anemia, thrombocytopenia, hyperfibrinogenemia, prolonged clotting times, elevated fibrin split products, and elevated creatinine kinase. In a retrospective study performed by Hackett et. al involving 100 client owned dogs, echinocytosis was the most common hematological change in prairie rattlesnake envenomation in dogs and was evident before substantial swelling took place. Possible mechanisms for the echinocytosis include depletion of ATP from cell membrane cation pumps by ATPase enzymes and alteration of erythrocyte membrane composition by phospholipases, both of which are present in rattlesnake venom. In a study performed by Walton et. al, the addition of ethylenediaminetetraacetic acid prevented the formation of echinocytes in vitro, suggesting a change in calcium or a metalloprotein participated in echinocyte formation. In cases of severe envenomation (e.g., large venom dose in a small dog), spherocytosis may be observed.[1,4,5,6]

Snake bites are common in the dog, horse, and to a lesser degree cats and are most commonly inflicted on the head or legs. Differential diagnoses for snake bites include trauma, angioedema (e.g., insect bites and stings), other animal bites, draining abscesses, and penetrating wounds.[1,7]

Conference participants briefly reviewed the intrinsic and extrinsic pathways of the coagulation cascade. Many agents or conditions can initiate coagulation by causing widespread endothelial damage exposing thrombogenic subendothelial collagen or by directly activating the coagulation cascade via the intrinsic or extrinsic pathway. Exposure of thrombogenic subendothelial collagen will cause the expression of tissue factor (factor III, thromboplastin) leading to activation of the extrinsic pathway. Although the coagulation cascade is divided into intrinsic

and extrinsic pathways for ease of understanding and for in vitro testing, this division does not exist in vivo. The tissue factor-activated factor VII complex is a potent activator of factor IX and factor X.[9] Included below is a table of agents or conditions known to induce DIC in animals from Jubb and Kennedy. Many of the agents listed in the table may initiate DIC by more than one route.[8]

Agents or Conditions Known to Induce Disseminated Intravascular Coagulation in Animals

Bacteria	Gram negative (endotoxin)
	Gram positive
Helminths	*Dirofilaria immitis*
Protozoa	*Theileria* sp.
	Sarcocystis sp.
	Babesia sp.
Rickettsia	*Rickettsia rickettsii*
Viruses	African swine fever
	Hog cholera
	Bluetongue
	Epizootic hemorrhagic disease of deer
	Infectious canine hepatitis
	Feline infectious peritonitis
	Aleutian disease of mink
Neoplasia	Carcinoma
	Leukemia
	Hemangiosarcoma
Other	Aflatoxicosis
	Antigen-antibody complexes (incompatible blood transfusion)
	Gastric dilation (volvulus)
	Heat stroke
	Hyperlipemia in ponies
	Hyperosmolality
	Immunologic endothelial injury
	Ingestion of red maple leaves
	Proteolytic enzymes (pancreatitis, snake bite)
	Shock, vascular stasis, prolonged anesthesia, acidosis
	Tissue necrosis (hepatic, pneumonia, postsurgery, burns)

Contributor: Department of Veterinary Microbiology and Pathology, College of Veterinary Medicine, Washington State University, Pullman, WA 99164-7040

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CASE III – D0604909 (AFIP 3027589).

Signalment: Adult, Angus cow, Bovidae, subfamily Bovinae, *Bos Taurus*.

History: An 880 lb cow on free range pasture started to show clinical signs of lethargy, dehydration, weight loss and alopecia which started one week prior to submission. Eight cows died within a week, all showing similar clinical signs. All cows that showed clinical signs died. Only cows that had been in the pasture the previous year died. None of the heifers on the same pasture or bulls on adjacent pasture died.

Gross Pathology: This 880 lb Angus cow was thin and had large confluent regions of alopecia and crusting on the head, neck, axillary region, and ventrum with scattered patchy foci on the skin of the trunk. There was consolidation of the anterioventral portion of the right lung. The kidneys were pale and swollen and the liver was uniformly red/brown and swollen. There was generalized enlargement of the lymph nodes which were uniformly tan and wet.

Laboratory Results: *Pasteurella mannheimia* was isolated from the consolidated region of the right lung.

Histopathologic Description: Adrenal gland: Diffuse dense lymphohistiocytic, plasmacytic and lesser granulocytic infiltrates extend from the capsular surface through the cortex and medulla with widely scattered single cell necrosis.

Kidney: Severe multifocal to coalescing regions of interstitial inflammation that is most prominent in the cortex but extends multifocally into the medulla. Inflammation separates and entraps tubules and glomeruli and is comprised of mostly lymphocytes with lesser numbers of eosinophils, macrophages, and multinucleated giant cells. Occasional entrapped tubules are mildly distended with luminal necrotic cell debris.

Skin: There is parakeratotic hyperkeratosis with occasional subcorneal pustules, mild acanthosis and spongiosis and light to moderate diffuse inflammatory cell infiltrates that extend from the superficial through the papillary dermis. The infiltrate is most prominent in the superficial dermis subtending the epidermis and around adnexa with some exocytosis into the follicular epithelium. Inflammatory cells are comprised of mostly lymphocytes with lesser numbers of macrophages, many pigment-laden, and eosinophils and plasma cells. There is superficial dermal edema and mild exocytosis of lymphocytes into the epidermis.

Contributor's Morphologic Diagnoses: Vetch toxicosis with:
1. Interstitial nephritis, severe, multifocal-coalescing, lymphohistiocytic, eosinophilic and granulomatous.
2. Adrenalitis, severe, diffuse, lymphogranulocytic.
3. Dermatitis, moderate, diffuse, lymphohistiocytic, eosinophilic with hyperkeratotic parakeratosis and subcorneal pustules.

Contributor's Comment: Vetch poisoning is a generalized disease characterized by multiorgan infiltration with lymphocytes, plasma cells, eosinophils, and multinucleated giant cells reported in cattle and horses.[1,2,3,4,5] Clinical signs include dermatitis, alopecia, diarrhea, weight loss, organ failure and death. Purple vetch (*Vicia benghalensis*), a hybrid variety (*Vicia villosa* subspecies *dasycarpa*), and hairy vetch (*Vicia villosa*) have been associated with vetch poisoning.[1,2,3,4] Reports from Oklahoma, Missouri, Kansas, Georgia, New York, California, Australia and Argentina suggest geographic distribution is extensive.[1] The cause(s) or factors associated with vetch toxicosis are unknown. Although vetch is widely used as forage for livestock, morbidity is typically low but has been reported as high as 68%.[1,5] Additionally, vetch-like disease has been described in cattle that have had similar clinical and pathologic signs/lesions but have not been exposed to vetch. Association with grass silage preserved with a formalin/sulphuric acid commercial additive, citrinin and citrus pulp have been described in these cases.[6,7,8]

In this case, the cows were on pasture that contained large stands of purple vetch (*Vicia benghalensis*). Only cows that had been on the pasture the previous year were affected suggesting these animals were previously sensitized to antigen associated with the vetch. The factor that previous exposure to the antigen is required to elicit clinical signs/lesions and the characteristic of the inflammatory response suggest the host response is likely a type-IV hypersensitivity reaction but neither the cutaneous hypersensitivity nor the lymphocyte blastogenesis tests have supported this theory thus far.[1]

AFIP Diagnoses:

1. Kidney: Nephritis, interstitial, granulomatous and eosinophilic, multifocal to coalescing, moderate, with mild tubular degeneration, necrosis, and regeneration, Angus, bovine.
2. Adrenal gland: Adrenalitis, granulomatous and eosinophilic, multifocal to coalescing, severe.
3. Haired skin: Dermatitis, lymphoplasmacytic, histiocytic, and eosinophilic, diffuse, moderate, with acanthosis, orthokeratotic hyperkeratosis, spongiosis, and superficial dermal edema.

Conference Comment: Hairy vetch is a legume that is cultivated and used as pasture, hay, and silage in most of the United States and in other countries. Vetch toxicosis occurs in cattle and to a lesser extent in horses after consumption of vetch-containing pastures. Vetch toxicosis is most commonly seen as a syndrome characterized by dermatitis, conjunctivitis, diarrhea, and multisystemic granulomatous and eosinophilic disease.[1,9]

The toxic principle in vetch seeds is prussic acid; however, the cause of the granulomatous inflammation remains unclear. One proposed pathogenesis involves a type IV hypersensitivity reaction secondary to ingestion of constituents of the plant that are absorbed and act as antigens that sensitize lymphocytes and evoke a multisystemic granulomatous response upon repeat exposure. Alternatively, vetch lectin may directly activate T lymphocytes to initiate the cellular response.[1,9,10]

Three syndromes associated with consumption of hairy vetch have been reported in cattle:

1. Acute nervous derangement and death after ingestion of seeds
2. Subcutaneous swellings if the head, neck, and body, herpetiform eruptions in the oral mucous membranes, purulent nasal discharge, rales, cough, and congestion associated with consumption of hairy vetch pasture
3. Dermatitis, conjunctivitis, diarrhea, and extensive infiltration of various organs by monocytes, lymphoplasmacytic cells, occasional multinucleated

giant cells, and often eosinophils also associated with consumption of hairy vetch pasture

Vetch-associated disease is more prevalent and severe in cattle over 3 years of age with Holstein and Angus breeds being disproportionately affected.[1]

Initial lesions in cattle include a rough coat with papules and crusts on the skin of the udder, teats, escutcheon, and neck progressing to involvement of the trunk, face, and limbs. The skin becomes alopecic and lichenified. Marked pruritis leads to excoriations secondary to self-induced trauma. Grossly, yellow nodular infiltrates of mononuclear leukocytes disrupt the architecture of a wide range of organs but are most severe in myocardium, kidney, lymph nodes, thyroid gland, and adrenal glands. In cattle, other species of *Vicia* and additional compounds such as diureidoisobutane, citrus pulp, and citrinin are capable of inducing disease indistinguishable from hairy vetch as pointed out by the contributor.[7,9,10]

Hairy vetch toxicosis in horses is similar to cattle; however, marked pruritis, diarrhea, and large numbers of eosinophils in the inflammatory infiltrate do not occur. Additionally, conditions very similar to vetch toxicosis have been reported in horses with no exposure to vetch. These cases have been referred to as "equine sarcoidosis," "idiopathic granulomatous disease involving the skin," "systemic granulomatous disease," or "generalized granulomatous disease." Scaling, crusting, and alopecia of the face or limbs are seen that progresses to a generalized exfoliative dermatitis. Organ involvement is variable.[9,11]

Contributor: Wyoming State Veterinary Laboratory, University of Wyoming, 1174 Snowy Range Rd., Laramie, Wyoming 82070, http://wyovet.uwyo.edu/

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CASE IV – S01262 (AFIP 3038505).

Signalment: 8-year-old, male, mixed breed dog.

History: The dog was presented to the local veterinarian with lethargy, anorexia, vomiting, bloody diarrhea, jaundice and seizures. Dogs die within a few days of liver and kidney failure and disseminated intravascular coagulation.

Gross Pathology: Severe diffuse jaundice. The liver was enlarged, pale, and yellow with multifocal petechial hemorrhages. Small amounts of blood-stained contents were found in the gastrointestinal tract, especially in the small intestine. In the respiratory tract, multifocal hemorrhages in the laryngeal mucosa were present. No other significant findings on post mortem examination.

Laboratory Results: A profile of the blood clinical chemistry parameters of the dog:

Parameter	Result	Lower normal limit	Upper normal limit
ALT (U/L)	691	0	60
ALP (U/L0	1113	0	150
AST (U/L)	203	0	50
GGT (U/L)	33.0	0.0	6.0
Amylase (U/L)	267	200	1480
Total Bilirubin (mg/dL)	11.7	0.1	0.5
Creatinine (mg/dL)	0.8	0.5	1.5

Urea (mg/dL)	5.4	10	28
Total protein (g/dL)	7.1	5.4	7.5
Albumin (g/dL)	3.6	2.6	4.0
Cholesterol (mg/dL)	195	135	280
Triglycerides (mg/dL)	121	50	100
Calcium (mg/dL)	11.7	9.0	11.7
Phosphorus (mg/dL)	6.4	2.5	6.2

Contributor's Morphologic Diagnoses: Liver: Hepatic degeneration and necrosis, hydropic and fatty, with bile duct proliferation, marked bridging fibrosis and mild histiocytic lymphocytic infiltration.

Contributor's Comment: Aflatoxicosis in dogs is a condition caused by the contamination of dog food by the fungal species *Aspergillus* with the production of aflatoxins. The first report of pathology in dogs due to aflatoxicosis was made in the United Sates in 1952; however, at that stage the etiology was unknown and the disease was referred to as "hepatitis X".[1] Aflatoxin production may occur both in the field and in storage when environmental conditions are favorable as occurs in warm, temperate, subtropical or tropical climates.[3] Dog food manufacturers regularly test their food products; however, small amounts may reach the final product undetected. The toxin produced by the fungus is usually aflatoxin B1.

Aflatoxins are hepatotoxic.[4] Hepatotoxicity is the result of widespread and nonspecific interactions between aflatoxins and/or their activated metabolites and various cell proteins. This interaction results in the disruption of basic metabolic processes and protein synthesis causing cell death.[3]

Besides being potent toxic compounds they are also carcinogenic, mutagenic and immunosuppressive agents. Aflatoxins are rapidly absorbed from the small intestine, metabolized in the liver to an epoxide active form by cytochrome P450 and conjugated with glutathione. The epoxide form results in oxidative damage via free-radical formation. Additionally, the epoxides may undergo further reactions including conjugation to glutathione, conversion to dihydrodiols and subsequently binding to macromolecules or to DNA, resulting in disruption of DNA and carcinogenesis.

The necrotizing effects and fatty changes seen in intoxicated animals are probably related to the inhibition of protein and RNA synthesis by the toxin. The bile duct hyperplasia seen in intoxication with aflatoxin may represent an attempt to regenerate parenchyma when the parenchymal cells have lost their ability to regenerate.[4] Anisocytosis, karyomegaly, binucleation and multinucleation probably represent the direct of effects of aflatoxin on the hepatocytes, as aflatoxin B1 is known to interfere with mitosis.[2]

Aflatoxin B1 is toxic to a wide range of species although there are significant differences in their sensitivity. Pigs are more sensitive that cattle which are more sensitive than sheep. Among laboratory animals, rats, guinea pigs and rabbits are significantly more sensitive than mice.[3] Dogs are considered to be quite sensitive with other susceptible species such as the duck, rabbit, cat and pig.[5] Dogs may be fatally intoxicated by a dose rate of less than 1.0 mg/kg bodyweight.[4]

Aflatoxicosis among dogs was identified in Israel in December 2005 due to the contamination of dog food from a specific supplier. Despite the warning by the manufacturer and the recall of the particular batch, some retailers apparently continued to sell the food with the resulting widespread toxicity.

In this outbreak, signs of toxicity covered a wide spectrum from acute to chronic. The aflatoxin dose and exposure duration determine the time of onset of clinical signs and their manifestations. Acute intoxication results from exposure to high concentrations of aflatoxin while chronic intoxication, which is more common, occurs following exposure to lower doses for a more prolonged period of time. A diagnosis of aflatoxicosis relies on the demonstration of aflatoxins in the feed and the occurrence of characteristic hepatic lesions. There is no specific treatment for affected animals.

AFIP Diagnosis: Liver: Hepatocellular vacuolar degeneration and necrosis, diffuse, severe, with biliary hyperplasia, and numerous pigment-laden macrophages, mixed breed, canine.

Conference Comment: The contributor provides a thorough overview of aflatoxicosis. Aflatoxins are a group of bishydrofurans produced by several strains of fungi, primarily *Aspergillus flavus*, *A. parasiticus*, and *Penicillium puberlum*. At least 13 aflatoxins have been identified with B_1, B_2, G_1, and G_2 being most common.[3,4]

In addition to hepatotoxic, carcinogenic, teratogenic, and immunosuppressive effects, aflatoxins also have anticoagulative effects due to decreased hepatic synthesis of coagulation factors, prothrombin, and fibrinogen. In acute aflatoxicosis with severe hepatic necrosis, disseminated intravascular coagulation (DIC) can cause coagulopathy which can lead to extensive hemorrhage and anemia.[1]

As the level of aflatoxin increases, the liver may show all or none of the following changes: enlargement, pallor, bile staining, increased firmness due to fibrosis, and nodular regenerative hyperplasia. In severe cases, edema of the gallbladder and

bile-tinged ascites may be observed. In cases of acute fulminating liver necrosis, after consumption of very high concentrations of aflatoxin, widespread hemorrhage and massive hepatic necrosis are observe.[3,4]

Typical light microscopic findings in cases of acute or subchronic aflatoxicosis in most species include hepatocyte degeneration, necrosis, hepatocellular vacuolation, anisocytosis, anisokaryosis, megalocytosis, bile duct or oval cell proliferation, cytosegresome formation and nodular regeneration that may progress to cirrhosis or cancer.[3,4]

Marked bridging fibrosis was not observed in the sections of liver received. Additionally, some slides had a section of essentially normal small intestine.

Contributor: Kimron Veterinary Institute, Department of Pathology, P.O. Box 12, 50250, Bet Dagan, Israel

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Michelle E. Thompson, DVM
Captain, Veterinary Corps, U.S. Army
Wednesday Slide Conference Coordinator
Department of Veterinary Pathology
Armed Forces Institute of Pathology
Registry of Veterinary Pathology*

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