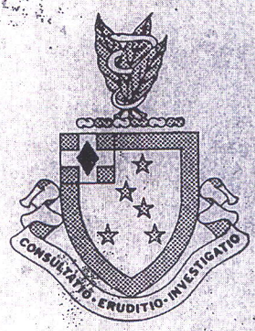
SYLLABUS

Veterinary Pathology Department Wednesday Slide Conference 1993-1994



Armed Forces Institute of Pathology
Washington, D.C. 20306-6000
1994

Syllabus

VETERINARY PATHOLOGY DEPARTMENT, AFIP
WEDNESDAY SLIDE CONFERENCE
1993-1994

126 microslides
34 lantern slides

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ML94002

PREFACE

The Registry of Veterinary Pathology, Armed Forces Institute of Pathology, has conducted the Annual Wednesday Slide Conference Program for more than two decades. The cases presented each Wednesday throughout the academic year are distributed to more than 135 active participants, including military and civilian veterinary pathologists throughout the United States and Canada, as well as many foreign countries. The diagnosis, comments, a synopsis of the discussion, and references for each case are forwarded to participants weekly. Our list of active contributors continues to grow.

This study set has been assembled in an effort to make the material presented at our weekly conferences available to a wider circle of interested pathologists and other scientists.

This set, composed of 120 cases, 126 microslides and 34 lantern slides, was assembled from the cases studied during the 1993-1994 conferences.

We wish to thank each contributor for his or her participation and for the permission to use cases in this study set.

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
1	Dog	Eye	*Blastomyces dermatitidis*
2	Dog	Liver, cerebellum	Hepatic encephalopathy
3	Goat	Meninges	Atypical meningothelial proliferation
4	Sheep	Liver	Sporodesmin toxicosis
5	Pig	Spinal cord	Selenium toxicosis
6	Dog	Cerebrum Spinal cord	Globoid cell leukodystrophy
7	Dog	Cerebrum	Laminar necrosis 2° to hypoxia
8	Pig	Cerebrum	Salt toxicity/water depravation
9	Mouse	Uterus, liver	Histiocytic sarcoma
10	Rat	Lung	Phospholipidosis
11	Rat	Kidney	Granulocytic leukemia
12	Macaque	Kidney	Glomerulonephritis, membranoproliferative
13	Rat	Nasal turbinates	Polypoid adenoma Large granular lymphocyte leukemia
14	Dog	Kidney	Glomerular lipidosis
15	Guinea pig	Lung	Adenovirus
16	Mouse	Skin	*Stapylococcus aureus* (Botryomycosis)
17	Dog	Intrathoracic mass	Thymoma
18,19	Pig	Placenta	*Leptospira icterohemorrhagiae*
20,L1	Bovine	Colon	Adenovirus

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
21	Cat	Gallbladder	*Salmonella* group D
22,L2	Macaque	Small intestine	Cytomegalovirus
23	Tamarin	Lung	*Klebsiella pneumoniae*
24,25	Sheep	Brainstem	*Listeria monocytogenes*
26	Frog	Skin	*Pseudocapillaria xenopi*
27	Macaque	Spinal cord	Poliovirus
28,L3	Macaque	Duodenum	Adenocarcinoma
29	Mouse	Eye	Retinal degeneration
30	Mouse	Liver	Helical bacteria
31,L4	Horse	Respiratory mucosa	Ethmoid hematoma
32	Horse	Skin	*Alternaria tenuis*
33	Horse	Eye,uvea	*Halicephalobus deletrix*
34	Horse	Liver	*Histoplasma capsulatum*
35	Cat	Lung	*Paragonimus kellicotti*
36	Bovine	Esophagus	Bovine viral diarrhea
37,L5-6	Pig	Lung	*Nocardia asteroides*
38,L7-8	Macaque	Lung	Ricin toxicity
39	Fish	Testicle	Seminoma
40	Fish	Skin, skeletal muscle	Lymphocystis virus Myxosoan cysts
41,L9	Fish	Skin,skeletal muscle,intestine	Myxosporidiosis
42	Bovine	Lung,liver	Brisket disease
43, L10-11	Dog	Skin	Epitheliotropic lymphoma
44	Dog	Skin	*Peloderma strongyloides*

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
45	Cat	Skin	Pemphigus foliaceus
46	Horse	Skin	Equine eosinophilic granuloma w/collagen degradation
47,L-12	Bovine	Cerebellum	GM_1 gangliosidosis
48	Duck	Small intestine Bursa of Fabricus esophagus	Duck viral enteritis (herpesvirus)
49	Goat	Lung	Caprine arthritis-encephalitis virus, *Muellerius* sp.
50	Sheep	Lung	Maedi/visna
51	Dog	Lung	Canine adenovirus type II, canine distemper virus
52,53	Wolf	Heart	*Bacillus piliformis*
54	Guinea pig	Skin	Trichofolliculoma
55	Rat	Kidney	Chronic progressive nephropathy
56	Pig	Cerebellum	Abiotrophy
57	Bovine	Rumen	Ruminal acidosis
58	Elk	Lung	*Mycobacterium bovis*
59	Bovine	Skeletal muscle	Eosinophilic myositis
60	Cat	Mammary gland	Fibroepithelial hyperplasia
61	Dog	Esophagus	*Spirocerca lupi*
62	Pig	Skin	*Staphylococcus hyicus*
63	Bovine	Nasal and buccal mucosa	Malignant catarrhal fever (Alcelaphine herpesvirus)
64	Chicken	Comb, wattles	Avian influenza

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
65	Pheasant	Liver	*Erysipelothrix rhusiopathiae*
66	Chicken	Liver	Myelocytomatosis
67	Peafowl	Crop	*Capillaria* sp.
68	Tamarin	Liver	Callitrichid hepatitis
69	Llama	Small intestine	*Mycobacterium pseudotuberculosis*
70	Bobcat	Lung	*Yersinia pestis*
71,72 L13	Camel	Colon	*Chlorella* sp.
73	Dog	Kidney	Amyloidosis, medullary
74,75	Ferret	Colon	*Camphylobacter*-like organism
76	Sea turtle	Skin	Fibropapilloma
77,L14	Coyote	Liver	*Hepatozoon canis*
78,L15	Macaque	Kidney	Renal cortical necrosis 2° to DIC
79	Squirrel	Skin,lung,liver kidney	Squirrel fibroma virus (Leporipox virus)
80,L16	Dog	Kidney	*Dioctophyma renale*
81	Dog	Liver	Islet cell carcinoma
82	Llama	Kidney,heart	*Candida* sp.
83	Cat	Skin	Fibrosarcoma, postvaccinal
84, L17-18	Dog	Bone, mandible	Alveolitis
85	Dog	Pancreas	Atrophy, radiation-induced
86, L19-21	Goat	Placenta	*Coxiella burnetti*

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
87	Bovine	Heart	Epithelial inclusions
88	Sheep	Brainstem	Scrapie
89	Mouse	Testicle	Malignant teratoma
90	Bovine	Kidney	Oxalate nephrosis
91	Deer	Small intestine	*Yersinia pseudotuberculosis*
92 L22-23	Pig	Lung, nasal turbinates	Cytomegalovirus
93	Monkey	Spleen,	Ebola virus
94	Bovine	Salivary gland, pancreas	Chlorinated napthalene toxicosis
95	Horse	Lung, liver	*Crotalaria juncea*
96,L24	Cat	Liver	Granulated round cell tumor
97	Bovine	Liver	*Microcystis aeruginosa*
98	Cat	Cerebrum	Feline ischemic encephalopathy
99	Dog	Anal sac	Adenocarcinoma of the apocrine glands
100	Dog	Colon	Histiocytic ulcerative colitis
101	Cat	Skin	Feline skin fragility syndrome
102,L25	Cat	Bone	Plasma cell myeloma
103	Mouse	Bone	Myelofibrosis
104	Sheep	Bone	Chondrodysplasia (spider lamb)
105 L26-27	Horse	Bone	Lymphosarcoma

LIST OF SLIDES

Slide #	Animal	Tissue	Diagnosis
106	Bovine	Lung, liver	*Salmonella dublin*
107 L28-29	Cat	Spleen	*Francisella tularensis*
108	Dog	Liver	*Mycobacterium avium*
109	Rabbit	Mammary gland, uterus	Adenocarcinoma, endometrial hyperplasia
110	Snake	Trachea	Adenocarcinoma
111, L30-31	Caiman	Skin	Caiman poxvirus
112	Ostrich	Ventriculus	Megalobacteriosis
113,L32	Oryx	Spinal cord	*Listeria monocytogenes*
114,L33	Horse	Spinal cord	Equine motor neuron disease
115	Donkey	Hoof	Laminitis
116	Horse	Lymph node	Malignant round cell tumor
117	Horse	Lung	Equine herpesvirus-1
118	Dog	Articular cartilage	Quinolone toxicosis
119	Sheep	Kidney; liver	Copper toxicosis
120	Cat	Lung	Lipid pneumonia
121	Pig	Lung	Porcine reproductive and respiratory syndrome virus
122,123	Dog	Skin; liver	Superficial necrolytic dermatitis, cirrhosis
124,L34	Llama	Spinal cord	*Parelaphastrongylus tenius*
125	Dog	Kidney	Aminoglycoside toxicosis
126	Dog	Testicle	Mixed germ cell-stromal tumor

COMMENTARY ON SLIDES

Microslide 1

History. A 2 1/2-year-old, black and rust, spayed female, Doberman Pinscher was presented to the University of Minnesota Veterinary Teaching Hospital on 4/13/93 with multiple nonpruritic draining fluctuant nodules and fistulous tracts on the face, trunk and extremities, exercise intolerance, lethargy, weight loss, difficulty breathing, and ocular discharge, of three months duration.

On physical exam, the dog was depressed and underweight. The cutaneous nodules and fistulous tracts contained thick reddish-yellow exudate. Multiple lymph nodes were enlarged. An ophthalmologic examination revealed bilateral superficial corneal ulcers. The right eye had grade 2/4 flare, rubeosis iridis and conjunctival injection; the pupil would not dilate and the fundus was not assessed. The left eye had a few bullous detachments of the retina and sub-retinal infiltrates in the non-tapetum. Radiographs showed general lung fields had a bronchointerstitial pattern, and there was a lobulated soft tissue density mass that impinged on the thoracic inlet suggestive of a granulomatous lymphadenopathy, abscess, or possible tumor in the cranial mediastinum. The pattern was thought to be atypical for blastomycosis.

The dog's condition deteriorated during treatment and it was returned to the Veterinary Teaching hospital for euthanasia on 4/22/93.

Gross Pathology. The dog was thin and had dependent edema involving the limbs. The entire body including the face and periorbital skin had multifocal exudative, ulcerated, raised cutaneous and subcutaneous nodules and tracts ranging from <5mm to 2 cm diameter, some of which extended into the underlying muscle. Nodules and tracts contained viscous purulent tan exudate. Smears of the exudate (new methylene blue stain) contained numerous thick walled, double contoured, broad based budding yeasts compatible with Blastomyces dermatitidis. The lungs were diffusely congested, edematous, and had numerous miliary gray-tan foci in all lobes, and multifocal infarcts. The pulmonary arteries had multifocal thrombi. The papillary muscles of the left ventricle had several well demarcated gray-tan foci. The submandibular, cervical, hilar, retroperitoneal and popliteal lymph nodes were enlarged and firm; on cut surface, these lymph nodes were yellowish white and had focal liquefied areas which contained thick, purulent yellow exudate. Impressions of the retroperitoneal and cervical lymph nodes had numerous budding yeasts compatible with Blastomyces dermatitidis (new methylene blue stain). The eyes had focal bilateral corneal ulcers.

Laboratory Results. Surgical biopsies of the skin had moderate orthokeratotic hyperkeratosis, mild to moderate epidermal and follicular acanthosis, mild to moderate superficial dermal lymphocytic and mastocytic infiltration, dermal glandular adnexal hypertrophy, and deep dermal pyogranulomas which extended into the panniculus muscle and surrounded follicles and adnexa. PAS, GMS, and acid-fast stains were negative for fungal and bacterial organisms.

Smears of the exudate from the draining cutaneous tracts contained yeasts compatible with Blastomyces dermatitidis.

Contributor's Diagnoses and Comments. 1. Systemic blastomycosis, involving the eyes (bilateral), skin, subcutis, lungs, lymph nodes, and heart.

2. Eyes, severe bilateral pyogranulomatous endophthalmitis, with retinal detachment and degeneration and mild pyohistiocytic keratitis, corneal edema and ulceration. Mycotic endophthalmitis. Blastomyces dermatitidis.

3. Skin/Subcutis, chronic severe multifocal pyogranulomatous dermatitis and cellulitis. Mycotic. Blastomyces dermatitidis.

4. Lymph nodes, multiple, chronic diffuse pyogranulomatous lymphadenitis with necrosis. Mycotic. Blastomyces dermatitidis.

5. Lung, chronic multifocal granulomatous pneumonia with pulmonary artery thrombosis and focal infarction. Mycotic. Blastomyces dermatitidis.

6. Heart, multifocal pyogranulomatous myocarditis with myocardial necrosis. Mycotic. Blastomyces dermatitidis.

Blastomycosis is distributed worldwide; it is known to affect most tissues and is the most frequently reported cause of intraocular mycosis in dogs. Blastomycosis occurs naturally in humans, dogs, cats, horses, and sea lions and has been experimentally produced in laboratory animals inoculated with the mycelial phase of Blastomyces dermatitidis. It is more common in dogs than in humans, and most commonly affects young to middle aged hunting or working male dogs. In dogs with systemic disease, 20 to 26% are reported to be blind, or have grossly observed ocular lesions.

Blastomycosis is a primary pulmonary disease which disseminates to other organs, including the skin. In cases with ocular involvement, the organism is thought to reach the eye hematogenously, becoming established in the choriocapillaris. At this point, it may break through the choriocapillaris and retinal epithelium, eliciting an inflammatory reaction between the sensory and epithelial portions of the retina causing retinal separation with little disturbance of the choroid. More commonly, it provokes an intense inflammation in the choroid before or while extending into other tissues. Organisms are usually absent in the anterior chamber; however, a secondary

inflammatory response in the anterior ocular tissues may be triggered by the release of diffusible mediators such as prostaglandins and other vasoactive compounds from inflammatory cells or other cells in the posterior ocular tissues, resulting in compromised outflow of aqueous humor and glaucoma in advanced cases.

The histologic appearance of ocular blastomycosis is that of a diffuse, pyogranulomatous endophthalmitis with retinitis, exudative separation of the sensory retina, and (commonly) granulomatous optic neuritis. Earliest lesions involve only the choroid, and with increased duration there is involvement of surrounding tissues. The inflammatory process is generally centered on the choriocapillaris, with minimal involvement of the choroid proper.

Other changes include neovascularization of the subsensory retinal exudate, lack of retinal invasion by the organisms in the retina, scleral thrombophlebitis, periorbital cellulitis, greater inflammation of the posterior ocular tissues as opposed to the anterior ocular tissues, rubeosis iridis, and sparing of the tapetum.

AFIP Diagnoses. 1. Eye: Endopthalmitis, pyogranulomatous, diffuse, severe, with retinal detachment, and budding yeasts, Doberman Pinscher, canine, etiology- consistent with Blastomyces dermatitidis.
2. Eye, cornea: Keratitis, chronic-active, diffuse, mild.

Conference Note. There is variation of ocular structures present among sections. The term endopthalmitis was preferred to panophthalmitis because of lack of involvement of sclera. Differential diagnosis discussed in conference included other fungi that cause systemic infections, such as Coccidioides immitis, Histoplasma sp. and Cryptococcus, as well as the algae Prototheca; however, the combination of broad-based budding, the size of the yeast-like cells (8-15 microns), and the "doubly contoured" refractile walls are found only in Blastomyces dermatitidis. Broad-based budding is the most distinctive feature. The rostral surface of the iris has vascular proliferation consistent with preiridal membrane, also known as rubeosis iridis.

Contributor. University of Minnesota, Department of Veterinary Pathobiology, College of Veterinary Medicine, 1971 Commonwealth Avenue, St. Paul, MN 55108.

References.

1. Albert RA, Whitley RD, and Crawley RR: Ocular blastomycosis in the Dog. Comp Cont Ed. 3:303-308, 1981.

2. Buyukmihci NC and Moore PF: Microscopic lesions of spontaneous ocular blastomycosis in dogs. J Comp Pathol 97:321-328, 1987.
3. Trevino GS: Canine blastomycosis with ocular involvement. Vet. Path. 3:652-658, 1966.

International Veterinary Pathology Slide Bank
Laser disc frame # 7705, 437, 438, 515, 1039, 1681, 2012, 2016, 2017, 2936, 3357, 4239, 6598, 10193.

Microslide 2

History. This 4-month-old Siberian husky, male, canine had sudden onset of seizures 3-4 weeks prior to necropsy. The dog was howling, pacing, and abnormally listless when not seizuring.

Gross Pathology. The liver was extremely small yet normal in color and consistency. A wide vascular connection between the portal veins and the vena cava was found in the right lateral lobe of the liver.

Laboratory Results.

	Pre	Post
Ammonia tolerance test	$176_{um/L}$	$522_{um/L}$

Contributor's Diagnosis and Comments. 1. Intrahepatic portal vein hypoplasia.
2. Discomminuted vacuolar encephalopathy.

Hepatoencephalopathy is a fairly common cause of neurological dysfunction in dogs. The condition is associated with a pathological mixing of blood from the portal vein and the systemic vasculature. Normally blood from the portal vein passes through the capillary sinusoidal vessels of the liver before returning to the systemic circulation. Ammonia is absorbed in the intestine as a product of bacterial digestion of proteins. The high levels of ammonia in the portal blood are normally lowered during the course of one passage through the liver. The portal blood bypassing the liver will be rich in ammonia resulting hyperammoniemia. Portal-systemic shunting can occur in several different ways. The condition can be congenital or acquired. In acquired portal-systemic shunting, blood usually flows through already existing, but not functioning, channels between the portal vein and the branches of the posterior vena cava. This usually occurs passively as a result of portal hypertension associated with chronic liver disease. This dog has a congenital portal-systemic shunt. Congenital shunting results from an abnormal vascular development leading to shunting of blood from the portal vein to the systemic circulation either through an intrahepatic shunt as in this dog, or through an

abnormal connection between the portal vein or its branches, and the posterior vena cava or the azygos vein. Congenital extrahepatic shunts are usually identified as a single widely dilated abnormal vascular connection on an angiographic study. Dogs with congenital portal-systemic shunting fail to develop a normal sized liver. Establishment of a normal arborizing portal vasculature is a determinant of ultimate hepatic size in dogs. The clinical manifestations of hepatic portal-systemic shunting result from hepatoencephalopathy. Seizures and behavior abnormalities are common manifestations of hepatoencephalopathy. Histopathologically, the lesions are characterized by widely disseminated multifocal encephalopathy. Affected areas characteristically show an increase in Alzheimer's type II astrocytes and varying degrees of vacuolar degeneration. The extent of histopathological alteration in the brain correlates poorly with the severity of clinical signs. This dog has a severe symmetrical widely disseminated vacuolar encephalopathy with increased numbers of Alzheimer's type II astrocytes. Controversy exists whether the encephalopathy is a direct result of the hyperammoniemia or the result of other as yet unnamed toxic substances which reach the systemic circulation as a result of portal-systemic shunting.

AFIP Diagnoses. 1. Liver: Portal vein hypoplasia and hepatic artery hyperplasia, diffuse, moderate, Siberian Husky, canine.
2. Brainstem; cerebellum: Vacuolar encephalopathy, focally extensive, severe, with gliosis.

Conference Note. Ammonia tolerance tests are helpful in diagnosing liver disease in which there has been a marked reduction in functional liver mass. Ammonia, which is absorbed from the lower intestinal tract, is normally removed by the liver via the portal veins and converted to urea, but this is dependant on adequate functional hepatic mass and portal blood flow.

The vacuolar encephalopathy observed in the brain was considered typical of hepatic encephalopathy. The section presented in conference also had extramedullary hematopoiesis in the choroid plexus. The neurologic changes in hepatic encephalopathy are believed to involve factors in addition to ammonia retention. Gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter that is normally metabolized by the liver, is elevated in plasma and the concentration of the GABA receptors within the brain is increased in liver failure. Other toxic amines, captans, and short-chain fatty acids which are normally removed from portal circulation by the liver may be responsible for breakdown of the blood-brain barrier and may also act as false neurotransmitters.

Contributor. School of Veterinary Medicine, 2015 Linden Drive West, Madison, WI 53705.

References.

1. Feronci P, Puspok A, Steindl: Current concepts in the pathophysiology of hepatic encephalopathy. Europ J Clin Invest 22:573-581, 1992.

2. Kelley WR, The liver and biliary system, in Pathology of Domestic Animals, Jubb, Kennedy, and Palmer, editors, Fourth edition, vol. 2, 1993, pp 323-324, 352, 357-358.

International Veterinary Pathology Slide Bank

Laser disc frame #2561, 3924-5, 4584-5, 5137, 10635, 13152-3, 15770, 16378, 16388-91, 16402, 16406-8.

Microslide 3

History. This 2-year-old Toggenburg doe presented with ataxia and weakness of 6 months duration. In addition, left horizontal nystagmus and stiff painful neck were present at the time of euthanasia.

Gross Pathology. A poorly demarcated dark grey mass was present in the roof of the fourth ventricle.

Contributor's Diagnosis and Comments. Choroid plexus epithelioma.

A clear transition from choroid epithelium to squamous epithelium is apparent in most sections. Although infiltration into the Virchow-Robin space is present, there does not appear to be parenchymal invasion. The cell cords were positive for actin, keratin and S-100 protein; positive/negative for NSE and negative for vimentin, EMA, alpha 1 AT, and GFAP. No citation of such a neoplasm was found in the English literature.

AFIP Diagnosis. Brainstem adjacent to fourth ventricle, periventricular meninges and Virchow-Robin space: Atypical meningothelial proliferation, Toggenburg, goat.

Conference Note. This lesion is unique in our experience. This case was reviewed by the Department of Neuropathology of the AFIP and was interpreted as meningio-angiomatosis, although the squamoid cells on the meningeal surface and in the Virchow-Robin spaces are not typical of this condition. The conference participants believed that the cells were too well-differentiated to be neoplastic and, thus, favored a nonneoplastic proliferative condition. A clear transition between choroid epithelium and squamous epithelium was not present in the sections examined. Immunohistochemical stains for keratin, vimentin and S-100 protein were performed, and the results were consistent with those reported by the contributor. The keratin positivity and vimentin negativity suggest epithelial differentiation. Meningothelial cells have many epithelial characteristics. This

remarkable lesion may represent epithelial differentiation of meningothelial cells.

Contributor. The Ohio State University, Department of Veterinary Pathobiology, 1925 Coffey Road, Columbus, OH 43210.

References.

1. Proceedings of the Forty-Second Annual Meeting of the American College of Veterinary Pathologists, December 8-13, 1991, Orlando, FL, p. 123.

2. Ribas JL, Carpenter J, and Mena H: Comparison of Meningio-angiomatosis in a Man and a Dog. Vet Path. 27:369-371, 1990.

3. Stebbins KE, and McGrath JT: Meningio-angiomatosis in a Dog. Vet Path. 25:167-168, 1988.

Microslide 4

History. The liver section is from an 8-month-old, castrated male, Polypay-cross icteric lamb that died during an outbreak of severe photosensitization.

Gross Pathology. Livers of all 4 of the necropsied lambs from this flock were swollen, firm, and had accentuated lobular patterns. There was edematous thickening of the extrahepatic bile ducts and gall bladders.

Laboratory Results. Bacterial culture of lungs (and one lamb's liver) yielded heavy growth of Pasteurella hemolytica.

Contributor's Diagnosis and Comments. Liver - bile duct hyperplasia, portal fibrosis, and mononuclear inflammatory cell infiltrates. Cause - chronic sporodesmin toxicity ("facial eczema").

Severe photosensitization was diagnosed in a flock of 200 lambs grazing an unshaded, irrigated, perennial ryegrass pasture in western Oregon. The pasture had a considerable amount of dead plant material from the previous season when it was neither grazed nor irrigated. About 4 weeks after being placed onto the pasture, during a period of unseasonably warm weather, jaundice and photosensitization were noted. Initially, the animals' faces were swollen and ears were swollen and dropped. Eyelids and muzzles became swollen and the overlying affected skin loosened and formed scabs that covered purulent exudate. Ear tips became desiccated and curled. Deaths of about 5% of the lambs were associated with pneumonia and septicemia, typically due to Pasteurella hemolytica.

Examination of the pastures revealed no poisonous plants. Spore counts of Pithomyces chartarum were 600,000 spores/gram

vegetation on initial examination and dropped to about 5000/gram over the next 3 weeks. Lambs that were moved to a shaded pasture area recovered. In contrast to what is seen in New Zealand, Australia, and South Africa, sporodesmin toxicity is rare in the United States and occurs only under very specific conditions when ambient temperature and humidity are high and sheep have grazed pastures down to where they are ingesting dead ryegrass containing the fungal spores. Hepatic damage and hepatogenous photosensitization then may result.

AFIP Diagnoses. 1. Liver, portal areas: Bridging fibrosis and biliary hyperplasia, diffuse, moderate, with lymphoplasmacytic cholangitis and pericholangitis, Polypay-cross, sheep.
2. Liver: Hepatitis, random, acute, multifocal, mild.

Conference Note. Sporodesmin is a mycotoxin produced by the fungus Pithomyces chartarum, which is most commonly found on dead ryegrass. This toxicosis is rare in the United States and is more commonly seen in South Africa, New Zealand, and Australia. The toxicity is related to the density of the spores found on the pasture. Sporodesmin typically causes chronic liver damage and severe hepatogenous photosensitization. The mycotoxin is not directly hepatotoxic. It is secreted in an unconjugated form into the bile causing biliary epithelial necrosis when concentrations are sufficiently elevated. Changes in the hepatic parenchyma are minimal. Several toxin-induced hepatic diseases were discussed in conference including aflatoxicosis, Lantana intoxication, and copper toxicosis.

The photosensitization (facial eczema) that occurs in sporodesmin toxicity is hepatogenous (type 3) as opposed to primary (type 1), or aberrant endogenous metabolism (type 2) forms. In hepatogenous photosensitization, phylloerythrin, a product of microbial transformation of chlorophyll in the intestinal tract, accumulates in tissues because of the liver's reduced ability to transport and excrete it. Phylloerythrin has photodynamic properties and induces skin lesions associated with photosensitization. Primary photosensitization occurs when photodynamic toxins that the normal liver cannot excrete are ingested and deposited in the skin. An example is hypericin in St. John's wort (Hypericum perforatum). The best known example of aberrant endogenous metabolism-induced photosensitization occurs in congenital porphyria of cattle in which photodynamic porphyrins accumulate because of deficiency of uroporphyrinogen cosynthetase.

Contributor. Veterinary Diagnostic Laboratory, Oregon State University, Corvallis, OR 97339.

Reference.

Kelley WR, The liver and biliary system. In: Pathology of Domestic Animals, Jubb, Kennedy, and Palmer, eds, 4th ed, vol. 2, 1993, pp 351-352 and 390-392.

Microslide 5

History. The owner of a farrow to finish swine herd reported that approximately one month following a feed change pigs of all age groups became anoretic, with several individuals progressing to exhibit hyperesthesia about the face, posterior paresis and paralysis, and death. Clinical signs were more pronounced and death losses were highest in the nursery and feeder pigs. Affected pigs were alert and some would eat if feed was placed in front of them.

Gross Pathology. The brain and spinal cord were unremarkable at gross necropsy examination. Following formalin fixation and sectioning, foci of softening were observed in the caudal cervical and caudal lumbar regions of the spinal cord.

Laboratory Results. Bacteriologic culture of meningeal swabs, brain tissue, lung, liver, kidney and spleen resulted in no growth.

Toxicologic analysis of the finished feed being fed to the grower/finisher pigs revealed 16.88 parts per million (ppm) selenium. The finisher base ration contained 203.00 ppm and the nursery concentrate contained 25.85 ppm selenium. These levels are approximately 17 times, and 43 times the levels reported on the respective feed labels.

Contributor's Diagnosis and Comments. Poliomyelomalacia, focal, ventral horns, bilaterally symmetric, cervical and lumbar intumescences, chronic, severe selenium toxicity.

Selenium in feed at a level of 7.0 ppm is reported to be toxic to swine. In this case, the source of the excess selenium was traced to the finisher and nursery premix or concentrates, apparently the result of a formulation or mixing mistake. The lesion caused by selenium toxicity in pigs is characterized by its bilateral symmetry and focal distribution confined to the ventral horns of the cervical and lumbar intumescences. A histologically similar focal lesion in this case was found in the brainstem. Brainstem nuclei reported to be affected in selenium toxicity in pigs include the motor nucleus of the fifth cranial nerve, facial nucleus, cuneate nucleus, and gracilis nucleus. The lesion is histologically characterized by neuronal degeneration and loss, gliosis, prominent vascularization, chromatolytic neurons near the margin of the lesions, and microcystic change around the periphery of the lesions.

AFIP Diagnosis. Spinal cord, ventral horns: Poliomyelomalacia, bilaterally symmetrical, severe, crossbred, porcine.

Conference Note. Selenium toxicity can present as an acute or chronic disease. In addition to neurologic lesions, skeletal and cardiac muscle degeneration, liver degeneration and necrosis, and in chronic cases, hair and hoof lesions may be seen. Organic selenium compounds, especially those from plants, are commonly more toxic than inorganic compounds. Plants that accumulate selenium are either obligate or facultative accumulators. Obligate accumulators, which require high levels of selenium for survival, include species of Xylorrhhiza (woody aster), Oonopsis (goldenweed), Stanleya, and Astragalus. Facultative accumulators include species of Asters, Atriplex, Sideranthus, Castilleia, Guitierrezia, and Machaeranthera.

The pathogenesis and mechanism of toxicity are not fully understood. Selenium is chemically related to sulfur and it has been speculated that selenium may replace sulfur in certain biochemical reactions; this mechanism may be involved in the development of hair and hoof lesions. Apparently, selenium's major toxic effect is enzymatic inhibition of oxidation/reduction systems. Selenium excess is also associated with decreased tissue ascorbic acid and glutathione. The decrease in ascorbic acid may contribute to the vascular damage seen with the disease.

Contributor. Kansas State University, College of Veterinary Medicine, Department of Pathology and Microbiology, VCS Building, Manhattan, KS 66506.

References.

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Microslide 6

History. This 2 1/2-year-old, Basset hound, male, canine had slowly progressive onset of incoordination and hind limb proprioceptive and placement deficits.

Gross Pathology. No gross lesions initially, but following formalin fixation there was a slight yellow discoloration of the white matter in the cerebrum, cerebellum, and dorsal funiculus of the spinal cord.

Contributor's Diagnosis and Comments. Leukodystrophy, with demyelination and perivascular globoid cell infiltration, severe, cerebrum, cerebellum, spinal cord.
Etiology: Globoid cell leukodystrophy (galactocerebrosidosis).

Globoid cell leukodystrophy, also known as galactosylceramide lipidosis, galactocerebrosidosis, and Krabbe's disease, is an invariably fatal lysosomal storage disease affecting the central nervous system. The disease was originally described in humans but has since been recognized in a number of domestic animals including the Cairn and West Highland White Terrier, Pomeranian, Miniature Poodle, Bluetick Hound, Beagle, Basset Hound, domestic cat, and polled Dorset sheep. The disease is due to an inherited (presumed autosomal-recessive) deficiency in the activity of galactocerebroside β-galactosidase. This deficiency eventually leads to progressive demyelination and the accumulation of the characteristic "globoid cells" in the white matter. Unusual features in this case were the late onset of the disease and the distribution of the lesions in the spinal cord. Signs of this disease usually appear within the first few months of age, but in this case, the onset of clinical signs was delayed for almost three years. A similar case of late onset globoid cell leukodystrophy has previously been reported in a Basset Hound.

AFIP Diagnosis. Brain, cerebrum; spinal cord: Globoid cell leukodystrophy, Basset Hound, canine.

Conference Note. Globoid cell leukodystrophy is a genetically determined disease caused by a deficiency of galactocerebroside β-galactosidase which catalyzes the degradation of galactocerebrosides. Galactocerebrosides, a major component of myelin, accumulate within lysosomes of oligodendrocytes and Schwann cells. The deficient enzyme is also involved in the breakdown of other metabolites, most notably galactosylphingosine (psychosin), which is also synthesized by oligodendrocytes. Psychosin accumulation is highly toxic to oligodendrocytes, resulting in widespread oligodendrocyte degeneration and necrosis and concomitant cessation of

myelination. Previously formed myelin degenerates, and is phagocytized by and accumulates within macrophages that are also deficient in galactocerebroside β-galactosidase. These macrophages give rise to the characteristic globoid cells.

Histologically, globoid cells are often clustered around blood vessels in the white matter, leptomeninges, and endoneurium of peripheral nerves. Additionally, diffuse demyelination, axonal loss, and dense astrogliosis are typical hallmarks of this disease.

In addition to several breeds of dogs, the domestic cat, and polled Dorset sheep, an excellent model for globoid cell leukodystrophy in humans is the twitcher mouse. The twitcher mouse is affected with the same genetic defect as in humans, and the fundamental aspects of the clinical course and pathologic changes are the same.

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International Veterinary Pathology Slide Bank
Laser disc frame #13106, 14238-9, 17006-7.

Microslide 7

History. This 9-year-old, male, mixed breed dog was found in front of a burning barn. The dog smelled intensely of smoke, was lying on its side, cried and showed severe dyspnoea. After symptomatic therapy with infusions, antiphlogistica and diuretics the dog was euthanized on the following day because of poor prognosis. The clinical diagnosis was intoxication by smoke inhalation.

Gross Pathology. At necropsy the tracheal mucosa was covered with masses of a firm, black mucus and the lung showed

severe acute diffuse alveolar edema. There were no other macroscopic findings.

Contributor's Diagnosis and Comments. Laminar edema, loss of neurons with acute neuronal necrosis predominantly in the deep cortical layers consistent with generalized hypoxia, brain, cortex, canine, mixed breed.

Laminar edema and neuronal necrosis in the cortex of the brain are considered to be typical findings in cases of acute respiratory hypoxia. Generalized hypoxia, caused by respiratory disease or diminished O_2-pressure in the atmosphere, leads to laminar edema and neuronal necrosis with resulting loss of neurons in the brain. Grey matter seems to be more susceptible to hypoxia than white matter. In the grey matter, Purkinje cells in the cerebellar cortex and the deep layers of the cerebral cortex seem to be most susceptible. In hypoxic disturbances, nuclei of neurons become triangular and deeply basophilic. The neuronal cytoplasm becomes deeply eosinophilic, and the whole neuron appears to be shrunken.

During massive smoke development, carbon monoxide intoxication can also occur. Carbon monoxide originates from incomplete combustion of carbonic substances. Neuropathological findings considered typical for carbon monoxide intoxication are symmetrical pallidal necrosis (in humans) and white matter degeneration and necrosis, which both could not be found in the present case. Furthermore, at necropsy there was no evidence of carboxyhemoglobin formation.

In the present case, the cause of hypoxia could be reduced O_2-pressure due to massive smoke inhalation.

AFIP Diagnosis. Brain, cerebrum: Degeneration and necrosis, neuronal, laminar, multifocal, moderate, mixed breed, canine.

Conference Note. The differential diagnosis for this lesion discussed in conference included lead toxicosis, thiamine deficiency, cyanide toxicosis, cardiac arrest and other causes of hypoxia. Neurons and oligodendrocytes are most sensitive to hypoxia, followed by astrocytes, microglia, and endothelial cells (in increasing order of resistance). Gray matter is more sensitive to hypoxia than white matter due to its higher metabolic rate and requirement for oxygen. Regional sensitivities also occur. The Purkinje cells of the cerebellum and the neurons of the cerebral cortex are the most sensitive and, within the cerebral cortex, the deeper laminae are more sensitive than the superficial laminae.

Smoke inhalation injury typically involves several mechanisms. In addition to low oxygen levels, three principal

nonirritant gases are often present which can contribute to hypoxia: carbon monoxide, hydrogen cyanide, and high concentrations of carbon dioxide. Carbon monoxide, in addition to binding hemoglobin, shifts the oxygen dissociation curve to the left, impairing oxygen unloading at the tissue level. Carbon dioxide, an asphyxiant gas, is a potent respiratory stimulant and can cause increased inhalation of other toxic constituents of smoke. Hydrogen cyanide is rapidly translocated into the brain. The cyanide binds the Fe+++ of cytochromes, causing cells to be unable to use O_2 in the production of ATP (histotoxic anoxia). Other injuries are attributed to various irritant gases, particulates, and thermal damage.

Contributor. Institut fur Veterinarpathologie, Frankfurterstrasse 96, D-35392 Giessen (FRG).

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International Veterinary Pathology Slide Bank
Laser disc frame #8577-8582.

Microslide 8

History. This 9-month-old, Vietnamese potbellied male porcine suddenly became weak and started to seizure. On presentation he showed full body muscle tremors every 2-3 seconds. At times, he was recumbent and quiet. Fecal pellets were dry, and body temperature was 96°F. He became comatose and was euthanized following the clinical diagnosis of salt intoxication.

Gross Pathology. Fibrous adhesions were present between pleural surfaces of lung and ribs. A chronic diffuse pericarditis was present as well. The brain was bilaterally symmetrical and moist.

Laboratory Results.

Chemistry:	sodium = 178 mEq/1	WBC = 15,900 /ul
	chloride = 134 mEq/1	Fibrinogen = 1000 mg/dl
	potassium = 5.6 mEq/1	

Contributor's Diagnosis and Comments. Meningoencephalitis, eosinophilic, subacute, multifocal, moderate, with neuronal necrosis and spongiosis, acute, multifocal, moderate, cerebral cortex. Etiology: salt intoxication/water deprivation.

Indirect salt intoxication is associated with water deprivation and results from reduced sodium excretion, excessive sodium intake or a combination oft the two. Clinical signs are neurologic. Death can result from respiratory failure and dehydration. Clinical analysis of serum and cerebrospinal fluid may confirm hypernatremia with levels of sodium above 160 mEq/l. Histological examination of the cerebrum will reveal in the acute stages of the disease the pathognomonic presence of eosinophils cuffing meningeal and cerebral vessels. Brains of affected pigs also show edema and subcortical polioencephalomalacia. The presence of eosinophils is intriguing and not fully understood. Differential diagnosis would include lead or mercury toxicosis, pseudorabies or rabies.

AFIP Diagnosis. Brain, cerebrum: Necrosis, laminar, cortical, diffuse, with eosinophilic meningoencephalitis, Vietnamese potbellied pig, porcine.

Conference Note. The complete pathogenesis of indirect salt intoxication is unknown, but the lesions are hypoxic in nature. Sodium flows freely into the CSF through the choroid plexus but requires active transport to return to the serum. Increased levels of sodium within cells inhibit anaerobic glycolysis limiting the energy available for return of sodium to the serum from the brain. When water is reintroduced and the animal is rehydrated, water flows into the cells of the CNS to adjust the osmolality, and edema is produced.

The differences between cytotoxic and vasogenic edema were discussed during conference. Cytotoxic edema, which is intracellular, results from osmotic disturbances, and is primarily dependent on the sodium/potassium pump and ATP as an energy source. This case is a classic example of cytotoxic edema. Vasogenic edema is primarily extracellular and is caused by derangement of vascular permeability which allows leakage of fluid into the neuropil. Vasogenic edema is commonly seen in traumatic, infectious, and hemorrhagic CNS lesions.

Contributor. University of Florida, Box 100145, Gainesville, FL 32610.

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International Veterinary Pathology Slide Bank

Laser disc frame #5197, 7483-5, 9006, 9599-9600, 14243-7, 16969, 17026-8.

Microslide 9

History. This 2-year-old CD-1 female mouse survived to terminal sacrifice in oncogenicity study in which there was no treatment-related neoplasia.

Gross Pathology. Uterus markedly enlarged, lobulated, purple. Liver - all lobes - multiple purple foci up to 3 mm in greatest dimension.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Histiocytic sarcoma, uterus. Histiocytic sarcoma, extramedullary hematopoiesis - liver. Differential diagnosis/synonyms - Endometrial sarcoma, reticulum-cell neoplasm, type A, malignant schwannoma, histiocytic lymphoma.

Microscopic examination reveals considerable variation within the uterine mass. The neoplasm is consistent with schwannoma with some areas having the Antoni type A pattern including Verocay bodies. Other areas are consistent with the Antoni type B pattern including cholesterol deposits. However, some or all of these same patterns have also been attributed to endometrial sarcoma and histiocytic lymphoma (sarcoma).

Dunn included uterine neoplasms similar to this case within her reticulum-cell neoplasm, type A category. Chouroulinkov et al., and Dawson et al. reported similar if not identical neoplasms as endometrial sarcomas. Stewart et al. considered at least some of the neoplasms of this type to be malignant schwannomas. Dunn, a co-author with Stewart, recanted her earlier position and agreed that these tumors were of nerve sheath and not reticular origin. Frith et al. reexamined the issue and concluded that most of these uterine neoplasms were of lymphoreticular origin and should be classified histiocytic lymphomas.

The liver involvement is more typical of histiocytic sarcoma and provided the impetus to select that diagnosis. The numerous foci of what was interpreted as extramedullary hematopoiesis within the neoplastic areas were considered unusual.

Hopefully, the last has not been written on this subject. Each of the reports cited appears to have validity but none is compelling. It may be that each of these tumor types can arise in the murine uterus and should be diagnosed independently. However, the criteria for differentiation seem inadequate and the temptation to place them under a single heading is strong.

AFIP Diagnoses. 1. Uterus; liver: Histiocytic sarcoma, Charles River CD-1 mouse, rodent.
2. Uterus, endometrium: Hyperplasia, cystic, focally extensive, moderate.

Conference Note. The differential diagnosis discussed in conference included histiocytic sarcoma, endometrial sarcoma, and schwannoma. These tumors share many common morphologic features and differentiation is difficult. Liver involvement is commonly seen with histiocytic sarcoma. The cell of origin in histiocytic sarcoma is thought to be a component of the mononuclear phagocyte system, possibly the tissue macrophage. A major product secreted by mononuclear phagocytes is the enzyme lysozyme. In the rat, lysozyme has been identified in the cells of histiocytic sarcomas, and the enzyme has been proposed as a reliable and specific marker for this tumor type. Conference participants noted the structures resembling Verocay bodies in the uterine mass, but immunohistochemical stains of the mass were negative for S-100 protein. Erythropoiesis has been reported to be common in mice with histiocytic sarcoma (Lemon, 1967).

Contributor. Pfizer Central Research, Bldg. 274, Eastern Point Road, Groton, CT 06340.

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Microslide 10

History. This 4-month-old high-dose Sprague-Dawley female rat was necropsied upon completion of a 12-week oral toxicity study and a 4-week recovery period. There were no clinical signs or clinical pathology abnormalities.

Gross Pathology. Necropsy revealed that the lungs were "puffy", failing to collapse evenly when the thorax was opened.

Laboratory Results. No abnormalities found.

Contributor's Diagnosis and Comments.

1. Drug-induced pulmonary phospholipidosis.
2. Alveolar histiocytosis.
3. Multifocal subacute-chronic bronchopneumonitis.
4. Moderate-severe multifocal chronic proliferative pneumonia.
5. Alveolar emphysema.

Etiology: Drug or its metabolites binds to phospholipid in type II pneumocytes and may be excreted along with surfactant (phospholipid) into alveoli.

Light microscopic examination of hematoxylin and eosin stained lung sections revealed alveoli filled with large histiocytes containing amorphous pale staining material. Besides the alveolitis, there was multifocal "bronchopneumonitis" with an admixture of inflammatory cells found in the thickened interstitium and bronchial lumens. Within one lobe there was a moderate sized subpleural area with inflammation, extensive proliferation of both type II pneumocytes and histiocytes, and loss of normal architecture. Electron microscopic examination revealed that the histiocytes contained abundant phospholipid; this was a drug-induced effect. All high dose recovery rats, except for this one, had only minimal residual pulmonary effects.

The drug behaved like an amphophilic cationic drug described in the references.

AFIP Diagnosis. Lung: Histiocytosis, alveolar, multifocal, moderate, with subacute proliferative interstitial pneumonia, Sprague-Dawley rat, rodent.

Conference Note. Phospholipids are structural components of cell membranes and cytoskeletons, and are a major component of surfactant. Their synthesis, utilization, and turnover can be influenced by drugs, chemicals, endogenous hormones, or cofactors. Phospholipidosis may occur as a result of metabolic dysfunction, genetic disorders, or long-term treatment with cationic amphophilic drugs. Human phospholipid storage diseases include Niemann-Pick, in which there is a deficiency of sphingomyelinase with an accumulation of sphingomyelin, and Tay-

Sachs disease, in which there is a deficiency of hexosaminidase A with an accumulation of G_{M2}-ganglioside.

The severity of phospholipidosis and the organs affected vary between species. Ultrastructurally, phospholipidosis is characterized by membranous lamellar bodies within lysosomes. A proposed mechanism of lamellar body formation is altered lysosomal metabolism. While it has been shown that some cationic amphophilic drugs concentrate within lysosomes and inhibit lysosomal function, the exact mechanism is undetermined.

A differential diagnosis for the histologic appearance of the lung in this case is Pneumocystis carinii infection. Organisms are primarily extracellular in pneumocystosis, however, while in this case the foamy material was within macrophages.

Contributor. Marion Merrel Dow Inc., 9550 Zionsville Road, Indianapolis, IN 46268-0470.

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Microslide 11

History. This 20-month-old male rat, Tif:RAIf (SPF) (Sprague-Dawley derived), was kept in the breeding unit and was not under an experiment. It was killed due to bad general condition and a sample of tissues was sent to pathology for histologic examination.

Gross Pathology. Moderate to marked enlargement of spleen, kidneys, liver and various lymph nodes; liver soft and fragile; grayish-greenish discoloration of kidneys and lymph nodes.

Laboratory Results. No clinical pathology was performed.

Contributor's Diagnosis and Comments. Granulocytic leukemia.

Cortex and medulla of the kidney are markedly infiltrated by mature and immature myeloid cells. The nuclei of these cells are kidney- or ring-shaped; mature granulocytes are also present. Mitotic figures are numerous, as are degenerated cells. The neoplastic cells have infiltrated the renal capsule and the surrounding perirenal adipose tissue. The kidney tubules are displaced and show signs of degeneration. Hyaline resorption bodies are numerous in tubular epithelial cells. In addition, large macrophages can be found within the neoplastic tissue. They contain numerous cytoplasmic granules. Additional organs involved were liver, spleen and lymph nodes (bone marrow was not supplied for examination).

Spontaneously occurring granulocytic leukemia is rare in most stocks and strains of rats, including Tif: RAIf. According to the literature, the incidence is usually less than 1%. At necropsy, a striking greenish coloring of affected organs may be present, hence the designation chloroleukemia. This phenomenon is due to the presence of myeloperoxidase and porphyrins.

Large macrophages are found fairly consistently in granulocytic leukemias. Their presence is unexplained. They seem to be involved in the removal of cellular debris from disintegrating neoplastic cells.

Granulocytic leukemia has to be distinguished from benign conditions of myeloid hyperplasia resulting from inflammatory or neoplastic processes elsewhere in the body. In the present case, the neoplastic nature of the myeloid proliferation is confirmed by the marked organ invasion and the presence of the characteristic macrophages.

AFIP Diagnoses. 1. Kidney: Granulocytic leukemia, Tif: RAIf rat, rodent.
2. Kidney, proximal convoluted tubules: Hyaline droplets, intracytoplasmic, with mild multifocal tubular epithelial necrosis.

Conference Note. Granulocytic leukemia is frequently diagnosed by quantitative and differential blood counts. Characteristically, there is a maturation arrest of granulocytic cells. Immature myeloid cells are present in peripheral blood, even in the early stages of the disease. Progression of the

disease may be accompanied by either a gradual or abrupt increase in the WBC. In the acute and subacute forms, WBCs usually range from 25,000-190,000/mm^3 ,and there is a predominance of immature myeloid elements. In the chronic form of the disease, the WBC count can be 600,000/mm^3 or greater and myeloblasts and promyelocytes are less numerous in the peripheral blood.

Hyaline droplets represent an accumulation of secondary lysosomes within the cytoplasm of proximal convoluted tubular epithelial cells. These lysosomes may contain $\alpha_{2\mu}$-globulin reversibly bound to the inducing chemical and/or metabolite. This bond interferes with lysosomal hydrolysis of $\alpha_{2\mu}$-globulin in the epithelial cell, leading to the accumulation of cellular protein as hyaline droplets. This condition is restricted to male rats. Male rats are physiologically proteinuric due to hepatic synthesis of large amounts of $\alpha_{2\mu}$-globulin and subsequent filtration via the kidney. Hyaline droplet formation has also been reported in association with histiocytic sarcoma in both sexes of rats. Lysozyme is the major component of these protein droplets. In contrast to the $\alpha_{2\mu}$-globulin hyaline droplet nephropathy, these protein droplets are thought to form because of excessive production of lysozyme by the neoplastic cells.

Contributor. Ciba-Geigy AG, Preclinical Safety, Pathology, K-135.2.26, CH-4002 Basel, Switzerland.

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International Veterinary Pathology Slide Bank
Laser disc frame #4688-93(canine), 6920(feline).

Microslide 12

History. This 8-year-old female Rhesus monkey (Macaca mulatta) had a mild episode of crusted bloody nasal discharge which appeared to respond to antibiotic therapy. Two weeks later the animal presented acutely moribund, and expired.

Gross Pathology. A large, 2 cm area of superficial gastric ulceration was present. A 4 cm hemorrhagic pulmonary infarct was seen in the right lung.

The kidneys were bilaterally and uniformly pale and swollen.

Laboratory Results. A heavy growth of coagulase negative Staphylococcus was cultured from the lung lesion.

Contributor's Diagnosis and Comments. 1. Membrano-proliferative glomerulonephritis, global and diffuse, marked-severe, with extensive glomerular crescent formation.
2. Tubular proteinosis, patchy, mild.

The most striking microscopic findings were within glomeruli, which were characterized by increased mesangial cellularity, thickening (and on PAS staining, splitting) of capillary basement membranes, accentuation of the lobularity of many glomerular tufts, and the formation of numerous crescent structures associated with Bowman's capsule. Small accumulations of fibrin were occasionally noted in Bowman's space.

The term membranoproliferative glomerulonephritis (MPGN) is frequently used as a morphological designation, describing conditions in which there is both an increase in glomerular cellularity and thickening of the capillary wall. In humans, the disorder can occur either primarily/idiopathically, or may be secondarily associated with a wide variety of well-defined disease states. Although the specific initiating etiologic and pathogenic mechanisms may vary, MPGN is generally thought to be the result of chronic antigenemia.

Glomerular crescent formation likewise is not a specific disease but an endpoint in numerous disorders creating glomerular capillary basement membrane damage through which intravascular contents escape with precipitation of fibrin in the capsular space. Fibrin is thought to be the primary stimulus for the formation of crescent structures, which can be comprised of a variety of cells including parietal and visceral epithelial cells, lymphocytes and monocytes.

In research primates, MPGN may be associated with sepsis secondary to chronic vascular catheterization. Reports of spontaneously occurring glomerular disease in macaques (with the exception of mesangioproliferative glomerulonephritis in M. nemistrina) appear to be rare. The final pathophysiologic cause of the glomerular disease present in this case was not definitively determined, but an infectious/post infectious etiology was strongly suspected.

We have seen a number of cases of MPGN in this colony which occurred in association with type D retroviral infections,

although a specific cause-effect mechanism has not been demonstrated. The retroviral status of this animal was not determined.

AFIP Diagnosis. Kidney: Glomerulonephritis, membranoproliferative, global and diffuse, severe, with crescent formation, Rhesus monkey (Macaca mulatta), primate.

Conference Note. Conference participants considered a majority of the tubular and interstitial changes to be associated with the glomerulonephritis, but the foci of interstitial lymphocytes and plasma cells may represent an unrelated interstitial nephritis. Multinucleated epithelial cells are present in the collecting ducts and represent a normal finding in Rhesus monkeys.

Glomerulonephritis in animals is usually classified as membranous when basement membrane thickening predominates, proliferative when cellular proliferation predominates, or membranoproliferative (mesangiocapillary, mesangioproliferative) when both changes are present. The most common pathogenesis of glomerulonephritis in animals is immune complex deposition. Ultrastructurally, immune complexes are seen as subendothelial, intramembranous, subepithelial, or mesangial electron dense deposits. Immune complex deposition usually occurs when there is a slight excess of antigen or equal antigen and antibody concentrations. These complexes usually contain complement as well as antigen and antibody.

Several mechanisms are responsible for glomerular injury in glomerulonephritis, the best-established of which is that of complement fixation with subsequent chemotaxis of neutrophils. Complement components C3a, C5a, and C567 are chemotactic for neutrophils which, in the process of phagocytizing immune complexes, release lysosomal enzymes, arachidonic acid metabolites, and oxygen-free radicals which damage glomerular basement membranes. C5b-9, the terminal membrane attack complex of complement, can independently damage glomeruli. Complement fragments can cause release of histamine from mast cells which leads to increased capillary permeability. A mechanism independent of complement and neutrophils also exists, but is not well understood.

Contributor. University of Pittsburgh, Department of Laboratory Animal Resources, A-115 Scaife Hall, Pittsburgh, PA 15261.

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International Veterinary Pathology Slide Bank
Laser disc frame #1195-6, 2995-6, 3018-9, 5015, 6109-13, 6116-33, 6140-2, 6608-10, 16481-94.

Microslide 13

History. This aged female Fischer 344 rat was found dead approximately 30 months after repeated aerosol exposure to hydrazine.

Gross Pathology. The spleen was enlarged and swollen (9.5 cm). There was also splenic rupture with approximately 5 ml of blood in the abdomen. Mesenteric lymph nodes were 0.2 to 0.3 cm in diameter.

Laboratory Results. None.

Contributor's Diagnosis and Comments. 1. Nasal turbinates: Polypoid adenoma (adenomatous polyp), Fischer 344 rat, rodent.
2. Nasal turbinates, vessels: Large granular lymphocyte (mononuclear cell) leukemia.

Hydrazine (N_2H_4) is a highly reactive reducing agent which is widely used as an intermediate in organic synthesis and as a missile propellant. It has been shown to be weakly oncogenic in rats and hamsters. In chronic hamster and rat studies, from which the submitted case was an exposed animal, the incidence of nasal polypoid adenoma was 3% (3 of 94 exposed hamsters) and 5% (10 of 194 exposed rats). Submucosal glandular adenoma, squamous cell carcinoma, and olfactory neuroblastoma were rarely observed in exposed animals. No nasal neoplasms were observed in untreated controls.

The cell morphology and pseudoglandular or microcystic arrangement of this neoplasm is typical for polypoid adenoma of the nasal cavity. Depending on the level of section this tumor originates from the dorsal wall of the lateral meatus with variable involvement of the adjacent nasoturbinate and extends to the ventral meatus. Squamous metaplasia and inflammation of the nasal lacrimal duct are likely secondary to the neoplasm. In the contralateral nasal sinus there is multifocal squamous metaplasia

and minimal to mild lymphoplasmacytic to acute inflammation (varies depending on the level of section). Some sections have respiratory epithelial cells of the dorsal meatus containing eosinophilic globules. The significance of these globules is not known and in this study there was no significant difference in the incidence between treatment and control animals.

There is a structure-function relationship that tends to determine the location and type of induced nasal tumors; cell type and air flow are principal factors. Knowledge of the gross and histologic anatomy of the nasal cavity is critical for interpretation of pathology data and for proper specimen selection. Good and slightly different descriptions of the histologic anatomy of the rat nose and methods of sampling for histopathologic examination can be found in Harkema (1991), Morgan (1991) and Jiang (1986).

Close examination of the vasculature reveals abnormally large numbers of circulating mononuclear cells. Histopathologic examination of the enlarged spleen confirmed the diagnosis of mononuclear (large granular lymphocyte) leukemia. A similar intravascular pattern was observed in the liver and lungs. There was no statistically significant difference in the incidence of leukemia between treatment and control groups [23% vs 27% (females) and 27% vs 30% (males)].

AFIP Diagnoses. 1. Nasal mucosa: Polypoid adenoma, Fischer 344 rat, rodent.
2. Nasal mucosa: Rhinitis, lymphoplasmacytic, chronic, focally extensive, moderate, with epithelial hyperplasia and squamous metaplasia.
3. Blood vessels, intraluminal: Large granular lymphocyte leukemia.

Conference Note. There was variation in the level of nasal cavity present among sections. Adenomas of the nasal cavity arise from the respiratory epithelium, septal glands, or Bowman's glands; however, the cell of origin is sometimes difficult to determine. They can be papillary or polypoid and usually consist of well-differentiated simple or pseudostratified epithelium overlying a scant fibrovascular stroma arranged in a villous, tubular or glandular pattern. Polypoid adenomas are usually found in the anterior nasal cavity and vary from microscopic nodules to large masses that protrude from the nares and cause dyspnea. It is a rare spontaneous tumor in the rat.

Large granular lymphocyte leukemia, also referred to as mononuclear cell leukemia, is one of the most common neoplasms of Fischer 344 rats. As a spontaneous neoplasm it occurs in 10-35% of Fischer rats over the age of 18 months. It arises in the spleen, and gross pathologic findings include severe splenomegaly, a pale mottled liver, enlargement of visceral lymph

nodes, and petechial hemorrhages in the lungs, brain, and lymph nodes. Leukocyte counts range from 5,000 to 370,000/μl with consistent findings of immune mediated hemolytic anemia, thrombocytopenia, and clotting abnormalities suggestive of disseminated intravascular coagulation. Large granular lymphocyte leukemia in the Fischer 344 rat is an animal model for human T-cell leukemias.

Contributor. Armstrong Laboratory (AL/OET), 2856 G Street; Bldg. 79, Wright-Patterson AFB, OH 45433-7400.

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Microslide 14

History. This 3-year-old male Boston Terrier canine was brought to a clinic for possible intestinal blockage. The dog had cardiac arrest during an exploratory laparotomy.

Gross Pathology. None provided.

Laboratory Results. None provided.

Contributor's Diagnosis and Comments. Glomerular lipoidosis.

In this case, the aggregates of so-called foam cells were shown to contain lipid material. The early observations of this lesion by other workers suggested that these cells were of endothelial origin. However, electron microscopic examination of this lesion in 33 beagle dogs showed the presence of intercellular substance and absence of luminal space between the cells. Further, these cells were surrounded by basal lamina which were covered by foot processes except on the endothelial surface. These findings confirmed the mesangial origin of the foam cells. Endothelial cells showed some vacuolation and the presence of irregular globular inclusions in their cytoplasm. This lesion is not thought to have any functional significance.

AFIP Diagnoses. 1. Kidney: Glomerular lipidosis, diffuse, segmental to global, severe, Boston Terrier, canine.
2. Kidney: Nephritis, interstitial, lymphoplasmacytic, chronic, multifocal, mild.
3. Kidney, pelvis: Pyelitis, lymphoplasmacytic, chronic, multifocal, mild.

Conference Note. Several conference participants commented that this is a remarkably severe case of glomerular lipidosis. Glomerular lipidosis is an infrequent spontaneous lesion of dogs that has no functional significance. This lesion is not associated with glomerulonephritis. The large lipid containing cells within the glomerulus, often referred to as "foam cells", have been shown to be altered mesangial cells. A differential diagnosis discussed in conference included lipid embolism, which occurs as a post-traumatic event and in diabetes mellitus.

Contributor. University of Arizona Diagnostic Laboratory, 2831 N. Freeway, Tucson, AZ 85705.

References.

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Microslide 15

History. This 8-week-old male guinea pig was euthanized due to respiratory distress two days after arrival into quarantine from a commercial vendor.

Gross Pathology. The lungs remained fully inflated after opening the chest.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Marked subacute necrotizing bronchopneumonia - intranuclear inclusions - guinea pig adenovirus infection.

This disease has been described in both young and old guinea pigs and is reported to have a low morbidity and high mortality. Virus antigen and serologic tests have not been available for this agent. The disease has been reproduced in guinea pigs using infected tissues, but attempts to propagate the virus *in vitro* have been unsuccessful.

AFIP Diagnosis. Lung: Bronchopneumonia, subacute, diffuse, moderate, with necrotizing bronchiolitis, atelectasis, and bronchiolar epithelial basophilic intranuclear inclusion bodies, Dunkin Hartley guinea pig, rodent, etiology- consistent with adenovirus.

Conference Note. Acute or subacute pneumonia is a common cause of death in guinea pigs, and is commonly associated with bacteria such as Bordetella bronchiseptica, Streptococcus pnuemoniae, Streptococcus zooepidemicus, Klebsiella pneumoniae, and Pasteurella multocida. Viral pneumonia is rare. There are several reports of necrotizing bronchopneumonia in guinea pigs associated with adenovirus. Findings included necrotizing bronchitis and bronchiolitis accompanied by basophilic intranuclear inclusion bodies. Electron microscopy has revealed numerous adenoviral particles, arranged in paracrystalline and crystalline deposits and filling the nuclei of pulmonary epithelial cells.

Adenoviruses cause respiratory disease in cattle, sheep, horses, quail, nonhuman primates, dogs, and man, and experimentally induce disease in swine and mice. Diagnosis of adenoviral infection is commonly based on isolation of the virus,

serology, or immunofluorescence. Hemagglutination and hemagglutination-inhibition can be performed on infected tissue or serum to demonstrate most types of adenovirus. Definitive diagnosis of guinea pig adenovirus infection is difficult. Tissue from guinea pigs with experimentally-induced adenoviral pneumonia were found not to hemagglutinate rat erythrocytes. Attempts to replicate guinea pig adenovirus in cell culture have not been successful. Currently, there is no serologic method to identify guinea pig adenoviral infection.

Contributor. Pennsylvania State University, M. S. Hershey Medical Center, Department of Comparative Medicine, P.O. Box 850, Hershey, PA 17033.

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Microslide 16

History. All SPF mice in a shipment housed in a hard plastic "hepa-filtered" isolator began to develop nodules on their heads and in their cervical regions one month after arrival from the vendor.

Gross Pathology. Subcutaneous nodules varying in number and ranging from 3-10 mm in diameter were observed in the cephalic and cervical regions. When lanced, pus of a thick consistency extruded from the nodule.

Laboratory Results.

1. A gram stained touch impression of the nodule content revealed large gram-positive cocci.
2. *Staphylococcus aureus* was isolated from the nodules of several mice.

Contributor's Diagnoses and Comments.

1. Skin, facial, subcutaneous abscesses, multiple.
2. Skin, botryomycotic dermatitis.
3. Skin, furunculosis.
4. Etiology: Staphylococcus aureus.

This is a common iatrogenic condition that occurs in nude mice that are not housed in sterile caging systems and not handled with aseptic procedures. Subsequent assessment of newly arrived mice indicated the mice were harboring Staphylococcus aureus upon arrival. Contamination from human contact has been reported to be the primary source of staphylococcal disease that develops in SPF mice.

AFIP Diagnosis. Haired skin: Microabscesses, chronic, multiple, coalescing, with colonies of cocci and Splendore-Hoeppli material, C57B1/6 nu nu mouse, rodent.

Conference Note. Botryomycosis is a chronic bacterial infection characterized by the presence of bacterial colonies surrounded by Splendore-Hoeppli material. It usually follows some form of trauma and typically involves the deep dermis, subcutis, and occasionally extends to the muscle, adjacent bone, and rarely viscera. The etiologic agent is usually coagulase positive Staphylococcus aureus, but species of Pseudomonas, Proteus, Streptococcus, Actinobacillus and other bacteria can also cause the condition. Microscopically, there are multiple foci of suppurative inflammation that surround bacterial colonies that are coated by an eosinophilic, amorphous substance referred to as Splendore-Hoeppli material. Splendore-Hoeppli material is not unique to botryomycosis and is seen in other microbial infections and foreign body reactions. It is thought to represent glycoprotein antigen-antibody complexes.

Furunculosis due to Staphylococcus aureus has been reported in nude mice. Homozygous nude mice (nu/nu) have been shown to be more resistant to experimental challenge with Staphylococcus aureus than heterozygous controls (nu/+). The increased resistance is attributed to the presence of naturally occurring activated macrophages in the reticuloendothelial organs. This enhanced activation of macrophages may be due to the lack of T lymphocyte suppressor cells in these animals.

Contributor. St. Jude Children's Research Hospital, Animal Resources Center, 332 North Lauderdale, Memphis, TN 38105.

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Microslide 17

History. This 18-month-old Rottweiler was presented to the veterinary teaching hospital with a history of ascites, poor growth and muffled heart sounds. X-rays revealed a mediastinal mass. Exploratory surgery was performed.

Gross Pathology. Firm, red to brown tissue with scattered black areas, assumed to be atelectatic lung lobes, was removed as was the mediastinal mass. Specimens were identified as representing the left cranial, right middle, and left and right caudal lung lobes. After surgery, there was little functional lung remaining. The dog died the following morning at 3:00 AM.

Laboratory Results. The animal was not necropsied. Examination of biopsy specimens was the only laboratory procedure performed.

Contributor's Diagnosis and Comments. Lymphocytic thymoma; possible intrapulmonary thymoma.

The tissue had prominent vasculature surrounded by variable amounts of collagenous stroma with anastomosing cords of monomorphic mature lymphocytes. Randomly distributed were individual and small clusters of thymic epithelial cells, occasionally keratinizing and forming definitive Hassall's corpuscles. The thymic epithelial component had no histologic evidence of atypia. Thirty-five (35) sections were examined, many of which had been indicated as representing "atelectatic lung lobes". The neoplastic tissue was identical in all sections

examined. Lung parenchyma could not be identified in any section. A few sections contained thymic (thyroglossal duct) cysts lined by cuboidal to columnar and occasionally ciliated cells containing a colloid like material, foamy macrophages, and occasional cholesterol clefts. Also present in a few regions were large numbers of melanophages.

Thymomas are rare neoplasms in domestic species. Thymomas of this type are seen most frequently in the dog, sheep, and goat, and rarely in the horse. Forty-seven canine cases had been reported in the veterinary literature from 1970–1984, with 15 diagnosed during an 11 year period at the Angell Memorial Animal Hospital. A search of the database of the Animal Health Diagnostic Laboratory from 1 Jan 81 to 31 May 93 revealed 19 cases of canine thymoma with 4 cases diagnosed in 1993, including this case. Over the same time frame, only three had been diagnosed in cats, one in a goat, and none in other species.

Tumors of the thymic epithelium are classified as benign (encapsulated) or malignant (invasive) with both main variants having epithelial, lymphocytic, or mixed types. A rare intrapulmonary variant has also been sporadically described in man. Malignant thymic tumors have also been classified as carcinomas of many subtypes. Thymic neoplasms of neuroendocrine, germ cell, lymphoid, and adipocyte origin have also been reported. Metastatic neoplasms may also affect the thymus. A number of paraneoplastic syndromes have been described in animals and man including myasthenia gravis. The symptoms shown by this dog were related to compression of mediastinal structures. Although an intrapulmonary thymoma was suspected, the inability to demonstrate the thymoma enveloped in pulmonary tissue led to its exclusion as a potential diagnosis.

The histologic appearance of this tumor was "classic" for the lymphocytic variant, with the predominant cell being the small mature lymphocyte. The mixed type typically has a spindle cell or mesenchymal appearance to the epithelial component, not apparent in this tumor.

AFIP Diagnosis. Intrathoracic mass (per contributor): Thymoma, Rottweiler, canine.

Conference Note. The nomenclature of tumors of the thymus is confusing. By a strict definition, the term thymoma would include tumors of all cell types normally present in the thymus. Such an approach led to terms such as lymphocytic thymoma, which seems to refer to a lymphoid neoplasm of the thymus, although it is often used to indicate a neoplasm of thymic epithelium with a predominant component of nonneoplastic lymphocytes. The AFIP takes the approach that defines thymoma as a tumor of thymic epithelial cells, regardless of the presence or absence of a

lymphoid component or the relative abundance of lymphocytes. Lymphoid tumors of the thymus are referred to as lymphosarcoma of the thymus.

Ultrastructurally, thymomas are usually well-differentiated and closely resemble normal thymic epithelium. The neoplastic cells contain tonofilaments and desmosomes. Immunohistochemically, the cells stain positively for keratin.

Myasthenia gravis is a common paraneoplastic syndrome in people, but it is less common in animals. It occurs when there is development of autoantibodies to acetylcholinesterase receptors caused by exposure of muscle antigens within the thymus.

Differential diagnosis for cranial intrathoracic tumors was discussed in conference and includes thymoma, chemodectoma, lymphosarcoma, and ectopic thyroid and parathyroid tumors.

Contributor. Animal Health Diagnostic Laboratory, P.O. Box 30076, Lansing, MI 48909-7576.

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Microslide 18 and 19

History. This crossbred porcine fetus was aborted at approximately 93-100 days gestation (114 days = normal gestation length).

Gross Pathology. No gross lesions were noted.

Laboratory Results. The thoracic fluid from this fetus had a microscopic agglutination microtiter (MAMT) of 1:50 against Leptospira icterohemorrhagiae.

Contributor's Diagnosis and Comments. Placentitis, chronic/suppurative, diffuse, mild to moderate, with vasculitis, placenta, porcine.

The allantochorion contains multifocal perivascular to diffuse interstitial infiltrates composed of neutrophils, lymphocytes, plasma cells and macrophages. Occasional aggregates of neutrophils are present at the tips of allantochorionic villi. In some sections, vessel walls are infiltrated by primarily lymphocytes, plasma cells and neutrophils. Although organisms are not readily visible with H&E staining, the Warthin-Starry method demonstrates many spirochetes (leptospires) within the connective tissue, vessel walls and epithelium of the allantochorion. These organisms measure 0.3 um in width and up to 20 um in length. The fetal thoracic fluid MAMT of 1:50 against serovar L. icterohemorrhagiae provides significant evidence of a prenatal leptospiral infection. No microscopic lesions were noted in the fetus.

Leptospiral abortions in pigs most commonly occur in the last 3 weeks of pregnancy, as in this case, and some pigs are born alive but weak. Mummification is occasionally present. Gross lesions are not common and the most severe lesions are seen in those piglets delivered alive but sick at or near term. Some of these will be icteric, and have multifocal hepatic necrosis and a fibrinous pleuritis and peritonitis. An interstitial nephritis characterized by focal and diffuse aggregates of lymphocytes in the medulla and pelvis is characteristic. A mild suppurative pneumonia and placentitis occurs rarely.

Abortion in swine is often the only evidence of leptospiral infection in a herd. Clinical signs are often mild and go undetected. Leptospires are chiefly saprophytic aquatic organisms found in river and lake water, in sewage, and in the sea. The principal reservoirs are rodents, especially rats, mice and voles, and domestic animals such as dogs, cattle and pigs. Infected swine develop a bacteremia before leptospires localize in the kidneys where they persist and can be shed for months. It is during the bacteremia that the organisms invade the placenta and infect the fetus.

AFIP Diagnosis. Placenta: Placentitis, subacute, diffuse, moderate, with necrotizing vasculitis, and numerous spirochetes, crossbreed, porcine.

Conference Note. A vasculitis with fibrinoid necrosis was present in some sections in larger vessels. Conference participants remarked on the large number of spirochetes evident

in the Warthin-Starry section compared with the relatively small numbers of inflammatory cells present.

Other serovars of Leptospira interrogans that commonly infect swine include canicola, grippotyphosa, bratislava, pomona, and tarassovi. Swine are thought to be the primary reservoirs for L. pomona. Leptospires are transmitted through the urine, milk, vaginal discharges, or transplacentally, and can infect hosts through penetration of intact mucous membranes or through breaks in the skin.

Other infectious causes of porcine abortion include Brucella suis, Pasteurella sp., porcine parvovirus, pseudorabies virus, porcine cytomegalovirus, bovine herpesvirus-1, hog cholera, African swine fever, encephalomyocarditis virus, and the recently recognized porcine reproductive and respiratory system virus. Protozoal organisms including Sarcocystis sp. and Toxoplasma gondii also cause abortion in swine.

Contributor. Veterinary Diagnostic and Investigational Laboratory, P.O. Box 1389, Tifton, GA 31793.

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Microslide 20; Lantern slide 1

History. This 3-week-old castrated male beef calf developed diarrhea at three days of age, improved, then relapsed and died at three weeks of age. A postmortem examination was done by the attending veterinarian.

Gross Pathology. Hemorrhage was noted in the jejunum, ileum, and spiral colon.

Laboratory Results. A Salmonella culture of the small intestine was negative. Direct examination of intestinal contents for cryptosporidia revealed no organisms. No viruses were isolated from the small intestine.

Contributor's Diagnoses and Comments. 1. Necrohemorrhagic colitis, diffuse, severe.

2. Necrotizing vasculitis, multifocal, severe, with amphophilic intranuclear inclusions in endothelial cells.
Etiology: Bovine adenovirus.

Isolation of bovine adenovirus in cell culture is often unsuccessful. In this case, electron microscopy was required for determination of an etiologic diagnosis. The submitted electron micrograph of a colonic endothelial cell reveals an array of unenveloped, hexagonal viral particles measuring 63.5 nm, which are consistent in appearance with adenovirus.

The majority of bovine adenoviral infections are asymptomatic. Of the ten serotypes of bovine adenovirus identified to date, bovine adenovirus 3, 5, and 7 have been associated with gastroenteritis. Bovine adenoviral gastroenteritis has been reported in cattle from 11 days of age to adulthood. The incubation period is seven to ten days. The pathogenesis is poorly defined, but is considered to involve viremia with localization of virus in endothelial cells. Viral infection of endothelial cells in the gastrointestinal tract results in vascular necrosis and subsequent ischemic necrosis of the mucosa.

AFIP Diagnosis. Colon: Colitis, necrotizing, acute, diffuse, mild, with endothelial intranuclear inclusion bodies, breed unspecified, bovine.

Conference Note. Adenoviruses infect a number of different species including horses, cattle, sheep, goats, dogs, chickens, turkeys, ducks, quail and geese. The majority of these viruses cause an acute, mild or subclinical respiratory disease. Some, as seen in this case, cause mild gastroenteric disease. Typically, infections are associated with a long latency period, and adenoviruses can often be isolated from apparently healthy individuals. Adenoviral disease is more significant in immunocompromised hosts.

Bovine adenoviral enteric infections occur sporadically in feedlot animals and calves ranging from one to eight weeks in age. Lesions are seen in the forestomachs, abomasum, and intestines and are characterized by multifocal to coalescing areas of necrosis which may be covered by a pseudodiptheritic membrane. Lesions tend to be more severe in the jejunum and ileum in young calves, especially over the Peyer's patches. In feedlot animals, the lesions are more severe in the colon.

Microscopically, the lesions consist of vascular thrombosis with ischemic necrosis of the overlying intestinal mucosa, accompanied by edema and congestion of the submucosa. Vascular endothelial cells often contain intranuclear inclusions. Necrosis and lymphoid depletion are seen in affected Peyer's patches. Inclusions may also be seen in vascular endothelial

cells of the adrenal glands, mesenteric lymph nodes, liver, spleen, kidney, and in the mucosa of the urinary bladder.

Ultrastructurally, adenoviruses have nonenveloped icosahedral capsids measuring 70-80 nm in diameter and composed of 252 capsomeres. Capsids often are arranged in crystalline arrays. Conference participants believed that the electron micrograph provided by the contributor demonstrated typical icosahedral viruses, although the crystalline array pattern was not evident.

Contributor. Department of Pathobiology, 166 Greene Hall, Auburn University, AL 36849.

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Microslide 21

History. This 11 1/2-year-old castrated male Domestic Shorthair feline was presented for recent onset of lethargy and anorexia. Physical examination revealed pyrexia (106.4°F).

Gross Pathology. None.

Laboratory Results. Urinalysis revealed bilirubinuria. SGPT was 78 U/L, alkaline phosphatase was normal, and bile acid was elevated. A complete blood count was unremarkable. An aspirate of the liver revealed pus. Bacterial culture of gallbladder contents yielded a group D Salmonella.

Contributor's Diagnosis and Comments. Gallbladder, cholecystitis, suppurative and hyperplastic, chronic active, due to Salmonella D, feline, Domestic Shorthair.

A cholecystectomy was performed and the excised gallbladder was submitted for histologic examination. Following surgery, the cat was placed on chloramphenicol and tube fed. The animal

responded well to treatment and is normal six months following the surgical procedure.

Sections of the submitted gallbladder feature marked hyperplasia of mucosal epithelium accompanied by diffuse hyperemia and edema of lamina propria, muscularis, and serosa. Intense infiltrates of neutrophils are present and traverse the overlying hyperplastic epithelium. Eosinophils and mononuclear cells are also evident with inflammatory infiltrates being most numerous within lamina propria, yet also evident within muscularis and serosa. Several serosal lymphatics are dilated. A few foci of mucosal loss are accompanied by variable amounts of hemorrhage and fibrin with occasional cellular debris. An artery undergoing fibrinoid necrosis is noted within serosa.

Acute and chronic forms of cholecystitis are rarely reported in small animals. The route of infection is thought to be either reflux of intestinal bacteria into the gallbladder or bacteremia associated with hepatic circulation. Suppurative cholecystitis has been described in the cat, generally in association with a concurrent cholangiohepatitis. Most described cats were aged and had a history of weight loss with intermittent vomiting. Cholelithiasis was a finding in two cases, with a cholelith from one case being positive for Escherichia coli.

The Salmonellae are found worldwide. Salmonella typhimurium is the species most commonly isolated from diseased animals and humans. Cats may have greater resistance than dogs accounting for lesser numbers of reported cases. Fecal isolation from normal cats has ranged from 0% to 14%. Experimentally, large numbers of Salmonellae are required to produce gastrointestinal colonization. Organisms surviving the low pH of the stomach attach preferentially to the tips of villi where they invade and multiply. Organisms may be shed continually or intermittently for up to six weeks following infection. Lymph nodes, liver, and spleen may harbor the organism even in the absence of shedding. The gallbladder and bile do not appear to be as important a site for localization of infection in animals as compared to humans infected with Salmonella typhi.

Clinical cases of salmonellosis in cats may present with fever, anorexia, vomiting, and diarrhea. Not all cases present with diarrhea, as was evidenced in this case which had no evidence of diarrhea throughout its clinical course. The most common isolate in cats is Salmonella typhimurium. Salmonella serotype D was isolated from this case. Serotypes included in D are S. typhi, S. pullorum, S. enteritis, and S. dublin. Serotyping was not pursued in this case.

AFIP Diagnosis. Gallbladder: Cholecystitis, proliferative, chronic-active, diffuse, moderate, with ulceration and hemorrhage, Domestic Shorthair, feline.

Conference Note. Diseases of the gall bladder and extrahepatic biliary tract in cats are uncommon. Cholelithiasis, choledocholithiasis, parasitic infection by several species of trematodes (Amphimerus pseudofelineus, Opisthorchis tenuicollis, Metorchis albidus, M. conjunctus, and Platynosomum concinnum), neoplasia (bile duct carcinoma), as well as cholangitis have been reported in cats. Chronic cholangitis in cats is often seen in conjunction with low grade pancreatitis. In cats and horses the bile duct and the major pancreatic duct have a common entry into the small intestine.

Salmonella sp. are usually eliminated through the bile following bacteremia. Salmonella sp. classically cause a fibrinous cholecystitis in cattle, especially calves.

Contributor. C. E. Kord Animal Disease Laboratory, P.O. Box 40627, Melrose Station, Nashville, TN 37204.

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Microslide 22; Lantern slide 2

History. This 12-year-old Rhesus monkey (Macaca mulatta) was inoculated with SIVmac239 (pathogenic molecular clone) 16 months prior to euthanasia.

Gross Pathology. The jejunal mucosa had multiple red, raised, circumferential bands (gross kodachrome).

Laboratory Results. CBC revealed anemia and thrombocytopenia, and a mild neutrophilia with a normal total WBC count. Total protein, albumin, sodium and potassium were subnormal and BUN was mildly elevated (see attached). Aerobic bacterial culture of the small intestine yielded no enteric pathogens.

Hematology and clinical chemistry:

	Case A93-143	Reference Range
WBC	6.9 x 10^3/ul	3.4 - 11.2
Seg	4.8	1.1 - 4.7
Band	0.1	0 - 0.1
Lymph	1.8	0.5 - 7.0
Mono	0.1	0 - 0.9
EOS	0.1	0 - 0.6
RBC	5.14 x 10^6/ul	4.98 - 6.42
HCT	33%	37 - 47
MCV	64 fl	69 - 79
MCH	20.4 pg	21.7 - 24.7
Platelets	59 x 10^3/ul	190 - 536
Total protein	5.7 g/dl	6.0 - 7.8
Albumin	2.3 g/dl	3.3 - 4.7
Na	236 mEq/l	140 - 152
K	2.8 mEq/l	3.1 - 5.1
BUN	33 mg/dl	9 - 23
Creatinine	0.8 mg/dl	0.7 - 1.3

Contributor's Diagnosis and Comments. Jejunum: Multifocal, moderate, subacute, hemorrhagic, suppurative enteritis, with lacteal dilatation and intranuclear and intracytoplasmic viral inclusions within cytomegalic cells.

Etiology: Cytomegalovirus.

There is diffuse mild to moderate crypt hyperplasia and multifocal villus blunting. In regions corresponding to the grossly observed raised, red bands, there is a marked neutrophilic infiltrate in the lamina propria and within the epithelium. Tips of villi are distended by hemorrhage and dilatation of lacteals. The dilated lacteals contain protein-rich fluid, erythrocytes and neutrophils, and are occasionally thrombosed. There is variable mucosal edema and multifocal necrosis in the superficial lamina propria. Scattered throughout the areas of neutrophilic inflammation are large (cytomegalic) cells with amphophilic intranuclear and/or intracytoplasmic inclusions. These are primarily endothelial cells or macrophages within the lamina propria. Where the inflammation extends into the submucosa, occasional endothelial cells contain inclusions. Using in situ hybridization with a digoxigenin-labelled DNA probe for macaque cytomegalovirus (CMV) (kindly provided by Dr. Peter Barry, UC Davis), CMV nucleic acid-containing cells,

corresponding to the cells containing inclusions observed on H&E, are confined to the areas of neutrophilic inflammation.

Other lesions present on some sections include glandular ectasia, crypt necrosis and a regional lymphoplasmacytic enteritis. In addition to the jejunal lesions, this animal had CMV-associated cerebral meningitis, myelitis and mesenteric lymphadenitis, as well as CMV inclusions in pulmonary arterial endothelial cells.

CMV infection is one of the most common opportunistic infections in AIDS patients, with 90% of patients developing active CMV infection, and up to 25% experiencing serious complications due to CMV. Its most prominent manifestations include retinitis, colitis, encephalitis and pneumonia, and lesions are often disseminated in affected individuals.

CMV infections are also common in SIV-infected Rhesus monkeys, with incidence from 10 to 33% in various studies. As in patients with AIDS, the nervous system and lung are most commonly affected, although lesions have been seen in many organs, and CMV inclusions in arteries are common.

In the intestine, primary CMV infection of endothelial cells is believed to induce a vasculitis which results in mucosal hemorrhage and ulceration, although it is not always clear whether CMV is a primary intestinal pathogen, or a secondary invader. In this case, the association of CMV inclusions confined to the areas of hemorrhage and neutrophilic inflammation in the jejunum, as well as the lack of evidence for other etiologic agents, suggests that CMV is the cause of the enteritis.

AFIP Diagnoses. 1. Small intestine: Enteritis, suppurative, hemorrhagic, multifocal, moderate, with karyomegaly and cytomegaly, and eosinophilic intranuclear inclusions, Rhesus monkey (*Macaca mulatta*), primate.
2. Small intestine, mucosal epithelium: Hyperplasia, diffuse, mild to moderate.

Conference Note. Inclusions were seen in the lamina propria often within endothelial cells. In addition to intranuclear inclusions, some conference participants believed there were intracytoplasmic inclusions. The moderator considered the changes in the small intestine to be more severe than would be expected with only CMV, suggesting that there might be a "background" of SIV enteropathy which is characterized by villus blunting and atrophy, variable crypt hyperplasia, and a lymphoplasmacytic and histiocytic infiltrate in the lamina propria.

Differential diagnosis for enteritis in SIV-infected

macaques includes infection with Shigella, Campylobacter, Salmonella, Yersinia, as well as adenovirus, morbillivirus, and simian varicella virus. Other opportunistic agents commonly found in SIV-infected monkeys include Cryptococcus neoformans, Cryptosporidium, Toxoplasma gondii, Mycobacterium avium, and Pneumocystis carinii.

Cytomegaloviruses are members of the Betaherpesvirinae subfamily of herpesviruses. These viruses typically have a narrow host range. Different strains infect a wide variety of hosts from humans to guinea pigs. Transmission is usually horizontal causing a subclinical chronic or latent infection. Clinical disease is important in immunodeficient individuals and fetuses. A variety of clinical syndromes may occur including encephalitis, chorioretinitis, pneumonia, and gastrointestinal infection such as seen in this case.

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Microslide 23

History. This 3-month-old male infant cotton-top tamarin was one of seven, ages 9 days to 3 months, that died in the infant nursery between June 1 and 17, 1991. This infant and a twin were born on March 23, 1991. They were rejected and abused by their parents and removed to the infant nursery where their wounds were treated and they were given antibiotics. They recovered and gained weight normally. This infant died on June 15.

Gross Pathology. The body was in good condition. The tail and left hand were missing but the stumps appeared to be healed. The lungs were congested. The spleen was slightly enlarged. A smear of heart blood contained myriads of bipolar bacilli, around some of which a mucoid capsule was visible as a halo.

Laboratory Results. Klebsiella pneumoniae was isolated from heart blood, lung, brain or other tissues of the seven infants at necropsy.

Contributor's Diagnoses and Comments. Lung: Congestion, diffuse; purulent pneumonia, multifocal. Blood vessels: Bacteremia; purulent vasculitis, multifocal. Saguinus oedipus, cotton-top tamarin, non-human primate. Etiology: Klebsiella pneumoniae.

The lung is diffusely congested and there are a few fibrin strands within alveolar lumens. There are numerous neutrophils and mononuclear cells in blood vessel lumens. Sections vary from focal perivascular purulent pneumonia to purulent vasculitis and more advanced neutrophilic infiltrate with focal hemorrhage. There are also lymphocytes, macrophages and mild extramedullary hematopoiesis as demonstrated by the presence of a few megakaryocytes and nucleated erythrocytes. The numerous bacteria in blood vessel lumens are short, plump, bipolar bacilli. Bacteria were also seen in hepatic sinusoids, the lumen of the heart and vascular lumens in other tissues.

Klebsiella pneumoniae, also known as Friedlander's bacillus, is a member of the family Enterobacteriaceae and is normally found in the intestinal tract of man and animals. It is a straight rod arranged singly, in pairs or short chains. The outer layer consists of a thick polysaccharide capsule which gives rise to large mucoid colonies.

K. pneumoniae is a common cause of mortality in New World monkeys, especially tamarins. Acute mortality in previously healthy animals may occur, especially among young animals. Cases occur sporadically or in mini-epizootics. In June 1991, seven juveniles between the ages of 9 days and 3 months in the same room died with K. pneumoniae infection. In another outbreak 28 tamarins died during a five month period. There were six cases of septic abortion with the loss of 13 fetuses and three cases of maternal bacteremia.

Large numbers of bipolar encapsulated bacilli are present in blood vessel lumens and in tissues, often with very little inflammation. The source of infection appears to be the intestine; in some cases, the bacteria are seen to invade the mucosa. In infants, the infection spreads from apparently healed wounds, usually of the tail, inflicted by the parents. Pneumonia, pyelonephritis, and meningoencephalitis are also seen.

Klebsiella peritonitis may be associated with the acanthocephalan, Prosthenorchis elegans, in the intestinal wall, in newly captive animals or in those with transmural colonic adenocarcinoma, also common in this species.

In man, K. pneumoniae may cause severe pneumonia or urinary tract infection. It is found in mixed infections of the biliary tract and less commonly in sinuses, middle ears, mastoids and meninges. The first stage of pneumonia is characterized by congestion, edema, a few neutrophils and often numerous bacteria. This stage is followed by widespread fibrinosuppurative consolidation of the lung. The abundant mucinous secretion by the bacteria protects the organisms against phagocytosis and favors spread. Abscess formation, organization of the exudate and bacteremia may follow.

AFIP Diagnosis. Lung: Pneumonia, interstitial, subacute, diffuse, moderate, with acute vasculitis and extracellular gram-negative bacilli, cotton-top tamarin (Saguinus oedipus), primate.

Conference Note. Differential diagnosis discussed in conference included Yersinia, Pasteurella, Streptococcus pneumoniae, and Klebsiella. The organisms seen within vessels were separated by clear spaces, consistent with the encapsulation characteristic of Klebsiella.

Klebsiellae are opportunistic pathogens that are gram-negative, nonmotile, encapsulated, facultative anaerobic bacilli. Clinical syndromes associated with this bacterium in animals include metritis in mares, mastitis in cattle, and urinary tract infections in dogs. Susceptible laboratory animals include non-human primates, guinea pigs, rats, and mice. Infections occur in both Old and New World monkeys; syndromes include septicemia, meningitis, pneumonia, peritonitis, and cystitis. In owl monkeys (Aotus trivirgatus), Klebsiella has been associated with thromboembolic airsacculitis.

Cotton-top tamarins are an endangered species of the Callitrichidae family. Because spontaneously occurring colorectal adenocarcinomas are common in cotton-top tamarins, they are recognized as an animal model (#286) for human colonic adenocarcinoma.

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Microslide 24 and 25

History. A 7-year-old female Dorset cross sheep used as a blood donor in a research laboratory developed a sudden onset of neurologic signs including nystagmus, opisthotonos, teeth grinding, excessive salivation, and recumbency. The ewe failed to respond to treatment with large doses of vitamin B and 20 mg of dexamethasone, and was euthanized 15 hours after the onset of clinical signs.

Gross Pathology. The brain and other organ systems were grossly unremarkable.

Laboratory Results. Listeria monocytogenes was cultured from the brainstem.

Contributor's Diagnosis and Comments. Brain, brainstem, and cervical cord: Encephalitis and myelitis, suppurative, subacute, moderate, with microabscesses, associated gram-positive bacilli, and lymphocytic perivascular cuffing.

The affected neuropil is infiltrated by a small to moderate number of neutrophils, lymphocytes, and macrophages, which form loosely arranged aggregates, sometimes in association with bacterial colonies. The neuropil in these areas is disrupted by vacuoles and small numbers of swollen axons. Blood vessels scattered throughout the section are surrounded by variably sized cuffs of predominantly lymphocytes, with few macrophages and occasional neutrophils. In some areas, the meninges are infiltrated by small numbers of lymphocytes. The microscopic changes are characteristic of listeriosis.

Listeria monocytogenes infection can cause three distinct syndromes: abortion, septicemia, and encephalitis which rarely occur simultaneously in the same animal. Encephalitic listeriosis of sheep, also known as circling disease, occurs sporadically and most commonly in the winter and early spring. Listeria monocytogenes is ubiquitous in nature and is able to survive in soil for years. Most animals are exposed to the organism during their lifetime. Latent infection may be widespread. Factors such as stress caused by pregnancy, climate, or concurrent disease predispose the animal to clinical disease. Current thinking suggests that stress diminishes the host's cell mediated immunity, resulting in activation of latent infection.

Listeriosis is most often associated with silage feeding where pockets of bacteria may go undetected in routine feed testing. Incompletely fermented silage, with a pH of 5.5 or higher can support bacterial multiplication. In encephalitic listeriosis, the bacterium is believed to penetrate the nasal mucosa and invade the brain via the cranial nerves, especially the trigeminal nerve. Infection of the dental branches of the trigeminal nerve is often seen in sheep that are losing and cutting teeth in winter and early spring. Clinical signs include mental confusion, depression, head pressing, and paralysis of one or more of the medullary centers. Neurologic signs commonly associated with listeriosis include deviation of the head to one or the other side without rotation of the head, circular walking patterns, paralysis of the pharyngeal and masticatory muscles, and paralysis of the facial nerve, with resultant eyelid, ear, and lip droop. The course of the disease can range from hours to two days. Animals that survive usually exhibit neurological handicaps. Typically, the brain is grossly unremarkable. Histologically, lesions predominate in the medulla and pons, with less severe involvement of the thalamus and cervical spinal cord. The characteristic lesion is the parenchymal microabscess, accompanied by perivascular lymphocytic cuffing and variable meningitis. Bacterial culture of the organism confirms the diagnosis.

AFIP Diagnosis. Brain, brainstem: Encephalitis, subacute, diffuse, moderate, with microabcsesses and gram-positive bacilli, Dorset cross sheep.

Conference Note. A mild meningitis was seen in several sections. The majority of bacteria appeared to be extracellular. This case was reviewed by the Department of Infectious and Parasitic Diseases of the AFIP. They considered the bacteria to be gram-positive bacilli arranged in chains. This arrangement is rare for Listeria in their experience; however, the morphology and staining characteristics of the bacteria are consistent with Listeria.

Differential diagnosis for the clinical signs in this case include rabies, polioencephalomalacia, clostridial infection, parasitic encephalitis, lead toxicity, and scrapie in addition to listeriosis. Since gross lesions are rare in listeriosis, culture of the pons and medulla, cerebrospinal fluid examination and culture, and blood culture may be helpful in confirming the diagnosis. Examination of other organs, especially the liver and kidney, in addition to the brain may be helpful in ruling out toxic and other causes.

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International Veterinary Pathology Slide Bank
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Microslide 26

History. An adult female albino Xenopus laevis, that was used for ova production, was submitted for necropsy. The frog had become thin and lethargic and had an area of brown discoloration on its dorsum.

Gross Pathology. The dorsal lumbar skin was covered by thick, brown, mucoid material; the underlying skin was grossly unremarkable. The animal's body fat stores were depleted. No other gross abnormalities were evident.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Skin: Epidermal hyperplasia with intraepidermal nematodes, multifocal, mild erosive dermatitis and mild epidermitis.

The nematodes are consistent with Pseudocapillaroides xenopi, also known as Capillaria xenopodis, a common pathogen in laboratory Xenopus frogs. Clinical signs associated with parasitism include an increase in the amount of desquamated skin found in tank water, inappetence, decreased activity, roughened, mottled skin, and decreased egg production in females. Untreated frogs progress to complete anorexia and death. Direct examination of unstained skin from tank water is useful in antemortem diagnosis; affected skin shows intraepidermal tunnels and may contain adult nematodes, larvae, and/or eggs.

Pseudocapillaroides xenopi is a white nematode measuring 2 to 4 millimeters in length. Eggs are thin-shelled, bioperculate, and barrel-shaped. Adult males are smaller than females and have a caudal spicule. Eggs develop to the first larval stage in utero, but do not hatch until they are laid. The life cycle of this cutaneous parasite appears to be direct with autoinfection possible, but this has not yet been well characterized. In a study performed by Cohen, et. al., thymectomized frogs had a high incidence of parasitism which was reversible with thymus grafting, indicating that a thymus-dependent immune response may be important.

AFIP Diagnosis. Skin: Hyperplasia, epidermal, diffuse, moderate, with intraepidermal nematodes and minimal multifocal subacute epidermitis, South African clawed frog (Xenopus laevis), amphibian.

Conference Note. Xenopus laevis is one of the most commonly used laboratory amphibians, especially as a source for ova for embryologic, genetic and molecular biologic research. They have a reported lifespan of up to fifteen years.

Infection with Pseudocapillaroides xenopi causes a wasting syndrome characterized by anorexia, color change, and desquamation of skin and can lead to death. Gross necropsy findings include thin frogs with rough skin. Histologically, the epidermis is riddled with tunnels containing nematodes and accompanied by mild to moderate granulomatous inflammation. Nematodes have also been reported in the kidneys of affected frogs, wrapped around glomeruli in Bowman's spaces.

Other important diseases of frogs include Lucke's tumor of leopard frogs caused by a Gamma herpesvirus; "red leg" in frogs caused by Aeromonas hydrophila and other bacteria; chromomycosis; mycobacteriosis caused by several species including Mycobacterium marinum, M. fortuitum, and M. xenopi; and tadpole edema disease caused by an iridovirus.

Other nematodes that localize in epithelium include Trichosomoides crassicauda in the urothelium of rats, Gongylonema

sp. in various locations including the esophageal mucosa of cattle and non-human primates, Anatrichosoma sp. in the nasal mucosa of monkeys, and Eucoleus boehmi in the nasal mucosa of dogs.

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Microslide 27

History. This 1-year-old Macaca mulatta was sacrificed after 17 days on a polio vaccine neurovirulence test. It developed partial paralysis of the right leg during the test.

Gross Pathology. None.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Diffuse, moderate, nonsuppurative poliomyelitis.

Poliovirus is a member of the enterovirus genus, family picornaviridae. The virus is spread by the fecal-oral route. The great apes are the only nonhuman primates to be naturally infected and can demonstrate the same clinical picture seen in man including paralysis. Old World monkeys are not generally susceptible to naturally occurring poliomyelitis although infant Rhesus and cynomolgus monkeys have been orally infected experimentally.

Oral ingestion of the virus is followed by viremia with the virus disseminating to the CNS, lymph nodes, and heart. In the CNS there is predilection for the anterior horn neurons of the spinal cord and the motor nuclei of the cranial nerves.

This animal was administered oral polio vaccine, which is a live attenuated strain of the virus, in the lumbar spinal cord. It is common for some animals to demonstrate spread of the virus from the inoculation site up the cord and even into the midbrain. This animal shows lesions in the cervical cord which are typical of a poliovirus infection. Lesions are seen predominantly in the grey columns of the spinal cord and consist of gliosis, perivascular cuffs, neuronal necrosis, neuronophagia, and chromatolysis.

AFIP Diagnosis. Spinal cord: Poliomyelitis, nonsuppurative, multifocal, moderate, with rare neuronal necrosis, Rhesus monkey (Macaca mulatta), primate.

Conference Note. Poliovirus strains differ in their antigenic type. Within each type, there are marked differences in virulence and invasiveness. Neuronal changes usually include chromatolysis, neuronolysis, and neuronophagia. These changes can be seen prior to the influx of inflammatory cells and have been shown to be associated with development of high virus concentrations suggesting that the lesions are a result of virus replication and not of the inflammatory process which follows nerve cell destruction. In the early stage of inflammation, three cells types predominate: neutrophils, lymphocytes, and macrophages. The neutrophils persist for only a few days, while the lymphocytes and macrophages persist for weeks to months.

Differential diagnosis discussed in conference included poliomyelitis virus, SIV, SV40, and measles. SIV lesions typically have multinucleate giant cells and no primary neuronal degeneration. SV40 would more likely cause progressive demyelination.

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Jones TC, editors). Vol. 1, Springer-Verlag, New York, 1978, pp 344-347.

Microslide 28; Lantern slide 3

History. This 30-year-old Rhesus (Macaca mulatta) male was exposed in March of 1965 to whole-body penetrating proton radiation. He had been maintained in the Brooks Air Force Base chronic radiation colony. Severe progressive weight loss was noted (3.4 kg loss over 6 months). However, weight loss from 1985 totaled 1/2 of his middle aged body weight. This animal had severe kyphosis and discospondylosis, which contributed to his debility. He was depressed with reduced feces and anorexia. Vomiting was reported the day prior to necropsy. He was euthanized and the whole body was perfused with Karnoskys' fixative.

Gross Pathology. There was severely reduced subcutaneous, pericardial and peritoneal fat. Pulmonary acariasis was present. Approximately 5 cm distal to the pylorus involving the ampulla of Vater was an intraluminal polypoid glandular mass approximately 2-3cm in diameter. The tumor invaded through the muscular tunics into the pancreas with increased connective tissue surrounding the pancreatic and bile ducts. The stomach was full but not distended. However, the small intestine was devoid of any ingesta, and the large intestine contained scant amounts. There was moderate colonic diverticulosis. Lesions in other organs were limited to senile changes.

Laboratory Results. Cultures of colon and cecum for enteric bacteria and Campylobacter were negative.

Clinical Pathology: Interpretation: Total protein and albumin levels are reduced, possibly also reflected in reduced serum calcium. Bilirubin levels are high normal. Sodium and chloride levels are reduced, anion gap is (129 + 3.6) - (89 + 22) = 22. Hematology values are with normal limits. Monkeys with pulmonary acariasis frequently have eosinophilia.

Clinical Chemistry and Hematology

Serum Chemistry:

Glucose	(mg/dl)	60
BUN	(mg/dl)	26
Creatinine	(mg/dl)	0.6
Na	(meq/l)	129
K	(meq/l)	3.6
Cl	(meq/l)	89
CO_2		22
Calcium	(mg/dl)	6.9
TP	(g/dl)	2.7

ALB	(g/dl)	1.4
AP	(u/l)	42
AST (SGOT)	(u/l)	25
LDH	(u/l)	225
BILI	(mg/dl)	0.3

CBC Results:

WBC	($X\ 10^3$)	6.5
RBC	($X\ 10^6$)	6.7
Hgb	(g/dl)	14.4
HCT	(%)	43.3
MCV	(fl)	64.6
MCH	(pg)	21.5
MCH	(g/dl)	33.3
PLT	($X\ 10^3$)	290

Differential (%)

SEG	74
Lymph	20
Mono	2
EOS	4

Contributor's Diagnosis and Comments. Duodenum (ampulla of Vater): Adenocarcinoma, well-differentiated, Macaca mulatta, nonhuman primate. Etiology, unknown.

The chronic radiation colony of Rhesus monkeys at Brooks AFB contains males and females that were irradiated between 1964-1969. As of this date, of 360 treated and control Rhesus, 23 have had intestinal neoplasia with no sex predominance. Seventeen (17) of these have been small intestinal tumors, and of these, 4 have been periampullary neoplasms. DePaoli (1982) cited 8 GI tumors in monkeys, 2 located in the duodenum, one involving the ampulla of Vater. Fanton and Hubbard (1984) reported 2 adenocarcinomas of the small intestine from this colony with no reference to specific site. Intestinal neoplasia in nonhuman primates has been reported in cotton-top tamarins and infrequently in the baboon, rhesus, and other monkey species.

Human colorectal tumors account for 15% of all cancer related deaths (second to lung cancer) in the United States. Although the small bowel represents 75% of the entire length of the human gastrointestinal tract, neoplasia in this location account for only 3-6% of all gastrointestinal tumors. Of these tumors, adenocarcinomas are the most common and are frequently found in the ampullary or periampullary area.

We find the periampullary neoplasms to be provocative. These tumors may produce obstructive jaundice. Like human cases, most clinical problems include weight loss, anorexia, jaundice, dark urine, pale or dark feces, pain, nausea, vomiting, fever, constipation or diarrhea. Positive fecal tests for occult blood are highly suggestive of intestinal neoplasia. False positives for our colony have been related to rectal mucosal trauma, diverticulosis/diverticulitis, and periodontal disease. False negatives may be related to lack of bleeding or ulceration and lack of proximity of the lesion to the rectum. Weight loss,

changes in gastrointestinal function and anemia continue to be the most prominent clinical clues.

Adenocarcinomas in areas other than the ampulla may cause low grade bleeding or massive hemorrhage. In humans, tumor incidence increases with age and dietary habits of affluence (low fiber, high fat) are contributory. Hereditary causes, such as polypoidosis, also exist as familial influences. Grossly, adenocarcinoma of the small intestine may have a polypoid, fungating, sessile, ulcerated or annular constricting appearance. Histologically, this case appeared as a polypoid mass involving the ampulla, with proliferative edges that curled in towards the wall. Neoplastic islands of cells invaded through all muscular tunics, serosa, and into the pancreatic tissue and ducts. Lobular acinar pancreatic atrophy and fibrosis was noted. No metastasis to regional lymph nodes was found in this case, although it has occurred within our colony in another case.

An established animal model of intestinal adenocarcinoma is ulcerative colitis induced/related colonic adenocarcinoma seen in cotton top tamarins (Model #286). Additional models are seen in rats exposed to a furan analog, DHNT (Model 178) and small intestinal adenocarcinoma seen in "fat lamb" type sheep in adulthood (Model 293). Small intestinal adenocarcinoma has been recently reported in a goat.

Theories regarding the reduced frequency of small intestinal tumors in humans compared to the frightening frequency of large bowel tumors include: (1) small bowel contents are diluted by liquid, therefore potential carcinogens are less concentrated, (2) transit time is more rapid in small bowel, and (3) large bowel bacteria may convert bile salts/lipid breakdown products to carcinogens.

The presence of duodenal/ampullary small intestinal tumors may be related to radiation exposure in our geriatric Macaca. Ileal and colonic cancers appear to be related more to old age and have been seen in our control animals (6/23). Further diagnostic workups, methods of early detection and determination of colony incidence with regards to radiation exposure is ongoing.

AFIP Diagnosis. Duodenum: Adenocarcinoma, Rhesus monkey (*Macaca mulatta*), primate.

Conference Note. The adenocarcinoma shows a broad range of differentiation. Within the mucosa, the tumor is composed of well-organized tubules, while deeper tunics are infiltrated by poorly-differentiated neoplastic epithelial cells separated by a marked scirrhous reaction. The attached pancreas has marked lobular atrophy with ductal regeneration. In some sections, a large pancreatic duct contains invading tumor.

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International Veterinary Pathology Slide Bank
Laser disc frame #9195, 10665-6 (bovine), 9247 (feline).

Microslide 29

History. Tissue from a 1.6 week old male B6C3F1 mouse and a 2.6 week old Fvb/NCr mouse. Mice are normal clinically and grossly. B6C3F1 mice have pigmented skin while Fvb mice are white.

Eyes were fixed in Bouin's fixative.

Gross Pathology. No visible lesions except color of skin and retina.

Laboratory Results. None.

Contributor's Diagnosis and Comments. 1. Genetic retinal degeneration (rd) - published diagnosis.

2. Our diagnosis - Hypoplasia or aplasia of inner and outer photoreceptor layers, outer nuclear layer and outer plexiform layer. Reduced thickness of inner nuclear and inner plexiform layers.

3. Normal eye is from B6C3F1 mouse which is also pigmented.

We are performing studies to determine the sequence of events in the fetus and newborn to produce lesions seen in 6 week old mice.

AFIP Diagnosis. Eye, retina, outer plexiform layer, outer nuclear layer, and photoreceptor layer: Atrophy, diffuse, severe, Fvb/NCr mouse, rodent.

Conference Note. Fvb/N is an inbred strain of mouse designated for Friend virus B-type susceptibility. The strain has been maintained since the 1970's and is useful for production of transgenic mice because they are good breeders, have large litters and produce fertilized eggs with large pronuclei which facilitate microinjection of DNA. Fvb/N mice are homozygous for the rd (retinal degeneration) allele which is recognized as a model for human retinitis pigmentosa. The degeneration is inherited in an autosomal recessive fashion and is characterized by a rapid degeneration of rod photoreceptor cells starting at 7-10 days of age. Eyes develop normally up to this age. By 15 days, a majority of rod cells have been lost and by 35 days all are gone. Cone cells degenerate at a slower rate and may survive up to 18 months of age. Experimentally, it has been found prior to detection of degeneration that the photoreceptor cells have elevated levels of cGMP with a reduction in cGMP phosphodiesterase activity. A recent study has shown this to be due to a defect in the B subunit of the cGMP phosphodiesterase (PDE) gene. Inherited retinal degenerations in Norwegian elkhounds, Irish Setters, and RCS rats also show a preferential loss of rod photoreceptor cells.

During the conference, differences between congenital aplasia and degenerative changes were discussed. Without the history of these mice being born with normal retinas it is impossible to distinguish between the two. Differential diagnosis would include light-induced retinal degeneration which produces a similar lesion.

Contributor. National Cancer Institute, NCI-FCRDC, Fairview 201, Frederick, MD 21702-1201.

References.

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Microslide 30

History. Tissue from a 7.5 month old male retired breeder A/JCr mouse that was clinically normal and had been breeding normally.

Gross Pathology. Pale liver, prominent lobular pattern.

Laboratory Results. Isolation of helical bacterium from similar livers in blood agar. Bacterium has 2-4 turns and single flagellum.

Contributor's Diagnoses and Comments. 1. Chronic active hepatitis.
2. Chronic cholangitis.
3. Oval cell hyperplasia.
4. Hepatocytomegaly with intranuclear inclusions of several types.
5. Postnecrotic cirrhosis, mild.

This case is from an outbreak of a new liver disease in mice from the National Cancer Institute's Frederick, Maryland facility. The disease, first thought to be a toxic hepatitis, was transmitted to mice with liver suspensions. The helical bacterium was isolated consistently from affected livers and seen in liver sections with Steiner's stain and on EM examination of livers. Organisms were only found within bile canaliculi.

In this case, Steiner's stain shows individual organisms within bile canaliculi. Organisms are found focally and not necessarily within lesions. This case does not have numerous organisms as do cases in SCID mice. Many pigment granules also stain black. The organisms are small, thread-like, thin structures, with 2-4 turns.

AFIP Diagnosis. Liver: Hepatitis, periportal, portal and bridging, lymphoplasmacytic, chronic, diffuse, moderate, with biliary hyperplasia and oval cells, A/JCr mouse, rodent.

Conference Note. Considerable karyomegaly was present in hepatocytes as well as numerous intranuclear inclusions interpreted to be cytoplasmic invaginations. The moderator believed that there was scarring as evidenced by hepatocellular loss with undulation of the capsular surface and commented that collagen fibrosis was not usually found after necrosis in mouse livers.

The as yet unnamed helical bacterium responsible for the lesions in this case has been found only to affect certain strains of mice including A/JCr, BALB/cAnCr, DBA/2NCr, SCID/NCr and C3H/HeNCr. Athymic NCr-nu, Cr:NIH-bg-nu, B6C3F1, C57BL/6NCr and C57BL/6NCr-bg strains appear to be resistant. Males are more severely affected than females. Lesions appear at 2-4 months of age and become more advanced at 8-10 months and consist of small areas of hepatocellular necrosis and nonsuppurative inflammation. Chronic lesions are characterized by oval cell hyperplasia, hepatocytomegaly, bile duct hyperplasia, and peribiliary leucocyte accumulations. The helical bacterium has been found only in bile canaliculi and has a smooth cell wall with a single flagella.

Contributor. National Cancer Institute, NCI-FCRDC, Fairview 201, Frederick, MD 21702-1201.

References.

1. Lee A, et al: Helicobacter muridarum sp. nov., a microaerophilic helical bacterium with a novel ultrastructure isolated from the intestinal mucosa of rodents. Int J Syst Bacteriol 42(1):27-36, 1992.

2. Ward JM, et al: A unique hepatitis in mice associated with a helical bacterium. In: Proceedings of the Society of Toxicologic Pathologists 12th International Symposium, June 27-July 1, 1993.

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Microslide 31; Lantern slide 4

History. Epistaxis, intermittent, 3 months duration. Became mucopurulent 3 weeks ago. Then became dyspneic. Endoscopy: Hemorrhagic mass in ethmoid region.

Gross Pathology. Macroscopically, the mass was large, irregular (90mm diameter X 40mm) with a pale, bosselated, convex surface that covered a large mass of lamellated blood clot. Cut surfaces revealed variably thick (2-10mm) pale, tough, outer tissue and inner soft, dark blood clot.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Hematoma, chronic, ethmoid.

The convex surface is formed by blood clot and inflammatory exudate in which there is heavy surface bacterial growth. There is some residual stratified squamous epithelium in which there are a few neutrophilic leukocytes. Beneath is a broad band of inflamed granulation tissue in which there is copious blood pigment and heavy siderotic basophilia of connective tissue and blood vessel walls.

Larger sections include surface upper respiratory epithelium. In the deeper tissue, chronic hemorrhage, macrophage and giant cell reaction, and remarkable hemosiderosis are present. Giant cell phagocytosis of crystalline material is conspicuous. The deepest part is blood clot. In some sections, there are extensive surface necrosis and ulceration with florid underlying granulation tissue and surface inflammation. Also present are pseudoepitheliomatous epithelial hyperplasia and entrapment and cystic distension of glands.

The histological appearance is of chronic organizing hematoma. The bleeding appears to have originated from mucosal connective tissue, but a definitive site of hemorrhage is not recognized in these sections.

AFIP Diagnosis. Respiratory mucosa: Rhinitis, granulomatous, focally extensive, severe, with granulation tissue, marked hemosiderosis and mineralization, Thoroughbred cross, equine.

Conference Note. Progressive ethmoid hematomas are nonneoplastic masses that usually originate from the ethmoid region and expand into the adjacent sinuses and caudal nasal cavity of horses. The hematomas are locally destructive and progressive. Treatment is difficult, warranting a poor prognosis for a cure. The pathogenesis of the lesion is poorly understood. Possible predisposing factors include chronic infection, repeated episodes of hemorrhage, and congenital or neoplastic conditions.

Although ethmoid hematomas are relatively uncommon, there are documented cases in Thoroughbreds, Arabians, Quarterhorses and warmblooded horses. Standardbreds have not been reported to be affected. There does not seem to be a gender predisposition. The average age of reported cases is 9.9 years with a range from 3 to 20 years. Epistaxis is the most consistent clinical sign and results from ulceration or discontinuity of the epithelium covering the lesion. Diagnosis is best confirmed by biopsy.

Histopathologically, the lesions typically consist of an outer covering of respiratory epithelium overlying an irregular zone of submucosal fibrous tissue and a central zone of recent

and old hemorrhage containing hemosiderin-laden macrophages and numerous multinucleated giant cells. Differential diagnosis of the gross lesion should include fungal granulomas, nasal amyloidosis, nasal polyps or neoplasia.

Contributor. Department of Veterinary Pathology, University of Liverpool, P.O. Box 147, Liverpool, UK.

References.

1. Cook WR, and Littlewort MCG: Progressive hematoma of the ethmoid region in the horse. Eq Vet J 6:101-108, 1974.
2. Platt H: Hemorrhagic nasal polyps of the horse. J Pathol 115:51-55, 1975.
3. Bell BT, Baker GJ, Foreman JH: Progressive ethmoid hematoma: Background, clinical signs, and diagnosis. Compendium Cont Vet Ed 15(8):1101-1111, 1993.
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International Veterinary Pathology Slide Bank
Laser disc frame #391, 15377-80, 15386-8.

Microslide 32

History. Sections are from solitary, non-painful nodules from the cheek and ear of adult horses. No other signs of illness were noted.

Gross Pathology. Smooth surfaced, solitary, firm nodules were examined from the haired skin. Case 92-11200 is from the left cheek and 93-11251 is from the ear.

Laboratory Results. Pure cultures of *Alternaria tenuis* were obtained from each nodule.

Contributor's Diagnosis and Comments. Dermal granuloma, with lymphoid hyperplasia. Etiology: *Alternaria tenuis*.

The differential diagnosis of solitary nodules from the skin of horses is extensive, and includes a variety of neoplasms, fungal and parasitic granulomas, foreign body reactions, collagenolytic granulomas (nodular necrobiosis), and others. A large number of mycotic granulomas have been described, including mycetomas, phaeohyphomycosis, sporotrichosis, zygomycosis, and alternariosis. Lesions due to *Alternaria* sp. in horses typically are associated with marked lymphoid hyperplasia, often with follicle formation. Lymphoid proliferations are often much more pronounced than the macrophages and multinucleated giant cells of the granulomatous response. The lesions submitted are typical

for alternariosis where lesions are usually seen on the face, neck, chest, or legs.

AFIP Diagnosis. Haired skin: Dermatitis, granulomatous, focally extensive, moderate, with lymphoid follicle formation and fungal hyphae, Quarterhorse, equine.

Conference Note. Alternaria spp. are saprophytic fungi which are sporadic opportunistic pathogens. Alternaria sp. can be isolated from normal skin of horses. They are classified as dematiaceous (naturally pigmented) fungi and are ubiquitous saprophytes of soil, wood, and decaying vegetable matter. The cutaneous and subcutaneous forms of the disease syndrome caused by dematiaceous fungi, phaeohyphomycosis, usually result from introduction of fungi via traumatic injuries. Other dematiaceous fungi isolated from horses include Drechslera spicifera and Hormodendrum sp.

An alternate morphologic diagnosis of multiple to coalescing granulomas was considered. Pigmentation of the hyphae was not found on examination of H&E-stained sections, deparaffinized unstained sections and sections treated by the Fontana-Masson method.

Contributor. Veterinary Diagnostic Laboratory, Oregon State University, Corvallis, OR 97339.

References.

1. Coles BM, Stevens DR, and Hunter RL: Equine nodular dermatitis associated with Alternaria tenuis infection. Vet Pathol 15:779, 1978.

2. Scott DW: Large Animal Dermatology, 1988, WB Saunders Co., Philadelphia, pp. 185-191.

International Veterinary Pathology Slide Bank
Laser disc frame # 2099, 10079 (feline).

Microslide 33

History. This 10-year-old, castrated male, bay Thoroughbred horse had a 1-month-long history of uveitis in the left eye.

Gross Pathology. The contents of the left eye including the lens and uveal tract were submitted to the surgical pathology service of the Department of Pathobiology at Texas A&M University.

Laboratory Results. None.

Contributor's Diagnosis and Comments. DX: Severe chronic granulomatous uveitis due to Halicephalobus deletrix.

The saprophytic nematode, Halicephalobus deletrix (formerly Micronema deletrix) has been associated with granulomatous inflammation in the central nervous system, kidneys, bone, gingiva and mammary glands of horses. The uveitis in this horse had granulomatous lesions typical for Halicephalobus deletrix infection. In the weeks following diagnosis of ocular disease, the horse developed severe neurologic disease and was euthanatized. Necropsy documented the presence of granulomatous and necrotizing meningoencephalitis due to the same organism.

AFIP Diagnosis. Eye, uvea: Uveitis, granulomatous, diffuse, severe, with larval and adult rhabditid nematodes, Thoroughbred, equine.

Conference Note. Tissue identification of the sections was challenging but the presence of large rod-shaped melanin granules of the retinal pigmented epithelium and small round melanin granules in uveal melanocytes is unique to the choroid of the eye. Halicephalobus deletrix is classified as a rhabditid nematode with the characteristic rhabditiform esophagus consisting of a corpus, isthmus and bulb. It is a saprophytic parasite of which only the females have been found in parasitic infections. It is hypothesized that the species has two cycles of development: an asexual parasitic cycle where only females are present and reproduce parthenogenetically and a sexual cycle in which male and female worms exist in a free-living state. This parasite has been most commonly reported as an infection of the brain or kidney in horses and humans. Lesions have also been seen, however, in the nasal cavity, oral cavity, lymph nodes, lungs, spinal cord, heart, liver, stomach, ganglion, and bone. The route of infection is unknown.

Contributor. Department of Pathobiology, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4467.

References.

1. Blunden AS, Khalil LF, and Webbon PM: Halicephalobus deletrix infection in a horse. Eq Vet J 19:255-260, 1987.
2. Spalding MG, Greiner EC, and Green SL: Halicephalobus (Micronema) deletrix infection in two half-sibling foals. J Am Vet Med Assoc 196:1127-1129, 1990.

International Veterinary Pathology Slide Bank
Laser disc frame #3654-6, 6270, 6346, 6612-4, 7942.

Microslide 34

History. A 5-year-old Arabian mare aborted her foal approximately 3 weeks premature. The mare was pyrexic (105°F) with harsh lung sounds and increased tracheal sounds. Borborygmi

were reduced in intensity in all abdominal quadrants. Otherwise, the mare was reportedly alert, standing, and with good appetite. The vaccination history of the mare was unknown.

Gross Pathology. The aborted fetus had dark, atelectatic lungs and the liver was covered by numerous, discrete, white foci. The placenta was passed complete and was grossly normal. A reproductive examination on the mare revealed no detectable abnormalities.

Laboratory Results. Results of serology (from mare): Equine Herpesvirus-1 1:64; Equine Influenza-A1 1:40; Equine Influenza-AS-Alaska 1:40; Equine Influenza A2-Miami 1:20.

The equine influenza antibody titers suggested prior vaccination. The equine rhinopneumonitis antibody titer indicated that the horse had been infected or vaccinated.

Contributor's Diagnosis and Comments. Multifocal granulomatous hepatitis. Etiology: Histoplasma sp.

Sections of lung, liver, kidney, jejunum, heart, pericardium and placenta from the aborted fetus were examined histologically, and lesions were limited to the severe inflammation in the liver and less severe inflammatory foci in the lung. The organisms stained positively with silver stains (Grocott's methenamine-silver nitrate) and are characterized by a uniform round to oval shape, 3 micron diameter, with a thin, smooth outer cell wall and a centrally located condensed nuclear structure. Occasionally, the organisms are seen in pairs connected at the most narrow portion of their oval shape (single, narrow based budding). The morphology is consistent with Histoplasma sp.

This case closely resembles that described in JAVMA Vol. 183, No. 10, pp 1097-98 in which a mare had a late gestational abortion with Histoplasma organisms seen in only the liver and lung of the abortus. The organism was confirmed to be Histoplasma capsulatum by immunofluorescent staining.

Unlike the case reported in JAVMA in which the mare was apparently healthy, the mare in our case had clinical signs that indicated pulmonary disease. The etiology of the mare's respiratory signs remains undetermined. Follow-up on her condition at two months post-abortion found her healthy. Her pulmonary signs abated following one to one and a half weeks of antibiotic and steroid therapy.

AFIP Diagnosis. Liver: Hepatitis, granulomatous, perivascular and random, multifocal to coalescing, moderate, with vasculitis and intracellular yeast, Arabian, equine, etiology-consistent with Histoplasma capsulatum.

Conference Note. A differential diagnosis of rhinopneumonitis was discussed in conference in which abortion of late-term, well-preserved fetuses is also seen. Lymphoid necrosis in spleen and lymph nodes in addition to typical inclusions are characteristic of rhinopneumonitis.

Histoplasmosis is acquired by inhalation of air-borne conidia followed by pulmonary infection and phagocytosis by macrophages which can disseminate to other sites in the body. Infection is associated with heavy exposure, young age, and possibly immunosuppression, particularly involving cell-mediated immunity. Latent infections have been demonstrated. Histoplasmosis has been reported as a rare cause of abortion in horses.

Contributor. NCSU-College of Veterinary Medicine, 4700 Hillsborough Street, Raleigh, NC 27606.

References.

1. Saunders JR, Matthiesen RJ, and Kaplan W: Abortion due to Histoplasmosis in a mare. J Am Vet Med Assoc 183:1097-1099, 1983.

2. Valli VE: The hematopoietic system. In Pathology of Domestic Animals, eds. Jubb KV, Kennedy PC, and Palmer N, Academic Press, 4th ed, 1993, vol 3, pp 247-249.

International Veterinary Pathology Slide Bank

Laser disc frame #2037(canine), 9303, 9592, 9677, 10684, 12892(feline), 5294-5, 5758, 6786-7.

Microslide 35

History. This 3-year-old domestic shorthair feline (spayed), presented with respiratory difficulty. Collapse and death occurred in spite of supportive care and oxygen therapy.

Gross Pathology. Section of lung submitted containing a 1.5 cm diameter red brown cyst. Within cyst there were two flattened red brown flukes approximately 12 x 6 mm.

Laboratory Results. None.

Contributor's Diagnoses and Comments. 1. Lung: Marked chronic granulomatous pneumonia and pleuritis.

2. Suppurative bronchiolitis and bronchiolectasis with squamous metaplasia.

3. Pleura: Marked chronic granulomatous pleuritis.

Etiologic diagnosis: Verminous pneumonia, pulmonary trematodiasis. Etiology: Paragonimus kellicotti.

All slides exhibited a marked inflammatory response to numerous oval golden brown fluke eggs. Although most of the eggs are broken and distorted, a few are intact and exhibit the operculated structure typical of trematode eggs. The bronchial changes were variably present among the submitted slides. The involvement of both parietal and visceral pleura surfaces indicates possible rupture of a fluke cavity into the pleural space, releasing the contents and possibly leading to pneumothorax in this patient. Infections by Paragonimus kellicotti are usually inapparent or produce only mild clinical signs unless there is heavy infection or rupture of parasitic cysts.

AFIP Diagnosis. Lung: Pneumonia and pleuritis, granulomatous, eosinophilic, fibrosing, diffuse, severe, with numerous trematode eggs, bronchiectasis, and squamous metaplasia, Domestic Shorthair, feline.

Conference Note. Paragonimus kellicotti belongs to the family Troglotrematidae which also includes the genus of intestinal flukes Nanophyetus. Other important members of the genus Paragonimus include P. westermanii, the common lung fluke of man which also infects dogs, cats, pigs, and other mammals, P. ohirai, which is found in pigs, dogs, weasels, badgers, and wild boars, and P. iloktsuensis, in rats and dogs. P. westermanii is the only species believed to develop in humans.

The life cycles of Paragonimus sp. are similar. Adult flukes, living as pairs in pulmonary cysts, release eggs which pass through connecting channels into bronchioles and are coughed up, swallowed, and pass in the feces. Miracidia, which are ciliated larvae, develop in the egg within 17-20 days. After hatching, the miracidia infect aquatic or amphibious snails from several genera including Melania, Ampullaria, Pomatiopsis, Semisulcospira, and Assiminea. Pomatiopsis lapidaria appears to be the only snail infected with P. kellicotti in North America. Sporocysts develop free in the lymphatic system of the snail. First generation redia emerge from the sporocyst approximately 28 days after infection and develop into second generation redia 63-75 days after infection. Cercariae emerge from the snail and enter a crayfish or crab where they mature into metacercaria and encyst in its heart, liver or muscle. In North America, crayfish of the genus Cambarus are the secondary intermediate host. After the definitive host ingests the crayfish, the metacercaria excyst in the small intestine, penetrate the intestinal wall, migrate through the peritoneal cavity, diaphragm, and pleural surface of the lung. The flukes then form a cystic cavity, grow and mature. Rarely, adult flukes localize to other areas of the body, including the central nervous system.

Within the section presented in conference, smooth muscle hypertrophy was evident in the lesser affected areas of the lung.

Some sections also contained pleura that exhibited reactive plump cuboidal mesothelial cells and fragments of mediastinum that contained similar granulomatous inflammation as was in the lung.

Contributor. Experimental Pathology Laboratories, Inc., P.O. Box 12766, Research Triangle Park, NC 27709.

References.

1. Dubey JP, et al: Induced paragonimiasis in cats: Clinical signs and diagnosis. JAVMA 173:734-742, 1978.

2. Hoover EA, and Dubey JP: Pathogenesis of experimental pulmonary paragonimiasis in cats. Am J Vet Res 39:1827-1832, 1978.

3. Weina PJ, and England DM: The American lung fluke, Paragonimus kellicotti, in a cat model. J Parasitol 76:568-572, 1990.

4. Rochat MC, et al: Paragonimiasis in dogs and cats. The Compend cont Ed 12:1093-1100, 1990.

International Veterinary Pathology Slide Bank
Laser disc frame #38, 4672-3, 6172-3, 6686-8, 7179-80, 7992, 10857.

Microslide 36

History. This 6-month-old Hereford X Holstein, female bovine developed diarrhea, did not respond to treatment and died.

Gross Pathology. The carcass was severely dehydrated and weighed 94.5 kg. All four feet had moderate to severe multifocal areas of ulceration with adhering plaques of fibrinonecrotic debris between the digits. A small number of 2-3 millimeter diameter mucosal erosions were present in the oral cavity. Similar small erosions with adhering bits of fibrin were present in the esophagus. Intestines contained a green watery fluid. Hemorrhagic cratering of intestinal lymphoid follicles was present mainly in the jejunum. The mucosa in scattered segments of intestine was congested.

Laboratory Results. No significant bacteria were isolated. Cytopathic bovine virus diarrhea virus was isolated in tissue culture.

Contributor's Diagnosis and Comments. Esophagus: Esophagitis, subacute, focally disseminated, fibrinonecrotizing. BVD virus.

Lesions in various stages of development are present in the section; similar lesions are common in cases of BVD-mucosal disease. Cytopathic BVD virus was isolated in tissue culture.

In the esophagus the squamous epithelium contained marked multifocal to coalescing areas of necrosis characterized by cellular swelling and eosinophilia, pyknosis and karyorrhexis, and pleocellular inflammatory infiltrates often extending into the basal layers. Spleen had moderate to severe lymphocytolysis, marked depletion of lymphoid follicles and presence of erythrocytes within follicles. In the liver there was mild periportal infiltration by small numbers of mixed inflammatory cells and mild bile stasis. Intestinal sections had severe segmental necrosis of crypt epithelium often with stromal collapse. Small amounts of necrosuppurative debris frequently were present within crypt lumina. There was extensive necrosis of intestinal lymphoid follicles. Occasionally there was extension of crypt epithelium into depleted follicles. The intestinal lamina propria was hypercellular and there were frequent multifocal hemorrhages.

AFIP Diagnoses. 1. Esophagus: Esophagitis, erosive and ulcerative, acute, multifocal, moderate, Hereford-Holstein cross, bovine.
2. Esophagus, ganglia: Ganglioneuritis, subacute, diffuse, mild.

Conference Note. Bovine viral diarrhea (BVD) virus infection produces a wide variety of clinical syndromes including diarrhea, immunosuppression, infertility, abortion and mummification, congenital defects, immunotolerance and persistent infection, acute and chronic mucosal disease, and subclinical infections, which are most common. Acute mucosal disease occurs when a fetus is infected with a noncytopathic strain of BVD virus during the first four months of gestation and develops immunotolerance and persistent viral infection, and subsequently becomes superinfected with a cytopathic strain of BVD generally between 6 months and two years of age. The progeny of persistently infected females are also persistently infected, making it possible to establish maternal families of these animals.

Transmission of the virus is usually by direct contact with a carrier via virtually all body secretions. Exposure to the virus in an immunocompetent host usually results in production of neutralizing antibodies and elimination of the virus.

Clinical signs in acute mucosal disease include depression, fever, anorexia, salivation, mucopurulent nasal discharge, lameness, lacrimation and corneal edema, and profuse watery diarrhea with blood and fibrinous casts. Progressive dehydration and weakness followed by death occurs within five to seven days after onset of clinical signs. Gross lesions include erosive lesions around the nasal and oral cavities, in the interdigital clefts, on the vulva, and scrotum; blunting of the oral papillae; and erosions and ulcerations throughout the alimentary tract.

Peyer's patches are often necrotic and hemorrhagic, a lesion also seen in rinderpest. Microscopically, acute inflammation in the mucosa over Peyer's patches with destruction of underlying glands, collapse of the lamina propria, and lysis of the follicular lymphoid tissue is seen.

This case was histologically characterized by acute multifocal ulcerative esophagitis. Areas of parakeratotic hyperkeratosis were evident on sections examined in conference. The differential diagnosis for the esophageal lesions includes infectious bovine rhinotracheitis, rinderpest, malignant catarrhal fever, and papular stomatitis.

BVD viral antigen has been demonstrated by immunohistochemical staining within the cytoplasm of myenteric ganglion cells. A cytoplasmic clearing and vacuolization of autonomic ganglion cells and myenteric plexuses has also been reported.

Contributor. B.C. Ministry of Agriculture, Fisheries & Food Animal Health Centre, P.O. Box 100, Abbotsford, B.C. V2S 4N8.

References.

1. Radostits OM, and Littlejohns IR: New concepts in the pathogenesis, diagnosis and control of disease caused by the bovine viral diarrhea virus. Can Vet J 29:513-528, 1988.

2. Wilhelmsen CL, Bolin SR, Ridpath JF, Cheville NF, and Kluge JR: Lesions and localization of viral antigen in tissues of cattle with experimentally induced or naturally acquired mucosal disease, or with naturally acquired chronic bovine viral diarrhea. Am J Vet Res 52:269-275, 1991.

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International Veterinary Pathology Slide Bank

Laser disc frame #271, 420-1, 1301-2, 1328, 1561, 1863-5, 1990, 2030-2, 2666-9, 2847-8, 3511-2, 4037, 4042, 4352-3, 4553, 4844-6, 5641, 7563-72, 8777, 9437, 9702-3, 12455-60, 12799-803.

Microslide 37; Lantern slides 5 and 6

History. Three of 11 crossbred piglets farrowed by a clinically normal sow were stillborn. One of these stillborn piglets was submitted for necropsy.

Gross Pathology. The lungs were diffusely swollen, and mottled pink, red, and gray, with disseminated, pinpoint, white-gray foci. Tracheobronchial lymph nodes were swollen. The placenta was red-gray with brown granular material on the chorion.

Laboratory Results. Cytology of impression smears of the lung demonstrated clear (non-staining), filamentous bacteria in the cytoplasm of degenerate neutrophils or macrophages.

Nocardia asteroides was isolated from the lung (NVSL sample ID #944811).

Selected tissues were negative for porcine parvovirus, encephalomyocarditis virus, and pseudorabies virus by FA.

Contributor's Diagnosis and Comments. Lung: Broncho-pneumonia, suppurative and necrotizing, diffuse, with vasculitis and nocardioform bacteria.

Etiology: Nocardia asteroides.

Filamentous bacteria were not identifiable in H&E-stained sections, but stained well with Gomori's methenamine silver (GMS). They were determined to be gram-positive with Brown and Brenn stain, and were not acid-fast. A few multinucleated giant cells were in the bronchial lymph node (included in the section submitted).

Suppurative placentitis was confirmed histologically and attributed to Nocardia asteroides. Infection of the placenta probably preceded fetal pneumonia. This bacterium probably gained entrance to the fetal membranes in the uterus via the cervix and is apparently a rare cause of fetal infection in swine.

AFIP Diagnosis. Lung: Pneumonia, necrosuppurative, diffuse, severe, with necrotizing vasculitis, thrombosis, and filamentous bacilli, crossbred, porcine.

Conference Note. Nocardia asteroides has been associated with sporadic abortions in cattle, swine, and rarely in horses. Abortion usually follows uterine localization of the organism in the uterus of subclinically infected dams. Placentitis and fetal pneumonia are the primary gross lesions. Nocardia is also associated with mastitis in cattle and infection in CID foals. Nocardial organisms are capable of growing in macrophages; cell-mediated immunity is important in clearance of organisms. Virulence of the bacteria has been associated with the thickness of the peptidoglycan layer.

Conference participants discussed a differential diagnosis that included actinomycetes and Fusobacterium. Filamentous bacteria, mononuclear cells, neutrophils, and occasional giant cells were observed in the H&E-stained sections. A Coates modified Fite stain for Nocardia demonstrated acid-fast staining of the filamentous bacteria, although the bacilli were not acid-fast when stained by Fite's method or the Ziehl-Neelsen method.

A degree of autolysis complicated interpretation of the sections.

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Laser disc frame #3191-3 (CID foal)

Microslide 38; Lantern slides 7 and 8

History. Under anesthesia, this 6.1 kg adult female Rhesus macaque (Macaca mulatta) received a calculated inhaled dose of 36.5 mg/kg aerosolized ricin; developed signs of acute respiratory distress shortly before death at 48 hours post exposure.

Gross Pathology. At necropsy, clear froth was present throughout the entire respiratory tract. Fluid and fibrin were present in the thoracic cavity. Lungs did not collapse and were wet, heavy, mottled red and purple, with rib impressions. Mediastinal lymph nodes were enlarged and edematous.

Laboratory Results. None.

Contributor's Diagnoses and Comments. 1. Lungs: Bronchitis, necrotizing, acute, multifocal, moderate.

2. Lungs: Bronchiolitis, acute, diffuse, severe.

3. Lungs: Pneumonia, fibrinous, acute, multifocal to coalescing, marked.

4. Lungs: Alveolar flooding (edema), multifocal to coalescing, severe.

5. Lungs: Interstitial perivascular edema, multifocal to coalescing, severe.

6. Lungs: Pleuritis, fibrinous, acute, multifocal, moderate (present in some sections).

The acute respiratory lesions were attributed to experimentally induced lethal inhaled ricin intoxication. The monkey also had acute diffuse mild laryngitis, acute diffuse mild tracheitis with acute segmental purulent peritracheitis/ mediastinitis and acute diffuse moderate purulent lymphadenitis of the draining mediastinal lymph nodes. Other microscopic lesions (mild lymphoplasmacytic gastritis, subacute mild portal hepatitis and multifocal mineralization of the inner adrenal cortices) were regarded as incidental findings.

The immediate cause of death was attributed to rapid progressive pulmonary edema resulting in massive alveolar flooding and asphyxiation. Acute pulmonary damage is induced directly or indirectly by inhaled ricin via an, as yet, unelucidated mechanism. There are three types of pulmonary edema, permeability edema, neurogenic edema and high pressure (osmotic or cardiogenic) edema. Ricin-induced pulmonary edema is probably of the permeability type.

AFIP Diagnosis. Lung: Pneumonia, interstitial, acute, diffuse, moderate, with abundant intra-alveolar fibrin and edema, Rhesus monkey (Macaca mulatta), primate.

Conference Note. Ricin is a highly toxic lectin found in seeds of Ricinus communis (castor bean plant) and is similar in structure and mechanism of action to abrin and modeccin. Ricin consists of two dissimilar peptide chains, a longer B-chain, responsible for binding the toxin to cell surface receptors, and an A-chain, which is solely responsible for the toxic activity. The A-chain inactivates the 60 S ribosomal subunits in cells thereby inhibiting protein synthesis. Evidence suggests that a single A-chain molecule within the cytosol of a cell is sufficient to cause cellular death. Ricin and abrin appear to be more toxic to certain neoplastic cells and may prove useful as anti-cancer therapeutic agents.

There is a delay after administration of the toxin before clinical signs become apparent, even when the toxin is administered by parenteral routes or inhalation, as protein synthesis is blocked. There are differences in species susceptibility to this toxin.

Conference participants discussed a differential diagnosis that included paraquat, oxygen, phosgene, and staphylococcal enterotoxin B toxicities, and acute respiratory distress syndrome (ARDS). Pleura was present in some sections and exhibited a fibrinous pleuritis.

Contributor. USAMRIID, Pathology Division, Ft. Detrick, Frederick, MD 21702-5011.

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Microslide 39

History. Tissue is an adult male zebra danio (Bracydanio rerio). The body cavity increased in size over a four-month period. Immediately before euthanasia and necropsy, the fish was having trouble moving and maintaining buoyancy.

The fish was a resident of a 15-gallon fresh water tank with a mixed population of tropical fish for more than three years. The fish were fed Tetra Ruby(R) twice daily. Although an occasional elderly fish died during the past two years, there was no evidence of any transmissible health problems. About six months after this fish was killed, another zebra danio in the tank developed an intrabody mass, but was not examined microscopically.

Gross Pathology. None.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Seminoma, testis, zebra danio (Bracydanio rerio), fish.

A large, well-circumscribed, lobulated mass was located posterior and dorsal to the liver, ventral to the kidneys, and dorsal to the intestines. The lobules were irregular in size and shape and some contained centrally located lumens. Some lumens were empty and others contained spermatogonia. A sparse, finely vascularized connective tissue stroma extended between lobules and around the periphery of the mass. The lobules were composed primarily of large pleomorphic, undifferentiated germ cells that were densely packed or arranged in acinar or ductular patterns. The cytoplasm was lightly eosinophilic and granular. Nuclei were large, vesicular and round or oval. Many mature, basophilic staining germ cells and spermatozoa were clumped throughout the lobules. Mitoses were not common. In some sections, clumps of mineral were scattered in the connective tissue stroma.

Testicular tumors have been reported rarely in fish and microscopic descriptions have not been detailed. Most large undifferentiated cells were presumed to be germ cells because many mature germ cells and spermatogonia were seen in the mass indicating that spermatogenesis was active. In addition, cytoplasmic vacuolation (lipid) was not a prominent feature of these cells which indicated they were less likely to be Sertoli cells.

The mass in this animal was considered to be a tumor rather than hyperplasia because the mass was affecting motion, the mass was likely to kill the fish and the shape, size and arrangement of the undifferentiated primary cells were pleomorphic.

The morphologic appearance of this tumor is similar to that seen in a zebra danio reviewed at the AFIP in 1979 (LA 179-79) and another zebra danio which has not been submitted (the histopathologic section was reviewed). The morphologic similarity of these masses in three different zebra danios indicates this tumor may be a common testicular tumor for this species.

AFIP Diagnoses. 1. Testicle: Seminoma, zebra danio (Bracydanio rerio), pisces.
2. Pancreas: Pancreatitis, chronic, focally extensive, moderate.

Conference Note. A discussion of germ cell hyperplasia versus seminoma was held in conference. The size of the mass, the degree of cellularity and the interference with mobility of the fish support a diagnosis of neoplasia. The presence of spermatogenesis, the seemingly orderly progression of cell maturation, and the mild degree of cellular atypia support a diagnosis of hyperplasia. Consultation with veterinary pathologists with expertise in fish pathology indicated agreement with the contributor's diagnosis of seminoma, and a comment was made that spermatogenesis has been previously noted in fish seminomas.

Possible causes of the pancreatic inflammation include fluke migration and mycobacteriosis. Some sections also contain trematodes in the oropharynx and gills, granulocytic inflammation around the swim bladder, and edema in the head kidney.

Contributor. Hazleton Wisconsin, Inc., P.O. Box 7545, Madison, WI 53707-7545.

References.

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Microslide 40

History. Ten fingerling red drum (Sciaenops ocellatus) were presented for necropsy with a complaint of "crusting" epithelial lesions and general poor condition. The fish originated from a commercial aquaculture grow out operation utilizing natural brackish surface waters. Mortalities at the time of presentation were reported as low, but slowly increasing. Morbidity was estimated at 10-15%. One month prior, cohorts from the same tanks had been evaluated for severe scale loss and epithelial erosion. Large numbers of monogenetic trematodes (Gyrodactylus sp.) were present and treatment with potassium permanganate was begun.

Gross Pathology. Multifocal clusters of raised, pinpoint, pearly-tan epithelial nodules were scattered randomly throughout body surfaces. Lesions were most prominent on fin bases, opercular flaps and corneas. General body condition was poor.

Laboratory Results. Bacterial cultures of liver and spleen were negative. Virus isolation was not attempted.

Contributor's Diagnosis and Comments. Dermal hyperplasia, multifocal, marked with intralesional intracytoplasmic viral inclusion bodies and mild perilesional granulomatous inflammation. Lymphocystis disease, iridovirus.

Lymphocystis is a chronic, generally benign, iridoviral induced hyperplastic disease of fibroblasts occurring in at least 125 species of fresh water and marine teleosts. Gross lesions appear as 0.3 to 2.0 mm pearly, cream to pink, gray or tan nodules. Nodules occur primarily externally, but can involve the internal organs.

Microscopically, nodules represent massively hypertrophied fibroblasts that may increase in volume 50,000-100,000 fold. The typical mature "lymphocystis cell" is oval to spherical and surrounded by a thick, laminated, PAS positive, hyaline capsule. The cell nucleus and nucleolus, when present, remain centrally located and are also markedly hypertrophied. Distributed around the periphery of the cytoplasm are the distinctive large, often cordlike, basophilic, Feulgen positive viral inclusion bodies. The surrounding unaffected connective tissue is generally invaded by a mixture of macrophages, lymphocytes and plasma cells.

The causative agent is a large, 200 ± 50 nm, icosahedral viral particle containing a dense DNA core within a capsid composed of two unit membranes, covered by globular subunits with projecting filaments. The virus is resistant to desiccation, but is ether, acid and heat labile. The diagnosis can be confirmed by virus isolation, using a variety of fibroblast-like fish cell lines or by IFA, but this is seldom necessary due to the characteristic histologic appearance.

Transmission is primarily by direct contact, ideally suited to intensive culture operations and is facilitated by skin trauma. These fish had been treated 1 month previously for infestation with monogenetic trematodes that had caused considerable scale loss and epithelial erosion. There also appears to be a strong stress mediated component and lesions may spontaneously resolve if environmental conditions improve. Young fish appear to be most susceptible, with some degree of resistance developing with age. The condition is seldom life threatening, but severely affected fish may be the objects increased predation. Extensive perioral, corneal or fin lesions may interfere with feeding activity, leading to reduced body conditions and occasionally to starvation. From a commercial standpoint, the infection is economically significant in cultured species due to decreased marketability.

An incidental microscopic finding was the presence of intracellular sporozoan parasites within myocytes. Examination of wet mounts prepared from fixed tissue, reveal 4 polar capsules, suggesting a myxosporean of the order Multivalvulida, genus Kudoa. Myxosporean infections by this genus are common in marine fish. They tend to incite little or no host reaction, but are responsible for significant mortalities in some fish species. Post mortem liquefaction of fillets due to enzymatic release from the parasites decreases economic value.

AFIP Diagnoses. 1. Skin: Dermatitis, granulomatous and proliferative, multifocal, moderate, with lymphocystis cells, red drum (Sciaenops ocellatus), piscine.
2. Skeletal muscle: Cysts, myxosoan, multifocal.

Conference Note. The large lymphocystis cells with their distinct capsule, which is composed of sulfated acid mucopolysaccharide, central enlarged nucleolus, and large, cytoplasmic inclusions are unique to lymphocystis infections. The virus tends to be dermatotropic; however, muscle, peritoneum, and visceral organs can also be affected. Other iridoviruses include tadpole edema virus, ranavirus of frogs, carp iridovirus, goldfish iridovirus, Japanese eel iridovirus, and perch iridovirus. African swine fever virus, which was previously classified as an iridovirus, is now considered an "ungrouped" virus because of major differences in its DNA structure and mode of replication.

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Laser disc frame #2101, 9397.

Microslide 41; Lantern slide 9

History. These fish were reintroduced into a stream in the Great Smoky Mountains National Park; netted fish were seen to have pinpoint, slightly elevated white foci in the integument of the head, body and fins.

Gross Pathology. See history.

Laboratory Results. Myxosporidial spores were seen in smears of the integumentary lesions.

Contributor's Diagnosis and Comments. Myxosporidiosis of skin, skeletal muscle and fascia, red line darter fish, species of myxosporidia undetermined.

Multiple cross sections of one fish reveal variable numbers of closely spaced, pyriform organisms within the integument, gill filaments, skeletal muscle and fascia adjacent to various other viscera. The organisms are surrounded by a thin-walled cyst with a rounded and conical end. Cysts measure up to 12 x 7.2 um. The cytoplasm, usually retracted from the cyst wall, contains one to two nuclei; the conical end contains two adjacent pyriform refractile bodies (cnidocysts). Mature spores stain light blue and have an acid-fast, birefringent cyst wall. Only very occasionally is there a lymphoid infiltrate associated with the parasites.

Myxozoa are found in a wide variety of cold blooded vertebrates. After ingestion, sporoplasm disseminates to various sites via the circulation where spores subsequently develop.

Extrasporogonic development may be seen as ameboid cells within parasitized blood cells.

Scrapings allowed identification of the etiology of the integumentary lesions but the severity of the infection was not appreciated until histology was done.

AFIP Diagnoses. 1. Epidermis: Hyperplasia, epidermal and mucus cell, multifocal, moderate, with myxosporidean parasites, red line darter (Etheostoma rufilineatum), piscine. 2. Dermis; skeletal muscle; small intestine; spinal cord: Myxosporidean parasites, numerous.

Conference Note. Of the more than 1,330 recorded myxosporean species, only a few are known to cause serious or fatal infections. In general, there is little humoral response to myxosporeans; inflammatory reactions are generally cell-mediated. Myxosporeans may avoid the host's limited immune response by mimicking host antigens. If the parasite develops in an atypical site, it may provoke a vigorous host tissue response and be destroyed. Similarly, if myxosporeans develop in an atypical host, they may be able to proliferate but not complete sporogony. Myxosporidia can affect any organ of fish and can cause a wide variety of lesions. Typically, the host reaction to myxosporean infection is proliferative. Phagocytosis, primarily by melanomacrophages, is important in control of the organisms.

Several genera, including Unicapsulada, Kudoa, and Hexacapsulada, can severely damage muscle due to proteolytic enzymes released by the parasite. Damaged tissue has a jelly-like appearance due to liquefaction of the muscle which results in economic loss for the producer. During the conference, a brief discussion was held on identification of different species of myxosporidia. Spore morphology including shape, shape of the polar capsules and their arrangement, and multi- or bivalvuate morphology is helpful in identification. Conference participants suspected this infection to be due to Myxobolus sp. Other myxosporidean infections were discussed, including Hennaguya, which causes "hamburger gill disease", and Myxobolus cerebralis, which causes "whirling disease". Some sections also contain intestinal trematodes, and coelomic nematodes between the body wall and kidney.

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References.

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Microslide 42

History. An eight-month-old castrated male Angus calf had been on pasture in Kremling, Colorado, elevation 2225m. Owner noted ventral edema. Presented to the teaching hospital with severe ventral edema of brisket and all four legs; and ascites. There was a grade II/VI holosystolic murmur and a prominent jugular pulse. The calf had tachycardia and ultrasound revealed a pleural effusion.

Gross Pathology. Severe subcutaneous edema of ventrum, legs and brisket. Left ventricular free wall thickness to right ventricular free wall thickness ratio is 2 to 1, and the right ventricle is dilated (right ventricular dilation with eccentric hypertrophy). Pulmonary edema and congestion. Pleural effusion. Liver with an accentuated lobular ("nutmeg") pattern and increased firmness. Ascites.

Laboratory Results. CBC normal. Blood gas indicates a metabolic and respiratory acidosis. EKG; Deep S wave.

Contributor's Diagnosis and Comments. Heart; right ventricular dilation with eccentric hypertrophy. Lungs, muscular pulmonary arteries and arterioles; medial hypertrophy and adventitial hyperplasia, diffuse, marked. Liver; centrilobular fibrosis and hepatic cord atrophy (chronic passive congestion).

The tissues submitted include lung and liver. The small and large muscular arteries of the lung section have markedly thickened walls. The thickening is due predominantly to subintimal and medial hypertrophy characterized by an abundant, well organized, pale amphophilic myxomatous tissue. There are occasional thin bands of mineralization in the subintimal areas of the largest vessels. There is marked thickening of the adventitia of the muscular arteries and arterioles throughout the section as well. The parenchyma is diffusely congested and there is moderate accumulation of an amorphous eosinophilic material (edema) within the alveolar spaces. The interlobular septa are also widened with widely separated collagen fibers (edema).

The liver section provided has a marked, diffuse fibrous tissue proliferation around and bridging the central veins. There is moderate to marked centrilobular hepatic cord atrophy due to hepatocellular drop out. The hepatocytes remaining in the

centrilobular areas frequently contain large, clear, round, intracytoplasmic vacuoles (macrovacuolar degeneration, centrilobular, mild, diffuse). There are occasional karyomegalic hepatocytes scattered widely throughout the parenchyma.

The presentation, clinical findings, gross and microscopic postmortem findings are characteristic of "high elevation disease" or "brisket disease." The disease is associated with cattle being grazed at elevations above 2,200m. Typically, young cattle are more susceptible than old and animals transported from low elevations to high elevations (naive animals) are more susceptible to the disease. Ingestion of locoweed (Oxytopis sericea) while at high altitude is associated with increased risk. Heritable risk factors have also been implicated in the pathogenesis.

The pathogenesis of the disease stems from the bovine's vascular sensitivity to hypoxia at high elevation. The decreased oxygen tension at high elevations result in a hypoxic state that induces vasoconstriction and increased pulmonary arterial pressure. In response to the chronic hypoxic conditions the smooth muscle cells of the tunica media undergo reactive hypertrophy.

The bovine is unusual in that the large and small pulmonary arteries and arterioles normally have a prominent smooth muscle component to the tunica media that may predispose the area to hypertrophy. The medial hypertrophy results in pulmonary hypertension exacerbating the hypoxic effects and increasing the preload on the right side of the heart. The right ventricle hypertrophies and dilates in response to the increased pulmonary pressure and eventually right-sided congestive heart failure ensues with associated ventral edema, ascites and the chronic passive congestion of the liver. The pathophysiology of the medial hypertrophy is incompletely understood; however, protein kinase C (PKC) activation has been shown to allow medial proliferation in response to hypoxia while PKC blockers prevent medial proliferation in vitro. Peptide growth factors may also be involved in the proliferative response of the media. Insulin like growth factor-I has been shown to have mitogenic effects on arterial smooth muscle cells.

AFIP Diagnoses. 1. Lung, pulmonary arteries: Intimal, medial and adventitial hypertrophy, diffuse, mild to severe, Angus, bovine.
2. Lung: Congestion and edema, diffuse, mild to moderate.
3. Liver: Fibrosis, centrilobular, bridging, diffuse, severe, with centrilobular fatty change.

Conference Note. Mineralization is present multifocally in larger arteries. The intimal hypertrophy is most prominent in large pulmonary arteries. Differential diagnosis for the

pulmonary changes includes congenital defects such as mitral valve stenosis, pulmonary embolism, and other causes of pulmonary hypertension. The similarity of liver lesions produced by gossypol, aflatoxin, and pyrrolizidine alkaloids were discussed. Monocrotalene in rats causes fibrosis in the liver and lungs with medial hypertrophy of vessels, megalocytosis, and pulmonary interstitial fibrosis. Factors that stimulate smooth muscle cells were discussed and include smooth muscle elastogenic factor, PDGF, TGF-β, insulin-like growth factor, and protein kinase C. A recent article also reported endothelin-1 to be a mitogen for smooth muscle cells and found that pulmonary hypertension was associated with increased expression of endothelin-1 in vascular endothelial cells, suggesting that this may contribute to the vascular changes in "high altitude disease".

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International Veterinary Pathology Slide Bank

Laser disc frame #4304-5, 15656-8.

Microslide 43; Lantern slides 10 and 11

History. This 9-year-old, mixed breed, spayed female, canine presented with multifocal alopecic, erythematous, scaly and crusty lesions of the skin on the muzzle, trunk and legs. Progressed to involve the mucocutaneous junction with oozing,

exudative lesions. Three months after diagnosis, weakness and lethargy developed and euthanasia was elected.

Gross Pathology. Skin: Generalized scaling and alopecia with oozing and crusting involving the oral mucocutaneous junction.
Liver: Scattered pale, firm 0.5-1.0 cm diameter masses.
Heart: Focal, pale, firm 1.2 cm diameter mass left ventricle.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Haired skin: Epitheliotropic lymphoma.

Histologically, both the lesions in the haired skin and oral mucosa were similar and consisted of multifocal infiltration of the basal, midlevel and, less often, the superficial epidermis and mucosal epithelium by small to large numbers of pleomorphic round cells. Infiltrates involved both surface and follicular epithelium, often with sparing or minimal involvement of the dermis. Cells had poorly defined borders, forming coalescing clusters in more densely infiltrated areas, with small to moderate amounts of light amphophilic cytoplasm. Nuclei varied from oval to irregularly folded and convoluted. The masses in the liver and heart were composed of densely packed pleomorphic, neoplastic lymphoid cells. These histologic findings are characteristic of those described with the epitheliotropic form of cutaneous lymphoma, in this case with involvement of visceral organs.

In human beings, cutaneous lymphomas have been classified into epitheliotropic and dermal variants. The epitheliotropic form is characterized by pronounced epidermal involvement, has been identified as being of T lymphocyte origin and is now referred to as cutaneous T-cell lymphoma. Cases of dermal cutaneous lymphoma generally have minimal superficial dermal infiltrates with a lack of epidermal invasion and have been demonstrated to be of B cell origin. Similar morphologic variants of cutaneous lymphoma are described in old dogs and initial reports indicate these cases may have the same histogenesis as in people.

Gross lesions in dogs have varied from erythematous, scaly areas of alopecia to more ulcerative, oozing lesions, often involving the mucocutaneous junctions and footpads, or actual cutaneous nodules. The prognosis in cases of canine epitheliotropic lymphoma is generally poor. Most owners have elected euthanasia within a few months of diagnosis as lesions progress and eventual visceral metastases, as seen in this case, are reported. More recently, there is a report of temporary remission achieved with the use of synthetic retinoids.

AFIP Diagnosis. Haired skin: Lymphosarcoma, epitheliotropic, mixed breed, canine.

Conference Note. In humans, epitheliotropic lymphosarcomas have been shown to arise from T-cells. T-cell origin has rarely been demonstrated in dogs. Hopefully, reliable canine immunohistochemical markers for B-cells and T-cells will become available in the near future. The moderator remarked that epitheliotropic lymphosarcomas usually start among the basal keratinocytes and spread into the more superficial epidermis with subsequent spread into the dermis and progression into the nodular form of lymphosarcoma. Metastasis of these tumors is usually to regional lymph nodes, liver, and spleen. In the section presented in conference, there is minimal dermal infiltration of neoplastic cells. The external root sheaths of hair follicles are involved in some areas. Also noted was a generalized loss of hair follicles and adnexal structures. Loss of hair follicles and adnexa must be differentiated from glabrous skin which is hairless but can be identified by elongated rete ridges which facilitate adhesion of the dermis and epidermis.

A new treatment regime for epitheliotropic lymphosarcoma using synthetic retinoids has shown promising results. The exact mechanism of action of these compounds is uncertain but may be linked to their ability to regulate growth and differentiation of epithelial cells. Other effects, including their ability to inhibit epidermal cells' response to tumor promoters, modification of gene suppression, decreasing gap junctions, as well as anti-inflammatory effects may contribute to the improvement seen clinically in animals treated with these compounds.

Contributor. College of Veterinary Medicine, Cornell University, Ithaca, NY 14853.

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International Veterinary Pathology Slide Bank
Laser disc frame #11782, 11786, 11802-3, 11807-8.

Microslide 44

History. This 1-1/2-year-old male Bull Mastiff had 2 weeks of severe pruritus, a moist dermatitis on the right facial region, and a region of alopecia on the right shoulder. Skin scrapings of these areas revealed abundant viable nematode larvae. These parasites remained viable 6 days after treatment with ivermectin (subcutaneous inoculation), pyrethrin dip, and shampoo.

Multiple, 4 mm haired skin punch biopsies were submitted for histopathologic examination on 2 different dates, approximately 2 weeks apart.

Gross Pathology. The only gross observation was that the dermis and subcutis were firm and tan-grey.

Laboratory Results. Results of direct and fecal floatation examinations were negative for intestinal parasites. Filter and occult heartworm test results were also negative.

Contributor's Diagnoses and Comments. Multifocal, severe, eosinophilic pyogranulomatous folliculitis and furunculosis with intrafollicular nematode larvae, Pelodera (Rhabditis) strongyloides; Multifocal, moderate, superficial, perivascular, and periadnexal plasmacytic, eosinophilic mastocytic (allergic) dermatitis; Staphylococcal folliculitis.

Pelodera (rhabditic) dermatitis is an erythematous, nonseasonal, pruritic dermatitis, caused by invasion of the skin by the larvae of the free-living nematode, Pelodera strongyloides. The nematode has a direct life cycle, and lives in decaying organic debris. Infection results from contact with contaminated straw or hay bedding. It is believed that a hypersensitivity reaction to the invading parasite is the mechanism for the observed histological changes.

Pelodera dermatitis occurs most commonly in dogs, but is seen occasionally in cattle, and rarely in horses. Gross lesions consist of crusting, erythema, and excoriation, accompanied by severe pruritus; secondary pyoderma is not uncommon. The ventral abdomen, limbs, paws, and perineum are the usual sites of infection, reflecting areas of exposure.

Histologically, there is a chronic inflammatory process characterized by diffuse, marked orthokeratotic hyperkeratosis; marked irregular epidermal and follicular acanthosis, and multifocal necrosis of individual acanthocytes. Many keratin plugged follicles, as well as superficial necrotic debris, contain transverse and longitudinal sections of elongate nematode larvae. The diagnostic morphology of these rhabditic larvae can be seen in many sections, and consists of a buccal capsule,

esophagus, isthmus, esophageal bulb, and intestine. The width of the larvae ranges from 15-30 microns, depending on the section. In addition, there is a multifocal, severe, eosinophilic pyogranulomatous folliculitis and furunculosis. Fragments of nematode larvae are present in the center of these granulomas.

Additional findings include staphylococcal folliculitis; dilation of apocrine glands and occasional larvae; multifocal, moderate, superficial, periadnexal and perivascular, plasmacytic, mastocytic eosinophilic (allergic) dermatitis.

Clinical differential diagnosis includes hookworm dermatitis, demodicosis, sarcoptic acariasis, contact dermatitis, canine dirofilariasis, allergic inhalant disease, and food hypersensitivity.

AFIP Diagnosis. Haired skin: Dermatitis, subacute, eosinophilic, periadenexal, multifocal, moderate, with folliculitis, perivasculitis, and intrafollicular and perifollicular larval rhabditid nematodes, Bull Mastiff, canine.

Conference Note. Pelodera dermatitis is an uncommon skin disease of dogs. The presumed mechanism of disease is a hypersensitivity reaction to the parasites. Pelodera strongyloides larvae are incapable of penetrating intact skin; the skin must be inflamed or otherwise injured prior to infection. Skin scrapings should reveal motile nematode larvae measuring up to 600μ in length. The presence of characteristic nematode larvae in hair follicles with an accompanying folliculitis and perifolliculitis on histopathologic examination is diagnostic. Demodicosis can present a similar histopathologic picture.

Coccoid bacteria are present multifocally in follicles suggesting a bacterial pyoderma component to the lesion. Conference participants believed that the section of skin was probably collected from the back or shoulder because of the presence of large arrector pili muscles.

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International Veterinary Pathology Slide Bank
Laser disc frame #4366-8.

Microslide 45

History. This 2-year-old domestic shorthair cat had a sudden onset of crusty, erythematous and alopecic lesions of both pinnae, the lips, tail and extremities. The cat was depressed, anorexic and hyperthermic. A CBC and chemistry panel showed a neutrophilia with left shift only. Punch biopsies revealed an intraepidermal (suprabasilar to subcorneal) vesiculopustular dermatitis with neutrophils and acantholytic keratinocytes, typical of pemphigus. The cat failed to respond to antibiotic-corticosteroid combinations and was euthanatized five weeks later. The owner was unable to administer oral corticosteroids.

Gross Pathology. There was a generalized dermatopathy characterized by areas of alopecia, crusting, erosions and ulcerations. The areas affected included the nose, periocular and periauricular areas, medial, lateral and tips of the pinnae, dorsal aspect of the head, ventral cervical region, right inguinal region, perianal and proximal ventral tail, distal 7.5 cm of the tail, digits and footpads of all four feet, cranial and caudal aspects of both forelegs, and all aspects of both metatarsal regions. Visceral organs had no significant lesions.

Laboratory Results. Direct immunoperoxidase staining for immunoglobulins on both punch biopsies and postmortem skin sections revealed intercellular granular deposits in the epidermis. The pattern in most areas was outer epidermal, consistent with pemphigus foliaceus, but in many areas, this extended down to the suprabasilar areas, suggestive of pemphigus vulgaris.

Contributor's Diagnosis and Comments. Intraepidermal vesiculopustular dermatitis with acantholytic keratinocytes, multifocal to locally extensive, severe.
Name of disease: Pemphigus, probably pemphigus foliaceus.

Pemphigus foliaceus is by far the most common autoimmune skin disease of the cat. Involvement of the footpads of all four feet and head regions is most commonly seen in the feline cases of our dermatohistopathology service. Pemphigus vulgaris was considered in this case, especially because acantholysis extended to the suprabasilar region in many areas, as well as the profound illness in this cat. The typical "tombstoning" histologic picture of suprabasilar acantholysis was not seen, however. In

our experience with pemphigus foliaceus in both dogs and cats, the epidermal pustules and acantholysis often extend almost full thickness through the epidermis. It is also common, as in these sections of skin, to see acantholytic keratinocytes only in the scale-crust material overlying an intact epidermis. This is because the acantholytic process occurs in "waves".

AFIP Diagnosis. Haired skin: Dermatitis, chronic, diffuse, moderate, with neutrophilic and eosinophilic subcorneal pustules and acantholysis, Domestic Shorthair, feline.

Conference Note. Pemphigus refers to a group of immune-mediated skin diseases that are characterized by the development of autoantibodies against the glycocalyx of keratinocytes resultintg in development of intraepidermal acantholysis. Pemphigus antibody-induced acantholysis is thought to represent a type II hypersensitivity reaction. Pemphigus foliaceus is reported to be the most common form of autoimmune skin disease in the dog and cat and has also been reported in the horse, goat, and human beings. In the dog, there is a breed predisposition in Bearded Collies, Akitas, Chow Chows, Newfoundlands, Schipperkes, and Doberman Pinchers. No predilections have been reported in the cat. Histologically, subcorneal intraepidermal clefts containing numerous acantholytic cells, neutrophils and often eosinophils are characteristically seen.

The moderator commented that in a study of cats affected with pemphigus foliaceus at the University of Pensylvania, 48% had a concomitant allergic dermatitis characterized by significantly elevated numbers of mast cells in the superficial dermis. Cats typically presented with lesions involving the nail beds, feet, face and ears. An average of 3.2 biopsies were performed on each animal prior to definitive diagnosis, emphasizing the difficulty of obtaining diagnostic biopsy material in this condition.

Contributor. Department of Veterinary Pathology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Saskatchewan S7N OWO.

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Microslide 46

History. Multiple cutaneous masses were evident within the dorsal and lateral aspects of the body of the horse. The masses were first noticed by the owner during the summer months. The lesions progressively enlarged and were removed 6 months later by the referring veterinarian.

Gross Pathology. The cutaneous masses were raised, firm and approximately 1.0 cm to 3.0 cm in diameter.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Severe multifocal to coalescing eosinophilic granulomatous dermatitis with

collagenolytic necrobiosis/necrosis (equine nodular collagenolytic granuloma; equine nodular necrobiosis).

One section of skin was submitted. A mild degree of superficial hyperkeratosis was noted. Large multifocal to coalescing sites of severe collagenolytic necrobiosis/necrosis were evident within the superficial and deep dermis, characterized by accumulations of necrotic cellular debris intermixed with foci of mineralization and collagen fibers displaying a homogeneous, eosinophilic appearance. Mild to moderate fragmentation of many of the collagen fibers within the affected dermis was also evident. Large accumulations of eosinophils intermixed with macrophages and lesser numbers of lymphocytes, plasma cells, mast cells, neutrophils and immature fibrous connective tissue were noted peripheral to the sites of dermal necrobiosis/necrosis, extending into the affected focus and to the deep and lateral edges of some sections.

Equine eosinophilic granuloma with collagen degeneration (equine nodular collagenolytic granuloma; equine nodular necrobiosis) is considered by some authors to be part of the eosinophilic granuloma complex which can affect cats, dogs, and horses. In the horse, the lesions are nodular, nonpruritic and nonulcerative, usually occurring in the saddle areas. Although insect bites and trauma have been postulated as possible causes,

the exact etiology has not been ascertained. Conditions which produce similar lesions include habronemiasis and hypoderma nodules.

AFIP Diagnosis. Haired skin: Dermatitis, nodular, eosinophilic and granulomatous, focally extensive, moderate, with dermal necrosis and collagen degeneration, quarterhorse, equine.

Conference Note. Equine eosinophilic granuloma with collagen degeneration is a common nodular skin disease of horses that occurs more frequently in warmer months and shows no sex, age, or breed predisposition. Lesions are single or multiple and most commonly affect the neck, back, and whithers. The etiology is uncertain, but may involve arthropod injury. Histologically, lesions contain areas of collagen degeneration surrounded by granulomatous inflammation with numerous eosinophils. Older lesions may contain extensive areas of dystrophic mineralization and must be differentiated from calcinosis circumscripta.

Contributor. Animal Diagnostic Laboratory, Department of Veterinary Science, The Pennsylvania State University, University Park, PA 16802.

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International Veterinary Pathology Slide Bank
Laser disc frame #2362, 2379.

Microslide 47; Lantern slide 12

History. This 3-month-old female Friesian calf was from a 50 cow herd of purebred Friesians in which natural service was used. At two weeks of age, the calf was rather dull and slow to feed. There was progression to neuromotor dysfunction with incoordination and high stepping gait at three months of age. Three calves with similar signs died during 1992; necropsies were not performed.

Gross Pathology. The cerebral subcortical white matter was dark grey producing a distinct line of demarcation between grey and white matter.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Cerebellum, extensive Purkinje cell necrosis; Golgi type II neurons, neurons of the 4th ventricle roof nuclei and occasional Purkinje cells swollen with foamy cytoplasm; glycolipid storage material consistent with GM_1 gangliosidosis.

Specific changes are limited to nervous tissues. Neuronal cytoplasmic swelling with peripheral displacement of nuclei indicates a storage condition. The storage material is strongly periodic acid-Schiff positive, is Oil-Red-O positive and is largely removed by lipid solvents. Purkinje cell necrosis is accompanied by an increase in Bergmann's glia and there is some dendritic swelling in the molecular layer. In the granular layer, Golgi type II cells are swollen with storage material and there is some loss of granule cells. Axonal spheroids are prominent in the white matter. White matter astrocytic response is variable in the cerebellum; it is marked in the cerebrum. Cytoplasmic storage is present in neurons and some glial components throughout the central and autonomic nervous systems. There is low grade perivascular leukocytic infiltration.

The clinical history, breed and histological/histochemical features are consistent with GM_1 gangliosidosis. Definitive confirmation requires fluorimetric demonstration of low levels of β-galactosidase activity, an enzyme involved in ganglioside catabolism. The disease has been recorded only in Ireland, is rare and confined to the Friesian breed and is probably an autosomal recessive trait.

AFIP Diagnosis. Brain, cerebellum and brainstem: Neuronal vacuolation and swelling, diffuse, moderate, with Purkinje cell necrosis and mild gliosis, Friesian, bovine.

Conference Note. Histologically, lysosomal storage diseases appear similar making definitive diagnosis difficult without knowledge of breed as well as biochemical identity of the accumulating material or of the deficient enzyme. A number of inherited lysosomal storage diseases have been identified in animals and humans and are grouped according to the class of defectively degraded macromolecule. GM_1 gangliosidosis, also known as Tay-Sachs disease in humans, is classified as one of the sphingolipidoses. Gangliosidosis has been reported in domestic and Korat cats, German Shorthaired Pointers, Potugese Water Dogs, Japanese Spaniels, and mixed breed dogs, Friesian cattle, Suffolk sheep, and Yorkshire pigs. In GM_1 gangliosidosis, there is a deficiency of β-galactosidase activity, and in GM_2 of β-hexosaminidase A.

Bovine GM_1 gangliosidosis is recognized as an animal model for human GM_1 gangliosidosis. It differs from the human disease in that no significant histological changes are noted in the liver, spleen, or kidney.

GM_1 gangliosidosis in Suffolk sheep has been shown to be associated with a dual enzyme deficiency consisting of a profound β-galactosidase deficiency with only 5% residual activity and a less profound deficiency of α-neuraminidase with a 20% residual activity. Histologically, central and peripheral ganglionic neurons, kidney, liver, lymph nodes, and cardiac Purkinje fibers contain abnormal storage material.

Other important storage diseases of animals include α-mannosidosis in Angus cattle, sphingomyelinosis in Siamese, Balinese, and Domestic Shorthair cats, Miniature Poodles, glucocerebrosidosis in the Sydney Silky Terrier, and β-mannosidosis in the Anglo-Nubian goat and Salers cattle.

Contributor. Department of Veterinary Pathology, Faculty of Veterinary Medicine, University College Dublin, Ballsbridge, Dublin 4, Ireland.

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Microslide 48

History. There was a sudden die-off of only Muscovy ducks in Venice, CA where many ducks of various type had been crowded into fewer canals and ponds than usual. "Roundup" pesticide exposure was suspected to be the cause of deaths.

Gross Pathology. The first submissions were moderately autolyzed sub-adult Muscovies. The only significant lesions identifiable were focal gray-yellow, friable, erythematous lesions scattered through the intestinal tracts and most severe around the cecae. Four weeks later, 4 young ducklings were examined after continuation of the mortality in spite of attempts to isolate and treat the birds. All ducklings had pinpoint white foci disseminated throughout the livers. There were 2-3 up to 15 discrete foci of annular hemorrhage in the intestines as well as several foci in the esophagus and proventricular border. Some of the plaques of hemorrhage were raised on the mucosal surfaces and seemed to correspond to areas of GALT. No large tissue hemorrhages were present in any duck, and no cutaneous ulcers were found.

Laboratory Results. *Pseudomonas* sp. was isolated from the livers. No parasites were found on fecal examination.

The National Wildlife Health Research Center in Madison, WI confirmed the diagnosis of duck viral enteritis by viral culture of shipped organ samples from the first ducks.

Contributor's Diagnoses and Comments. 1. Bursitis, necrotizing, acute, moderately severe.
2. Enteritis, necrohemorrhagic, acute, severe.
Etiology: Herpesvirus, duck viral enteritis (duck plague)

Viral inclusions range from few and focal to numerous in areas of the submitted sections of bursa and necrotic intestine. Epithelium and lymphoid cells are infected. Other histologic lesions included multifocal hepatic degeneration and necrosis. Those foci were sometimes subtle but numerous typical Cowdry type A and type B intranuclear inclusions were found in adjacent hepatocytes, bile duct epithelium and Kupffer cells. In the esophagus, vasculitis was more prominent with endothelial hypertrophy and occasional inclusions. There was diffuse degeneration of the basal epithelium with extension into the submucosal glands. Viral inclusions were noted in the epithelial cell cytoplasm as well as nuclei, in concordance with the recent observations of Barr et al. The spleens had focal areas of fibrinoid necrosis, and inclusions were found in lymphoreticular and a few endothelial cells.

This diagnosis prompted quarantine of the county and the decision by U.S. Fish and Wildlife Service, with support from the Audubon Society and California Fish and Game, to totally depopulate ducks in the canals, resulting in considerable local community turmoil that quickly became a prolonged media event. Vaccination was suggested as an alternative but wildlife officials were not convinced that this would assure protection to waterfowl of the Pacific Flyway. In fact, a later isolated Muscovy epornitic in San Diego County has been blamed by some on illegal traffic of the Venice ducks. To date, no other waterfowl species has been affected, consistent with some authors' observations of resistance to the lethal effects of this virus in mallards (*Anas* sp.).

AFIP Diagnoses. 1. Small intestine: Necrosis, mucosal, multifocal, severe, with hemorrhage, lymphoid necrosis, and eosinophilic intranuclear inclusion bodies, Muscovy duck, avian.
2. Bursa of Fabricius: Necrosis, lymphoid, diffuse, severe, with eosinophilic intranuclear inclusion bodies.
3. Esophagus, epithelium: Degeneration and necrosis, multifocal, mild, with eosinophilic intranuclear and intracytoplasmic inclusion bodies.

Conference Note. Duck viral enteritis (DVE) is caused by an alpha herpesvirus. Domestic ducks, including Muscovy and Pekin, are most susceptible to the disease. Mallards are relatively resistant and are often implicated as the source of the infection. DVE can be transmitted by direct contact with infected birds or indirectly through contaminated water or other environmental sources. The gross lesions of DVE vary with the species and age of the affected duck. The initial viral injury occurs in endothelial cells of small arterioles, venules and capillaries, causing vascular wall disruption and hemorrhage with coagulation necrosis secondary to ischemia. The earliest lesions are necrosis and petechial to ecchymotic hemorrhage of the mucosa and submucosa of the esophagus and cloaca. Hemorrhage and necrosis are often concentrated in lymphoid tissue of the digestive tract, grossly appearing as annular bands in the intestines of ducks and as discoid foci in geese and swans. The spleen, thymus, and bursa of Fabricius are similarly affected. Other gross lesions can include petechial to paint-brush hemorrhages in the heart, ovary, kidney and pancreas, pinpoint hepatic necrosis, and a bloody nasal discharge. Histologic lesions include necrosis, hemorrhage, severe lymphoid depletion, and prominent eosinophilic intranuclear inclusions.

Differential diagnosis includes duck viral hepatitis (picornavirus), avian cholera (pasteurellosis), necrotic enteritis (Clostridium perfringens), hemorrhagic enteritis (adenovirus), Newcastle disease (paramyxovirus), avian pox, and avian plague (influenza virus).

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International Veterinary Pathology Slide Bank
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Microslide 49

History. This 5-year-old female La Mancha goat had been sick for approximately two weeks with signs of dyspnea. There was slight improvement with antibiotics. Two young goats on the premises have had a respiratory syndrome.

Gross Pathology. The most significant lesions were in the lungs which were diffusely plum colored and firm. Eighty per cent of the parenchyma was affected with the caudal and dorsal lobes most predominantly involved. There were no other significant gross lesions.

Laboratory Results. An agar gel immunodiffusion (AGID) test was positive for caprine arthritis encephalitis virus (CAEV). Lung cultures produced no bacterial growth.

Contributor's Diagnoses and Comments. Gross morphologic diagnosis: Diffuse, severe, proliferative interstitial pneumonia.

Gross Etiologic diagnosis: Lentiviral pneumonia; suspected etiology: CAEV-induced pneumonia.

Histopathologic morphologic diagnoses: Severe proliferative and exudative bronchiolar and interstitial pneumonia; moderate lymphoproliferative interstitial pneumonia; mild verminous pneumonia with intralesional adult and larval nematode parasites.

The lungs had a diffuse and severe interstitial pneumonia characterized by proliferation of type II epithelium, bronchiolar epithelial cells, and lymphoid elements. There was a prominent intra-alveolar and bronchiolar eosinophilic to slightly amphophilic proteinaceous exudate which contained sloughed type II cells, occasional macrophages, and rare neutrophils. Hyperplastic lymphoid aggregates were within alveolar regions and in perivascular, subpleural, and peribronchiolar regions. Alveoli were lined by hyperplastic tall cuboidal to low columnar epithelium. Bronchiolar epithelium was equally hyperplastic with even small bronchioles lined by pseudostratified epithelium. The exudate was mineralizing in some regions. There was a mild interstitial smooth muscle hyperplasia. Primarily within alveoli, but occasionally in bronchioles, were cross sections of adult and larval nematode parasites morphologically compatible with *Muellerius capillaris*. These parasites were more evident in the rectangular than in the triangular lung sections, with some of the parasitic forms being degenerate and mineralized. The

larger airways had less luminal exudate but occasional mucus accumulations.

The histologic changes were felt to be diagnostic for caprine lentiviral pneumonia, with the suspicion confirmed by the positive AGID for the CAEV virus. The prominence of the alveolar exudate seems peculiar to the caprine, is much less evident in ovine lentiviral pneumonia (OPP), and suggests increased permeability of alveolar lining cells and/or capillaries. The verminous pneumonia in this case was mild and an incidental finding. The typical gross lesions of subpleural emphysematous nodules were obscured by the severity of the interstitial pneumonia.

Potential etiologic rule-outs would include a variety of infectious agents (viruses, mycoplasms, parasites), inhaled dusts, hypersensitivity reactions, ingested toxicants (pyrrolizidine alkaloids), and other unknown or ill-defined agents.

AFIP Diagnoses. 1. Lung: Pneumonia, interstitial, chronic, diffuse, severe, with lymphoid proliferation, type II pneumocyte hyperplasia, intra-alveolar proteinaceous exudate and mild pleuritis, La Mancha, caprine.
2. Lung: Pneumonia, eosinophilic, subacute to chronic, multifocal, mild, with metastrongyle nematode adults, larvae, and eggs, etiology -- consistent with Muellerius sp.

Conference Note. Caprine arthritis-encephalitis virus (CAEV) is classified as a lentivirus and is biologically similar to ovine lentivirus. CAEV causes leukoencephalomyelitis in goats 1 to 4 months of age and chronic proliferative synovitis/arthritis, lymphocytic mastitis and pneumonia in adults. Virus replication occurs primarily in monocytes and macrophages and is linked to cell maturation, as found in the primate lentiviral diseases. Promonocytes and monocytes in the bone marrow are infected but viral replication is restricted and the virus remains in a proviral DNA form until maturation and differentiation into macrophages occurs. This mechanism allows infected cells to remain latently infected for long periods of time without host detection of the virus. Transmission of sheep and goat lentiviruses occurs both horizontally by inhalation of respiratory exudates containing virus and vertically by ingestion of milk containing infected macrophages.

The parasites in the lung are characterized by a smooth cuticle, polymyarian-coelomyarian musculature, an intestine lined by a few multinucleate cells, and lateral cords; these features are consistent with the suborder Metastongyloides. The larval parasites in the lungs have an undulating conical tail with a dorsal spine which is characteristic of the genus Muellerius. Muellerius capillaris has an indirect life cycle with a snail as

the intermediate host. In contrast, Dictyocaulus filaria has a direct life cycle.

Contributor. Animal Health Diagnostic Laboratory, P.O. Box 30076, Lansing, MI 48909-7576.

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International Veterinary Pathology Slide Bank
Laser disc frames #269, 2390, 3302, 3855, 4972-3, 10317.

Microslide 50

History. A flock was known to be seropositive (24% of flock in 1984; 65% in 1988) for maedi-visna, but the farmer had "cleaned up" by culling so that by 1989, he claimed none of the flock was seropositive. He did, however, admit to occasional cases of "pneumonia"; these sheep were culled also. This 3-year-old Texel cross-bred ewe was culled because she had reduced ability to keep up with other sheep when moved and had an increased respiratory rate. On auscultation, no abnormalities were detected other than an increased respiratory rate and louder than normal respiratory sounds without adventitious sounds.

Gross Pathology. Body condition was good and significant changes were confined to the lungs. The lungs were pink with a grey tinge and were large in volume for the size of ewe. They had a uniform pleural surface with sharp free borders. The lungs were heavier than normal at 0.78 kg (normal range for breed 0.4 to 0.6 Kg) and had an elastic, firm texture on palpation. On gross section, the parenchyma was firm and uniform without edema or congestive changes. No abscesses or areas of necrotic consolidation were found on multiple gross sectioning. The airways were unremarkable. No parasites were detected.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Lymphoid hyperplasia with chronic low grade interstitial pneumonitis and alveolar smooth muscle hypertrophy. Characteristic of maedi infection.

Histological section shows empty airways and absence of blood in vessels. The terminal bronchioles are moderately dilated and lined by single layered cuboidal epithelium or double-layered cuboidal epithelium without prominent goblet cells. Some airways and vessels are surrounded by loose, edematous connective tissue. The alveoli are angular in outline with variable degrees of thickening occasionally by interstitial and alveolar wall edema. The thickening is often the result of laminar or irregularly crescentric smooth muscle hypertrophy and hyperplasia. In many sites the intra-alveolar septa are edematous with sparse infiltrations by lymphocytes, macrophages and occasional neutrophil polymorphs. There are scattered alveolar macrophages containing hemosiderin. Scattered throughout the section, there are focal aggregates of lymphocytes and macrophages adjacent to both bronchioles and blood vessels. These foci often form germinal center-like structures. Within many alveolar lumens, there are small aggregates of hemosiderin-containing macrophages and distorted sloughed epithelial cells, the later probably of alveolar and terminal bronchiolar origin.

AFIP Diagnosis. Lung: Pneumonia, interstitial, chronic, diffuse, moderate, with lymphoid proliferation, smooth muscle hyperplasia, and alveolar histiocytosis, Texel cross, ovine.

Conference Note. Lentiviral diseases of sheep have been recognized worldwide and have been referred to as maedi/visna, ovine progressive pneumonia, and ovine lentiviral pneumonia. Clinical disease generally occurs in adult animals and is most commonly manifested as chronic interstitial pneumonia. Mastitis, arthritis, and neurologic manifestations are less common. There appears to be a genetic susceptibility to the development of clinical ovine lentiviral disease with the Texel, Border Leicester, and Finnish Landrace breeds being highly susceptible and the Suffolk, Hampshire, and Dorset breeds being relatively resistant.

In the examined sections, type II pneumocyte hyperplasia is not as prevalent as is usually the case in this condition. In some bronchioles, there are transmigrating inflammatory cells which may represent a response to a superimposed mycoplasmal or bacterial infection. Hemosiderin-laden macrophages are present in alveoli. There is multifocal bronchiolar squamous metaplasia.

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International Veterinary Pathology Slide Bank
Laser disc frames #2407-8, 4960-1, 10885.

Microslide 51

History. An 8-month-old female Beagle dog weighing 12 pounds was surrendered to the local animal shelter. It was given a distemper, adenovirus type II, parvovirus and parainfluenza virus combination vaccination and orally wormed with pyrantel pamoate on the day of entry. It was adopted about 10 days later. The dog developed a cough that was unresponsive to treatment. The animal died and was submitted for necropsy examination.

Gross Pathology. The dog was thin and mucous membranes were pale. About 35% of the lung parenchyma had foci of craniodorsal deep dark red patchy to coalescing consolidation. The stomach and jejunum had multifocal areas of mucosal hyperemia, affecting the mucosal ridges.

Laboratory Results. Bacterial cultures of liver and lung were negative. *Bacillus* sp., *Alpha streptococcus* and *E. coli* were isolated from the intestine. Adenovirus was detected in the intestine by negative contrast electron microscopy and virus isolation. Direct FA for canine distemper virus was positive on lung tissue and negative on brain tissue.

Contributor's Diagnosis and Comments. Lung: Bronchiolitis, necrotizing, subacute, diffuse, moderate, with amphophilic to basophilic intranuclear inclusions and eosinophilic intracytoplasmic inclusions compatible with canine adenovirus type II infection and canine distemper virus infection respectively, canine, Beagle.

Bronchial and bronchiolar epithelium was variably hyperplastic or, more frequently, vacuolated and necrotic. Bronchioles and alveoli contained mixed inflammatory cells, primarily neutrophils (many degenerative) and desquamated and necrotic epithelial cells. Bronchiolar and alveolar epithelial cells contained large amphophilic to basophilic intranuclear inclusions within swollen nuclei. Occasional nuclear inclusions contained a clear zone surrounded by swollen nuclear membrane (Cowdry type A). Some cells contained small ovoid eosinophilic intracytoplasmic inclusions, as well.

Canine adenovirus type II may become a respiratory pathogen causing bronchiolitis when canine distemper virus acts as an immunosuppressant. Adenovirus type II, however, can cause necrotizing bronchiolitis lesions in susceptible animals without coinfection with other viruses. This has limited the use of adenovirus type II as a vector for use in wildlife rabies vaccination programs.

AFIP Diagnosis. Lung: Pneumonia, bronchointerstitial, subacute, diffuse, moderate, with basophilic intranuclear inclusion bodies and eosinophilic intracytoplasmic inclusion bodies, Beagle, canine, etiologies -- consistent with adenovirus and morbillivirus.

Conference Note. Canine adenovirus type I causes infectious canine hepatitis. Canine adenovirus type II is usually associated with respiratory disease and plays a role in infectious tracheobronchitis ("kennel cough"), along with parainfluenza type 2, canine distemper and Bordetella bronchiseptica. Naturally occurring canine adenovirus type II pulmonary disease occurs most commonly in association with canine distemper virus infection or other immunosuppressive agents and is characterized by a necrotizing bronchiolitis with large basophilic intranuclear inclusions. Inclusions are most frequently seen in degenerate bronchiolar epithelial cells and less often in alveolar and bronchial epithelial cells and alveolar macrophages.

Small numbers of syncytial cells and eosinophilic intranuclear inclusions typical of canine distemper virus infection were present in some sections.

Contributor. Murray State University Breathitt Veterinary Center, P.O. Box 2000, Hopkinsville, KY 42241-2000.

References.

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International Veterinary Pathology Slide Bank

Laser disc frame #1248, 3052, 3367, 4155, 4678, 6664, 7515, 10122, 11762, 15512, 11758-9, 19945-6.

Microslide 52 and 53

History. This 8-week-old, unvaccinated wolf (Canis lupus)-dog hybrid pup was presented after three days of lethargy and diarrhea, and died within 24 hours despite treatment. During the past week, two of the five littermates had been found dead but were not necropsied.

Gross Pathology. The heart had extensive, irregular, multifocal to coalescing raised, pale, gray areas throughout the myocardium. The mucosae of the ileum, cecum and upper large intestine were reddened, and there were foci which had a granular surface covered by an adherent, cream-colored exudate. The lumen contained small amounts of blood admixed with mucus.

Laboratory Results. A fecal ELISA test was negative for parvovirus. The white blood cell count was 9600 with a left shift and absolute lymphopenia. The significant serum chemistry abnormalities included hypoproteinemia, hypoglobulinemia and an elevated ALT (182).

Contributor's Diagnoses and Comments. 1. Heart: Myocarditis, necrotizing, histiocytic, neutrophilic, multifocal to coalescing, severe, subacute, with intralesional bacilli.

2. Liver: Hepatitis, necrotizing, histiocytic, neutrophilic, multifocal, moderate, subacute, with intralesional bacilli.

3. Intestines: Enterocolitis, fibrinonecrotic, mild, subacute, with intralesional bacilli.

4. Intestines: Leiomyositis, necrotizing, multifocal, mild to severe, subacute, with intralesional bacilli.

5. Adrenal gland: Adenitis, necrotizing, suppurative, focal, moderate, acute, with intralesional bacilli.

6. Tyzzer's disease (Bacillus piliformis).

Necrotizing lesions were found in the heart, liver, adrenal gland and intestinal mucosa, muscularis mucosa and tunica muscularis. Clusters of pleomorphic, filamentous bacilli were demonstrated with Warthin-Starry and/or Steiner stains within the necrotic foci and the intact cells surrounding these lesions. In addition, there was severe, diffuse lymphoid depletion of the spleen and a mesenteric lymph node.

B. piliformis is a pleomorphic, gram-negative, spore-forming, obligate intracellular bacillus which is typically found within hepatic, intestinal epithelial, smooth muscle and myocardial cells of affected animals. The organism can be readily identified with silver impregnation and Giemsa stains, and stains faintly with Gram stains, periodic acid-Schiff reaction and hematoxylin-eosin. B. piliformis is difficult to culture and cannot be grown on cell-free media.

Tyzzer's disease is typically an epizootic, fatal infection of young animals. Stresses such as weaning, overcrowding, poor sanitation, shipping and corticosteroid administration are often associated with clinical disease. In the canine, Tyzzer's disease has been associated with canine distemper virus infection, and immunosuppression has been suspected in other cases. Myocarditis has been described in other species, but this is the first reported case of canine myocarditis due to B. piliformis.

AFIP Diagnosis. Heart: Myocarditis, histiocytic and neutrophilic, necrotizing, multifocal to coalescing, severe, with silver-positive bacilli, wolf (Canis lupus) -dog hybrid, canine.

Conference Note. Tyzzer's disease was first described in 1917 as a fatal epizootic diarrheal disease in Japanese waltzing mice and is caused by the pleomorphic gram-negative bacillus, Bacillus piliformis. The disease has been reported in a variety of laboratory, domestic, and exotic animals. It classically presents as an enteric, hepatic, and cardiac infection. Only a few cases have been reported in dogs and cats, usually in association with immunosuppression.

Contributor. Colorado State University, Department of Pathology, Fort Collins, CO 80523.

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International Veterinary Pathology Slide Bank
Laser disc frame #2456, 2934, 3086, 3090, 9305, 9412.

Microslide 54

History. This 30-month-old, Dunkin-Hartley, female guinea pig (Cavia porcellus), had a skin tumor which developed on the left side of the thorax and was surgically removed.

Gross Pathology. The mass was firm, appeared to be pigmented, and was approximately 2.5 x 2.5 x 2.5 cm in size.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Trichofolliculoma, skin, guinea pig.

Trichofolliculoma is a common skin tumor of guinea pigs. Some authors consider trichofolliculomas to be hamartomatous lesions which should be distinguished from trichoepitheliomas. Trichoepitheliomas contain "horn cysts" composed of keratinized material and islands of basophilic cells which resemble hair papillae, but contain no hair. Trichofolliculomas usually contain a central cyst with keratinized material that represents a large distorted primary hair follicle. The epithelial cells surrounding the cyst are contiguous with smaller secondary well-developed hair follicles which contain hair.

AFIP Diagnosis. Haired skin: Trichofolliculoma, Dunkin-Hartley guinea pig, rodent.

Conference Note. Trichofolliculomas are reported to be the most common skin tumor of guinea pigs. They also occur in humans and rarely in dogs and cats. A sebaceous trichofolliculoma variant is recognized in humans and occurs in areas rich in sebaceous glands, such as the nose. Other follicular tumors include trichoepithelioma, tricholemmoma, intracutaneous cornifying epithelioma, pilomatrixoma, and malignant hair follicle tumor. A unique feature of trichofolliculoma is the pattern of arborizing secondary follicular structures.

Contributor. The M. S. Hershey Medical Center, The Pennsylvania State University, Department of Comparative Medicine, P.O. Box 850, 500 University Drive, Hershey, PA 17033.

References.

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Microslide 55

History. This fuzzy rat was retired as a breeder at 11 months of age and was euthanized 4 months later because of weight loss and inactivity.

Gross Pathology. The left kidney (submitted) is enlarged with an irregular capsular surface. The right kidney is slightly reduced in size, also with an irregular surface. Combined organ weight is 7.608 grams.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Kidney: Chronic progressive nephrosis, diffuse, severe.

The fuzzy rat is derived from the Wistar-Firth rat. The only inbred strain of fuzzy rats in this country is maintained at Wright-Patterson Air Force Base, Ohio. The animal in this case report was from a longevity study on this strain.

The features of chronic progressive nephrosis observed in this case are tubular dilatation with proteinaceous casts, basement membrane thickening, variable stages of interstitial inflammation, and occasional hyperplastic and/or hypertrophic tubular and glomerular changes.

The histologic features of chronic progressive nephrosis in fuzzy rats does not differ from the same condition that is more commonly reported in Fischer 344 or Sprague-Dawley rats. The main difference in the inbred fuzzy is that the maximuum lifespan of male rats is 17 months. The primary cause of these animals' deaths is renal failure (severe anemia- hematocrit down to 15%; and severe azotemia - BUN up to 380 mg/dl and creatinine up to 3 mg/dl; with the nephrotic syndrome). Female fuuzzy rats of the same age are clinically normal.

AFIP Diagnosis. Kidney: Nephropathy, chronic, diffuse, severe, WF/PmWp-fz rat, rodent.

Conference Note. Chronic progressive nephropathy is the most common renal disease of aged laboratory rats. Albino strains are predisposed. A high incidence is seen in Fischer 344, Wistar, and Marshall rats. Males have a higher incidence than females. Castrated males are less suceptible while testosterone administration accelerates lesion development. Glomerular damage appears to be the initial lesion in this disease although the initiating events are not clearly understood. In people, it has been postulated that protein-rich diets induce glomerular hyperfiltration and hyperperfusion resulting in age-associated functional and structural deterioration. Reduction in caloric and protein content of rats' diets has correlated with a decrease in severity of the disease.

Glomerular lesions vary from mild basement membrane thickening with mesangial proliferation to sclerosis with synechia formation. The amount of protein in the urine increases as the disease progresses.

The fuzzy rat is an inbred strain of the Wistar Furth rat that has a mutant gene, designated *fz*. Homozygous *fz/fz* rats are born with curled or twisted vibrissae and hair that becomes short and broken by two months of age, giving them a fuzzy appearance.

By six months of age, the rats are usually hairless. Histologically, the hair follicles are poorly developed, often cystic, and contain keratinous debris.

Contributor. Toxic Hazards Division, Armstrong Laboratories (AL/OET), Bldg 79; Area B, Wright-Patterson Air Force Base, OH 45433.

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International Veterinary Pathology Slide Bank
Laser disc frame #10937.

Microslide 56

History. At 5 to 7 weeks of age, several pigs (both male and female) in a litter of Large White pigs developed signs of ataxia, with hindquarter swaying and a wide-based stance. When walking, they fell sideways and backwards. Over a 3-week period, affected pigs lost the ability to stand, adopting sternal and finally lateral recumbency. Muscle strength was maintained, and the pigs remained alert and continued to eat and drink. This case was a 9 week old piglet of unknown sex.

Gross Pathology. No significant changes.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Cerebellar abiotrophy. Etiology: Heritable disorder (suspected autosomal recessive).

Lesions associated with this postnatal syndrome of cerebellar disease are confined to the cerebellar cortex and the white matter of the cerebellar folia. The most consistent findings are of numerous fusiform to spheroidal segmental swellings of Purkinje axons ('torpedoes', 'spheroids') in the granular layer of the cerebellum, and smaller axonal swellings, Wallerian-type axonal degeneration and gliosis in the white matter of the cerebellar folia. In pigs surviving for several months, there is also segmental loss of Purkinje cells.

Cerebellar abiotrophy in Large White pigs of Canadian Yorkshire bloodlines has been recognized in Australia since the

early 1980's. It has been reported in Yorkshire pigs in New York State (Gardner, 1972).

AFIP Diagnosis. Cerebellum: Axonal swelling, multifocal, moderate, granular cell layer, with axonal degeneration and gliosis, folial white matter, Large White pig, porcine.

Conference Note. Abiotrophy is defined as the pathologic premature degeneration of neurons and is generally limited to lesions presumed to be caused by inborn metabolic deficits. In contrast, atrophy refers to degeneration caused by an exogenous insult. Hypoplasia indicates defective or incomplete development.

Nervous system abiotrophies can be divided into four groups based on anatomic location: motor neuron degenerative diseases, multisystemic degenerations, cerebellar degenerations, and miscellaneous degenerations. Of these, cerebellar abiotrophy is the most common in domestic animals and has been reported in pigs (Yorkshire), sheep (Merino), dogs (Gordon Setters, Airedales, German Shepherd Dogs, Rough Coated Collies, Kerry Blue terriers, and others), horses (Arabian), and cattle (Holstein, Angus, and Charolais). The condition is presumed to be caused by an autosomal recessive trait.

In cerebllar abiotrophy, the Purkinje cells are most susceptible to degeneration. Secondary depletion of granule cells may also occur. Other cortical layers are normal.

Causes of cerebellar hypoplasia include hog cholera vaccination, feline panleucopenia and bovine viral diarrhea. The granular cell layer is the primary area of the brain affected in these diseases.

Contributor. Regional Veterinary Laboratory, Wollongbar NSW 2477, Australia.

References.

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International Veterinary Pathology Slide Bank
Laser disc frame #9707, 11119, 12754.

Microslide 57

History. This yearling Charolais heifer was found dead without premonitory signs. The animal was housed in a small feed lot. The owner was in the process of increasing the "concentrate" in the ration.

Gross Pathology. Gross alterations were limited to failure of the rumen mucosa to slough in spite of mild autolysis in other organs. The rumen mucosa appeared slightly granular and was pale yellow.

Laboratory Results. The pH of the rumen contents was <5.

Contributor's Diagnosis and Comments. Acute diffuse necrotizing rumenitis due to rumen acidosis, rumen, ox.

Histomorphology of the rumen lesion is typical of that described for chemical rumenitis (ruminal acidosis, carbohydrate overload). The cells of the upper layers of the epithelium (mainly stratum granulosum) are severely vacuolated. Neutrophils are present in the epithelium within the epithelial cell vacuoles and vesicles formed by separation of cell layers and disruption of cell membrane. Multifocally, areas of degeneration and vacuolation involving the basal layers of the epithelium are evident. Neutrophilic infiltrates and mild hemorrhage accompany these basal foci. The lamina propria/submucosa of the rumen have mild infiltrates of lymphoid cells. Propria/submucosal capillaries are congested.

The pathogenesis of ruminal acidosis is as follows: Ingestion of feeds containing high concentrations of readily fermentable carbohydrates results in proliferation of microorganisms capable of using that substrate. These microorganisms, mainly streptococci, produce lactic acid as a product of fermentation causing ruminal pH to fall. The normal flora, which is sensitive to pH changes, is killed after the pH drops below 5. At pH 5, lactobacilli proliferate and form large amounts of lactic acid. When ruminal pH becomes acid, rumen atony ensues and salivary secretion decreases, reducing the buffering normally provided by the saliva. Osmotic pressure increases in the rumen by virtue of increased lacate concentration, resulting in hemoconcentration and circulatory shock. Absorption of lactic acid from the rumen results in marked acidosis. Both contribute to the death of the animal.

AFIP Diagnoses. 1. Rumen: Rumenitis, subacute, diffuse, moderate, with intraepithelial microabcesses.
2. Rumen: Rumenitis, granulomatous, multifocal, mild, with fungal hyphae, condition- consistent with zygomycosis.

Conference Note. Ruminal acidosis with acute rumenitis is often associated with excessive carbohydrate ingestion. While the condition is most commonly seen in intensive beef or dairy production herds, it can occur in sheep, goats, and exotic ruminants. Brahman cattle may be more susceptible than Angus or Hereford to development of ruminal acidosis and its sequelae, while Holsteins appear to be more resistant.

The amount of feed required to induce ruminal acidosis depends on the type of feedstuff. Grains are more commonly associated with the syndrome but other feeds high in carbohydrates, including fruit crops, root crops, molasses and grain meals may also induce the condition. The increased proportion of dietary carbohydrate appears to be more important than the absolute amount ingested.

Ruminal acidosis is initially due to an increase in dissociation of volatile fatty acids which causes a decrease in rumen motility and the death of normal ruminal flora. This initial lowering of ruminal pH causes a rapid proliferation of Streptococcus bovis which produces lactic acid and other organic acids which further decrease the rumen pH. When the pH falls below 4.5, the growth of S. bovis is inhibited and the growth of Lactobacillus organisms is promoted. D-lactic acid is primarily responsible for the ensuing systemic acidosis because it is poorly metabolized. Acute chemical rumenitis develops due to the low pH.

Common sequelae to ruminal acidosis include secondary bacterial and fungal infections, hepatic abscesses, venal caval syndrome, abomasal and duodenal ulcers, polioencephalomalacia, renal cortical necrosis, and laminitis. Fusobacterium necrophorum is reported to be the most common secondary invader.

Fungal hyphae are present multifocally within epithelium and propria/submucosa of some sections. Hyphae range from 5 to 20 microns in diameter, are infrequently septate, and branch at right angles; these features are consistent with a mucoraceous zygomycete. Zygomycetes are common opportunistic invaders associated with this condition in cattle.

Contributor. Veterinary Diagnostic Center, University of Nebraska-Lincoln, Lincoln, NE 68583-0907.

References.

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International Veterinary Pathology Slide Bank
Laser disc frame #3319-20, 5728-9.

Microslide 58

History. This animal was one of a herd of captive North American elk which were depopulated after several tuberculin skin test reactors were identified. The animals were euthanitized, necropsied, and tissues were collected by a USDA Veterinary Medical Officer and submitted to the National Veterinary Services Laboratory (NVSL).

Gross Pathology. Multiple pulmonary abscesses and granulomas were noted in this animal.

Laboratory Results. Mycobacterium bovis was isolated from tissues submitted to NVSL.

Contributor's Diagnosis and Comments. Multiple pulmonary pyogranulomas to caseocalcareous granulomas with intralesional acid-fast bacilli.

Histopathologic examination of lung from a mature elk revealed multiple pyogranulomas and caseocalcareous granulomas with intralesional acid-fast bacilli. The pulmonary granulomas contained large, irregular central accumulations of granular, eosinophilic debris with scattered areas of mineralization intermixed with and bordered by polymorphonuclear leukocytes, macrophages, and occasional giant cells. There was a regionally variable lymphoplasmacytic infiltrate on the margins and usually a thick, collagenous connective tissue capsule enclosed the granulomas. Adjacent bronchioles sometimes contained clumps of caseonecrotic debris. The overlying pleura was thickened and had fibrous tags. When an acid-fast stain was applied, rare acid-fast bacilli were identified within the granulomas.

The State-Federal Bovine Tuberculosis Eradication Program has nearly eliminated Mycobacterium bovis from the cattle population of the United States. Most newly identified M. bovis positive herds have been traced back to commingling of domestically produced animals with imported Mexican steers.

There have been several recent outbreaks in captive elk herds in the United States and Canada. These infected elk represent a serious potential for the zoonotic spread of bovine tuberculosis to humans, domestic livestock, and nondomestic ruminants.

The characteristics of the gross lesions in elk and other cervids are many times not typical of the lesions found in affected bovine animals. Lesions found in this herd of elk were

often suppurative or liquefied, or resembled lesions of caseous lymphadenitis. The most common sites for gross lesions were the lungs and retropharyngeal lymph nodes.

The high incidence of pulmonary lesions as well as the abscess-like characteristic of the lesions have lead to public health concerns, especially for exposed slaughterhouse, meat inspection and rendering facility workers. Canadian meat inspection personnel are now provided with protective equipment and are encouraged to follow special safety precautions when working with tuberculin reactor cervids. These measures were taken after several slaughterhouse workers became skin test positive after contact with culture positive cervids.

AFIP Diagnosis. Lung: Granulomas, caseocalcareous, multiple, with pyogranulomas, elk (Cervus elaphus), artiodactyl.

Conference Note. Although lesions in cervid M. bovis infection may include caseous necrosis, mineralization, epithelioid macrophages, giant cells, and fibrosis as seen in bovine cases, significant differences are often present. The centers of granulomas frequently contain numerous neutrophils. Mineralization is generally not as extensive as is found in bovine cases, and it occurs around the periphery of the necrotic centers of the lesions. Giant cells are less numerous. Finally, lesions may contain large numbers of acid-fast bacilli while in cattle bacilli are rare.

Mycobacterium bovis is most commonly spread via inhalation or ingestion. Prior to routine pasteurization of milk, the ingestion of contaminated milk was a common mechanism of human infection. With the presence of liquified pulmonary lesions that contain numerous organisms, the potential for aerosol spread in slaughterhouses is enhanced.

Gross lesions of mycobacteriosis in elk must be differentiated from other causes of pulmonary abscesses and granulomas, such as Actinomyces pyogenes and Yersinia pseudotuberculosis, fluke migration tracts, lungworms, and Coccidioides immitis infection.

Contributor. USDA, FSIS, Science, PSD, Pathology Branch, Bldg. 318-C BARC-East, 10300 Baltimore Avenue, Beltsville, MD 20705.

References.

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elaphus nelsoni) in Colorado. J Vet Diagn Invest 4:428-433, 1992.

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International Veterinary Pathology Slide Bank
Laser disc frame# 11885-6, 2463, 4091-2, 11708, 13147.

Microslide 59

History. Carcass condemned at slaughter for multiple abscesses. Formalized sections of the masseter muscle, diaphragm, and shoulder muscles submitted for evaluation.

Gross Pathology. See above.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Myositis, multifocal, diffuse, eosinophilic, granulomatous, sarcocyst.

Eosinophilic myositis is a relatively rare condition primarily seen in abattoir carcasses. Although the exact cause is unknown, there is good evidence to suggest that it is caused by degenerating Sarcocystis sp. tissue cysts. Sarcocyst remnants have been seen in the centers of lesions and Sarcocystis specific IgE has been found to be associated with degranulated eosinophils. It is the masses of eosinophils that make the muscle fibers green. Both acute and chronic inflammation exist in the same section, and in some sections there is a granulomatous response.

AFIP Diagnosis. Skeletal muscle: Myositis, eosinophilic, multifocal, coalescing, moderate, with eosinophilic granulomas and protozoal cysts, Hereford cross, bovine, etiology- consistent with Sarcocystis sp.

Conference Note. Although the pathogenesis of eosinophilic myositis (EM) is unknown, sarcocyst specific type-I hypersensitivity may be involved. Sarcocystis sp. organisms have been identified in the centers of EM lesions accompanied by degranulated eosinophils and mast cells. Sarcocystis cruzi specific IgE and IgG have been demonstrated in EM lesions and in serum of EM-affected cattle.

Sarcocystis infection in cattle is common worldwide. Cattle serve as intermediate hosts of S. cruzi, S. hirsuta, and S. hominis while the respective definitive hosts are dogs, cats, and humans. Intermediate hosts become infected by ingestion of

sporocysts usually via food contaminated with feces. Asexual replication occurs in the intermediate host initially in vascular endothelial cells and then in myocytes of striated muscle. Sexual replication occurs in the intestinal epithelial cells of the definitive host after ingestion of infected muscle.

Contributor. Animal Health Centre, P.O. Box 100, Abbotsford, B.C., Canada V2S 4N8.

References.

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International Veterinary Pathology Slide Bank

Laser disc frame #2533, 9141, 11604, 11607, 15217-9, 18969, 22145.

Microslide 60

History. Cat arrived on 4 March to be used for toxicity study. Palpation during a physical examination on 5 March revealed the presence of small masses on the abdomen. By 17 March the masses increased in size to become confluent along both sides of the ventral abdomen. Each mass varied within a range of 3 to 5 cm in diameter. Palpation of the masses did not elicit any sign of discomfort from the cat. On 18 March the masses were accompanied by marked edema. The animal was not suitable for use on study and was euthanatized.

Gross Pathology. Sectioning of the masses revealed subcutaneous and periglandular edema around discrete pale brown-red masses of apparent mammary tissue. No secretions exuded from the sectioned surfaces of the gland.

The uterus was normal for a non-gravid animal. The pituitary and ovaries appeared normal.

Laboratory Results. Radiographs of the masses revealed them to be a tissue of relatively uniform density.

Contributor's Diagnosis and Comments. Mammary fibroepithelial hyperplasia (feline mammary hypertrophy). Etiology: Unknown, hormonal imbalance.

This lesion is seen infrequently. Various authors state that the lesion is presumed to be the result of hormonal imbalance occurring typically in young nonpregnant female cats. Histologic evaluation of the ovaries, uterus, and pituitary revealed no morphologic abnormalities in this case.

AFIP Diagnosis. Mammary gland: Fibroepithelial hyperplasia, diffuse, moderate, Domestic Shorthair, feline.

Conference Note. Fibroepithelial hyperplasia has been referred to as fibroadenomatous hyperplasia, feline mammary hypertrophy, fibroadenoma, and total fibroadenomatous change. The exact cause is unknown but a hormonal basis is suspected. It occurs primarily in young female cats but has also been reported in neutered male and female cats following prolonged treatment with progesterone-like compounds such as megestrol acetate. Progesterone hormone receptors have been identified in the hyperplastic tissue, but not estrogen receptors. Uteri of affected queens often show changes consistent with progesterone influence and ovaries contain large corpora lutea and follicles of normal types and sizes.

Administration of megestrol acetate has also been associated with development of diabetes mellitus, pyometra, uterine adenocarcinoma, and adrenocortical suppression. A veno-occlusive disease of snow leopards and cheetahs may be associated with phytoestrogen administration as well as a variety of other factors.

Feline mammary fibroepithelial hyperplasia resembles fibroadenomas and fibrocystic mastopathies of women. The condition has also been reported rarely in dogs.

Contributor. The Upjohn Company, 301 Henrietta Street, Kalamazoo, MI 49007.

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International Veterinary Pathology Slide Bank
Laser disc frame #6388-9.

Microslide 61

History. This 5-year-old German Shepherd Dog had a 5 month period of anorexia, vomition and weight loss. Later, it developed paresis of the hind limbs. The dog was treated for ehrlichiosis and urinary infection. Hematology and urinalysis were performed as well as radiography of the thorax and pelvic region. Radiography demonstrated spondylosis between T10 - T13 and a suspected aneurysm of the thoracic aorta. In a barium study, esophageal dilation was demonstrated in the region caudal to the heart. The dog was euthanatized on the owners request.

Gross Pathology. Esophagus: Multiple nodules ranging from 1-4 cm in diameter. Most nodules had a fistula from which a nematode protruded into the esophageal lumen. Scarring and multiple aneurysms in the thoracic aorta were seen. Spondylosis of T10-T13 area was present.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Esophagus: Esophagitis, pyogranulomatous, multifocal, severe, with various sections of different levels of Spirocerca lupi.

The adult worms have a thick cuticle surrounding a muscle wall. Numerous ova within the gravid uterus are seen. The eggs are small (5 x 11 to 15 x 37 mm), thick-shelled, flattened and ovoid with parallel sides, and are embryonated before they are discharged through the genital pore.

Myxofibrous nodules, formed of reactive pleomorphic fibroblasts with hyperchromatic nuclei, are seen next to nodules containing the parasites . This may be early evidence of mesenchymal neoplasia formation and is not seen in all sections.

AFIP Diagnosis. Esophagus: Esophagitis, nodular, granulomatous and eosinophilic, chronic, moderate, with spirurid nematodes, German Shepherd Dog, canine.

Conference Note. The genus Spirocerca contains two species: S. arctica, found in Northern Russia, and S. lupi, found in

tropical and subtropical climates including areas of the United States. Spirocerca lupi has been reported in dogs, foxes, wolves, jackals, coyotes, wild and domestic felids, goats, and donkeys. The life cycle is indirect. Coprophagous beetles are intermediate hosts, and paratenic hosts include domestic and wild birds, rodents and other small mammals, reptiles and amphibians. Infection occurs when either intermediate or paratenic hosts are ingested. Infective third-stage larvae are released in the stomach and penetrate the gastric wall. Larvae migrate to a branch of the gastric or gastroepiploic artery, then to the celiac artery, and finally to the thoracic aorta where they develop within the adventitia for two to four months. Finally, larvae migrate to the adjacent esophagus and develop into adults in the submucosa. Adults penetrate the esophageal mucosa in order to deposit larvated eggs in the lumen.

Lesions associated with S. lupi infection are most commonly seen in the esophagus, stomach, and aorta. Less frequently, urinary bladder, kidneys, and subcutaneous tissues are affected due to aberrant larval migration. Clinical signs are often minimal but may include persistent vomiting and sudden death due to rupture of an aortic aneurysm. Associated conditions include ankylosing spondylosis of thoracic vertebrae and hypertrophic pulmonary osteopathy.

Spirocerca lupi has been associated with the development of esophageal sarcomas. Other parasites associated with neoplasms include Cysticercus fasciolaris of rats associated with hepatic sarcomas, Schistosoma haemotobium of humans associated with urinary bladder carcinoma, and Opisthorchis sp. and Clonorchis sinensis in humans and cats respectively associated with biliary carcinoma.

Contributor. Department of Veterinary Pathology, Kimron Veterinary Institute, Beit-Dagan, 52050, Israel.

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International Veterinary Pathology Slide Bank

Laser disc frame #21464, 23871, 2488-9, 3458, 4663-5, 10561-2, 20198.

Microslide 62

History. Tissue was from a 4-week-old female crossbred pig.

Gross Pathology. Pig was covered by a greasy and yellow-brown exudate.

Laboratory Results. Staphylococcus hyicus was isolated from the skin and superficial lymph nodes.

Contributor's Diagnosis and Comments. Intraepidermal pustular dermatitis. Etiology: Staphylococcus hyicus.

In the skin sections submitted, the epidermis is hyperplastic with elongation of the rete ridges. There are several intraepidermal or subcorneal pustules. Hyperkeratosis is also present. The superficial dermis is edematous with dilated capillaries and mononuclear perivascular infiltrate.

Exudative epidermitis ("greasy pig disease") is still a common problem in suckling or early-weaned pigs. In neonatal pigs, the skin lesions are often generalized and characterized by the presence of a malodorous, greasy, dirty yellow-brown exudate. In older pigs, skin lesions are more localized.

AFIP Diagnosis. Haired skin: Dermatitis, subacute to chronic, diffuse, moderate, with intraepidermal microabscesses, orthokeratotic and parakeratotic hyperkeratosis, and intracorneal fungal hyphae, crossbred pig, porcine.

Conference Note. The fungal hyphae are interpreted to be secondary invaders. Exudative epidermitis is an acute, generalized, vesicopustular dermatitis of young pigs caused by Staphylococcus hyicus. It occurs most commonly in pigs one to seven weeks of age with no sex or breed predilection. There is no seasonal pattern to the disease, and it often occurs despite good hygiene and management practices. The cause may be a toxin produced by S. hyicus, as bacteria-free culture supernatants have been shown to reproduce the disease when injected subcutaneously into pigs. Staphylococcal "scalded skin syndrome" is a similar condition of humans in which certain strains of staphylococci elaborate exfoliative toxins that produce subcorneal cleavage in the epidermis and oral mucosa.

Differential diagnosis includes dermatosis vegetans, swinepox, dermatophytosis, and pityriasis rosea.

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International Veterinary Pathology Slide Bank

Laser disc frame #1721-2, 1739-40, 4436-43.

Microslide 63

History. A 12-month-old steer was inoculated intravenously with a lethal dose of alcelaphine herpesvirus-1. Two weeks post-infection the animal was severely clinically ill, with high fever, conjunctivitis, corneal edema, rhinitis, and generalized lymphadenopathy.

Gross Pathology. There was a severe, ulcerative, necrotizing rhinitis affecting the stratified squamous epithelium of the muzzle and nasal cavity. Conjunctiva was multifocally eroded and covered by a mucopurulent exudate. There were numerous oral erosions as well as blunting of buccal papillae. Lymphoid tissue throughout the carcass was markedly expanded.

Laboratory Results. None.

Contributor's Diagnoses and Comments. 1. Stomatitis, ulcerative, necrotizing, with lichenoid lymphoid cell infiltrate, severe, subacute, buccal mucosa.

2. Rhinitis, ulcerative, necrotizing, with lichenoid lymphoid cell infiltrate, severe, subacute, nasal mucosa.

3. Vasculitis, transmural, lymphoid, moderate, subacute, buccal mucosa, nasal mucosa.

Etiology: Alcelaphine herpesvirus-1.

Malignant catarrhal fever (MCF) is a severe, multisystemic disease of cattle with low morbidity and high mortality.

There are two forms of MCF. One, caused by alcelaphine herpesvirus-1, occurs in cattle exposed to calving wildebeest. This form of the disease, referred to as "wildebeest-derived" MCF, occurs primarily in Africa but is also seen in zoos and game parks around the world, whenever cattle are housed in proximity to wildebeest. The second form of MCF occurs when cattle are commingled with lambing sheep. This form of the disease is caused by a less well-characterized virus and is known as "sheep-associated" MCF. Both forms of the disease are clinically and pathologically identical.

The pathogenesis of MCF is complicated. It is thought that the virus infects and transforms a subset of lymphocytes which

then undergo a clonal expansion and attack host tissue. Consequently, the lesions have features of both lymphoma and graft-versus-host disease. A very characteristic histologic feature is generalized vasculitis.

AFIP Diagnoses. 1. Nasal mucosa: Rhinitis, ulcerative, lymphocytic and lymphoblastic, diffuse, severe, with vasculitis, Hereford, bovine.
2. Buccal mucosa: Stomatitis, lymphocytic and lymphoblastic, diffuse, moderate, with ulceration and vasculitis.
3. Salivary duct: Sialodochitis, lymphocytic and lymphoblastic, diffuse, moderate.

Conference Note. Malignant catarrhal fever is a disease that affects domestic cattle and a wide range of wild ruminants, including most species of deer, bison, cape buffalo, and greater kudu. The wildebeest-associated form of the disease is caused by a cell-associated lymphotropic herpesvirus, provisionally assigned to the Gammaherpesvirinae subfamily, and designated strain alcelaphine herpesvirus-1. The wildebeest (Connochaetes taurinus) carries the virus as a latent infection. Wildebeest calves, which become infected at 2-3 months of age, are the main source of infection for cattle. Route of infection is by direct contact with nasal or ocular secretions or via aerosols. Virus entry is through the upper respiratory tract mucosa or tonsils. Primary viral replication occurs within small and medium-sized lymphocytes.

Characteristic lesions include lymphoproliferation of T-lymphocytes and lymphoblasts, vasculitis, tissue necrosis, and erosions and ulcerations of mucosal and cutaneous tissues. The exact pathogenesis of the lesions is not well-characterized but is probably immune-mediated. Latent infection and transformation of large granular lymphocytes by the virus may result in derepression of T-lymphocyte replication, permitting lymphoproliferation. The tissue necrosis may result from deranged natural-killer cell activity.

Differential diagnosis includes bovine viral diarrhea, infectious bovine rhinotracheitis, bluetongue, and Jembrana disease of Bali cattle.

Contributor. Foreign Animal Disease Diagnostic Laboratory, NVSL-VS-APHIS-USDA, P.O. Box 848, Greenport, NY 11944.

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Laser disc frame #8322, 8364-7, 8371-3, 12447-54, 12804, 13140-1, 18971-3, 21107-10.

Microslide 64

History. An 18 month old, adult female White Leghorn chicken was experimentally inoculated in the left caudal thoracic air sac with $10^{5.7}$ median embryo infective doses of highly pathogenic avian influenza (HPAI) virus type A/Chicken/Pennsylvania/1370/1983 (H5N2). The bird was very depressed with ruffled feathers at 48 hours postinoculation. At 72 hours, there was moderate facial edema, especially apparent in comb and wattles. She was euthanized by cervical dislocation.

Gross Pathology. Postmortem findings included subcutaneous facial edema, generalized dehydration, and petechiation over visceral surfaces.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Subcutaneous thrombosis and hemorrhage, multifocal, moderate to severe, comb and wattles.

Etiology: Highly pathogenic avian influenza virus. A/Chicken/Pennsylvania/1370/1983 (subtype H5N2).

The avian influenza viruses are type A influenza viruses. Classification is by subtype, based on the envelope antigens hemagglutinin (H) and neuraminidase (N). Different subtypes may cause very different clinical disease. Those which cause high mortality are referred too as "highly pathogenic" avian influenza (HPAI).

In 1983, there was an extensive outbreak of HPAI in the eastern United States. This outbreak originated in Pennsylvania and is thought to have arisen as a result of some very simple nucleic acid mutations which caused a mildly pathogenic strain to become very virulent. Eradication efforts took the lives of 17 million birds and cost U.S. taxpayers 63 million dollars.

Clinical features seen with this subtype of HPAI include depression, comb and wattle edema, markedly decreased egg production, and sudden death. At postmortem, there may be widespread superficial edema, which is most evident in the head and neck region. Hemorrhages may be found on many surfaces.

Generally, birds are very dehydrated with darkened pectoral muscles. Histologically, blood vessels of comb and wattles are distorted and degenerating. Late in the disease, inflammation may be widespread, especially affecting heart and external ocular muscles.

Immunohistochemical studies indicate that HPAI H5N2 has an affinity for capillary endothelium throughout the body. In some tissues, virus spills out of infected endothelium to specifically infect parenchymal cells, especially muscle, brain and kidney.

AFIP Diagnosis. Comb and wattles: Edema, diffuse, severe, with congestion, hemorrhage, and fibrin thrombi, white leghorn chicken, avian.

Conference Note. Different avian influenza strains can produce a wide variety of clinical signs and disease courses. Different presentations are due to differences in tissue tropism of various virus strains. Most strains are non-pathogenic unless combined with concurrent infections. The virus in this case was highly virulent and appeared to be endotheliotropic.

The viral subtypes of avian influenza are classified according to their hemagglutinin (H) and neuraminidase (N) antigens. Fourteen H and nine N subtypes have been identified in birds. Highly virulent strains usually belong to the subtype H5 or H7. The isolates are further coded by the following formula: type (A or B)/species/geographic location/number of isolate/year(H and N subtypes).

While domestic birds including chickens and turkeys are most susceptible to disease, disease can also occur in pheasants, quail, guinea fowl and partridges. Wild ducks and geese seem to be refractory to disease and are regarded as reservoirs.

Contributor. Foreign Animal Disease Diagnostic Laboratory, NVSL-VS-APHIS-USDA, P.O. Box 848, Greenport, NY 11944.

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International Veterinary Pathology Slide Bank

Laser disc frame #8112, 12513-23, 14603.

Microslide 65

History. A live, 30-week-old, ringneck pheasant was submitted for diagnosis. The submitted bird was listless. It's walk was stiff with little neck movement. Over 3 to 4 hours it became very docile. Fifteen 30-week-old birds were found dead in a pen of forty.

Gross Pathology. Moderate hepatomegaly and splenomegaly seen at necropsy.

Laboratory Results. Erysipelothrix rhusiopathiae was isolated in pure culture from liver.

Contributor's Diagnoses and Comments. 1. Hepatitis, diffuse, peracute, with intracytoplasmic bacteria, endothelium, and Kupffer cells.
2. Bacteremia, acute.

Liver, endothelium, Kupffer cells, intravascular leukocytes, and rarely hepatocytes, contain densely packed, sometimes granular, basophilic cytoplasmic material. Cytomegaly, and cellular degeneration result from the cytoplasmic accumulations. Degenerate cells are vacuolated, detached from basal lamina, and occasionally lytic. Lilies gram stain demonstrated the material to be gram-positive and it is consistent with bacterial colonies.

This case demonstrates the minimal inflammatory response present in the peracute stages of infectious processes. Other birds dying from the disease had similar hepatic changes, and the possibility of an insufficient immune response exists. Erysipelothrix infection is zoonotic and the pathologist in this case developed localized cellulitis and lymphangitis after being scratched by the bird. The disease in man is termed erysipeloid and local physicians were unfamiliar with this disease. Erysipelas in human medicine refers to cellulitis and lymphadenitis caused by beta hemolytic group A Streptococci and resembles erysipeloid clinically. E. rhusiopathiae was isolated from the pathologist's skin lesion.

AFIP Diagnosis. Liver: Hepatitis, peracute, diffuse, moderate, with intracellular bacteria, ringneck pheasant, avian.

Conference Note. Erysipelothrix rhusiopathiae infects a wide range of domestic and wild animals causing a variety of disease syndromes including acute septicemia, skin lesions such as "diamond skin disease" in swine, vegetative endocarditis, and arthritis. Transmission of the organism is by ingestion or wound infection. Wild birds present with either non-specific acute illness or sudden death. Lesions in pheasants are typically suggestive of septicemia, but are not pathognomonic; diagnosis depends on culturing the organism.

The virulence of different strains of Erysipelothrix rhusiopathiae is in part due to the amount of neuraminidase produced. Bacterial neuraminidases act by removing N-acetylneuraminic acid (NANA) from a number of substrates resulting in anemia, leukopenia, and thrombocytopenia.

Contributor. North Dakota Veterinary Diagnostic Laboratory, Van Es Hall, NDSU, Fargo, ND 58105.

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Microslide 66

History. An increased mortality in the broiler breeders was noted after placement in the breeding house.

Gross Pathology. Large multifocal to coalescing light tan masses of variable size were evident within the liver, spleen and ovaries of many of the birds.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Moderately severe to severe, intrasinusoidal, periportal and centrilobular hepatic myelocytoma (avian myelocytomatosis; avian leukosis/sarcoma viral complex).

The section was taken from an enlarged liver. Moderately severe to severe multifocal to coalescing accumulations of round to slightly ovoid cells were evident within sinusoidal spaces, periportal and centrilobular sites. Periportal and centrilobular areas were most severely affected. The cells contained numerous large eosinophilic cytoplasmic granules and displayed a mild degree of nuclear and cellular pleomorphism. Nuclei were round to slightly ovoid, vesicular and contained occasional prominent nucleoli. Three to four mitotic figures per high power field were also noted. Marked, multifocal cellular distension of sinusoidal spaces and secondary atrophy and obliteration of

hepatic cords were also evident. A moderate degree of vascular congestion was also noted.

The gross and microscopic postmortem findings in this case are consistent with avian myelocytomatosis. Avian myelocytomatosis is considered part of the avian leukosis/sarcoma group of diseases. The avian leukosis/sarcoma viruses (avian type C oncoviruses) are grouped together due to sharing of important physical and chemical characteristics and a common group specific antigen. The virus contains an electron dense core, approximately 35-45 nm in diameter, an intermediate membrane and an outer membrane. The overall diameter of the viral particle is approximately 80-120 nm. Myelocytomatosis often involves the periosteum of bone in addition to visceral organs, including liver and spleen. The neoplastic cells characteristically are large, relatively uniform in size and shape, and contain numerous eosinophilic cytoplasmic granules. In this case, the neoplasm was multicentric with liver, spleen and ovaries affected in many of the birds.

AFIP Diagnosis. Liver: Myelocytomatosis, chicken, avian.

Conference Note. Avian retroviruses are divided into three classes: endogenous, exogenous replicant-competent, and exogenous replicant-defective. The exogenous leukosis viruses are replicant-competent containing *gag*, *pol*, and *env* genes. With the exception of the Rous sarcoma virus, the rapidly transforming exogenous viruses that contain an oncogene are replicant-deficient requiring helper viruses for replication. The virus strains that cause myelocytomatosis belong to this exogenous replicant-defective group.

The target cells in myelocytomatosis are non-granulated myelocytes. Typical lesions involve bone and start in the marrow cavity with extension through the bone to the periosteum. Any organ may become affected. Various viral strains have been associated with causing myelocytomatosis, including MC29. These strains can also induce a spectrum of different neoplasms including nephroblastomas, renal carcinomas, erythroblastosis, myeloblastosis, and hemangiomas/hemangiosarcomas.

Contributor. Animal Diagnostic Laboratory, Department of Veterinary Science, The Pennsylvania State University, University Park, PA 16802.

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International Veterinary Pathology Slide Bank
Laser disc frame #8101-2.

Microslide 67

History. A five-month-old male peafowl (Pavo sp.) was lethargic, anoretic, and refused to roost with other birds on the farm for about one week prior to death. The owner added piperazine to the birds water supply following onset of symptoms.

Gross Pathology. Body condition was thin. The crop mucosa was thickened with a rough, raised surface.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Moderate diffuse proliferative ingluvitis associated with nematode parasites. Etiology: Capillaria annulata or C. contorta.

Crop mucosa is 0.5 to 1 mm thick due to epithelial hyperplasia and retained keratin layers. Cross sections of helminths from 100 to 250 microns in diameter are present deep in the mucosa. The parasites have a thin outer cuticle, 10-15 micron wide body wall and clear body cavity containing tubular digestive tract and occasional reproductive organs. These features are typical of nematodes. Occasional heterophils are present near the junction of the mucosa and submucosa.

AFIP Diagnoses. 1. Crop: Hyperplasia, epithelial, diffuse, moderate, with hyperkeratosis and intraepithelial aphasmid nematodes, peafowl (Pavo sp.), avian.
2. Crop, adipose tissue: Atrophy, diffuse, severe.

Conference Note. The sections contained several tangential sections of intra-epithelial nematodes characterized by a pseudocoelom, thin cuticle, coelomyarian-polymyarian musculature,

stichosome, and paired bacillary bands. These findings are consistent with aphasmids of the family Trichinellina. Capillaria sp. have either direct or indirect life-cycles in which earthworms are utilized as intermediate hosts. In addition to Capillaria annulata and C. contorta, Capillaria obsignata should be included in the differential diagnosis since it appears similar histologically and has been reported in the intestinal tract of peafowl (Pavo sp.). Infected birds can become weakened and emaciated in severe infections. Fat atrophy indicates that this bird was in poor nutritional condition.

Other aphasmid parasites include Trichuris sp., Anatrichosoma sp., Trichosomoides sp., Trichinella sp., Cystoopis sp., and Eucoleus sp.

Contributor. Mississippi State University, College of Veterinary Medicine, P.O. Drawer V, Mississippi State, MS 39762.

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International Veterinary Pathology Slide Bank
Laser disc frame #20201, 21203, 21240.

Microslide 68

History. One of a pair of golden lion tamarins (Leontopithecus rosalia) whose mate died a few days earlier. It was found on the floor of a large indoor jungle exhibit in a depressed state. It did not respond to supportive therapy and died 30 minutes later.

Gross Pathology. Lungs were dark red. Gastrointestinal tract was discolored dark green. Cecum had hemorrhagic bands and appeared thickened. Liver and spleen appeared within normal limits.

Laboratory Results. Few Campylobacter sp. were isolated postmortem.

Contributor's Diagnosis and Comments. Hepatitis, acute, necrotizing, multifocal, with acidophilic bodies. Etiology: LCMV (Lymphocytic choriomeningitis virus, Arenaviridae).

Callitrichid hepatitis (CH) is an acute highly lethal viral disease that occurs in sporadic outbreaks in zoos and animal parks among many species of marmosets and tamarins in the family Callitrichidae and in Goeldi's monkeys (Callimiconidae sp.) with a particularly high incidence in the endangered golden lion tamarin (Leontopithecus rosalia). Since its initial description in 1981, there have been fourteen outbreaks in the United States and one in Great Britain, with 79 deaths in total. The etiologic agent of CH has been shown to be lymphocytic choriomeningitis virus (LCMV), an arenavirus. The natural host of this virus is the mouse, but other species, including humans, are sometimes infected. In humans, infection with LCVM causes a flu-like illness with neurologic manifestations.

Clinical signs of CH are nonspecific and include dyspnea, anorexia, weakness, and lethargy often followed by prostration and death. Necropsy findings include jaundice, pleural and pericardial effusions, subcutaneous and intramuscular hemorrhage, and hepatosplenomegaly. Histologically, there is an acute hepatitis characterized by hepatocellular necrosis with inflammation and acidophilic bodies.

LCMV has long been recognized as a serious zoonotic disease. Identification of LCMV-infected tamarins and marmosets is important in reducing the risks of exposure of zoo staff and visitors. In the outbreaks to date, human infections have been identified by seroconversion of two veterinarians, one had necropsied an animal with CH, and the other had been bitten by an infected animal. Caution is recommended for veterinary staff exposed to infected primates, their tissues, or excreta.

AFIP Diagnoses. 1. Liver: Hepatitis, necrotizing, acute, multifocal, moderate, with acidophilic bodies, golden lion tamarin (Leontopithecus rosalia), non-human primate.
2. Liver: Hemosiderosis, diffuse, mild to moderate.

Conference Note. Multifocally, there are necrotic hepatocytes, swollen hepatocytes and accompanying infiltrates of small numbers of lymphocytes and neutrophils. Necrotic hepatocytes often appear as 7-15 μm diameter, round, deeply eosinophilic structures, known as acidophilic bodies. Such bodies are the remnants hepatocytes that have undergone apoptosis.

Diffusely, hepatocytes contain variable amounts of a granular brown pigment that was more concentrated in areas of necrosis. Special stains demonstrated that the pigment is iron-positive, and thus consistent with hemosiderin. Hepatic pigmentation in golden lion tamarins may be a manifestation of the Dubin-Johnson-like syndrome; however, the pigment is iron-negative in that condition.

Contributor. Department of Pathology, National Zoological Park, Washington, DC 20008.

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Microslide 69

History. A six-year-old female llama (Llama glama) had weight loss and diarrhea for 1.5 months; however, the animal remained alert and had a good appetite. Weight loss continued until the animal became emaciated, recumbent, and unable to stand. A thickened intestinal wall and enlarged mesenteric lymph nodes were palpated rectally. The animal was euthanatized.

Gross Pathology. There was a lack of subcutaneous and abdominal fat; serous atrophy of fat was present around the coronary arteries. There was approximately 150 ml of serous fluid in the peritoneal cavity. The distal one third of the ileum was diffusely thickened and corrugated. Mucosal folds were prominent and resisted stretching. Intestinal lymphatics were dilated and filled with clear fluid. All mesenteric lymph nodes

were enlarged. On cut surface, there were multifocal, variable sized, chalky, firm foci within lymph nodes.

Laboratory Results. Mycobacterium paratuberculosis was isolated in pure culture from the intestine and lymph nodes.

Contributor's Diagnosis and Comments. Enteritis (ileitis), granulomatous, diffuse, severe, ileum. Johne's disease due to Mycobacterium paratuberculosis infection.

The microscopic lesion in the intestine was characterized by a severe diffuse infiltration of the mucosa and submucosa by epithelioid macrophages. Lymph nodes were also diffusely infiltrated with epithelioid macrophages. Multiple foci of necrosis were present throughout the nodes. Intracellular acid-fast bacilli were seen throughout the intestinal and lymph node lesions. Lesions were typical of Johne's disease in cattle and sheep. Mycobacterium paratuberculosis has been isolated from or suspected as a cause of intestinal disease in various animal species. To our knowledge, it has not been a frequent finding in llamas.

AFIP Diagnosis. Small intestine: Enteritis, histiocytic, diffuse, severe, with lymphatic histiocytic emboli, llama (Llama glama), artiodactyl.

Conference Note. Paratuberculosis (Johne's disease) is caused by Mycobacterium avium paratuberculosis, a short acid-fast bacillus. This bacterium is now classified as a subspecies of M. avium on the basis of high DNA homology with M. avium avium. The disease in cattle typically presents as a chronic wasting disease accompanied by diarrhea. It has been reported in various other species including llamas, camels, moose, white-tailed deer, sika deer, mouflon, and aoudads.

M. a. paratuberculosis is difficult to culture and grows slowly. Successful culture requires the addition of mycobactin as a source of iron. In a recent outbreak in a zoological park, the organism was identified by radiometric culture followed by use of a PCR-amplified DNA probe. Other diagnostic methods include lymphocyte stimulation tests, gene probes, and serology. Serologic tests have frequent false-positives and false-negatives. Delayed-type hypersensitivity skin tests are not considered reliable for M. a. paratuberculosis.

The moderator and some attendees did not consider the macrophages in this case to be epithelioid macrophages. Epithelioid macrophages are large, pale-staining macrophages having an ovoid nucleus and an angular shape that causes them to resemble epithelial cells. They contain abundant endoplasmic reticulum, Goli apparatus, vesicles, and vacuoles. They are believed to be adapted for extracellular secretion rather than

phagocytosis. The macrophages in this lesion have rounded contours and are adapted for phagocytosis rather than secretion.

Contributor. Department of Veterinary Pathology, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK 74078.

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International Veterinary Pathology Slide Bank

Laser disc frame #1112, 1239-41, 1870-1, 1996, 2468-9, 2630, 2815, 3586, 3702, 4187-8, 4320-2, 4842, 5602, 5630-2, 5702, 7947, 8855, 9171, 9500, 10380-2, 16059-64.

Microslide 70

History. A free-roaming bobcat was observed to be ataxic and frequently fell down. It was euthanized and presented for postmortem examination.

Gross Pathology. Bilaterally, the cranial and middle lung lobes were firm, heavy and dark red.

Laboratory Results. Yersinia pestis was isolated from the lung.

Contributor's Diagnosis and Comments. Pneumonia, acute, diffuse, fibrinopurulent, severe. Yersinia pestis.

Sections from the brain, trachea, lung, heart, liver, kidney, spleen, pancreas, stomach, small and large intestine were examined. Lesions were present only in the lung.

AFIP Diagnosis. Lung: Pneumonia, interstitial, acute, diffuse, moderate to severe, with myriad coccobacilli, bobcat (Lynx rufus), feline.

Conference Note. Plague, caused by Yersinia pestis, has been reported in numerous species of animals including various rodents, lagomorphs, domestic and wild felids and canids, and humans. Most infections are thought to result from the bite of infected fleas; however, direct transmission from ingestion or handling of infected tissues can occur. Resistant rodents such as deer mice serve as disease reservoirs. Sylvatic epizootics in susceptible animals such as prairie dogs amplify the infection, resulting in exposure of domestic species. Carnivores are relatively resistant to plague and have been used as sentinel animals.

Pulmonary infection can occur secondary to systemic spread or as a primary infection typified by the pneumonic form of the disease which is transmitted by inhalation of infectious aerosols. Either type of pulmonary infection is of great public health significance.

Plague bacilli produce two classes of toxin. Lipopolysaccharide endotoxin may be responsible for development of disseminated intravascular coagulation. Murine toxins are released following lysis of the cell wall and are responsible for tissue edema and necrosis. Several virulence factors have been identified including: a) Fraction 1, which is antiphagocytic and anticomplementary, b) two antigens designated *V* and *W* which promote resistance to intracellular killing, c) pestacin which, when linked to fibrinolysin and coagulase, contributes to invasiveness, and d) absorption of pigments which is associated with virulent strains.

Tissue Gram stains confirmed the presence of numerous bipolar-staining, gram-negative coccobacilli in the lung.

Contributor. Montana Veterinary Diagnostic Laboratory, P.O. Box 997, Bozeman, MT 59771.

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International Veterinary Pathology Slide Bank
Laser disc frame #3642, 24653-4.

Microslide 71 and 72; Lantern slide 13

History. This 8-year-old female one-humped camel (Camelus dromedarius) was slaughtered at Gedarif abattoir, Sudan, after a history of persistent chronic diarrhea.

Gross Pathology. At necropsy, performed immediately after death, there were irregular areas of green discoloration of the mucosa of the distal ileum, cecum and the proximal half of the right colon. The mucosal folds were thickened and showed scattered circular ulcers. The mesenteric lymph nodes were enlarged and green, especially those located at the ileocecal junction.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Colon: Granulomatous enteritis, severe, diffuse, ulcerated, with intrahistiocytic microorganisms. Green algae (Chlorella spp.).

Microscopically, the thickened mucosa and submucosa are infiltrated by numerous macrophages, giant cells, some plasma cells, and lymphocytes. The giant cells and most of the macrophages contain one or more algal organisms; extracellular algae are extremely rare. These organisms, about 9 μm in diameter, are characterized by a single nucleus and a slightly basophilic cytoplasm. They are surrounded by a thick, refractile wall that stained with PAS, GMS, and GF stains. PAS procedure reveals multiple intracytoplasmic, diastase sensitive, granules. The granules are also accentuated by the GMS method. Partial or complete internal septation and well-developed sporangia containing 2 to 4 endospores are common. Electron microscopic examination shows the presence of numerous elliptical and electron-lucent starch granules at the periphery of the algal cytoplasm; these granules are surrounded by multiple membranes (thykaloids) characteristic of chloroplasts. Immunofluorescent staining results for Prototheca wickermanii and Prototheca zopfii were negative.

Infections of mammals caused by unicellular algae are rare and most are due to the achlorophyllous microorganisms of the genus Prototheca. Green algal infections (chlorellosis) are usually recognized in slaughtered cattle and sheep with the

typical green discoloration of affected organs (mainly retropharyngeal lymph nodes in cattle, liver and the hepatic lymph nodes in sheep). Subcutaneous infections in a beaver and in a woman have also been described. Although H&E sections do not allow differentiation between Prototheca sp. and Chlorella sp., the green color of the macroscopic lesions, light microscopic detection of numerous PAS and GMS positive starch granules, ultrastructural detection of typical chloroplasts, and the negative immunofluorescence for pathogenic Prototheca sp. warrant a diagnosis of green algal infection or chlorellosis in this case.

To our knowledge, this is the first report of such an infection in a camel and the first associated with granulomatous enteritis in any species.

AFIP Diagnosis. Colon:- Colitis, erosive, granulomatous, diffuse, severe, with numerous algae, camel (Camelus dromedarius), artiodactyl.

Conference Note. Green algae infections caused by Chlorella sp. are rare in animals and must be differentiated from colorless Prototheca sp. algae by the presence of diastase-sensitive starch granules, chloroplasts, and green color in unfixed tissue. These algal organisms are ubiquitous in fresh and marine water, sewage, vegetation, and feces. Exposure may occur through oral ingestion of contaminated water. Infections with Prototheca sp., also uncommon, have been reported to cause cutaneous lesions in cats and humans, mastitis in cattle, and disseminated infections in dogs.

Other endosporulating organisms include Coccidioides immitis and Rhinosporidium seeberi.

Contributor. Pfizer, Centre de Recherche - B.P. 159, 37401 Amboise cedex, France.

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Microslide 73

History. This forty month-old, 18 kg., male Chinese Shar Pei dog presented in acute oliguric renal failure. Previous disorders include chronic otitis externa, generalized demodecosis, and chronic pyoderma.

Gross Pathology. Sections of formalin fixed right and left kidney were similar. Within the cortex there were disseminated cystic spaces up to 0.5 mm diameter. Kidneys were diffusely firm, and renal capsule was nodular. The medulla was firm and waxy.

Laboratory Results.

Calcium	12.9	WBC	12,800
Phosphate	21.2	PMNs	11,648
Sodium	150	Lymphocytes	1152
Potassium	4.9	Hematocrit	41.9
Chloride	99	MCV	60
Glucose	141	MCHC	36.2
BUN	207		
Creatinine	16.7	Urine pH	6.0
Total Protein	7.8	Urine Protein	-
Albumin	3.4	Urine glucose	2+
ALT	66	Specific gravity	1.020

Ear culture: Pseudomonas aeruginosa

Contributor's Diagnoses and Comments. 1. Kidney: Amyloidosis, medullary, diffuse, mild, Shar Pei, canine.
2. Kidney: Fibrosis, interstitial, diffuse, marked, with chronic-active moderate interstitial nephritis and capsulitis.
3. Kidney: Degeneration and necrosis, renal tubular epithelium, with diffuse severe mineralization and tubular regeneration.

While chronic nephritis or end-stage kidney disease is uncommon in the Shar Pei breed, renal medullary amyloidosis with chronic nephritis has been recently reported in 14 Shar Pei dogs. Abyssinian cats, cows, mice, and Dorcas gazelles similarly manifest with medullary amyloidosis. Three of the 14 cases were associated with a poorly characterized syndrome of recurrent fever and tibiotarsal joint swelling, known as, "Shar Pei fever". A similar syndrome called Mediterranean fever occurs in people. Clinicopathological changes in affected Shar Pei dogs may include hypoproteinemia, non-regenerative anemia, decreased antithrombin-

III, leukocytosis, pulmonary thromboembolism, hypercalcemia, increased serum phosphorus, uremia, and proteinuria. These animals may develop the nephrotic syndrome with normochloremic metabolic acidosis (titrational metabolic acidosis, due to uremia). Histological changes commonly include medullary amyloidosis, variable glomerular involvement, chronic interstitial nephritis, soft tissue mineralization, and glomerular atrophy/sclerosis, as seen in this case.

AFIP Diagnoses. 1. Kidney, interstitium: Amyloidosis, diffuse, severe, Chinese Shar Pei dog, canine.
2. Kidney: Fibrosis, interstitial, diffuse, severe, with tubular and glomerular atrophy and loss, mineralization, and lymphoplasmacytic interstitial nephritis (end-stage kidney).

Conference Note. Sections of kidney show severe changes at all levels of the nephron. Congo red stains demonstrate the preponderance of the amyloid to be medullary. Some sections also contain small deposits of oxalate crystals.

Amyloid refers to a group of proteins possessing a characteristic β-pleated sheet appearance on x-ray crystallographic analysis. Several proteins have been identified and include serum amyloid-associated (SAA), amyloid light chain (AL) protein, transthyretin, β2 microglobulin, β2 amyloid protein, and islet amyloid polypeptide (IAPP). SAA, an acute phase protein produced in the liver, is most commonly associated with secondary amyloidosis. AL is produced by plasma cells and is the predominent material in primary amyloidosis.

Amyloidosis occurs as systemic or localized disease and can affect a variety of organs. Renal medullary amyloidosis, as seen in this case, has been reported in Shar Pei dogs, Abyssinian cats, cows, mice, and Dorcas gazelles. Systemic amyloidosis occurs in Rhesus monkeys with clinical signs of cachexia with muscle wasting, chronic diarrhea, and lameness and predominant AA amyloid deposits in the intestines and spleen. Hamsters also have systemic amyloidosis associated with chronic infections and commonly associated with development of the nephrotic syndrome and right atrial thrombosis. Cutaneous or respiratory (nasal) amyloidosis is the form usually seen in horses.

Contributor. Walter Reed Army Institute of Research, Washington, DC 20307-5100.

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International Veterinary Pathology Slide Bank
Laser disc frame #10490-1, 10667-8, 10685-6, 10799-800, 13260-1, 16469-72.

Microslide 74 and 75

History. This adult female sable ferret (*Mustela putorius furo*) had sudden onset of mucohemorrhagic diarrhea with rectal prolapse and was humanely killed with an overdose of sodium pentobarbital.

Gross Pathology. The walls of the distal small intestine and of the large intestine were thicker than normal. The mucosa, and with lesser frequency, the submucosa and the muscular layers in affected areas were thicker than normal. The mucosal surfaces were nodular to irregularly rugose with exaggeration of the normal circumferential (small intestine) and longitudinal (colon) folds. Ingesta and fecal material were flecked with blood and mucus.

Laboratory Results. Routine culture of material obtained by colonic swab yielded only normal flora.

Contributor's Diagnosis and Comments. Colon and ileum: Proliferative colitis and ileitis, multifocal to coalescing, with intralesional intraepithelial *Campylobacter*-like organisms, ferret, mustelidae.

Pertinent histologic changes are mucosal hyperplasia with glandular dysplasia (loss of polarity, cytoplasmic basophilia, glandular branching), elongation and dilation; multifocal extension of dysplastic mucosal glands through the muscularis mucosa into submucosa and tunica muscularis; mononuclear cell inflammation around affected glands; and chronic active inflammation around dysplastic glands in submucosa and tunica muscularis. By Warthin-Starry stain, intracellular silver-positive, short, curved rod-shaped organisms were detected in dysplastic epithelial cells. These organisms were most common in apical cytoplasm of affected cells and were absent in adjacent normal epithelial cells.

Ferrets are one of several species in which similar enterocolonic mucosal hyperplasia with intracellular *Campylobacter*-like organisms (CLO) occur. Similar syndromes

occur in swine, guinea pigs, hamsters, rabbits, and rats. While the disease in ferrets is usually confined to the colon, it has been reported in the distal small intestine with metastasis of dysplastic epithelial cells containing CLO to regional lymph nodes. Such metastasis also occurs in swine and rats. In ferrets and swine it is not considered to be neoplastic; in rats it is. Change in classification of the rat disease may occur now that CLO have been found in "neoplastic" cells at metastatic sites.

AFIP Diagnosis. Colon: Colitis, proliferative, subacute, multifocal to coalescing, severe, with silver positive bacilli, sable ferret (Mustela putorius furo), mustelid.

Conference Note. Proliferative bowel disease in ferrets is believed to be caused by a Campylobacter-like organism (CLO), although the syndrome has not been successfully reproduced with the organism alone. It occurs sporadically in ferrets less than fourteen months of age, most commonly between four and six months old. Clinical signs include emaciation, dehydration, green mucoid to mucohemorrhagic diarrhea, and occasionally rectal prolapse. Neurologic signs such as ataxia and posterior paralysis have been reported in chronic cases. The disease is fatal if not treated, but affected ferrets respond to treatment if initiated early in the course of the disease.

Other species reported with CLO infections include pigs, hamsters, rabbits, mice, and Wistar rats. Two syndromes are reported in pigs: a sporadic infection of weanling pigs that produces regional ileitis and intestinal adenomatosis, and proliferative enteritis in older pigs (4-6 months) that is characterized by enteric hemorrhage.

Other Campylobacter sp. reported in ferrets are C. jejuni and C. coli, which cause necrosuppurative enteritis similar to that in humans and non-human primates. Helicobacter mustelae is the etiologic agent of chronic atrophic gastritis in ferrets.

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International Veterinary Pathology Slide Bank
Laser disc frame #811, 2450-1, 5414-5.

Microslide 76

History. These turtles were captured by a team from the National Marine Fisheries Service, Honolulu Laboratory, during routine tagging studies. Both turtles had multiple skin tumors.

Gross Pathology. One turtle (W93-16) had sessile and pedunculated firm masses (4 total) affecting the skin of the left and right front flippers and the cornea. The second turtle (W93-34) had tumors (7 total) affecting all limbs, tail, and cornea.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Cutaneous fibropapillomatosis, etiology unknown.

The tumors have a pattern similar to cutaneous fibromas of white-tailed deer (W93-16) or fibropapillomas of mule deer (W93-34). Most sections contain one or more intravascular trematodes eggs. Various degrees of inflammation is associated with the eggs and vessels. However, papillomaviruses have not been found in lesions. Transmission studies with the trematodes or eggs have been unsuccessful. Some cases in Florida green sea turtles have contained herpes virus in the epidermis. This may be a secondary invader similar to the bacteria and fungi evident in the stratum corneum of many of these sections.

AFIP Diagnosis. Skin: Fibropapilloma, green sea turtle (Chelonia mydas), reptile.

Conference Note. Green sea turtles (Chelonia mydas) are the only species of sea turtle documented with this type of fibropapilloma. The etiology for these fibropapillomas is as yet unknown, however; possible causes include an immune response to trematode eggs, secretion of hirudin by marine leeches, viruses including papilloma and herpes viruses, excess solar radiation, chemical pollutants, stress, and genetic predisposition to neoplasia. Clinical signs in affected turtles can include vision impairment and blindness, disorientation, impaired swimming due to physical obstruction, emaciation, and an apparent increased susceptibility to parasitism by the marine leech Ozobranchus branchiatus.

Several sections contained thick-walled trematode eggs in capillaries. Learedius learedi, a cardiovascular fluke, has been associated with fibropapillomas in sea turtles.

Most papillomas in other species are caused by papillomaviruses, with cattle, horses, and dogs being most frequently affected. Six different papillomaviruses have been identified in cattle: types 1,2 and 3 cause cutaneous fibropapillomas, types 5 and 6 cause papillomas of the teats, and type 4 causes papillomas in the gastrointestinal tract. Affected cattle are usually less than two years of age, with single or multiple lesions that regress spontaneously. Sarcoids in horses have been associated with bovine papillomavirus type 2, and the lesion reproduced by intradermal inoculation of the virus. Aural plaques in horses, oral and cutaneous papillomas in dogs, and fibromas in deer have been associated with papillomavirus. Papillomavirus-induced lesions have also been reported in several strains of laboratory and wild mice.

Contributor. The Jackson Laboratory, 600 Main Street, Bar Harbor, ME 04609-1500.

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International Veterinary Pathology Slide Bank
Laser disc frame #7340, 7387, 9587, 9623, 11485, 16666.

Microslide 77; Lantern slide 14

History. Los Angeles county coyotes are trapped and euthanized as part of an ongoing predator abatement program. Over 500 necropsies on these animals have been documented in the past 7 years.

Gross Pathology. The animals are generally found in fair to excellent nutritional condition with variably severe ectoparasite and endoparasite burdens. This includes fleas, ticks tapeworms and occasionally roundworms. No heartworms have been found and other gross observations are usually limited to incidental trauma. The livers appear grossly normal in all cases.

Laboratory Results. Serology has been limited to plague analysis in which about 6% have detectable antibody titers. Blood smears were never available. Random blood samples from several dogs living in the mountains were negative for gametocytes.

Contributor's Diagnosis and Comments. Hepatitis, granulomatous with eosinophils, multifocal, mild to moderate. Etiology - Hepatozoon sp., consistent with Hepatozoon canis.

The histologic picture is variable in these slides as multiple animals were sampled. There is moderate autolysis with postmortem bacterial growth in many sections, a complication that seems unavoidable in this species even though the necropsies were consistently finished within 4-6 hours of death. The highly variable diet of coyotes may cause the liver to encounter unusually heavy bacterial loads. The granulomas are best described as random but there seems to be a definite predilection for the terminal hepatic veins and portal triads. There are well-formed granulomas with central necrosis and epithelioid macrophages rimmed by eosinophils and lymphoid cells, but other foci are poorly organized and composed of lymphocytes, plasma

cells and eosinophils replacing hepatocytes. Giant cells are relatively rare.

The intracellular organisms can be difficult to detect in hepatocytes and are not present in all slides, but depicted typically in the photomicrograph. Several other forms have been observed both earlier with prominent peripheral nuclei and later as the schizonts break down and lose their merozoites, often leaving an empty shell-like residuum. Less than 20% of the granulomas contain organisms and schizonts are often seen apart from the inflammatory reaction. They remain visible even in the most autolyzed samples and are accentuated with GMS stain.

This hepatic infection is present in about 50% of Los Angeles County coyotes sampled and the organism can be demonstrated in about 30% of those on single routine histologic section. No matter how severe and disseminated the reaction may be, no adverse effect on the host has been detected. Infection has not been detected in any other organ.

The mode of infection and transmission is uncertain in this species, but appropriate invertebrate vectors are abundant in these feral canids. Infection has not been reported in domestic dogs in the L. A. Basin. The primary host for Hepatozoon sp. can include birds, reptiles and amphibians, although other authors claim that the tick, Rhipicephalus sanguineus, is the only known vector in wild carnivores. There few reports of hepatozoonosis in coyotes, largely limited to parasite surveys in the Gulf Coast region.

AFIP Diagnosis. Liver: Granulomas, multiple, random and portal, with protozoal schizonts, coyote (Canis latrans), canine.

Conference Note. Hepatozoon sp. infects canids, felids, rodents, squirrels, raccoons, mink, birds, and reptiles. The life cycle is indirect with blood-sucking arthropods as intermediate hosts. Sporogony occurs in the arthropod host after ingestion of a blood meal containing gametocyte-infected leukocytes. When the arthropod is subsequently ingested by the vertebrate host, sporozoites are released, penetrate the intestinal wall, and are carried via the blood or lymph to various tissues including spleen, bone marrow, liver, lungs, lymph nodes, and myocardium where they form schizonts. After undergoing several generations of schizogony, merzoites are released, enter mononuclear leukocytes, and become microgamonts and macrogametes.

Intermittent fever and emaciation are the most frequently reported clinical signs in dogs with Hepatozoon canis infections. Periosteal bone formation is frequently seen with Hepatozoon infections, often occurring in areas of concurrent granulomatous myositis. The pathogenesis of this lesion is not known but

interference with medullary or periosteal circulation may be the cause.

Contributor. Los Angeles County Comparative Medical & Veterinary Services, 7323 Descanso Avenue, Downey, CA 90242.

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International Veterinary Pathology Slide Bank
Laser disc frame #11084, 11088, 14304-5.

Microslide 78; Lantern slide 15

History. Tissue is from a 12-year-old, captive-reared, female Rhesus monkey (Macaca mulatta) whose previous history included delivery of a stillborn fetus (04-06-89) and rectal prolapse corrected by manual reduction (07-08-91). Approximately 24 hours post-delivery of a viable full-term infant, this animal became depressed and displayed ecchymoses on the right superior palpebra. The lower right abdomen was painful on palpation, and the uterus was enlarged. The animal's condition deteriorated rapidly with a delayed capillary refill time and hemorrhage from

the nose, mouth, and rectum; she collapsed and died during emergency treatment.

Gross Pathology. Copious amounts of thin, reddish-black, sanguinous exudate stained the perineal fur and drained from the vulva. There was focal hemorrhage in the right caudal lung lobe. Both kidneys were swollen with a striking capsular variegated display of irregular, alternating to confluent, red to pale yellow-white patches. On cut section, these changes were strictly limited to the renal cortices. The turgid, egg-shaped uterus measured 7 x 4 x 4 cm. Friable reddish-black clots, resembling grape jelly, were loosely adherent to the endometrial surface. Thin, watery black contents partly filled the colonic lumen.

Laboratory Results. The following abnormalities were noted on the day of death:

Glucose	202 mg/dl
BUN	252 mg/dl
creatinine	15 mg/dl
Phos	15.6 mg/dl
ALT	504 IU/L
WBC	42.5 x $10^3/\mu l$
neutrophils	52%
bands	2%
lymphs	31%

Fecal occult blood: positive
Group D streptococcus was the predominate organism recovered from the endometrium.

Contributor's Diagnosis and Comments. Necrosis, ischemic, acute, multifocal to confluent, severe, cortical, bilateral with intraglomerular capillary microthrombosis, kidneys, Rhesus monkey (Macaca mulatta).

Other microscopic changes included pulmonary intra-alveolar hemorrhage and acute, focal, fibrinous interstitial pneumonia (presumably secondary to bacteremia/toxemia); microthrombosis of splenic and hepatic sinusoids; multifocal, mild, suppurative hepatitis and hepatic necrosis; and acute, diffuse, superficial necrotizing and suppurative deciduitis/endometritis.

The gross and microscopic changes are characteristic of disseminated intravascular coagulation (DIC) with thrombosis of glomerular afferent arterioles and glomerular capillaries leading to bilateral renal cortical infarction. When bilateral and symmetrical, renal cortical necrosis causes peracute anuria and uremia and is uniformly fatal. The predisposing event to acute renal cortical necrosis in this animal was felt to be acute, ascending Group D streptococcal endometritis.

Acute, bilateral renal cortical necrosis often follows septic or hemorrhagic shock. In humans, the condition most often complicates obstetrical emergencies such as placental abruption, acute septic endometritis, prolonged intrauterine death, uterine hemorrhage, and amniotic fluid embolism. The diagnosis is based on the clinical setting of postpartum acute renal failure combined with renal biopsy and/or selective arteriopathy. Renal cortical necrosis has also been reported in endotoxemia of metritis, mastitis, and enteritis in cattle, azoturia in horses, hemorrhagic shock from bleeding esophageal ulcers in pigs, and from unknown antecedent events of kenneled dogs.

It is not clear whether DIC and microthrombosis are the cause of ischemic injury or result from previous endothelial injury; both mechanisms may operate simultaneously. Bilateral renal cortical necrosis has been considered the counterpart of the Shwartzman reaction. Pregnancy can prime experimental animals for the Shwartzman reaction so that a single injection of endotoxin induces DIC, whereas two injections are necessary in non-pregnant animals. Gram-positive bacterial sepsis or gram-negative endotoxemia can cause endothelial injury to glomerular capillaries, mediated in part by monocyte/macrophage elaboration of TNF, thus predisposing to microthrombosis and ischemic infarction. Hypotension secondary to shock also leads to a redistribution of renal perfusion with confinement of the lesions to the cortex. PGE_2 produced in the medulla during ischemia modulates the angiotensin II and catecholamine-induced vasoconstriction.

AFIP Diagnosis. Kidney, cortex: Necrosis, coagulative, multifocal to coalescing, moderate, with fibrin thrombi, Rhesus monkey (*Macaca mulatta*), primate.

Conference Note. Gross appearance of acute ischemic renal necrosis can vary considerably depending on the distribution and duration of the ischemia and the amount, timing, and extent of reperfusion. Lesions vary from a diffuse finely mottled appearance to distinct patchy areas of necrosis.

Causes of disseminated intravascular coagulation (DIC) are many and include gram-negative (endotoxemia) and gram-positive bacteria, viruses, parasites, neoplasia, toxins, shock, vascular stasis, acidosis, and tissue necrosis. The two general mechanisms of DIC initiation are release of tissue factor or thromboplastic substances into the circulation and widespread injury to endothelial cells. Both mechanisms result in activation of the extrinsic and intrinsic clotting pathways. In obstetrical cases, the cause of DIC is often multifactorial, including release of placental thromboplastins or amniotic fluid into the circulation, hypoxia, acidosis, and shock, as well as infectious complications that cause widespread endothelial damage. In addition to bilateral renal cortical necrosis seen

with generalized Shwartzman-like reaction, postpartum pituitary necrosis (Sheenan's syndrome) is reported in humans with DIC. Tubular proteinosis was present in most sections.

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International Veterinary Pathology Slide Bank
Laser disc frame #1052, 18532, 18594, 18513-4, 4891.

Microslide 79

History. Two-month-old orphan baby gray squirrel (Sciurus carolinensis) was being hand raised by a wildlife rehabilitator.

Gross Pathology. Corrugated, thickened skin in patches over the body surfaces. Multiple white to pale tan rounded and occasionally raised foci 1-3 mm in diameter in lung, liver and kidney.

Laboratory Results. None.

Contributor's Diagnoses and Comments. 1. Skin: Multifocal epidermal hyperplasia and intradermal and subcutaneous fibroplasia with intracytoplasmic inclusions.
2. Lung: Multifocal fibroplasia and alveolar epithelial hyperplasia with intracytoplasmic inclusions.
3. Liver and kidney: Multifocal fibroplasia with intracytoplasmic inclusions.

Etiologic Diagnosis: Squirrel fibromatosis. Etiology: Leporipox virus.

The skin lesions were the most obvious and dramatic manifestations of this disease and intracytoplasmic inclusions were easily found in both the proliferating epidermis and dermal fibroblasts. Similar proliferation of both epithelial and fibroblastic stromal components were seen in lung and liver, with inclusions more difficult to identify in these tissues. The epithelial proliferation in the lung has been termed "adenomatoid" and compared to pulmonary adenomatosis in sheep. In the kidney, stromal proliferation is most prominent with no appreciable epithelial component. Disseminated pox viral infection in squirrels is usually limited to immature animals.

AFIP Diagnoses. 1. Haired skin: Mesenchymal and epidermal proliferation, focally extensive, with eosinophilic intracytoplasmic inclusion bodies, epidermal ballooning degeneration, ulceration, and orthokeratotic and parakeratotic hyperkeratosis, gray squirrel (Sciurus carolinensis), rodent.
2. Lung: Mesenchymal and type II pneumocyte proliferation, nodular, multifocal, with eosinophilic intracytoplasmic inclusion bodies.
3. Kidney: Mesenchymal and tubular epithelial proliferation, diffuse, with eosinophilic intracytoplasmic inclusion bodies.
4. Liver: Mesenchymal and biliary epithelial proliferation, multifocal to coalescing, with eosinophilic intracytoplasmic inclusion bodies, multifocal necrosis, and hemorrhage.

Conference Note. Squirrel fibroma virus is a poxvirus antigenically related to the Shope fibroma virus. Natural infection has been reported in juvenile grey squirrels. Woodchucks (Marmota monax) and domestic rabbits have been successfully infected experimentally. The pathogenesis of the viral infection is not completely understood, but it is believed that the virus is transmitted by mosquitoes and that it spreads hematogenously to multiple sites where tumor formation is induced. The virus has been shown to replicate in vascular endothelial cells.

Other poxviruses that cause tumors or tumor-like lesions include yabapox in monkeys, molluscum contagiosum in people, lumpy skin disease in cattle, genital papillomatosis in swine, sheep pox and contagious ovine exanthema in sheep, myxomatosis in Oryctolagus sp. rabbits, and fibromas in cottontail rabbits.

Contributor. Experimental Pathology Laboratories, Inc., P.O. Box 12766, Research Triangle Park, NC 27709.

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International Veterinary Pathology Slide Bank

Laser disc frame #2771-2, 5346.

Microslide 80; Lantern slide 16

History. This two-year-old male mongrel dog was submitted for unilateral (left) nephrectomy. The dog became progressively depressed, dying 6 days after the surgery. The excised kidney was slightly enlarged but otherwise normal and was kept in formalin.

Gross Pathology. Ammoniacal odor was present in the mouth and stomach. The right kidney was small, with a convoluted surface, and contained a female specimen of Dioctophyma renale, 53 cm in length. The renal parenchyma was reduced to a vesicle with a 3 mm thick wall and was tightly adhered to the capsule.

Laboratory Results. BUN = 163 mg/dl one day prior to the death.

Contributor's Diagnosis and Comments. Compressive atrophy, marked, right kidney. Etiology: Dioctophyma renale.

Histologically, the renal parenchyma is thinned and obliterated by fibrous tissue. Atrophy and loss of glomeruli and tubules are frequent. Hyperplasia of the transitional epithelium of the pelvis is present. D. renale (giant kidney worm) is a cosmopolitan nematode the principal host of which are mink (Mustela vison). Other hosts include dogs, cats, other carnivores and rarely pigs, horses, cattle and humans. The adult female is 20-100 cm in length and the male 14-45 cm. The eggs measure approximately 65 x 42 micrometers. The life cycle is complex and not completely understood. The eggs are passed in the urine and then encyst in the body cavity of annelids (Lumbricus variegatus), reportedly the only essential intermediate host for completion of the cycle. Paratenic hosts such as fish, frogs and crustaceans are reported. The final host can be infected by ingesting any of them. Dogs are most frequently affected among the domestic species even though they are considered abnormal hosts. Adult worms live in the renal pelvis, usually in the right kidney, where they cause pyelitis,

frequently purulent progressive pressure atrophy of the renal parenchyma, and hydronephrosis. In dogs, in most of the cases of dioctophymosis (60%), the adult worm is free in the abdominal cavity causing complications including peritonitis, internal hemorrhage and peripancreatitis.

In intrarenal parasitism, the hypertrophied contralateral kidney usually compensates for the failing atrophic parasitized kidney. In this case, the excised left kidney was hypertrophied. The unfortunate nephrectomy deprived the animal of its only functional kidney. The BUN and clinical signs support renal failure as the cause of death. We prefer to call this lesion marked compression atrophy rather than hydronephrosis since we did not see fluid or any kind of exudate within the hollow parenchyma.

AFIP Diagnosis. Kidney, cortex and medulla: Atrophy, diffuse, severe, with fibrosis and urothelial and tubular epithelial hyperplasia, mixed breed dog, canine.

Conference Note. Dioctophyma renale ("giant kidney-worm") is the largest parasitic nematode. It is thought to secrete an enzyme which is cytolytic to the renal parenchyma. This, in addition to pressure necrosis, secondary pyelonephritis and hydronephrosis leads to the severe renal atrophy exemplified by this case. Adult worms are most commonly found in the renal pelvis or free in the peritoneal cavity, but have also been reported in the urinary bladder, urethra, uterus, ovaries, mammary gland, stomach, abdominal wall, and thorax of affected animals.

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International Veterinary Pathology Slide Bank
Laser disc frame #3653, 6045, 6215, 6624, 13680, 13682, 13686.

Microslide 81

History. This 9-year-old, male (recently castrated), Shepherd mix canine had a 2 month history of anorexia, weight loss, lethargy, constipation and tenesmus. Physical examination revealed a mitral cardiac murmur, a caudal abdominal mass and prostatmegaly.

Gross Pathology. Necropsy revealed multiple, round, variably sized (1-5 cm diameter), white, firm, often umbilicated hepatic masses that were easily extirpated. A large (8 x 8 x 5 cm), irregular, solitary, firm, white parapancreatic mass was seen associated with the left pancreatic lobe in the dorsal leaf of the greater omentum. The fluctuant prostate was symmetrically enlarged and displayed several large, thin-walled cavities containing purulent yellow-green material.

Laboratory Results. Urinalysis revealed a marked bacterial urinary tract infection. The dog displayed a persistent, mature neutrophilia (WBC = 43,000). On two occasions 3 weeks apart, fasting blood glucose levels were 97 mg/dL (normal 85-120). The serum pancreatic polypeptide level measured 838,526 pg/ml (normal 100-170). Multiple sections of liver and parapancreatic tumor masses stained consistently only for neuron specific enolase (NSE), chromogranin and pancreatic polypeptide using avidin-biotin-peroxidase complex immunohistochemical methods.

Contributor's Diagnosis and Comments. Pancreatic polypeptide cell adenocarcinoma - pancreas with metastasis to liver.

The parapancreatic mass grossly represented focal outward extension of a superficial pancreatic neoplasm. Metastases were seen only in the liver. Within the liver, tumor cell morphology and arrangement were variable. In some areas, single rows of discrete columnar cells with basophilic, apical nuclei rested upon fine fibrovascular stroma which formed incomplete packets. In other areas, cells were more cuboidal or polygonal with central nuclei, granular cytoplasm and were arranged in acinar or cord patterns.

Immunohistochemical staining was performed for the following: insulin, glucagon, somatostatin, NSE, chromogranin, pancreatic polypeptide (PP), serotonin, gastrin, islet amyloid polypeptide and ACTH. Of these, only NSE, chromogranin and PP were consistently present in mild to strongly positive fashion.

This tumor was unusual in that it appeared to represent a nearly pure population of neoplastic pancreatic F cells secreting only pancreatic polypeptide. Most pancreatic endocrine tumors secrete multiple substances with insulin by far the most common.

Humans with PP cell tumors are reportedly asymptomatic. This was likely true in this case with most, if not all, of the dog's symptoms related to the chronic, cystic, septic prostatitis.

AFIP Diagnosis. Liver: Islet cell carcinoma, metastatic, Shepherd mix, canine.

Conference Note. Six distinct types of islet cells have been identified. Alpha cells typically comprise about 15% of cells in islets and produce glucagon. Beta cells are the most numerous, commonly comprise up to 80% of islet cells, and secrete insulin. Delta cells are present as two populations; one that produces somatostatin and one that produces vasoactive polypeptide. F cells produce pancreatic polypeptide and enterochromaffin cells produce serotonin. G cells, which are normally found in the mucosa of the pyloric antrum and proximal duodenum of adult dogs, produce gastrin. G cells have been identified immunocytochemically in fetal and neonatal islets but are absent in normal mature islets. Several clinical syndromes have been described in association with functional tumors. Hyperinsulinism, hypoglycemia, and neurologic signs are associated with functional beta cell tumors. Zollinger-Ellison syndrome is associated with hypergastrinemia and hyperglycemia. Vacuolar hepatopathy and superficial necrotizing dermatitis are associated with glucagonemia. Amyloid deposition may be a feature of these tumors.

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International Veterinary Pathology Slide Bank
Laser disc frame #250.

Microslide 82

History. This eight-year-old, male llama developed chronic obstructive bronchitis with clinical signs of respiratory distress similar to "heaves" in horses. The condition was treated with oral dexamethasone for eight months. The animal became lethargic and anorexic with low-grade colic the last ten days.

Gross Pathology. Multiple, small white foci were noted in the heart and kidney by the clinician at necropsy.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Nephritis and myocarditis, chronic active, multifocal, necropurulent, severe, due to Candida sp. (systemic candidiasis).

This represents a steroid-induced disease, i.e. an iatrogenic disease. Systemic candidiasis is unusual in immunocompetent hosts. The lungs and liver of this animal were not affected by the fungus. The distinctive morphology of Candida sp. in tissue sections is the production of pseudohyphae, hyaline yeast-like cells with blastoconidia, germinating yeast forms and true hyphae.

AFIP Diagnoses. 1. Kidney: Abscesses, multiple, coalescing, with fungal organisms, llama (Lama glama), artiodactyl.
2. Heart: Myocarditis, pyogranulomatous, multifocal, moderate, with fungal organisms.

Conference Note. Special stains demonstrated hyphae, pseudohyphae, and yeast-like cells characteristic of Candida sp. The yeast-like cells are oval and 3 to 6 μm in diameter. Pseudohyphae consist of yeast-like cells that are attached end-to-end in chains. They differ from true hyphae by the presence of constrictions at points of attachment between cells.

Candida sp. are opportunistic invaders, usually requiring a compromise in host defenses. Candida infections are categorized into three forms: cutaneous, mucocutaneous and systemic. Systemic infection has been associated with severe defects in neutrophil function and with multiple host defense deficiencies. In systemic candidiasis the organism has a predilection for the kidneys which may be damaged to the extent that renal failure occurs. Vegetative valvular endocarditis is also frequently seen

and may progress to myocarditis and pericarditis secondary to mycotic emboli. Lesions are typically acute with suppuration and necrosis.

Contributor. Montana Veterinary Diagnostic Laboratory, P.O. Box 997, Bozeman, MT 59771.

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Microslide 83

History. Tissue is from a six-year-old, male, castrated, Domestic Longhair cat with a history of a thoracic vertebral dislocation/fracture as a kitten, resulting in neural deficits (Schiff-Sherrington syndrome). The cat had received routine feline vaccinations. One rabies vaccination had been administered subcutaneously in the interscapular space 18 months prior to tumor diagnosis. The site developed hair loss six to eight months postvaccination. In September 1992, a 3.0 x 1.5 x 1.5 cm subcutaneous mass was palpated in the interscapular space. An excisional biopsy was performed and the mass was diagnosed as a fibrosarcoma, characterized by abundant fibrous connective tissue with focal areas of anaplasia that became more pronounced toward the center. By October 1992 there were numerous recurrences (dermal and subcuticular), at which time the cat underwent four weeks of orthoradiation. The masses disappeared, but in January 1993, one large mass appeared at the periphery of the radiation-induced alopecia. This mass was treated with cesium needles, after which it disappeared only to reappear five months later (May 1993). At that time the mass was surgically excised using a 3 cm margin. In October 1993, multiple dermal masses developed along the suture line and one subcutaneous mass was found 4 cm craniad to the previous excision site. These masses continue to increase in size.

Gross Pathology. As described in the history.

Laboratory Results. FeLV negative.

Contributor's Diagnosis and Comments. Haired skin, dermis and subcutis: Fibrosarcoma, Domestic Longhair, feline.

Fibrosarcoma in cats is generally accepted to occur in two forms. The first is solitary, occurs in older cats, is similar to fibrosarcoma in other species, and is the more common of the two forms. The second form occurs in young cats (less than five years), is multicentric, more anaplastic, and is associated with feline sarcoma virus which is a recombinant hybrid of host genome and feline leukemia virus. This form is found only in cats serologically positive for feline leukemia virus.

For several years there have been reports describing an increased incidence of fibrosarcomas and other sarcomas at sites routinely used by veterinarians for subcutaneous and intramuscular vaccinations. Many of these sarcomas are bordered by an inflammatory infiltrate resembling previously recognized vaccine-induced inflammatory nodules. There is growing epidemiologic evidence that this unique fibrosarcoma may be the consequence of postvaccinal panniculitis. It is currently hypothesized that the chronic inflammatory and immunologic reactions predispose the cats to a derangement of their fibrous connective tissue repair response, eventually resulting in neoplasia. Aluminum-based adjuvants have been the prime suspects for initiating the inflammatory response. Electron probe x-ray microanalysis has identified the material found within the macrophage cytoplasm to be composed of aluminum and oxygen, which are combined with hydroxide and phosphate to serve as adjuvant gels in some feline vaccines. Breed, sex or age predilections have not been described. The reported interval between vaccination and tumor development ranges from a few months to 4 years. Although similar focal necrotizing granulomatous panniculitis at some vaccination sites has also been reported in dogs, there are no references to subsequent tumor development.

Although the etiology of the fibrosarcoma described for this case is unknown, the associated inflammatory response, though not pronounced, is readily evident around the periphery of the mass as angiocentric lymphoid nodules admixed with scattered eosinophils and macrophages that contain an amphophilic foreign material; this is considered to be consistent with vaccinal sarcoma in cats.

AFIP Diagnosis. Haired skin: Fibrosarcoma, with amphophilic intrahistiocytic foreign material and perivascular lymphocytes, Domestic Longhair, feline.

Conference Note. Postvaccinal sarcomas have been reported as fibrosarcomas, malignant fibrous histiocytomas, osteosarcomas, rhabdomyosarcomas, and chondrosarcomas, with fibrosarcomas and malignant fibrous histiocytomas comprising the majority of the tumors. In a recent study, most of these tumors had histological and immunohistochemical staining characteristics consistent with fibroblastic/myofibroblastic origin. Posttraumatic sarcomas in the eyes of cats are thought to have similar origins.

Contributor. Walter Reed Army Institute of Research, Washington, DC 20307.

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Microslide 84; Lantern slides 17 and 18

History. This four-month-old, female Beagle was received from a commercial vendor at two months of age. After acclimation, the research protocol involved an 80% partial hepatectomy with subsequent gene therapy. Human clotting factor IX was introduced and expressed by a defective packaging adenovirus 5 vector infused via the vascular access port placed in the spleen during hepatectomy. Recovery was uneventful until three days prior to sacrifice, at which time the dog was reported by the animal care person to have a swollen jaw.

Physical examination revealed bilateral firm swelling of the rami of the mandible. Palpation of the swelling was very painful to the patient. The gingiva showed hemorrhagic areas and focal ulcerations. Clinical chemistries were unremarkable with the exception of alkaline phosphatase, which was elevated to 697 IU/L. Radiographs revealed a proliferative lesion with areas of lysis also present in the rami of the mandible. During the two days following initial presentation, swelling continued to increase and spread. Pyrexia developed on the second day (temp. 104.2°F). Pain, rapid progression, and clinical suspicion of a fungal infection aided in the decision to euthanize the dog and perform a necropsy on the third day of illness.

Gross Pathology. The mandible contained several semi-circumscribed, dark red raised masses, which were fluctuant. The cervical lymph nodes were enlarged, measuring 4 cm x 1 cm x 1.5 cm and had dark red centers. Fibrous attachments were present between the venous access port, spleen and the omentum. Between the liver and the lesser curvature of the stomach there were also a few small fibrous adhesions. At the root of the mesentery there were many 1.5 mm spidery veins.

Laboratory Results. Cultures and special stains for infectious agents and other organisms were negative.

Contributor's Diagnosis and Comments. Canine craniomandibular osteopathy. Etiology unknown.

This case was interesting in several areas. It occurred at an earlier age than is typical, was much more aggressive than normal, and occurred in a breed not mentioned in the literature previously. The radiographic appearance, physical location, negative culture results and histologic appearance, however, provide adequate justification for this diagnosis.

Proliferation of bone and evidence of resorption in what appears to be a random fashion with the formation of a mosaic pattern (formation lines and resting lines) in the osteoid is the significant lesion. Bone marrow is replaced by mesenchymal immature-appearing connective tissue, and spicules of bone formation distort the periosteal margin to the point that it is often not evident. Large accumulations of multinucleate osteoclasts are seen in some sections which appear to have completely resorbed the spicule of bone they originated on. Surrounding the lesion in the bone, there are large areas of hemorrhage and necrosis in the margin between the lesion in the bone and the surrounding soft tissue. Associated with these areas of hemorrhage and necrosis, there are large accumulations of polymorphonuclear neutrophils.

AFIP Diagnosis. Bone, mandible: Alveolitis, chronic-suppurative, diffuse, severe, with osteolysis and osteonecrosis, Beagle, canine.

Conference Note. This case was reviewed by the Departments of Oral, Orthopedic, and Radiologic Pathology of the AFIP, as well as by a veterinary pathologist with expertise in orthopedic pathology not affiliated with the AFIP. The consensus opinion is that this is a case of chronic suppurative osteomyelitis with bone resorption and internal and external root resorption. This lesion is not typical of craniomandibular osteopathy in several respects, including net loss of bone rather than periosteal bone proliferation, the involvement of alveolar bone, and the presence of multifocal edema and hemorrhage. Sections were interpreted to be from alveolar regions rather than from the rami which radiographically demonstrated irregular radiopacities and which may have been more representative of the contributor's diagnosis of craniomandibular osteopathy. The radiograph showed diffuse sclerosis of both mandibular rami with extension into the soft tissue. Conference participants believed that there might also be a concomitant fibrous osteodystrophy.

Contributor. Center for Comparative Medicine, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030.

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International Veterinary Pathology Slide Bank
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Microslide 85

History. This 10-month-old, female Beagle was a subject in a study of autologous stem cell reconstitution. She was approximately 5 months old when she received total body irradiation sufficient to deplete marrow elements. Marrow reconstitution was successful. The animal was killed and tissues evaluated as part of the study. The animal was considered to be clinically normal at the time of death.

Gross Pathology. The pancreas was small, firm and finely nodular. Both kidneys were of normal size but had a few faint, pale steaks radiating through the cortex and medulla.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Pancreatitis, atrophic and sclerotic, diffuse, severe. Etiology: Radiation-induced injury.

This pancreatic lesion is recognized as a sequela to either severe organ targeted or total body irradiation. Evolution of the change occurs over a 2-5 month post-irradiation period. The condition culminates in nearly total loss of the pancreas with nodular regeneration occurring along main and accessory ducts. Diabetes is reported as a complication. It is speculated that the lesion is a result primarily of vascular and connective tissue injury rather than direct epithelial cell injury. Grossly observed renal lesions were consistent with chronic interstitial nephritis on histological examination.

AFIP Diagnosis. Pancreas: Atrophy and loss, diffuse, severe, with fibrosis and regeneration, Beagle, canine.

Conference Note. Conference participants commented that islets of Langerhans were indistinct in sections examined. Pancreatic atrophy can be primary or secondary to other pancreatic injury. Primary atrophy is usually a diffuse change and can be caused by a variety of nutritional deficiencies including those of essential amino acids, zinc, copper, and selenium. Secondary atrophy is usually multifocal and occurs most commonly following duct obstruction by fibrous connective tissue. Histologically, atrophy presents as a depletion of zymogen granules and development of basophilic cytoplasm. Cells progressively shrink and the normal acinar or glandular pattern is lost.

Periductal pancreatic stem cells are thought to be the proliferating cell type during regeneration and are capable of differentiating into acinar cells, ductal cells, and islet cell precursors. Pancreatic cells share a common ancestry with hepatocytes and biliary epithelium and also have the ability to differentiate into hepatocytes.

Contributor. Department of Comparative Medicine, School of Medicine, T142 Health Sciences SB-42, University of Washington, Seattle, WA 98195.

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Microslide 86; Lantern slides 19, 20 and 21

History. A neonatal female kid and placenta from a near-term Pygmy goat were submitted for pathologic examination. A farm in western Pennsylvania experienced 21 abortions in their sheep and goats over 3 months in the winter of 1993. Thirteen of 80 ewes and 7 of 12 does aborted near-term fresh and/or autolyzed fetuses and had weak twin lambs or kids. Some goats had bloody vaginal discharges and returned to heat in the fall of 1992. Abortions did not occur in the other farm animals (cattle, pigs, horses, donkeys). Leptospira spp. caused some abortions 5 years previously, and there was a recent lapse in vaccination for leptospirosis. The farmer had recently bought some sheep and goats from an Illinois herd with a history of chlamydiosis and toxoplasmosis.

Gross Pathology. Most of the cotyledons were brown-red, soft and streaked with viscous, opaque, yellow-white fluid. Intercotyledonary spaces were edematous, roughened, and mottled grey-green, brown, and pink-brown. Soft, irregular, plaque-like, yellow, raised areas were often present around the cotyledons. No significant lesions were present in the kid.

Laboratory Results. Placental bacterial isolates consisted of light growths of E. coli and non-hemolytic Staphylococcus. No bacteria were isolated from the kid. Chlamydial isolation attempts were negative. Serum from the heart blood of the kid was negative for antibodies against Toxoplasma gondii, Chlamydia psittaci, and Coxiella burnetii.

Contributor's Diagnosis and Comments. Severe, diffuse, subacute necrosuppurative placentitis with intralesional and intracellular microorganisms (Coxiella burnetii).

Based on the light microscopic morphology and staining characteristics, the etiology of the placentitis was presumed to be Coxiella burnetii. The microorganisms stained bright red with Machiavello stain, weakly gram-negative, blue-purple with Giemsa and Giemeniz stains, and positive with Steiner's silver method. Equivocal results were obtained with 4 monoclonal and 1 polyclonal immunoperoxidase stains for Chlamydia psittaci (D. Haines and E. Clark, University of Saskatchewan). Two of the monoclonal antibodies gave positive reactions but in a pattern inconsistent with chlamydial infections. Transmission electron microscopy revealed microorganisms free within trophoblast cytoplasm and within cytoplasmic membrane-bound spaces. The ultrastructural morphology of the organisms was consistent with that of Coxiella burnetii.

Moderate to marked, diffuse hepatocellular vacuolar degeneration was the only significant finding in tissues from the kid.

AFIP Diagnosis. Placenta: Placentitis, necrotizing, acute, multifocal, severe, with intratrophoblastic coccobacilli, pygmy goat, caprine.

Conference Note. The Department of Infectious and Parasitic Diseases of the AFIP reviewed this case and agreed that the organisms had ultrastructural features consistent with Coxiella burnetii. Ultrastructurally, Coxiella burnetii is characterized by two trilaminar membranes separated by a periplasmic space with the inner plasma membrane often in close association with peripheral ribosomes. Numerous ribosomes are present peripherally in the cytoplasm while nucleoid filaments are present centrally in either a dispersed state or packed together to form a dense nucleoid mass.

Differential diagnosis for placentitis associated with intratrophoblastic organisms includes Coxiella burnetii, Brucella sp., and Chlamydia sp.

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Microslide 87

History. This 1-week-old male Holstein calf was sacrificed for the collection of cardiac tissue for experimental purposes. The animal was clinically normal at time of sacrifice.

Gross Pathology. A white raised umbilicated mass about 2.5 cm in diameter was found in the interventricular septum. A smaller similar mass was in the right ventricular free wall.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Heart: Myocardial epithelial inclusions.

Epithelial inclusions are an occasional incidental finding in the myocardium of cattle. These inclusions are composed of ductular and/or acinar structures lined by cuboidal to squamous epithelium. Myocardial epithelial inclusions are likely of endodermal origin and are choristomas. They are believed to

arise early in embryogenesis, when endodermal cells from the foregut become trapped within the adjacent heart rudiment. Similar intracardiac epithelial masses have also been reported in swine and humans.

AFIP Diagnosis. Heart, myocardium: Epithelial inclusions, multifocal, Holstein, bovine.

Conference Note. Myocardial epithelial inclusions have been reported in cattle, swine, rats, and humans. The lesions in cattle closely resemble those seen in human atrioventricular nodes; however, several differences exist. The lesions in cattle contain cells with silver-positive cytoplasmic granules less frequently than is found in the epithelial inclusions of humans. The lesions in cattle are not associated with clinical signs while in humans they have been associated with complete heart block and sudden death. Epithelial inclusions are proliferative in neither cattle nor humans. Atriocaval mesotheliomas in aged rats appear somewhat similar histomorphologically. They occur most frequently in the atrial free wall. In contrast to epithelial inclusions, these lesions are proliferative and occasionally metastasize.

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Microslide 88

History. This 4-year-old Suffolk ewe was one of four which were purchased five months previously. This was the third ewe of the four which had pruritus of the hindquarters and had become recumbent. The ewe had lambed approximately three weeks prior to presentation.

Gross Pathology. The ewe was euthanatized by electrocution. Patchy alopecia of the hindquarters was seen. The caudal portion of the dependent lung lobe was diffusely dark red and firm. Numerous adult Haemonchus spp. were present in the abomasum. A retained placenta was present in the uterus.

Laboratory Results. None.

Contributor's Diagnosis and Comments. 1. Degeneration and vacuolation, neuronal, multifocal, moderate, medulla, Suffolk, ovine.

2. Spongiform change, multifocal, mild to moderate, medulla, Suffolk, ovine.

Etiology--consistent with ovine scrapie.

Sections of medulla are provided. Lesions are centered primarily in gray matter. Multiple, round, clear neuronal vacuoles and neuronal pyknosis are seen. Focal areas of hemorrhage are noted in some sections and are likely a result of euthanasia.

Scrapie is an insidious, degenerative disease which affects the central nervous system of sheep and goats. Other names for the disease include la tremblante (French: trembling) and Traberkrankheit (German: trotting disease). Scrapie is the prototype of the group of diseases known as transmissible spongiform encephalopathies; i.e. bovine spongiform encephalopathy (BSE), transmissible mink encephalopathy, kuru, and Creutzfeldt-Jakob disease. Evidence suggests that BSE results from oral infection of cattle with the scrapie agent from infected processed sheep protein. The cause of scrapie is believed to involve interactions among one or more strains of an infectious agent (scrapie agent) and one or more host genetic factors.

AFIP Diagnosis. Brainstem: Neuronal vacuolar degeneration and spongiform change, diffuse, moderate, with mild astrocytosis, Suffolk, ovine.

Conference Note. There are decriptions of a disease syndrome of sheep compatible with scrapie over 300 years old. The scrapie agent is believed to be a prion particle consisting of a neuronal cell surface sialoglycoprotein of 27-30 kDa (PrP 27-30) that contains no nucleic acid. It is derived from a larger protein of 33-35 kDa designated PrP^{SC} which is a protease resistant isoform of a normal cellular protein (PrP^{C}). PrP^{SC} is synthesized from PrP^{C} by a posttranslational process, believed to be a conformational change. The gene encoding PrP^{SC} is not a component of the infectious prion protein but may play a role in the genetic transmission of the disease. In addition, the Sip gene in sheep and Sinc gene in mice play roles in the incubation period of scrapie. There are two alleles (sA and pA) of the sheep gene. Experimentally infected sheep homozygous for the sA allele develop the disease after a shorter incubation period than do heterozygotes. Sheep homozygous for the pA allele are less likely to develop scrapie.

The characteristic microscopic lesions of scrapie include neuronal vacuolation and degeneration, astrocytosis, and vacuolization of the neuropil, primarily in the grey matter of

the brainstem. Vacuolation is most frequently found in the medulla, pons, midbrain, and thalamus. Amyloid plaques may also be present and are immunoreactive for PrP^{SC}.

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Microslide 89

History. One of several mice with a "knockout" (gene deletion) for the p53 tumor suppressor gene. This mouse was a homozygote.

Gross Pathology. A 4.0 x 2.5 x 1.5 cm multilobulated, dark red, mottled mass was observed at necropsy replacing the right testicle.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Malignant teratoma, testis, transgenic mouse. Cause: null mutation for p53 tumor suppressor gene.

Mice in this study have developed a high incidence of malignant tumors at an early age. Tumors have consisted of lymphoblastic lymphomas, osteosarcomas, rhabdomyosarcomas, hemangiosarcomas, mammary adenocarcinomas, malignant schwannomas, and several benign and malignant testicular tumors. Testicular teratomas have been reported in the 129 strain for years. We have seen four malignant teratomas in this study to date. Since the original publication, we have approximately 20 additional heterozygotes with malignancies. This appears to be the first animal model for Li-Fraumeni syndrome in man.

AFIP Diagnosis. Testicle: Teratoma, malignant, C57BL/6 x 129 transgenic mouse, rodent.

Conference Note. Teratomas are uncommon tumors of mice that frequently occur in the gonads and are classified as germ cell tumors composed of elements of two to three different germ cell layers. Tissue elements may be immature or mature and may undergo malignant transformation. Malignant teratomas contain poorly differentiated tissue of which immature nervous tissue with neural rosettes often predominates. Stratified squamous, respiratory, and sebaceous epithelium, as well as neuronal tissue, ocular tissue, and cartilage, in both immature and mature forms, are present in this case with the neuroepithelial and cartilaginous tissues having characteristics of malignancy.

The p53 gene is recognized as a tumor suppressor gene and plays a role in transcription, cell cycle control, and programmed cell death (apoptosis). Part of p53's tumor suppression ability seems to be linked to its ability to turn on a newly discovered gene (WAF1/Cip1) which is responsible for producing a protein, named p21, that arrests cells in mid-cycle by binding to cyclin-dependent kinases and inhibiting their action. When mutated, p53 tumor suppression is not only lost but the mutated forms can stimulate abnormal cell growth. It is the most commonly mutated gene in human tumors occurring in approximately 50% of all human cancers including 70% of colorectal cancers, 50% of lung cancers, and 40% of breast cancers. Mutations in p53 gene in these tumors correlate with more agressive tumors that are more likely to metastasize.

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Laser disc frame #8446, 8449.

Microslide 90

History. This 3-week-old Beefmaster calf was born with hypotrichosis. The animal failed to thrive and died at 3 weeks of age.

Gross Pathology. Renal calyces were dilated and contained cloudy colorless gelatinous material and yellow granular calculi.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Nephrosis, chronic, diffuse, degenerative, marked, with associated oxalate-nephrolithiasis and diffuse interstitial fibrosis.

The lesions in this case are suggestive of congenital oxalate nephrosis. The crystals were identified as calcium oxalate by the Pizzolato method. The history, marked nephrolithiasis and interstitial fibrosis suggest that this was a congenital lesion. Fetal renal oxalosis has been experimentally produced in lambs by feeding pregnant ewes oxalic acid. The owner of this calf reported no significant quantity of oxalate-containing plants in his pasture or hay.

Renal oxalosis has been associated with other congenital defects in neonatal calves. Primary renal oxalosis is an inherited metabolic disease in man caused by one or two different disorders of glyoxylate metabolism. These disorders are clinically similar and are characterized by recurrent calcium oxalate nephrolithiasis, chronic renal failure and early death from uremia. The occurrence and incidence of primary renal oxalosis in animals has not been established.

AFIP Diagnosis. Kidney: Tubular epithelial degeneration and necrosis, diffuse, moderate, with interstitial fibrosis, oxalate crystals, and multifocal chronic-active tubulointerstitial nephritis, Beefmaster, bovine.

Conference Note. Renal oxalosis in ruminants occurs most frequently secondary to ingestion of plants containing high levels of oxalates such as Amaranthus spp., Beta vulgaris, Chenopodium album, Halogeton glomeratus, Oxalis spp., Rumex spp., Rheum rhaponticum, and Sarcobatus vermiculatus. Generally, the highest oxalate concentration is in leaves, with lesser amounts in seeds, and the least amount in stems. Under range conditions, sheep are more susceptible than cattle to toxicosis and horses are relatively resistant. Other causes of renal oxalosis include ethylene glycol, fungi such as Aspergillus and Penicillium spp.,

pyroxidine (vitamin B_6) deficiency, and methoxyflurane anesthesia.

Primary hyperoxaluria has been reported in humans, cats, a family of Tibetan Spaniels, and recently in Beefmaster cattle. In humans, the condition is due to an autosomal recessive trait and is classified into two types. Type I, the most common form, is caused by a deficiency of the hepatic peroxisomal enzyme alanine:glycoxylate aminotransferase. In type II primary hyperoxaluria, there is a defect in hydroxypyruvate metabolism.

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Laser disc frame #102, 3070-1, 7142.

Microslide 91

History. This adult, male fallow deer was found dead. It was kept in a zoo with other deer which seemed normal.

Gross Pathology. Animal in good condition. Fibrinonecrotic ileitis with perforation and locally extensive fibrinous peritonitis. Presence of several small white nodules, 1-3 mm in diameter, in the lungs, liver, and in the wall of the ileum and corresponding mesenteric lymph nodes.

Laboratory Results. *Yersinia pseudotuberculosis* isolated in large amounts from the lungs, liver, ileum and mesenteric lymph nodes.

Contributor's Diagnosis and Comments. Severe multifocal and coalescing necropurulent ileitis with multiple bacterial microcolonies. Cause: *Yersinia pseudotuberculosis*.

In all layers of the ileal wall, there are multiple, often confluent, necropurulent foci around bacterial colonies (gram-negative coccobacilli). Similar lesions are present in the mesentery and mesenteric lymphatics. Yersiniosis has been reported in domestic (cattle, sheep, goats, pigs, dogs and cats) and wild captive (deer and others) animals. Yersiniosis has been reported in several breeds of deer, but the fallow deer does not seem very susceptible to the disease. The disease is caused by Yersinia enterocolitica or Y. pseudotuberculosis and these organisms can occur together in a herd and even in an individual animal.

AFIP Diagnosis. Small intestine: Enteritis, necrosuppurative, circumferential and transmural, multifocal to coalescing, severe, with colonies of coccobacilli, fallow deer, cervid.

Conference Note. Yersiniosis refers to diseases caused by either Yersinia pseudotuberculosis or Y. enterocolitica. It occurs in a variety of mammals, birds, and reptiles. Most outbreaks are precipitated by stress, and the disease commonly occurs during the winter. The natural route of infection is oral; the initial enteric infection is followed by bacteremia and dissemination to other organs. A severe, acute syndrome is typically seen in non-human primates, artiodactyls, and edentates. A subacute, less severe manifestation is most often found in birds. A chronic form of the disease occurs in rodents.

Several virulence factors have been identified. In virulent strains, a plasmid gene is present that encodes V and W antigens that are responsible for resistance to intracellular destruction. V and W antigen production is linked to temperature and Ca^{++} concentrations. Virulent strains also produce invasin, an outer surface membrane protein that attaches to a B_1 integrin cell surface receptor for fibronectin. Invasin has a greater affinity for the receptor than fibronectin and its binding results in internalization of the bacteria. In addition, the gene attachment invasion locus, ail, codes for a surface protein which promotes adhesion.

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International Veterinary Pathology Slide Bank
Laser disc frame #2837, 18263, 19454, 19494.

Microslide 92; Lantern slides 22 and 23

History. Ten minimal disease (MD) grower swine with anorexia, sneezing and respiratory distress were obtained from a MD farm in Taiwan. The farm had 252 MD grower swine which were bought from a SPF farm about 25 days ago.

Gross Pathology. Large amount of clear fluid was accumulated in the thorax and pericardial cavities. Severe edema of the lungs were seen in all cases. The epithelium of both turbinates and nasal cavity had marked hyperemia.

Laboratory Results. Numerous viral particles, ultrastructurally indistinguishable from herpesvirus, were observed by electron microscopy in the affected turbinates.

Contributor's Diagnosis and Comments. Rhinitis with intranuclear inclusions, subacute, diffuse, nasal turbinate, porcine. Etiologic diagnosis: Cytomegalovirus.

Porcine cytomegalovirus (PCV) infection usually induces a clinically silent infection in the adult but often a fatal generalized infection in the young animal. In herds under good management conditions, the virus may be endemic with less significant clinical disease. The occurrence of the disease may be associated with secondary infections such as swine infertility and respiratory syndrome (SIRS) virus, or pseudorabies virus infection. Serological evidence indicates that over 90% of herds have been exposed to infection in the United Kingdom. Diagnosis of PCV infection in swine can be made on the basis of virologic and histological examinations. Large basophilic intranuclear inclusions and cytomegaly are consistently seen in the nasal mucous gland and acinar and duct epithelium of Harderian and lacrimal glands.

AFIP Diagnoses. 1. Nasal turbinates: Rhinitis, subacute, diffuse, moderate, with glandular epithelial cytomegaly, karyomegaly, and basophilic intranuclear inclusions, Landrace, porcine.
2. Lung: Pneumonia, interstitial, subacute, diffuse, moderate, with interlobular and pleural edema.

Conference Note. Inclusion body rhinitis is caused by porcine herpesvirus 2, a betaherpesvirus, and infection is generally species specific. The virus typically causes rhinitis, pneumonia, and reduced growth in young pigs; mummification, stillbirths, and neonatal deaths are also seen. Infection is via the nasal cavity with primary replication of the virus in the nasal mucosal glands, lacrimal or Harderian glands, followed by viremia. The virus disseminates to various epithelial sites, frequently including renal tubules. Gross lesions in young pigs often include widespread petechia and edema, including diffuse pulmonary edema with a prominent interlobular component.

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International Veterinary Pathology Slide Bank
Laser disc frame #15562-6.

Microslide 93

History. One of six adult male African green monkeys (Cercopithecus aethiops) inoculated intraperitoneally with 1000 plaque-forming units of Ebola (Zaire type) virus. The six monkeys were a placebo group in a drug therapy protocol and were treated with saline IM every eight hours beginning one day prior to virus inoculation. All six monkeys died 6 to 7 days postinoculation.

Gross Pathology. Petechiae were present on the eyelids. The liver was mottled dark red-brown to light tan, was friable, and had rounded capsular borders. The stomach mucosa had numerous petechiae.

Laboratory Results. #1 - one day prior to Ebola inoculation. #2 - day of death.

Serum Chemistry:		#1	#2	Normal
Glucose	(mg/dl)	104	27	79-111
BUN	(mg/dl)	15	68	6-20
Creatinine	(mg/dl)	1.0	7.5	0.6-1.4
Na	(mmol/1)	129	139	136-144

K	(mmol/l)	3.7	4.6	3.9-5.1
Cl	(mmol/l)	106	97	99-107
CO_2	(mmol/l)	28	23	24-32
AMYL	(u/l)	926	730	30-110
Calcium	(mg/dl)	8.6	6.3	9.0-10.2
PHOS	(mg/dl)	2.6	16.5	2.6-4.2
TP	(g/dl)	6.2	6.5	6.5-8.1
ALB	(g/dl)	3.5	3.4	3.9-4.7
ALKP	(u/l)	58	1266	36-108
GGT	(u/l)	97	476	8-78
AST	(u/l)	145	10279	10-42
ALT	(u/l)	213	4587	0-50
LDH	(u/l)	2492	3489	290-546
CPK	(u/l)	3523	2000	35-374
CHOL	(mg/dl)	129	166	120-200
TRIG	(mg/dl)	64	1212	35-160
TBIL	(mg/dl)	0.8	3.4	0.3-1.1

CBC Results:		#1	#2
WBC	(X 10^3)	5.1	8.5
RBC	(X 10^6)	7.3	5.7
Hgb	(g/dl)	17.9	14.6
HCT	(%)	54.0	41.6
MCV	(fl)	74.4	72.8
MCH	(pg)	24.7	25.5
MCHC	(g/dl)	33.1	35.1
PLT	(X 10^3)	337	296

Differential(%)	#1	#2
SEG	47	57
Lymph	52	11
Mono	1	0
EOS	0	32

Coagulation:	#1	#2	Normal
PT	9.0	12.8	9.8-12.8
PTT	22.0	78.9	23.3-34.0

Contributor's Diagnosis and Comments. 1. Liver: Hepatocellular degeneration and necrosis, multifocal to coalescing, random, moderate with minimal acute inflammation, Kupffer cell hypertrophy, and multifocal eosinophilic intracytoplasmic hepatocellular inclusions.

2. Spleen, cords of Bilroth: Fibrin deposition and histiocyte loss/necrosis, diffuse, moderate.

3. Spleen, white pulp: Lymphoid depletion and lymphocytolysis, diffuse, moderate.

4. Spleen, white pulp: Fibrin thrombi, multifocal, mild.

5. Spleen, marginal zone: Congestion/hemorrhage, diffuse, mild.

Etiology: Ebola (Zaire type) virus.

The filoviridae family consists of one genus, Filovirus. Marburg virus and Ebola (Zaire type, Sudan type, and Reston type) virus are the two species in the genus. Marburg virus and Ebola (Zaire type and Sudan type) virus are clearly associated with the

African continent. The recent exportations of Ebola (Reston type) virus infected monkeys from the Philippines may indicate the existence of other filoviruses. During the 1976 Ebola outbreaks in Zaire and Sudan, the estimated case fatality rates in human beings were 88% for the Zaire type and 53% for the Sudan type. More recently, the Ebola (Reston type) virus was isolated from cynomolgus monkeys imported into the U.S. in 1989-1990, and from monkeys at the export facility in the Philippines. While highly lethal for naturally and experimentally infected monkeys, Ebola (Reston type) virus may be less virulent for humans, having infected four animal caretakers without causing clinical illness.

The natural sources and ecology of filoviruses are unknown. These viruses have a tropism for cells of the mononuclear phagocyte system and fibroblasts. The mode of entry of the filoviruses into cells remains unknown. Virion assembly involves budding from the plasma membranes of preformed nucleocapsids; nucleocapsids also accumulate in cytoplasm, forming prominent inclusion bodies.

In Rhesus and African green monkeys inoculated with Ebola (Zaire type), the virus replicates to high titer in liver, spleen, and lymph nodes during the incubation period. Lesions include necrosis in liver and adrenal glands, fibrin thrombi in multiple organs, and interstitial hemorrhage, which is most evident in the gastrointestinal tract. Necrosis in liver and adrenal glands is caused directly by virus infection of parenchymal cells, and typically there is very little inflammatory response. Biochemical dysfunction of endothelial cells and platelets during Ebola (Zaire type) viral infection has been demonstrated and has been associated with edema, multiple effusions, hemorrhage, and hypovolemic shock. In primate infections, the intrinsic clotting pathway is affected and the extrinsic pathway is spared.

AFIP Diagnoses. 1. Spleen, red pulp: Fibrin deposition and necrosis, diffuse, moderate, African green monkey (Cercopithecus aethiops), non-human primate.
2. Spleen, white pulp: Lymphoid depletion and lymphocytolysis, diffuse, moderate, with marginal zone congestion/hemorrhage.
3. Liver: Hepatocellular degeneration and necrosis, multifocal to coalescing, random, moderate, with minimal acute hepatitis, and multifocal eosinophilic intracytoplasmic hepatocellular inclusions.

Conference Note. Differential diagnosis for the splenic lesion was discussed and includes Ebola, simian hemorrhagic fever, anthrax, Rift Valley fever, severe endotoxemia or other causes of disseminated intravascular coagulation. Hepatic necrosis with formation of Councilman-like bodies (apoptotic bodies), as seen in this case, is not a feature of simian hemorrhagic fever but is seen in the other viral hemorrhagic

fevers including Ebola, Marburg, and yellow fever. Yellow fever virus typically produces midzonal hepatic necrosis and nephrosis. Ebola virus is pantropic and produces large amphophilic intracytoplasmic inclusion bodies in many tissues, most commonly including the liver, spleen and adrenal gland.

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Microslide 94

History. Tissue from a one-year-old female Angus cross that was one of ten in a group of 101 yearling cattle grazing a winter small-grain pasture that developed chronic, nonpruritic dermatitis, lacrimation, diarrhea, and wasting.

Gross Pathology. Cutaneous thickening and folding, corneal ulceration, multiple raised eroded lesions of tongue; focal, raised multicystic lesions in gallbladder and biliary mucosa; small, very firm pancreas; diffusely pale, moist renal cortices; cystic changes in Gartner's ducts and mesonephric remnants of mesosalpinx.

Laboratory Results. Serum vitamin A - 63 ng/ml (normal 250-450 ng/ml). Toxicologic investigation - Assay of 4 different sources of grease revealed one to contain > 500 ppm tetrachlornaphthalene.

Contributor's Diagnosis and Comments. 1. Pancreas, fibrosis, interlobular and intralobular (moderately severe) with acinar atrophy.
2. Salivary gland, mandibular, squamous metaplasia of ductal epithelium.
3. Salivary gland, sialoadenitis, interstitial, lymphocytic/ plasmacytic, mild.

AFIP Diagnoses. 1. Salivary gland, ducts: Metaplasia, squamous, multifocal, moderate, Angus cross, bovine.

2. Salivary gland: Sialoadenitis, subacute, multifocal, mild.
3. Pancreas: Fibrosis, interstitial, diffuse, moderate, with mild acinar atrophy.

Conference Note. Bovine hyperkeratosis or X-disease is caused by chlorinated naphthalene toxicosis and is primarily a disease of historical interest since the causative chemicals have not been in use for over thirty years. Chlorinated naphthalenes were used as lubricants, wood preservatives, and in asphalt roofing paper. In oral toxicity studies, di- and trichloronaphthalene do not to produce clinical signs, while tetra-, penta-, hexa-, hepta-, and octachloronaphthalene are toxic with hexa- and heptachloronaphthalene being most toxic. The toxin is cumulative and intoxication can result from a large single exposure or chronic low levels of exposure.

Clinical signs of intoxication include excessive lacrimation, salivation, depression, and weight loss with subsequent development of non-pruritic dermatopathy characterized by hyperkeratosis and alopecia. In addition to the changes in the skin, widespread epithelial hyperplasia and metaplasia is seen throughout the body including ducts of salivary glands and pancreas, gallbladder, bile ducts, and epithelial linings of the genital tract. Pancreatic fibrosis and acinar atrophy have also been reported but are not specific to this disease. Secondary infections with papular stomatitis virus and dermatophytes are common.

Intoxication with chlorinated naphthalenes is thought to interfere with the conversion of carotene to vitamin A, but the exact mechanism is poorly understood. Plasma levels of vitamin A drop prior to the onset of clinical signs and remain low for several weeks. Vitamin A therapy can alleviate some clinical signs but is usually not curative.

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International Veterinary Pathology Slide Bank
Laser disc frame #417-19.

Microslide 95

History. Tissue is from a ten-year-old male horse, one of twenty horses that were fed with 40% of Crotalaria juncea seeds in the diet. After 30 and 60 days of treatment, all of them showed staggering, dyspnea and fever, culminating in death. Cattle that received the same diet presented no signs of intoxication.

Gross Pathology. The lungs had edema, congestion, and diffuse areas of consolidation of the parenchyma. The liver was enlarged by congestion. The cause of death was diagnosed as pulmonary failure.

Laboratory Results. Male guinea pigs were fed with C. juncea seeds in the diet at the same level as the horse diet (40%). Three animals died with dyspnea 4 months after the beginning of the treatment. Pulmonary and hepatic lesions were similar to those in the horses.

Contributor's Diagnosis and Comments. The lungs showed a characteristic diffuse fibrosing alveolitis, with thickening of the alveolar walls by edema, an inflammatory infiltrate and fibrosis, and the alveoli were flooded by edema and lined by hyaline membranes. The liver was congested with dilatation of sinusoids and compression of hepatocyte trabeculae.

Several species of Crotalaria are poisonous to man and domestic animals. C. spectabilis is probably the most poisonous species. Other toxic species include C. retusa, C. burkeana, C. sagitallis, C. juncea, C. dura, C. equorum, C. globifera and C. striata. The toxic manifestation can be observed in the liver, but can also occur in lungs by the release of the reactive metabolite into the sinusoidal blood. In the present case, pulmonary lesions were most prominent, and are compatible with a blood borne insult.

The toxic principles capable of causing the lesions of Crotalaria poisoning have been identified. The pyrrolizidine alkaloid monocrotaline is found in the leaves and seeds of Crotalaria spectabilis. Two other alkaloids, fulvine and crispatine, have been isolated and identified as macrocyclic esters of retrorsine. In C. juncea seeds, trichodesmine was identified as the principal toxic pyrrolizidine alkaloid by Zhang, 1985, and other chemical constituents identified are senecionine and junceine.

Pyrrolizidine alkaloids are known to be hepatotoxic. After their absorption from the alimentary tract they are metabolized in the liver and converted to highly reactive pyrrolic derivatives. Their metabolites are considered to bind rapidly to

tissue components and are believed to be responsible for the cell injury that occurs.

The reproduction of the disease in experimental animals confirmed the diagnosis of C. juncea poisoning.

AFIP Diagnoses. 1. Lung: Pneumonia, interstitial, chronic, diffuse, moderate, with interstitial fibrosis, hyaline membranes, and edema, breed unspecified, equine.
2. Liver: Sinusoidal dilatation, diffuse.

Conference Note. Pyrrolizidine alkaloids are found in a number of different plants including the genera Crotalaria, Senecio, Heliotropium, Cynoglossum, Amsinckia, Echium, and Trichodesma. Most toxic plant species contain more than one of the over 100 chemically defined pyrrolizidine alkaloids. The toxins must be metabolized by dehydrogenation of the parent alkaloid to highly reactive pyrroles before the full toxic effect is seen. The toxicity of the alkaloid for a specific organ depends on the rate at which the parent alkaloid is converted to the pyrrolic derivative, the proportion of alkaloid converted, and the reactivity or binding capacity of the pyrrole. These can vary with species, sex, and age of the animal intoxicated. Sheep and goats tend to be most resistant to intoxication, cattle and horses are intermediate, and swine are the most susceptible of domestic animals to intoxication.

The most characteristic hepatic lesions induced by this toxin are megalocytosis and bile duct proliferation, which were not apparent in this case. Pulmonary vascular and interstitial changes, as seen in this case, are also reported lesions. The alkaloids from Crotalaria sp. are more likely to affect a wide range of tissues in intoxicated animals than are other alkaloid-containing plant species.

The differential diagnosis for the chronic interstitial pneumonia includes pyrrolizidine alkaloid toxicosis and crofton weed (Eupatorium adenophorum) toxicosis.

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International Veterinary Pathology Slide Bank
Laser disc frame #13554, 20627, 20939-41, 23321, 23881, 23918-9.

Microslide 96; Lantern slide 24

History. This 13-year-old, castrated male Domestic Shorthair cat had chronic renal disease that had been managed well for 6 years. He was examined in November 1992 at the Auburn University Small Animal Clinic for progressive weight loss over the past 6 months. He was cachectic (6 lbs) and had palpable abdominal masses. Hepatomegaly, splenomegaly, a markedly thickened colon wall, and a mass caudal to the left kidney were seen on abdominal radiographs.

Gross Pathology. No necropsy was performed. At the time of abdominal laparotomy, the liver was enlarged, mottled, and slightly pale. The mesenteric lymph nodes were enlarged with a granulated grey/pink appearance. The walls of sections of the jejunum and ileum were thickened and firm.

Laboratory Results. The cat was negative for FeLV (ELISA) and FIV (Cite), and had a FIP (IFA) titer of <1:100 which is considered negative. His T_4 concentration was 54 nmol/L (10-50) which is above the reference range, but the cat was not considered to have hyperthyroidism as his primary disease.

CBC results:

Hct	31.9%	(30-45)
total WBC	18,900/ul	(5,500-19,500)
segmented neutrophils	17,010/ul	(2,500-12,500)
lymphocytes	378/ul	(1,500-7,000)
monocytes	1,134/ul	(0-850)
eosinophils	378/ul	(0-750)
platelets	291,000/ul	(300,000-700,000)

Clinical chemistry results (abnormal)

ALT	715 IU/L	(26-52)
SAP	471 IU/L	(6-51)
CK	442 IU/L	(100-250)
creatinine	2.4 mg/dl	(0-1)
BUN	51 mg/dl	(5-30)
Ca^{+2}	8.7 mg/dl	(9.5-11.6)
inorganic phosphate	3.2 mg/dl	(4.3-5.9)
total protein	5.9 g/dl	(6.2-7.7)
albumin	2.4 g/dl	(2.8-3.7)
total bilirubin	4.3 mg/dl	(0.15-0.2)
anion gap	17.6	(8.2-14.0)

Cytologic Findings: An ultrasonically guided fine needle aspirate obtained from an abdominal mass (mesenteric lymph node) consisted of a highly cellular population of mixed lymphoid cells. Approximately 60% of the cells were medium to large discrete round cells with round to oval nuclei, fine, dispersed chromatin and multiple nucleoli, and scarce to numerous small to large acidophilic granules in the cytoplasm. The nuclei were eccentrically located and the granules were to one side of the nucleus or next to the nuclear indentation. Small mature lymphocytes made up approximately 30% of the cells, with fewer plasma cells, macrophages, and neutrophils.

Contributor's Diagnosis and Comments. Large granular lymphoma.

The normal hepatocellular architecture is disrupted by large multifocal areas of increased cellularity owing to variably sized densely packed cells. These cells have oval to irregular nuclei with marginated chromatin, one to several prominent nuclei, and moderate amounts of acidophilic cytoplasm with a grainy appearance. Mitotic figures are 1-2 per HPF. There is granular brown pigment in hepatocytes and between hepatocytes.

The neoplastic cells do not stain with toluidine blue (T-blue), Prussian blue, or periodic acid-Schiff (PAS). Granules within the neoplastic cells stain faintly pink with Giemsa and black with phosphotungstic acid-hematoxylin (PTAH).

Ultrastructurally, the cells are discrete with no intercellular junctional complexes. There are numerous intracytoplasmic 1 to 1.5 μm diameter granules usually located within indentations of the nucleus. The granules are membrane bound with variably dense cores. Some contain membrane whorls.

Neoplasms characterized by large round to oval cells with round to indented nuclei and having few to numerous granules or globules within the cytoplasm, involving the intestines, liver, spleen, lymph nodes and other tissues of cats have been previously diagnosed as either neoplasms of globule leukocytes or as large granular lymphoma. Only three cases of neoplasia of globule leukocytes and approximately 20 cases of large granular lymphoma have been reported in the literature. Descriptions of signalment, clinical signs, neoplasm distribution, and cytologic, histologic and ultrastructural characteristics are similar between the two neoplasms. Cellular cytochemical staining results are varied as are histochemical staining results. The authors of a review article state that a difference between these two types of cells is that large granular lymphocytes fail to stain with phosphotungstic acid-hematoxylin (PTAH), while globule leukocytes are reported to stain strongly. Additionally, the granules of large granular lymphocytes are either not visible or

are faintly visible with H&E, while granules of globule leukocytes are readily visible. However, one early case report and another recent article state that their large granular lymphoma cells stained strongly with PTAH as did the cells of the neoplasm presented here. I suggest, as did Drs. J. W. Harvey and M. Calderwood Mays in a letter to the editor of Veterinary Pathology in 1987 and Drs. M.F. McEntee, S. Horton, J. Blue, and D.J. Meuten in an article in Veterinary Pathology 30:195-203, 1993, that these cases may represent the same disease with somewhat different presentations.

AFIP Diagnosis. Liver: Granulated round cell tumor, Domestic Shorthair, feline.

Conference Note. Conference participants preferred the more general terminology of granulated round cell tumor due to the uncertainty in distinguishing large granular lymphocyte tumors from globule leukocyte tumors. Features of granulated round cell tumors of cats include eosinophilic cytoplasmic granules on H&E sections that stain deep blue with phosphotungstic acid-hematoxylin (PTAH), prevalence of abdominal involvement, especially distal small intestine and lymph nodes, and a feline leukemia-negative status. These tumors have a poor prognosis with frequent metastasis and rapid progression. The cell of origin of these tumors is unknown but may include B and T lymphocytes, granulated intraepithelial lymphocytes, globule leukocytes, mucosal or cutaneous mast cells, or other myelogenous cell types.

Contributor. Auburn University, Department of Pathobiology, 166 Greene Hall, Auburn University, AL 36849-5519.

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International Veterinary Pathology Slide Bank
Laser disc frame #14281-5, 14457-8, 23336.

Microslide 97

History. This 1-year-old Angus/Hereford cross, female bovine was one of a group of 17 found seemingly "in a daze" in sternal recumbency, but still able to rise. She was loaded into a truck and taken home where she died that night. The pasture in which the cow had been kept bordered a glacial lake which was covered by a thick layer of green algae on the day the heifer was discovered. Water samples were collected the day after the heifer's death.

Gross Pathology. There were ecchymotic to paint brush hemorrhages in the subcutaneous tissue, abdominal fat, submucosa of the trachea, epicardium, and endocardium. The intestines from the mid-duodenum posteriorly were filled with blood. The liver was swollen and mottled. The mesentery was edematous and there was excessive ascitic fluid.

Laboratory Results. Bacterial and virologic isolation techniques did not yield positive results. Microcystis aeruginosa, a cyanobacteria (blue-green algae) was identified in the 3 water samples. A portion of one of the water samples was frozen and thawed. After centrifugation, the supernatant was filtered through a 0.45 μm pore diameter filter. Four of four mice injected intraperitoneally (IP) with 0.5 ml of the filtrate and two of four mice injected IP with 0.25 ml of the filtrate died in less than two hours. Histologic lesions in the liver were similar to those in the heifer. Further analysis of the algae determined the estimated LD_{50} for ICR-Swiss male mice was 50 mg/kg which indicated moderate to high levels of toxicity. Enzyme linked immunosorbent assay demonstrated about 4 mg of microcystin per gram of dried algae cells. (Toxicity LD_{50} and microcystin identification by Dr. W. W. Carmichael, Department of Biological Sciences, Wright State University, Dayton, Ohio).

Contributor's Diagnosis and Comments. Acute confluent submassive necrosis and hemorrhage, liver, bovine. Etiology: microcystin produced by Microcystis aeruginosa.

Ingestion of toxic cyanobacteria (blue-green algae) has been responsible for intermittent sickness and death of livestock, pets, and wildlife. All continents, except Antarctica, have documented blooms (the visible coloration of a water body due to suspended cells, filaments and/or colonies) of toxic cyanobacteria. Conditions that favor water blooms are: 1) nutrient loading, 2) retention of water within a water body, 3) stratification, and 4) increased water temperature. Nutrient loading, due to nitrates and phosphates from agricultural run-off and sewage plant discharge, is probably the most important controllable factor affecting the occurrence of cyanobacterial blooms.

Microcystins are a group of related hepatotoxin produced by cyanobacterial species of the genera Microcystis, Oscillatoria, Anabaena, and Nostoc. Microcystins are absorbed from the ileum and apparently are transported preferentially into hepatocytes. Within hours, there is massive hepatocellular necrosis. In animals dying acutely, it is felt that death results from hypovolemic shock due to intrahepatic hemorrhage. In animals surviving the acute phase, hepatic insufficiency and photosensitization are not uncommon. Toxicity due to hepatotoxin, microcystins, nodularin, and unidentified hepatotoxins is the most commonly reported form of cyanobacteria poisoning. However, neurotoxins are produced by species of Anabaena, Aphanizomenon, Oscillatoria, and Trichodesmium. Most of these toxins act as postsynaptic cholinergic nicotinic agonists which cause a depolarizing neuromuscular blockade, or they inhibit cholinesterase.

AFIP Diagnosis. Liver: Necrosis and hemorrhage, submassive, diffuse, Angus/Hereford cross, bovine.

Conference Note. Microcystin-LR, a cyclic heptapeptide hepatotoxin, is the major toxin produced by Microcystis aeruginosa. It is taken up by hepatocytes by binding to a hepatocyte-specific, bile acid carrier. Microcystin-LR causes a rearrangement of filamentous actin via an unknown mechanism in hepatocytes; however, it does not involve actin depolarization or prevention of actin assembly as seen with other low molecular weight peptides. This disruption of actin results in shape changes in the plasma membrane leading to cell rounding and hepatocellular dissociation and necrosis. Sinusoidal endothelium is disrupted leading to hemorrhage into the adjacent parenchyma. Death occurs due to loss of hepatic function and circulatory collapse.

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International Veterinary Pathology Slide Bank
Laser disc frame #22489.

Microslide 98

History. This 8-year-old Domestic Shorthair spayed female cat had a four day history of hind end paresis, hyperesthesia, hypersalivation, and depression. After being released back to owner had several five-hour episodes of "rage"-type activity.

Gross Pathology. Cut surface of the brain demonstrated small (up to 1 mm in diameter) multifocal areas of dark red discoloration (interpreted as hemorrhages) and locally extensive areas of softening (malacia) within the right hippocampus.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Acute severe diffuse ischemic necrosis - hippocampus. Feline ischemic encephalopathy.

This section of brain is characterized by perivascular cuffing, multifocal areas of hemorrhage, diffuse moderate microgliosis, neuronal loss and widespread areas of spongiform degeneration within the hippocampus. Surviving neurons of the pyramidal layer of the hippocampal cortex and the granular layer of the dentate gyrus exhibit nuclear pyknosis, karyolysis and a small amount of shrunken strongly eosinophilic cytoplasm. Hypertrophy of the vascular endothelium is present in areas of hemorrhage. Moderate numbers of neutrophils are seen within the Virchow-Robin spaces and the adjacent neuropil. These lesions are compatible with those reported in feline ischemic encephalopathy. Feline ischemic encephalopathy is a neurological syndrome recognized in adult cats of any breed and sex. This syndrome is characterized by an acute onset of predominantly unilateral cerebral signs, behavioral changes and seizure disorders. Aggressive behavior and hysteria are associated with involvement of limbic system (amygdala and hippocampus). Although most of the reported cases have been seen in summer, this particular case occurred in winter. Histologically, feline ischemic encephalopathy is characterized by extensive ischemic necrosis of the cerebral cortex and subcortical limbic system structures. Although the lesions occur in the areas perfused by

the middle cerebral artery, evidence of occlusion is often not detected. The cause and pathogenesis are unknown.

AFIP Diagnosis. Brain, cerebrum, hippocampus: Necrosis, diffuse, with multifocal hemorrhage, Domestic Shorthair, feline.

Conference Note. The necrosis involves all elements of the hippocampus and is compatible with an infarct. Differential diagnosis for this lesion would include feline ischemic encephalopathy, thiamine deficiency, trauma to the base of the brain, migrating parasites such as seen in aberrant heartwom disease, or possibly toxic causes. The minimal inflammatory response is incompatible with most infectious causes.

Feline ischemic encephalopathy is an uncommon disease of adult cats of unknown etiology. The onset of the disease is acute to peracute with non-progressive clinical signs that sometimes regress.

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International Veterinary Pathology Slide Bank
Laser disc frame #273, 1186, 2653-5, 7278-84, 7645, 15754.

Microslide 99

History. This 12-year-old spayed female Afghan Hound had a history of discomfort when defecating and had tenesmus. A mass was palpated in the region of the left anal sac. The mass was surgically removed.

Gross Pathology. A discrete lobulated 2 X 3.5 X 3.5 cm firm mass is received fixed in formalin. A tag of black mucosa is attached to one margin of the mass. On cross section, the mass is irregular, tan-white and firm throughout.

Laboratory Results. Serum chemistry data indicated hypercalcemia (23.4 mg/dl) and hypophosphatemia (2.8 mg/dl).

Contributor's Diagnosis and Comments. Adenocarcinoma of anal sac gland.

The section consists of a multilobular, discrete, proliferation of neoplastic epithelial cells adjacent to non-haired squamous epithelium and perianal apocrine glands. The cells form numerous variably sized tubules and frequently contain eosinophilic secretory material. The neoplastic cells are cuboidal to columnar, have a moderate complement of eosinophilic cytoplasm and prominent hyperchromatic round-to-oval nuclei. Mitotic figures are found in small numbers. The lobules are surrounded by fibrovascular stroma which contains scattered infiltrates and islands of lymphocytes.

Neoplasms arising in the perianal region of dogs are common. The majority of tumors arise from the perianal glands (hepatoid glands) which are modified sebaceous glands. In contrast, tumors arising from the apocrine glands of the anal sac are rare. Anal sac gland adenocarcinomas are more common in females whereas perianal gland tumors are found more commonly in males. Metastases occur via lymphatics to regional nodes. The paraneoplastic syndrome of hypercalcemia and hypophosphatemia is a consistent finding in animals with these tumors. The serum calcium and phosphorus will return to normal upon excision of the primary mass if metastatic disease is not present. Practically all anal sac apocrine gland tumors are carcinomas. Despite the fact that there is little anaplasia, foci of stromal or lymphatic invasion can frequently be identified in histologic sections.

AFIP Diagnosis. Anal sac (per contributor): Adenocarcinoma of the apocrine glands of the anal sac, Afghan Hound, canine.

Conference Note. Humoral hypercalcemia of malignancy (pseudohyperparathyroidism) is a paraneoplastic disorder in which bone-resorbing substances such as parathyroid hormone, parathyroid hormone-like peptides, prostaglandin E_2, osteolytic sterols, and osteoclast-activating factor are secreted by malignant neoplasms of nonparathyroid origin. In the case of adenocarcinoma of the apocrine glands of the anal sac, parathyroid hormone-like peptide is secreted by neoplastic cells. This substance causes hypercalcemia by increasing both osteoclastic bone resorption and renal 1 α-hydroxylase activity, resulting in inappropriately high levels of 1,25-dihydroxycholecalciferol. In dogs and cats, lymphosarcoma is the most common neoplasm associated with hypercalcemia. Hypercalcemia has been reported in horses with lymphosarcoma, squamous cell carcinoma, and malignant mesenchymoma. It has also been reported in granulomatous diseases such as blastomycosis, possibly due to abnormal vitamin D metabolism.

Grossly, adenocarcinomas of the apocrine glands of the anal sac are usually unilateral but occasionally bilateral. They occur in the perineal subcutaneous tissue ventrolateral to the anus and appear as multilobulated, tan masses with foci of necrosis and cystic spaces which may contain blood-tinged fluid. Other lesions, primarily associated with pseudohyperparathyroidism, include hypoplasia of the parathyroid glands, renal mineralization, and decreased trabecular bone volume with an increase in the number of osteoclasts.

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International Veterinary Pathology Slide Bank
Laser disc frame #3815, 8346-8.

Microslide 100

History. This 2-year-old neutered female Boxer had intermittent blood-tinged diarrhea since 6 months of age. It was best managed on low fat diets. Repeated fecal examinations were negative. Treatment with metronidazole was ineffective. With onset of severe weight loss and anorexia, the dog was submitted to the Mississippi State teaching hospital. During IV catheter placement, she went into cardiac arrest and died.

Gross Pathology. Dehydration and thin body condition. Purulent vaginal discharge associated with pyometra of the remnant of a uterine horn. Rectal wall was 2 to 4 mm thick with mucosal congestion and dark blood on the surface.

Laboratory Results. Microbiology: No pathogens isolated. BUN 50 mg/dl, Creatinine 1.4 mg/dl, Total protein 7 mg/dl, Albumin 3.1 mg/dl, ALT 22 mg/dl, Alkaline Phosphatase 37 mg/dl, WBC 17,900, Seg 63%, Lymph 20%, Monos 13%, Bands 4%.

Contributor's Diagnosis and Comments. Chronic multifocal ulcerative histiocytic colitis. Etiology: Idiopathic histiocytic Boxer colitis of unknown etiology.

The colon contains multifocal areas of ulceration up to 1 mm in diameter characterized by loss of mucosa extending to the muscularis mucosa. The lamina propria, submucosa, and portions of the muscular layers are diffusely infiltrated by PAS-positive macrophages and moderate numbers of lymphocytes.

Chronic ulcerative histiocytic colitis associated with PAS positive macrophages is consistent with a diagnosis of "idiopathic boxer colitis". The causative agent and pathogenesis of this condition are unknown.

AFIP Diagnosis. Colon: Colitis, ulcerative, histiocytic, chronic, diffuse, severe, Boxer, canine.

Conference Note. Histiocytic ulcerative colitis is an uncommon condition characterized by mucosal ulcerations and the accumulation of histiocytes that contain abundant PAS-positive material. It occurs primarily in Boxers under two years of age, but has also been reported in French Bulldogs and cats. The etiology is unknown but several theories have been proposed including a deficiency in lysosomal enzymes, inability of the macrophages to process normal amounts of absorbed foreign material, or inhibition of foreign material degradation by some ingested material with normal macrophage function. An infectious etiology has also been proposed due to ultrastructural studies that have found Chlamydia-like organisms in some cases; however, the disease has not been reproduced experimentally by the transmission of organisms. Affected dogs may be genetically predisposed.

Contributor. Mississippi State University, College of Veterinary Medicine, P.O. Drawer V, Mississippi State, MS 39762.

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International Veterinary Pathology Slide Bank
Laser disc frame #4720, 14006.

Microslide 101

History. This 2-year-old spayed Persian cat was presented with a one month history of anorexia. The cat was depressed, cachectic and approximately 8% dehydrated. Blood count showed a non-regenerative anemia. The cat was very sensitive on its dorsal cervical region. The cat was treated with intraveneous fluid, ampicillin and vitamin supplementation and was sent home the day after. It became alert with a good appetite and continued with oral therapy. Two weeks later the cat presented with a skin tear of about 5 cm in diameter without bleeding in the dorsal cervical area. The skin was very thin and fragile, and was easily torn while clipping the hair. Following the clinical workup a diagnosis of feline hepatic lipidosis was made. Three days later, further sloughing of the skin was noticed. The cat was euthanized.

Gross Pathology. Parts of the skin were missing from different areas of the body. In some areas the skin was still connected but looked like degloving wounds. Areas of skin which looked intact were easily pulled off the cat. (Postmortem was done 20 minutes after death.) The liver was enlarged, yellow to orange and had a fatty appearance. No other changes were noticed.

Laboratory Results. Blood count showed a non-regenerative anemia.

HB	9.0 g/dl
PCV	28%

Blood chemistry:

ALT	586 U/L
AST	157 U/L
ALP	1259 U/L
T. Bil.	1.45 G/DL

Ultrasound of the liver showed no abnormality in size and echoicity. FIV/FeLV tests were negative. Blood sample at that time showed very lipemic serum.

Triglyceride	3361 mg/dl
ALT	131 U/L
AST	49 U/L
T. Bil.	2.35 mg/dl

Contributor's Diagnosis and Comments. Skin: Severe dermal atrophy. Moderate sebaceous gland atrophy. Feline skin fragility syndrome.

Feline skin fragility syndrome is a rare disease of multifactorial etiology characterized by markedly fragile thin skin. During 1993 we have seen two cases of this syndrome associated with severe hepatic lipidosis as it was described by Diguelou. Secondary inflammation was seen in the dermis that was already separated from hypodermis and was absent or very mild in affected skin which was still connected to the subcutis. The severe dermal atrophy is due to the very small amounts of collagen fibers and less due to adnexal atrophy.

AFIP Diagnosis. Haired skin, dermis, epidermis, and adenexa: Atrophy, diffuse, moderate, with follicular and epidermal hyperkeratosis, Persian, feline.

Conference Note. Grossly, cutaneous fragility is associated with collagen dysplasias (cutaneous asthenia, dermatosparaxis, Erlers-Danlos syndrome), feline fragility syndrome, and hyperadrenocorticism from endogenous or exogenous causes. Histopathologically, feline skin fragility sydrome is distinct from dermatospraxis in that there is severe attenuation of dermal collagen, epidermis, and adenexa. In contrast, the amount of dermal collagen in collagen dysplasias is often normal. If depleted, it is not as severely depleted as is seen in this case. Ultrastructural evaluation is often necessary to identify the collagen deformity.

Contributor. Department of Pathology, Institute Beit-Dagan 52050, Israel.

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International Veterinary Pathology Slide Bank
Laser disc frame #7905-6, 14526-7.

Microslide 102; Lantern slide 25

History. A seven-year-old, castrated, male Domestic Shorthair cat presented with a firm mass in its left elbow and history of progressive lameness over several months. Radiographs revealed bony erosions and lysis in distal humerus, proximal radius, and ulna. The left foreleg was disarticulated.

Gross Pathology. The left elbow joint was swollen around the anterior and lateral aspects by a pinkish white mass with mixture of dark purple-grey areas. Erosions and lysis of bone were observed in the cortex and medulla of distal humerus and proximal radius and ulna.

Laboratory Results. Serum biochemical analysis revealed total serum protein of 7.3 g/dl (reference range 5.3-7.6 g/dl) with 3.8 g/dl (reference 3-4.1 g/dl) in the globulin fraction.

Contributor's Diagnosis and Comments. Tumoral amyloidosis with variably dense infiltrates of plasma cells in the soft tissues around the left elbow joint, distal humerus, and proximal radius and ulna.

Histopathologically, large areas of musculature, synovial and juxta-articular tissues and cancellous bones in and around the elbow joint had been replaced by homogeneous to fibrillar eosinophilic deposits mixed with debris and individual or clustered plasma cells. These lesions are different from those in cats with multiple myeloma, in which sheets of closely packed plasma cells replace the bone marrow elements and destroy the adjacent trabeculae. Markedly increased numbers of active osteoclasts are seen on the bone-resorbing surface areas with heavy infiltration of plasma cells.

AFIP Diagnosis. Bone, humerus, and adjacent soft tissue: Plasmacytoma/myeloma, with tumoral amyloidosis, Domestic Shorthair, feline.

Conference Note. This case was reviewed by the Department of Orthopedic Pathology of the AFIP. The moderator, conference participants and the Department of Orthopedic Pathology believed the plasma cells were neoplastic based on the presence of anisocytosis, atypia, and high mitotic rate. The amyloid exhibits an apple green birefringence when stained with Congo Red and viewed under polarized light. In myeloma, neoplastic plasma cells may produce a homogenous immunoglobulin or immunoglobulin fragment termed M-component. The amyloid is usually composed of abnormal immunoglobulins (β or γ globulins) or their light or heavy chain components. The Department of Orthopedic Pathology commented that this case resembles tumoral amyloidosis associated with plasmacytoma/multiple myeloma in humans. An associated pathologic fracture of the humerus was present in most sections.

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International Veterinary Pathology Slide Bank

Laser disc frame #1198, 2633, 7863, 8942, 12205.

Microslide 103

History. Femoral and maxillary bone from a two-year-old female $B6C3F_1$ mouse that was on a 2-year inhalation study to evaluate the carcinogenic potential of a particulate compound. The mouse was sacrificed for evaluation at the termination of the study after being exposed 6 hours/day, 5 days/week for 104 weeks.

Gross Pathology. The marrow cavity of the femoral bone was irregularly narrowed by yellow, rubbery tissue.

Laboratory Results. None.

Contributor's Diagnoses and Comments. 1. Femoral bone, diaphysis and metaphysis: Myelofibrosis, moderate.

2. Maxillary bone: Myelofibrosis, moderate.

Myelofibrosis occurred in control and exposed mice with approximately equal frequency. In the femur, the metaphyseal and diaphyseal bone and subcortical marrow spaces are generally affected. In the maxilla, myelofibrosis generally occurs in the marrow spaces of the maxillary bone of the dorsal nasal cavity, and lateral and ventral to the roots of the incisor teeth. The severity of the lesion varied among animals. In general, it is characterized by minimal to mild proliferation of spindle cells in an eosinophilic, often fibrillar, extracellular matrix in the cortex of the bone. However, in the more advanced cases such as shown here, the spindle cell proliferation is more extensive and the lesion appears osteosclerotic. The proliferating spindle cells partially or completely replace the bone marrow and often are associated with extensive or focal proliferation of trabecular bone (hyperostotic enostosis). In some cases, the presence of osteoclasts in association with the trabeculae is an indication that active remodeling of the bone was in progress. A

section of the nasal cavity contains an adenoma of the harderian gland; this neoplasm is not present in all of the sections.

Myelofibrosis is a spontaneously occurring alteration that is commonly seen in various strains of aging female mice. The lesion is frequently multicentric involving the vertebrae, sternebrae, femur, and bones of the skull, and varies in severity. Synonyms used to describe this alteration include: fibro-osseous lesion, osteosclerosis, myelosclerosis, endocrine osteomyelofibrosis and myelostromal proliferation. Osteosclerosis is believed to be an end stage of myelofibrosis.

The pathogenesis of myelofibrosis and the respective roles of bone and the bone marrow have not been completely elucidated. Experimental data suggest that the proliferation of the spindle cell is under micro-environmental or hormonal control. It has been suggested that necrosis of marrow tissue is a prerequisite. Female sex hormones, in particular estradiol, appear to play a major role in the spontaneous development of myelofibrosis. Subcutaneous administration of B-estradiol to 8 to 10-week-old female mice resulted in decreased marrow cellularity and replacement of the bone marrow by trabecular bone. In some long term bioassay studies, the development of myelofibrosis has been linked to estrogen stimulation as manifested by the concomitant occurrence of uterine and ovarian cysts, and metritis. The mechanism of estrogen-induced myelofibrosis has been linked to the depletion of bone marrow macrophage, erythroid, myeloid, fibroblast and pluripotent stem cells known as colony forming units (CFUs). Administration of estrogens to various mouse strains resulted in decreases in the number of pluripotent, macrophage, myeloid and fibroblast CFUs in the bone marrow and spleen.

Myelofibrosis in mice must be differentiated from fibrous osteodystrophy, viral induced osteomas, and osteopetrosis. Fibrous osteodystrophy is usually associated with renal lesions of hyperparathyroidism and is characterized by the proliferation of periosteal new bone and softening of bone. Osteomas may be associated with invasive destruction of bone. In osteopetrosis, the entire skeletal system is affected early in life. Neonatal long bones are club-shaped and remain so into adulthood. Agents that can induce myelofibrotic-like lesions in mice include irradiation, viruses, and a variety of chemicals.

AFIP Diagnoses. 1. Bone, maxilla and femur: Fibro-osseous proliferation, B6C3F1 mouse, rodent
2. Harderian gland: Adenoma.

Conference Note. The term fibro-osseous proliferation was preferred by the moderator and conference participants due its more descriptive nature. This condition commonly affects multiple bones, with a fairly sharp demarcation between the

normal and abnormal bone. The lesion is characterized by increased bony resorption as well as increased bone formation with osteoblastic proliferation. This lesion differs from estrogen-induced metaphyseal sclerosis in which osteoclasis and thus remodeling is inhibited, resulting in retention of primary trabeculae. A differential diagnosis would include a metabolic bone disorder such as fibrous osteodystrophy; however, the lesions associated with most metabolic conditions tend not to be as sharply demarcated.

The harderian gland adenoma was not present in all sections.

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Microslide 104

History. This six-month-old, male, Suffolk lamb was the result of a breeding program utilizing frozen semen from a ram to a ewe both of which were affected by hereditary chondrodysplasia.

This lamb had progressive angular limb deformities and was euthanized to confirm a diagnosis of hereditary chondrodysplasia (spider lamb syndrome).

Gross Pathology. The lamb had severe valgus deformities of both front and hind limbs. There was moderate thoracic scoliosis present. Sections of thoracic vertebral bodies contained irregular reticulated growth plates. Both olecranons had numerous irregularly shaped centers of ossification and irregular growth plates. A 2 cm diameter area of skin necrosis was noted on the lateral surface overlying the right tibiotarsal joint. Within the center of this lesion, a puncture wound extended into the joint space. Bilateral distension of tibiotarsal joints by yellow-green thick liquid exudate and small fibrin clumps was present. The exudate extended both proximally and distally 5 cm within tendon sheaths. Articular surfaces of the distal tibias contained multiple fracture lines extending transphyseally to the metaphyses.

Laboratory Results. None.

Contributor's Diagnoses and Comments.

1. Hereditary chondrodysplasia affecting multiple bones including thoracic vertebrae, olecranons, distal tibias (spider lamb syndrome).
2. Polyarthritis, tibiotarsal joints, septic, severe, acute.
3. Pathologic transphyseal fractures, distal tibia, bilateral, severe, acute.

The signalment, clinical, gross and histologic findings in this case are consistent with a diagnosis of hereditary chondrodysplasia (spider lamb syndrome). Spider lamb syndrome almost exclusively affects Suffolk, Suffolk cross, and Hampshire breeds of sheep. The disease is thought to have a simple recessive type inheritance.

Lambs affected by the syndrome can appear normal or abnormal at birth. The lambs which appear normal at birth generally develop obvious lesions by 4 to 6 weeks of age. As the animals age, the deformities progressively worsen. The most common gross lesions include: mild to severe carpal valgus, mild to severe tarsal valgus, thoracic scoliosis, dorsal deviation of sternum, Roman nose, and pathologic fractures.

Histologic lesions are generally seen in areas with growth cartilage in the long bones and vertebrae. There is general unevenness and an increase in width of growth cartilage. Large tongues of disorganized cartilage extend from growth zones into the metaphysis, epiphysis and even into cortical bone.

The slide submitted in this case was from a thoracic vertebra and contained similar histologic findings to those previously described. The elbows were also examined histologically and had similar findings. The pathologic transphyseal fractures of the distal tibias were not examined histologically, but were thought to have resulted from this disease syndrome. The septic polyarthritis was likely caused by traumatic puncture of one or both hock joints.

AFIP Diagnosis. Bone, vertebra: Chondrodysplasia, Suffolk, ovine.

Conference Note. In all sections, growth plates are uneven and characterized by inactive endochondral ossification with retention of cartilage capped by bone. There is osteopenia beneath the growth plates with inadequate primary and secondary trabecular formation. In the epiphysis, areas of hyaline cartilage are replaced by fibrocartilage. Some sections contain a focal osteophyte-like change near the intervertebral disc. Bone marrow hypoplasia and serous atrophy of fat are present in the sections. A differential diagnosis for this lesion would be osteochondrosis; however, no abnormal arborization of the growth plate typically seen in this condition is present.

Contributor. Department of Pathology, School of Veterinary Medicine, University of California, Davis, CA 95616.

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International Veterinary Pathology Slide Bank
Laser disc frame #5525-27, 7960-1, 10615, 20688-91.

Microslide 105; Lantern slides 26 and 27

History. Tissue is from a nineteen-year-old, male Quarterhorse gelding with a one week history of weight loss and non-localized lameness. After a diagnostic nerve block at the fetlock of the left foreleg, the horse would not bear weight on that leg.

Gross Pathology. Multiple fractures were present on the condyles of the left third metacarpus. Bones examined (left foreleg and left rear leg) had moderate to marked porosity of the cortical and subchondral bone.

Laboratory Results. Hemogram and blood chemistry profiles were within normal limits.

Contributor's Diagnosis and Comments. Lymphosarcoma with osteopenia, proximal left first phalanx (10) and proximal left third metacarpus (14).

Survey radiographs indicated widespread involvement of all long bones. The cervical spine did not appear to be involved. Microscopic evidence of lymphosarcoma was also present in the anterior mediastinal lymph nodes and spleen. Osteoclasis is dramatic on surfaces adjacent to the neoplastic infiltrates but not on other surfaces. This suggests the resorption may be mediated by lymphokines released by the tumor and only locally active. These lymphokines may be acting indirectly by stimulating IL-6 secretion from stromal cells. Lymphosarcoma presenting with primarily bone involvement appears to be unusual in the horse.

AFIP Diagnosis. Bone: Lymphosarcoma, Quarterhorse, equine.

Conference Note. Artifactual changes due to tissue processing and autolysis make interpretation of the tissue challenging. Cellular detail is best preserved in the periosteum near the synovium and becomes less so near the articular cartilage. Neoplastic cells are present periosteally, infiltrating through the cortex, and in multifocal aggregates in the marrow. Subchondral osteolysis and villous hyperplasia of the synovium are present. A differential diagnosis of osteomyelitis was discussed during conference. The localization of the bone resorption to the sites of the cellular infiltrate is not typical of inflammation. Sections of mesenteric lymph nodes were infiltrated by similar neoplastic cells and extended through the capsule into the perinodal adipose tissue.

Lymphosarcoma in the horse may be of a mixed cell type, as seen in this case. Bone resorption is thought to be due to local stimulation of osteoclastic bone resorption by humoral factors either directly or indirectly through osteoblasts.

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International Veterinary Pathology Slide Bank
Laser disc frame #2091-4, 3469, 4615, 7425-6, 19045-8, 20685.

Microslide 106

History. This eight-week-old, female, Holstein calf was one of three animals presented for acute onset of depression and dyspnea. The animals were from a 65-cow purebred Holstein herd that initially experienced acute onset of fever, depression, and often respiratory distress in 2 to 4-week-old calves with high death losses. Some animals developed diarrhea and arthritis. Affected calves decreased to 10-15% following initiation of antibiotic therapy. Most of the affected animals, subsequently, presented with respiratory distress and arthritis.

Gross Pathology. The calf was in poor body condition; the eyes were sunken into the orbits. The lungs were diffusely reddened, wet, and heavy and had a notable rubbery consistency. No exudates were present in the trachea or bronchi. The spleen was markedly enlarged; a meaty consistency was seen on cut surface with very little oozing blood. Hock joints contained fibrin and excess synovial fluid. The contents of the small intestine were watery and yellow.

Laboratory Results. Culture of the lungs and ileum yielded Salmonella dublin. Virus isolation of the lung for BRSV was negative.

Contributor's Diagnoses and Comments. 1. Necrotizing interstitial pneumonia with septal thrombosis, acute, diffuse, severe. Etiology: Salmonella dublin.
2. Necrotizing hepatitis with paratyphoid nodules, acute, multifocal, severe. Etiology: Salmonella dublin.

The problem in this herd is typical of epizootics of Salmonella dublin infection in cattle. The tissues from this calf represent the typical consequences of bacteremia and dissemination of the infection. The liver has multifocal, randomly distributed paratyphoid nodules or granulomas associated with extensive necrosis. The lungs have widespread interstitial thickening of alveolar septa by edema and mononuclear cell infiltrates. Fibrinous thrombi in alveolar septa are common, as well as alveolar septal necrosis. Alveoli variably contain edema, fibrin, hemorrhage, and macrophages. In addition to necrotizing hepatitis and necrotizing interstitial pneumonia, this calf also had severe necrotizing splenitis, multifocal suppurative nephritis, fibrinous arthritis, enteritis with focal crypt necrosis, bone marrow myeloid hyperplasia with multifocal necrosis, and widespread lymphocyte depletion and necrosis involving mesenteric lymph nodes, spleen, and Peyer's patches. This pattern of disease expression, often seen in Salmonella

dublin infection, is attributed to a plasmid-encoded virulence factor. This factor is also common to Salmonella choleraesuis.

Morbidity and mortality in the herd have persisted despite early recognition and treatment of individual animals. This is consistent with the persistent carrier state of Salmonella dublin in adult dairy cattle in which the infection may persist for years or life. The possibility of shedding of organisms in colostrum with transfer to calves is likely; similar shedding in milk can result in human infections from unpasteurized dairy products.

AFIP Diagnoses. 1. Lung: Pneumonia, interstitial, acute, diffuse, moderate, with fibrin thrombi and random necrosis, Holstein, bovine.
2. Liver: Hepatitis, necrotizing, random, subacute, multifocal to coalescing, moderate, with vasculitis and thrombosis.

Conference Note. Multifocally within the lung, intra-alveolar fibrin appears compressed, forming vague hyaline membranes. Fibrin thrombi are present multifocally in the lung and liver. Differential diagnosis discussed for interstitial pneumonia in cattle includes septicemias, especially salmonellosis and colibacillosis, bovine respiratory syncytial virus, oxygen toxicity, acute respiratory distress syndrome (ARDS), and atypical interstitial pneumonia. Differential diagnosis for the hepatitis includes colibacillosis, salmonellosis, Tyzzer's disease, toxoplasmosis, listeriosis, and other septicemias.

Salmonella dublin typically causes an enteritis and septicemia in adult cattle and calves. In calves, the disease occurs in outbreaks with acute onset and high mortality. Salmonella sp. have several virulence factors including lipopolysaccharide, cytotoxins, enterotoxins, flagella, adhesion pili, and a plasmid-encoded virulence factor. A gross lesion often observed in salmonellosis is fibrinous cholecystitis or gallbladder edema.

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International Veterinary Pathology Slide Bank
Laser disc frame #86-87, 16238-41

Microslide 107; Lantern slides 28 and 29

History. A 1-year-old male orange tabby Domestic Shorthair cat from Edgewood, New Mexico (on the high plateau east of Albuquerque) was submitted for necropsy. The cat had been well until 3 days earlier when the owner noticed that he was lethargic and anorectic. He was taken to a local veterinarian who found pyrexia (T 106 F), dehydration, and marked cervical lymphadenopathy. Despite treatment with fluids and antibiotics, the cat became unresponsive and died.

Gross Pathology. The cat was in poor nutritional condition, with scant body fat reserves. Numerous yellow 1.5-2 mm foci resembling grains of millet were seen throughout the spleen. Cervical and mesenteric lymph nodes were markedly enlarged, with 2-3 mm yellow foci in the cortex, visible on capsular and cut surfaces. The lungs were slightly wet and heavy, but the cat appeared slightly overhydrated, with modest subcutaneous edema and mild pleural and peritoneal effusions.

At the end of the necropsy, the pathologist inadvertently cut her left middle finger. The cut was immediately irrigated and scrubbed with betadine for several minutes, and bandaged to help stop rather profuse bleeding.

Laboratory Results. Impression smears were made of lymph node and spleen, and were negative by fluorescent antibody (FA) staining for *Yersinia pestis*. Thirty hours later, the pathologist had painful left axillary lymphadenopathy with mild fever (99 F). At 40 hours, a gram-negative rod forming a characteristic blue-white round smooth colony was found to be growing from the cultures of spleen and lymph node. It was negative for *Y. pestis* by FA, but positive for *Francisella tularensis*.

Contributor's Diagnosis and Comments. Severe diffuse coagulative necrosis, lymphoid follicles, spleen and cervical lymph node. Etiology: *Francisella tularensis*.

Also, there was a moderate multifocal fibrinous interstitial pneumonia with accompanying edema and macrophages in alveoli. No lesions were seen in the liver, kidney, intestine, heart, adrenal and thyroid glands, pancreas, skeletal muscle, urinary bladder, or brain.

The first six months of 1992 were unusual in that more cases of tularemia than normal were diagnosed in New Mexico. Both plague and tularemia occur mainly on the high plateau or in the foothills in New Mexico. Many species of wild and domestic animals can be hosts for tularemia. Rodents and rabbits are the best known hosts. The disease in rodents causes miliary white foci in the liver, spleen, and lymph nodes. Tularemia is readily transmitted through many insect vectors, as well as by inhalation, ingestion, or through abrasions.

F. tularensis is a dangerous laboratory pathogen because of the risk of infectious aerosols. An inoculum of only 10-50 organisms can cause disease if inhaled or injected. Typically, a laboratory acquired infection causes disease in 24-36 hours, whereas the disease in the field has a longer incubation period (3-7 days). Our pathologist recovered uneventfully once the appropriate treatment (80 mg gentamicin intravenously twice daily for 3 days, followed by doxycycline 100 mg twice daily for 10 days) was initiated. The diagnosis was confirmed by a rise in serum titer over the next five weeks from <1:20 at week 0, to 1:80 at week 4 by the tube agglutination and microagglutination methods. The titer typically rises slowly in people with tularemia, peaking at 4-5 weeks. Very high titers (1:1,000-10,000) can occur in untreated cases. Although infection can confer lifelong immunity, both relapses and reinfections can occur.

AFIP Diagnoses. 1. Spleen: Splenitis, necrotizing, acute, multifocal to coalescing, severe, with vasculitis and thrombosis, Domestic Shorthair, feline.
2. Lymph node: Lymphadenitis, necrotizing, acute, diffuse, severe.

Conference Note. Differential diagnosis for the gross lesions would include infections with Francisella tularensis, Yersinia pestis, Y. pseudotuberculosis, Salmonella sp., other gram-negative bacteria, and Toxoplasma gondii. Histologically, the lesions are more typical of Francisella tularensis due to the lack of visible bacterial colonies as seen with yersiniosis, or protozoal zoites and pseudocysts, often seen in toxoplasmosis.

Francisella tularensis can penetrate intact skin, enter through cuts or abrasions, or via arthropod inoculation; ingestion and inhalation are other potential routes of infection. The exact pathogenesis is poorly understood, although the ability of the organisms to survive intracellularly is important in establishing infection.

In acute septicemia, an initial neutrophilia is often followed by neutropenia. Toxic neutrophilic changes are commonly seen in cats and include cytoplasmic vacuolation, increased

basophilia, toxic granulation due to increased permeability of lysosomal membranes and lysosomal swelling, and formation of Doehle bodies which are composed of ribosomes and compressed lamellae of rough endoplasmic reticulum.

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International Veterinary Pathology Slide Bank
Laser disc frame #3476-7, 5307-8, 11121-4, 22253

Microslide 108

History. Maggie, a two-year-old, spayed female Miniature Schnauzer, an indoor dog current on vaccinations that was housed with no other pets, developed a submandibular lymphadenopathy which was unresponsive to antibiotics. The lymph node subsequently abscessed, was drained and different antibiotics were prescribed. Maggie became clinically worse and was referred to the University of Georgia Veterinary Medical Teaching Hospital. Maggie presented depressed, 7% dehydrated, pyrexic (104°F), with left-shifted neutrophilic leukocytosis and generalized peripheral lymphadenopathy. At least three abdominal masses were palpated, visualized radiographically and presumed to be enlarged mesenteric lymph nodes. After fine needle aspirates of the lymph nodes allowed a disease diagnosis, specific therapy was begun. After initial improvement for a few weeks the dog's condition began to deteriorate and she was euthanized.

Gross Pathology. The peripheral and mesenteric lymph nodes were enlarged and splenic nodules were present.

Laboratory Results. The National Veterinary Services Laboratory in Ames was not able to isolate the organism; however, the Centers for Disease Control and Prevention in

Atlanta was able to diagnose Mycobacterium avium by polymerase chain reaction. No serotype was determined.

Contributor's Diagnosis and Comments. Multifocal granulomatous hepatitis characterized by periportal, venous and sinusoidal accumulations of epithelioid macrophages with intracellular acid-fast bacilli. Similar infiltrates of macrophages effaced the lymph nodes, and were also present in spleen, lung, and intestines. Etiologic diagnosis: Systemic mycobacteriosis. Cause: Mycobacterium avium.

Dogs are considered to be more susceptible to M. tuberculosis and M. bovis than M. avium. Mycobacteriosis is considered an inverse zoonosis in dogs. The direction of transmission is from human to animal, with dogs being more likely than cats to contract the disease via inhalation. Dogs can get the alimentary form from cattle via ingestion of milk of other contaminated products, but if experimentally fed large doses of M. avium, they do not become infected yet pass viable bacilli in their feces. Mycobacteriosis due to M. avium usually does not form discrete granulomas restricted to a few organs, but is usually a progressive disseminated disease as in this case. The bacilli, as in other species, tend to be more numerous than with M. bovis or M. tuberculosis. In the literature, basset hounds are overrepresented. In these reports, there are suggestions of an inherited immune defect; however, no definitive conclusions have been reached regarding the immune defect in these dogs. Many mycobacterial compounds are implicated in the mechanisms of pathogenicity and virulence. The mechanisms by which mycobacteria survive intracellularly vary with the pathogenic species; for example, it has been shown that M. tuberculosis inhibits the normal phagosome-lysosome fusion primarily due to surface sulfo-lipids, while M. avium forms a capsule-like electron-transparent zone due to C-mycosides which act by impairing normal diffusion of lysosomal enzymes. Intradermal skin testing which is widely used in people has been reported to be inconsistent and unreliable in dogs. Culture of mycobacteria is difficult and many are slow growers. The polymerase chain reaction provides a more rapid diagnosis but like culturing, it is only performed at a few labs.

In most cases, aspiration and biopsy along with an acid-fast stain can give a disease diagnosis. With newer techniques using fluorescent antibodies and immunohistochemistry, speciation of mycobacteria can be determined.

AFIP Diagnosis. Liver: Hepatitis, histiocytic, periportal and random, multifocal, moderate, with intrahistiocytic bacilli, Miniature Schnauzer, canine.

Conference Note. The differential diagnosis includes infections with other intrahistiocytic bacteria; however,

demonstration of numerous acid-fast organisms, as in this case, is diagnostic of Mycobacterium sp. Immunity to mycobacterium is cell-mediated. Nonspecific immunosuppression mediated by monocytes and lymphocytes or specific immunosuppression mediated by T-suppressor cells may modify the cellular response of the host to mycobacteria allowing persistent infection. Mycobacterium avium has been shown to survive and grow in macrophages. Production of superoxide dismutase by the organism may protect it against host defenses. Killing of M. avium may be mediated by tumor necrosis factor and dependant on 1,25-dihydroxycholecalciferol.

In chronic inflammatory diseases, such as this case, the most common clinical pathologic change is anemia. This anemia, often referred to as the anemia of chronic disease, is due to the sequestration of iron in the monocyte/macrophage system with impaired reutilization of iron. Clinically, it presents as a nonregenerative anemia with low serum iron, low transferrin (measured as total iron-binding capacity), high levels of hemosiderin in the bone marrow, and high ferritin. In contrast, an iron deficiency anemia is characterized by low serum iron and a high transferrin.

Contributor. Department of Veterinary Pathology, College of Veterinary Medicine, The University of Georgia, Athens, GA 30602-7388.

References.

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International Veterinary Pathology Slide Bank
Laser disc frame #9126-7, 21897

Microslide 109

History. This 23-month-old New Zealand white female rabbit was used for an antibody study.

Gross Pathology. The rabbit presented in good body condition. The mammary glands were mildly swollen, some were discolored blue and 4-5 ml of a serosanguinous fluid was obtained when incised. Other teats contained small amounts of milk. The ovaries were speckled tan and had a granular appearance. Several cysts 2-3 cm in diameter were noted on the surface. No normal follicles or corpora lutea were detected. The endometrium of both horns was diffusely thickened up to 3-4 mm and was interpreted to be hyperplastic. Gross assessment of remaining major organ systems revealed essentially normal tissue.

Laboratory Results. Cultured samples of mammary secretions were negative for bacteria.

Contributor's Diagnosis and Comments. 1. Mammary gland: Adenocarcinoma, intraductal, cystic and papillary, New Zealand white, lagomorph.
2. Uterus, endometrium: Hyperplasia, adenomatous, diffuse, moderate.

Other morphologic diagnoses believed to be associated with the above entities, but not included in the submitted sections, included: 1. Ovaries: Luteninization, bilateral, diffuse, marked.
2. Adrenal gland, zona reticularis: Lipoidal degeneration, diffuse, moderate.
3. Pituitary gland, chromophobes: Hyperplasia, diffuse, moderate.

While the dominating lesion seen in this animal was the mammary cystic and papillary adenocarcinoma, other pathologic changes, such as endometrial hyperplasia, ovarian luteinization, pituitary chromophobe hyperplasia, and adrenal cortical lipoidal degeneration, are all suggestive of putative endocrine dysregulation, and that the neoplasia present in the mammae only reflects a local manifestation of a more profound constitutional disorder. In both organs there is a continuum of proliferative changes that range from hyperplasia to neoplasia. As such, the adenomatous uterine hyperplasia, given sufficient time, might progress to uterine adenocarcinoma.

Concurrent proliferative lesions within the mammary gland and uterus are common in aged does (2-3 years of age). Three endocrine organs are consistently involved in mammary carcinoma that is preceded by cystic disease; namely the adrenals, the pituitary and the uterus. It is generally accepted that the mammary and uterine changes are predetermined by more fundamental endocrine changes, namely hyperestrogenism, possibly secondary to pseudopregnancy (rabbits are induced ovulators*) that may result from mismatings, proximity of bucks, or mounting by other does. However, it should be noted that neither the uterine nor mammary

adenocarcinomas have been experimentally induced by hyperestrogenism alone.

*Other animals that are induced ovulators include cats, mustelids and llamas.

AFIP Diagnoses. 1. Mammary gland: Adenocarcinoma, cystic, New Zealand white rabbit, lagomorph.
2. Uterus, endometrium: Hyperplasia, papillary, diffuse, moderate.

Conference Note. The pathogenesis of this condition is undetermined. A better understood estrogen-associated condition is supression of bone marrow precursors leading to aplastic anemia due to damage of stromal cells. Early in the course of the anemia, there is neutrophilia, thrombocytosis, and leucocytosis due to release of previously committed stem cells. During the recovery phase, monocytes are the first cell population to increase in peripheral blood due to the lack of a monocyte storage pool and their release at an early stage of development.

A variable schirrous reaction is present in the mammary gland adenocarcinoma.

Contributor. Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Reference.

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International Veterinary Pathology Slide Bank
Laser disc frame #394, 3673, 3922-3, 8431-2, 8499-8501

Microslide 110

History. A 3.5 meter, 648 gm, male black rat snake was presented to veterinary clinic after two-week history of lethargy and anorexia. During the week prior to presentation, a firm, 6 cm diameter swelling had developed at a point approximately 70 cm caudal to the head. Radiographs revealed a distinct soft tissue mass that extended from just caudal to the heart into the pulmonary region, obscuring the trachea.

Gross Pathology. Necropsy revealed a mass adhered to the ventral aspect of the trachea and the ventral body wall.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Adenocarcinoma, tracheal or bronchial origin.

Neoplasms are uncommonly reported in snakes, but the sparse literature includes references to tracheal or bronchial adenocarcinomas. Tracheal carcinomas were produced in Python reticulatus by oral administration of N-nitroso-diethylamine, which has also been found to be carcinogenic in 19 species of mammals, two bird species, one amphibian, and three fish species.

AFIP Diagnosis. Trachea: Adenocarcinoma, black rat snake, reptile.

Conference Note. Tumors of tracheal origin are rare in most species. Papillomas and squamous cell carcinomas are the more commonly reported epithelial tumors. Other reported primary tumors include leiomyomas, rhabdomyosarcomas, chondromas, chondrosarcomas, osteochondromas, and osteosarcomas. Adenocarcinomas of tracheal origin are considered very rare while bronchogenic or bronchioloalveolar adenocarcinomas are more commonly seen.

There is a slight variation in tissue sections; most sections have small segments of respiratory epithelium and some sections contain cartilage. A prominent desmoplastic response is present surrounding neoplastic tubules. Prominent intranuclear eosinophilic structures are present in most cells and most likely represent prominent nucleoli as they are commonly found in normal black rat snake tissues.

The moderator believed this tumor to be of either pulmonary, tracheal, or esophageal origin. Its location on the convex surface of the trachea is more suggestive of a bronchial or esophageal origin.

Contributor. Biotechnics, 111-A Carpenter Drive, P.O. Box 1278, Sterling, VA 20167.

References.

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Microslide 111; Lantern slides 30 and 31

History. In a commercial farm, juvenile caimans (Caiman crocodylus yacare) approximately one year of age showed cutaneous and oral mucosal lesions which had been medicated for dermatomycoses. These animals suffered from nutritional stress and had been receiving a low-protein diet. All animals showing lesions had normal appetite and no other clinical alterations. This infection proved to be self-limiting.

Gross Pathology. Animals had gray-white, round, superficial cutaneous lesions approximately 1-3 mm in diameter that were occasionally coalescent. Lesions primarily involved the feet, eyelids, maxillary and mandibular regions, being more frequent in the tail, back, sides and mouth. Skin biopsies were performed and the fragments obtained were submitted for histopathological and ultrastructural evaluations.

Laboratory Results. Transmission electron microscopic examination revealed large electron-lucent inclusions containing large numbers of virions within the cytoplasm of infected epithelial cells. The virions were round to oval with a double coat surrounding a central granular nucleoid. They contained dumbbell-shaped nucleoids and lateral bodies typical of poxvirus.

Contributor's Diagnosis and Comments. Epithelial hyperplasia of the lesion edges, accompanied by acanthosis and necrosis. The epithelial cells showed ballooning degeneration and a large number of eosinophilic intracytoplasmic viral inclusions. These varied in size and resembled Bollinger and Borrel bodies. A discrete inflammatory process of the dermis was also present composed predominantly of agranulocytic mononuclear cells.

The first report of poxvirus in ectothermic vertebrates was made by Jacobson et al, in 1979, in skin lesions of Caiman sclerops (presently C. crocodylus fuscus, Penrith et al, 1991). Viral dermatitis due to poxvirus has been described by other researchers working with crocodillians and lizards in outbreaks or isolated cases, but the origin of the infections remained undetermined. Many authors suggest that the poxvirus remain "latent" until activated by stressing conditions producing recurrent clinical manifestations. No reptilian poxvirus has been isolated, although several trials have been made in avian and reptilian cell cultures.

AFIP Diagnosis. Skin, epidermis: Hyperplasia, focally extensive, moderate, with eosinophilic intracytoplasmic inclusion bodies, caiman (Caiman crocodylus yacare), reptile.

Conference Note. The lack of an inflammatory cell component to this lesion is striking. Caiman poxvirus is an unclassified

References.

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Microslide 113; Lantern slide 32

History. This 3-year-old male Arabian Oryx (Oryx leucoryx) was found lying in its pasture, in right lateral recumbency. The animal was alert but unable to stand. The oryx was moved into a stall and treated parenterally with dexamethasone, flunixin meglumine, and oxytetracycline. The following day, the animal could maintain sternal recumbency with assistance and it was given fluids intravenously and dexamethasone, thiamin, and ivermectin subcutaneously. The next day, the oryx's condition was unchanged; fluids and DMSO were administered IV and thiamine and oxytetracycline were given subcutaneously. On the following day, the oryx was in lateral recumbency and was depressed and unresponsive. Due to the poor prognosis, euthanasia was performed.

Gross Pathology. Gross lesions were limited to the central nervous system. The cerebrospinal fluid (CSF) was yellow-white and turbid. Extensive cavitating poliomalacia was present in the distal cervical spinal cord and proximal thoracic cord.

Laboratory Results. Hematologic and serum chemical analyses were performed each day. Abnormal findings were as follows:

	WBC	Segs	Fibr	SAST	SALT
Units	(k/ul)	(k/ul)	(mg/dl)	(I.U.)	(I.U.)
Normal	5.0-8.3	4.0-6.7	100-400	41-95	18-43
Day 1	16.8	14.6	700	307	50
Day 2	17.0	15.9	900	1410	211
Day 3	17.3	15.1	1000	1235	210
Day 4	15.2	14.3	700	NA	NA

Cytologic examination of the CSF revealed high numbers of monocytes, macrophages, and lymphocytes with fewer neutrophils. Listeria monocytogenes serotype 4 was isolated in pure culture from the CSF.

Contributor's Diagnoses and Comments. 1. Spinal cord: Poliomalacia, cavitating, focally-extensive. Etiology: Infarction.

2. Spinal cord: Meningomyelitis, suppurative, multifocal, moderate. Etiology: Listeria monocytogenes.

Listeriosis is a common disease of ruminants that typically manifests as encephalitis, abortion, or septicemia. The causative organism, Listeria monocytogenes, is widespread in the environment and can often be isolated from the intestinal tracts of healthy animals. Although the pathogenesis of listeriosis is not well understood, it is believed that the encephalitic form develops via ascending bacterial migration along trigeminal or other craniofacial nerves. In domestic species, disease outbreaks may be associated with feeding of contaminated silage.

Histologic lesions characteristic of listeriosis were present in the midbrain, cerebellum, and brainstem of this oryx and consisted of multifocal hemorrhage and microabscessation in the white matter with perivascular cuffing by mononuclear cells and fewer neutrophils in the neuropil and meninges. The segmental malacia present in the spinal cord of this animal is not typical of listeriosis; this lesion is consistent with infarction due to blockage of the ventral spinal artery branch supplying this area. The rapid onset of clinical signs in this oryx was probably caused by sudden infarction of the spinal cord associated with Listeria-induced vasculitis and/or thrombosis.

Clinically, the differential diagnosis in this case included trauma, cerebrospinal nematodiasis caused by Parelaphostrongylus tenuis, listeriosis, thiamin deficiency, and rabies.

AFIP Diagnosis. Spinal cord: Meningomyelitis, subacute, focally extensive, moderate, with grey matter cavitation, Arabian Oryx (Oryx leucoryx), artiodactyl.

Conference Note. The lesions in this section consist of a focally extensive area of cavitation restricted to the grey matter and a meningomyelitis that consists of perivascular and random concentrations of lymphocytes, plasma cells, macrophages, and neutrophils. Sections of brainstem and other segments of spinal cord from this animal were examined during the conference; lesions more typical Listeria sp. including microabcesses and lymphocytic cuffing of vessels were present.

Listeria monocytogenes is an infrequent cause of disease in domestic and exotic ruminants. It causes four primary syndromes that consist of central nervous system infection, abortion, generalized septicemia, or mastitis. The central nervous system form commonly presents as a meningitis in young animals and a meningoencephalitis in adults. Often, there are no gross lesions visible in the brain of affected animals.

Conference Note. Equine motor neuron disease is aracterized by degeneration of motor neurons in the ventral rns of the spinal cord and some brainstem nuclei with secondary onal degeneration and atrophy of skeletal muscle. Clinical gns and histologic and ultrastructural lesions are similar to yotrophic lateral sclerosis in humans. In the human disease, wever, there is extensive degeneration of the pyramidal tracts ile only mild degeneration of these tracts is seen in horses.

Other diseases affecting the equine spinal cord include uine degenerative myeloencephalopathy, cervical stenotic elopathy, protozoal encephalomyelitis, and rabies. These seases have different clinical and pathologic findings from uine motor neuron disease and should be easily differentiated.

Contributor. Department of Pathology, Cornell University, haca, NY 14853.

References.

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croslide 115

History. This 8-year-old female donkey came from a herd of nkeys which had exhibited mild signs of respiratory distress llowed by mild lameness. Radiographs indicated rotation of P3 the majority of the animals. This donkey was within 6 weeks foaling and recovering from the respiratory condition when she veloped anorexia and lipemia. She was euthanatized due to ntinuing progression of clinical signs. Total time from onset lameness to euthanasia was 2 weeks.

Gross Pathology. Rotation of coffin bones, both front feet; in pregnancy.

Laboratory Results. None.

Contributor's Diagnosis and Comments. Laminitis, subacute, th secondary epidermal necrosis and blunting.

Extensive structural alterations of the secondary epidermal minae are present, being most pronounced at the distal djacent to P3) aspect of the epidermal laminae. These changes

range from blunting and irregularity of orientation to areas which are devoid of secondary epidermal laminae. There is extensive necrosis and/or cytoplasmic vacuolation of secondary epidermal lining cells. In occasional slides there are focal regions of epidermal proliferation at the proximal aspect of the epidermal laminae (adjacent to the keratinized tissue), with resultant bridging of cells between epidermal laminae. The secondary dermal laminae are moderately hypercellular due to an accumulation of mononuclear inflammatory cells; this hypercellularity is most prominent at the distal aspect of the epidermal laminae. The vasculature within the secondary epidermal laminae is dilated and is frequently lined by large basophilic endothelial cells.

AFIP Diagnosis. Hoof: Necrosis, laminar, epidermal, multifocal, minimal, with edema, donkey, equine.

Conference Note. The pathogenesis of laminitis is not fully understood. Ischemia of the distal digit seems to be a central event. Several theories exist as to the inciting mechanism. Three vascular mechanisms have been proposed and include initial venoconstriction with increased postcapillary resistance, prolonged arteriovenous shunting of blood, and peripheral vasospasms. Other theories include metabolic abnormalities or endotoxemia as inciting events in the pathogenesis.

Histopathological changes seen in acute laminitis include edema, swelling of endothelial cells, capillary congestion and thrombosis, epithelial cell necrosis and hyperplasia, and hyperkeratosis. The vascular changes precede the other changes.

Contributor. Abbott Laboratories, D-469, AP 13A, Abbott Park, IL 60064-3500.

References.

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International Veterinary Pathology Slide Bank
Laser disc frame #100-1, 223, 715, 859-63, 1271-2, 1468, 2399, 2465, 3268, 3338, 7617, 12855, 15282, 20417-8.

Microslide 116

History. This fifteen-year-old standardbred was a teaser stallion. He became emaciated and developed an enlarged scrotum on the right side which was diagnosed as a hematoma. The horse

ide 122 and 123

story. This obese, 11-year-old, neutered, male terrier-
og exhibited severe, progressive hyperkeratosis and
g of the footpads and adjacent haired skin of all four
The elbows were also thickened with scaly crusts. The
sions were obviously painful. On excisional biopsies, a
is of superficial necrolytic dermatitis was made.

oss Pathology. In addition to the skin lesions described
the liver was smaller than normal with a diffusely nodular
r surface. The nodules extend throughout the parenchyma,
10 mm in diameter and pale tan to dark red-brown.

boratory Results. A total body panel at this time
i elevated glucose of 7.9 MMol/L, a mildly elevated
e-phosphatase of 93 U/L and mildly elevated ALT of 75 U/L.
id analysis and total bilirubin were within the normal

ntributor's Diagnoses and Comments. 1. Superficial
tic dermatitis, diffuse and moderate, with epidermal
cell necrosis, outer epidermal edema, and severe scale-
g of the epidermal surface.
ronodular cirrhosis of the liver, diffuse and moderate,
ilular hyperplasia.

y: Unknown metabolic or hormonal disturbance.

e distribution of the skin lesions, the mild to moderate
ons of liver enzymes, and gross and histologic lesions of
i liver are strongly supportive of a diagnosis of
itaneous syndrome. This syndrome resembles necrolytic
ry erythema of man, caused in most cases by pancreatic
nomas. Most canine cases are instead associated with an
type of severe hepatocellular vacuolation and nodular
asia, not entirely typical of hepatic cirrhosis, in that
or no fibrosis is present. The condition in dogs is also
y referred to as metabolic epidermal necrosis and diabetic
pathy. The unusual feature of this case, compared to most
ed cases, is the relative absence of hepatocellular
tion and the presence of epidermal single cell necrosis
sis). The latter finding is a much more common feature of
a multiforme. The typical "red-white-blue" histologic
in the epidermis however, due to parakeratosis, outer
al pallor/edema and inner epidermal hyperplasia is more
ent with superficial necrolytic dermatitis. The necrosis,
nd pallor of the epidermis are thought to result from a
lowering of the plasma amino acid levels, the existence of
as not established in this case.

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AFIP Diagnoses. 1. Haired skin and footpad: Dermatitis, subacute to chronic, superficial, diffuse, moderate, with parakeratotic hyperkeratosis, superficial epidermal edema and pallor, and basilar epidermal hyperplasia, terrier cross, canine. 2. Liver: Hyperplasia, nodular, diffuse, moderate, with hepatocellular necrosis and vacuolization, biliary hyperplasia, and portal, septal and periportal subacute to chronic hepatitis. 3. Liver: Congestion, diffuse, moderate, with hemorrhage, micronodular hemosiderosis, and lymphangiectasis.

Conference Note. The histologic findings of parakeratotic hyperkeratosis, epidermal pallor and edema, and basilar hyperkeratosis are virtually pathognomonic for this entity; however, these lesions may not be uniformly present in every biopsy. As seen in this case, footpads are the most common sites of the skin lesions followed by mucocutaneous junctions, edges of the pinnae, and friction-points such as elbows and hocks. The pathogenesis of the skin lesion is unknown but hypoaminoacidemia has been documented in affected dogs.

The liver lesion is characterized by severely disrupted hepatic architecture, nodular hyperplasia, and hepatocellular vacuolation. Hepatocellular necrosis is uncommon in the canine disease but is present in this case. A Masson trichrome-stained section revealed very little collagen. Hyperglucagonemia has been associated with cirrhosis due to a reduction in hepatic degradation of glucagon secondary to abnormal liver function. High glycogen levels in the blood have been shown to lead to decreased plasma amino acid levels which may be a mechanism for hypoaminoacidemia. The hepatic congestion, hemosiderosis, and lymphangectasis may have been caused by concominant chronic passive congestion.

Contributor. Department of Veterinary Pathology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO.

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International Veterinary Pathology Slide Bank

Laser disc frame #16379, 22756, 22758-9.

Microslide 124; Lantern slide 34

History. This three-year-old male llama (Lama glama) began circling six months ago but remained ambulatory until four days prior to presentation when quadraparesis developed. There was torticollis to the left and ventral nystagmus with the slow component to the left indicating vestibular involvement.

Gross Pathology. The llama's body condition was judged to be fair. Small amounts of clear yellow fluid containing some fibrin strands were present in the thoracic, pericardial, and abdominal cavities. There were multiple fibrous adhesions between the liver and diaphragm.

Laboratory Results. CSF tap: glucose 98 mg/dl; protein 63 mg/dl; RBC 2000/µl; WBC 15/µl, primarily eosinophils. At necropsy bacterial cultures of brain, including cold enrichment culture for Listeria, yielded no growth.

Contributor's Diagnosis and Comments. Brain: Meningoencephalitis, necrotizing, multifocal, acute to chronic, severe due to Parelaphostrongylus tenius.

Lesions were present in the cervical spinal cord, brainstem, cerebellum, and cerebrum, and ranged from areas of leukocytic infiltration to malacic foci containing primarily gitter cells to necrotic and hemorrhagic foci. Sections of nematode were found near the corpus callosum. Leukocytic infiltrates were present in the leptomeninges, in perivascular spaces, and in the neuroparenchyma. Lymphocytes, macrophages, plasma cells, and fewer eosinophils were found commonly as infiltrating cells. Fibrous astrocytes and macrophages were predominating cell types in many necrotic foci. A few glial or cell nodules and dilated axon sheaths were present chiefly in sections of medulla and cerebellar peduncle. Leptomeningeal fibrosis was common in sections from cervical spinal cord and all levels of the brain. The photomicrograph contains sections of nematode from the llama near the corpus callosum and has hemorrhage and leukocytic infiltration associated with the parasite. Sections of the parasite contain well developed ovary and oviduct indicative of the 5th stage larval form. In the natural host, the white-tailed deer, migration to the subdural space would have been completed before development to the 5th stage larvae occurs. Several other cases of presumed and confirmed P. tenius infection have been seen in llamas and sheep presented to the ISU Veterinary Teaching Hospital. Infection in cattle has not been recognized at our hospital.

AFIP Diagnosis. Brain, cerebrum: Meningoencephalitis, necrotizing, subacute to chronic, eosinophilic, multifocal, moderate, llama (Lama glama), artiodactyla.

Conference Note. The natural host for Parelaphostrongylus tenius is the white-tailed deer (Odocoileus virginianus); infected white-tailed deer show few or no clinical signs. In aberrant hosts, usually other cervids or ungulates, infection often causes severe neurologic disease. The parasite has an indirect life cycle in which the infective larvae (L3) are present in snails or slugs which are inadvertently ingested while grazing. The larvae then penetrate the abomasal wall and migrate from the body cavity to the spinal nerves and on to the spinal cord. In deer, the larvae develop and migrate in the dorsal horns of the gray matter for 20-30 days with subsequent migration out of the cord and into the subdural space where they mature and lay eggs. The eggs hatch into L1 larvae which travel hematogenously to the lungs where they are coughed up, swallowed, and passed in the feces. In aberrant hosts, the larvae fail to migrate out of the spinal cord into the subdural space and cause extensive damage to the spinal cord and brain.

Contributor. Department of Veterinary Pathology, College of Veterinary Medicine, Iowa State University, Ames IA 50011.

References.

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International Veterinary Pathology Slide Bank

Laser disc frame #10278, 13679.

Microslide 125

History. As part of a renal transplant study protocol, this adult, male, crossbred hound dog had surgery for bone marrow removal, and then was profoundly immunosuppressed with cyclophosphamide and concurrently given ampicillin and gentamicin to prevent bacterial infection. As anticipated with the cyclophosphamide therapy, the dog developed severe nausea and began vomiting. Serum chemistry values were BUN > 100 and creatinine 8.2, and he was hypokalemic and hypochloremic. He was treated with cimetidine and metoclopramide to counteract cyclophosphamide side effects; however, the dog continued to vomit. Urine specific gravity was 1.013 and protein and blood

were detected in the urine. Gentamicin was discontinued. Twelve hours later, the BUN and creatinine had risen to 139 and 10.0, respectively, and no improvement was seen in the urinalysis. The dog was euthanized by intravenous overdose of barbiturates.

Gross Pathology. The capsular surfaces of the kidneys were pale cream-tan and the cut surfaces were paler than normal.

Laboratory Results. Included in the above history.

Contributor's Diagnosis and Comments. Urogenital system, kidneys, nephropathy, toxic, diffuse, necrotizing, tubular, moderate, crossbred hound, canine.

At necropsy, in addition to the renal changes, there were multifocal gastric mucosal reddening and more diffuse reddening of the mucosae of both large and small intestine. The urinary bladder was diffusely dark purple on both mucosal and serosal surfaces; the mucosa was turgid and several times the expected thickness. Microscopic changes included severe, diffuse, necrotizing enteropathy of both large and small intestine and diffuse, severe, hemorrhagic necrosis and edema of the urinary bladder mucosa.

Urinary bladder and gastrointestinal changes were attributed to cyclophosphamide toxicity. The renal changes were attributed primarily to the well-documented toxicity of aminoglycoside antibiotics in the kidney functionally impaired by dehydration. The possibility of cyclophosphamide renal tubular toxicity contributing to the development of tubular necrosis was not excluded.

AFIP Diagnosis. Kidney: Necrosis, proximal tubular epithelium, diffuse, moderate, with granular and hyaline casts and tubular regeneration, crossbred hound, canine.

Conference Note. Aminoglycosides are excreted primarily by glomerular filtration and without metabolic alteration. They accumulate selectively in proximal renal tubular epithelium and cause damage via inhibition of lysosomal phospholipases which results in formation of myelin figures and rupture of lysosomes; this, in turn, leads to mitochondrial dysfunction and cell death. Members of this group of antibiotics, in decreasing order of toxicity, include neomycin, kanamycin, gentamicin, streptomycin, and tobramycin. Factors enhancing aminoglycoside nephrotoxicity include dehydration, fever, and pre-existing renal and hepatic disease. Nephrotoxicity is dose related and is reversible. Aminoglycoside toxicosis also affects the inner ear and neuromuscular junctions.

The differential diagnosis for acute tubular necrosis includes ischemic causes, most commonly associated with shock,

and nephrotoxic causes including a wide variety of drugs and toxins. Ischemic acute tubular necrosis is characterized by necrosis of short widely separated segments of the nephron and is often accompanied by tubulorrhexis and casts. Toxic acute tubular necrosis typically affects extensive areas of the proximal convoluted tubules.

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Laser disc frame #6891, 12279, 18449.

Microslide 126

History. This ten-year-old, male Chihuahua was presented for castration with a retained right testicle and perineal hernia.

Gross Pathology. Enlarged right testicle with grey-tan tissue. Left testicle has no significant lesions.

Laboratory Results. Nothing remarkable.

Contributor's Diagnosis and Comments. Mixed germ cell-stromal tumor of the testis of dog (right).

These testicular neoplasms in the dog have at least two distinct cell populations, germ cells and sex cord stromal

(Sertoli) cells and can be distinguished morphologically and immunohistochemically. These tumors are closer to the mixed germ cell-sex cord stromal tumors than to the gonadoblastomas of the testis in humans. These tumors in the dog are possibly being classified as seminoma or Sertoli cell tumor, depending on the predominance of germ cells or Sertoli cells.

AFIP Diagnosis. Testicle: Mixed germ cell-stromal tumor, Chihuahua, canine.

Conference Note. This tumor is composed of cells that exhibit regional variation in cellular morphology. Some areas contain tubules filled with round to polygonal cells that have abundant deeply eosinophilic cytoplasm, round nuclei with finely stippled chromatin and single, central, prominent, magenta nucleoli similar to cells found in seminomas. Other areas contain tubules lined by polygonal to columnar cells that often palisade perpendicular to the basement membrane and have moderate amounts of a vacuolated to lacy eosinophilic cytoplasm, round to oval vesicular nuclei with marginated to stippled chromatin; these resemble Sertoli cells. Areas are present in which both cell types are intermixed in the same tubule. Immunohistochemical staining for vimentin produced diffuse cytoplasmic staining of the Sertoli-like cells and perinuclear staining of the germ cell-like cells while immunostaining for neuron specific enolase caused diffuse cytoplasmic staining of the Sertoli-like cells.

Multiple testicular tumors are common in dogs. Recently, mixed germ-cell stromal tumors were proposed as a separate, distinct group of testicular neoplasms of dogs. These tumors may represent comingling of neoplastic cells from independently arising seminomas and Sertoli cell tumors.

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Laser disc frame #5721.