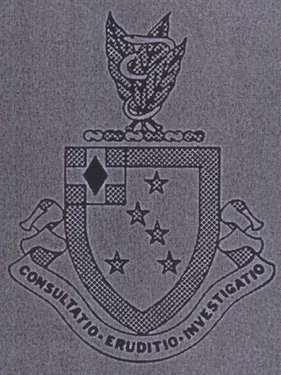
Syllabus

Veterinary Pathology Department Wednesday Slide Conference 1990-1991



Armed Forces Institute of Pathology
Washington, D. C. 20306-6000
1992

ML 92001

SYLLABUS

VETERINARY PATHOLOGY DEPARTMENT, AFIP
WEDNESDAY SLIDE CONFERENCE
1990 - 1991

126 microslides
26 kodachromes

Prepared by

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PREFACE

The Department of Veterinary Pathology, Armed Forces Institute of Pathology, has conducted the annual Wednesday Slide Conference for more than two decades. The cases presented each Wednesday throughout the academic year are also distributed to over 120 active participants, including military and civilian veterinary pathologists throughout the United States and Canada, as well as many foreign countries. The list of active contributors continues to grow. The diagnosis, comments, and a synopsis of the discussion for each case is to participants weekly.

This study set has been assembled in an effort to make the material presented at our weekly conferences available to a wider range of interested pathologists and other scientists. Discussions and comments have been abbreviated for succinctness.

A selection of 120 cases, with 126 microslides and 26 kodachromes, has been made from cases studies during the 1990-1991 conferences.

We wish to thank all contributors for their participation and for the permission to use their cases in this study set.

LIST OF SLIDES

SLIDE NUMBER	LANTERN NUMBER	AFIP NUMBER	ORDER/ ANIMAL	ORGAN/ TISSUE	DIAGNOSIS
1	1	2285063	CANINE	LUNG	PNEUMONIA, GRANULOMATOUS AND EOSINOPHILIC
2		2287123	CANINE	HEART	PARVOVIRAL MYOCARDITIS
3		2286499	PORCINE	LUNG	PNEUMOCYSTIS CARINII
4		2286754	MINK	LUNG	ALEUTIAN MINK DISEASE
5,6		2201061	FELINE	KIDNEY	FELINE INFECTIOUS PERITONITIS
7		2287577	CANINE	BRAIN	ALEXANDER'S DISEASE
8		2287620	FELINE	BRAIN	CYTAUXZOON FELIS
9,10		2287584	EQUINE	LIVER KIDNEY	HYPERLIPIDEMIA SYNDROME
11		2286495	EQUINE	LIVER	LISTERIA MONOCYTOGENES
12		2285432	CANINE	LUNG	CANINE ADENOVIRUS II
13	2	2287971	PRIMATE	LIVER	HERPES B VIRUS
14		2286470	PRIMATE	LUNG	PARAGONIMUS WESTERMANI
15		2285547	CANINE	KIDNEY	ASPERGILLUS TERREUS
16		2285551	FELINE	LYMPH NODE	CRYPTOCOCCUS NEOFORMANS

LIST OF SLIDES (Cont'd)

17	3	2286456	CANINE	SKIN	PYTHIOSIS
18		2287619	CANINE	NASAL POLYP	RHINOSPORIDIUM SEEBERI
19		2286727	EQUINE	LIVER	EQUINE INFECTIOUS ANEMIA
20		2287506	EQUINE	KIDNEY	ACTINOBACILLUS EQUULI
21		2285439	EQUINE	SKIN	MOLLUSCUM CONTAGIOSUM
22		2287645	EQUINE	LIVER SKIN	TYZZER'S DISEASE, DERMATOPHILOSIS
23,24		2287127	RAT	LUNG	CAR BACILLUS, MYCOPLASMA SENDAI VIRUS
25	4	2287366	RABBIT	SKIN	SHOPE FIBROMA
26		2237858	MOUSE	LIVER	MOUSE HEPATITIS VIRUS
27	5	2237470	RABBIT	LUNG	PASTEURELLA PNEUMONIA
28		2285555	MOUSE	SPLEEN	HEMANGIO-SARCOMA
29	6	2286724	RAT	THORACIC MASS	CHORDOMA
30	7,8	2286467	PRIMATE	STOMACH LIVER	ENTAMOEBA HISTOLYTICA
31	9	2237857	RABBIT	INTESTINE	CAMPYLOBACTER LIKE ORGANISM
32		2288942	FELINE	KIDNEY	VITAMIN D TOXICITY

LIST OF SLIDES (Cont'd)

33		2184633	EQUINE	PITUITARY	ADENOMA
34		2287626	EQUINE	HEART	MONENSIN TOXICITY
35		2289404	RAT	ADRENAL GLAND	ADRENAL PHAEO-CHROMOCYTOMA, GANGLIONEUROMA, LEUKEMIA
36		2292388	LEOPARD	PANCREAS	ISLET AMYLOIDOSIS
37	10	2133003	CANINE	OVARY	DYSGERMINOMA
38,39		2240201	BOVINE	PLACENTA	ASPERGILLOSIS
40	11	2186904	CHICKEN	OVIDUCT	SALPINGITIS
41		2287618	FELINE	EYE	MYCOTIC ENDOPHTHALMITIS, MYELOPROLIF-ERATIVE DISEASE
42	12	2292197	FELINE	SKIN	POXVIRUS
43		2288690	BOVINE	LIVER	SALMONELLA DUBLIN
44	13	2287369	GOLDFISH	KIDNEY	RENAL CYSTIC DISEASE
45		2288247	BOVINE	INTESTINE	ENTERITIS, LEUKOCYTOSIS
46		2288236	PORCINE	LIVER	PSEUDORABIES
47		2285966	BOVINE	COLON	CORONAVIRUS, CRYPTOSPORID-IOSIS
48		2237306	BOVINE	LUNG	RESPIRATORY SYNCYTIAL VIRUS

LIST OF SLIDES (Cont'd)

49		2288032	PRIMATE	LUNG	KLEBSIELLA PNEUMONIA
50		2238187	COCKATOO	LIVER PANCREAS	PACHECO'S DISEASE
51	14	2188575	DEER	SKIN	PARAPOX VIRUS
52		2237474	CANINE	KIDNEY	LYME DISEASE
53	15	2017975	CANINE	KIDNEY	NEPHRITIS
54	16	2289065	BOVINE	LIVER	LANTANA CAMERA TOXICITY
55		2292838	CANINE	KIDNEY	ZINC TOXICITY
56		2253097	CANINE	URINARY BLADDER, INTESTINE	MORBILLIVIRUS, CRYPTOSPORID-IOSIS, COCCIDIOSIS
57		2288672	PARROT	LIVER	AVIAN REOVIRUS
58		2288939	GOOSE	SKIN	SQUAMOUS CELL CARCINOMA
59		2219673	RACCOON	LUNG	MORBILLIVIRUS
60		2236460	FELINE	INTESTINE	ADENOCARCINOMA
61	17	2295207	OCTOPUS	INTESTINE	AGGREGATA SP.
62		2131393	ELEPHANT	LUNG	MYCOBACTERIUM TUBERCULOSIS
63		2185162	PARROT	LIVER	AVIAN ADENOVIRUS
64		2236727	TORTOISE	HEART	PERICARDITIS
65	18	2295201	EQUINE	LUNG	GLANDERS
66		2288055	BOVINE	HEART	CLOSTRIDIUM CHAUVOEI

LIST OF SLIDES (Cont'd)

67		2286763	BOVINE	LIVER	PYRROLIZIDINE ALKALOID TOXICITY
68		2287112	BOVINE	LIVER	DICROCOELIUM DENDRITICUM
69	19	2282704	GUINEA PIG	MAX. W/ TEETH	VITAMIN C DEFICIENCY
70		2285771	RAT	UTERUS	DECIDUOMA
71		2131343	CANINE	SPLEEN	MYCOBACTERIUM AVIUM
72		2287576	MOUSE	VENTRAL MASS	RHABDOMYO-SARCOMA
73		2194381	BOVINE	LIVER	PYRROLIZIDINE ALKALOID TOXICITY
74		2287969	BOVINE	LUNG	INFECTIOUS BOVINE RHINOTRACHEITIS
75		2289157	FELINE	MAMMARY GLAND	ADENOCARCINOMA
76		2295204	EQUINE	BRAIN	EASTERN EQUINE ENCEPHALITIS
77,78	20	2182075	OVINE	INTESTINE LYMPH NODE	MYCOBACTERIUM PARATUBER-CULOSIS
79		2292167	BOVINE	BRAIN	POLIOENCEPH-ALOMALACIA
80		2288937	MOUSE	BRAIN	ANAPLASTIC GLIOMA
81		2186362	ORYX	LIVER	YERSINIA ENTEROCOLITICA

LIST OF SLIDES (Cont'd)

82		2286508	PORCINE	LUNG	ACTINOBACILLUS PLEUROPNEUMONIA
83		2302201	HAMSTER	INTESTINE	CLOSTRIDIUM DIFFICILE
84		2295198	CAPRINE	LUNG	PESTE DES PETITS RUMINANTS
85		2302194	DUCK	PANCREAS	ZINC TOXICITY
86		2292827	BOVINE	LYMPH NODE	HYPERPLASIA
87		2286826	PRIMATE	INTESTINE	SIMIAN IMMUNO-DEFICIENCY VIRUS
88		2286830	PRIMATE	LYMPH NODE	MALIGNANT LYMPHOMA
89,90		2311140	PRIMATE	EYE, KIDNEY	SIMIAN IMMMUNO-DEFICIENCY VIRUS
91		2288945	PORCINE	BONE	VITAMIN D TOXICITY
92	21	2287616	KUDU	MANDIBLE	FIBROUS OSTEO-DYSTROPHY
93		2292829	CANINE	BONE	HYPERTROPHIC OSTEOPATHY
94		2287575	CANINE	RIB	HEMANGIO-SARCOMA
95		2288648	MOUSE	LIVER	HEPATOCELLULAR CARCINOMA, CHO-LANGIOCARCINOMA
96		2240203	RAT	KIDNEY	NEPHROPATHY
97		2177606	PANDA	PANCREAS	MORBILLIVIRUS
98		2185695	FERRET	SKIN	SCHWANNOMA

LIST OF SLIDES (Cont'd)

99		2288230	AGAMA	LIVER	HERPESVIRUS
100		2288053	CATFISH	GILL	GRANULOMATOUS BRANCHITIS
101		2292826	SNAKE	STOMACH	HYPERTROPHIC GASTRITIS
102		2292188	DOLPHIN	LUNG	PULMONARY NEMATODIASIS
103		2186867	FELINE	LYMPH NODE	FRANCISELLA TULARENSIS
104		2130815	BOVINE	ESOPHAGUS	BOVINE PAPULAR STOMATITIS
105		2289185	CANINE	GLANS PENIS	TRANSMISSIBLE VENEREAL TUMOR
106		2085247	CANINE	HEART	ATHEROSCLEROSIS
107		2286510	PORCINE	SKIN	MELANOMA
108		2285061	CANINE	SKIN	HEPATOCUTAN-EOUS SYNDROME
109		2288674	FELINE	SUBCUTIS	INJECTION SITE
110		2218359	CANINE	SKIN	LYMPHOSARCOMA
111	22	2289155	EQUINE	KIDNEY	LEPTOSPIROSIS
112		2185693	RAT	EPIDIDYMIS	MESOTHELIOMA
113	23,24	2075745	FELINE	HEART	TOXOPLASMA GONDII
114		2289149	EQUINE	BRAIN	HALICEPHALOBUS DELETRIX
115	25	2288076	OVINE	NASAL TURBINATE	ADENOCARCINOMA

LIST OF SLIDES (Cont'd)

116		2291782	OVINE	TONGUE	EPIDERMOLYSIS BULLOSA
117		2291784	BOVINE	MAMMARY GLAND	NOCARDIA ASTEROIDES
118	26	2286502	LLAMA	STOMACH	CLOSTRIDIUM PERFRINGENS
119		2285556	MOUSE	LIVER	HEPATOCELLULAR CARCINOMA
120		2293544	HAMSTER	LIVER	METAZOON PARASITE
121		2236853	MOUSE	SKIN	CYSTIC DEGEN-ERATION
122		2145835	RAT	LIVER	MYELOID LEUKEMIA
123		2287591	CANINE	VERTEBRAE	ASPERGILLUS SP
124		2288227	CANINE	LUNG	HISTIOCYTIC PNEUMONIA
125		2287100	CANINE	KIDNEY SKIN	LEISHMANIASIS
126		2296428	EQUINE	STOMACH	SQUAMOUS CELL CARCINOMA

COMMENTARY ON SLIDES

Slide 1, L1 (AFIP 2285063)

History. This suburban, 8-year-old, female German shepherd dog, kept both indoors and outdoors, was referred for a productive cough and progressive weight loss of a few weeks duration. It had not responded to treatment with chloramphenicol. Physical examination revealed dyspnea, panting (respiratory rate = 64 bpm), and diffuse rales. Thoracic radiographs were interpreted as consolidation of the right middle, caudal, and accessory lung lobes and diffuse interstitial infiltrate of the remaining lobes. Percutaneous needle biopsy of the right caudal lung revealed an abundance of eosinophils admixed with macrophages, lymphocytes, neutrophils and erythrocytes. The dog required oxygen therapy and underwent exploratory thoracotomy and triple pulmonary lobectomies.

Gross Pathology and Laboratory Results. The caudal lobe was firm, consolidated, and failed to collapse. The right middle and accessory lobes were partially atelectatic with regional edema and congestion. There were multifocal to regionally extensive, greenish/tan discrete nodules ranging from 3 to 15 cm. in diameter and peribronchial fibrosis. Three adult heartworms (male and females) were located within a branch of the caudal pulmonary artery.

Hematology	RBC	5.51 x 10^6/ul
	PCV	40%
	WBC	31.2 x 10^3/ul
	Neutrophils	23,400/ul (75%)
	Lymphocytes	2,800/ul (9%)
	Monocytes	2,500/ul (8%)
	Eosinophils	2,500/ul (8%)

Filaria filter screen: Negative

Diagnoses. 1. Lung: Pneumonia, granulomatous and eosinophilic, chronic, diffuse, moderate to severe, with eosinophilic granulomas. 2. Lung, arteries: Arteritis and endarteritis, eosinophilic, proliferative, multifocal, moderate.

Contributor's Comment and Conference Note. Chronic eosinophilic and granulomatous pneumonia with eosinophilic arteritis is one of a diverse group of clinical and pathologic entities that are included under the syndrome known as pulmonary infiltrates with eosinophilia (PIE). The PIE syndrome refers to hypersensitivity disorders characterized by having both eosinophilic pulmonary infiltrates and an eosinophilic leukocytosis. The disorders range in clinical severity from a mild, self-limiting, transient course such as simple pulmonary eosinophilia (Loeffler's syndrome) to the usually fatal course seen in two rare conditions known as pulmonary eosinophilia associated with angiitis and granulomatosis (Wegeners granulomatosis) and hypereosinophilic syndrome. The best known causes of chronic eosinophilic pneumonia are parasitic infections such as dirofilariasis and migration of helminth larvae. A causative role by inhalant allergens, drug

reactions, hypersensitivity reactions to fungal or bacterial infections, or other immune-mediated disorders has been suggested but not documented in the dog. The cause of these disorders remains unclear not only because of the difficulty in identifying a specific cause but also because the dramatic recovery of most patients given corticosteroids precludes the need to determine an etiology. The role that the occult heartworm disease played in this case is not determined. The lesions may be a pulmonary manifestation of hypersensitivity to secretions or other allergens of microfilaria and adult heartworms. There have been reports of pulmonary lesions associated with retained microfilariae in occult canine heartworm infection, but examination of many sections of lung in this case did not reveal any microfilaria.

This syndrome is also referred to in the literature as pulmonary nodular eosinophilic granulomatosis. Participants considered lymphomatoid granulomatosis in the differential diagnosis.

Contributor. Angell Memorial Animal Hospital, Department of Pathology, 350 S. Huntington Avenue, Boston, MA 02130.

Suggested reading.

Bauer T: Pulmonary hypersensitivity disorders. In: Current Veterinary Therapy X, Small Animal Practice, ed. Kirk RW, pp. 369-376, W.B. Saunders Company, 1989.

Castelman WL, Wong MM: Light and electron microscopic pulmonary lesions associated with retained microfilariae in canine occult dirofilariasis. Vet Pathol 19:355-364, 1982.

Confer AW, Qualls CW Jr., MacWilliams PS, Roo CR: Four cases of pulmonary nodular eosinophilic granulomatosis in dogs. Cornell Vet 73:41-51, 1983.

Dungworth DL: The Respiratory System. In: Pathology of Domestic Animals ed. Jubb KVF, Kennedy PC, Palmer N, Vol. 2, 3rd ed., p. 468. Academic Press, Orlando, 1985.

Lord PF, Shaer M, Tilley L: Pulmonary infiltrates with eosinophilia in the dog. J Am Vet Rad Soc 16:115-20, 1975.

Neer TM, Waldron DR, Miller RI: Eosinophilic pulmonary granulomatosis in two dogs and literature review. J Am Anim Hosp Assoc 22: 593-599, 1986.

Shatz M, Wasserman S, Patterson R: Eosinophils and immunologic lung disease. Med Clinics of North America 65(5):1055-1071, 1981.

Slide 2 (AFIP 2287123)

History. This 5-week-old, female, mixed breed canine was one of a litter of 5 puppies dying over a one week interval. Clinical signs in most of the animals were similar including sudden onset of lethargy, hyperpnea and/or dyspnea, gagging, and death occurring within 24 hours. One pup died without showing clinical signs. The dam, a young adult stray, showed no clinical signs of disease and had an uncertain vaccination history.

Gross Pathology. Renal cortices and the left lung were markedly congested. The small intestine contained numerous adult nematodes identified as Toxocara canis.

Diagnosis. Heart: Myocarditis, interstitial, subacute, diffuse, with myocardial fiber degeneration and necrosis and intranuclear inclusions.

Contributor's Comment and Conference Note. The myocardium contains patchy coalescing areas of myocellular loss and degeneration with interstitial edema and infiltration of varying numbers of inflammatory cells, predominantly lymphocytes, macrophages, and plasma cells, with a few neutrophils. A few myocellular nuclei, generally near areas of marked degeneration, contain ovoid to rectangular, basophilic, intranuclear inclusions. Microscopic changes are consistent with lesions described in both natural and experimental neonatal infection of puppies with canine parvovirus.

Attendees agreed that the lesions and clinical history are consistent with parvovirus induced myocarditis. The ability of the myocardium of a puppy to support a canine paroviral infection was discussed. The possibility that the inflammation might be immune mediated rather than directly attributable to viral activity was also raised.

Contributor. University of Illinois Veterinary Diagnostic Laboratory, 2001 South Lincoln Avenue, Urbana, IL 61801.

Suggested reading.

Mennier PC, Cooper BJ, Appel MJG, Slauson DO: Experimental viral myocarditis: parvoviral infection of neonatal pups. Vet Pathol 21:509-515, 1984.

Robinson WF, Huxtable CR, Pass DA: Canine parvoviral myocarditis: A morphologic description of the natural disease. Vet Pathol 17:282-293, 1980.

Yates RW, Weller RE: Have you seen the cardiopulmonary form of parvovirus infection? Vet Med 83:380-386, 1988.

Slide 3 (AFIP 2286499)

History. This 1-month-old pig was from a nursery with respiratory problems characterized mainly by pumping. Morbidity was high, but mortality low. Many of the affected pigs displayed retarded growth and wasting.

Gross Pathology and Laboratory Results. Both lungs were enlarged with a reddish color and rubbery texture.

Routine bacteriology gave negative results. The lungs were also negative for Mycoplasma hyopneumoniae, influenza A, respiratory coronavirus, porcine parvovirus and encephalomyocarditis virus (immunofluorescence technique).

Diagnoses. 1. Lung: Pneumonia, interstitial, subacute, diffuse, moderate, with type II pneumocyte and bronchiolar epithelial cell hyperplasia. 2. Lung, alveoli: Alveolitis, histiocytic, subacute, with flocculent eosinophilic material and pneumocystis organisms.

Contributor's Comment and Conference Note. Lesions are characterized mainly by a proliferative pneumonia (proliferation of type II pneumocytes and bronchiolar epithelium). In several slides, there are also necrotic cells, probably macrophages, in the alveolar

lumina. A mild peribronchiolar-perivascular mononuclear cell infiltration is also present. Multifocal pneumocystosis is present and is characterized by the presence within the alveoli of an eosinophilic foamy or honeycomb material. This proliferative pneumonia with necrotic macrophages is a common problem in farrowing and finishing operations. This is the most important health problem in Quebec swine herds. The disease has appeared in the fall of 1988 and has become widespread. The cause is unknown at this time, but a viral etiology is suspected. Superimposed bacterial pneumonias are common. These pigs seem also very susceptible to Glasser's disease and Streptococcus suis type 2 infection. Pneumocystis carinii is also another common secondary invader. We suspect the causal agent to impair phagocytosis by killing the macrophages.

The conference moderator and participants agreed that Pneumocystis carinii was probably not the primary cause of the pneumonia in this case. The type II pneumocyte hyperplasia was particularly striking, more than is usually seen in pneumocystosis. Equivocal intranuclear inclusions in the bronchial submucosal glandular epithelium cells were observed by several participants. Bullous interlobular emphysema was present in some sections.

Contributor. Department of Pathology and Microbiology, C.P. 5000, St-Hyacinthe, Quebec, Canada, J2S 7C6.

Slide 4 (AFIP 2286754)

History. Four, 4-month-old, female minks that had displayed dyspnea and a mild serous nasal discharge, were submitted from a mink farm that was experiencing losses in the kit crop.

Gross Pathology and Laboratory Results. The lungs displayed mottled irregular dark red areas and were firm and failed to collapse. The spleens were enlarged.

Bacteriological cultures of the lung were negative.

Diagnosis. Lung: Pneumonia, interstitial, subacute, diffuse, moderate, with type II pneumocyte hyperplasia, amphophilic to basophilic intranuclear inclusions and peribronchial and perivascular lymphoplasmacytic infiltrates.

Contributor's Comment and Conference Note. The lung lesions consist of thickening of alveolar walls with hypertrophy and hyperplasia of type II pneumocytes and interstitial edema. There are intra-alveolar macrophages and occasional neutrophilic granulocytes. There are areas of desquamating pneumocytes and cellular debris. Plasma cells are accumulating loosely around blood vessels. There are variable numbers of amphophilic intranuclear inclusion bodies, some completely fill the nuclei and others demonstrate a clear halo and marginated chromatin. Interstitial pneumonia - (parvovirus) Aleutian Disease.

The kits from this ranch that developed interstitial pneumonia were from Aleutian Disease serologically-negative dams. There were, however, infected animals on the ranch. The owner failed to eliminate serologically-positive animals when they were tested. He only placed them in a separate building.

Aleutian Disease is a persistent, eventually fatal, immune complex disease of mink. The classical disease is characterized by plasmacytosis, hypergammaglobulinemia, and immune mediated glomerulonephritis and arteritis. Interstitial pneumonia in kits is an unusual and uncommon manifestation of the disease.

The interstitial pneumonia that occurs in parvovirus infected mink kits whose mothers are serologically negative for Aleutian disease is believed to be caused by primary viral injury to type II pneumocytes. Although interstitial accumulation of mononuclear cells has not been described as a feature of experimental parvovirus infection in mink kits, most participants believed there were significantly increased numbers of perivascular lymphocytes and plasma cells in this case. As these mink were older than usual for the viral specific pneumonia, this lesion may reflect immune mediated changes typical of Aleutian disease.

Contributor. Animal Disease Diagnostic Laboratory, Utah State University, Logan, UT 84322-5600.

Suggested reading.

Alexandersen, S: Acute interstitial pneumonia in mink kits. Experimental reproduction of the disease. Vet Pathol 23:579-588, 1986.

Slides 5 & 6 (AFIP 2201061)

History. This 6-month-old, sexually intact male DSH cat was purchased from a local pet store in December 1987. The cat appeared normal until January 1988, at which time it was noted that there had been no weight gain since the previous visit to the referring veterinarian. Other clinical abnormalities were not noted at that time. When the animal was presented in April 1988 for routine orchidectomy, the cat was icteric and thin. The cat was euthanatized.

Gross Pathology. At the time of necropsy, the cat was thin and all mucous membranes were icteric. Body fat reserves were minimal, and remaining fat was yellow in color. Approximately 200 cc of clear, straw-colored fluid was present in the abdominal cavity. The surface of the liver was very finely granular in texture, and was diffusely speckled with extremely small black spots. Approximately 8 cm of the distal jejunum/proximal ileum was hyperemic. Black flecks, interpreted as digested blood, were present throughout the length of the GI tract. Several petechial hemorrhages were present on the capsular surface of the left adrenal gland. Following fixation, hypopyon and keratitic precipitates were noted in the right eye.

Diagnoses. 1. Kidney: Phlebitis and interstitial nephritis, pyogranulomatous, multifocal, moderate, domestic shorthair, feline. 2. Kidney, microvasculature: Fibrin thrombi, diffuse, severe.

Contributor's Comment and Conference Note. The presence of pyogranulomatous vasculitis in multiple organs is highly suggestive of disease due to feline coronavirus (feline infectious peritonitis [FIP]).

The highest incidence of FIP is seen in cats between the ages of 6 months and 2 years, and occurs more frequently in purebred than domestic cats. The type of immunity that develops during infection determines which form of the disease occurs clinically. Lack of a cell-mediated immune response results in the wet form, which occurs as essentially a peritonitis and/or pleuritis, with an outpouring of fluid into either or both of these body cavities. With a partial cell-mediated immune response, lesions of the dry form occur which are more granulomatous in nature and are localized primarily in parenchymatous organs; there is minimal or no exudation of fluid into the body cavities. The clinical history and histologic lesions present in this case are consistent with the dry form of the disease; although it was not analyzed, the abdominal fluid was likely ascitic fluid secondary to liver disease.

The presence of fibrin thrombi in capillary beds of multiple tissues is evidence of disseminated intravascular coagulation (DIC). The basic mechanism underlying this syndrome is the intravascular activation of blood coagulation in concert with the activation of the fibrinolytic system. The subsequent formation of thrombin leads to widespread platelet aggregation and fibrin formation. This may result in thrombosis of capillaries, arterioles, and venules, and infarctions in many organs. Several mechanisms are possible for the activation of the clotting system in this case. Endothelial damage may activate the intrinsic pathway of coagulation. The liver damage present may release thromboplastin-like material, triggering the clotting cascade, or more likely, activation of the clotting cascade may occur due to endotoxemia secondary to the damaged liver's inability to clear endotoxin that is normally absorbed in small quantities from the intestinal tract.

Conference participants agreed that, based on the history and the histological lesions, this case most likely represents feline infectious peritonitis virus infection. There was some variation pertaining to the inflammatory component. In many sections it was clearly perivascular, while in others the orientation was not obvious.

Contributor. Division of Pathology, Department of Comparative Pathology, U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Ft. Detrick, MD 21701.

Suggested reading.

Greene, GE: Clinical Microbiology and Infectious Diseases of Dog and Cat. W.B. Saunders Co., Philadelphia, 1984, pp 514-524.

Slappendel, RJ: Disseminated intravascular coagulation. Vet Clin North Am 18(1):169-184, 1988.

Slide 7, (AFIP 2287577)

History. This 6-month-old female miniature poodle developed a slowly progressive (2-3 mo) course of posterior leg weakness, ataxia and tremors.

Gross Pathology. No gross changes.

Diagnosis. Brain, mesencephalon: Astrocytosis and astrocytic hypertrophy, subpial, subependymal and perivascular, with eosinophilic refractile bodies (Rosenthal fibers), miniature poodle, canine.

Contributor's Comment and Conference Note. Histologic examination reveals prominent accumulation of Rosenthal fibers in a primarily perivascular and subpial distribution. There is mild rarefaction of the myelin and moderate astrocytic gliosis.

Rosenthal fibers are irregularly shaped, elongated or round hyaline eosinophilic bodies found within the cell bodies and processes of astrocytes. They are PAS negative and not sudanophilic. Their precise nature has not been determined but they do consist mainly of proteins including glial fibrillary acidic protein.

Ultrastructurally, Rosenthal fibers consist of granular osmophilic deposits that are intimately associated with a matrix of glial filaments. They are not membrane bound.

The disease is rare in humans and has been reported in two Labrador retriever littermates, a Scottish terrier dog and in a white Alpine sheep. Cases have been so sporadic that no familial or genetic basis has been established.

The distribution of the eosinophilic refractile bodies (Rosenthal fibers) was felt to be characteristic of Alexander's disease. Alexander's disease in people is characterized by the deposition of Rosenthal fibers. The fibers are usually oriented perpendicularly along all subpial surfaces of the central nervous system extending into the neuropile around perivascular spaces. Rosenthal fibers are not specific for Alexander's disease; they are also observed in glial scars and in piloid astrocytomas, the only difference being their occurrence within these lesions rather than in a subpial distribution. Alexander's disease in people is also characterized by a less well defined demyelination of the white matter. Both changes may be seen together, but the relationship is not consistent.

Contributor. Department of Pathology, Division of Comparative Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75235.

Suggested reading.

Cox, NR, et al: Myeloencephalopathy resembling Alexander's disease in a Scottish terrier dog. Acta Neuropathologica (Berl). 71:163-166, 1986.

Fankhauser R, et al: Encephalopathy with Rosenthal fiber formation in a sheep. Acta Neuropathologica (Berl). 50:57-60, 1980.

Friede, RL: Alexander's Disease. Archives of Neurology 11:414-422, 1964.

Sorjonen, DC, Cox, NR, Kwapian, RP: Myeloencephalopathy with eosinophilic refractile bodies (Rosenthal fibers) in a Scottish Terrier. J Am Vet Med Assoc 190(8):1004-1006, 1987.

Slide 8 (AFIP 2287620)

History. This domestic shorthair cat, M/C, 3 years, 11 lbs, was presented to a local clinic with signs of pain, lethargy, and anorexia. Temperature was 105.4. Puncture wounds, but no abscesses were noted. The following day the cat was readmitted with nystagmus, collapse, and dehydration. The cat died 24 hours later.

Gross Pathology and Laboratory Results. Icterus and a mildly mottled liver were noted.

FA test for rabies was negative. Bands, metamyelocytes, and basophils were increased in number; lymphocytes were decreased. BUN and total bilirubin values were elevated.

Diagnosis. Brain, cerebrum: Parasitemia, protozoal, intrahistiocytic, diffuse, moderate, with minimal subacute meningoencephalitis, domestic shorthair, feline, etiology--consistent with Cytauxzoon felis.

Contributor's Comment and Conference Note. Microscopic evaluation of this case was limited to kidney, liver, and brain. Macrophages/monocytes filled with protozoal organisms were seen in blood vessels of all sizes in all three organs.

Many participants observed 1 u in diameter basophilic bodies suggestive of piroplasms on or in erythrocytes. There was some variation in slides in that several sections contained a minimal perivascular infiltrate consisting of small numbers of lymphocytes, plasma cells and rare neutrophils.

Cytauxzoonosis is described as a fatal disease of domestic cats. Bobcats are considered the natural host, with ticks as possible vectors. Schizonts initially appear in macrophages; these schizonts develop into distinct nucleated macroschizonts that undergo division by schizogony and binary fission. The macrophages eventually rupture and release merozoites which infect RBC's.

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

Suggested reading.

Franks PT, Harvey JW, Shields RP, Lawman MJP: Hematological findings in experimental feline cytauxzoonosis. J Am Anim Hosp Assoc 24:395-401, 1988.

Kier AB, Wagner JE, Kinden DA: The pathology of experimental cytauxzoonosis. J Comp Path 97:415-432, 1987.

MacWilliams PS: Erythrocytic rickettsia and protozoa of the dog and cat. In: Vet Clin N Am, ed. R.B. Grieve pp. 1443-1461.

Simpson CF, Harvey JW, Carlisle JW: Ultrastructure of the intraerythrocytic stage of Cytauxzoon felis. Am J Vet Res 46:1178-1180, 1985.

Slides 9 & 10 (AFIP 2287584)

History. This 6-year-old, female donkey, in late gestation, was presented for a 1 week history of anorexia, depression, and weakness. Physical examination revealed increased heart rate and respiration, moderate dehydration and dependent edema. Blood obtained for laboratory analysis was grossly lipemic.

Gross Pathology and Laboratory Results. The liver was markedly enlarged and diffusely pale yellow with rounded blunt edges. On cut surface, the parenchyma was pale yellow, greasy and friable. Liver sections floated in formalin. Bilaterally, the kidneys were

slightly swollen and when cut, the cortices were pale yellow and bulged slightly from beneath the capsule. Intestinal contents were very fluid. Mild mucosal erosion was present in the large colon. Mild dependent edema and abdominal effusion were present.

Gross serum lipemia		
Total Triglyceride (mg/100 ml)	7655	(110)
Alkaline Phosphatase (mU/ml)	951	(66-210)
Aspartate Aminotransferase (mU/ml)	800	(300)
BUN (mg/dl)	77	(8-26)
Creatinine (mg/dl)	53	(2.0)
Urine Protein	2+	
Urine Glucose	1+	
Urine /Quantitative Protein (mg/dl)	47.4	
Urine Creatinine (mg/dl)	17.8	
Protein/Creatinine	2.66	(1)

Diagnoses. 1. Liver, hepatocytes: Vacuolar change, diffuse, severe, breed unspecified, equine (donkey). 2. Kidney, proximal convoluted tubules: Vacuolar change, diffuse, moderate to severe, with multifocal mild tubular epithelial necrosis, regeneration and mineralization.

Contributor's Comment and Conference Note. Signalment, clinical history and pathologic findings are consistent with "hyperlipemia syndrome." The initiating cause of this disease syndrome is unknown. However, it is believed to be stress related or a disturbance of fat metabolism and most common in late pregnancy or postpartum equids.

Note: (Oil Red O stains confirmed the presence of lipid within vacuoles present in hepatocytes and renal tubular epithelium.)

Conference participants agreed that the clinical history and histological lesions are consistent with the condition described in ponies as "hyperlipemia syndrome." The disease is usually fatal. Ponies may also develop ventral subcutaneous edema, a moderate diarrhea, metabolic acidosis, and signs of disseminated intravascular coagulation.

Hepatic lipidosis syndromes have also been described in other animals, including macaques, guinea pigs and domestic cats. The feline condition is similar to hyperlipemia of ponies in that both occur in obese nutritionally stressed animals, hypertriglyceridemia is present and the mortality rate is high. The condition in cats differs from that in ponies in several ways, however. In cats there is no sex predilection, icterus is common and severe periacinar hepatocellular necrosis may occur.

Contributor. North Carolina State University, 4700 Hillsborough Street, Raleigh, NC 27606.

Suggested reading.

Gay, CC, et al: Hyperlipemia in ponies. Aust Vet J 54:459-462, 1978.

Jubb, KVF, Kennedy, PC, Palmer, N: Pathology of Domestic Animals, Vol 2: 254, 1985.

Schotman, AJH, and Wagenar, C:P Hyperlipemia in ponies. Zentralbl Vet Med A16, 107, 1969.

Slide 11 (AFIP 2286495)

History. This 4-day-old, female Tennessee walking horse was delivered normally and showed no signs of illness for 2 days. The foal was reluctant to stand and nurse on day 3. Treatment with antibiotics and enemas was ineffective and the foal died on day 4.

Gross Pathology and Laboratory Results. The subcutaneous fat, articular cartilages and aortic intimal surfaces were yellow tinged. The liver was swollen and had a diffuse finely mottled red tan color. The spleen was enlarged, dark red, and meaty.

Listeria monocytogenes was isolated from the spleen, liver, lung, kidney, and intestine.

Diagnosis. Liver: Hepatitis, necrotizing, acute, multifocal to coalescing, moderate, with intralesional bacilli, Tennessee walking horse, equine.

Contributor's Comment and Conference Note. In addition to the necrotizing hepatitis noted in the section there was an acute multifocal interstitial pneumonia, numerous glomerular microvascular thrombi, and multiple areas of fibrinosuppurative necrosis in the bone marrow.

Listeria septicemia, abortion, and encephalitis are more common in ruminants, but have been reported in swine and horses. The M cells overlying Peyer's patches may serve as the portal of entry for Listeria, with subsequent phagocytosis of the bacteria by macrophages. A sulfhydryl-dependent cytotoxin (listeriolysin) may serve as a critical virulence factor, allowing intracellular survival of Listeria. In mice, binding of listeriolysin to the lysosomal membranes exerts a protective effect against proteolytic degradation, presumably allowing intracellular survival. Listeriolysin also causes in vitro lysis of macrophages and hepatocytes.

Participants observed bacteria in areas of necrosis. Other bacteria considered in the differential diagnosis included Bacillus pilliformis and Actinobacillus equuli.

The role of listeriolysin and the expression of T-cell mediated immunity was discussed. T-cell recognition of Listeria antigens on the surface of antigen-presenting cells may be potentiated by the binding of listeriolysin to membrane cholesterol. Listeriolysin belongs to a group of sulfhydryl (SH)-activated cytotoxins produced by streptococci as well as by certain species of Listeria, Clostridium and Bacillus.

Contributor. C. E. Kord Animal Disease Laboratory, P.O. Box 40627, Melrose Station, Nashville, TN 37220.

Suggested reading.

Berche P, Gaillard JL, Geoffrey C, and Alouf JE: T-cell recognition of listeriolysin is induced during infection with Listeria monocytogenes. J. Immuno. 139: 3813-3821, 1987.

Gaillard JL, Berche P, and Sansonetti P: Transposon mutagenesis as a tool to

study the role of hemolysin in the virulence of Listeria monocytogenes. Infect. Immun. 52: 30-55, 1986.

Jubb RVF, Kennedy PC, and Palmer N: Pathology of Domestic Animals. Vol 1, p 288 and Vol 2, p 54.

Slide 12 (AFIP 2285432)

History. This 8 to 10-week-old, Bichon Frise, female pup was purchased from a pet store that routinely obtained large numbers of pups through various breeders in the midwestern United States. Two pups from the same litter had persistent respiratory signs with fever. The condition was unresponsive to antibiotics and the pups were euthanatized.

Gross Pathology and Laboratory Results. Gross pathology not available. Formalin fixed tissue was received by the contributor.

Viral isolation: Adenovirus. This was done on frozen tissue retrieved from this pup.

Diagnosis. Lung: Pneumonia, suppurative, multifocal to coalescing, moderate, with basophilic intranuclear inclusion bodies, Bichon Frise, canine--etiology consistent with canine adenovirus type II.

Contributor's Comment and Conference Note. This lesion with the large number of inclusion bodies was unique. There were two pups in the group affected and no history to suggest the pups were ill prior to shipment. They had been vaccinated with modified live canine distemper and parvovirus vaccines. Two discrete foci of recent hepatic necrosis with similar intranuclear inclusions were present in one pup. All other tissues were unremarkable (kidney, spleen and gallbladder were also submitted).

Many participants felt the suppuration indicates there may have been a bacterial infection secondary to the adenoviral infection. Some attendees believed they observed toxoplasma cysts within areas of necrosis.

The pathologic picture of canine adenovirus type 2 (CAV-2) infection is typically a bronchointerstitial pneumonia, with necrotizing bronchiolitis and the presence of large basophilic intranuclear viral inclusions, as seen in this case. The disease is sometimes seen with canine distemper and therefore should be suspected of requiring some type of immunosuppression. Clinically, it is usually mild without secondary bacterial infection. CAV-2 can also be involved in canine infectious tracheobronchitis complex caused by Bordetella bronchiseptica and a number of other viruses. Canine parainfluenzae type-2 virus is probably the most common viral isolate but CAV-2 is also important in the etiopathogenesis.

Contributor. Central Laboratory for Veterinarians, c/o Box 8110-80, 264 H Street, Blane, WA 98230.

Suggested reading.

Jubb KVF, Kennedy PC, and Palmer, N.: Pathology of Domestic Animals, Vol 2;

Academic Press 1985, pg 483.
Clinical Microbiology and Infectious Diseases of the Dog and Cat. C.E. Greene; W.B. Saunders, 1984, pg 305-306.

Slide 13, L2 (AFIP 2287971)

History. This 4-year-old, colony born, female cynomolgus monkey (Macaca fascicularis), had a cesarean section for dystocia, at which time a macerated fetus was removed from the uterus. Despite antibiotic therapy, her condition deteriorated, until a week following the c-section, when an exploratory laparotomy revealed severe peritonitis. The monkey was euthanatized.

Gross Pathology and Laboratory Results. The entire small intestine was contained within an omental sac. There were multiple adhesions involving the intestines, pancreas, omentum and peritoneum. The lungs were multifocally hemorrhagic, with areas of consolidation. The liver contained miliary white foci throughout all lobes. The uterine wall was friable and multifocally thinned; the lumen contained a large blood clot.

Glucose	51 MG/DL	ALT/SGPT	221 U/L
BUN	83 MG/DL	AMYLASE	543 U/L
CREAT	3.3 MG/DL	CPK	691 U/L
TOT PRO	4.2 G/DL	CO2	16 MEQ/L
ALBUMIN	1.4 G/DL	DBILI	0.13 MG/DL
CALCIUM	6.6 MG/DL	TRIGLY	1201 MG/DL
PHOSPHORS	8.3 MG/DL	Na	124 MEQ/L
ALKPHOS	3050 U/L	K	2.1 MEQ/L
GGT	25.6 IU/L	CL	93 MEQ/L
AST/SGOT	173 U/L	GLOB	2.8 G/DL
LDH	1588 U/L	A/G	0.500
CHOLESTER	221 MG/DL	AGAP	17
TOTBILI	0.59 MG/DL	B/CR	25.2

Cultures of heart blood, uterine contents and peritoneum yielded no bacterial growth. The hepatic lesions, as well as control Herpesvirus simiae (B virus) infected Vero cells, were immunoreactive for Herpesvirus hominis (simplex) envelope antigen.

Diagnoses. 1. Liver: Hepatitis, necrotizing, multifocal to coalescing, moderate, with syncytial cell formation and eosinophilic intranuclear inclusion bodies, Macaca fascicularis, primate--etiology consistent with Herpesvirus simiae (B-virus). 2. Liver, hepatocytes: Vacuolar change, diffuse, moderate.

Contributor's Comment and Conference Note. Typical Herpesvirus lesions were also seen in lung, adrenal gland, bone marrow and spleen, but not in central nervous system, nor were there any abnormalities of the oral cavity, skin or eyes. The fetus and placenta contained no characteristic lesions, and immunohistochemical staining of these tissues was negative.

B virus is enzootic in macaques, but it rarely causes systemic disease. Following infection, vesicles and ulcers may occur on mucous membranes or on the skin, accompanied by seroconversion. Once infected, a monkey should be considered to be infected for life. Immunosuppression has been shown to intensify the natural lesions. In this case, the stress of the dystocia and c-section may have contributed to the severity of the infection.

The major importance of B virus is its zoonotic potential. Human infection is fortunately rare, but frequently fatal. Fatal B virus infections have also been reported in patas and colobus monkeys.

Several participants felt there was a segmental phlebitis associated with some areas of hepatocellular necrosis. The zoonotic potential of Herpesvirus B was discussed in detail. Although the morbidity rate of human infections is relatively low, the mortality rate is strikingly high. Most infections follow a monkey bite, although minor accidental self trauma incurred while performing necropsies is also a potential route of infection. The disease in humans is characterized clinically and pathologically by necrotizing encephalomyelitis with necrosis also occurring in the liver, spleen, lymph nodes and adrenal glands. Characteristic intranuclear inclusion bodies can be found in affected tissue, but have not been demonstrated in all cases.

Contributor. New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772.

Suggested reading.

Jones TC, and Hunt RD: Veterinary Pathology, 5th edition, Lea and Febiger, Philadelphia, 1983, pp. 316-318.

Kalter SS, and Heberling RL: B virus infection of primates in perspective. Lab Anim 18: 31, 1989.

Whitley RJ: Cercopithecine Herpes Virus 1 (B virus). In Fields, BN et al., Eds. Virology, 2nd edition, Raven Press, Ltd., New York, 1990, pp 2063-2073.

Slide 14 (AFIP 2286470)

History. This 6-year-old, female, Cynomolgus monkey (Macaca fascicularis) arrived at the facility on 10/19/88 and cleared quarantine with normal laboratory results. Coughing was noted on 3/31/89. The coughing cleared following treatment, but returned on 4/28/89. TB tests were negative. The radiographs showed increased nodular densities in the lungs (especially caudo-dorsal lobes). There was no response to further treatment.

Gross Pathology. There was extensive pleural fibrosis. Multiple pulmonary masses were present, and contained tan necrotic material. The lung was submitted for microscopy and culture.

Diagnosis. Lung: Bronchopneumonia, lymphoplasmacytic and eosinophilic, multifocal, severe, with bronchiectasis and bronchiolectasis and intrabronchiolar trematode adults and eggs, Macaca fascicularis, primate--etiology consistent with

Paragonimus westermani.

Contributor's Comment and Conference Note. Paragonimiasis is not uncommon in Macaca fascicularis (crab eating macaque). The disease results from ingestion of fresh water crayfish or crabs. The intermediate hosts, containing the metacercariae were ingested prior to arriving at this laboratory.

Infection with Paragonimus kellicotti in North America and Paragonimus westermani in Asia is not uncommonly seen in fish eating species of animals. Dogs and cats in North America may also acquire the infection by eating crayfish. Flukes are normally found in pairs in the parenchyma of the lung. Overt clinical signs may not be observed; however, pneumothorax may occur if there is rupture to the pleural surface of a cyst that communicates with an airway.

Contributor. Syntex Research Laboratories, 3401 Hillview Avenue, Palo Alto, CA 94304.

Suggested reading.

Abbott, DP and Majeed, SK: A survey of parasitic lesions in wild-caught, laboratory-maintained primates (Rhesus, Cynomolgus, and Baboon). Vet Pathol 21: 198-207, 1984.

Slide 15 (AFIP 2285547)

History. A sample of formalin fixed kidney from an 8-year-old female German shepherd with no case history was submitted for evaluation.

Diagnoses. 1. Kidney: Nephritis, granulomatous, diffuse, moderate, with necrotizing arteritis and fungal hyphae, German shepherd dog, canine. 2. Kidney: Fibrosis and hemorrhage, interstitial, multifocal, with tubular degeneration and regeneration.

Contributor's Comment and Conference Note. The changes in the glomeruli are thickened capsule and mesangial matrix. The tubular epithelium shows focal coagulative necrosis, focal mineralization (dystrophic calcification) and denudation into the lumen. Focal hemorrhage was evident. The perirenal adipose tissue shows hemorrhagic necrosis with sinusoidal dilation of few blood vessels. Giant cells are present in some granulomas.

The tissue was divided into parts to make the necessary number of histology slides. Consequently, not all the above features are present in all the slides.

The moderator was able to demonstrate, within the areas of granulomatous inflammation, numerous fungal hyphae. The hyphae, evident with both Gomori's methenamine silver and Gridley fungus techniques, were branching, septate, of uniform diameter, and had both terminal and lateral spores. The terminal spores were especially large and prominent. The moderator believes that these morphologic characteristics are most consistent with Aspergillus terreus[2,5]. Paecilomyces sp. may have similar morphological characteristics and cannot be ruled out based on its appearance in tissue sections alone[3,6]. Another differential to be considered is systemic candidiasis because of

the presence of septate hyphae, pseudohyphae, and budding yeast-like cells[1]. In this case, the moderator indicated that cultural studies or immunofluorescence would be necessary for a definitive diagnosis. A case of canine protothecal nephritis[4] was shown for comparative purposes; the presence of daughter cells or endospores within the parent cell are distinguishing histologic features for the genus Prototheca, an achlorophyllous algae.

The interstitial fibrosis and tubular epithelial degeneration and regeneration were also of interest. Several participants believe this may have been due to hypoxia secondary to the vascular lesions or nephrotoxicity secondary to antifungal therapeutic agents.

Contributor. Mobil Oil Corporation, Toxicology Division, P.O. Box 1029, Princeton, NJ 08543-1029

Suggested reading.

1. Chandler FW and Watts JC: Pathogenic Diagnosis of Fungal Infections, ASCP Press, Chicago, 1987, p 100-110.

2. Kalbay MJ, et al: The pathology of disseminated Aspergillus terreus infection in dogs. Vet Pathol 22: 540-547, 1985.

3. Littman MP and Goldschmidt MH: Systemic paecilomycosis in a dog. J Am Vet Med Assoc 191: 445-447, 1987.

4. Migaki G, et al: Canine protothecosis: review of the literature and report of an additional case. J Am Vet Med Assoc 181: 794-797, 1982.

5. Mullaney TP, et al: Disseminated aspergillosis in a dog. J Am Vet Med Assoc 182: 516-518, 1983.

6. Patnaik AK, et al: Paecilomycosis in a dog. J Am Vet Med Assoc 161: 806-813, 1972.

Slide 16 (AFIP 2285551)

History. An enlarged (0.5x1x1 cm) right prescapular lymph node was noticed for a week in a female DSH cat of unknown age.

Diagnosis. Lymph node, prescapular (per contributor): Lymphadenitis, granulomatous, diffuse, mild, with abundant intralesional budding yeast, domestic shorthair, feline, etiology--consistent with Cryptococcus neoformans.

Contributor's Comment and Conference Note. Majority of the lymph node architecture was replaced. Many budding yeast like forms are present.

Participants agreed that the morphology of the budding yeast is consistent with Cryptococcus neoformans. Contrary to most pathogenic yeast, C. neoformans is not dimorphic. The involvement of the prescapular lymph node suggests a primary cutaneous lesion in the neck, shoulder, or arm.

Cryptococcosis occurs worldwide in many species, but cats are affected most frequently. Animals that are compromised immunologically, such as by feline leukemia virus, corticosteroid therapy or malnutrition are most susceptible. A wide variety of

lesions and clinical signs have been reported; however, rhinitis, pneumonia, ulcerative skin lesions, encephalitis and ocular infections are the most commonly reported. The pulmonary lesion is a multifocal granulomatous pneumonia and, as with those infections involving other internal organs, has the gross characteristic appearance of small, gelatinous, white foci. The characteristic infection in the central nervous system may involve the meninges and neuropile. The microscopic features of the infection may vary from one having no significant cellular reaction and containing many organisms (gelatinous form) to a more granulomatous reaction characterized by macrophages, giant cells, lymphocytes and a fibrous stroma. Extension of infection from the meninges or hematogenous spread may result in ocular involvement, the organisms becoming trapped in the choriocapillaries. On H&E stained sections, C. neoformans appears as thin-walled, slightly basophilic spherical cells with single narrow-based buds, and surrounded by a wide clear zone or halo. The halo represents the mucinous capsule. The capsular material is positive with Mayer's mucicarmine technique. Use of this stain in the diagnosis of cryptococcosis was first suggested by Dr. C.N. Barron (see reference). Though not seen in this case, short septate hyphae may also be seen in tissue sections.

Contributor. Mobil Oil Corporation, Toxicology Division, P.O. Box 1029, Princeton, NJ 08543-1029.

Suggested reading.

Chandler FW and Watts JC: Pathologic Diagnosis of Fungal Infection. ASCP Press, Chicago, 1987, pp 164-173.

Barron CN: Cryptococcosis in animals. J Am Vet Med Assoc 127: 125-132, 1955.

Howlett CR, et al: Systemic cryptococcosis in a cat. Aust Vet J 49: 535-538, 1973.

Jubb KVF, Kennedy PC, Palmer N: Pathology of Domestic Animals, Academic Press, 1985, Vol. 1, pp. 278, 371, 385.

Thomson RG: Special Veterinary Pathology, BC Decker Inc., 1988, pp. 110, 552, 571.

Slide 17, L3 (AFIP 2286456)

History. A 4-1/2-year-old female, spayed poodle had a firm, nodular lesion removed from the skin over the sternum and submitted for histopathology. The owners had been treating the lesion with "Preparation H" topically for several weeks.

Diagnosis. Haired skin: Necrogranulomas, multifocal and coalescing, moderate, with branching septate hyphae, poodle, canine.

Contributor's Comment and Conference Note. Hyphae were stained best by Gomori's methenamine silver. Although the organism was not cultured and a specific immunofluorescent stain was not available in our laboratory, the morphologic features of the organism were considered diagnostic of pythiosis. The lesion had not recurred 10 months after surgery.

The moderator pointed out that the morphologic characteristics of the branching, septate hyphae observed within the granulomatous and necrotizing dermal lesions are indicative of a fungal infection. Definitive diagnosis would require cultural studies or immunofluorescence. The differential diagnosis should include zygomycosis, aspergillosis, and pythiosis. The organisms in the former two infections tend to be angioinvasive, a feature not observed in this case.

The genus Pythium, originally designated as Hyphomyces destruens, has been reclassified from the fungi to the protista based on the demonstration of sporangial structures from which biflagellated zoospores are formed[2,3,4] in cultures. Horses are thought to acquire the infection when standing in water for extended periods. As a result, the lesions tend to be more frequent on the lower limbs and ventral abdomen. Because of the worm-like appearance of the necrotic material in fistulous tracts, the gross lesions are often called "leeches" in horses. In dogs, the skin and the gastrointestinal tract are common sites of infection[1,5].

Contributor. Animal Disease Diagnostic Laboratory, Purdue University, West Lafayette, IN 47907.

Suggested reading.

1. Bentinck-Smith J, et al: Canine pythiosis - isolation and identification of Pythium insidiosum. J Vet Diag Invest 1: 295-298, 1989.

2. Bridges CH and Emmons CW: A phycomycosis of horses caused by Hyphomyces destruens. J Am Vet Med Assoc 138: 579-589, 1961.

3. Miller RI, et al: Gastrointestinal phycomycosis in a dog. J Am Vet Med Assoc 182: 1245-1246, 1983.

4. Miller RI and Campbell RSF: The comparative pathology of equine cutaneous phycomycosis. Vet Pathol 21: 325-332, 1984.

5. O'Neill Foil CS, et al: A report of subcutaneous pythiosis in five dogs and a review of the etiologic agent Pythium spp. J Am Anim Hosp Assoc 20: 959-966, 1984.

Slide 18 (AFIP 2287619)

History. This 9-year-old, male, Blue Tick Hound had a 1 year history of sneezing, decreased tracking ability, decreased interest in females, and nasal discharge. Treated with Ketaconazole for 3 months with "clinical response". Following discontinuation of treatment, sneezing and nasal discharge resumed.

Gross Pathology. A friable, 1 x 2 cm diameter red, polypoid mass in the right nasal vestibule.

Diagnosis. Nasal mucosa: Rhinitis, polypoid, chronic, moderate, with sporangia and trophocytes, blue tick hound, canine, etiology--consistent with Rhinosporidium seeberi.

Contributor's Comment and Conference Note. The structures in the mucosa are consistent with trophocytes and sporangia of Rhinosporidium seeberi.

Rhinosporidiosis is very rare in dogs. Nasal polyps are the most common clinical presentation of rhinosporidiosis in other more commonly affected species.

Participants agreed that the morphology of the organism is characteristic for Rhinosporidium seeberi. The presence of the different stages, i.e. sporangia, trophocytes and endospores, of the life cycle of R. seeberi are characteristic findings and allow a definitive diagnosis.

Rhinosporidiosis is a mycotic disease which, in addition to dogs, affects cattle, horses, goats, water fowl and humans. It is seen mainly in tropical areas and considered enzootic in India and Sri Lanka. Histologically, the lesions consist of variably sized polyps, up to 3 cm in diameter, composed of fibrous tissue stroma containing the spherical organisms and inflammatory cells.

Contributor. N.C. State, 4700 Hillsborough Street, Raleigh, NC 27606.

Suggested reading.

Allison N, et al: Nasal rhinosporidiosis in two dogs. J Am Vet Med Assoc Vol 188, No. 8, April 15, 1986.

Chandler FW, et al: Color Atlas and Text of the Histopathology of Mycotic Diseases, Year Book Medical Publishers, Inc., p 109-110, 1980.

Easley JR, et al: Nasal rhinosporidiosis in the dog. Vet Pathol 23: 50-56, 1986.

Levy MG, et al: Cultivation of Rhinosporidium seeberi in Vitro: Interaction with Epithelial Cells, Science, Vol 234, p 474-476, 1986.

Wilson RB, et al: Canine rhinosporidiosis. Compendium, Vol. 11, No. 6, p. 730-732, 1989.

Slide 19 (AFIP 2286727)

History. This 9-year-old, male, Appaloosa was presented with anorexia, ataxia, behavioral changes and possible photosensitivity. The horse had bitten the owner and referring veterinarian and subsequently was euthanatized. It was submitted for necropsy and rabies examination.

Gross Pathology and Laboratory Results. 1. Hepatitis, chronic, severe, diffuse, liver. 2. Arteritis, verminous, chronic, focal, cranial mesenteric artery. 3. Guttural pouch calculi, chronic, diffuse, severe, bilateral. 4. Gastritis, chronic, diffuse, severe, stomach (Etiology: endoparasites).

Rabies examination by indirect immunofluorescence was negative. Fecal flotation analysis revealed strongyle ova.

Abnormal Clinical Chemistry Data:

Albumin: 2.1 g/dl
Alkaline Phosphatase: 2802 U/L
SGOT/AST: 491 U/L
Total bilirubin: 2.6 mg/dl
Globulin: 5.8 g/dl
Bile acids: 54 umol/1

Diagnosis. Liver: Hepatitis, subacute, diffuse, moderate, with multifocal hepatocellular necrosis, Appaloosa, equine.

Contributor's Comment and Conference Note. Hepatitis, chronic, multifocal, severe, with necrosis, multifocal, moderate, liver. Etiology: Equine retrovirus (EIA virus).

This horse most likely suffered from hepatic encephalopathy, although budgetary constraints prevented a detailed clinical work-up of liver function. It also was heavily parasitized with some evidence of liver involvement. The presence of typical clusters of lymphocytes, randomly distributed through hepatic lobules suggested equine lentiviral infection. A retrospective Coggin's test verified this suspicion. Of interest is the fact that a Coggin's test performed a year prior to euthanasia was negative.

Several conference participants commented that many of the small mononuclear cells with hyperchromatic nuclei within the sinusoids may be nucleated erythrocytes (EMH). The moderator commented that hepatic extramedullary hematopoiesis is not a common histologic finding in the horse and although EMH may be present in this case, most of the cells are lymphocytes and plasma cells. In addition, some attendees believed that the relatively small amount of hemosiderin in the Kupffer cells may indicate a recent infection.

Equine infectious anemia is an arthropod-borne retroviral (lentiviral) infection of horses, mules and donkeys. The virus replicates in macrophages and possibly other cells, with eventual release of large amounts of virus. The hemolytic crises seen with EIA, each caused by a different antigenic variant of the virus, result from virus, antibody and complement interaction with erythrocytes and subsequent erythrophagocytosis. There is usually bilirubinemia, leukopenia (neutropenia and marginal lymphopenia) and thrombocytopenia, the mechanism of which is poorly understood. Animals dying during an acute hemolytic crisis exhibit icterus, anemia and widespread focal hemorrhages. In chronic cases emaciation and serous atrophy of fat are seen.

Contributor. Department of Comparative and Experimental Pathology, University of Florida, Box J-103, HSC, Gainesville, FL 32610.

Suggested reading.

Issel CJ and Coggins L: Equine infectious anemia: current knowledge. J Am Vet Med Assoc 174: 727-733, 1979.

McGuire TC and Crawford TB: Immunology of a persistent retrovirus infection - equine infectious anemia. Adv Vet Sci 23: 137-159, 1979.

Slide 20 (AFIP 2287506)

History. This full-term standardbred foal had a normal delivery, stood and nursed but always seemed a little listless. IgG was less than 200 dl; transfusion elevated it to less than 800 mg/dl. At 2 days of age, it stopped nursing, became recumbent, had purple membranes, cardiac arrhythmias, and pulmonary edema. It was treated with antibiotics.

Gross Pathology and Laboratory Results. The peritoneal cavity contained 50 mls of light red, watery fluid. Ecchymoses were present in the subcutis, epicardium, trachea,

esophagus, oral cavity, small and large intestine, urinary bladder, and joints. Kidneys were mottled on the subcapsular surface and deep red on the cut surface.

Bacterial culture: lung - no growth after 7 days
liver - 2 colonies, Pasteurella spp. and Actinobacillus spp.

Diagnosis. Kidney: Nephritis, suppurative, embolic, multifocal, moderate, with interstitial and capsular congestion and hemorrhage and numerous colonies of coccobacilli, standardbred, equine, etiology--consistent with Actinobacillus equuli.

Contributor's Comment and Conference Note. The renal capsule, cortex, and medulla were congested. There were many bacterial emboli, some associated with foci of polymorphonuclear leukocytes (microabscesses), and, in many sections, lodged in branches of the renal artery. This is considered to be typical of Actinobacillus equuli infection in neonatal foals. The clinical history in this foal is also considered typical of this disease. Antibiotic treatment probably compromised the culture results.

The moderator and conference participants believed this case typified Actinobacillus equuli embolic suppurative nephritis in young horses. Infection is thought to be acquired *in utero*, during parturition, or shortly after birth, probably from an umbilical infection. In foals that survive the early fulminating septicemia, typical microabscessation is seen in kidneys and other organs. Polyarthritis is a common sequelae.

Contributor. CIBA-GEIGY Corporation, 556 Morris Avenue, Summit, NJ 07901.

Suggested reading.

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Jubb KVF, Kennedy PC, and Palmer N: "Diseases of Bones" p 110 in Pathology of Domestic Animals, Vol 2, 3rd edition 1985 Academic Press New York.

Maxie MG: "The Urinary System" p343 in Pathology of Domestic Animals, Vol 2, 3rd edition Ed. by Jubb KVF, Kennedy PC, and Palmer N. 1985 Academic Press New York.

Slide 21 (AFIP 2285439)

History. This 8-year-old boerperd stallion from northern Transvaal, Republic of South Africa developed slowly progressing papular dermatitis over several months. Scrotal edema developed over several weeks. This was the only horse affected from a herd of five.

Gross Pathology and Laboratory Results. The stallion presented with a severe scrotal edema. A fair number of Rhipicephalus spp. ticks were present in the groin. There was an extensive papular dermatitis over the lateral neck, thorax, shoulders and sternum. Lesions varied from 2-20 mm in diameter (most fell into smaller groups of the range). Small superficial scabs could be removed without leaving a haemorrhagic area.

The hair over the papules was raised in tufts.
Moderate eosinophilia on hematology.

Diagnosis. Haired skin: Epidermal hyperplasia, diffuse, severe, with intraepidermal molluscum bodies, boerperd, equine.

Contributor's Comment and Conference Note. Molluscum contagiosum is caused by a hitherto unisolated poxvirus. Morphologically similar lesions have been found in horses, quokas, kangaroos, chimpanzees and man. It has been reported from northern Africa and was recently reported in Zambia. It has never been recorded in the Republic of South Africa but a clinically similar syndrome has been seen previously. The disease is not very contagious but apparently can be transmitted to other horses by injecting suspensions of the skin lesions intravenously.

Electron microscopic examination of the lesions in this case, as in other cases reported elsewhere, revealed virions with the classical biconcave morphology of a poxvirus. Affected animals may recover spontaneously but apparently corticosteroid therapy can lead to a flare-up of the lesions. It has been suggested that the disease is identical to uasin gishu skin disease of Kenya.

Conference Note. Conference participants agreed that the histomorphological lesions in this case are consistent with molluscum contagiosum. Epidermal histological lesions in this condition were compared and contrasted with those of horsepox. Molluscum contagiosum is characterized by epidermal downgrowth with large, usually single, intracytoplasmic inclusions. With horsepox, there tends to be an outward epithelial hyperplasia and smaller, occasionally multiple, eosinophilic intracytoplasmic inclusions.

In addition to uasin gishu in Kenya, molluscum contagiosum has also been described as resembling viral papular stomatitis, a similar, although incompletely characterized, poxvirus disease of horses, occurring in the United States, Australia and New Zealand. Both diseases differ from molluscum contagiosum in that they are highly contagious, have a more generalized cutaneous distribution, and typically have larger lesions.

Contributor. Veterinary Research Institute, P.O. Box 12502, Onderstepoort 0110 R.S. Africa.

Suggested reading.

Lange L, Marrett S, Maree C, and Gerdes T: An outbreak of poxvirus infection in horses. Electron Microscopy Society of Southern Africa - Proceedings Vol 19: 79-80, 1989.

Moens Y and Kombe AH: Molluscum contagiosum in a horse. Equine Veterinary Journal 20(2): 143-145, 1988.

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Slide 22 (AFIP 2287645)

History. This 1-month-old Arabian colt was presented with a severe skin rash around genitalia, feet, muzzle. The mare also had mild lesions on the muzzle. The colt became acutely ill and died.

Gross Pathology. Severe icterus. Swollen, mottled liver.

Diagnoses. 1. Haired skin: Dermatitis and epidermitis, necrosuppurative, diffuse, severe, with epidermal filamentous and coccoid bacteria, Arabian, equine, etiology--consistent with Dermatophilus congolensis. 2. Liver: Hepatitis, necrotizing, acute, multifocal to coalescing, severe, with intrahepatocellular filamentous bacilli, etiology--consistent with Bacillus piliformis.

Contributor's Comment and Conference Note. The epidermal crust contained numerous branching chains of Dermatophilus congolensis as well as groups of cocci which may be Staphylococcus, or other bacteria, or possibly fragments of D. congolensis. We did not attempt to differentiate these organisms. Both are easily seen with hematoxylin and eosin. In the liver, hepatocytes at the margins of necrotic foci often contained sheaves of basophilic fine filamentous bacteria, some of which are easily visible in the intact cell cytoplasm with standard hematoxylin and eosin stain at high magnification.

Organisms in both the epidermis and within hepatocytes were demonstrated with gram stains. Conference attendees agreed that the morphology of the organisms coupled with the histologic lesions in the skin and liver were consistent with dermatophilosis and Tyzzer's disease respectively.

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

Suggested reading.

Hall WC, Van Kruiningen HJ: Tyzzer's disease in a horse. J Am Vet Med Assoc 164(12): 1187-1189, 1974.

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Slides 23 & 24 (AFIP 2287127)

History. The submitted tissues are from a group of aged Long-Evans rats that had chronic respiratory disease (wheezing, sniffles, and weight loss).

Gross Pathology and Laboratory Results. The cranioventral lobes of the lungs were pale red and depressed. Some small airways were dilated; many contained

moderate quantities of cloudy mucinous fluid.

Serology: Positive for Mycoplasma pulmonis and Sendai virus. Culture (lungs): Negative.

Diagnosis. Lung: Bronchopneumonia, chronic, suppurative, multifocal, with bronchiectasis and ciiia-associated filamentous bacteria, Long-Evans rat, rodent.

Contributor's Comment and Conference Note. The lungs have variable peribronchiolar infiltration of lymphocytes and plasma cells, intrabronchiolar accumulation of neutrophils and mucin, segmental necrosis and loss of bronchiolar epithelial cells, and suppurative bronchiectasis. Occasional bronchioles have focal ulceration of the epithelium with marked locally extensive edema, inflammation and fibroplasia. Silver stained sections reveal heavy colonization of the ciliary borders of bronchiolar epithelial cells with slender filamentous bacteria.

Histopathologic changes are compatible with infection by cilia-associated respiratory (CAR) bacillus. The spatial correlation between bacterial colonization and bronchiolar lesions suggests a direct effect. The case is complicated by a positive serologic diagnosis of M. pulmonis and Sendai virus infection and the fact that Mycoplasma pulmonis can induce similar histopathologic changes. This case most likely represents a severe CAR bacillus infection secondary to pulmonary mycoplasmosis.

Concurrent infection of CAR bacillus with other murine respiratory pathogens such as M. pulmonis, Sendai virus or sialodacryoadenitis virus is commonly reported in the literature. Most authors suggest that spontaneous CAR bacillus-induced respiratory disease occurs only in the presence of other stressors (concurrent infections, depressed, immunologic function, etc.). A recent report of primary CAR bacillus-induced respiratory disease in obese (OB/OB) mice, which have depressed cell mediated immunity, supports this concept. Alternatively, rats inoculated intranasally with large doses of CAR bacillus can develop chronic respiratory disease and typical microscopic lesions (lymphocytic peribronchiolitis, suppurative bronchiectasis, suppurative bronchopneumonia) independent of concurrent viral or bacterial infections. These findings suggest that CAR bacillus also has the potential to be a primary respiratory pathogen at high doses.

Conference participants agreed that the morphology of the cilia-associated filamentous bacteria was consistent with CAR bacillus. The distinguishing histomorphological features of the infectious agents identified in this case were discussed in detail. The moderator commented that a prominent lymphoplasmacytic response around airways is a common feature of Mycoplasma pulmonis infections. The prominent type II pneumocyte hyperplasia, fibrosis and histiocytic infiltrate are more typical of CAR bacillus. In mice infected with Sendai virus, squamous change in the terminal bronchioles is common; in rats the changes are often minimal or absent. Several participants thought they saw occasional syncytial cells within areas of inflammation.

Contributor. Department of Veterinary Pathobiology, University of Illinois, 2001 S. Lincoln Avenue, Urbana, IL 61801.

Suggested reading.

Ganaway JR, Spencer TH, Moore TD, Allen AM: Isolation, propagation and

characterization of a new recognized pathogen, cilia- associated respiratory bacillus of rats, an etiologic agent of chronic respiratory disease. Infect and Immun 47: 472-479, 1985.

Griffith JW, White WJ, Danneman PJ, Lang CM: Cilia-associated respiratory (CAR) bacillus infection in obese mice. Vet Pathol 25: 72-76, 1988.

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Matsushita S, Joshima H: Pathology of rats intranasally inoculated with cilia-associated respiratory bacillus. Laboratory Animals 23: 89-95, 1989.

Slide 25, L4 (AFIP 2287366)

History. The tissue is from a wild rabbit (Sylvilagus floridanus) approximately 4 weeks of age. Eleven orphaned rabbits were being hand-raised in a private home. Ten of the rabbits developed soft tumor-like growths on all areas of their bodies and subsequently died. One of the dead rabbits was submitted for necropsy examination.

Gross Pathology and Laboratory Results. A mass measuring 1.5 cm in diameter was found in the subcutaneous tissue of the left nasomaxillary region. The overlying skin was alopecic. The mass was soft and white on cut surface. A similar nodule on the medial aspect of the right hind limb measured 0.5 cm in diameter. Macroscopic lesions were not observed in any other organs or tissues.

Negative contrast electron microscopy on ground tumor tissue failed to reveal virus particles.

Diagnosis. Haired skin: Shope fibroma, eastern cottontail rabbit (Sylvilagus floridanus), lagomorph.

Contributor's Comment and Conference Note. Rabbit fibroma is a cutaneous neoplasm induced by poxvirus in the genus Leporipoxvirus. Myxoma virus, another member of the genus Leporipoxvirus, causes myxomatosis in the European rabbit (Orcytolagus cuniculus) and cutaneous fibroma in wild rabbits (Sylvilagus sp.). However, myxoma virus has only been reported in wild rabbits in California and Oregon in the U.S. The natural host of the fibroma virus is the eastern cottontail rabbit (Sylvilagus floridanus). Fibromas induced by this virus may be myxomatous and difficult to differentiate histologically from myxoma. Both the fibroma virus and the myxoma virus are transmitted mechanically by arthropods such as fleas, mites and mosquitoes. Typical poxviral inclusion bodies may occur in tumor cells and epithelial cells in the epidermis, and were observed in this case. The diagnosis was based on history, gross and microscopic appearance of multiple cutaneous neoplasms, and the known host and geographic range of rabbit fibroma virus.

Most participants agreed that the history and the gross and microscopic appearance are consistent with Shope fibroma, although the loosely arranged edematous dermal stroma is not a typical feature. The cytoplasm of neoplastic cells was negative with the PAS reaction and the alcian blue stain, further supporting a diagnosis of Shope fibroma. The cytoplasm of neoplastic cells in cases of myxomatosis typically stains

positively for mucin.

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

Suggested reading.

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Szeczech GM, Carlton WW, Hinsman EJ, Jacobson JJ: Fibroma in Indiana cottontail rabbits. J Am Vet Med Assoc 165: 846-848, 1974.

Slide 26 (AFIP 2237858)

History. This mouse was one of several among a shipment of pathogen-free mice that died suddenly a few days after arrival.

Gross Pathology and Laboratory Results. The liver was pale yellow-tan and finely mottled with slightly darker areas. There were no other gross lesions.

No bacterial pathogens were isolated from the nasal passages, liver, or cecum. Results of serologic tests for antibodies to Sendai virus, pneumonia virus of mice, mouse hepatitis virus (MHV), minute virus of mice, GD-VII virus, reovirus type 3, lymphocytic choriomeningitis virus, mouse pox (ectromelia), K virus, polyoma virus, and mouse adenovirus were negative.

Diagnoses. 1. Liver: Hepatitis, necrotizing, acute, multifocal to coalescing, BALB/c mouse (Mus musculus), rodent. 2. Liver: Extramedullary hematopoiesis, diffuse, mild.

Contributor's Comment and Conference Note. MHV infections usually do not cause clinical disease in adult immunocompetent mice. However, strains of MHV differ in virulence, and strains of mice differ in susceptibility. BALB/c mice are among the most susceptible; severe disease can occur in non-immune adult BALB/c mice infected with virulent strains of MHV. Our diagnosis was based on the characteristics of the liver lesions, which included a few syncytia at the edges of necrotic areas in some sections, and the presence of numerous syncytia in the cecal epithelium. The major differential diagnosis in this case includes salmonellosis, mousepox, and Tyzzer's disease. In salmonellosis, the lesions tend to be more suppurative and to affect the walls of veins, resulting in thrombophlebitis, and Salmonella was not isolated from the liver. Acute virulent mousepox features necrosis of lymphoid tissues as well as liver, with cytoplasmic inclusions. In Tyzzer's disease, the causative bacillus can be demonstrated within hepatocytes with stains such as Warthin-Starry; such organisms were not present in this mouse.

The moderator commented on the presence of several cytomegalic, karyomegalic hepatocytes containing abundant nuclear heterochromatin. These cells were often located adjacent to areas of necrosis and are typical of mouse corona virus hepatitis.

Mouse hepatitis virus has two patterns of infection, respiratory and enteric, depending on the virus strain. Respiratory strains infect the upper respiratory mucosa, with dissemination to secondary target organs, such as liver, in susceptible hosts. Enteric strains infect enteric mucosa in all ages with minimal dissemination. Pathognomonic lesions are multinucleated syncytia. The ascending colon is the most frequent site of infection with the enteric strain. Immunosuppression increases the susceptibility to a disseminated infection.

Contributor. Department of Comparative Medicine, University of Alabama at Birmingham, Birmingham, AL 35294.

Suggested reading.

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Barthold SW: Mouse hepatitis virus infection, intestine, mouse. In Jones TC, Mohr U, Hunt RD (eds), Monographs on Pathology of Laboratory Animals. III. Digestive System. Springer-Verlag, New York, 1985.

Slide 27, L5 (AFIP 2237470)

History. This conventionally-housed rabbit had a rapid onset of respiratory disease characterized by rapid respiration and a fever of 104.5°F. It was treated with oral and injectable tetracycline without effect. Due to its deteriorating condition, the rabbit was euthanatized. Other rabbits in the same room have had similar signs.

Gross Pathology and Laboratory Results. The right pleural cavity was completely filled with turbid, pink fluid that compressed the right lung. The pleural surface of the right lung lobe was covered with white, fibrinous material.

Culture of pleural fluid yielded Pasturella multocida.

Diagnosis. Lung: Pleuropneumonia, fibrinopurulent, chronic, diffuse, severe, with pulmonary edema, fibrosis and hemorrhage, Flemish giant rabbit, lagomorph.

Contributor's Comment and Conference Note. Infection with Pasturella multocida, a gram-negative bacillus, causes one of the most common diseases of laboratory rabbits. Pasteurellosis can result in rhinitis, conjunctivitis, otitis media, abscesses, bronchopneumonia, metritis and septicemia. Rabbits may die suddenly with the systemic form of the disease without any significant gross or histologic lesions.

P. multocida is ubiquitous in most conventionally housed rabbits and was the cause of respiratory disease in the other rabbits housed in the room with this rabbit. Transmission is by direct contact or aerosol and asymptomatic carriers are common and an important source of infection.

Pasteurellosis is the leading cause of morbidity and mortality in rabbits, the prevalence ranges between 20-70%. Pasteurella organisms may also be isolated from the nasopharyngeal area of rabbits with no clinical signs or pathologic lesions. Transmission is by aerosol and direct contact. The prevalence increases with age. Predisposing factors such as increased atmospheric ammonia levels, concomitant disease, stress of pregnancy and travel are thought to be significant. The most common presentation is a serous to mucous to mucopurulent rhinitis/sinusitis (snuffles), ascending the nasolacrimal duct to a conjunctivitis. Other infections may produce pneumonia, osteomyelitis, meningoencephalitis, nephritis, orchitis, septicemias and subcutaneous abscess. Subclinical infections may remain. The disease is considered to be incurable.

Contributor. Emory University, School of Medicine, P.O. Drawer II, Atlanta, GA 30322.

Suggested reading.

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Slide 28 (AFIP 2285555)

History. This female, 112-week-old B6C3F1 mouse was euthanatized at the termination of a 2-year carcinogenesis bioassay.

Gross Pathology. Spleen: Irregularly shaped, 14x10x6mm, firm red mass.

Diagnosis. Spleen: Hemangiosarcoma, B6C3F1 mouse, rodent.

Contributor's Comment and Conference Note. This case is a typical example of the hemangiosarcomas commonly seen as incidental lesions in the spleen and other organs of aging mice. The section is from an irregularly-shaped, 14 x 10 x 6mm, firm, red splenic mass. Except for an intact external capsule and scattered small foci of lymphoid cells (not present in every slide), the usual splenic architecture has been replaced by sheets of densely-packed abnormal vascular channels supported by a moderately abundant, focally edematous fibrous stroma. These vascular channels vary widely in diameter and shape, and frequently exhibit branching and interconnection. The channels are lined by usually single layers of endothelial cells with plump, oval, hyperchromatic nuclei. Lumina contain variable numbers of red blood cells as well as proteinaceous fluid and occasional fibrin thrombi. The fibroblast-like stromal cells are elongated with large elliptical vesicular nuclei. A few neutrophils are scattered throughout, but inflammatory cell infiltrates are generally inconspicuous. A focal area composed of similar vascular channels was present in the medullary cavity of the femur.

Conference attendees agreed the features of this neoplasm were consistent with a hemangiosarcoma. The moderator added that although hemangiosarcomas in mice may have marked cellular pleomorphism; the monomorphic cytological features of this particular neoplasm were more typical of the classically described condition.

Hemangiosarcomas often occur in up to 2-5% of control mice in long-term studies. In certain breeds the rate may be as high as 40%. These neoplasms can occur in multiple sites and differentiating metastasis from multicentric origin can be difficult. Grossly, hemangiosarcomas may often be distinguished from soft tissue neoplasms by their cystic, sometimes firm, irregularly nodular appearance and red or red-brown color.

Contributor. National Institute of Environmental Health Sciences/National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

Suggested reading.

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Squire RA, Goodman DG, Valerio MG, et al: Tumors-cardiovascular system. In: Pathology of Laboratory Animals, Vol. II, (eds) K Benirschke, FM Garner, TC Jones, pp. 1083-1092, Springer-Verlag, New York, 1978.

Stewart HL: Tumours of the soft tissues. In: Pathology of Tumours in Laboratory Animals, Vol. II, The Mouse, (ed) VI Turusov, pp. 487-509, IARC, Lyon, France, 1979.

Slide 29, L6 (AFIP 2286724)

History. This CRL; CD(SD)BR male rat was obtained from Charles River Breeding Labs as part of a larger shipment to be placed on a two-year carcinogenicity study. It was about 28 days old on arrival, was quarantined for 14 days then placed on study in one of the dose groups. It was housed in an environmentally controlled room and fed powdered Purina rat chow (5002). It was killed in moribund condition after 617 days on study.

Gross Pathology. The terminal body weight was 400 g and the rat appeared in generally good flesh. There was a small dark firm nodule (0.2-0.5cm) in the pancreas; both testes were small and soft (slight) and each hindlimb had a moderately severe raised lesion involving the plantar tarsal region. There was an invasive mass in the thoracic cavity; it was pale, mottled, firm, measuring 5.5cm long x 3.0cm wide x 2.5cm thick. The mass was largest near the thoracic vertebral bodies and extended ventrally into the dorsal thoracic wall.

Diagnosis. Mass from thoracic cavity (per contributor): Chordoma, CRL; CD(SD)BR rat, rodent.

Contributor's Comment and Conference Note. Light microscopic examination revealed typical physaliphorous (bubble) cells arranged in irregular lobules by connective tissue strands. These cells contained numerous large unstained cytoplasmic vacuoles, a central or eccentric oval nucleus and a small centrally located nucleolus. The cells resembled microscopically the notochordal remnants found in the central portion of the intervertebral discs in fetal rats.

Chordomas have been reported in people, dogs, mice, mink, rats, ferrets and a cat. The tumor usually arises from residual foci of notochord most commonly located within the sacrococcygeal vertebrae or skull. In rats, up to 56% of chordomas

metastasize to the lungs. In human beings, they are locally destructive and invasive and metastasize in up to 43% of the cases. Chordomas are more common in males in both rats and people.

Contributor. Merrell Dow Research Institute, P.O. Box 68470, Indianapolis, IN 46268.

Suggested reading.

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Reuber MD, Reznik-Schuller HM: Benign chordoma (sacrococcygeal) in the rat: A light and electron microscopic study. Vet Pathol 21: 536-538, 1984.

Stefanski SA, Elwell MR, Mitsumori K, Yoshitomi K, Dittrich K, and Giles HD: Chordomas in Fischer 344 rats. Vet Pathol 25: 42-47, 1988.

Slide 30, L7, L8 (AFIP 2286467)

History. An adult dusky leaf monkey (Presbytis obscurus), originally imported from Indonesia, had been kept individually in a private primate zoo for more than 3 years. He started to develop intermittent diarrhea and anorexia a week before death. The diarrhea was watery and green.

Gross Pathology. The stomach was empty and there were multiple, 0.5 to 1.5 cm circumscribed raised, pale yellow-green areas randomly present in the mucosa. Most of the affected regions had ulcerated centers. The liver showed generalized enlargement with multiple variably shaped, white to pale yellow, raised foci on the surface, ranging from 0.2 x 0.2 - 4 x 1.2 - 6 cm, some of which had a slightly depressed center. Similar foci were also noted on the cut surface of the liver parenchyma.

Diagnoses. 1. Stomach: Gastritis, erosive, multifocal, subacute, mild to moderate, with intralesional amoebae sp., dusty leaf monkey (Presbytis obscerus), primate. 2. Liver: Hepatitis, necrotizing, subacute, multifocal to coalescing, severe, with multifocal necrotizing phlebitis and intralesional amoebae sp.

Contributor's Comment and Conference Note. There were areas of necrosis in the gastric mucosa covered by thick layers of fibrin and mucin mixed with some exfoliated degenerate and necrotic epithelial cells, bacterial colonies, few neutrophils and scattered trophozoites of E. histolytica (PAS positive). Large numbers of trophozoites and mild infiltration of macrophages and plasma cells were present in or along the edge of the necrosis. The submucosa showed diffuse edema and focal mononuclear inflammatory cell infiltration.

The liver contained multiple discrete to coalescing foci of zones of caseous

necrosis with a laminated appearance and a minimal to mild inflammatory cell response of macrophages and lymphocytes along the edge. Trophozoites of E. histolytica of varying numbers were seen in most affected areas, primarily at the edges of the lesions. The blood vessels adjacent to the necrosis were often involved as well with changes characterized by focal necrosis of the wall and early thrombus formation.

It is known that the stomach of leaf monkeys is adapted for digesting leaves and leafy vegetables and consists of presaccular, saccular, tubular and pyloric portions. The presaccular and saccular portions have a neutral pH for fermentation that makes them a suitable environment for excystation of amebas and trophozoite invasion.

Although hepatic involvement without gastric lesions or vice versa occurs in some cases of amebiasis, we suspect that the infection in this case was initiated from the stomach with secondary vascular spreading to the liver. This speculation is based on the fact that there were much lower numbers of trophozoites in the liver lesions than in those of stomach and they generally required special stain to be visualized. In comparison with the extensive tissue destruction, the inflammatory response was rather mild in this case. It has been indicated that except for the earliest stages and advanced lesions with bacterial superinfection the host inflammatory response of amebic lesions is generally poor. This is because the tissue destruction is due largely to liquefactive necrosis caused by the lytic substance released from the trophozoites.

Conference participants agreed that the history and histological lesions were consistent with Entamoeba histolytica. Variation of the vascular component was present in the slides.

Contributor. Animal Industry Res. Inst. TSC, #1 Tapu, Chunan, Miaoli, Taiwan ROC, and Pig Research Institute of Taiwan.

Suggested reading.

Frank H: Pathology of amebiasis in leaf monkeys (Colobidae). In: Proceedings, 24th Int. Symp. Dis Zoo Anim., pp. 321-326, 1982.

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Von Lichtenberg F: Infectious disease. In Robbins Pathologic Basis of Disease, ed. Cotran RS, Kumar V, and Robbins SL, 4th ed., pp. 307-443. W.B. Saunders Co., Philadelphia, 1989.

Slide 31, L9 (AFIP 2237857)

History. This 1 kg weanling, female New Zealand white rabbit (Oryctolagus cuniculus) was one of four submitted by the owner of a commercial rabbitry that produces rabbits for biomedical research. The rabbits had soft, gelatinous, or mucinous feces, were lethargic, and had poor appetites.

Gross Pathology and Laboratory Results. The contents of the cecum and colon were semifluid and mucinous, and the rectum did not contain formed fecal pellets. There were no other gross lesions.

No bacterial pathogens were isolated from the cecum, small intestine, liver, or nasal passages.

Diagnoses. 1. Small intestine and cecum: Enteritis and typhlitis, proliferative, diffuse, New Zealand white rabbit (Orcytolagus cuniculus), lagomorph. 2. Small intestine: Enteritis, histiocytic, diffuse, moderate.

Contributor's Comment and Conference Note. There was similar but milder epithelial hyperplasia in the distal ileum and proximal sacculated colon. In Warthin-Starry-stained sections, numerous small curved bacilli were visible in the apical cytoplasm of hyperplastic epithelial cells. In immunofluorescence tests performed by Dr. James G. Fox, the bacteria were stained by antibody specific for intracellular Campylobacter-like organisms (CLO) present in proliferative intestinal lesions in swine, hamsters, and ferrets. The condition in rabbits thus appears to be similar to proliferative enteritides in these and possibly other species. It also has some similarities to an acute cecitis of young rabbits associated with intracellular CLO and with a histiocytic enteritis reported from Japan. Since 1983, we have identified the condition in rabbitries in three different states, suggesting that the condition is widespread geographically. The identity of the organisms has not been determined. Those in swine and hamsters are recognized by monoclonal antibody against an antigen common to several known Campylobacter spp, and some reports indicate that they are recognized by rabbit antisera against known Campylobacter spp. such as C. hyointestinalis. However, because the serum of many rabbits contains naturally occurring antibodies against the intracellular CLO, Campylobacter antisera prepared in rabbits not determined to lack such pre-existing antibodies cannot be regarded as specific. Specific antisera against intracellular CLO extracted from intestines of pigs with proliferative enteritis do not recognize known species of Campylobacter.

Marked tissue variation was present in several slides. Of interest was the presence of numerous macrophages within the lamina propria of the small intestine in several sections. Many of these cells contain apparent intracytoplasmic silver positive organisms morphologically similar to the organisms both within the lumen and in the apical cytoplasm of enterocytes. Similar cells were observed in tissue sections by Schoeb and Fox (11). Foreign body giant cells were not present in the sections presented.

Contributor. Department of Comparative Medicine, University of Alabama at Birmingham, Birmingham, AL 35294.

Suggested reading.

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2. McOrist S, Lawson GH: Reproduction of proliferative enteritis in gnotobiotic pigs. Res Vet Sci 46: 27-33, 1989.

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the faeces of normal and contact pigs. Vet Rec 124: 40, 1989.

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Slide 32 (AFIP 2288942)

History. A 6-month-old domestic shorthair male (castrate) cat was presented to the referring veterinarian for anorexia, vomiting, hypersalivation, polydipsia, muscle weakness and halitosis.

Gross Pathology and Laboratory Results. The cat had eaten a cholecalciferol-based rodenticide several days previously. It was fed a proprietary diet with no vitamin or mineral supplementation. White, firm plaques were present on the buccal mucosa. The lungs were congested and edematous. The kidneys were swollen with white streaks through the cortices. Focal, gritty pale areas were present transmurally through the stomach and small intestine. Multifocal pale areas were present in the myocardium.

Serum biochemistry:

creatinine:	405 umol/l (normal 70-159 umol/l)
urea:	25 mmol/l (normal 7-10.7 mmol/l)
calcium:	7.9 mmol/l (normal 1.6-2.6 mmol/l)

Diagnosis. Kidney, cortex, basement membranes, tubular epithelium, and periglomerular and perivascular connective tissue: Mineralization, multifocal, moderate, with multifocal tubular epithelial cell necrosis, domestic shorthair, feline.

Contributor's Comment and Conference Note. There was evidence of widespread metastatic calcification in most organs and blood vessels. There was extensive calcification in lungs and heart, both of which may have led to the severe pulmonary edema that was present. Cholecalciferol (Vitamin D_3) used as a rodenticide has only recently been released in Australia. In North America, it has been known for some time as a potential toxin in domestic animals. Reported cases suggest that the levels required for illness and death are lower than the reported LD_{60} of 88 mg/kg BW in dogs.

The calciferols (Vitamin D and its metabolites) are fat soluble, biologically active secosteroids. Secosteroids are steroid-related molecules in which one of the four rings has been opened.

Toxicosis of Vitamin D_3 is believed to result from high circulating levels of 25-hydroxycholecalciferol which can substitute for 1,25-$(OH)_2D_3$ on receptors when present in excessive amounts. Mineralization is common in the dog and cat, but unusual in other species. Solanum malaçoxylon and Cestrum diurnum in cattle, horses and pigs that ingest the leaves and stems can produce a toxicosis when the 1,25-$(OH)_2D_3$ is cleaved from the carbohydrate moieties in vivo to release active D_3. Clinical signs include progressive emaciation, joint stiffness, increased serum phosphorus and greatly increased serum calcium. The bones may be thickened due to hyperostosis.

Biochemical studies using subcellular fractionation suggest localization of 1,25$(OH)_2D_3$ in the nuclei of the target organs where it acts on DNA to make mRNA. The mRNA codes for specific enzymes/proteins that are responsible for calcium transport; the resultant hypercalcemia causes inactivation of adenyl cyclase. This in turn results in decreased levels of adenosine monophosphate which impairs Na transport in the kidneys with loss of sodium in the urine (natriuresis). The resultant PU/PD are reversible if the cause of the increased calcium is removed. If it is not, a progressive mineralization occurs, beginning with the tubular basement membranes and epithelium, especially at the corticomedullary junction and eventually involving the glomeruli. The tubular epithelial mineralization and the cast formation cause tubular obstruction and eventual loss of nephrons.

Rabbits are very sensitive to Vitamin D_3. Outbreaks of toxicosis have occurred with five times the normal feed levels of Vitamin D_2/D_3.

Contributor. School of Veterinary Studies, Murdoch University, Murdoch Western Australia 6150.

Suggested reading.

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Slide 33 (AFIP 2184633)

History. This 26-year-old female Iceland pony was presented with suppurative

pulpitis of the right upper P2 and P3 and empyema of the adjacent maxillary sinus. Ten days following surgery the pony developed treatment-resistant fever and became lethargic. As the pony's condition deteriorated rapidly it was euthanatized 15 days post surgery.

Gross Pathology. The pony was found to have an empyema of the right maxillary sinus. Both lungs had multifocal greyish-white foci, approximately 3 cm in diameter. The pituitary gland showed a greyish-white nodule, 2 cm in diameter, with scattered areas of hemorrhage on cut surface and compression of the overlying hypothalamus. Both adrenal glands showed multifocal nodular hyperplasia. The liver was slightly enlarged, pale and yellowish. The meninges of the brain were opaque and hyperemic and the basal cisterns were filled with creamy pus. Verminous arteritis was present in the mesenteric vessels, and intestinal infestation with Anoplocephala perfoliata was observed.

Diagnosis. Pituitary gland, pars intermedia: Adenoma, Iceland pony, equine.

Contributor's Comment and Conference Note. Histologically, the tumor is subdivided by fibrovascular stroma into several nodules with focal hemorrhages and compression of the pars distalis. The tumor is composed of large columnar, spindle-shaped or polygonal cells, which are arranged in cords forming palisades and pseudoacini. Occasionally, cuboidal cells form follicular structures containing colloidal-like, PAS-positive material. Nuclear pleomorphism is absent and mitotic figures are rare.

The greyish-white foci observed grossly in the lungs consisted of pyogranulomatous infiltrates and fungal colonies. Histological examination of the meninges of the brain revealed a diffuse suppurative leptomeningitis.

Although no clinical history was available from the present case, the owner mentioned, on request, that the pony suffered from polydipsia and polyuria. The clinical syndrome, generally associated with adenomas of the PI, includes hirsutism, muscle wasting, hyperglycemia, glucosuria, and diabetes insipidus. This syndrome was considered to result from hypothalamic compression and damage to the hypothalamic-neurohypophyseal tract by suprasellar extension of silent pituitary adenomas. Recent studies have challenged this view by demonstrating elevated plasma ACTH and cortisol levels, loss of circadian fluctuation and relative resistance to glucocorticoid negative feedback inhibition of ACTH secretion in affected horses. It was demonstrated that equine Cushing's disease caused by adenomas of the PI is associated with ACTH hypersecretion. Furthermore, PI proopiomelanocortin (POMC) peptides such as alpha-MSH, beta-MSH, corticotropinlike intermediate lobe peptide (CLIP), and beta-endorphin are also secreted.

Immunocytochemistry of the present case revealed strong cytoplasmic reaction for POMC (human$^{1\text{-}48}$ N-POMC and human$^{1\text{-}76}$ N-POMC) and alpha-MSH. In contrast, immunostaining was weak to moderate for ACTH and beta-endorphin and negative for prolactin. These results are in accordance with the above mentioned biochemical studies. The bacterial and fungal infections could be due to the hypercortisolism.

The frequency of pituitary tumors within various animal species was discussed. Adenomas derived from cells of the pars intermedia are by far the most common

type of pituitary tumor in horses. Functional tumors arising from corticotroph (ACTH-secreting) cells in either the pars distalis or the pars intermedia are encountered most frequently in dogs. Pituitary adenomas are frequently seen in female rats and are associated with increased levels of prolactin.

Contributor. Institut für Veterinär-Pathologie, FrankfurterstraBe 96, D-6300 Giessen, West Germany.

Suggested reading.

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Slide 34 (AFIP 2287626)

History. 1-year-old male thoroughbred was one of 13 out of a herd of 36 to die or be euthanatized. All herd members showed varying degrees of illness. Of those to die, some were sudden and unexpected, but most had a one to several day history of depression and weakness with dyspnea and tachycardia. Sweating and signs of colic were common. Treatment for nonspecific colic was initiated.

Gross Pathology. The heart was soft and moderately flaccid. Streaks and irregular patches of pale tan and dark red tissue were multifocally distributed in the ventricular myocardium. An effusion of clear, bright yellow fluid was found in the pleural and peritoneal cavities.

Diagnosis. Heart, myocardium: Myocyte loss, multifocal, moderate, with degeneration and necrosis, thoroughbred, equine.

Contributor's Comment and Conference Note. The myocardium contains numerous foci devoid of muscle. Adjacent myocardial cells are necrotic and fragmented. Many congested thin-walled vessels are present. The skeletal muscle of the diaphragm (not included) has mild, multifocal phagocytosis and fragmentation of muscle fibers.

Monensin is a growth promoter and coccidiostat commonly added to cattle and poultry feeds. There is a wide range of toxicity among domestic species. The horse is

exquisitely sensitive to the chemical. The veterinary literature documents a number of incidental and experimental intoxications. Myocardial degeneration is the most pronounced postmortem finding.

In this outbreak, a mislabelled pelleted feed containing Monensin was distributed as horse feed. Twenty-five deaths occurred over a two month period. Echocardiographic evaluation revealed ventricular dyskinesis. Serum creatine kinase (CK), the myocardial isoenzyme for creatine kinase (CKMB), and hydroxybutyrate dehydrogenase (HBDH) were all markedly elevated. Necropsy findings were dark red to tan mottling of the ventricular myocardium and effusion of a clear yellow fluid into the body cavities.

A group of survivors was studied for 10 months. Nine were necropsied, because their exercise fatigue was of cardiac origin. The hearts were moderately flaccid but lacked significant histopathology.

Monensin, a polyether antibiotic, is a metabolic fermentation product of Streptomyces cinnamonenis. Monensin is a sodium-selective carboxylic ionophore by virtue of its ability to form lipid-soluble cation complexes that can readily traverse cell membranes. Monensin is used extensively as a feed additive to control coccidiosis in chickens and as a growth promotant in cattle. In ruminants monensin results in a higher recovery of energy from rumen fermentation by increasing the proportion of proprionic acid produced.

Monensin toxicosis is characterized by myodegeneration and necrosis with species variation of severity within cardiac and/or skeletal muscle. Toxicosis has been reported in cattle, sheep, pigs, horses, dogs, chickens, turkeys, and guinea fowl, although only approved for use in cattle and poultry. Horses are the most susceptible to monensin toxicosis.

Toxicity results most frequently from feed mixing errors or from the accidental feeding of a nontarget species, especially monogastric animals. Toxicity also often results from drug incompatibilities such as with concurrent treatment with tiamulin, used to control swine dysentery, and triacetyloleandomycin. The LD_{50} of monensin varies from 200 mg/kg in broiler chickens to 2-3 mg/kg in horses.

Microscopic lesions of monensin toxicity differ very little from those of nutritional or exertional myopathy, except that mineralization of degenerate tissue usually is less marked.

Differential diagnosis in a horse would include: exertional, and nutritional myopathy, blister beetle intoxication, white snake root and coffee senna poisoning, colic and laminitis of variable causes.

Contributor. New Bolton Center (University of Pennsylvania), 382 West Street Road, Kennett Square, PA 19348.

Suggested reading.

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Slide 35 (AFIP 2289404)

History. This male, Fischer 344 rat was on a longevity study in which it received a moderate reduction in caloric intake.

Gross Pathology. Right adrenal enlarged (8x8x8 mm), round, pale, firm.

Diagnoses. 1. Adrenal gland: Ganglioneuroma, with vascular invasion, Fischer 344 rat, rodent. 2. Adrenal gland: Pheochromocytoma. 3. Adrenal gland: Large granular cell leukemia.

Contributor's Comment and Conference Note. This tumor is a malignant mixed cell tumor of adrenal gland containing leukemia cells.

Adrenal gland contains a neoplastic mass centrally and a compressed rim of preexisting adrenal gland (mainly cortex) at the periphery. In the center of the mass is a well-differentiated pheochromocytoma. A ganglioneuroma containing ganglion cells and abundant Schwann (support) cells surrounds the pheochromocytoma. Ganglion cells are present in nests or as individual cells between Schwann cells or in the pheochromocytoma. The ganglioneuroma has penetrated the adrenal capsule and has infiltrated the periadrenal tissue. Many blood-filled spaces (especially in the pheochromocytoma) contain numerous lymphocytes. Necrosis of lymphocytes and pheochromocytoma cells is evident. Ganglioneuroma and leukemia cells are present within vessels inside and outside of the adrenal capsule.

Metastatic foci were not observed.

There was variation in slides; several contained small fragments of liver with a mild hepatocellular degeneration and leukemia. Several participants felt there was evidence of extramedullary hematopoiesis within the adrenal gland and hepatic sinusoids. In several sections the ganglioneuroma was also seen in periadrenal vascular spaces.

Histological data on more than 60,000 F344 rats revealed 28 ganglioneuromas (2). Ganglioneuromas were always associated with pheochromocytomas. Ganglion cells and pheochromocytes are both thought to be derived from fetal sympathoblasts. The tumor cells in these two tumors probably represent two differentiation stages of the stem cell, rather than two independently developing neoplastic cell types.

Contributor. Pathology Associates, Inc., National Center for Toxicological Research, Jefferson, AR and Arkansas Livestock and Poultry Commission.

Suggested reading.

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Slide 36 (AFIP 2292388)

History. A 13-1/2 year old male clouded leopard (Neofelis nebulosa) was presented for a one month history of vomiting and loose stools, increased frequency of defecation, progressive weight loss.

Gross Pathology and Laboratory Results. Degenerative joint disease; chronic nephritis; hepatic telangiectasia and biliary cysts.

Glucose (2 weeks pre-necropsy 121 mg/dl; Glucose (day of necropsy) 92 mg/dl.

Diagnoses. 1. Pancreas, Islets of Langerhans: Amyloidosis, multifocal, moderate, clouded leopard (Neofelis nebulosa). 2. Pancreas, exocrine: Nodular hyperplasia, multifocal, moderate. 3. Pancreas: Lobular fibrosis and ductular hyperplasia, multifocal, moderate, with exocrine acinar atrophy and chronic inflammation.

Contributor's Comment and Conference Note. Islet amyloid is similar to that seen in domestic cats. In domestic cats, this amyloid is derived from polymerization of islet-amyloid polypeptide (IAPP), which is synthesized in normal islet beta cells. Affected cats are normoglycemic, but have glucose intolerance. Studies are in progress (Dr. Ken Johnson, University of Minnesota) to determine if the amyloid in this leopard is due to IAPP. Islet amyloidosis also has been identified in another clouded leopard, a puma, and a jaguar.

Pancreatic atrophy likely is secondary to stenosis or inflammation of the pancreatic ducts from an ascending infection. Because cats have a common bile duct/pancreatic duct at the entrance to the duodenum, this lesion often coexists with chronic cholangitis, as was true for this leopard. Ductal hyperplasia would result from the chronic irritation. The hyperplastic epithelium in some lobules has the appearance of either ductal or acinar epithelium, supporting evidence of a common stem cell for these two populations.

Pancreatic acinar adenomas are also referred to as nodular hyperplasia and are common in older cats. Adenoma would be the preferred terminology in this case because of compression of the adjacent parenchyma.

The various types of amyloid were discussed. Islet amyloid polypeptide (IAPP) has recently been identified as the principle constituent of amyloid deposits in a human insulin producing tumor (insulinoma), human patients with Type II (non-insulin dependent) diabetes mellitus, and adult cats with diabetes. IAPP is synthesized by normal islet beta cells and probably co-secreted with insulin. Although the physiological role of IAPP has not been completely worked out, it may be important in development of Type II diabetes mellitus by apposing the action of insulin in peripheral tissues. Polymerization, forming extracellular islet-amyloid deposits, may further contribute to the development of diabetes by destroying islet cells and disrupting the passage of glucose and hormones.

In humans, approximately 90% of amyloid consists of fibril proteins, the remaining 10% is composed of a glycoprotein designated as "P component". Two major classes of amyloid have been identified. AL (amyloid light chain) is derived from plasma cells and is composed of complete immunoglobulin light chains, NH_2-terminal fragments or both.

Most of the light chains are of the lambda type (particularly lambda VI); however, in some cases, kappa chains have been identified. The second major class (AA) does not have structural homology to immunoglobulins or any other known protein. AA is commonly referred to as "secondary amyloidosis" because it is often associated with inflammatory conditions. AA fibrils are derived from a large precursor in the serum called SAA (serum amyloid associated) protein that is synthesized in the liver.

Other biochemically distinct proteins found in amyloid deposits include transthyretin, beta 2-microglobulin and beta 2-amyloid protein.

After treatment with potassium permanganate, AA protein loses affinity for congo red, whereas other forms of amyloid do not.

Contributor. National Zoological Park, Smithsonian Institution, Washington, DC 20008.

Suggested reading.

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2. Johnson KH, O'Brien TD, Hayden DW, et al: Relationships of islet amyloid polypeptide (IAPP) to spontaneous diabetes in adult cats. In: Isobe T, Araki S, Uchino F, Kito S, Tsubura E, eds. Amyloid and amyloidosis. New York: Plenum Press, 1988, pp 673-678.

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Slide 37, L10 (AFIP 2133003)

History. A 12-year-old, female Yorkshire terrier was presented for vomition of solid food for several weeks. A mid-abdominal mass was palpable. Exploratory laparotomy revealed gross enlargement of the left ovary and ovariohysterectomy was performed.

Gross Pathology. An ovariohysterectomy specimen with normal-looking, slender uterine horns and small right ovary. The left ovarian bursa was tense and was expanded by a grossly enlarged (4.5 cm diameter) ovoid gonad with soft, pale cut surfaces

containing central, softer, red areas. No normal left ovarian tissue was recognized.

Diagnosis. Left ovary (per contributor): Dysgerminoma, Yorkshire terrier, canine.

Contributor's Comment and Conference Note. Histological features which support this diagnosis are the extensive effacement of ovarian tissue by sheets of polyhedral and pleomorphic cells with numerous mitoses, patchy cystic degeneration and hemorrhage and occasional loose foci of lymphoid cells.

No clinical evidence of metastasis is recognized to date (one month after surgery) in this case.

Dysgerminoma is a neoplasm composed of large cells with large vesicular nuclei indistinguishable from primordial germ cells of the sexually indifferent embryonic gonad. It closely resembles a seminoma of the testis. Dysgerminomas are rare in animals, occurring in dogs, cats and cows (in order of decreasing frequency). These neoplasms rarely metastasize; a 10-20% incidence is reported. When metastasis does occur, it may involve the regional lymph nodes, liver and kidneys. Grossly, dysgerminomas have a yellow-white to gray-pink appearance and are often soft and fleshy.

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Suggested reading.

Nielsen SW, Misdorp W, McEntee K: "Tumours of the Ovary" Bulletin WHO 53, 1976, pp 203-216.

Slides 38 & 39 (AFIP 2240201)

History. Male bovine (holstein) fetus, 6.5 months gestation. Second abortion in the last 3 months; prior to abortion, the cow developed a swollen, edematous udder. The placenta was retained. The animal had been on a dry hay winter ration for several months prior to the abortion.

Gross Pathology and Laboratory Results. The male fetus was approximately 6-1/2 months gestation. No skin abnormalities detected, no gross anomalies observed. There were no remarkable findings on internal inspection. Lungs did not float upon immersion in buffered formalin solution. Significant necropsy findings were restricted to the placenta. Intercotyledonary areas were a yellow-tan to brown color, thickened, and leathery in consistency. Cotyledons were swollen, cupped, and appeared necrotic. There were multiple foci of adventitial placentation present within the intercotyledonary stroma.

Tissues submitted for bacterial and fungal studies included placenta, lung, liver, and stomach contents. For virology, placenta, thymus, spleen, lung, liver, kidney and fetal heart blood were examined. Liver and kidney were taken for trace mineral toxicologic analysis. Specimens of all major body organs including eyelid, thyroid and adrenals were examined histologically.

The placenta yielded a heavy, pure growth of Aspergillus sp. on Mycosel agar. Lung, liver and stomach contents were negative on bacterial and fungal culture. All tests for viruses were negative; tests for chlamydia utilizing McCoy cell tissue culture and FA

antibody conjugate were also negative. Fetal heart serum IgG levels were within acceptable normal limits, at 11 mg/ml, while IgM levels were elevated at 40 mg/ml.

Diagnosis. Placenta: Placentitis, necrosuppurative, diffuse, severe, with necrotizing vasculitis, mineralization and fungal hyphae, holstein, bovine.

Contributor's Comment and Conference Note. Histopathological examination revealed numerous inflammatory cells throughout the chorioallantois, including degenerate neutrophils. Some sections examined have a severe vasculitis. There is widespread necrosis and mineralization of trophoblast cells, together with focally dense clusters of degenerate inflammatory cells. Grocott's methenamine silver stain demonstrated the presence of numerous parallel-sided, septate, branching hyphae within the exudate adjacent to necrotic villus trophoblasts and frequently within the placental stroma per se. Other tissues have nonspecific changes, though the liver has diffuse periacinar atrophy of hepatocytes, narrowing of hepatic cords, and sinusoidal edema and dilation.

Gross and microscopic findings strongly suggest Aspergillus to be the cause of abortion; the organism was detected on direct smear, on fungal culture, and readily seen microscopically utilizing special stains. The gross appearance of the placenta was also typical of mycotic abortion, though Brucella abortus and Campylobacter fetus were also considered initially. It is noteworthy that a diagnosis in this case would not have been possible had placenta not been included for examination.

Fungal agents have been consistently reported in studies on bovine abortion (1,2), the first case in cattle presented by Theobald Smith in 1920 (3). As in this case, the greatest majority of mycotic abortions are due to Aspergillus spp. in the Northern hemisphere, the species A. fumigatus being most commonly reported (3). Unfortunately, in this case, specific typing of the organism cultured from the placenta was not done. The highest incidence appears to be from December to May, the time of feeding hay which may be infected with fungal spores (1,2,3).

Aspergillus sp and other molds are widespread in nature; cattle are believed to be most commonly infected by the aerogenous route (5), with hematogenous spread accounting for placental involvement (4,5,6). The possibility of contaminated semen as a source of the organisms, or the gastrointestinal tract, has also been mentioned (3,7). Most fetuses expelled are between 3 and 7 months gestation (3). Apparently pregnancy confers extraordinary susceptibility of the uterus and its contents to the growth of fungi; both Aspergillus spp. and the zygomycetes (Mucor, Absidia, and Rhizopus spp.) have an affinity for the invasion of blood vessel walls with ensuing vasculitis as seen in some of the slides in this case. Thrombosis is often a result (5).

Fungal agents such as Aspergillus spp. are believed to produce irritating and toxic metabolites locally, thus accounting for the lesions seen, though at least one author states that very little is known specifically about the pathogenesis of lesions caused by these organisms (1,8).

In this case no skin lesions were seen, though they are present in about 20% of mycotic abortions (2). The liver of this fetus demonstrated mild inflammatory changes with portal lymphomononuclear aggregates, together with evidence of hypoxia characterized by periacinar atrophy. Radial immunodiffusion analysis of fetal heart serum indicates the fetus had elicited a primary immune response, with serum IgM levels elevated to 40 mg/ml (normal levels 6-19 mg/ml). Serum IgG levels were within normal

limits (9,10). Such measurement of fetal (preclostral) immunoglobulin levels can be a useful aid in appraising the likelihood of infectious abortion, though there is always a possibility of transplacental absorption of maternal antibody. Trace mineral analysis on fetal liver and kidney, particularly for Se and Cu, were within normal limits (11).

Aspergillus colonies grow with a distinct margin, fluffy and white during early growth but later becoming velvety and blue-green in color due to the production of pigmented conidia. Microscopically, as in this case, the hyphae are septate and hyaline, and stain well with Grocott's methenamine silver; PAS and other stains have also been used, though in the contributor's experience Grocott's is most satisfactory. Other species sometimes involved are A. niger, A. flavus and A. terreus (8).

A diagnosis of mycotic abortion may be reasonably made when the organism is demonstrated in fetal tissue with the characteristic lesions of placentitis, dermatomycosis, or bronchopneumonia. The finding of fungi in abomasal contents without demonstrable lesions should be interpreted with care as yeasts and molds of unknown source may be present (2).

Conference participants agreed that the histomorphologic lesions and morphology of the fungal structures were consistent with placentomal aspergillosis. Agents capable of causing inflammation of the placenta and fetus were discussed.

Placentitis caused by fungi and Brucella spp. are difficult to differentiate grossly. Placental lesions in sheep, caused by Coxiella burnetti (Q fever in humans) are most severe in intercotyledonary areas. Enzootic abortion in ewes is caused by a chlamydial organism and typically characterized by marked necrosis of the cotyledons with intercotyledonary edema.

Contributor. Animal Health Center, 1874 Gladwin Road, P.O. Box 100, Abbottsford, British Columbia, Canada.

Suggested reading.

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Slide 40, L11 (AFIP 2186904)

History. A 45-day-old female, broiler chicken carcass was condemned from the poultry processing plant.

Gross Pathology and Laboratory Results. The entire tubular portion of the female reproductive tract was distended by a core of firm, yellow material.

Escherichia coli was isolated from the oviduct. No viruses were isolated (3 serial, blind passages in 10-day SPF chicken embryos, allantoic sac inoculation).

Diagnosis. Oviduct: Salpingitis, chronic-active, diffuse, with heterophilic exudation, broiler chicken, avian.

Contributor's Comment and Conference Note. Coliform salpingitis may develop in broiler chickens as a consequence of E. coli infection of the left greater abdominal air sac, as occurs during systemic colibacillosis. In contrast to the descending infection in broilers, coliform salpingitis is thought to be an ascending infection in laying hens.

Salpingitis in commercial poultry is of economic importance due to reduced egg production and/or poor eggshell quality. Several viral and bacterial diseases have been reported. Some strains of infectious bronchitis virus (coronavirus) have a tropism for the oviduct, resulting in epithelial cell hyperplasia and nonpatency associated with lymphoid cell hyperplasia and germinal centers in the oviducts. Heterophil infiltration and lymphoid hyperplasia have been described in the oviduct with Newcastle disease infection of mature hens. Adenovirus may cause lesions restricted to the uterus (egg-drop syndrome-76).

Bacteria that have been associated with salpingitis include Escherichia coli and Mycoplasma spp. Mycoplasma gallisepticum salpingitis may follow yolk sac or air sac infections in immature chickens. In turkeys, Mycoplasma meleagridis causes an egg-transmitted infection.

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Suggested reading.

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Slide 41 (AFIP 2287618)

History. A 10-year-old, mixbreed, male, feline was presented for a corneal ulcer in the left eye of 4-6 weeks duration. The ulcer was treated with topical and systemic

antifungal agents. The cat also had myelogenous leukemia, severe anemia and was feline leukemia virus positive. A pedicle flap to the affected eye was performed.

Gross Pathology. Not described by referring veterinarian.

Diagnoses. 1. Eye: Myeloproliferative disease, mixed breed, feline. 2. Eye, cornea and iris: Keratitis and iritis, suppurative, chronic, focally extensive, moderate to severe, with fungal hyphae. 3. Eye, anterior chamber: Inflammation, fibrinosuppurative, moderate, with fungal hyphae. 4. Eye, posterior chamber: Inflammation, fibrinosuppurative, mild to moderate.

Contributor's Comment and Conference Note. The tumor cells in the eye were differentiated towards megakaryocytes. They had abundant eosinophilic cytoplasm with marked anisokaryosis and nuclear lobation. Adjacent to the megakaryocytic line were smaller mononuclear cells interpreted as part of the myeloproliferative disease. Tumor cells mixed with the inflammatory infiltrate at the junction of iris and anterior chamber, making the distinction of tumor and inflammatory cells in these areas difficult. Interestingly, no multinucleated giant cells were noted in the areas of inflammation and the hyphae. In the hematopoietic tissues the tumor cells were also differentiated towards megakaryocytes and were admixed with smaller mononuclear cells as in the eye. The pattern of infiltrate (bone marrow, spleen, liver, lymph node, peripheral blood) and cellular morphology combined with the feline leukemia virus infection were compatible with myeloproliferative disease in the cat. We thought this slide was particularly interesting because of the unique metastasis to the eye, the difficulty in differentiating it from inflammation and the concurrent mycotic infection.

Mycotic keratitis is apparently uncommon in the cat. Trauma, exposure keratitis or long term corticosteroid use have been listed as predisposing causes. Candida, aspergillus and rhinosporidium have been listed as etiologic agents. In this case, cultures were not taken so a definitive etiologic diagnosis was not established. The microscopic features of an average wall diameter of 3-4 um, would be consistent with Ascomycetes (higher fungi); septate walls and 45 degree branches are consistent with aspergillus or fusarium. Possibly the feline leukemia virus caused immunosuppression predisposing to the mycotic infection in the eye. Mycotic organisms were not noted in tissues other than the eye.

The presence of megakaryocytic cells was confirmed by positive immunostaining for Factor VIII related antigen. Conference participants discussed the oncogenic viruses of cats. Feline leukemia virus (FeLV) is a retrovirus with a genome consisting of a single strand of RNA, containing "gag" (group specific antigen) and the "env" (envelope) genes, which code for structural viral proteins. In addition, FeLV genome contains a gene known as the "pol" (polymerase) gene which codes for an RNA-dependent DNA polymerase (reverse transcriptase) enzyme. This enzyme copies viral RNA into complementary DNA which is inserted into the chromosomes (provirus) of proliferating cells (cells undergoing DNA synthesis). Following viral RNA transcription from the integrated provirus and translation on host ribosomes, precursor structural and envelope proteins and reverse transcriptase are generated. Eventually intact virus particles bud from the cell surface. The viral genome does not possess an oncogene (cancer inducing gene) and induces

leukemia by an indirect, as yet unknown mechanism. A tumor specific antigen called feline oncornavirus-associated cell membrane antigen (FOCMA) is found on the surface of FeLV-induced neoplastic cells.

Feline sarcoma virus, an acute transforming retrovirus possessing transforming genes or oncogenes ("onc" genes), induces polyclonal tumors shortly after infection, and is a recombinant virus, generated by the insertion of a cellular gene (protooncogene) into the helper chronic leukemia virus genome. FeSV is thus formed by the insertion of a cat cellular gene into the FeLV RNA genome. When the FeLV genome acquires an "onc" gene and becomes an FeSV, it loses part of the "gag" gene, most of the "env" gene and usually all of the "pol" gene. FeSV is able to infect and transform cells but can only replicate if the cells are concurrently infected with FeLV. FeSV-transformed cells express FOCMA.

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Suggested reading.

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Slide 42, L12 (AFIP 2292197)

History. This 10-week-old male castrated domestic cat, living in a rural environment, was presented with a "bite-like" lesion at the left nostril. After one week of treatment with antibiotics and glucocorticoids, the animal developed multiple ulcerated skin lesions. Due to its poor condition the animal was euthanatized.

Gross Pathology and Laboratory Results. The cat was emaciated. Multifocal ulcerated skin lesions, which were partly covered by yellowish, greasy, scabbing masses and numerous firm dermal nodules, up to 2 cm in diameter, were noticed. No other gross lesions were observed.

Electron microscopically orthopoxvirus particles were seen in scab material from the skin lesions and poxvirus was isolated in primary calf lung cells.

Diagnosis. Haired skin: Dermatitis, subacute, necrotizing, multifocal, severe, with epidermal and follicular epithelial hyperplasia and eosinophilic intracytoplasmic inclusion bodies, domestic shorthair, feline.

Contributor's Comment and Conference Note. The skin lesions consist of acanthosis with large eosinophilic intracytoplasmic inclusion bodies, ulceration and moderate to severe infiltration of neutrophils and mononuclear cells extending into the upper and deep corium. The etiologic diagnosis was confirmed by electron microscopy

and tissue culture techniques. There was no evidence of systemic infection.

The present case shows the typical clinical, histological and virological findings of feline poxvirus infection. The causative virus is a member of the vaccina/variola (orthopoxvirus) genus, indistinguishable, so far, from cowpoxvirus. Little is known about the epidemiology of this virus but limited serological studies suggest that the natural reservoir is a wild mammal, e.g. voles and mice. In cats, the course of the disease is in general, self limited and restricted to the skin. Systemic and fatal infections are rare. Generalization or development of more severe skin lesions has been seen following the administration of corticosteroids as appears to have occurred in this case. The FeLV and FIV status, which might contribute to the disease process were not determined in the present case.

The owner of the cat developed, 14 days after appearance of the first lesions in the cat, a firm nodule 2 cm in diameter on the back of the right hand. This lesion ulcerated and scabbed and healed by scar formation after four weeks. Cowpoxvirus was also isolated from this lesion.

Although cat-to-human transmission of this disease is apparently rare, this case shows that precautions should be taken when handling infected cats.

Additional morphologic features include furunculosis with associated eosinophilic infiltrates and epidermal microabscesses. Multifocally, accumulations of necrotic debris were present between the dermis and epidermis. Cowpox is found only in Europe and is accepted as being endemic in wild small mammal reservoir hosts. Antibodies, but not virus, have been detected in British voles and mice. Isolation of closely related viruses from wild rodents in Eastern Europe and typical clinical histories of infected cats further support this. Other zoonotic poxviruses include vaccinia, pseudocowpox, monkeypox, buffalopox, orf and bovine papular stomatitis.

Cats are thought to become infected when hunting; most cases occur in the autumn when numbers of reservoir host species are greatest. Cat to cat transmission can occur but generally causes subclinical infection.

A recent case of fatal poxvirus infection in a domestic cat with feline immunodeficiency virus (FIV) infection suggests that FIV status may be an important prognostic indicator in poxvirus infected cats.

Several outbreaks of "cowpox" virus infection have also been reported in cheetahs. Attempts to find the sources of infection have failed. There are indications that at least three different poxviruses infect carnivores: the raccoon poxvirus in the USA, the "cowpox" virus in the United Kingdom and the carnivore poxvirus in the USSR.

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Suggested reading.

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Slide 43 (AFIP 2288690)

History. This 12-day-old Jersey cross, male, bovine (Bos taurus) was normal for the first week of life, before becoming depressed and reluctant to stand during the four days before submission to the laboratory for necropsy.

Gross Pathology and Laboratory Results. Liver: Slightly enlarged with blunt edges and a finely granular capsular surface. The parenchyma was mottled with pinpoint pale foci. Lung: Patchy atelectasis. Small intestine: Segmental congestion with sparse contents.

Microbiology: Aerobic culture/gallbladder, liver: Dense growth of Salmonella dublin.

Diagnoses. 1. Liver: Hepatitis, necrotizing, histiocytic and neutrophilic, multifocal, moderate, with necrotizing thrombophlebitis, Jersey cross, bovine. 2. Liver: Hepatitis, portal, subacute, diffuse, mild, with biliary hyperplasia.

Contributor's Comment and Conference Note. Throughout the liver there are multiple small foci of necrosis, most of which have proceeded to the reactive phase. These foci comprise a central area of degenerate cells and fibrin surrounded by a zone of histiocytes. There is also moderate infiltration of portal areas by mainly mononuclear cells with thrombosis of some medium sized vessels. The lung is congested with areas of atelectasis, prominence of alveolar septa due to histiocytosis and formation of multiple microgranulomas.

A member of the Enterobacteriaceae, salmonellae are short (1 to 3.5μ long by 0.5 to 0.8μ in diameter), usually motile, Gram-negative rods which are both aerobic and facultatively anaerobic, do not ferment lactose, and can be selectively isolated using tetrathionate- or sodium selenate-containing broths. More than 2000 serotypes have been identified based on O (somatic, determined by the lipopolysaccharide of the cell wall), H (flagellar) and Vi (virulence, found only on S. typhi) antigens.

The fecal-oral route is the most important mode of transmission in animals and man. As sources, contaminated feeds, water, bedding, wild birds, rodents, reptiles, and recovered shedding carriers, have all been implicated. Many predisposing factors to salmonellosis exist, including young age, poor sanitation, crowding, and other stresses such as parturition, parasitism (such as coccidiosis in chickens), poor nutrition, transportation, intercurrent viral infection, oral antibiotics, and surgery.

Generally speaking, salmonellae can produce an acute or chronic enterocolitis or systemic disease with bacteremia. Salmonella affects the young more frequently and more severely than adults and the young are more apt to succumb to septicemia. When adults become infected they are more likely to recover or become symptomless carriers. The carrier state is an unstable one; if a carrier is stressed it may succumb (especially

cattle). Occasionally antibiotics appear to convert enterocolitis or simple carrier states to systemic disease.

Salmonellae have several virulence factors that contribute to development of diarrhea, bacteremia, and septicemia. These factors include adhesion pili, flagella, cytotoxin, lipopolysaccharide and enterotoxin. In cattle, the serotypes usually incriminated include Salmonella typhimurium, S. enteritidis and S. dublin. S. dublin is not common in North America east of the Rockies, shows some specificity to cattle and usually occurs in epizootics rather than sporatic cases as is common in the others. In chronic salmonellosis there is almost always an anterior bronchopneumonia and purulent exudation into synovial cavities. Septicemia is the usual syndrome in newborn calves. Enteritis with fibrinous casts is the common form in adults, and many occur in calves 26 weeks of age. The gross and histologic hallmark of salmonellosis is the enlargement and surface necrosis of Peyer's patches, cecal and colonic lymphoid nodules.

In the ileum of the pig, the oval elongated Peyer's patches are ulcerated and coated with a necrotic pseudomembrane, whereas in the colon, the solitary nodules are raised and ulcerated, creating "button ulcers". In the septicemic form, violet discoloration of the skin and petechiation of the kidneys ("turkey egg kidney") is often seen. Anal stricture is a possible sequella to Salmonella typhimurium infection in pigs, secondary to an ulcerative proctitis. The pigs are stunted, obstipated and have a pendulous abdomen.

Horses usually have acute fatal colitis; dogs have sudden bouts of acute, but not life-threatening diarrhea; and cats typically die with a fibrile enterocolitis. Life-threatening pseudomembranous colitis occurs in primates.

Contributor. Regional Veterinary Laboratory, Wollongbar N.S.W. 2480, Australia.

Suggested reading.

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Slide 44, L13 (AFIP 2287369)

History. This privately owned, 10-year-old goldfish (Carassius auratus) had a 4-month history of a gradual increase in size and of sinking to the bottom of the tank and lying upside down. Appetite had remained good. It was presented to a veterinary clinic where it died about 1/2 hour after a small sample of fluid had been taken from its abdomen.

Gross Pathology and Laboratory Results. The general body condition was good. Some fat could be detected in the mesentery and abdominal cavity. Two very large masses, approximately 5cm long and 2cm in diameter and more or less bilaterally symmetrical, were along the dorsal wall of the abdominal cavity. These masses consisted of multiple fluid-filled cystic cavities. (In the projection slide provided, the left mass has

been removed, together with the heart, liver and digestive tract.) The fish was fixed in its entirety.

No bacterium was isolated from the fluid within the abdominal masses on routine culture.

Diagnosis. Kidney: Cystic change, diffuse, severe, with intracystic glomerulus-like structures, goldfish (Carassius auratus), piscine.

Contributor's Comment and Conference Note. The tissue involved was recognized as kidney, as indicated by the presence of tubules and occasional glomeruli in the mesenchyma. The high cellularity of this mesenchyma was compatible with the presence of hemopoietic tissue in normal fish kidneys. The lesion consisted of numerous, usually large, cystic spaces of variable size and shape lined by a simple epithelium that was mostly squamous but also cuboidal in several places. In one or a few locations within each of several cysts, this epithelium formed a small aggregate of cells morphologically similar to a glomerular tuft, including the presence of capillaries.

There exist a few reports of polycystic kidney disease in goldfish. A prevalence of 6.3% was found in a population of goldfish from a heavily polluted industrial basin in Canada. The cause of this condition is unknown. The cystic spaces are thought to represent an extreme dilatation of the capsular space of individual glomeruli, the lesion originating during embryogenesis as a result of occlusion of the neck segments of nephrons.

Renal cystic disease may be inherited, congenital, or acquired. It is most common in pigs and calves, but may occur in any species. Although the etiology is known or has been speculated for several species, in most it is yet to be worked out. Cysts can develop in any part of the nephron, including the glomerular space, or in the collecting system. There is no evidence that cysts are caused by failure of nephrons to unite with the collecting system. By analysis of the fluid content of cysts, it has been shown that many are part of functioning nephrons. Most renal cysts are not caused by obstructive lesions (except acquired retention cysts of chronic renal disease, some dysplastic diseases, and possibly glomerulocystic disease). Current theories on the formation of cysts include: a) partial intratubular obstruction with proximal dilatation, b) production of defective tubular basement membrane components resulting in increased basement membrane compliance, and c) epithelial hyperplasia with altered transtubular transport.

Many chemicals, such as long-acting corticosteroids, diphenylamine, 5,6,7,8,-tetrahydrocarbazold-3-acetic acid, alloxan, diphenylthiazole, and nordihydroguaiaretic acic, cause renal cysts in experimental animals.

Acquired cysts of the kidney develop when tubules are obstructed by scar tissue. These rarely exceed 1 cm in diameter; most are located in convoluted tubules and Bowman's spaces. In dogs with renal failure, hyperplastic collecting tubules are sometimes visible as elongated cysts in the medulla. Excessive scarring differentiates these from primary cysts.

In the goldfish, polycystic kidney disease is described as a rare, spontaneous entity with large cysts that affect agility and buoyancy. The cysts vary in size, and may extend over the swim bladder to encroach on the coelomic cavity. The cysts are a dilatation of Bowman's space with no apparent communication between the cyst and the tubular portion of the nephron. No signs of renal impairment are seen, probably because

other organs compensate (i.e., spleen-hematopoiesis, gills- elimination of nitrogenous wastes, and gut-water balance).

In pigs, there are usually one or a few unilocular cysts, 1-2 cm across, which are usually bilateral incidental findings in young pigs. In pigs, lambs, calves, puppies, kittens, and foals, a congenital form of polycystic kidney associated with cystic bile ducts, bile duct proliferation, and at times pancreatic cysts occurs, and show clinically as stillbirths or death due to renal failure during the first few weeks of life.

In laboratory animals, a strain of rats was developed in which renal cysts became visible after 20 days of age (9). In addition, a report of diphenylthiazole-induced renal cystic disease in the rat (4) describes distention of medullary collecting tubules, and occasionally cortical collecting and distal tubules. In C57BL/6J mice, a model for infantile polycystic kidney disease has been developed (6). Cysts are bilateral, noticeable by the 17th day of gestation, and death occurs by 5 wks of life. There is progressive dilatation of PCTs and collecting ducts. In rabbits, an autosomal recessive disease with incomplete penetrance is described in the III_{vo} strain. Polycystic disease has also been seen in an adult squirrel monkey, Persian cat, and a pig-tailed macaque.

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Suggested reading.

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2. Bernstein J, et al: Epithelial hyperplasia in human polycystic kidney diseases. Am J Pathol 129: 92-101, 1987.

3. Biller DS, et al: Polycystic kidney disease in a family of Persian cats. J Am Vet Med Assoc 196: 1288-1290, 1990.

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Slide 45 (AFIP 2288247)

History. This 6-week-old, female Holstein calf was healthy at birth, but at seven

days of age developed a fever that persisted despite antibiotic therapy. At 46 days of age, the calf became recumbent and died two days later.

Gross Pathology and Laboratory Results. The calf had moderately enlarged mesenteric lymph nodes and enlarged Peyer's patches which were ulcerated and covered by fibrinohemorrhagic exudate. The kidneys were slightly swollen.

Periodic blood samples showed a progressive leukocytosis characterized by a marked neutrophilia without a left shift. Neutrophil function tests showed impaired random migration, oxidative metabolism, iodination, ingestion, bacteriocidal activity, elastase release, and cytoplasmic calcium flux, but cytotoxicity assays were normal or above normal. Blood counts and neutrophil functions of the dam were normal. Lymphocyte blastogenesis and MTT reduction were normal in both animals. A monoclonal antibody (R 15.7) against canine CD18 (β subunit) molecule demonstrated a decrease in the surface molecule on neutrophils from the calf's dam, sire, and some of the half-siblings, indicating a carrier state. Lectin blotting of neutrophil membranes of the affected calf failed to demonstrate any Mac-1 glycoprotein whose subunit has an affinity for the lectin, ConA.

To check for viruses, blood from the affected calf was infused into two healthy calves (which subsequently remained healthy). In addition, in vitro tests for syncytial virus, BLV, and BIV were negative.

Diagnoses. 1. Small intestine: Enteritis, ulcerative, chronic, focal, with numerous intraluminal bacteria, holstein, bovine. 2. Small intestine, blood vessels: Leukocytosis, marked, diffuse.

Contributor's Comment and Conference Note. Etiology: Neutrophil Mac-1 deficiency. Leukocyte adhesion: deficiency (LAD) is a rare disease of humans and has been demonstrated in inbred Irish Setter dogs and Holstein calves. Most of the calves die of recurrent bacterial infections of the respiratory or intestinal tracts. The hallmark of necrotic lesions in these animals is a lack of neutrophil infiltrate in spite of a persistent and high neutrophilia.

The LAD syndrome is due to a defect in membrane integrin proteins (LFA-1, Mac-1; p150,95) needed for adherence. These proteins have an α, β, stoichiometry with a common β subunit. The Mac-1 protein adheres to iC3b, ICAM-1, and serum coated zymosan.

Endothelium-leukocyte interaction is important for normal migration of leukocytes from blood to tissues during inflammation. Following margination, white blood cells adhere to the endothelium in great numbers. Since this process is a prelude to all subsequent cellular events, its mechanism is the topic of much current research.

One group of adhesion molecules on leukocytes consists of three heterodimer glycoproteins, each having identical beta subunits with different alpha subunits. Current nomenclature for these glycoproteins can become quite confusing. The beta subunits (94 kd) are noncovalently associated with the distinct, higher molecular weight alpha polypeptides. Currently, there are three leukocyte adhesion proteins, also referred to as leukocyte cell adhesion molecules, Leu-CAM's or CDW18 complexes. LFA-1 (gp 170,94) expressed on phagocytes and lymphocytes and promotes lymphoid cell adhesion interactions. Mac-1 (gp 155,94) also referred to as Mo-1 and CR3, has a complement

(C3bi) receptor and plays a role in amyloid cell adhesion phenomena. P150,95, (gp 150,94) also referred to as Leu-M5 is the most recently characterized, and may represent a lectin-like surface molecule. Mac-1 (Mo-1, CR3) and p150,95 (Leu-M5) are present in intracellular vesicles as well as on the surface of unstimulated cells. Inflammatory mediators such as C5a trigger an increase in Mac-1 and P150,95 (but not LFA-1) surface expressions.

In contrast to the leukocyte-dependent effect on adhesion, surface proteins on endothelial cells (ELAM-1 and ICAM-1) have been identified. ICAM-1 serves as a receptor for LFA-1 adhesion. Mediators of endothelial-leukocyte adhesion include bacterial products (endotoxins), complement fragments (C5a), chemotactic peptides, leukotriene B4, platelet activating factor, transferrin and cytokines (IL-1 and TNF). The mechanisms include stimulation of leukocyte adhesion molecules (C5a and LTB4), the stimulation of endothelial adhesion molecules (IL-1 and endotoxin) and a combination of both effects (TNF).

The role of integrins in cell-cell and cell-matrix interactions was discussed. Integrins are transmembrane glycoprotein surface receptors which recognize extracellular matrix (ECM) proteins. The intracellular protein interacts with the cytoskeleton to induce differentiation and signal cell locomotion. Many integrins bind the matrix proteins by recognizing the specific amino acid sequence of the tripeptide arginine-glycine-aspartic acid (RGD), a sequence thought to play a role in cell adhesion. ECM proteins containing an RGD sequence include fibrinogen, fibronectin, vitronectin, Von Willebrand Factor, osteopontin, thrombospondin and collagens (type I).

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Suggested reading.

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Slide 46 (AFIP 2288236)

History. Fifteen out of fifty-six 4 day-old, crossbreed, mixed sexes, piglets died suddenly in a two day period.

Gross Pathology and Laboratory Results. Pinpoint (< 1 mm) white foci were noted on the livers and spleens of these piglets.

FA examination of tonsil for pseudorabies virus was positive. Pseudorabies virus was isolated from the brain.

Diagnosis. Liver: Hepatitis, necrotizing, acute, random, with eosinophilic intranuclear inclusions, crossbreed, porcine.

Contributor's Comment and Conference Note. Inclusion bodies are present in many but probably not all slides. These foci of necrosis correspond to the white foci noted at necropsy. Although these foci are not always visible at necropsy, when present they are highly suggestive of pseudorabies. These pigs also had typical nonsuppurative encephalitis.

Pseudorabies, caused by Herpesvirus suis, usually occurs sporadically, is almost always fatal in 1-2 days and is characterized by fever and neurologic disturbances. In swine, several clinical diseases can be seen, depending on the age, dosage, route of exposure and incidence of the viral strain. Reproductive effects, abortions in the 1st trimester, and macerated or mummified fetuses later in gestation may be secondary to fever or related to fetal infection by a route yet undetermined. In Europe, acute respiratory tract signs are the most common. Pruritus is rarely seen in pigs. Gross lesions are usually minimal.

Pseudorabies is a pantropic virus which affects numerous organs with lesions commonly observed in the liver, adrenal gland, kidney, lungs and CNS. Histologically these lesions are presented with focal areas of necrosis, mild inflammatory changes and rare intranuclear inclusion bodies.

The major reservoir of Pseudorabies virus is the pig. The role of feral animals (raccoon, opossum, and cat) is unclear, and circumstantial. Inhalation and/or ingestion of nasal secretions are considered to be the major modes of transmission among pigs; other hosts are infected on contact with swine or ingestion of pig meat. The virus gains entry into the central nervous system via the olfactory, glossopharyngeal and trigeminal cranial nerves.

Of interest is the species infectivity of Herpesvirus suis. Where most herpesviruses are host specific, Herpesvirus suis infects other species including dogs, cats, cattle and raccoons. In mink, the herpesvirus is endotheliotropic, infecting both arteries and veins. Ptyalism has been reported as the most common sign in dogs.

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Suggested reading.

Pathology of Domestic Animals, 3rd Ed., Jubb, Kennedy and Palmer, p. 296-7.

Slide 47 (AFIP 2285966)

History. Approximately 2 weeks old, Hereford, male, Bos taurus. Several calves in this herd developed diarrhea with dehydration at approximately 10 days to 2 weeks of age. Three had died at the time of the submission.

Gross Pathology and Laboratory Results. The colon was filled with mucoid to fluid contents.

E. coli was recovered in pure culture from the small intestine. Coronavirus was identified by electron microscopy from colonic contents.

Diagnoses. 1. Colon: Colitis, necrotizing, acute, diffuse, with crypt ectasia, hereford, bovine. 2. Colon: Cryptosporidiosis, multifocal, mild.

Contributor's Comment and Conference Note. Coronavirus is a single stranded RNA virus, is 100-120 mm in diameter and has projecting peplomers or spikes that account for the characteristic solar corona-like appearance of the virion. Calves up to 21 days of age are susceptible. The severity of infection is influenced by viral serotype, colostral antibody and concomitant pathogens. The course of infection, severity of lesions and clinical signs are more pronounced in coronaviral enteritis than in rotavirus-induced disease. Grossly, coronaviral lesions in the small intestine cannot be distinguished from rotavirus enteritis or enterotoxogenic colibacilliosis. Rotavirus is usually confined to the small intestine (proximal portions first). Coronavirus typically descends the small intestine and infects the colon; the virus is present in both enterocytes on the villar surface and in the crypts.

Coronavirus can cause a variety of clinical symptoms in a wide range of species. These include feline infectious peritonitis (FIP) in cats, avian infectious bronchitis in chickens, blue comb in turkeys, hemagglutinating encephalomyelitis virus and transmissible gastroenteritis (TGE) in swine, acute enteritis in dogs and cats, sialodacryoadenitis (SDA) and rat coronavirus (RCV) infection in rats and mouse hepatitis virus (MHV) in mice. Coronavirus-like virions have been associated with a wasting syndrome in guinea pigs.

Contributor. Department of Veterinary Science (Vet Diag Lab), NDSU, Fargo, ND 58105.

Suggested reading.

1. Veterinary Pathology by T.C. Jones and R.D. Hunt, 5th Edition 1983, p495.
2. Mebus, CA, Stair, EL, Rhodes, MB, and Twiechaus, MJ: Pathology of neonatal calf diarrhea induced by a coronavirus-like agent. Vet Pathol 10: 45-64, 1973.
3. Jaax, GP, et al: Coronavirus-like virions associated with a wasting syndrome in guinea pigs. Lab An Sci 40(4): 375-378, 1990.

Slide 48 (AFIP 2237306)

History. This 4-year-old Hereford cow was found dead in the meadow during the spring season.

Gross Pathology and Laboratory Results. Pulmonary emphysema. IFA results (lung) bovine respiratory syncytial virus positive, parainfluenza-3 negative. Bacteriological culture (lung, liver, kidney) negative.

Diagnosis. Lung: Pneumonia, interstitial, proliferative, subacute, diffuse, severe,

with syncytia, Hereford, bovine.

Contributor's Comment and Conference Note. This lung has the gross (according to submitting veterinarian) and histologic features of the pneumonic lesions associated with BRSV infection in cattle. The pathogenesis of lesions (and nature of protective immune response) associated with BRSV infection remain controversial. Recently BRSV-specific IgE has been detected in cattle with clinical disease following BRSV infection, supporting the notion that hypersensitivity to the virus may be an important component in lesion development. Studies in mice suggest that cell-mediated (CTL) immune responses may enhance pathology while eliminating virus infected cells. It has also been suggested that BRSV infection predisposes cattle to acute interstitial pneumonia of dietary (L-tryptophan/3-methyl indole) or other origin, or that BRSV infection is coincidental in animals dying of acute interstitial pneumonia.

Conference Note. Most conference participants agreed that while the clinical history, laboratory results and histological lesions are consistent with bovine respiratory syncytial virus (BRSV) infection, parainfluenza type 3 (PI-3) infection could not be ruled out histologically. PI-3 typically has less syncytia than BRSV.

BRSV is a paramyxovirus, genus Pneumovirus. It is antigenically but it is not serologically identical to human RSV. Paramyxoviruses carry a single strand of RNA, in most, the infective strand (negative strand) is impotent, but serves as a template for its complimentary strand (positive strand).

Enzootic pneumonia is a disease complex caused by a combination of one or more respiratory viruses commonly complicated by secondary bacterial invasion and predisposed to by environmental factors such as inadequate ventilation and housing. The pathogenesis has not been fully elucidated. Immunofluorescence studies have revealed RSV antigen in the following locations: 1) ferret - nasal epithelium and scattered pulmonary alveolar cells, 2) cotton rats - bronchiolar epithelium, not in alveoli, 3) cebus monkey - alveolar cells, bronchiolar and tracheal epithelium, 4) cattle - alveolar cells, bronchiolar and bronchial epithelial cells, 5) children - alveolar cells, bronchiolar and bronchial epithelial cells. The ferret and cotton rat have been reported as useful models of the human disease. These animal models differ in that the susceptibility of ferrets to RSV infection decreases with age, while the cotton rat remains susceptible throughout life. Experimentally, RSV can cause a moderate to severe disease in young lambs. A caprine RSV has also been isolated.

Atypical interstitial pneumonia was discussed. A variety of toxic substances such as 4-ipomeanol, L-tryptophan and perilla mint ketone can induce fatal respiratory disease in cattle. 4-ipomeanol is the toxic component found in mold damaged sweet potatoes.

The L-tryptophan is converted to indolacetic acid which is decarboxylated to 3-methylindole (3MI). 3MI is absorbed and metabolized by a mixed function oxidase (MFO) system in the lung to produce pneumotoxicity. Monensin can inhibit ruminal conversion of L-tryptophan to 3-methylindole. 3MI selectively damages the nonciliated bronchiolar epithelial (Clara) cells in horses. In calves and goats, pulmonary edema induced by 3MI has been linked to Type I alveolar epithelial cell injury and to vascular lesions. Necrosis and exfoliation of the Clara cells were also reported with oral 3MI administration in the goat in one report (10). In mice, 3MI induced pulmonary edema is

associated with early alveolar capillary endothelial damage (6). In the rat lung, the Clara cell is the apparent site of cytochrome P-450 dependent monooxygenase activity and the main target cell for pulmonary toxins that are activated by this enzyme system; however, one report states that 3MI is not toxic to rodents (10). Chemicals which are toxic to Clara cells in mice, rats, or other rodents include naphthalene, carbon tetrachloride, 4-ipomeanol and 3-methylfuran.

Contributor. Wyoming Veterinary Laboratory, 1190 Jackson Street, Laramie, WY 82070.

Suggested reading.

1. Cannon, MJ, Openshaw, PJM, Askonas, BA: Cytotoxic T cells clear virus but augment lung pathology in mice infected with respiratory syncytial virus. J Exp Med 168: 1163-1168, 1988.

2. Castleman, WL, Lay, JC, Dubovi, EJ, Slauson, DO: Experimental bovine respiratory syncytial virus infection in conventional calves: Light microscopic lesions, microbiology, and studies on lavaged lung cells. AJVR 46: 547-553, 1985.

3. Dungworth, DL: The respiratory system In: Pathology of Domestic Animals, V.3, Jubb, KVF, Kennedy, PC, Palmer, N (eds.) Academic Press 1985 pp. 482, 530.

4. Kerschen, RP, Bennett, BW, Flack, DE, Jensen, RL, Collins, JK: Bovine respiratory syncytial virus infection in yearling feedlot cattle. Agri-Practice, April 23-26, 1987.

5. Stewart, RS, Gershwin, LJ: Detection of IgE antibodies to bovine respiratory syncytial virus. Vet Immunology and Immunopath 20: 313-323, 1989.

6. Castleman, WL, et al: Pulmonary lesions induced by 3-methylindole and bovine respiratory syncytial virus in calves. AJVR 51(11): 1806-1814, 1990.

7. Prince, GA and Porter DD: The pathogenesis of respiratory syncytial virus infection in infant ferrets. Amer Jour Path 82(2): 339-352, 1976.

8. Prince, GA, et al: The pathogenesis of respiratory syncytial virus infection in cottonrats. Amer Jour Path 93(3): 771-792, 1978.

9. Lehmkuhl, HD, Smith, MH and Cutlip, PC: Morphogenesis and structure of caprine respiratory syncytial virus. Archives Virol 65: 264-276, 1980.

10. Turk, MA, et al: Pathologic changes in 3-methylindole-induced bronchiolitis. AJP 110(2): 209-218, 1983.

Slide 49 (AFIP 2288032)

History. This 5-year-old, male rhesus monkey (Macaca mulatta) was depressed for three days after being anesthetized for a routine MRI scan. On the fourth day, he was found down in his cage, dehydrated and in shock. During emergency treatment, respiratory arrest occurred and resuscitation attempts failed. Prior to the MRI scan, no clinical problems had been noted. Negative TB test 6-12-89. SRV and SIV seronegative 8-88. Housed alone (open pan - no bedding) in a room with 23 other apparently healthy rhesus.

Gross Pathology and Laboratory Results. All lung lobes are firm, congested and

consolidated - the right lobes are more severely affected. The pleura and pericardium are diffusely thickened by a fibrinous exudate, and there are multiple foci of pus and hemorrhage on pleural surfaces. No visible body fat stores.

Microbiology reported heavy growth of Klebsiella pneumoniae from both pleural exudate and lung tissue. In addition, Escherichia coli was isolated from the pleura and Streptococcus bovis from lung.

Diagnosis. Lung: Bronchopneumonia, fibrinosuppurative, diffuse, severe, with fibrinous pleuritis, necrotizing bronchiolitis, gram-negative rods and gram-positive cocci, rhesus monkey (Macaca mulatta), primate.

Contributor's Comment and Conference Note. Pneumonia is a serious cause of illness and fatality in captive nonhuman primates. Of the 316 nonhuman primates necropsied at our facility for research or diagnostic purposes between January 1989 and May 1990, pneumonia was the cause of death in 25, and 21 of these cases were bacterial pneumonias. The affected nonhuman primate species included 10 rhesus, 5 cynomolgus, 2 owl monkeys, 2 squirrel monkeys, and 2 pygmy marmosets. The most common isolate was Klebsiella pneumoniae followed in decreasing order by Escherichia coli, Streptococcus pneumonia, Bordetella bronchiseptica, Corynebacterium pseudotuberculosis, and Mycobacterium tuberculosis. Klebsiella pneumoniae has also been recognized as the most common cause of bacterial pneumonias in nonhuman primates at other facilities (1964-1967 U.C. Davis, Good and May 1971; 1974-1979 Southwest Foundation, Boncyk and Kalter 1980). At the Pasteur Institute, Klebsiella pneumoniae infections were threatening a squirrel monkey breeding colony (mortality close to 100% in the young) which lead to the successful development of a protective strain-specific capsular polysaccharide vaccine.

Conference participants agreed that the histomorphologic lesions in this case were consistent with a bacterial pneumonia. Of particular interest was the presence within alveoli of bacterial organisms surrounded by a capsular clear space or "halo." This feature is characteristic of Klebsiella sp. and may be a useful morphological feature on H&E stained tissues.

Klebsiella pneumoniae is frequently isolated from the laryngeal air sacs of monkeys with air sac infections. Air sacs are found in most monkeys and all anthropoid apes, with the exception of the gibbon. Air sacs communicate with the larynx by slit-like openings at the base of the epiglottis. Histologically they are lined by stratified, cuboidal and ciliated pseudostratified columnar epithelium with occasional goblet cells.

Contributor. National Institutes of Health, Comparative Pathology 28A/111, 9000 Rockville Pike, Bethesda, MD 20892.

Suggested reading.

1. Berendt RF, Schneider MA, Young HW, and Frola FR: Protection against Klebsiella pneumoniae respiratory tract infection of mice and squirrel monkeys given kanamycin by aerosol and injection. Am J Vet Res 40(9): 1231-1235, 1979.

2. Boncyk LH, and Kalter SS: Bacteriological findings in a nonhuman primate colony. IN Developments in Biological Standardization, Vol 45, Kalter SS and Hennessen

W (Ed.), p 23-28, 1980.

3. Crouch TW, Higuchi JH, Coalson JJ, and Johansen WG: Pathogenesis and prevention of nosocomial pneumonia in a nonhuman primate model of acute respiratory failure. Am Rev Respir Dis 130(3): 502-504, 1984.

4. Giles RC, Hildebrandt PK, and Tate C: Klebsiella pneumoniae air sacculitis in the owl monkey (Aotus trivirgatus). Lab Anim Sci 24(4): 61-616, 1974.

5. Good RC, and May BD: Respiratory pathogens in monkeys. Infect Immun 3(1): 87-93, 1971.

6. Houser WD, Norback DH, and Ragland WL: Atypical Klebsiella infections in infant monkeys. Mainly Monkeys 1: 20, 1970.

7. Hunt DE, Pittillo RF, Deneau GA, Schabel FM, and Mellett LB: Control of an acute Klebsiella pneumoniae infection in a rhesus monkey colony. Lab Anim Care 18(2): 182-185, 1968.

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10. Schmidt RE, and Butler TM: Klebsiella - Enterobacter infections in chimpanzees. Lab Anim Sci 21(6): 946-949, 1971.

11. Snyder SB, Lund JE, and Bone J, et al: A study of Klebsiella infections in owl monkeys (Aotus trivirgatus). J Am Vet Assoc 157(11): 1935-1939, 1970.

Slide 50 (AFIP 2238187)

History. Two Amazon parrots died acutely in a large aviary. Within 3 days of the deaths of the two parrots, this cockatoo developed signs of vomiting and diarrhea. Within 2 days convulsions, muscle tremors, and hyperexcitability became evident. The bird died on the 4th day of illness.

Gross Pathology and Laboratory Results. An adult white male cockatoo in fair nutritional condition and good postmortem condition was received for necropsy examination. Very little body fat was present. There was only mild atrophy of the breast musculature. No leg band was present. The spleen was enlarged (1.1 cm diameter) and was pale tan. The liver was markedly enlarged. The liver had a red and tan mottled appearance. Abundant serous fluid is present in the abdominal cavity. The lungs were wet (edematous). A small amount of tan gruel-like ingesta was present in the crop. The sinuses were clear. The meninges of the brain were congested.

Parasitology - No parasites or parasite ova observed in intestinal content. Bacteriology - Liver: No growth aerobically. Colon: No growth on enteric media. Chlamydia culture - No Chlamydia isolated from liver, spleen and colon. Toxicology - Lead analysis on liver = 0.19 ppm (wet weight basis).

Diagnoses. 1. Liver: Cholangiohepatitis, necrotizing, multifocal, acute to subacute, moderate, with intranuclear inclusions, cockatoo, avian. 2. Pancreas: Pancreatitis, necrotizing, chronic, diffuse, severe, with intranuclear inclusions.

Contributor's Comment and Conference Note. Tissue samples were submitted to the National Veterinary Services Laboratory for viral culture. Psittacine herpesvirus was isolated from the tissues.

This case is unusual in our experience, because of the severe pancreatitis present. Psittacine herpesvirus typically causes severe necrotizing hepatitis with intranuclear inclusions in hepatocytes. In the present case, both hepatitis and pancreatitis were found, and inclusion bodies were observed only in the pancreas.

Microscopic findings in other organs from this bird were reticuloendothelial cell hyperplasia and plasmacytosis in the spleen and mild focal bronchopneumonia in the lung.

Pacheco's disease is a potentially latent systemic disease; clinically, the disease manifests as gastrointestinal, respiratory or neurologic signs depending on which organ system is affected most severely. Herpesvirus may be demonstrated in the liver, lungs and brain, and in this respect, resembles pigeon herpesvirus disease. The virus is shed in the feces of asymptomatic and clinically ill birds. Spread of disease is primarily from ingestion of infected feces. Lesions in affected organs are characterized by multifocal coagulative necrosis. Nuclei of the cells around affected areas often contain large, centrally located, eosinophilic or basophilic inclusions which displace the nuclear chromatin to the periphery.

As with many herpesviruses, psittacine herpesvirus may be transferred from cell to cell without viremia. This is accomplished by construction of a "pocket" of cytoplasm containing infective particles with uptake of these "pockets" into cytoplasmal pseudopods of noninfected cells.

Psittaciformes harbor three serologically distinct herpesviruses: Pacheco's virus, Amazon tracheitis virus, and Budgerigar herpes virus. In more classic cases of Pacheco's disease, in which the liver, spleen, kidney and lung are involved, the differential diagnosis includes psittacosis, salmonellosis, Newcastle disease and, lead poisoning.

There was some variation in slides in that the intranuclear inclusion bodies were more numerous in some sections than in others.

Contributor. New Mexico Department of Agriculture, Veterinary Diagnostic Services, 700 Camino de Salud, NE, Albuquerque, NM 87106.

Suggested reading.

1. Simpson CF, and Hanley JE: Pacheco's parrot disease of psittacine birds. Avian Dis 21: 209-219, 1977.

2. Gerlach H: Viral diseases. In Clinical and Avian Medicine and Surgery by Harrison GJ, Harrison LR, pp. 415-419, 1986.

3. Panigrahy B, Grumbles LC: Pacheco's disease in psittacine birds. Avian Dis 28: 808-812, 1984.

Slide 51, L14 (AFIP 2188575)

History. Two-year-old red deer stag (Cervus elaphus). 200 of 400 two-year-old stags on this property developed multiple coalescing scabs over their muzzle, face, ears and velvet.

Gross Pathology and Laboratory Results. In affected areas there was alopecia with crusting and fissuring of the skin. Removal of the scabs revealed a red, raw surface.

No dermatophilus organisms were cultured or seen in smears prepared from scabs. Pox virus particles were detected by negative contrast electron microscopy.

Diagnosis. Skin (velvet): Dermatitis, subacute, multifocal, moderate, with a superficial serocellular crust, red deer (Cervus elaphus), cervid.

Contributor's Comment and Conference Note. Several outbreaks of parapoxvirus infection have occurred on deer farms in New Zealand with morbidity rates sometimes reaching 100 percent. In stags the velvet is often the principal site of infection.

The deer virus resembles a parapoxvirus morphologically but restriction endonuclease analysis has shown that its DNA fragment patterns are distinct from those of orf (contagious ecthyma) virus.

Conference participants agreed that although poxvirus inclusions were not obvious on sections reviewed in conference, the presence of poxvirus demonstrated by electron microscopy makes this a valid case of pox dermatitis.

Parapoxviruses infect a range of species, but are most important in cattle, sheep, goats, and camels. The viruses are zoonotic; individuals that handle infected livestock can develop local lesions, usually on the hands. Other diseases caused by parapoxvirus include pseudocowpox, bovine papular stomatitis, and orf. Ultrastructurally, poxviruses have a 170x250nm brick-shaped virion (nucleosome and core membrane), lateral bodies, an outer membrane with short surface tubules, and sometimes an envelope.

Contributor. Palmerston North Animal Health Lab, P.O. Box 1654, Palmerston North, New Zealand.

Suggested reading.

Horner GW, Robinson AJ, Hunter R, Cox BT, Smith R: Parapox virus infections in New Zealand farmed red deer (Cervus elaphus). New Zealand Vet J 35: 41-45, 1987.

Slide 52 (AFIP 2237474)

History. This 5-year-old, spayed female, doberman had sporadic polyuria/polydipsia of about 3 months duration. In week prior to first chemistries, decreased appetite, lethargy, 10% weight loss.

Gross Pathology and Laboratory Results. Small, pale kidneys; hemorrhagic enteritis.

	BUN	CREAT	K	ALB	ELISA titer for B. burgdorferi
Day 1	100	6.4	5.8	2.4	greater than 1/1000
Day 6	283	11.0	4.9		
Day 8	Euthanatized				

Day 1 CBC - normal

Day 1 CBC - normal 1130,000**

** due to the highest titers ever seen by the reporting lab

Diagnoses. 1. Kidney (PAS reaction): Glomerulonephritis, membranoproliferative, diffuse, moderate, doberman pinscher, canine. 2. Kidney (PAS reaction): Nephritis, interstitial, subacute, mild.

Contributor's Comment and Conference Note. This dog was a house pet which, when outside, was confined to a fenced yard. The yard was surrounded by woods frequented by deer and other wildlife. In retrospect, the owners reported occasional episodes of nocturia, polyuria and polydipsia over the 3 months prior to examination, but it had been so sporadic that it did not cause concern. There was no history of joint pain, lameness or other illness. The animal was febrile. Antibiotic, steroid and electrolyte therapy was instituted, but the animals' condition rapidly deteriorated.

A cause-and-effect relationship between borreliosis and canine renal disease remains to be proven. However, in the past 5 years we have seen 15 cases of dogs with similar renal changes and highly positive Lyme disease titers. Most of the dogs were under 5 years old; some had a history of lameness, but most presented in renal failure.

Conference participants agreed that although the histomorphological appearance of the sections reviewed in conference suggests an immune mediated glomerulonephritis, a definitive diagnosis could only be made ultrastructurally by demonstrating a thickened basement membrane, immune complex deposition and increased mesangium.

Lyme disease is an immune-mediated disease of people initiated by the spirochete Borrelia burgdorferi and characterized by a primary skin lesion (erythema chronicum migrans) that may be followed by cardiac, neurologic or arthritic complications. The organism is transmitted by Ixodes sp. hard ticks. The natural host of the larval and nymph stages is the white-footed mouse while the host of the adult stage is the white-tailed deer. Borreliosis has also been reported in dogs; clinical signs in dogs include arthritis, arthralgia, fever, and anorexia. Recently there have been reports in dogs associating glomerulonephritis with positive titers for B. burgdorferi.

Contributor. Pathology Department, Pfizer Central Research, Groton, CT 06340.

Suggested reading.

1. Grauer GF, et al: Renal lesions associated with Borrelia burgdorferi in a dog. J Am Vet Med Assoc 193(2): 237, 1988.

2. Greene RT, et al: Clinical and serologic evaluations of induced Borrelia burgdorferi infection in dogs. Am J Vet Res 49(6): 752, 1988.

3. Habicht GS, Beck G, and Benach JL: Lyme disease. Sci Amer 257: 78, 1987.

4. Kornblatt AN, Urband PH, and Steere AC: Arthritis caused by Borrelia burgdorferi in dogs. J Am Vet Med Assoc 186(9): 960, 1985.

5. Lissman BA, Bosler EM, Camay H, Ormiston BG, and Benach JL: Spirochete-associated arthritis (Lyme disease) in a dog. J Am Vet Med Assoc 185(2): 219, 1984.

6. Madigan JE, and Teitler J: Borrelia burgdorferi borreliosis. J Am Vet Med Assoc 192(7): 892, 1988.

7. Magnarelli LA, Anderson JF, Schreier AB, and Ficke CM: Clinical and serologic studies of canine borreliosis. J Am Vet Med Assoc 191(9): 1089, 1987.

Slide 53, L15 (AFIP 2017975)

History. A 4-year-old, spayed, female Rhodesian ridgeback was presented with a two month history of weight loss and anorexia. Over a 7 day hospital stay, the dog's condition deteriorated to include pitting edema of the extremities, bloody diarrhea and thrombocytopenia. Cardiac arrest ensued and the dog died.

Gross Pathology and Laboratory Results.

1. Bilateral pale granular renal cortices. 2. Pleural and gastric serosal mineralization. 3. Gastrointestinal ecchymoses. 4. Multiple tan linear myocardial foci.

BUN	75 mg/dl	UA	ANA - negative
Creatine	4.2 mg/dl	S.G.	1.015 BP 190/140 (doppler)
P04	10.8 mg/dl	Protein	60/mg/dl CVP 3 cm H_2O
Albumin	1.9 gm/dl	WBC	35-40
WBC	30,500	Bact	3+
Platelets	35,000	Culture	E. coli
		RBC	NS

Diagnosis. Kidney: Nephritis, membranoproliferative, global, diffuse, moderate, with synechia and crescent formation, Rhodesian ridgeback, canine.

Contributor's Comment and Conference Note. Microscopic examination of the glomeruli revealed diffuse severe glomerular hypercellularity, multifocal parietal epithelial proliferations or crescents, periglomerular sclerosis, and segmental granular eosinophilic foci within the peripheral glomerular tufts. These segmental foci were sometimes associated with nuclear pyknosis and likely represent glomerular capillary thrombosis and necrosis.

The predominantly plasmacytic interstitial nephritis is reported to occur often in many forms of glomerulonephritis. In addition, moderate multifocal dilatation and atrophy of tubules with hyaline casts and mineralization of tubular basement membranes was evident.

Immunofluorescence for IgM revealed granular positivity along peripheral glomerular capillaries. Electron microscopic studies demonstrated marked subendothelial basement membrane immune complex deposition, characteristic of MPGN, Type I as seen in man.

The gastrointestinal tract had extensive hemorrhage and fibrinoid necrosis of larger vessels with adjacent lymphocytic inflammation. Multifocal severe myocardial necrosis was compatible with infarction. The vasculopathy in this case is ascribed to uremia and hypertension.

In man, numerous crescents are indicative of rapidly progressive or crescentic glomerulonephritis, which carries a poor prognosis. The ultrastructural, immunofluorescence, and microscopic findings are suggestive of MPGN, Type I although an essential cryoglobulinemia and polyarteritis cannot be ruled out. Glomerular thrombi hallmark essential cryoglobulinemia; in polyarteritis, the changes in the glomerulus are usually focal and segmental and have extensive fibrinoid necrosis. C3 immunofluorescence is more strongly positive in MPGN than in cryoglobulinemia, and the

immune complexes of cryoglobulinemia have a unique "fingerprint" ultrastructural morphology distinguishing them from immune complexes in MPGN.

The different types of membranoproliferative glomerulonephritis were discussed. In all types, with light microscopy, the glomeruli are large and hypercellular, largely due to proliferation of mesangial cells. Infiltrating leukocytes and parietal epithelial crescents are present in many cases. The glomerular capillary wall often exhibits a "double contour" or "train track" appearance, especially evident with PAS/silver stains. This is due to splitting of the basement membrane as a result of mesangial cell processes extending into the peripheral capillary loops.

Type I glomerulonephritis is characterized by the presence of subendothelial electron-dense deposits. C3 along with IgG and early complement components C1q and C4 are deposited in a granular pattern, suggesting an immune complex pathogenesis. Type II glomerulonephritis is caused by deposition of dense material of unknown composition within the glomerular basement membrane, giving rise to the term "dense deposit disease." C3 is present in irregular granular foci in the basement membranes on either side, but not within the dense deposits. IgG is usually absent, as are complement components. A rare variant, type III glomerulonephritis, has both subendothelial and subepithelial deposits with clinical features similar to type I.

Contributor. Angell Memorial Animal Hospital, 350 S. Huntington Avenue, Boston, MA 02130.

Suggested reading.

1. Heptinstal, RH: Pathology of the Kidney, 3rd Ed., Little, Brown and Co., 1983.
2. Krakowka, S: Glomerulonephritis in dogs and cats. Vet Clin North Am 8(4): 629-39, 1978.
3. Osborne, CA and Vernier RL: Glomerulonephritis in the dog and cat: A comparative review. JAAHA 9: 101-127, 1973.
4. Slauson, DO and Lewis RM: Comparative pathology of glomerulonephritis in animals. Vet Pathol 16: 135-164, 1979.
5. Cheville, NF: Uremic gastropathy in the dog. Vet Pathol 16: 292-309, 1979.
6. Müller-Peddinghaus, R and Trautwein, G: Spontaneous glomerulonephritis in dogs. Vet Pathol 14: 1-13, 1977.

Slide 54, L16 (AFIP 2289065)

History. Seven of eight 4-month-old, shorthorn calves in a herd showed severe weight loss, anorexia and photophobia. They were fed grain, lucerne hay and grazed reclaimed land.

Gross Pathology and Laboratory Results. The calf was in very poor body condition, clinically jaundiced with crusty excoriations around the eyes and muzzle. Fat and elastic tissues were extremely jaundiced grossly. The liver showed a mild exaggeration of the lobular pattern and the gallbladder was grossly distended.

Creatinine Kinase	799 U/1 (50-200)
Gamma Glutamyl Transferase	115 U/1 (9-30
Aspartate Aminotransferase	268 U/1 (44-150)
Glucose	4.9 mmol/1 (2.5-4.2)
Urea	4.9 mmol/1 (4.1-10.5)
Creatinine	83 umol/1 (70-154)
Calcium	2.47 mmol/1 (2.00-2.70)
Phosphate	2.19 mmol/1 (1.40-2.60)
Bilirubin Total	170.5 umol/1 (0-17)
Magnesium	0.4 mmol/1 (0.8-1.2)
Protein	73.1 g/l (57-75)
Albumin	29.2 g/l (26-35)
A/G Ration	0.7 (0.63-1.20)
Ammonia	64 umol/1
Serum Bile Acids	257.8 umol/1

Diagnosis. Liver, hepatocytes: Vacuolar change, hepatocellular, diffuse, severe, with megalocytosis, bile duct hyperplasia, multifocal necrosis and multinucleated hepatocytes, shorthorn, bovine.

Contributor's Comment and Conference Note. Lantana camera contains at least 2 toxic triterpines, lantadene A and B, which cause disease by cholestasis. Lantadene A will cause severe periacinar necrosis when given in large doses. However, the naturally occurring disease involves hepatocellular injury, with apoptosis or mild multifocal necrosis rather than widespread necrosis. Histological evidence of cholestasis in the form of canalicular plugging is commonly a finding, although not a feature of this section. The most consistent histological finding is hepatocellular enlargement and vacuolar or hydropic degeneration; generally less satisfying than the intensity of clinical findings would suggest. Gross findings usually include marked icterus and often spectacular enlargement of the gallbladder, as found in these calves. Lesions in other organs can include a nonspecific renal tubular nephrosis and myocardial necrosis, neither of which were seen in this case.

This disease is seen commonly in cattle, rarely in sheep and goats, which although equally susceptible to the toxin, will generally not eat the plant.

Naturally occurring disease caused by ingestion of Lantana camera is a subacute to chronic condition characterized by anorexia, severe icterus, constipation, polyuria, dehydration and photosensitization. Hepatocellular enlargement and fine cytoplasmic vacuolation, together with some degree of bile accumulation in canaliculi, hepatocytes and Kupffer cells, is the predominant histologic change in the liver. Electron microscopy has demonstrated increased smooth endoplastic reticulum and a characteristic form of bile canaliculi collapse. Also seen are distended canaliculi with damaged microvilli. Cholestasis seems to be due to interference with canalicular transport of bile resulting in increased amounts of conjugated bilirubin.

A cholestatic agent, icterogenin (found in Lippia schmanni), is chemically identical to lantadene A.

Contributor. Murdoch University Veterinary School, Murdoch University, Murdoch, WA 6150.

Suggested reading.

1. Pass, MA: Current ideas on the pathophysiology and treatment of Lantana poisoning of ruminants. Aust Vet J 63:6, p169, 1986.
2. Seawright, AA et al: The oral toxicity for sheep of triterpene acids isolated from Lantana camara. Aust Vet J 153: 231, 1977.
3. Seawright, AA, Allen, JG: Pathology of the liver and kidney in Lantana poisoning of cattle. Aust Vet J 48: 323, 1972.
4. Pass, MA et al: Toxicity of reduced Lantadene A (22 B-Angelocycloxyoleanolic acid) in the rat. Tox App Pharm 51: 515, 1979.

Slide 55 (AFIP 2292838)

History. This mature, female Saluki dog was presented because of weakness, malaise and depression. Temperature was mildly elevated. Mucous membranes were so "dark" that it was impossible to test capillary refill accurately. Hemolysis was present in capillary tube. There was dehydration noted. IV fluid with steroid therapy was instituted. The pet was referred for further immunosuppressive treatment but died 2 days later. There was no history of ingestion or exposure of any foreign substance or viral illness. Owner owns grooming and boarding facility, however, there have been no other illnesses so far observed.

Gross Pathology and Laboratory Results. Necropsy by practitioner. Submitted pancreas, spleen, liver, kidney. No gross description.

Toxicology - formalin-fixed liver. Zinc 136 ppm dry wt.

Diagnosis. Kidney: Tubular degeneration and necrosis, diffuse, moderate to severe, with tubular regeneration and prominent eosinophilic crystalline casts, Saluki, canine.

Contributor's Comment and Conference Note. Histopathology: Pancreas - No significant lesions. Kidney - Severe hemoglobinuric nephrosis - many tubules contain hemoglobin, occasional tubules are necrotic, and some tubular epithelial cells contain bile pigment. Liver - Marked cholestasis; distended sinusoids. Spleen - Marked congestion. Moderate erythrophagocytosis.

The development of acute hemolytic anemia and confusion with immune-mediated hemolytic anemia is typical of acute zinc toxicity in dogs. We do not have definitive hematologic back-up support of the hemolytic anemia, but there is morphological evidence of intravascular (hemoglobinuria) and extravascular (erythrophagocytosis) hemolysis in this dog to support the clinical diagnosis of anemia. The liver zinc concentration of 136 ppm is diagnostic (Breitschwerdt et al., 12 normal dogs, 17.5-32.1 ppm, average 26.2 ppm). We did not determine the source of zinc in this case, but reported sources are zinc nuts from transport cages, pennies, and zinc oxide ointment (1,2,3).

The specific mechanism by which zinc causes hemolysis in acute and subacute

cases of toxicosis is not known. Chronic zinc toxicosis has been shown to cause anemia by interference with absorption and utilization of iron and copper (both important in hematopoiesis) and the inhibition of enzyme systems which may affect erythrocyte fragility.

Recently, a report of Heinz body hemolytic anemia was associated with high plasma zinc concentration in a dog. Normally, erythrocytes are protected from oxidative damage by the preferential oxidation of glutathione, which is then returned to a reduced state via glutathione reductase or enzymes of the hexose monophosphate shunt necessary for the production of NADPH, the cofactor of glutathione reductase. However, zinc may not have to act as the oxidant causing damage to erythrocytes; by inhibition of one or more of the enzymes that normally protect erythrocytes from oxidative damage (eg, glutathione reductase or enzymes of the hexose monophosphate shunt), it may render them susceptible to oxidative damage via other agents.

Hemolytic anemia associated with zinc toxicosis has been reported in humans, canines, and ferrets. In humans, the most common cause is related to inhalation of zinc fumes or dust and is referred to as "metal fume fever". In animals, oral ingestion of zinc-containing compounds is more frequently recognized.

Contributor. Ontario Ministry of Agriculture and Food, Veterinary Laboratory Services, Box 3612, Guelph, Ontario N1H 6R8.

Suggested reading.

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Slide 56 (AFIP 2253097)

History. This 3-month-old female, poodle was admitted for hemorrhagic diarrhea and vomiting, that began three weeks earlier. During the following days of hospitalization, it exhibited progressive weakness, anorexia, and muscular tremor. Symptomatic treatment consisted of antibiotics. Antidiarrheal fluid therapy was given, without any real effects. Finally, euthanasia was decided.

Gross Pathology and Laboratory Results. There was a 10 cm long invagination of the distal portion of the ileum. The ileum was congestive and its mucosal surface seemed dull as in Parvovirus enteritis. There was melena in the colon. Mesenteric lymph nodes were congestive.

No parvovirus was found in the fecal samples examined.

Diagnoses. 1. Urinary bladder, epithelium: Intracytoplasmic inclusions, eosinophilic, multifocal, mild, poodle, canine. 2. Small intestine, lamina propria and epithellum: Coccidial microgamonts, macrogametes, meronts and oocysts. 3. Small intestine, villar brush border: Cryptosporidiosis.

Contributor's Comment and Conference Note. Sections of the ileum show atrophy and fusion of the villi. The lamina propria and submucosa are infiltrated by lymphocytes, macrophages and some neutrophils.

In the brush border of the enterocytes, especially at the tips of the villi, a great number of small round organisms are observed. Their shape, size and predilection site help to conclude these organisms as Cryptosporidium spp.

Beneath the basal membrane of the intestinal epithelium or deeper in the lamina propria, numerous developmental forms of Coccidias (macrogametes, microgametes, sporulated oocysts) are noted. Their subepithelial localization leads to the identification of the genus as Sarcocystis.

In addition, intracytoplasmic inclusion bodies are found in many epithelial cells (gallbladder joined to the sections of ileum) and in some intestinal macrophages. These inclusions are characteristic of canine morbillivirus.

This case represents a good example of the association between cryptosporidiosis and distemper in pups. Despite no information about the immune status of the animal, it is very likely that the immunosuppressive effect of distemper virus has played a role in the development of cryptosporidiosis in this dog. Similar observations were reported by Fukushima and Helmann (1984) and Turnwald et al (1988).

Concerning the pathogenesis of the enteritis observed and the history of hemorrhagic diarrhea given, some suggestions can be made. Cryptosporidium spp. is often incriminated as a cause of villous atrophy and malabsorption, so we think villous atrophy observed in this case is most probably because of the cryptosporidiosis. On the other hand, the pathogenesis of sarcosporidial infection is not clearly understood. It is known that pups and kittens of less than one month old may suffer hemorrhagic diarrhea due to intestinal coccidiosis. In our case, even though a clear hemorrhagic enteritis was not observed in the histopathological preparations, it is likely that the clinical observation of hemorrhagic diarrhea and the melena that was noted at necropsy may be because of Sarcocystis spp.

Finally, what we can conclude is that Cryptosporidium spp., a very important cause of neonatal diarrhea in calves and piglets, has probably also a greater importance in dogs that was thought before. In the diagnosis of cryptosporidiosis one needs to discover good sections of the intestine for the organisms may be easily overlooked.

In addition to the eosinophilic, intracytoplasmic inclusions within the urothelium, several conference participants observed similar intracytoplasmic inclusions in enterocytes and mononuclear cells adjacent to and in a depleted Peyer's patch. In several sections, numerous (up to 12) meronts were observed within the lamina propria. The presence of coccidial meronts within the subepithelial lamina propria of the small intestinal villi, in addition to the lack of oocysts deep within the lamina propria, is most consistent with Isospora canis infection. Merogony with sarcocystis is extraintestinal, occurring in arterial

vessels in the intermediate host (prey), where they develop into meronts. Merozoites liberated from these meronts initiate a second generation of meronts in capillaries throughout the body. Sarcocystis spp. sporulate within the intestine and are shed as infective oocysts or sporocysts while Isospora spp. shed unsporulated oocysts in the feces which sporulate in the environment to become infectious (as do Eimeria spp.).

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Suggested reading.

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Slide 57 (AFIP 2288672)

History. Three juvenile African grey parrots (Psittacus erithacus) died during a 40 day period in a pet store in Maryland after receipt from a commercial breeder in California. The 3 birds were not nestmates. Clinical signs prior to death in all three were lethargy, sitting with fluffed feathers, partial anorexia, and dyspnea. In previous weeks, this pet store had confirmed fatal cases of canarypox and salmonellosis in other species of caged birds. This parrot was treated with nystatin and Baytril without noticeable improvement.

Gross Pathology and Laboratory Results. 1. Liver: Necrotizing hepatitis, acute, disseminated, moderate. 2. Pericardial sac: Mucopurulent (gelatinous) pericarditis, diffuse, severe. 3. Lungs: Caseous and hemorrhagic bronchopneumonia, nodular, multifocal, mild. 4. Musculature: Atrophy, diffuse, mild.

Parasite Examinations: No worm eggs or protozoa were found in the feces or blood. Fluorescent antibody tests for Chlamydia, psittacine herpesvirus, and cryptosporidia were negative. Aspergillus fumigatus was cultured from the lung and pericardial sac. Special cultures for Salmonella, Candida, Hemophilus and Campylobacter were negative. Chlamydia cultures were negative. Virus cultures produced a plaque-forming virus on chicken eggs, which was identified as reovirus by the National Veterinary Services Lab.

Diagnosis. Liver: Necrosis, random, multifocal, moderate, African grey parrot (Psittacus erithacus), psittacine.

Contributor's Comment and Conference Note. The histologic features of the liver

are primarily linear and anastomosing foci of acute acidophilic necrosis with minimal inflammatory cell reaction. Hepatocellular necrosis is mostly random and in some regions is lobular or spans multiple lobules. Variable numbers of Councilman-like bodies are present in the sinusoids, some of which have been phagocytosed by Kupffer cells. No distinct inclusion bodies, organisms or parasites are present.

This case is presented to stimulate a discussion of the differential diagnoses of psittacine viral hepatitides. The hepatitis in this bird was caused by a psittacine reovirus. The recognized causes of psittacine viral hepatitis include reovirus, poxvirus (septicemic form), NDV, budgerigar fledgling disease polyomavirus, psittacine beak-and-feather disease syndrome diminuvirus, Pacheco's disease herpesvirus, adenoviruses, budgerigar coronavirus, and possibly other agents (such as avian influenza viruses).

At least 11 serotypes of avian reoviruses have been identified, but the serologic classification of psittacine reoviruses has been poorly studied. Avian reoviruses are versatile pathogens, but do not seem to share any common antigens with human or mammalian reoviruses. Avian reoviruses are commonly isolated from imported Old World psittacine birds. African grey parrots appear most susceptible to serious disease caused by reovirus, and several reports in the literature suggest reoviral infections are frequently complicated by numerous other pathogens, such as Salmonella, E. coli, paramyxovirus, Candida and Aspergillus spp.

In African grey parrots, the clinical syndrome is often difficult to distinguish from signs due to concurrent (or opportunistic) infections. Clinical findings in reovirus infected African grey parrots include hemorrhaging, diarrhea, ophthalmic infections, dyspnea, pneumonia, anemia, depression and death. Necropsy findings in African grey parrots with reovirus infection commonly include hepatitis as the major finding, with pulmonary edema, hydropericardium (or pericarditis), ascites, generalized palor (anemia), bursal atrophy, splenic atrophy (or splenomegaly early in the course of infection), uveitis and enteritis. In experimentally-inoculated parrots, ascites and pericarditis are not seen, suggesting these lesions are due to concurrent or opportunistic infections. In this case the pericarditis was attributed to acute aspergillosis.

Histologically, bland randomly distributed hepatic necrosis is the most consistent finding. Psittacine reovirus is also lymphohematotropic, enterotropic and may be mildly endotheliotropic. The spleen, bursa of Fabricius, thymus and bone marrow commonly show necrosis. Reoviral enteritis is presumed to be present in most cases, but rarely are fresh intestinal sections available from necropsy specimens to detect the mild villar lesions.

Lymphohematotropism of the virus and the common concurrent infections by E. coli, Salmonella, Aspergillus, Candida, paramyxoviruses and other pathogens, suggests that reovirus may have dire consequences on the immune status of infected African grey parrots. Significant immunologic suppression by this virus is suspected.

The vast majority of cases of reovirus infection and positive reovirus cultures occur in recently imported birds and birds still in quarantine facilities. This case, therefore, is unusual in that the affected birds were domestically hatched and raised. The source of the infection was not precisely determined but was assumed to be the breeding facility in California since the breeder admitted there was an on-going problem with coliform (E. coli) hepatitis among breeding birds; reoviral infections are assumed to be the predisposing factor in the cases of coliform hepatitis.

Ultrastructurally, psittacine reoviruses are slightly larger than poultry reoviruses; most psittacine reoviruses are about 80 nm diameter, lack and envelop, and are roughly cubic in shape. Virus particles can form crystalline arrays within the cytoplasm of infected cells, but in light microscopy, inclusions are not a feature.

Conference attendees agreed that the predominant light microscopic lesion was multifocal hepatic necrosis, with absence of viral inclusions and bacterial organisms. Although laboratory results in this case confirm the presence of avian reovirus in pooled tissue cultures, a more definitive correlation between the hepatocellular necrosis and the presence of reovirus would depend on electron microscopic demonstration of reovirus within degenerating hepatocytes.

Contributor. Animal Health Laboratory, Maryland Department of Agriculture, 3740 Metzerott Road, College Park, MD 20740.

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Slide 58 (AFIP 2288939)

History. This captive-raised 3-year-old male Barnacle goose developed large crusty nodules on the skin of one wing. Euthanasia was recommended following examination of a surgical biopsy.

Gross Pathology and Laboratory Results. No gross pathology.

Mycobacterial cultures were overgrown by contaminants. Special cultures for Salmonella, Candida and Campylobacter were negative. Mild numbers of capillaria eggs were observed in fecal examinations. Virus cultures were negative.

Diagnoses. 1. Skin: Squamous cell carcinoma, barnacle goose, avian. 2. Skin: Dermatitis, granulomatous, multifocal, moderate.

Contributor's Comment and Conference Note. This case was presented because of the unusual combination of a neoplasm and an infectious disease in the same tissue.

Squamous cell carcinomata are not common in birds. Increasing numbers of SCCs have been reported in poultry, but the vast majority of these tumors are discovered after

the carcass has been through a scalding vat and histologic features are often altered.

The carcinoma in this goose was characterized by cords of neoplastic cells invading the dermis and subcutis, a moderate mitotic rate with occasional bizarre mitotic figures, mitoses located among non-basal cells, keratin formation in neoplastic cells, and intercellular bridges among neoplastic cells. Invasion of the bone was not detected in this case, but has been reported in other cases of SCC of limbs.

Mycobacteriosis was evident as a granulomatous dermatitis. Between the cords of neoplastic squamous cells there were moderate numbers of multinucleated giant cells, macrophages, epithelioid macrophages and lymphocytes. Large numbers of acid fast bacilli were present in the multinucleated giant cells and many macrophages. Attempts to culture the mycobacteria failed because of overgrowth of the cultures by contaminants.

Additional histologic lesions in this goose included 1) moderate nodular amyloidosis of the spleen, 2) granulomatous splenitis with moderate numbers of acid fast bacilli, 3) very mild multifocal granulomatous hepatitis with minimal numbers of acid fast bacilli, and 4) proliferative lymphocytic synovitis. A moderate superficial suppurative epidermitis was evident in most sections/slides; a Gram stain of the skin lesions revealed a mix of Gram-positive and Gram-negative bacteria, the majority of which were Gram-positive cocci.

This case was initially presented as a surgical biopsy of the wing nodule. The biopsy consisted entirely of sloughed keratinized cells and moderate numbers of inflammatory cells in which acid fast bacilli were found. The squamous cell carcinoma was not diagnosed in the biopsy. Euthanasia was recommended because of the mycobacteriosis.

Conference participants agreed the histomorphologic characteristics of the skin neoplasm were consistent with squamous cell carcinoma. Acid fast stains revealed the presence of numerous acid fast bacilli within multinucleated giant cells and macrophages.

Recent reports indicate the frequency of squamous cell carcinoma in young chickens is increasing (11). Two surveys verified the neoplasm occurred in all geographic locations in the United States. No site predilection was observed. Presently, the frequency averages 2 per 10,000 birds slaughtered.

In humans, 4 cases of epidermoid carcinomas arising from chronic (between 3 and 20 years) plantar ulcers of leprosy patients were recently reported (12). Plantar ulcers are a commonly observed complication in human leprosy, resulting from peripheral nerve damage. Increased mitogenesis associated with chronic lesions is thought to predispose to the neoplasm.

Contributor. Animal Health Laboratory, Maryland Department of Agriculture, 3740 Metzerott Road, College Park, MD 20740.

Suggested reading.

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Slide 59 (AFIP 2219673)

History. The raccoon was found dead in the Connecticut Bass River State Forest, by rangers. Several grey foxes had been dying in the area with symptoms of distemper.

Gross Pathology. Alopecia was accompanied by a crusty exudate near the margins of hair loss, most pronounced on the ventral surface. The skin was erythematous. A lacrimal exudate encrusted the eye lids. The foot pads were thickened and fissured with some desquamation. Diarrhea was evident with perirectal feces accumulation. The left lung was purple and consolidated about the bronchioles. The stomach contained vegetable matter. The liver was swollen.

Diagnosis. Lung: Pneumonia, bronchointerstitial, subacute, diffuse, severe, with type II cell hyperplasia, syncytial cell formation and eosinophilic intranuclear inclusion bodies, raccoon (Procyon lotor), procyonid.

Contributor's Comment and Conference Note. Distemper is an ubiquitous disease of dogs and other canidae worldwide. Infections have also been reported in raccoons, weasels, otters, ferrets, mink and skunks. It is caused by a Morbillivirus. The virus is considered a "pantropic" virus which invades the epithelium of the upper respiratory tract, proliferates in lymphoid tissue, becomes viremic, and in dogs with an inadequate antibody response, infects nearly all body tissues, particularly epithelial cells. Grossly, the lungs

are edematous and exhibit varying degrees of interstitial pneumonia; they may appear mottled due to variations in cellularity. Secondary infection with bacteria is common, often resulting in a purulent bronchopneumonia. Histologically, both intracytoplasmic and intranuclear eosinophilic inclusion bodies may be present in many tissues; they are most persistent in the pulmonary epithelium and the epithelium of the stomach, renal pelvis and urinary bladder. Systemic conditions, such as toxoplasmosis, are common sequelae.

In the raccoon, distemper, rabies, larval migrans, toxoplasmosis, listeriosis, plumbism, methylmercurialism, ethylene glycol poisoning and an astrocytoma have been reported as causes of neurologic disease. Raccoons are also experimentally susceptible to pseudorabies and transmissible mink encephalopathy. A recent study indicated that the raccoon may serve as a short-term reservoir for pseudorabies, but it is unlikely to have an epizootiologic role as a long-term, subclinical carrier of the virus (2).

Contributor. University of Connecticut, N.E. Research Center for Wildlife Diseases, Storrs, CT 06268.

Suggested reading.

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Slide 60 (AFIP 2236460)

History. This 13-year-old domestic shorthair, neutered, male cat had been anorexic for 3 weeks, no vomiting or diarrhea. A palpable abdominal mass was present during the physical examination.

Gross Pathology and Laboratory Results. Abdominal mass involving ileocecocolic region of intestine. Cat died in postoperative period, following resection of 20 cm segment of intestine mesenteric lymph nodes large and friable at necropsy.

CBC/profile/T_4/FeLV tests were within normal limits.

Diagnosis. Ileum (per contributor): Adenocarcinoma, signet ring, poorly differentiated, domestic shorthair, feline.

Contributor's Comment and Conference Note. This neoplasm appears to have arisen in the ileum, grew by extension along the submucosa and muscle layers to the colon, and metastasized to the mesenteric lymph nodes. The morphologic features of the neoplastic epithelial component, as well as the scirrhous response, are classical features for this neoplasm.

In a recent study (3) gastrointestinal neoplasms other than lymphosarcomas and mast cell tumors were diagnosed in 44 cats; of these, 42 were classified as adenocarcinomas. The remaining two were diagnosed as fibrosarcoma and leiomyosarcoma. All tumors were malignant; 31 metastasized or recurred. The cats averaged 10.6 years of age, there was no sex predisposition and Siamese cats had a

higher frequency of adenocarcinomas than other breeds. The ileum was the most commonly reported.

Lymphosarcoma is reported as the most common gastrointestinal tumor in surveys of neoplasms in cats. Because of this neoplasm's multicentricity and classification under the hematopoietic system, the true prevalence is difficult to establish.

Conference participants in general preferred a diagnosis of a poorly differentiated signet ring adenocarcinoma because of the prominence of signet ring cells. The amount of extracellular mucin was considered too scant to warrant a diagnosis of mucinous adenocarcinoma. The presence of "lakes" of extracellular mucin is usually a morphological requisite for diagnosis of mucinous adenocarcinoma.

Contributor. The Upjohn Company, 301 Henrietta Street, Kalamazoo, MI 49001.

Suggested reading.

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Slide 61, L17 (AFIP 2295207)

History. Three weeks before the observation of the first young, this female mud flat octopus (Octopus bimaculoides) stopped eating and did not come out of the den. She had been eating only irregularly previous to this.

Gross Pathology. The nutritional status of this adult, female mud flat octopus is judged to be poor based on no food or ingesta within the stomach or intestinal tract and the small size of the digestive gland. The mantle is in overall good condition with one pinpoint healed scar identified on the right side. The beak and radula are unremarkable. Diffusely scattered over the mucosal and serosal surface of the entire intestinal tract are many white, pinpoint slightly raised foci with a moderate amount of thick mucoid material admixed within the lumen. This material is present affecting the esophagus, crop, stomach, cecum, and intestinal tract sparing the distal 5 mm of rectum. There is no food material or ingesta present in the GI tract. The digestive gland appears small, measuring approximately 11 mm by 6 mm at its greatest width 4 mm in depth. It is pale brown-grey. The gills, bronchial hearts, renal appendages and kidneys are unremarkable.

The ovary contains abundant eggs of somewhat different sizes. The oviducts and oviductal glands are normal. The eyes, white bodies, optic lobes, optic glands and brain all appear normal.

Diagnosis. Small intestine: Protozoal cysts, transmural, diffuse, etiology--consistent with Aggregata sp., mud flat octopus (Octopus bimaculoides), cephalopod.

Contributor's Comment and Conference Note. The apicomplexan Aggregata is a parasite of the digestive tract of cephalopods. The genus has been extensively studied in the cephalopods Sepia and Octopus in Europe, but little studied in North America (Hochberg, 1983).

Despite the role of Octopus in the marine ecosystem, and their importance to man as food items and for biomedical research, aspects of their parasite fauna are little known. Studies in Europe (Dobell, 1925) have shown that the protozoan parasite Aggregata commonly infects cephalopods. In the pioneering studies of this genus, Dobell showed that A. eberthi has a two host life cycle. Merogony (or vegetative reproduction) takes place in a crab. When the crab is eaten by a cephalopod, the parasite passes to the new hosts digestive tract, where gametogony (production of gametes) and sporogony (production of spores) occurs. The life cycle is completed when mature sporocysts, which have been passed from the cephalopod in the feces, are eaten by a crab.

Taxonomy of species of Aggregata is based upon morphology of the sporocysts and sporozoites. Although there are numerous reports of Aggregata infection in cephalopods, few species have been well documented. Three species are reported from European cephalopods, namely A. eberthi (Dobell, 1925), A. octopiana (Moroff, 1908; Wurmbach, 1935), A. spinosa (Moroff, 1908); A. kudoi is reported from Sepia in India (Narasimhamurti, 1979).

Reports on the histopathology of the infections in the final host include observations of the intracellular nature of the parasites, and enlargement of the host cells.

We have recently examined tissues from ailing North Pacific Giant Octopus, Octopus dofleini martini and California two-spotted octopus, Octopus bimaculoides held at the National Aquarium in Baltimore between 1981 and 1989. Histological sections have been prepared from a number of different sites in the digestive tract. Development of the Aggregata gametes and sporocysts in the two hosts has been recorded, as has the distribution of the parasites in different layers and regions of the digestive tracts. The histopathology of the infections has been observed.

A review of the life cycle of Aggregata species was presented by Dr. Sarah L. Poynton.

Aggregata sp. does not infect the octopus stomach, presumably because of its heavy cuticle. The cuticle is histologically similar to the koilon layer of the avian ventriculus. Infection of the nutrient uptake portions of the digestive tract of both cephalopod and crustacean hosts is typically seen.

This case was considered to be a severe infection. In such instances the submucosal tissue of the cephalopod may be almost completely replaced by parasites. The mechanical effects of compressing and deforming host tissue may prevent circulation and muscular activity in the gut wall; this is thought to contribute to the animal's demise.

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

Suggested reading.

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Slide 62 (AFIP 2131393)

History. This 30-year-old female Asian elephant (Elephas maximus) had chronic arthritis in both front legs. She was euthanatized. Selected tissues were submitted for histopathologic examination.

Gross Pathology and Laboratory Results. Several sections of lung were received. Some of the lung lobules were firm and contained multiple, 0.2 to 0.3 cm diameter, white, firm to hard nodules on cut section.

Unfixed lung tissue was cultured on Herrold's egg yolk agar. Monomorphic colonies grew on the slants after 4 weeks of culture. The colonies stained positive with acid-fast stains. The colonies were identified as Mycobacterium tuberculosis by the National Veterinary Services Laboratories in Ames, Iowa.

Diagnosis. Lung: Granulomas, caseonecrotic, multiple and coalescing, moderate, Asian elephant (Elephas maximus), proboscid.

Contributor's Comment and Conference Note. Very few bacilli can be demonstrated in the lung sections with acid-fast staining. Otherwise, the lesions are typical for pathogenic mycobacteria. Elephantine tuberculosis is difficult to diagnose antemortem. Inhalation was probably the route of infection. The possibility that tuberculous elephants constitute an occupational hazard to veterinarians, keepers and public should be considered.

Unfixed tissue from the lung was cultured on Herrold's egg yolk agar. Monomorphic cultures grew after 4 weeks on the slants. The isolates were acid-fast positive on direct smear. They were identified as Mycobacterium tuberculosis by the National Veterinary Services Laboratories in Ames, Iowa.

Although special stains failed to reveal acid-fast organisms, conference participants agreed the clinical history, microscopic lesions and laboratory data support the diagnosis of mycobacterial pneumonia.

A previous report of tuberculosis in an Asiatic elephant described microscopic lesions similar to those seen in man and domestic animals; however, an important difference was the absence of Langhans type giant cells (5). Tuberculosis is not often diagnosed antemortem in elephants due to the lack of clinical signs in that species. Since domesticated elephants live in close association with man and are frequently exposed to large crowds, man may likely be the source of infection. The possibility that tuberculous elephants constitute an occupational health hazard to veterinarians and zoo keepers (or vice versa) remains to be established. Three cases of tuberculosis were diagnosed in elephant keepers in Ceylon (9).

The moderator added that chronic arthritis is not an uncommon finding in elephants. Although still controversial, mycoplasmal or Mycoplasma arthritis has been reported in elephants.

Contributor. Department of Comparative and Experimental Pathology, Box J-103, JHMHC, Gainesville, FL 32610.

Suggested reading.

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2. Thoen, CO, Mills, K, and Hopkins, MP: Enzyme-linked protein A: an ELISA assay reagent for detecting antibodies in tuberculous exotic animals. Am J Vet Res 41: 833-835, 1980.

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Slide 63 (AFIP 2185162)

History. This adult, male, yellow-naped Amazon parrot (Amazona ochrocephala) was one of 7 psittacine birds from a pet store which died in about a 5 day period.

Numerous other species of birds (including passerines and columbiformes) were present in the same room with the dead psittacine birds, but only psittacines died. Among the dead birds were two species of cockatoos, macaws, one lovebird and an Alexandrian ring-necked parakeet; psittacines in the pet store which did not suffer mortalities included conures, parakeets, cockatiels, Pionus spp. and various spp of lovebirds.

Gross Pathology and Laboratory Results. 1. Miliary hepatic necrosis, moderate, liver. 2. Pulmonary edema and congestion, diffuse, moderate, lungs. 3. Splenomegaly, mild, spleen. 4. Hemorrhage, meningeal, focal, acute, moderate to severe, leptomeninges of brain. 5. Dilation, severe, proventriculus.

Parasite examination of feces: No worm eggs or protozoa were found.

Fluorescent antibody tests for chlamydia and "Pacheco's disease": Negative.

Bacteria, yeast and fungus culture results: No pathogenic organisms were cultured.

Virus culture results: An adenovirus was isolated and identified by EM by the National Veterinary Services Lab, Ames, Iowa.

Diagnosis. Liver: Hepatitis, necrotizing, multifocal to coalescing, moderate to severe, with basophilic intranuclear inclusion bodies, yellow naped Amazon parrot (Amazona ochrocephala), psittacine.

Contributor's Comment and Conference Note. This case was submitted because of the striking gross and histologic lesions in the liver, and to add a disease which must be differentiated from Pacheco's disease herpesvirus infection. Initially, Pacheco's disease was considered the likely cause of the pet store epornitic, however, specimens were collected for Newcastle's disease and AI cultures, since these latter diseases are of great concern to the poultry and pet bird industries. Adenovirus was cultured only from this Amazon parrot; NDV and AI virus were not isolated from any of the dead birds from this pet store.

Grossly, the liver of this bird had prominent miliary white foci of necrosis in all lobes. The necrotic foci were slightly sunken when near the capsule; the foci ranged from 0.5 mm to 4 mm diameter. Differential diagnosis of the gross liver lesions included Pacheco's disease, salmonellosis, pasteurellosis, listeriosis and reovirus infection. Other gross lesions in this bird included splenomegaly (spleen was about twice the expected size, but was normal in shape and color); focally severe acute hemorrhage into the leptomeninges overlying the occipital poles of the cerebrum; pulmonary edema and congestion; and prominent dilation of the proventriculus. Inasmuch as no other infectious agents were detected in numerous laboratory tests on this bird, it is assumed that most of these lesions were due to adenovirus infection.

Histologically, typical adenoviral inclusion bodies were present in many hepatocytic nuclei. These inclusions were large, basophilic often filled the nucleus and often caused marked swelling of the nucleus. The inclusion bodies associated with Pacheco's disease herpesvirus are usually much smaller, eosinophilic, and cause only mild swelling of the hepatocytic nuclei.

A review of the literature was attempted; only two case reports of adenoviral hepatitis in psittacine birds could be found (Scott et al, 1986; Graham, 1984). Adenoviral

pancreatitis, enteritis and encephalitis have been reported in various species of psittacine birds, but hepatitis was not considered a feature of the infections (Gerlach, 1986). Adenoviral infections or isolation of adenoviruses from yellow-naped Amazon parrots has, apparently, never been reported. Accordingly, further studies involving experimental infections of parakeets and cockatiels with this isolate of adenovirus are planned.

Conference participants agreed the prominent basophilic intranuclear inclusion bodies observed histologically are consistent with adenoviral infection.

Adenovirus infections in poultry and other avians were briefly discussed. Adenoviruses are unenveloped DNA viruses which range in size from 70-80 nm, and tend to be host specific. Because most adenoviruses are egg transmitted, they can be present in developing embryos. Avian adenoviruses have been divided into three major group types. Type I adenoviruses include the chick embryo lethal orphan (CELO) virus and numerous other serotypes including viruses associated with inclusion body hepatitis of chickens. Type II encompass the viruses causing marble spleen disease in pheasants and hemorrhagic enteritis in turkeys. Type III is the hemagglutinating agent responsible for egg drop syndrome - 1976.

In most species, adenovirus infection is common but disease is rare, especially for those adenoviruses associated with respiratory infections. Infectious canine hepatitis (canine adenovirus type I) is one of the few mammalian adenoviral diseases where virulent viruses produce disease in susceptible hosts. Fetal infection in primates has been reported to produce pulmonary hypoplasia. Other mammalian adenoviral diseases include 1) respiratory disease and renal infection, often with glomerulonephritis, in dogs (CAV-2), 2) pneumonia in horses (especially in immunosuppressed neonates), 3) respiratory and enteric infection in cattle, and 4) contagious pneumoenteritis of lambs.

Contributor. Maryland Department of Agriculture, Animal Health Laboratory, 3740 Metzerott Road, College Park, MD 20740.

Suggested reading.

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2. Jack SW, Reed WM, and Bryan TA: Inclusion body hepatitis in bobwhite quail (Colinus virginianus). Avian Dis 31: 662-665, 1987.

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Veterinarians, 1984. pp 267-280.
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Slide 64 (AFIP 2236727)

History. This 240 kg, male, Aldabra tortoise (Megalochelys gigantea) began showing gradual loss of condition in April 1988, with progression to anorexia and listlessness. The animal died on 28 April 1989.

Gross Pathology and Laboratory Results. The prosector noted many firm nodules on epicardium and pericardium. A fibrotic cyst containing amorphous exudate was on the hepatic capsule. Pale yellow discrete nodules were noted within the subcapsular areas of the liver.

A few days before death:
BUN 318 mg/dl
inorg P 7.6 mg/dl
SGOT 153 IU/l
CPK 975 IU/l
LDH 572 IU/l
Na 109 mE/l
K 12.0 in E/l
Uric acid 31.5 mg/dl

Diagnosis. Heart, epicardium: Fibrous and mesothelial proliferation (fibrous tags), papillary, diffuse, marked, with acicular clefts, Aldabra tortoise (Megalochelys gigantea), reptile.

Contributor's Comment and Conference Note. Tissue is cardiac muscle. Epicardial surface is covered with villous and papillary projections having a vascularized collagenous tissue stroma and a simple epithelial covering of cells that vary from flattened through cuboidal to tall columnar profiles with nuclei centrally located and cytoplasm foamy and pale-staining. Mitoses are not prominent.

This case was reviewed by both the Department of Veterinary Pathology and the Department of Cardiovascular Pathology. Although full consideration was given to the contributor's diagnosis of mesothelioma, conference participants felt the overall benign appearance to the cells, lack of cellular atypia and absence of mitotic figures are more consistent with a reactive lesion such as chronic pericarditis. Within the papillary projections of several sections acicular clefts were visible. In humans this is commonly associated with prior episodes of pericardial hemorrhage. Several sections also contained occasional surface associated gram-positive bacilli; their significance is unknown.

Contributor. Department of Veterinary Science, University of Arizona, Tucson, AZ 85721.

Suggested reading.

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2. Harrison MH, and Godleski JJ: Malignant mesothelioma in urban dogs. Vet Pathol 20: 531-540, 1983.

3. Magnusson RA, and Vert HP: Mesothelioma in a calf. J Am Vet Med Assoc 191: 233-234, 1987.

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Slide 65, L18 (AFIP 2295201)

History. An adult female donkey was inoculated intravenously with a broth culture of Pseudomonas mallei. Six weeks later she was not noticeably depressed and dyspneic.

Gross Pathology and Laboratory Results. Embolically distributed throughout both lungs were multiple, coalescing, soft, white, nodular foci.

In the skin of the muzzle were multiple variably-sized, firm, slightly raised, alopecic areas.

In the nasal cavity were several foci of ulceration and proliferation.

By fluorescent antibody testing, Pseudomonas mallei was identified in large numbers in the lung.

Diagnosis. Lung: Pneumonia, necrosuppurative, chronic, multifocal to coalescing, moderate to severe, breed unspecified, donkey, equine.

Contributor's Comment and Conference Note. Originally described by Aristotle in 330 B.C., glanders is a disease of solipeds and occasionally other animals, including humans. It is currently present in the Middle East, the Orient, and parts of Africa. Historically very common in cavalry horses, glanders was successfully eradicated from the United States in 1939 through the use of the mallein skin test.

In horses the principal lesions are in the lung, although nasal cavity and skin may also be affected. The pulmonary involvement is characterized as miliary distribution of pyogranulomas, with the proportions of exudative and proliferative components varying from case to case. In the nasal cavity, Pseudomonas mallei induces the formation of submucosal pyogranulomas which often ulcerate. Skin lesions in glanders, often referred to as "farcy", consist of similar ulcerating pyogranulomas, often associated with cord-like thickening of subcutaneous lymphatics.

There was some variation in the sections in that several sections had multifocal emphysema and a focal chronic pleuritis.

Glanders is caused by a bacterium variously known as Pseudomonas, Loefflerella, Pfeifferella, Actinobacillus, or Maellomyces mallei. Clinical signs usually relate to the respiratory tract, although a cutaneous form "farcy" and a nasal form may predominate. Nodules may arise in the nasal submucosa and reach 1 cm in diameter. These frequently ulcerate and result in a characteristic stellate scar. As with strangles, there may be only

fever and cough, but frequently there is death, especially in mules and donkeys. Horses are more prone to a chronic pulmonary form.

Glanders occasionally occurs in humans; carnivores may be infected by eating diseased flesh from horses. Goats are susceptible to infection by contact; cattle, sheep and pigs are not. Lesions of glanders in the alimentary tract are rare, although they do occur in experimental infections where large doses of the organism are given orally.

The principle tests used in the clinical diagnosis of glanders are the mallein test, complement fixation test, and guinea pig injection test. The mallein test is similar to the tuberculin test: 0.1 ml of mallein (an allergen made from growth products of Pseudomonas mallei) is injected into the lower eyelid with a tuberculin syringe. A positive reaction at 48 hours post injection is indicated by marked edema of the lid with blepharospasm and a severe, purulent conjunctivitis. The complement fixation test is the most accurate of the serological tests, but some strains of P. mallei have been reported to cross react with P. pseudomallei, the cause of pseudoglanders. A positive guinea pig injection test using intraperitoneal injection of either cultured organism or pus is the elicitation of the "Strauss" reaction, a severe orchitis and inflammation of the scrotal sac; however, this is not highly specific for P. mallei.

Contributor. Foreign Animal Disease Diagnostic Lab., NVSL-S&T-APHIS-USDA, P.O. Box 848, Greenport, NY 11944.

Suggested reading.

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2. Monlux, WS: Glanders. In: GS Trevino, JL Hyde, eds., Foreign Animal Diseases. pp. 178-185. US Animal Health Association, 1984.

3. Blood, DC, et al: In Diseases caused by bacteria, p 544-545, in Veterinary Medicine, 6th Ed. Lea & Febiger, Philadelphia, 1983.

4. Gillespie, JH, et al: In The pathologenic bacteria, The Genus Pseudomona in Hagans and Bruner's Infectious Diseases of Domestic Animals, p 55-5, Cornell Univ. Press, 1980.

5. Piggott, JA: Melioidosis, In Binford, CH, and Connor, DH (eds.): Pathology of Tropical and Extraordinary Diseases. Washington, DC, Armed Forces Institute of Pathology, p 169-174, 1976.

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Slide 66 (AFIP 2288055)

History. This 3-month-old, Hereford X Simmental, female, bovine was found

down and unable to rise. The dam was near the calf and was bellowing. The calf was observed less than 24 hours prior and was clinically normal at that time. This was the only calf affected. The herd consisted of 20 cows and 15 calves. No vaccines had been given. Adult cattle had been vaccinated for clostridial disease.

Gross Pathology and Laboratory Results. Large crepitant dry dark areas were evident within the muscles of right hind leg and rump area. Many darkened areas were present within the muscle of the left ventricle. Fine moist sheet of fibrin was adhered to the pericardial surface. The lungs were markedly congested.

FA test on heart and skeletal muscle samples were positive for Clostridium chauvoei.

Diagnosis. Heart, myocardium: Myositis, necrotizing, acute, multifocal to coalescing, severe, Hereford X Simmental, bovine.

Contributor's Comment and Conference Note. Blackleg is endemic in south Georgia. Blackleg generally has a rapid clinical course and most cases are found dead. The crepitant taunt swellings involving pelvis and/or pectoral muscles frequently are not present in cases with multiple sites of infection. Myocardial infection commonly occurs in cases of blackleg in this area (Table). Clostridium chauvoei infection reportedly is most common in cattle between 9 months to 2 years with a great reduction above and below this age range. Cases seen in this laboratory are mostly between 2 and 6 months of age. Most cattle in this area are vaccinated for clostridial diseases by 6 months of age. Occasionally we receive only formalized tissues from cases of suspected blackleg. A modified FA procedure using paraffin sections works well as a diagnostic procedure.

Table - Blackleg Cases Occurring Between 1 and June 30, 1990, VDIL Tifton.

				Sites of Muscle Lesions	
Age		Sex	Breed	Skeletal	Myocardium
3 mo	F	Mixed		X	X
3 mo	M	Limousin			X
8 mo	M	Limousin X		X	
4 mo	M	Brahma X		X	X
4 mo	M	Hereford		Septicemia	
2 mo	M	Limousin X		X	
6 mo	M	Hereford		X	
5 mo	M	Hereford		X	
3 mo	F	Sim X Her		X	X
2 mo	F	Angus		Septicemia (Practitioner necropsy-no muscle samples received).	

Blackleg, also known as black quarter, symptomatic anthrax, or emphysematous

gangrene, is caused by Clostridium chauvoei and initiated by the activation of latent spores in muscle. This definition separates blackleg from gas gangrene, in which, if C. chauvoei is involved, it is initiated as a wound contaminant. Blackleg can sometimes be mimicked closely by the syndrome known as "stable blackleg" or "pseudoblackleg", caused similarly by germination of latent spores of Clostridium septicum in cattle. Attempts at making distinctions between the two must take into consideration that C. septicum proliferates rapidly after death while C. chauvoei does not.

In domestic animals blackleg occurs only in cattle and sheep most frequently during the summer in young, well conditioned pastured animals. While the pathogenesis is still somewhat uncertain, many of the crucial points have been confirmed in experimental animals. Following ingestion of spores and a possible germinative cycle in the gut, the spores cross the intestinal mucosa (possibly involving macrophages) and are distributed to many tissues, including muscle. The spores germinate following a local event such as muscle damage or low oxygen tension. Degeneration of the muscle fiber is caused by both diffusing toxin and injury to blood vessels.

The lesions are usually found in large muscles of the pelvic and pectoral girdles, but may be in any striated muscle including heart, diaphragm and tongue. There may also be parenchymous degeneration of liver, kidney and endocrine glands as well as fibrinohemorrhagic pleuritis. If there is atrioventricular involvement, it is usually on the right side.

Blackleg in sheep, although much less common, closely resembles the disease in cattle.

Contributor. Veterinary Diagnostic & Investigational Laboratory, P.O. Box 1389, Rt. 7 Brighton Road, Tifton, GA 31793.

Suggested reading.

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Therapy: Food Animal Practice 2, Howard, JL (ed), WB Saunders Co. pp 567-575, 1986.

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Slide 67 (AFIP 2286763)

History. This 6-month-old, female Holstein, bovine, was from a herd of approximately 50 of similar age that were being fed baled alfalfa hay. The animal was emaciated and had been noticeably losing condition for the preceding 3 weeks. One other pen mate had died with similar signs.

Gross Pathology. The animal was submitted alive to the diagnostic laboratory. She was depressed and in poor condition. There was depletion of fat with serous atrophy of fat in the renal areas and at the base of the heart. The liver was pale, firm and indurated. There was edema along the mesentery and the abomasal wall.

Diagnosis. Liver: Hepatocellular loss and fibrosis, diffuse, moderate, with biliary hyperplasia and karyocytomegaly, Holstein, bovine.

Contributor's Comment and Conference Note. The microscopic changes in the liver were suggestive of pyrrolizidine alkaloid intoxication. Only a limited number of hay bales were available for examination. Most of the hay stores had been consumed. No toxic plants were found in the remaining bales. The field where the hay was cut was subsequently examined and found to contain areas with abundant first-year and second-year growth stages of hound's tongue plants (Cynoglossum officinale). The plant has a disagreeable odor and taste and is not commonly found as a cause of intoxication. Animals usually avoid grazing C. officinale on the range, however when the plant is dried and mixed with other forage it is consumed.

Pyrrolizidine alkaloids (PA) have been found in a variety of plants, particularly in the genera Senecio, Crotalaria, Heliotropism, Cynoglossum, Amsinckia, Echium, and Tuchodismin. Most plants contain more than one PA and it is often difficult to determine which is the primary toxin involved. PA's are relatively innocuous, but in the liver they can be converted to highly reactive pyrroles which can produce a variety of cell injuries by inhibiting membrane bound enzymes, inhibiting protein synthesis, and by reacting with low molecular weight sulfhydryl groups. The inhibition of cytoplasmic protein synthesis causes centrolobular necrosis seen in acute toxicities. This case represents a more chronic situation. The exact mechanism by which pyrrols exert their effects are not well understood; however, it is known that they have a high affinity for the nucleus and interfere with mitosis, (most likely by binding to tubulin and preventing formation of the mitotic spindle). DNA and RNA synthesis continue, resulting in the formation of megalocytic hepatocytes with large, single nuclei. The megalocytes eventually die, usually as single cells rather than in clusters. Hepatocellular regeneration with formation of normal-sized hepatocytes is not unusual, particularly if the animal has intermittent exposure to the toxins.

Associated lesions/conditions may include hepatic encephalopathy, thought to be due to the high concentrations of ammonia or amino acids in the blood, and

veno-occlusive disease, resulting from fibrosis and occlusion of central and hepatic veins due to endothelial damage and fibrosis.

Other alkylating agents such as nitrosamines and aflatoxins will also produce megalocytosis; however, rarely is this change as prominent as with PA toxicity. Cirrhosis is common in a variety of chronic toxicities.

There is a marked species difference in susceptibility; this is due in part to differences in metabolism of these substances. Pigs are most susceptible, cattle and horses are approximately 15 times more resistant than pigs, and sheep are approximately 200 times more resistant than pigs.

Contributor. Dr. R. A. Smart, Animal Disease Diagnostic Laboratory, Utah State University, Logan, UT 84322-5600.

Suggested reading.

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12. Shulman, HM, et al: Induction of hepatic veno-occlusive disease in dogs.

Slide 68 (AFIP 2287112)

History. Meat inspectors on routine abattoir examination found an enlarged, firm liver in this adult bovine. The liver was submitted to the Diagnostic Services at the Atlantic Veterinary College.

Gross Pathology. The liver and gallbladder were submitted for evaluation. The gallbladder was distended with watery, yellow-green bile and hundreds of small organisms which measured roughly 1 mm x 10 mm. The bile ducts were moderately enlarged and contained similar 1 x 10 mm structures free within the lumen. The bile ducts were surrounded by firm, white tissue and were prominent in deep sections.

Diagnosis. Liver: Cholangitis, chronic, multifocal, moderate, with intraductal trematodes, breed unspecified, bovine.

Contributor's Comment and Conference Note. Numerous adult flukes are present within the major bile ducts. Inflammation, proliferation and ulceration of the bile duct epithelium is prominent. Fibrous connective tissue is moderate surrounding major bile ducts and within portal triads. Bile ductular proliferation and fibrous connective tissue characterize the portal reaction. Pleocellular inflammatory cells and focal areas of mineralization are often associated with the adult flukes. An eosinophilic, granular material is also seen associated with occasional flukes.

Identification of this parasite is based on the lack of calcareous corpuscles, its leaf-shaped appearance, and the presence of digestive tract and ventral suckers. The body is filled with parenchyma and as is typical for Dicrocoeliidae, the ovary is posterior to the testes. The location and size of this fluke are helpful in identification (1).

Dirocoelium dentriticum (synonym D. lanceolatum), the lancet fluke, can result in liver lesions in the definitive host. Sheep, goats, and cattle are the most common domesticated definitive hosts. Human beings and numerous other wild and domesticated animals are known to serve, although less commonly, as definitive hosts. The prevalence in North America is low and this parasite has been reported to produce disease in New York State, Eastern Alberta and now the Atlantic Provinces.

Adults measure 1.5 to 2.5 mm wide by 10 mm in length and are pointed toward the anterior end. The damage to the host is directly proportional to the number of flukes in the liver and the length of time of the infection. Losses are seen in the form of reduced production of meat, milk and fiber as well as condemnation of livers at slaughter. It has been suggested that the bile duct hyperplasia is the result of a secreted substance by the intraluminal trematodes (2).

The intermediate hosts include land snails primarily of the genus Cionella (although 38 species of snails and nine families are known to be vectors), and ants of the genus Formica. Adults lie in the bile ducts or gallbladder; embryonated eggs containing miracidia reach the outside by passing down the common bile duct and deposited in feces. The eggs hatch when eaten by a snail. Two generations of sporocysts give rise to cercariae about three months after infection. Cercariae are expelled from the branchial chamber of the host in a mucoid envelope, known as a slime ball. Cercaria are eaten with the slime by ants and develop into metacercariae. Infected ants are eaten by the definitive host and the juvenile flukes reach the liver through either the common bile duct or the circulation. The prepatent period is about 70 days (3).

Most participants agreed that, based on the host and the location and size of the trematodes, the most likely etiology is Dirocoelium dentriticum; however, without light microscopic examination of an intact parasite, a definite etiologic diagnosis is not possible.

The amino acid proline has been reported as the active agent inducing the bile

duct hyperplasia of hepatic fascioliasis (2). Hepatic proline concentration increases by more than 10,000 times during infection by Fasciola. Increase in bile proline concentration and hyperplasia of the main bile duct both are reported to occur prior to parasites entering the duct. This suggests bile duct hyperplasia is induced by chemical rather than mechanical stimulation. The role of flukes in black disease and bacillary hemoglobinuria was discussed.

Black disease (infectious necrotic hepatitis), principally a disease of sheep and cattle, and occasionally seen in horses and swine, is caused by type B strain Clostridium novyi exotoxins (alpha, beta, and zeta). Black disease is essentially an intoxication caused by exotoxins: its development requires a nonimmune host, a latent spore infection of tissue (usually liver) and an anaerobic environment in which spores can germinate and vegetate. Fasciola hepatica, Dirocoelium dentriticum and Cysticercus tenuicollis have been reported to produce such an environment. If latent spores are present in the liver, vegetation quickly takes place within a thin zone of coagulative necrosis about the tunnels produced by wandering immature flukes.

Bacillary hemoglobinuria, a counterpart of black disease, occurs in cattle and rarely other species. It is caused by Clostridium haemolyticum (which also produces a beta toxin) and its pathogenesis is comparable to black disease. Fasciola hepatica is reported as the main cause of the incitatory lesion. The pathognomonic hepatic lesion has been described as an infarct secondary to portal thrombosis. Thrombosis occurs in affected areas, but may be a result rather than a cause of the initial lesion. In the liver the clostridial organisms are reported to reside in Kupffer cells.

Contributor. Department of Pathology & Microbiology, Atlantic Veterinary College, U.P.E.I., 550 University Avenue, Charlottetown, Prince Edward Island, Canada C1A 4P3.

Suggested reading.

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2. Isseroff, H, Sawma, JT, Reino, D: Fascioliasis: Role of proline in bile duct hyperplasia. Science 198: 1157-1159, 1977.

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Slide 69, L19 (AFIP 2282704)

History. This adult, female guinea pig (pet store animal) was sacrificed for diagnosis because of lethargy.

Diagnosis. Teeth, mandibular and maxillary: Odontodystrophy, characterized by odontoblast disorganization and loss, and periodontal fibrous tissue proliferation, breed unspecified, guinea pig.

Contributor's Comment and Conference Note. Vitamin C is an essential dietary vitamin in guinea pigs; it is a factor in many metabolic processes as it is needed in the production of collagenous, extracellular matrix (hydroxylation of proline in collagen

synthesis). Both dentin and osteoid matrix formation is abortive in the scorbutic guinea pig. Abnormal disorganized dentin and odontoblasts are seen in the pulp of the decalcified dental sections.

There was some variation in tissue sections in that several sections contained variable amounts of hemorrhage. The moderator commented that cartilage is normally present within the molar pulp of guinea pigs.

Vitamin C deficiency occurs only in species unable to synthesize ascorbic acid endogenously. Ascorbic acid is synthesized in the liver of most mammals and in the kidney of reptiles and amphibians. Most birds produce the vitamin in the liver, but in a few the kidney serves this function; however, the red vented bulbul bird reportedly depends on food sources to fulfill ascorbic acid requirements. Man, nonhuman primates, guinea pigs and fruit eating bats lack the enzyme L-gulonolactone oxidase which is required for synthesis of ascorbic acid. Insects, invertebrates, and fish generally do not synthesize vitamin C. Vitamin C is rapidly and readily absorbed in the small intestine. Even prolonged periods of negative balance often fail to produce scurvy since the vitamin is stored in many tissues and organs throughout the body, principally in the adrenal and pituitary glands. Other organs with substantial reserves are the brain, liver, spleen, pancreas, kidney and heart muscle.

Vitamin C is essential for the formation of collagen, ground substance, osteoid, dentin, and intracellular cement substance. Vitamin C functions as a co-factor in the post-translational hydroxylation of proline within the cistern of the rough endoplasmic reticulum. Vitamin C also functions in hydroxylation reactions involved in the synthesis of carnitine from lysine. Vitamin C may be involved in the sulfation of the acid mucopolysaccharides of ground substance. Poorly formed capillaries rupture easily because of defects in connective tissue and ground substance of capillary walls (the collagen of vessel walls has the highest content of hydroxyproline). Ascorbic acid inactivates histamine in guinea pigs, thus a deficiency may potentiate the development of capillary leakage and hemorrhage in scurvy. Hemorrhages can occur in any tissue or organ, but principle sites are the subperiosteum, the subcutaneous tissues and the joints of the extremities.

Bone changes result from the deficiency in osteoid matrix formation. In the growth plate the palisade of cartilage cells is found as usual and is provisionally calcified but the osteoblasts are incapable of forming bone matrix. Resorption of the cartilaginous matrix then fails and there is a downgrowth of long spicules into the marrow shaft similar to that seen in rickets. Fibroblasts proliferate in this scorbutic zone and form a loose, disorganized connective tissue, but no collagen is formed. The long-term lack of endochondral bone formation in chronic cases results in extensive loss of trabecular bone. The resultant weakened growth plate and metaphysis are susceptible to distortion and microfractures. Subperiosteal new bone may form along the diaphysis in an attempt to provide compensatory support. Resorption of alveolar bone causes the teeth to loosen, fall out, or become displaced.

Vitamin C is also required for the hydroxylation of dopamine to form norepinephrine; by virtue of its reducing potential, the prevention of oxidation of tetrahydrofolate, thereby maintaining the folic acid pool; maintaining iron in its reduced state, and, enhancement of both the absorption of non-heme iron in the diet and the bioavailability of stored iron.

Contributor. SVM - University of Wisconsin-Madison, 2015 Linden Drive W, Madison, WI 53706.

Suggested reading.

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3. Benirschke, K, Garner, FM, and Jones, TC: Pathology of Laboratory Animals, Springer-Verlag, New York, 1978, pp 734-740.
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Slide 70 (AFIP 2285771)

History. Tissue is from a 2-3 month old, female Wistar rat. This lesion was an incidental finding at necropsy.

Gross Pathology. Intraluminal uterine mass, focal, unilateral.

Diagnosis. Uterus: Deciduoma, Wistar rat, rodent.

Contributor's Comment and Conference Note. Deciduomas were first described in the guinea pig and were thought to be a tumor. They also occur in the rabbit, mouse, dog, hamster and monkey. Grossly, deciduomas appear as single or multiple, unilateral or bilateral, intraluminal uterine masses that are indistinguishable from normal implantation sites. Deciduomas arise from proliferation of decidual tissue (connective tissue cells of the uterine mucosa that enlarge and specialize during pregnancy) in response to nonspecific stimuli in the nonpregnant, usually pseudopregnant, animal. Sensitivity to decidualization occurs during days 3-5 of pseudopregnancy following exposure to progesterone and minute amounts of estrogen. The uterine epithelium may then proliferate following a mechanical stimulus, inducing stromal differentiation and deciduoma formation. Deciduomas spontaneously regress after days 12-16 of pseudopregnancy. Larger deciduomas may persist till day 21. Many stimuli can induce deciduoma formation (endometrial trauma), or, as in this case, they may occasionally occur spontaneously.

Conference Note. Conference participants agreed that the history and light microscopic characteristics are consistent with previous reports of deciduoma in rats.

Microscopically, deciduomas contain six regions which are variably discernible depending on the stage of development. 1) The basal zone is the outermost boundary containing basal endometrial gland remnants; 2) The capsule is immediately adjacent to the inner border of the basal zone and consists of a band of flattened cells. 3) The antimesometrial region is characterized by closely packed antimesometrial cells separated by small capillary channels. 4) The mesometrial region (decidua basalis) consists of both spiny mesometrial cells and granulated metrial gland (GMG) cells. 5) The glycogenic area represents a transition between the antimesometrial and mesometrial regions. 6) The mesometrial glands contain both GMG cells and fibroblastic stromal cells.

A typical GMG cell is large (up to 40 μm in diameter), frequently binucleated, and contains eosinophilic intracytoplasmic granules that are diastase-fast and periodic acid-Schiff (PAS)-positive. The peripheral cytoplasm is PAS-positive and diastase-sensitive. Recent studies indicated that GMG cells originate from bone marrow-derived lymphoid cells (2).

Contributor. Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, MI 48105.

Suggested reading.

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2. Elcock LH, et al: Deciduoma, Uterus, Rat. In: Jones TC, Mohr U, and Hunt RD (eds) Genital system. Springer-Verlag, New York, 1987, pp 140-146.

Slide 71 (AFIP 2131343)

History. Six months before death this 5-year-old, female beagle developed lesions of the ventral thorax characterized by draining fistulous tracts. The skin lesions persisted and the dog developed undefined systemic disease. The dog was euthanatized after developing bloody diarrhea.

Gross Pathology and Laboratory Results. Fistulous tracts associated with hemorrhagic fibrotic lesions of the subcutaneous tissue are present in the thoracic and perineal region. Internally, hemorrhage of colonic mucosa and serosa, splenomegaly with multiple peripheral infarcts, and mesenteric lymphadenopathy are observed.

Mycobacterium avium serotype I was identified in cultures of the colon by The National Veterinary Services Laboratories.

Diagnoses. 1. Spleen: Splenitis, histiocytic, diffuse, severe, beagle, canine. 2. Brain, cerebrum: Meningoencephalitis, lymphohistiocytic, multifocal, moderate. 3. Spleen: Lymphoid depletion, diffuse, severe.

Contributor's Comment and Conference Note. Granulomatous splenitis and meningitis due to Mycobacterium avium; splenic infarction.

The cutaneous lesions were biopsied six months prior to death after the animal

failed to respond to amoxicillin. The cutaneous lesions were "controlled" by continuous treatment with gentocin and doxycycline. At necropsy, granulomatous inflammation with numerous acid fast bacteria was also found in skin, liver, mesenteric lymph node, and bone marrow. The colonic hemorrhage was associated with vasculitis and venous thrombosis.

Dogs are more susceptible to M. bovis and M. tuberculosis and less so to M. avium. Dogs are reportedly more prone than cats to contract tuberculosis, usually by inhalation, in households with tuberculous people. Ingestion of milk or meat from infected cattle may result in alimentary infection.

Lesions of tuberculosis in carnivores differ from those in other species. Typical tubercles are not as common and when they occur, caseation necrosis is not prominent. More often, there is nonspecific granulation tissue with scattered macrophages and rare giant cells.

The typical dorsally and caudally distributed primary foci in the lungs of dogs have a tendency to fistulate onto the pleura causing a serofibrinous or serohemorrhagic pleuritis. Rapid intrabronchial dissemination usually occurs with a resultant tuberculous bronchitis and bronchiolitis rather than a bronchopneumonia. Peritoneal tuberculosis occurs with lesions in the mesenteric lymph nodes and liver and is accompanied by ascites. Tuberculous processes are not common in other organs, although involvement of meninges, uveal tract of the eye, genitalia, bones, and skin have all been reported. Hypertrophic osteopathy is sometimes a sequel to pulmonary tuberculosis.

Contributor. Department of Veterinary Pathology, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA 70803.

Suggested reading.

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March/April 1984, 295-299.

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Slide 72 (AFIP 2287576)

History. This 5-month-old BALB/cJ female mouse was used in trio matings to generate CAF1/J hybrids. Animal caretakers noticed a "tumor" on the underside of the animal during their routine evaluation of mice in the breeding colony.

Gross Pathology. A firm mass was located on the ventral abdomen in the subcutaneous tissue between the right hind leg and the tail. It was 1.5 X 1.0 cm in diameter. The mass was red, cavitated, and filled with red fluid.

Diagnosis. Subcuticular tissue, ventral abdomen (per contributor): Rhabdomyosarcoma, well differentiated, BALB/cJ mouse, murine.

Contributor's Comment and Conference Note. Rhabdomyosarcomas are rare malignant neoplasms of skeletal muscle. The spontaneous tumor is diagnosed in large breeding colonies at a relative incidence rate of 2.4 per 100,000 BALB/cJ mice and very rarely in all other strains. Cross striations can be demonstrated with a Bodian stain. Rhabdomyosarcomas react with monoclonal antibodies directed at sarcomeric actin but not smooth muscle actin, thus verifying the diagnosis. Southern blot analysis of DNAs prepared from a series of BALB/cJ rhabdomyosarcomas and hybridized with a murine leukemia virus probe that recognizes both ectotropic and dualtropic viruses did not demonstrate genomic fragments in addition to those known to occur in the strain.

Conference participants agreed that the light microscopic characteristics of this neoplasm were consistent with rhabdomyosarcoma. These tumors, diagnosed infrequently in domestic animals, are considered to be one of the rarest spontaneous neoplasms in laboratory rodents. The murine retrovirus (Molony murine sarcoma virus), isolated from a transplantable sarcoma, has been shown to induce rhabdomyosarcomas in mice. Rhabdomyosarcoma occurs most often in BALB/cJ mice or related inbred strains, suggesting a possible genetic predisposition. A variety of metals and carcinogens will induce these neoplasms in rodents, the latter with an incidence of greater than 50%.

Demonstration of cross striations, at either light or electron microscopic levels, is an important criterion for diagnosis. In poorly differentiated neoplasms, these may be difficult to demonstrate. Immunohistochemical stains utilized to confirm the diagnosis include desmin, myoglobin and actin.

Contributor. The Jackson Laboratory, 600 Main Street, Bar Harbor, ME 04609.

Suggested reading.

Sundberg, JP, Adkinson, DL, Bedigian, HG (Accepted for publication) Rhabdomyosarcomas in inbred laboratory mice. Vet. Pathol.

Slide 73 (AFIP 2194381)

History. This tissue is from an 18-month-old Friesland ox, which was dosed with toxic plant material collected on a farm where 70 cattle out of a herd of 200 animals died within a period of 12 months. Animals died after being clinically ill for a period varying from 1 week to 2 months. Affected cattle were thin and became progressively weaker and anorexic, and some were dyspneic and anemic. This animal was dosed plant material at a rate of 10g/kg/day for 17 consecutive days and euthanasia was performed on day 69.

Gross Pathology and Laboratory Results. Postmortem examination revealed a carcass in poor condition with the most noticeable changes occurring in the liver. The liver was small, pale and of markedly firm consistency. On cut sections clear lymph-like fluid exuded from the parenchyma in which diffuse fibrosis was evident. There was a pale grey discoloration of the lungs which were of slightly firmer consistency.

Indications of hepatic damage were manifested by a gradual fourfold increase in the activity of gamma- glutamyltransferase (GGT) in the serum, which after peaking at day 20, declined progressively to previous baseline values by day 45.

Diagnosis. Liver: Hepatocyte loss, diffuse, severe, with fibrosis, bile duct proliferation and mild hepatocellular megalocytosis.

Contributor's Comment and Conference Note. The histopathological changes in the liver were compatible with those described in chronic pyrrolizidine alkaloid poisoning. Microscopic lesions in the lung included mild thickening of the interstitium by mononuclear cells and connective tissue, hyperplasia of the epithelium of the smaller bronchioles and karyomegaly of some of the alveolar epithelial cells.

The Crotalaria genus is a member of a group of genera containing toxic pyrrolizidine alkaloids: of these plants, Crotalaria spp. cause disease in the broadest range of tissues in most domestic species. Of all the locally known Crotalaria spp. the dune bush or C. spartioides appears to be most hepatotoxic and occasionally in the past has been associated with liver failure in cattle. The mature plant is rather unpalatable, and poisoning in cattle occurs when the grazing is sparse. The specific alkaloid in C. spartioides has not been identified.

Conference participants agreed the clinical history and light microscopic lesions were consistent with pyrrolizidine alkaloid toxicity. Megalocytosis is not a change specific for pyrrolizidine alkaloidosis; it is also seen in intoxication by other alkylating agents such as nitrosamines and aflatoxins. Pyrrolizidine alkaloids are found in various plants including the genera Senecio, Crotolaria, Heliotropium, Cynoglossum, Amsinkia, Echium and Trichodesma. Metabolites of pyrrolizidine alkaloids may cause lesions in organs other than liver. Death may be due in some instances to renal damage and in others to pulmonary vascular and interstitial lesions. Hepatic fibrosis is reported as minimal in sheep, moderate in horses and marked in cattle.

Contributor. Section of Pathology, Veterinary Research Institute, P.O. Box 12502, Onderstepoort 0110.

Suggested reading.

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2. Hooper, PT: Pyrrolizidine alkaloid poisoning - pathology with particular reference to differences in animal and plant species. In: The effects of poisonous plants on livestock, Keeler, RF, Van Kampen, KR, James, LF (eds). Academic Press, pp. 162-187, 1978.

Slide 74 (AFIP 2287969)

History. Calves were not processed upon arrival at a feedlot and ultimately developed respiratory disease that was non-responsive to treatment. One hundred fifty of three hundred calves had respiratory signs; ten died. Tissue samples from affected calves were submitted to the Veterinary Diagnostic Center, University of Nebraska, for evaluation.

Gross Pathology and Laboratory Results. Lungs submitted had anteroventral consolidation (approximately 30% each lung). Tracheas submitted had locally extensive mucosal necrosis, severe hyperemia, and adhered "diphtheritic membranes."

The FA tests for IBR virus (bovine herpesvirus-1) performed on samples of lungs and tracheae were positive. Bovine herpesvirus-1 was isolated from samples of lungs and tracheae. The FA tests and attempts at virus isolation for other bovine respiratory viruses were negative. Bacterial pathogens were not isolated.

Diagnosis. Lung: Pneumonia, necrotizing, diffuse, severe, with necrotizing bronchiolitis and fibrin thrombi, breed unspecified, bovine.

Contributor's Comment and Conference Note. Inclusion bodies in this case are best seen in alveolar epithelial cells and macrophages; careful examination may be required in some sections. Additional changes include interlobular emphysema, fibrinous exudate within the pleura and interlobular spaces, and variably-sized foci of purulent inflammation. Foci of coagulative necrosis seen in most sections are suggestive of infarcts.

Infectious bovine rhinotracheitis is a common respiratory disease of feedlot cattle in the midwestern United States. The disease typically is an upper respiratory tract disease and can be controlled by vaccination. Fulminating infections such as the case described here generally are seen in unvaccinated feedlot calves. Severe pulmonary lesions resulting from fulminating bovine herpesvirus-1 infections may or may not be complicated by secondary bacterial infections.

Although most conference participants agreed the light microscopic lesions were consistent with a necrotizing viral pneumonia, they could not agree that unequivocal eosinophilic intranuclear inclusion bodies were present.

Infectious bovine rhinotracheitis is an acute contagious disease of cattle caused by bovine herpesvirus-1. The disease is characterized by inflammatory lesions of the upper respiratory tract and trachea. The virus can also cause a wide variety of other syndromes to include conjunctivitis, infectious pustular vulvovaginitis or balanoposthitis, abortion,

meningoencephalitis, enteritis and a generalized infection in young calves. The lesions in typical and uncomplicated infections are a seromucinous rhinotracheitis and, in some cases, conjunctivitis. Secondary bacterial infections with Pasteurella spp., Mycoplasma spp. and Fusobacterium necrophorum may contribute to the severity of disease. Eosinophilic intranuclear viral inclusion bodies in bronchial and alveolar epithelium appear for a transient period 2 or 3 days after infection.

Accurate assessment of the role of bovine herpesvirus-1 in causing pneumonia in cattle is complicated due to its propensity to predispose to secondary bacterial infections or even confound the effects of preexisting pneumonic lesions. Currently, it is thought that the lung is not significantly affected in mild cases. Severe viral infections can, however, impair pulmonary defenses and lead to severe fibrinous pneumonia, usually involving Pasteurella spp. The most severe viral lesion is a severe necrotizing bronchitis and bronchiolitis with extensive serofibrinous flooding of alveoli.

Aborted fetuses usually have no characteristic gross lesions. Microscopically, foci of intense necrosis and leukocyte infiltration in the fetal liver must be differentiated from listeriosis.

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

Suggested reading.

1. Jubb, KVF, Kennedy, PC, and Palmer, N. eds. Pathology of Domestic Animals. 3rd edition, Vol. 2, pp 425-427, Academic Press, New York, 1985.

2. Reed, DE, Bicknell, EJ, Bury, RJ: Systemic form of infectious bovine rhinotracheitis in young calves. J. Am. Vet. Med. Assoc. 163: 753-755, 1973.

Slide 75 (AFIP 2289157)

History. This 12-year-old, female, domestic shorthair cat had a rapidly growing subcutaneous inguinal mass.

Gross Pathology. Well-demarcated subcutaneous mass with areas of caseous material (approximately 3.5 x 5.0 x 6.0 cm).

Diagnosis. Mammary gland, inguinal (per contributor): Adenocarcinoma, tubulosolid, domestic shorthair, feline.

Contributor's Comment and Conference Note. The typical feline mammary adenocarcinoma has frequent mitoses, areas of necrosis and neoplastic cells within lymphatics. Mammary neoplasms in felines are usually malignant, solitary, and occur in older (8-12 yrs.) animals. The histological patterns are usually of the papillary variety, although solid patterns are also observed. Metastatic spread to lymph nodes or adjacent mammary glands via lymphatics is common.

Mammary gland is the fourth most common site of neoplasia in cats, following skin, lymphoid and hematopoietic tissues. The ratio of malignant to benign mammary tumors in the cat is 9:1. The percentage of carcinomas (86%) is much higher in the cat

than in the dog. The Siamese breed has twice the incidence of developing mammary carcinomas than other breeds combined. Almost all mammary neoplasms (99%) appear in intact females. The sparing effect of ovariohysterectomy is stronger in the cat than in the bitch. Ovariectomized cats have 0.6% of the risk of intact cats for developing carcinomas. The rare occurrence of estrogen receptors in feline mammary carcinomas compared to human and canine mammary neoplasms suggests a lack of estrogen dependency in this species. The possibility remains that the tumors may be dependent on other hormones.

The role of viruses in the etiology of feline mammary tumors remains unknown; however, type-A and type-C virus particles have been detected in these neoplasms. Cats with carcinomas generally have a short survival time after diagnosis; 25% show invasion of lymphatics and blood vessels. The average time between tumor detection and death is 12 months.

Fibroepithelial hyperplasia, also referred to as feline mammary hypertrophy, is occasionally reported in feline mammary glands. Spontaneous cases tend to occur in intact, nonpregnant queens less than two years of age; there is no breed predilection. It usually involves all or most of a gland and, unlike a neoplasm, often affects paired glands. This condition has a number of features that suggest a hormonal basis. Fibroepithelial hyperplasia in megestrol acetate-treated cats is reported to occur in older (average age 8.1 years) neutered male and female cats (3).

Contributor. Sterling Research Group, 81 Columbia Turnpike, Rensselaer, NY 12144.

Suggested reading.

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Slide 76 (AFIP 2295204)

History. This 2-year-old standardbred mare exhibited a period of hyperactivity followed by stupor and recumbency during a 12 hour period. Rectal temperature reached 102°F and the animal's clinical progress deteriorated rapidly. Death ensued 36 hours after the first signs of illness. A CSF tap sampled 12 hours before death revealed the following:

Protein	97 mg/dl	(normal 70)
Glucose	52 mg/dl	(normal 48-57)
WBC	603/μl	(normal 5)
	70% PML	
	20% large mononuclear cells	
	10% small mononuclear cells	
	18% small mononuclear cells	
RBC	18/ul	

Gross Pathology and Laboratory Results. No significant gross lesions were evident.

Laboratory Results. Eastern encephalitis virus was isolated from brain tissue.

Diagnosis. Brain: Meningoencephalitis, diffuse, moderate to severe, with neuronal necrosis and vasculitis, standardbred, equine.

Contributor's Comment and Conference Note. All histologic sections show severe, diffuse infiltration of the neuropil and meninges with lymphocytes and neutrophils in addition to a diffuse glial response. Microabscessation is present in areas where this response is most severe. Neuronal necrosis characterized by intensely eosinophilic, shrunken neurons with pyknotic nuclei is striking. Vasculitis is also a prominent feature of this lesion and consists of lymphocytic and neutrophilic infiltration of all vascular layers. Multifocal perivascular hemorrhage is associated with this lesion in some locations.

Eastern encephalitis (EE) virus is a togavirus of the alphavirus subfamily. It represents one of the most lethal viruses present on the North American Continent. Transmission occurs from the bite of infected mosquitoes with horses and humans having equal susceptibility. Death occurs in nearly 100% of infected horses, usually within 24-48 hours after initial clinical signs are observed. A lower mortality is encountered with human infection but severe mental compromise is often present in survivors. Swine and ring-necked pheasants are also susceptible to lethal infection with EE virus.

Much uncertainty exists concerning the epizootiology of EE. Migratory birds, many of which winter in Central and South America are considered the reservoir of infection. However, the mere presence of infected birds and the appropriate mosquito vector (Aedes sp.) do not guarantee that disease in mammals will occur. Anecdotally, a seven to ten year interval has been noted where EE is endemic in the United States.

The case submitted occurred in Massachusetts in September of 1982. The owner claimed the horse had been vaccinated for EE and WE in April.

Eastern, Western and Venezuelan equine encephalomyelitis (EEE, WEE, VEE) virus are members of the family togaviridae, genus alphavirus. CNS lesions produced by all three are similar, but some differences do exist. Grossly, there is cerebral congestion, edema, hyperemia, petechiation, focal necrosis and meningeal edema. Microscopic lesions are most prominent in the brain and spinal cord gray matter. These lesions consist of perivascular cuffing (with lymphocytes, macrophages and neutrophils), variable neutrophil infiltration into the gray matter, focal parenchymal necrosis, perivascular edema and hemorrhagic, necrotizing vasculitis, thrombosis, choroid plexitis and meningitis.

Neutrophilic infiltration occurs in the early stages of EEE and VEE infection.

Vasculitis, thrombosis and cerebrocortical necrosis occur more commonly in VEE but are occasionally seen in EEE.

Following inoculation (by mosquito) EEE virus infects several tissues. A second viremia results in hematogenous infection of the CNS. The virus may replicate in endothelial cells before entering the nervous system and infecting neurons, for which it has an affinity.

Contributor. Tufts University School of Veterinary Medicine, Department of Pathology, 200 Westboro Road, N. Grafton, MA 01536.

Suggested reading.

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2. Veterinary Virology, Fenner, et al, Academic Press, 1987.

3. Murphy, FA, and Whitfield, SG: Eastern equine encephalomyelitis virus infection: Electron microscopic studies of mouse central nervous system. Exp. Mol. Pathol. 13: 131, 1970.

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Slides 77, 78, L20 (AFIP 2182075)

History. This 4-year-old, male Merino sheep was at pasture over the summer. Dramatic weight loss was noted 10 weeks prior to euthanasia. The appetite remained good but the animal continued to lose weight. No diarrhea was noted. The other rams in the flock presented with similar signs; one died, the other 3 improved. This animal became very weak, was recumbent and paddling prior to euthanasia.

Gross Pathology and Laboratory Results. Carcass slightly dehydrated. Fat at all sites was starting to show serous atrophy. Moderate degree of muscle wastage.

Lungs - well expanded - no abnormality detected.

Liver - A few 1 mm. white calcified nodules.

Spleen - Contracted; white pulp only just visible on cut surface.

Rumen - Full of well chewed grass

Abomasum - Little coarse material, mucosa normal.

Small Intestine - Progressive thickening and corrugation of mucosa becoming bright yellow in caudal third. Contains a moderate amount of thin green fluid.

Caecum and first coils of colon - Mucosa slightly thickened but not yellow - contents fluid brown nonfibrous material.

Remainder of colon almost empty.
Rectum - Dark but otherwise normal faeces.
Mesentery - Lymphatic vessels prominent but walls not thickened.
Mesenteric lymph node - Not very enlarged but cut surface exhibits moderate cortical hyperplasia.

Bacteriology: Microscopic examination demonstrated the presence of acid-fast bacteria typical of Mycobacterium paratuberculosis. Cultural examination proved negative for the presence of members of the Salmonella group.

Feces Sample: Many oocysts seen but no fluke eggs. 9500 Strongyloides papillosus eggs per gram.

Blood Sample	This Case	Normal Mean	Normal Range
R.B.C. ($X10^{12}$)/l	7.16	12	9 - 15
P.C.V. (1/1)	0.19	0.33	0.26 - 0.42
Hg. (g/dl)	6.4	12	8 - 16
M.C.V. (f1)	26.5	32	28 - 40
M.C.H.C. (%)	37.7	33	31 - 38
i.e. Normochromic microcytic anaemia			
W.B.C. ($X10^9$/1)	17.2	8	4 - 12
Neutrophils (%)	88%	30	10 - 50
Eosinophils (%)	-	4	2 - 12
Basophils (%)	-	0.5	0 - 1
Lymphocytes (%)	11%	63	50 - 75
Monocytes (%)	1%	3	2 - 8
i.e. Neutrophilic leukocytosis			
(AST) Aspartate Aminotransferase (IU/l at 37°C)	176.5		45 - 34
(GGT) Gammaglutamyl transferase (IU/l at 37°C)	94.3		34 - 100
(LD) Lactate dehydrogenase (IU/l at 37°C)	480.0		200 - 600
(GD) Glutamate dehydrogenase (IU/l at 25°C)	4.9		1 - 12
Chlorides (mmol/1)	106		98 - 115
Total protein (g/l)	40.7		73 - 89
Albumin (g/l)	13.4		24 - 35
Globulin [by difference] (g/l)	27.3		49 - 54

i.e. hypoproteinaemia due to reduction of both albumin and globulin

Diagnoses. 1. Small intestine: Enteritis, granulomatous, diffuse, severe, Merino, ovine. 2. Lymph node, mesenteric (per contributor): Lymphadenitis, histiocytic, diffuse, mild. 3. Small intestine: Coccidia, intraepithelial, multifocal, mild.

Contributor's Comment and Conference Note. In Z-N stained sections the epithelioid cells contain many short acid-fast rod-like bacteria. In the colon the submucosal lymphoid nodules (follicles) are surrounded by cells containing organisms but only occasionally are such cells are found within the nodule. No acid-fast organisms could be detected in the reaction around the serosal lymphatic vessels.

The lymphoid tissue of the cortex is not active; the nodules are hardly visible. The sinuses of the cortex contain epithelioid cells but these have only a few acid-fast bacteria in their cytoplasm. The medulla is likewise not very active with only a few plasma cells present.

This is a typical case of Johne's disease in sheep caused by the pigment producing strain of Mycobacterium paratuberculosis.

Paratuberculosis in sheep should be suspected by the clinician investigating a progressive loss of weight in older sheep when parasitism has been eliminated at postmortem examination. The bright orange color of the terminal ileum, when present, is characteristic. It must be remembered that nonpigmented strains of the organism can infect sheep and loss of condition may be produced in cases where the gross changes in the intestine are minimal. Similarly, the granulomatous lymphangitis in the mesentery may not be present except in advanced cases; the serous atrophy of the mesenteric fat makes the thickened twisted lymphatics more easily seen.

Mycobacteria are small gram-positive, nonbranching, acid-fast bacilli, and are facultative intracellular parasites. The bacterial cell wall is composed of complex lipids including glycolipids, lipopolysaccharides, lipoproteins, and waxes. Mycolic acid is the lipid that results in the acid-fast property, but the precise role of other lipids in contributing to virulence and immunogenicity is unclear. These lipids are thought to be important in inducing the foreign body response and adjuvant activity of mycobacteria, and in the attraction of antigen presenting cells. There are strain variations within M. paratuberculosis and virulence variation is related to cell wall glycolipid content. Mycoside, a glycolipid, forms a barrier against lysosomal digestion and partly explains survival after phagocytosis by macrophages. These bacteria also prevent fusion of phagosomes and lysosomes in monkeys.

Paratuberculosis occurs worldwide and appears to be on the increase in many areas. Channel Island breeds (Jersey and Guernsey) and beef shorthorn cattle are most susceptible. The organism survives in the environment for 6-9 weeks. Cattle are infected as calves (usually less than 3-months-old) by ingesting feces containing this bacterium. The typical clinical manifestation is profuse diarrhea passed effortlessly, with only one affected animal in the herd. Emaciation progresses but appetite and alertness are retained until the terminal stages. Although the fecal-oral route is the primary mode of transmission, a bacteremia results in generalized infection with organisms excreted in milk, semen, and urine. Intrauterine infections may occur.

Following oral infection, M. paratuberculosis enters the lymphatic system through the tonsils and intestinal mucosa, specifically the membranous epithelial cells (M cells) which form the dome epithelium of the ileal lymphoid tissue. The presence of M cells and

prominent GALT in the ileum may explain the presence of predominant early lesions in this location. Some animals clear the infection and become carriers without clinical signs. This tolerance may result from compromised immunologic reactivity at the time of infection. Fetal infection may also result in tolerance. With a breakdown of tolerance, hypersensitivity and cell-mediated immunity develop, mucosal lesions progress, and disease results.

The pathological response to M. paratuberculosis is divided by some authors into a lepromatous form indicative of infection-tolerant state, a tuberculoid form indicative of an infection-resistant state, and intermediate variants. The lepromatous response is characterized by presence of foamy eosinophilic macrophages that contain numerous organisms but are unable to lyse the bacteria. These animals have increased B cell response but decreased T cell response. The tuberculoid response is characterized by aggregates of epithelioid and giant cells with T-4 and T-8 cells at the center and a rim of T-8 and B cells. Organisms are not seen in these lesions.

The pathogenesis of diarrhea in paratuberculosis is complex. Moderate villous atrophy is believed to result from the immune response in the lamina propria. There is also leakage of plasma proteins, malabsorption of amino acids and increased gut motility with decreased transit time. Type I and III hypersensitivity reactions may occur in the intestinal mucosa and result in increased flow of fluid and diarrhea. Excessive local production of immunoglobulins in the mucosa with subsequent formation of immune complexes and/or release of histamine from mast cells may participate in the pathogenesis since the diarrhea is responsive to antihistamines.

Paratuberculosis is one of the most important diseases of cattle, but has also been reported to occur in sheep, goats, and other ruminants including deer, moose, mouflon, camel, yak, gnu, and llama (11,14,20). Recently, M. paratuberculosis was documented in a colony of stumptail macaques (with no mention of an associated retrovirus), extending the natural host range and supporting current suggestions of pathogenicity for humans (6). Experimental studies suggest monogastrics, e.g., hogs, horses and chickens, may become infected under certain circumstances (21). In addition, strains of M. paratuberculosis have been recovered from diseased tissues of patients with Crohn's disease (22).

The disease in goats is similar to that described in cattle with minor differences. Contrary to cattle, tubercle-like caseation and calcification develop in goats and sheep. Focal areas of degeneration and necrosis in the media of the aorta have been described in the disease in goats (16,23).

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Slide 79 (AFIP 2292167)

History. This 3-year-old Hereford-cross cow was one of 25 cows in a 200 cow herd on range pasture that were depressed and blind. Eleven died. Three live affected cows were submitted for necropsy, along with range water for chemical analysis.

Gross Pathology and Laboratory Results. The three cows had widespread serous atrophy of fat and patchy septal pulmonary emphysema. There was bilateral multifocal malacia with yellow discoloration, petechiation and cleavage of parietal, occipital and frontal cerebral cortex. Yellow cortex was fluorescent in UV light.

Range water contained 6,000-7,000 ppm sulfate.

Diagnosis. Cerebrum, cortex: Necrosis, laminar, diffuse, severe, (polioencephalomalacia), Hereford, bovine.

Contributor's Comment and Conference Note. Polioencephalomalacia is a common neurological problem of cattle which is most frequently seen in young (0.5-2.0 years old) feedlot animals. A similar disease occurs in sheep, goats and some wild ruminant species. The characteristic gross lesions of soft, yellow discolored cortex can be highlighted as in this case by illuminating slices of fixed brain with UV light. Autofluorescence has been claimed to be due to lipopigment accumulation in phagocytic cells (1). The amount of intracellular autofluorescent lipopigment in cryosections of grossly fluorescent cortex is in fact small and the distribution of pigment-laden cells does not correspond to the widespread fluorescence. Fluorescence is most intense where cortical necrosis is advanced, involving both neuronal and glial elements. Noncerebrocortical lesions of neuronal necrosis and edema may also be found in thalamus, hippocampus and superior colliculus.

The presence of high sulfate levels in the range water may be significant. Epidemiological data suggested that polioencephalomalacia was 43 times more likely to be diagnosed in herds fed high sulfate diets than in herds not fed high sulfate diets (3). Weaned calves fed an experimental diet high in sulfates developed polioencephalomalacia in a 12-21 day period (2). Identical lesions can be induced in cattle by exposure to hydrogen sulfide, acute thiamine deficiency and a high molasses diet.

The term "polioencephalomalacia" generally is used to refer to laminar softenings restricted to the cerebrocortical gray matter. Polioencephalomalacia is a well recognized syndrome in cattle, sheep and goats. It is also the lesion of salt poisoning in swine, lead poisoning of cattle, and is described as one of the residual neurologic lesions in cyanide poisoning (10). Apart from this, laminar cortical necrosis is sporadically observed in swine, dogs and cats (10).

The cause of polioencephalomalacia in ruminants is considered to be a thiaminase deficiency, although it is unlikely the condition is etiologically specific. Thiamine deficiency is often associated with diets high in concentrate; such diets may lead to a reduction in the number of ruminal organisms that synthesize thiamine and permit an increase in bacteria that produce thiaminase I (13). In addition, the associated decrease in ruminal pH results in a pH nearly optimal for bacterial thiaminase I. Histamine also accumulates to become a potent co-substrate for activity of the enzyme (14). Amprolium, thiabendazole and hydrochloride may exacerbate the deficiency (14). Additionally, there is a high incidence in cattle fed diets based on molasses and in sheep eating the thiaminase-containing fern Marsiela drummondii. The disease has been reproduced experimentally with analogs of thiamine and feeding the thiaminase-containing rhizomes of bracken fern (Pteridium aquilinum) (9). The distribution of lesions has also been related to the field of supply of the middle cerebral artery, suggesting a local vascular event is involved in the etiopathogenesis (9).

Cats fed exclusively fish-based diets, which can contain thiaminase, may develop thiamine deficiency. Many fresh- and saltwater fish contain an antithiamine compound; its concentration is highest in carp. The greatest antithiamine activity is in spleen, liver, intestines, and heart. The specific compound appears to be hemin, a partially degraded metabolite of hemoglobin. There is no clear breed or sex predilection, but one study reported a family of Burmese cats with fish-diet induced, thiamine-responsive signs (12).

Chastek's paralysis in foxes and mink, characterized by depression, tremors, ataxia, blindness, opisthotonus, convulsions, coma, and death, is associated with feeding 10-25% raw carp in the diet (11). Both bracken fern (Pteridium aquilinum) and horsetail (Equisetum arvense) can produce a thiamine deficiency syndrome (due to thiaminase activity) when ingested by horses (9).

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Slide 80 (AFIP 2288937)

History. This 23-month-old Long-Evans:CRBL male rat had a four month history of swollen hocks and progressive weight loss of 320 gm to 120 gm during the last two weeks of life. Food consumption during this period was reduced.

Gross Pathology. The rat was thin but still retained some body fat. The kidneys were pale with a roughened surface. The spleen was enlarged three times normal and the hocks were swollen and ulcerated.

Diagnosis. Cerebellum: Glioma, anaplastic, Long-Evans:CRBL rat, rodent.

Contributor's Comment and Conference Note. The dorsal cerebellum contained an infiltrating mass of plump to spindle-shaped glial cells interspersed with large pleomorphic and anaplastic cells. The neoplastic cells infiltrated and destroyed most of the dorsal cerebellum. There were areas in which the smaller astrocytes palisaded around small areas of necrosis or around vascular structures. Elsewhere in the brain were small focal hemorrhages.

Although this rat was in the high dose group of a two year carcinogenicity study, this was the only such neoplasm seen. It is also the first case seen in approximately 10,000 aging rats. This neoplasm is very similar in both presentation and morphology to that reported by Wyand, et. al.

The nomenclature of rodent astrocytic tumors was discussed. Both naturally occurring and chemically induced brain tumors may be anaplastic and show a variety of cellular morphology and growth patterns; however, in the rat, anaplasia is more common in the latter. An astrocytic or oligodendrocytic differentiation is often not apparent. Cellular atypia is common and an occasional multinucleated giant cell may be present. The latter features are sometimes used to diagnose glioblastoma multiforme; however, this is a pre-committed term in human neuro-oncology and should not be used in cases of rat astrocytomas.

Special stains demonstrated an abundant fine reticular network within the neoplasm. Neoplastic cells were nonreactive with GFAP, S-100 and keratin immunohistochemical stains. The Department of Neuropathology commented that the histomorphological features and negative immunohistochemical staining are most consistent with a sarcoma, possibly of leptomeningeal origin.

By light microscopy, glioblastoma multiforme as recognized in domestic animals and humans is always highly cellular but may be uniform or extremely pleomorphic. Fields can contain well differentiated astrocytes or poorly differentiated cells with a lack of cytoplasmic processes and pleomorphic dark staining nuclei. There may be many or few

mitotic figures, often atypical. Tumor cells frequently palisade around the areas of necrosis, a diagnostic feature of glioblastoma multiforme. Giant cells and multinucleated cells are often found. There may be marked proliferation of endothelium of small capillaries with tufts of heaped cells.

Electron microscopically, the small undifferentiated cells with hyperchromatic nuclei are the poorly differentiated cells. They are GFAP negative, but have characteristic astrocytic processes. The larger, more pleomorphic cells display bizarre nuclei and large nucleoli, an increased number of mitochondria and RER cisterne, abundant lysosomes, prominent endocytotic vesicles, and complex undulating cytoplasmic processes. Of the domestic species, glial tumors are observed most frequently in the dog. There may be predilection for brachycephalic dogs. Most authors agree that the cell of origin is the astrocyte. In man, glioblastoma multiforme is the most anaplastic form of primary intracranial neoplasia in older people. It is believed that most are derived by anaplasia from a preexisting astrocytoma of relatively restricted size. In man, glioblastoma multiforme accounts for more than 50% of all primary gliomas. The peak incidence is 45-55 years, and males are affected more than females. The frontal lobe is the most common site.

Primary brain tumors in rats are reported infrequently compared to tumors found in other organ systems. Astrocytoma was reported as the most frequent glial cell tumor in Sprague-Dawley rats (2). A high incidence (up to 100%) of brain tumors can be induced by multiple injection of small doses of methyl nitrosourea (MNV) intravenously (3). Administration of ethylnitrosourea to rats during pregnancy caused approximately 50% of offspring to develop brain tumors and all offspring developed peripheral nervous system tumors (4). Glioblastoma multiforme was diagnosed in a 448-day-old female Charles River rat in a treated group of a 2-year study (1). There was no evidence of increased neoplasia or non-neoplastic disease associated with treatment in the study. Walker (5) states that this tumor is reported not to occur in rats due to the absence of vascular proliferation or areas of spongioblastic astrocytes.

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Slide 81 (AFIP 2186362)

History. This adult, female Oryx (Oryx gazella) calved approximately 6 weeks previously and calf died at birth. No clinical signs of illness. Found dead.

Gross Pathology and Laboratory Results. Diffuse fibrinous peritonitis. Colonic wall markedly thickened with numerous abscesses noted on cross section. Colonic mucosal necrosis and mesenteric lymphadenopathy. Multifocal granulomatous hepatitis with prominent fungating pale, firm nodules.

Bact: Heavy Yersinia pseudotuberculosis from colon, liver and peritoneal swab.

Para: 3+ gastrointestinal nematodes on fecal flotation.

Diagnosis. Liver: Hepatitis, necrosuppurative, multifocal to coalescing, moderate, with intralesional bacterial colonies, oryx (Oryx gazella), artiodactyle.

Contributor's Comment and Conference Note. The results of gross and microscopic examination were strongly suggestive of pseudotuberculosis and bacteriology results were confirmatory. As reported in other cases in the literature, giant cells were not seen histologically and bacterial colonies were prominent. This animal originated at a game farm which has many problems with feral birds, predominantly crows, starlings and seagulls; rodents were not common. It is presumed wild birds introduced the organism. Other cases in blackbuck (Antelope c. cervicapra) have also been diagnosed on this premise in association with abortion and metritis. Unfortunately, the neonate from the oryx was not submitted for examination.

Yersinia enterocolitica is a gram-negative, facultative coccobacillus that has the unusual ability to replicate at cold temperatures (e.g. 4°C).

The genus Yersinia has six species: Y. pestis, Y. pseudotuberculosis, Y. enterocolitica, Y. frederiksenii, Y. kristensenii and Y. intermedia. Y. pestis, the etiologic agent of human plague, and Y. pseudotuberculosis and Y. enterocolitica are the major species of the genus; the later two species are considered primarily enteric pathogens. Until recently, Y. frederiksenii and Y. intermedia were classified as atypical Y. enterocolitica; they tend to cause skin and wound infections.

The factors responsible for the virulence of T. enterocolitica are poorly understood. Properties that appear to be related to virulence include the presence of V and W antigens (which mediate the organisms ability to survive inside of mammalian phagocytic cells), and temperature-related calcium dependency, which is plasmid mediated. Other factors, such as the ability to penetrate human epithelial cells, are presumably encoded for by chromosomal genes. Many isolates from human or environmental sources also produce a heat-stable enterotoxin that is similar to the heat-stable toxin produced by E. coli. The enterotoxin is produced at 4°C and 22°C, but not at 37°C; its importance as a cause of diarrhea in yersiniosis is uncertain.

Y. enterocolitica has been isolated from many mammalian species including a variety of rodents, lagomorphs, and domestic animals, including swine, sheep, cattle, horses, dogs, and cats. Naturally occurring infections have also been reported in several species of nonhuman primates, including African green monkeys (Cercopithecus aethiops), cynomolgus monkeys (Macaca fascicularis), patas monkeys (Erythrocebus patas) and Galagos spp. Wild rodents and birds have been suggested as reservoir hosts, as have dogs and swine. Little is known about the epizootiology of Y. enterocolitica infections among reservoir hosts. Transmission from animal to animal or animal to man has not been conclusively demonstrated. The predominant serotypes in man can often be isolated from swine, which have been suggested as an important reservoir for the organism. Y. enterocolitica has been isolated from lakes, streams, and drinking water in the United States and Europe; however, few human cases of the disease have been linked to ingestion of contaminated water.

Epidemiologic studies have found that ingestion of raw pork is an important source of human infections in Europe. The organism is a common inhabitant of the porcine pharynx and tonsils. Masseter muscle is frequently trimmed for use as ground meat and adjacent tonsillar tissue is often included.

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Slide 82 (AFIP 2286508)

History. This 3-month-old feeder pig was from a herd which experienced several sudden deaths. Others in the herd were coughing and pumping.

Gross Pathology and Laboratory Results. This animal had a severe fibrinous pleuropneumonia affecting the entire right lung. The left lung was normal.

Actinobacillus pleuropneumoniae serotype I was isolated in large amounts from the pneumonic lesions.

Diagnosis. Lung: Pleuropneumonia, fibrinonecrotic, histiocytic, diffuse, severe, with intralesional gram-negative bacteria, breed unspecified, porcine.

Contributor's Comment and Conference Note. Severe fibrinous pleuropneumonia with oat-shaped cells. Cause: Actinobacillus pleuropneumoniae.

In this lung, there is a fibrinous pleuropneumonia with many macrophages and streaming oat-shaped cells (degenerate macrophages). Thrombosis of blood vessels and interlobular lymphatics is common. A severe unilateral fibrinous pleuropneumonia is a common manifestation of porcine pleuropneumonia. The large number of streaming degenerate macrophages is almost pathognomonic for the disease.

In the past, porcine pleuropneumonia was referred to as "Haemophilus pleuropneumonia" as the etiologic agent was originally named Haemophilus parahaemolyticus because of its requirement for V factor (nicotinamide adenine dinucleotide) and its similarity to the human isolate. The name was later changed to H. pleuropneumoniae.

Currently, the accepted cause of porcine pleuropneumonia is Actinobacillus pleuropneumoniae.

There are at least eight serotypes of the organism, most of which can cause typical pleuropneumonia. Although the pathogenesis is not well understood, endotoxins and cytotoxins may damage capillaries and impair phagocytic capabilities with resultant vascular leakage, thrombosis and decreased clearance mechanisms. The gross lesion is characterized by a hemorrhagic, necrotizing, fibrinous pleuropneumonia very similar, except in distribution, to pneumonic pasteurellosis in cattle. All lobes may be affected, but the most common site is the dorsal area of the caudal lobes. A large area of pleuropneumonia in the caudal lung lobe is almost pathognomonic for this disease in pigs. Histologically, lesions consist of necrotic areas bordered by alveoli packed with streaming macrophages and wide edematous interlobular septa and lymphatics. Fibrin thrombi are a common finding throughout the lung.

Haemophilus spp. which cause well recognized disease in domestic animals include H. parasuis, the usual cause of Glasser's disease, and H. somnus, the cause of thromboembolic meningoencephalitis of cattle.

A. pleuropneumoniae is known to produce a heat stable, trypsin resistant, formalin resistant hemolysin in culture medium; however, the role of the hemolysin in porcine pleuropneumonia is not understood. A recent report indicated erythrocytes of horses, rabbits and sheep were highly susceptible to the hemolysin, those of pigs and guinea pigs were less susceptible, and erythrocytes of 60-day-old chicks were not susceptible (2). Other organisms capable of producing a hemolysin which lyses erythrocytes of various species include Escherichia coli, Listeria monocytogenes, Moraxella bovis, Pseudomonas aeruginosa, Staphylococcus aureus, streptococci, and Vibrio parahaemolyticus (2).

Contributor. Department of Pathology and Microbiology, Faculty of Veterinary Medicine, University of Montreal, C.P. 5000, St-Hyacinthe, Quebec, Canada, J2S 7C6.

Suggested reading.

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3. Nicolet, J: Haemophilus infections. In: Diseases of Swine. Lemon, AD, Straw, B, Glock, RD, Mengeling, WL, Penny, RHC, Scholl, E (Eds.), Iowa State University Press, 426-436, 1986.

4. Sebunya, TNK, Saunders, JR: Haemophilus pleuropneumonia infection in swine--a review. J. Am. Vet. Med. Assoc. 182: 1331-1337, 1983.

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Slide 83 (AFIP 2302201)

History. This adult male Syrian hamster (Mesocricetus areatus) was submitted for euthanasia and necropsy from a room in which two male hamsters had recently died without clinical signs. This hamster was lethargic, mildly ataxic, and had a ruffled hair coat. There was a recent thermostat malfunction in the room with widely fluctuating temperatures. The male hamsters had recently been moved to this room, and were placed directly across from a bank of cages containing female hamsters. The male hamsters were active, agitated, and fought frequently.

Gross Pathology and Laboratory Results. The perineum was matted with a small amount of fecal material. The cecum was mildly distended with tan semisolid contents.

Cultures were negative; tissue culture technique for Clostridium difficile toxin B (cytotoxin) identification using HeLa cell line was positive at 1:1024.

Diagnosis. Cecum: Typhlitis, necrotizing, acute, diffuse, mild, Syrian hamster (Mesocricetus auratus), cavian.

Contributor's Comment and Conference Note. Clostridium difficile is a leading cause of antibiotic-induced typhlitis and colitis in hamsters, guinea pigs, and rabbits, and has been less frequently reported in cases of non-antibiotic-associated enteropathies in hamsters and foals. C. difficile causes pseudomembranous colitis (PMC) in human patients with or without history of antibiotic therapy. In humans, C. difficile is the causative agent in approximately 99% of cases of PMC and 20-30% of cases of antibiotic-associated diarrhea. The hamster is the animal model for human antibiotic-induced colitis. The disease syndromes in hamsters and humans differ in two features: (1) the terminal ileum, cecum, and proximal colon are affected in hamsters while lesions are restricted to the distal colon in man; (2) the hamster rarely develops grossly visible pseudomembranes, while this lesion predominates in human cases. Antibiotics that induce clostridial enteropathy in the hamster include erythromycin, lincomycin, clidamycin, streptomycin, kanamycin, neomycin, chloramphenicol, tetracycline, sulfaguanidine, and penicillin. Antibiotics alter the normal intestinal flora and allow colonization of the intestine by C. difficile. Clinical signs of depression, anorexia, hypothermia, and diarrhea may precede death. Gross lesions in the hamster are restricted to the terminal ileum, cecum, and proximal colon. The distal ileum and proximal colon may be distended with fluid and are occasionally hyperemic or hemorrhagic. The cecum

is frequently distended with watery to semiliquid contents that are cream, tan, or bloody in appearance. Microscopic lesions range from mild acute typhlitis to pseudomembranous typhlitis. The terminal 2 cm of ileum and the proximal 2 cm of colon sometimes have similar microscopic changes.

The differential diagnosis in the hamster includes Salmonella, enteroinvasive E. coli, and Bacillus piliformis, all of which can produce similar cecal lesions. Both Salmonella and B. piliformis affect other tissues, while C. difficile lesions are restricted to the intestine. C. difficile does not invade epithelial cells, while Salmonella, E. coli, and B. piliformis do enter epithelial cells and can be observed within the cytoplasm with special stains or electron microscopy. This case is representative of nonantibiotic-associated typhlitis due to C. difficile. Predisposing factors such as stress, hypochlorhydria, diet, antineoplastic drug therapy, and housing of hamsters treated with antibiotics with untreated hamsters have been implicated in the development of enteric C. difficile infections.

The pathogenesis is thought to involve altered gastric acidity or disruption of the intestinal bacterial barrier allowing C. difficile to colonize the intestinal tract. In this case, predisposing factors may have been the stress of temperature fluctuations and housing male hamsters with female hamsters. While speculative at present, there is epidemiological evidence that there are both exogenous (environmental) and endogenous reservoirs of C. difficile as sources of infection. C. difficile produces at least four significant toxins: toxin A (enterotoxin), toxin B (cytotoxin), a myoelectric factor, and a labile toxin. Toxin B is 213,000 times more cytopathic than toxin A. Testing for the cytopathic effect of toxin B on tissue cultures is the most sensitive means of diagnosis of C. difficile, especially when combined with neutralization tests: Clostridium sordellii antitoxin cross-reacts with C. difficile cytotoxin and is more widely used than antitoxin to C. difficile cytotoxin. Successful isolation of the cytotoxin depends on immediate collection of cecal contents after death. This poses a diagnostic challenge, as in our experience clinical signs are subtle or absent prior to death. C. difficile should be included in the differential diagnosis of sudden death and typhlitis in hamsters with a history of antibiotic or other drug therapy, of housing with other treated hamsters, or of recent stress.

Although most conference participants agreed the histomorphological changes in the cecum were consistent with those described for Clostridium difficile infection, some participants felt there were a few morphologic differences, such as evidence of segmental enterocyte proliferation and the presence of pseudomembranes. The moderator added that the Clostridium difficile is usually present in low numbers in the gut of hamsters.

Contributor. Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Suggested reading.

1. Borriello, SP, et al: Clostridium difficile--a spectrum of virulence and analysis of putative virulence determinants in the hamster model of antibiotic-associated colitis. J. Med. Microbiol. 24: 53-64, 1987.

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Slide 84 (AFIP 2295198)

History. This 9-month-old mixed breed goat was found dead 8 days after being inoculated subcutaneously with 1.0 ml of blood stabilate made from a goat showing clinical signs of peste des pestis ruminants.

Gross Pathology. The anteroventral portions of the lungs were consolidated and reddened. There was a modest accumulation of fibrin on the overlying pleura. The colonic mucosa was edematous and roughened.

Diagnosis. Lung: Pneumonia, bronchointerstitial, proliferative, subacute, diffuse, severe, with syncytial cells and intranuclear and intracytoplasmic eosinophilic inclusion bodies, mixed breed, caprine.

Contributor's Comment and Conference Note. Peste des petits ruminants (PPR) is a viral disease of goats and sheep characterized principally by stomatitis, diarrhea, oculonasal discharge and pneumonia. Originally described in West Africa, the disease is now known to be responsible for morbidity and mortality throughout much of subsaharan Africa north of the equator, the Arabian peninsula, and, recently, India. The causative agent is closely related to rinderpest virus, and these two are classified, along with the viruses of measles, canine distemper, and seal distemper, in the genus Morbillivirus of the family Paramyxoviridae.

Kids and lambs infected with PPR generally succumb due to severe dehydration engendered by the ulcerative stomatitis and enterocolitis. Older animals usually survive the gastrointestinal phase but may develop a severe bronchointerstitial pneumonia, which has many histologic similarities to the pneumonias associated with canine distemper and measles.

Other histomorphological features present include squamous cell metaplasia of the respiratory epithelium and moderate to large numbers of intra-alveolar neutrophils (often degenerate).

Although peste des petits ruminants virus (PPRV) cross reacts with rinderpest virus in immunodiffusion and complement fixation tests, it can be differentiated by serum neutralization tests.

Usually introduced to susceptible herds with newly purchased animals, PPRV is excreted and most likely transmitted via oculonasal discharges, saliva and feces at the onset of clinical signs. The usual incubation period before fever and mucosal erosions occur is two to six days. Diarrhea follows in two to three days. Death is usually preceded by pneumonia. Young animals are more susceptible than adults. West African dwarf goats are reported as more susceptible to infection than sheep (2). Cattle and pigs

can be infected experimentally, and although they do not develop clinical disease, there is subsequent protection against challenge with rinderpest virus (RPV). Goats recovered from PPRV infection when challenged with RPV do not develop rinderpest (2). Likewise, infection of goats and sheep with RPV reportedly protects them against PPRV infection (3). Necropsy findings in PPRV infection include mucosal erosions, hemorrhagic gastroenteritis and pneumonia.

The reported pathogenesis involves viral entry through the respiratory system with localization in pharyngeal and mandibular lymph nodes and tonsils. Subsequent viremia results with dissemination to visceral lymph nodes, spleen, bone marrow and mucosa of gastrointestinal and respiratory tracts.

The differential diagnosis in this case includes such conditions as rinderpest, bluetongue, heartwater, contagious ecthyma, sheep and goat pox, caprine pleuropneumonia, Nairobi sheep disease, salmonellosis, pasteurellosis, coccidiosis and plant and mineral poisonings.

Contributor. Foreign Animal Disease Diagnostic Lab., NVSL-S&T, APHIS-USDA, P.O. Box 848, Greenport, NY 11944.

Suggested reading.

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2. Brundza, A, Afshar, A, Dukes, TW, Myers, DJ, Dulac, GC, and Becker, SAWE: Experimental peste des petits ruminants (goat plague) in goats and sheep. Can. J. Vet. Res. 52: 46-52, 1988.

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Slide 85 (AFIP 2302194)

History. This 10-month-old, male, Barrows Goldeneye (Bucephalo islandica) duck was found recumbent under a boardwalk, with legs stretched out behind him. On physical examination the bird was depressed, ataxic, and unable to stand. Radiographs demonstrated two round metallic foreign bodies in the gizzard. The bird was anesthetized and two pennies, one with smooth surface devoid of the copper coating, were removed via endoscopy. The bird died following the procedure.

Gross Pathology and Laboratory Results. There is generalized decrease in muscle mass, with prominent keel. Subcutaneous and internal body fat is scant (inanition).

Serum zinc is elevated (12.5 ppm); Calcium is low (52.7 ppm); Copper is low (0.15 ppm).

Diagnoses. 1. Pancreas, acini: Degeneration and necrosis, diffuse, severe, Barrows Goldeneye (Bucephalo islandica), avian. 2. Small intestine: Enteritis, necrotizing, subacute, segmental, mild to moderate. 3. Kidney, tubules: Degeneration and necrosis, multifocal, minimal.

Contributor's Comment and Conference Note. Zinc, an essential trace mineral, is a component of up to 96 metalloproteins active in carbohydrate, lipid, protein, and nucleic acid metabolism, including carboxypeptidases, alkaline phosphatase, alcohol dehydrogenase, aminopeptidases, thymidine kinase, superoxide dismutase, and carbonic anhydrase (CA ii). CA ii contributes to maintenance of acid/base balance, particularly in red blood cells, renal tubular epithelial cells, gastric parietal cells, exocrine pancreatic cells, and salivary glandular cells. Next to calcium and magnesium, zinc is the most concentrated intracellular cation. Zinc toxicosis has been described in rats, chicks, ducks, cats, ferrets, lambs, cattle, horses, nonhuman primates, and man. Exposure occurs through ingestion of zinc-containing objects such as pennies minted since 1983 (96% zinc), nuts, or bolts; zinc oxide top-dressing; milk replacement diets for calves; or pasturing next to zinc smelters. A wide range of lesions have been attributed to zinc toxicosis, including depressed growth, hemolytic anemia, nephrosis, enteritis, nutritional myopathy, pancreatic atrophy and necrosis, lameness, osteochondrosis, pneumonia, and death. The threshold of acute toxicity is reported to be between 500 and 1500 ppm dietary zinc in ferrets, and between 1400 and 2500 ppm fed to rats, hens, lambs, cattle, and horses. Zinc is concentrated in the exocrine pancreas and renal tubular epithelial cells, and is primarily excreted via the pancreatic secretions. The pathogenesis of zinc toxicosis may be indirect or direct. Indirect toxicosis occurs through inhibition of selenium, copper, iron or calcium absorption, leading to deficiencies in these trace minerals. The lesion associated with secondary selenium deficiency is myopathy of striated and smooth muscle (skeletal muscle and gizzard), while arthropathies in cattle, rats, foals and pigs have been associated with hypocuprinemia or hypocalcemia secondary to zinc excess. Direct toxicity results from irritation of mucosal surfaces or from saturation of high-affinity binding sites with subsequent binding of zinc to lower affinity ligands via displacement of other divalent cations. These aberrant zinc complexes may lead to gene amplification, depression of genes, and derangements in protein and nucleic acid function. The most severe lesions would be expected to occur in those cells with large storage depots of zinc, such as liver, pancreas, and kidney. Pancreatic alterations have been described in experimentally intoxicated cats, sheep, calves, chickens, and ducklings, and in naturally intoxicated ferrets, sheep and calves. Lesions, limited to pancreatic acinar cells, consist of loss of zymogen granules, loss of basophilic staining, cytoplasmic vacuolization, cellular atrophy, and necrosis of individual acinar cells. End stage pancreatic lesions consist of ductlike structures (tubular complexes) separated by fibrous connective tissue. While the origin of these structures is unknown, they may arise by atrophy and dedifferentiation of acinar cells. Inflammation is generally minimal or absent. Similar pancreatic lesions have been described in a 28-year-old blue and gold macaw, although exposure to zinc and zinc levels were not reported. In an ultrastructural study of zinc toxicosis in ducklings, the predominant form of cell death was apoptosis (controlled, programmed cell death accompanied by little or no inflammation). The first stage of apoptosis consisted of margination of chromatin, condensation of cytoplasm, and formation of membrane-bound blebs of cytoplasm containing intact organelles. The second stage was phagocytosis and degradation of apoptotic bodies by acinar cells. Apoptotic bodies were distinguished from autophagosomes by the presence of both cytoplasmic and nuclear material. The pathogenesis of pancreatic lesions is undetermined, but may involve displacement of calcium leading to inhibition of

calcium-dependent cellular events such as stimulus-secretion coupling in acinar cells. Lesions may also be due to displacement of copper; experimental copper deficiency leads to acinar cell degeneration and atrophy. Pancreatic acinar cellular atrophy and necrosis are unusual findings in domestic animals, and zinc toxicosis should be included in the differential diagnosis in such cases.

Conference participants agreed that the clinical history and histomorphological changes were consistent with zinc toxicosis. Some sections of small intestine also contained trematode eggs within the lamina propria, (some surrounded by multinucleated giant cells) and occasional intraluminal sections of an unidentified nematode.

Contributor. Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Suggested reading.

1. Graham, TC, et al: A pathologic and toxicologic evaluation of veal calves fed large amounts of zinc. Vet. Pathol. 25: 484-491, 1988.

2. Gunson, DE: Environmental zinc and cadmium pollution associated with generalized osteochondrosis, osteoporosis, and nephrocalcinosis in horses. J. A. Vet. Med. Assoc. 180(3): 295-299, 1982.

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4. Latimer, KS, et al: Zinc-induced hemolytic anemia caused by ingestion of pennies by a pup. J. Am. Vet. Med. Assoc. 195(1): 77-80, 1989.

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6. Van Vleet, JF: Amounts of eight combined elements required to include selenium-vitamin E deficiency in ducklings and protection by supplements of selenium and vitamin E. Am. J. Vet. Res. 43(6): 1049-1055, 1982.

Slide 86 (AFIP 2292827)

History. Five-month-old, Holstein, steer, bovine. Thoracic lymph node from a calf that received an intravenous injection of 100 ml of blood from another calf and was euthanatized 34 days later.

Gross Pathology and Laboratory Results. Lymph nodes throughout the body were turgid and slightly reddened. The parenchyma bulged above the capsule when the nodes were incised. Several small lymph nodes were noticeable that usually are difficult to find, such as along the cervical trachea. Hemal nodes up to 1 cm in diameter were present but were within the size range of normal.

Two episodes of pyrexia (103-104) were detected during the first and third weeks post transfusion. Neutropenia (737, 828, 558) occurred on days 13, 29 and 30 post transfusion with total leukocyte counts of 6700, 6900 and 6200 respectively.

Diagnosis. Lymph node, thoracic (per contributor): Hyperplasia, follicular and paracortical, diffuse, moderate, Holstein, bovine.

Contributor's Comment and Conference Note. The calf was one used for in vivo serial passage of BIV. In calves killed 5-7 weeks post infection, hyperplasia was principally associated with the germinal centers and was seen microscopically in tonsil, spleen and gut associated lymphoid tissue as well as lymph nodes and hemal nodes. Morphologic alterations in the thymus were not detected. Germinal centers contain increased mitotic figures, blastic cells, scattered karyorrhectic cells and tingible body macrophages resulting in a starry sky pattern. The mantle of small lymphocytes becomes reduced or obscured. Lymph node changes are similar to those described in human immunodeficiency virus infection in the early lymphadenopathy stage (follicular hyperplasia without follicular fragmentation). Lymphoid hyperplasia from BIV infection is not distinguishable morphologically from other cases of lymphoid hyperplasia. Positive serology or virus isolation is needed to make the association with BIV.

Conference participants agreed that the diffuse follicular and paracortical hyperplasia observed in this animal was not specific for BIV infection and that definitive diagnosis would require virus isolation or positive serology.

Bovine immunodeficiency virus is a member of the family retroviridae and subfamily lentiviridae. It is also referred to as bovine visna-like virus, bovine visna virus and bovine lentivirus. Bovine immunodeficiency virus is antigenically and morphologically distinct from bovine leukemia virus (subfamily cornavirinae) and bovine syncytial virus (subfamily spuma virinae).

In one report (3), following experimental infection of calves, there was a transient leukopenia followed by a lymphocytosis and enlargement of subcutaneous lymph nodes. More recently, calves inoculated with tissue culture virus failed to develop lymphocytosis or lymphoproliferative responses 1-2 years later (4,5).

In another experiment (6), BIV from an original study was serially passaged 6 times in 2-4 month old calves. Clinical signs following BIV infection were transient and included pyrexia, neutropenia and lymphocytosis. Macroscopic observations at necropsy (4-6 weeks PI) were essentially normal with slightly swollen lymph nodes. Microscopically, follicular hyperplasia was the prominent change in lymph nodes. Changes in the paracortex and medullary cords were less conspicuous or absent.

BIV is detectable by the presence of syncytia after inoculation of peripheral blood leukocytes onto monolayer cultures of bovine embryonic spleen cells, or other susceptible cells (1). Identity of the virus can be confirmed by reacting cells with a known antiserum to BIV coupled with an indicator system (1). The indirect fluorescent antibody test is the most widely used system for detecting antibodies (1). For monitoring experimentally infected calves, blot analysis has proven more useful and sensitive (1).

Contributor. Iowa State University, Department of Veterinary Pathology, Ames, IA 50011.

Suggested reading.

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2. Ost A, Baroni CD, Biberfeld P, Diebold J, Moragas A, et al: Lymphadenopathy in HIV infection: histological classification and staging. Acta Pathol Microbiol Immunol

Scand Supp 8, 7-15, 1989.

3. Van Der Maaten MJ, Boothe AD and Seger CL: Isolation of a virus from cattle with persistent lymphocytosis. J Natl Cancer Inst 49: 1649-1657, 1972.

4. Van Der Maaten MJ, Whetstone CA, Roth JA, Miller JM: Bovine immunodeficiency-like virus. Abst. 10th Annual Food Animal Disease Research Conference, Marriott Hotel, Ft. Collins, CO 80523, Mar. 9-11, 1989.

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6. Carpenter S, Roth JA, Van Der Maaten M, Whetsone C, Miller LD: Early pathogenesis of bovine immunodeficiency-like virus infection in calves. Abst. Ann. Mtg. of the Laboratory of Tumor Cell Biology, National Cancer Institute, Hyatt Regency Hotel, Bethesda, MD, Aug. 20-26, 1989.

Slide 87 (AFIP 2286826)

History. Male juvenile rhesus monkey. Experimentally infected with Simian Immunodeficiency Virus (SIV-Delta) 7 months prior to sacrifice. Clinical signs of diarrhea, weight loss, pneumonia.

Gross Pathology and Laboratory Results. Cecum and colon - no gross lesions. Lungs - pneumonia. Monkey was perfused at time of necropsy.

Immunohistochemistry-SIV antigens in macrophages and multinucleated giant cells in various tissues including lamina propria of colon. Serology - antibodies to SIV.

Diagnosis. Small intestine: Enteritis, lymphohistiocytic, diffuse, mild, with multifocal crypt abscesses and syncytial cells, rhesus monkey (Macaca mulatta), primate.

Contributor's Comment and Conference Note. The pathogenesis of the intestinal lesions is not known. SIV-Delta was not reported to induce these types of lesions. The new SIV/SMM strain (Fultz et al) causes intestinal lesions with numerous antigen positive macrophages in lamina propria, similar to the lesions in this case (Dr. Phil Zack, unpublished).

Both human and simian immunodeficiency viruses (HIV and SIV) are lentiviruses which share 40 to 75% nucleotide sequence homology, depending on whether SIV is compared to HIV-1 or HIV-2, respectively (1-3). Lentiviral infections are classically associated with persistent infection and a slowly progressive clinical course, which appears to be a consequence of infection and eventual elimination of CD4+ T-helper cells (4).

Recently, a strain of SIV isolated from naturally infected sooty mangabey monkeys (SIV/SMM) was reported to be nonpathogenic for mangabeys, but when injected into macaques caused an immunosuppressive disease characteristic of lentivirus infection (5).

Several conference participants commented that they had seen occasional protozoal organisms in the villar crypts, along with rare surface associated bacteria.

Contributor. National Cancer Institute, NCI-FCRDC, Building 538, Frederick, MD 21701.

Suggested reading.

1. Chakrabarti L, Guyader M, Alizon M, Daniel MD, Desrosiers RC, Tiollais P, and Sonigo P: Sequence of simian immunodeficiency virus from macaque and its relationship to other human and simian retroviruses. Nature 1987;328:543-547.

2. Franchini G, Gurgo C, Guo H-G, Gallo RC, Collalti E, Fargnoli KA, Hall LF, Wong-Staal F, and Reitz MS Jr: Sequence of simian immunodeficiency virus and its relationship to the human immunodeficiency viruses. Nature 1987;328:539-542.

3. Guyader M, Emerman M, Sonigo P, Clavel F, Montaginer L, and Alizon M: Genome organization and transactivation of the human immunodeficiency virus type 2. Nature 1987;326:662-669.

4. Haase AT: Pathogenesis of lentivirus infections. Nature 1986;322:130-136.

5. Fultz PN, McClure HM, Anderson DC, et al: Identification and biologic characterization of an acutely lethal variant of simian immunodeficiency virus from sooty mangabeys (SIV/SMM), Aids Research and Human Retroviruses 1989;85:397-409.

6. Ward JM, O'Leary TJ, Baskin GB: Immunohistochemical localization of human and simian immunodeficiency viral antigens in fixed tissue sections. Am J Pathol 1987;127:199-205.

Slide 88 (AFIP 2286830)

History. Seventeen-year-old, female, Papio cynocephalus anubis, Olive baboon. This feral born was clinically lethargic, had a generalized lymphadomegaly, bilateral ocular discharge, and swollen breasts. Chest radiographs revealed multifocal variably sized opacities consistent with neoplasia or fungal disease.

Gross Pathology and Laboratory Results. The lymph nodes were white to yellow, moist, and uniform on the cut surface. Variably sized white to yellow foci consistent with those of the lymph nodes were seen in the lungs, kidney, mammary gland, spleen, bone marrow, and skin.

Clinical pathology results were unremarkable except for an eosinophilia.

Diagnosis. Lymph node, unknown origin: Malignant lymphoma, diffuse, large cell, immunoblastic type, olive baboon (Papio cynocephalous anubis), primate.

Contributor's Comment and Conference Note. Sections revealed diffuse nodal architectural effacement by a predominant large lymphoid cell infiltrate. The neoplastic cells had complex, often multilobulated vesicular nuclei with distinct eosinophilic nucleoli. There was widespread individual cell necrosis and moderate to marked mitotic activity. In some areas there was associated sclerosis. There was definite reactivity for pan-T antigen UCHL-1, in contrast to lack of reactivity for pan-B antigen L26.

Simian T-cell leukemia virus type I (STLV-1) is a retrovirus associated with leukemia/lymphoma in old-world non-human primate species such as Rhesus macaques, African green monkeys, and baboons. This virus is very closely related to human T-cell

leukemia virus type-I, the etiologic agent of adult T-cell leukemia/lymphoma in humans. The incidence of seropositivity to STLV-1 in non-human primate populations has been reported to be as high as 60%, however, the incidence of neoplasia is low. Spontaneous leukemia/lymphoma has been reported in STLV-1 antibody positive P.c.anubis and hamadrayas baboons. Cases of spontaneous malignant lymphoma and one case of Hodgkin's lymphoma have been reported in the baboon colony at Southwest Foundation for Biomedical Research (SFBR). A subsequent seroepidemiological survey of STLV-1 antibodies in SFBR baboons revealed an incidence of 39% in P.c.anubis baboons. An STLV-1 positive cell line has been established from peripheral blood leukocytes obtained from this animal before death. This is the first such case and was morphologically similar to HTLV-1-associated lymphoma in humans. These results further implicate STLV-1 as the etiologic agent of T-cell leukemia/lymphoma in baboons.

This case was reviewed by both the Departments of Veterinary Pathology and Hemolymphatic Pathology. The histomorphological characteristics of the lymph node were felt to be most consistent with diffuse, large cell, immunoblastic malignant lymphoma.

Contributor. School of Aerospace Medicine/VS, Brooks AFB, Texas 78235-5260.

Suggested reading.

1. McCarthy, TJ, Kennedy, JL, Blakeslee, JR, and Bennett, BT: Spontaneous malignant lymphoma and leukemia in a simian T-lymphotropic virus type I (STLV-I) antibody positive olive baboon. Lab Anim Sci 40(1): 79-81, 1990.

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3. Ishikawa, K, et al: Serological survey and virus isolation of Simian T-cell leukemia/T-lymphotropic virus type I (STLV-I) in nonhuman primates in their native countries. Int. J. Cancer 40: 233-239, 1987.

Slides 89, 90 (AFIP 2311140)

History. This monkey was challenged with a SIV strain of sooty mangabey origin on 8 Nov 88. At 23 days prior to death (DPD) splenomegaly was noted; at 8 DPD she was lethargic and her stools were loose and hemorrhagic; at 2 DPD she was anorectic, lethargic, and lying down at times; at 1 DPD she appeared very depressed, predominantly recumbent and had bloody diarrhea. Her condition remained unchanged on the day of necropsy. The cadaver was perfused with 4% paraformaldehyde.

Gross Pathology and Laboratory Results. No gross pathology.

PCV = 34.7
BUN = 200 mg/dl
Creatinine = 6.2 mg/dl
Phosphorus = 12.7 mg/dl
Calcium = 7.9 mg/dl
Total Protein = 5.6 g/dl

Albumin = 2.4 g/dl
Bilirubin = 1.1 mg/dl
Sodium = 135 mEq/L
Chloride = 93 mEq/L
LDH = 1780 U/L

Urinalysis: specific gravity = 1.020 protein = 4+ (2000 mg/dl); pH = 5.5; blood = 20-35 RBC's/HPF; WBC's = 2-5/HPF; no casts seen.

Diagnoses. 1. Kidney: Glomerulonephritis, membranoproliferative, global, diffuse, mild, rhesus monkey (Macaca mulatta), primate. 2. Kidney, glomerular capillaries, small arteries and arterioles: Vasculitis, necrotizing, with fibrinoid necrosis. 3. Eye, retina: Edema, diffuse, severe, with detachment and hemorrhage.

Contributor's Comment and Conference Note. This case was reviewed by both the Departments of Veterinary Pathology and Renal Pathology. Conference participants agreed the diagnosis in this case could not be made based entirely on light microscopic changes, but requires electron microscopic evaluation as well.

Contributor. Pathology Division, USAMRIID, Ft. Detrick, MD, and Retroviral Pathogenesis Section, Georgetown University/Laboratory of Infectious Diseases, NIAID, NIH, Rockville, MD.

Slide 91 (AFIP 2288945)

History. This 5-month-old, Yorkshire cross pig (Sus scrofa) was from a barn of 1300 feeder and finishing pigs. The farm experienced a sudden onset of illness with a morbidity rate of 15-20% and a mortality rate of 5%. Numerous pigs in all pens exhibited inappetence, respiratory distress, lameness, emaciation, multiple fractures and acute deaths over a one week period. Losses apparently coincided with a new batch of commercial pelleted feed delivered to the farm 6 weeks previously.

Gross Pathology and Laboratory Results. Long bones showed severe osteoporosis with marked loss of metaphyseal and epiphyseal trabecular bone and acute to subacute pathologic fractures of both femurs. The kidneys were pale with tiny white streaks and irregular foci throughout the cortical areas. The epicardial and myocardial cut surfaces of the heart had numerous tiny white foci. The lungs showed severe suppurative bronchopneumonia. The caudal lobes were firm, noncollapsed and gritty on sectioning ('pumice lung'). Tiny chalky white foci were on the free edges of the laryngeal vocal folds.

Fixed tissues submitted 1 week previously (heart, lung, kidney) showed extensive mineralization of blood vessels, myocardial myofibers, bronchiolar basement membranes, lung alveolar septae and renal tubular and glomerular basement membranes.

Diagnoses. 1. Bone (unknown location), metaphysis: Osteodystrophy, multifocal, moderate, characterized by basophilic matrix, osteopenia, and metaphyseal

infarction, Yorkshire cross pig (Sus scrofa), porcine. 2. Bone (unknown origin), epiphysis, blood vessels: Myointimal proliferation, tunica intima and tunica media, multifocal, moderate, with adventitial and perivascular calcification.

Contributor's Comment and Conference Note. The feed company involved admitted to a feed mixing error; approximately 400 times the recommended levels of vitamin D_3 (N.R.C. recommends 550-850 I.U./Kg of feed) was accidentally added to the batch of feed delivered to the farm.

The pathogenesis of hypervitaminosis D lesions is thought to be due to a combination of direct cell toxicity, with initial mitochondrial damage, as well as mineralization of damaged cells and elastic fibers because of the severe hypercalcemia and hyperphosphatemia which also occurs.

We have seen several incidents of this toxicity problem in feeder pigs, pregnant sows, dairy cows and dogs in our diagnostic laboratory but we had not seen the skeletal vascular lesions seen in several pigs necropsied from this farm.

This case was reviewed both by the Department of Veterinary Pathology and the Department of Orthopedic Pathology. Conference participants agreed the clinical history and the histomorphological changes evident in the sections of bone were consistent with vitamin D toxicity.

The conference moderator commented on the presence of abundant prominent basophilic scalloped borders along trabeculae of mature bone, often surrounded by less mature (pale eosinophilia) bone with an absence of osteoclasts with resorption bays (Howship's lacunae). These morphologic features suggest the condition may occur in waves with periods of high osteoclastic activity followed by periods of immature bone deposition. Both the lack of osteoclasts and abnormal poorly formed matrix are diagnostic of vitamin D toxicity. Histologically, similar structures lined by numerous active osteoclasts would be suggestive of fibrous osteodystrophy. The moderator further added that since specific osteoclastic receptors for 1,25 dihydroxycholicalciferol have not been identified, its mechanism of activation is unknown.

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Slide 92, L21 (AFIP 2287616)

History. This 4-year-old female greater kudu (Strepsiceros strepsiceros) was examined for mild chronic swelling of the mandibular symphysis with gradual enlargement. This was one of four kudus in a zoo that developed this lesion over a period of several years.

Gross Pathology and Laboratory Results. Focal spherical enlargement of the mandibular symphysis was present. This enlargement was firm to hard and white on cross section. No other gross lesions were present.

Serum calcium, phosphorus, urea nitrogen and creatinine were 7.8, 9.2, 41 and 2.1 mg/dl respectively.

Diagnosis. Mandible (per contributor): Fibrous osteodystrophy, hyperostotic, moderate to severe, focally extensive, greater kudu (Strepsiceros strepsiceros).

Contributor's Comment and Conference Note. Microscopic lesions in the kidneys consisted of mild chronic lymphoplasmacytic interstitial nephritis. There were mild lesions of fibrous osteodystrophy in the vertebral bodies. Fibro-osseous lesions of the mandible of greater kudus have been reported previously and considered to be either ossifying fibroma or fibrous osteodystrophy. This case supports an association of the mandibular lesion with renal disease and lesions indicative of hyperparathyroidism in other bones. Interesting in this case is the apparent decrease in serum calcium and elevation in serum phosphorus. These apparent disturbances were thought to be greater than would be suspected from the mild renal lesions and a mild degree of uremia. The International Species Information System lists these values for serum calcium and phosphorus as relatively normal for adult kudus. This could mean that feeding protein supplements to these animals in captivity could contribute to nutritional hyperparathyroidism and result in clinical disease in those animals which also develop renal disease. The cause of the renal disease was not apparent.

Hyperparathyroidism as a complication of chronic renal failure is a condition characterized by excessive parathyroid hormone (PTH) in response to chronic hypocalcemia. Hyperphosphatemia may develop with retention of phosphorous as the primary renal disease progresses to a point at which there is significant reduction in the

glomerular filtration rate. Phosphorous itself has no direct affect on PTH synthesis or secretion, but it may contribute by its ability to lower serum calcium. Impaired intestinal absorption also plays a significant role. Prior to acting on target cells in the intestine and bone, vitamin D_3 (cholecalciferol) is metabolized to 1,25 dihydroxycholecalciferol (1,25-DiOH-CC) in the renal convoluted proximal tubules.

Chronic renal failure impairs production of 1,25-DiOH-CC by the kidney and therefore diminishes intestinal transport and increases mobilization of calcium from the skeleton. In addition to the fibrous osteodystrophic changes, parathyroid glands undergo marked chief cell hyperplasia. Electron microscopic changes reflect an actively synthesizing stage of the secretory cycle, including extensive endoplasmic reticulum, numerous ribosomes, large mitochondria, prominent Golgi apparatuses, and numerous presecretory granules.

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Slide 93 (AFIP 2292829)

History. This 12-year-old, female beagle was exposed to a radioactive (^{91}Yttrium) aerosol that resulted in brief irradiation of the lung, 11 1/2 years before death. Slightly more than a week prior to death, the bitch was hospitalized due to depression, multiple joint swellings and mild dyspnea. Radiographs showed a collapsed disc space at C6-7 as well as periosteal proliferation of the distal humeri, radii, ulnas, femurs, tibias, fibulas, bones of the carpal and tarsal joints and metacarpal and metatarsal bones. An 8 x 4 cm radiopaque mass was noted in the right diaphragmatic lung lobe. A few days later, the dog developed pneumonia and died.

Gross Pathology. The thoracic cavity contained a small amount of serosanguinous fluid. A 5x5x4 cm, firm mass filled most of the caudal portion of the right diaphragmatic lung lobe. The pulmonary parenchyma adjacent to the tumor was dark red. On section,

the neoplasm was yellow and contained multiple necrotic foci. Tracheobronchial, sternal, and mediastinal lymph nodes were enlarged and firm.

The periosteal surfaces of most of the long bones of the appendicular skeleton were hard and rough. Bones involved were, specifically, the humeri, ulnas, radii, carpals, metacarpals, femurs, tibias, tarsals, and metatarsals.

Diagnosis. Bone, unknown origin: Periosteal new bone growth (hyperostosis), diffuse, moderate.

Contributor's Comment and Conference Note. This is a classic case of hypertrophic osteopathy and is presumed secondary to the bronchioloalveolar carcinoma present in the right diaphragmatic lung lobe. The majority of the new bone is woven bone but portions adjacent to the old cortex are compact bone. The pathogenesis of hypertrophic osteopathy remains obscure. This rare disorder is most commonly affected in veterinary medicine in the dog.

Conference participants agreed the clinical history and histomorphological lesions are consistent with those described for hypertrophic osteopathy. This syndrome, reported in all domestic species as well as in humans, consists of diffuse periosteal bony proliferation secondary to a chronic, usually intrathoracic, lesion. The lesion may be either inflammatory or neoplastic (2). Exceptions to this periosteum-thorax association include typical osseous lesions reported in mares with ovarian tumors, dogs with botryoid rhabdomyosarcomas of the urinary bladder (2,3), and chronic hepatitis in humans. Thoracic lesions associated with this condition are diverse and include pulmonary tuberculosis, primary and secondary neoplasms, granulomatous pleuritis and lymphadenitis of bronchial or mediastinal lymph nodes, chronic bronchitis, Dirofilaria immitis infection, Spirocerca lupi induced esophageal lesions (3), and neoplasia involving the thoracic wall. With the exception of pulmonary metastasis from central osteosarcomas, hypertrophic osteopathy is not commonly associated with intraosseous neoplasms (2).

The pathogenesis is obscure. None of the proposed mechanisms, including both neurogenic and humoral, consistently fit the clinical and experimental observations.

Craniomandibular osteopathy ("lion jaw"), which occurs most frequently in West Highland White or Scottish Terrier dogs, is another poorly understood disease characterized by proliferation of new bone on periosteal surfaces. Although the lesions usually involve only the rami of the mandibles and the bones of the skull (occipital and temporal), new periosteal bone formation on the limbs has been reported (4).

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Slide 94 (AFIP 2287575)

History. A 2-3/4-year-old, 25.4 kg male Belgian Malinois dog was presented (day 0) with a 5-cm diameter raised, non-painful, non-fluctuant mass over the ventral portion of the right tenth rib. The dog had been purchased in the Netherlands eight months previously for the Department of Defense Military Working Dog Program and, at the time of presentation, was beginning explosives detector training. The prior history included current, routine vaccinations, an eight-day course of prophylactic metronidazole for Giardia given seven months prior to presentation and 0.57 kg/day of a standard medicated diet.

Gross Pathology and Laboratory Results. Abnormalities noted on necropsy were limited to the liver, spleen, right chest wall and lung. A pedunculated mass, 1 cm in diameter, was present on the right anterior lung lobe. Several other 1 mm dark red nodules were noted on the surface of other lung lobes. The right chest wall had a 9x4x2 cm firm mass bulging into the pleural cavity, encompassing the right tenth rib and centered just above the costochondral junction. This mass also bulged outward from the rib cage and was covered by healed scar tissue from the previous surgery. The spleen was very engorged and contained one large blood-filled mass with a tear near its attachment to the capsule. Numerous other masses of variable size were present within the body of the spleen. The liver had eight large masses distributed near the mesenteric attachment of several lobes. Several of these masses were perforated and had large blood clots attached. The diaphragm was adhered to the surfaces of the chest wall mass in the thoracic cavity and to one large liver mass in the abdomen.

	DAY							
	9	9	10	12	15	16	18	
WBC ($x10^3$)	26.2	25.9	21.1	23.4	28.0	31.7	13.7	(15.4)*
HCT %	60	35	24	31	21	22	26	(28)*
Hgb (g/dl)	20.1	11.5	8.0	10.3	7.0	7.4	8.8	(9.8)*
Platelets ($x10^3$)	168	401	260	235	117	111	166	(14)*

*Values in parentheses denote abdominal fluid analyzed on day 18.

Diagnosis. Rib (per contributor): Hemangiosarcoma, Belgian Malinois, canine.

Contributor's Comment and Conference Note. Tissue sections of the chest wall mass showed neoplastic cells organized in sheets of cells which contained many vascular spaces. Individual cells had poorly defined cell borders in some areas while in other areas were spindle-shaped. Nuclei were oval and contained prominent nucleoli. Mitotic figures were common. The cytoplasm was abundant and slightly eosinophilic. The mass invaded and replaced the marrow cavity and cortex of the rib and extended into adjacent tissues. There were scattered fragments of bone within the mass along with large areas of hemorrhage or thrombosis. Factor VIII stains were positive in some of the neoplastic cells.

Hemangiosarcoma can arise from any site. It is possible that the large rib mass in this case was a metastasis from the spleen. Primary splenic hemangiosarcomas will frequently metastasize to the lung; however, in this case, only a few metastases were present. The size of the rib mass, the young age of the dog and the paucity of lung lesions suggest the possibility that this hemangiosarcoma could have originated in the rib rather than the spleen.

The conference moderator agreed that, although immunohistochemical staining for factor VIII related antigen failed to decorate the neoplastic cells, the clinical and histomorphological characteristics were consistent with hemangiosarcoma.

Hemangiosarcoma (malignant hemangioendothelioma) occurs most frequently in older dogs. German shepherd dogs (Alsatians) are most commonly affected. Hemangiosarcoma also occurs in horses, sheep and cats. It is the most common primary cardiac tumor of dogs, occurring most commonly subepicardially in the right atrial wall. Hemangiosarcomas arise de novo and not from preexisting hemangiomas. Hemangiosarcomas typically metastasize widely, especially to the lung ("cannonball" metastasis). In some cases the primary tumor site may be difficult to establish and multicentric origin is a possibility.

Primary hemangiosarcoma of bone, a relatively rare tumor in animals, occurs

mostly in dogs. Most cases occur in young adults of large and medium sized breeds with both sexes being equally represented. The breeds most commonly affected are Boxers, Great Danes and German shepherd dogs (13,15). Long bones are the most common sites of involvement, followed by pelvic bones, sternum, ribs, maxilla and vertebral column (13). Tumors of bone which may be similar in gross appearance include telangiectatic osteosarcoma, aneurysmal bone cyst, and tumors metastatic to bone including osteosarcoma and hemangiosarcoma of soft tissue origin. Histologically, hemangiosarcoma stroma does not form a calcifiable matrix (13). Hemangiosarcomas typically destroy extensive areas of bone before producing clinical signs. By this time, most have already metastasized hematogenously (13). Histological grading is reported to be of little or no prognostic value (15).

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Slide 95 (AFIP 2288648)

History. The Simian virus 40 (SV40) early region, which encodes the large and small viral tumor antigens (T-Ags), was fused to the mouse albumin enhancer/promoter, and this construct (Alb-SV) was introduced into fertilized mouse ova. Two transgenic founder mice that expressed the transgene were used to establish breeding lines. Mice were sacrificed and examined at one, two, three, four, and five months of age.

Gross Pathology. Between 3 and 5 months of age, all transgenic mice developed distended abdomens. Livers were severely enlarged, weighing 9-25 grams compared to normal adult liver weight of 1-1.5 grams. All livers contained multiple (up to several hundred) coalescing nodules.

Diagnoses. 1. Liver: Hepatocellular carcinoma, C57BL/6XSJL mouse, rodent. 2. Liver: Cholangiocarcinoma. 3. Liver: Foci of cellular alteration, clear cell variety.

Contributor's Comment and Conference Note. Mice expressing Alb-SV40 transgene developed moderate to severe hepatic dysplasia at one month of age, altered hepatocyte foci and nodules at two months of age, and multifocal hepatic adenomas, carcinomas, cholangiomas, and cholangiocarcinomas at 3 to 5 months of age. Histologically, there was loss of normal hepatic architecture with multiple nodules of varying types in each section. No evidence of metastasis was observed in any mouse. Nucleic acid from liver and liver tumors was assayed for transgene mRNA. T-Ag transcripts averaged less than 20 molecules/cell and did not vary greatly between untransformed transgenic liver and tumor nodules. A similar pathogenesis accompanied hepatic expression of T-Ag in two other transgenic models of liver neoplasia.

Conference participants agreed that multiple neoplasms were present within the sections of liver.

Creating transgenic animals begins with injecting DNA fragments (genes) in the pronucleus of a fertilized egg. If successful, the gene becomes part of the zygote's genetic makeup. Once inserted in the uterus of a recipient female, DNA injected fertilized eggs undergo implantation and placentation and continue development. Mice, compared to other animal embryos, have the best success rate for transgenic procedures, approximately 25%(4). In addition to introducing oncogenes, their uses include the study of transgenic animal models for human diseases, viral diseases, insertional mutagenesis, and gene regulation, as well as immune system and genetic diseases (4). The list will no doubt continue to grow.

Viral oncogenes (v-oncs) are part of the viral genome capable of causing cancer. DNA hybridization studies have indicated v-onc sequences are almost identical to normal cellular DNA. The normal cellular genes are referred to as proto-oncogenes in recognition

of their transforming potential. Much evidence suggests v-oncs may not be viral genes but rather wayward copies of proto-oncogenes incorporated into the viral genome during viral replication within a normal cell (5). Hepatic neoplasia has been induced by directing the expansion of SV40 T-antigens, an oncogenic mutant of c-H-ras, or e-myc to the liver of transgenic mice using an albumin enhancer/promotor (1).

Neoplastic transformation of cells in culture and induction of cancer in vivo is broadly divided into two stages: initiation and promotion (5). An initiated cell is altered in some manner, increasing the likelihood it will give rise to a tumor. Initiation is rapid, irreversible and has memory. Promotors can induce tumors in initiated cells. Promotors are nontumorigenic by themselves and must be applied after, rather than before, initiators. Promotors are reversible. Promotors also have a threshold level, subthreshold or mildly special doses are without effect.

In addition to the liver, depending on the specific promotor with which the T-antigen coding region is associated, SV-40 T-antigen coding region has induced neoplasia in the choroid plexus, exocrine pancreas, stomach, kidney, lens, thymus, heart and multiple endocrine organs (1,2,3).

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Slide 96 (AFIP 2240203)

History. Tissue from an adult male Fischer-344 rat which was used as a sentinel as part of a chronic toxicologic/carcinogenic study.

Gross Pathology. Kidney, bilateral, capsule, focus, irregular, pale, granular, multiple.

Diagnosis. Kidney: Nephropathy, chronic, progressive, severe, F344 rat, rodent.

Contributor's Comment and Conference Note. This case is a good example of the

common renal disease syndrome which effects a large percentage of aged adult Fischer 344 rats. Among other ancillary conditions which can occur as a result of this disease, secondary renal hyperparathyroidism is not common. Enlarged parathyroid glands and fibrous osteodystrophy of both long bones and bones of the skull is not an uncommon finding in addition to mineral deposition in soft tissues of various organs.

Chronic progressive nephropathy (CPN) is the most common spontaneous renal disease in adult aged laboratory rats, making it difficult to distinguish age-related from drug-related effects in chronic toxicity studies. The confusion in terminology stemmed from unclear cause and pathogenesis. Lesions are rarely observed in rats less than 1 year old but by 2 years of age (depending on the strain) 75% or more of the animals may have lesions. Several variables other than age affect the incidence of lesions.

Albino strains and stocks have higher incidence; nonalbino strains seem to be less affected. Sprague-Dawley rats are more susceptible than other strains, occurring also with high incidence in Fischer 344, Wistar and Marshall rats. It occurs with lower incidence/absence in Osborne-Mendel, Buffalo, Long-Evans, WAG/Rij and BN/Bi/Rij rats. Although the incidence and severity of CPN vary among the different rat strains, progression is qualitatively similar.

Male rats are more susceptible to age-related nephropathy than females. In Sprague-Dawley rats the incidence of CPN in males increases from 12 to 81% between 1 and 2 years of age; in females this age-related incidence increases from 8 to 44% which suggests a dramatic onset and/or development of this disease in the second year of life. Castrated males are less susceptible. Testosterone treatment accelerates lesion development.

Many attempts have been made to identify factors influencing the incidence and severity of CPN in laboratory rodents. By 20 months of age male Sprague-Dawley rats fed a diet containing 35% protein have more pronounced focal segmental glomerular sclerosis and tubular interstitial damage than rats fed their standard diet which contains 20% protein (13). Development of tubulo-interstitial damage and focal glomerular sclerosis were correlated with heavy and sustained proteinuria. By contrast, low protein diet (6%) was associated with a mild proteinuria, and no development of these lesions. A different conclusion was reached concerning the influence of dietary protein on nephropathy in the rat ablation model (1). Restriction of caloric intake (carbohydrate, fat, and minerals except for calcium and phosphorous) by 36% retarded growth and prevented the development of end-stage renal pathology in the remnant kidney model of chronic renal failure in rats regardless of whether protein was restricted or not. In contrast, protein restriction (38%) without restriction of any other dietary component failed to retard growth or protect the remnant kidney. The authors pointed out that in many of the studies in which protein restriction was found to protect against nephropathy, no information was provided on food intake.

Lesions can also be accelerated by unilateral nephrectomy and irradiation, thyroxin and adrenal hormone administration (5).

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Slide 97 (AFIP 2177606)

History. This female, 13-year-old lesser panda (Ailurus f. fulgens) was vaccinated on July 3. Serum from other lesser pandas was administered on July 6 and 8. The animal gradually developed diarrhea, inappetence, lethargy, and became moribund. She was euthanatized on July 24.

Gross Pathology and Laboratory Results. The lungs were mottled brown and had increased density. The left ventricle of the heart was slightly dilated and the aorta was slightly yellow. The cortex of both kidneys was finely granular.

Brain, lung, spleen, and lymph node were positive for canine distemper virus by fluorescent antibody tissue section test.

Diagnoses. 1. Pancreas, ducts, interlobular and intralobular: Inflammation, proliferative, chronic, multifocal, with ductal epithelial eosinophilic intranuclear and intracytoplasmic inclusion bodies and syncytia, lesser panda (Ailurus f. fulgens), procyonid. 2. Pancreas: Pancreatitis, necrotizing, chronic, multifocal, moderate, mild, with acinar cell eosinophilic intranuclear and intracytoplasmic inclusion bodies. 3. Salivary gland, mixed: Sialoadenitis, necrotizing, multifocal, mild, with acinar and ductal cell eosinophilic intranuclear and intracytoplasmic inclusion bodies.

Contributor's Comment and Conference Note. Degeneration of epithelium accompanied by viral inclusions was seen in many organs, but transitional epithelium did not appear affected. Degenerative changes in the kidney were judged to be age related. Fatal disease has been produced in lesser pandas by the administration of modified-live canine distemper virus vaccines.

Conference participants agreed the clinical history and histological lesions were consistent with a canine distemper virus (CDV) infection. There was variation in the location and severity of lesions in the sections of salivary gland.

Canine distemper virus is a naturally occurring disease in members of the family Canidae (e.g. dogs, foxes, coyotes and wolves), and Mustelidae (e.g. mink, ferrets, weasels, skunks) (2). Members of the family Procyonidae including raccoons, lesser pandas and kinkajous are susceptible (2). CDV infection in lesser pandas caused by both a modified live distemper vaccine (1,3) and spontaneous cases in a zoological garden have been described (2). This is the first reported case which demonstrated canine distemper virus (FA test) in the brain.

Contributor. Gerald G. Long, Pathology Department, Lilly Research Laboratories, Greenfield, IN 46140.

Suggested reading.

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Slide 98 (AFIP 2185695)

History. This is tissue from a 1-year-old, female, Fitch ferret (Mustela furo L.) that had a 1x1.5 cm, firm, subcutaneous mass located on the dorsum of the back.

Gross Pathology. The epidermis covering the 1x1.5x1 cm, firm, subcutaneous mass is focally ulcerated and reddened. The mass on cut surface is mottled yellow to white firm, multilobulated and has a coarse texture.

Diagnosis. Haired skin: Schwannoma, ferret (Mustela furo L.), mustelid.

Contributor's Comment and Conference Note. The superficial dermis has a compressive, well-demarcated, non-invasive multilobulated mass. The lobules vary from 1 to 5 mm diameter, are focally necrotic, and are encased by dense mature collagenous connective tissue. Individual lobules contain pleomorphic spindle-shaped cells that have indiscrete cytoplasmic borders, eosinophilic fibrillar cytoplasm, and large oval to round nuclei that have a fine chromatin pattern and inconspicuous nucleoli. Mitoses range from 0 to 2 per high power field. The cells are arranged into highly cellular interlacing bundles that are separated by a scant collagen stroma. In some lobules, the bundles form herring shoals and Verocay bodies. The epidermis has slight acanthosis and orthokeratotic hyperkeratosis.

Peripheral nerve sheath tumors have a broad spectrum of histological and ultrastructural appearances. Classical schwannomas are usually diagnosed by light microscopy alone; however, all nerve sheath neoplasms should be studied by electron microscopy if the cell type is to be established with certainty. Peripheral nerve sheath tumors may originate from three possible cell populations. First, nerve sheath neoplasms arise from Schwann cells located in the endoneurium. Schwann cells originate from the neural crest, contain S-100 protein, and have distinctive ultrastructural features (cytoplasmic features wrap around axons; ensheathed in a continuous basement membrane; pinocytotic vesicles are rare). The other two cell types that comprise nerve sheath tumors include the perineural cell of the perineurium and the fibroblast located in the epineurium. In contrast to the Schwann cell, these cells originate from mesenchyme, do not stain for S-100 protein, and have different ultrastructural characteristics (long thin cell processes invested in an interrupted basement membrane; terminal processes joined by tight junctions; numerous pinocytotic invaginations in the plasma membrane).

Positive immunohistochemical staining of the neoplastic cells for S-100 protein confirmed the neoplasm as Schwann cell origin. A recent report (1) summarized the disease states/abnormalities in a population of 350 ferrets as follows: Supernumerary incisors (26), infranumerary incisors (5), bifurcated incisors (4), broken canines (3), cataracts (6), respiratory tract infections (22), haemothorax (2), fractured rib (1), bifid spleen (2), splenic infarcts (2) accessory adrenal tissue (6), hydronephrosis (1), kidney cysts (5 out of 50 animals), monorchidism (1), accessory gallbladders (2), suspected leukemia (1), adenocarcinoma (1), neurofibroma (1) and buccal ulcer (1).

A review of 95 ferret tumors included ovarian stromal tumors, hemangiomas, hemangiosarcomas and adnexal skin tumors as comprising 50% of the total (5).

Contributor. Merck, Sharp & Dohme, Department of Safety Assessment, West

Point, PA 19486.

Suggested reading.

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Slide 99 (AFIP 2288230)

History. This young adult, Red Headed (Common) Agama (Agama agama) was one of a group of nine wild caught animals which were purchased from an animal dealer for display at a local zoological park. A number of problems have been diagnosed in animals which have died, including ectoparasitism, and endoparasitism (trematodes, cestodes, nematodes, microfilariasis). One had died from a necrotizing bacterial enteritis. This animal had also died unexpectedly. Multiple tissues collected at necropsy were submitted for examination.

Gross Pathology and Laboratory Results. Multiple pin-point white foci were noted in the liver. There were no other significant gross lesions.

Microbiology and virology were not performed.

Diagnosis. Liver: Hepatitis, necrotizing, acute, multifocal, with eosinophilic intranuclear inclusion bodies, Red Headed Agama (Agama agama), reptile.

Contributor's Comment and Conference Note. The liver contained multiple variably-sized foci of hepatocellular necrosis which were randomly distributed. These regions had little associated inflammation, but at the periphery numerous Type A eosinophilic to slightly amphophilic intranuclear inclusion bodies with peripheral halos were seen. They were considered to be characteristic of herpesvirus inclusion bodies. Within some of the necrotic foci clusters of rod-shaped gram-negative bacterial organisms were also present. The lung contained an occasional inclusion body (usually Type B) within airway epithelium. With the exception of mild autolysis, there were no significant lesions in the remaining tissues. Electron microscopy revealed intranuclear and intracytoplasmic virions of a size and morphology consistent with a herpesvirus (magnification 57,000 X). In one electron micrograph viral particles were budding from the nuclear membrane, acquiring an outer coat. In the second, several intranuclear viral particles were present with no outer coat, while several, present within an intranuclear invagination, had acquired outer coats, likely derived from the nuclear membrane. This behavior was also felt to be consistent with a herpesvirus, and explains the wide variability in sizes reported

for herpes viruses (150-200 nm).

Several reports have described "herpes-like" viruses in reptilian species including Pacific pond turtles, Green sea turtles, tortoises, Map turtles, and Siamese cobras. The characteristic intranuclear inclusions, combined with the EM findings support a diagnosis of herpesvirus disease in this Agama. A second animal which was submitted at the same time as this animal had numerous Type B inclusion bodies in airway epithelium, and a mild exudative pneumonia, but no evidence of hepatic necrosis or hepatic inclusion bodies. The viral particles in the lung of this animal were identical to those in the liver. Of the nine Agamas received, only one is still alive, and at this time is doing well.

Conference participants agreed the electron microscopic presence of hepatocellular intranuclear and intracytoplasmic virions was consistent with a herpesvirus. Only in recent years have herpes viruses been identified as presumptive agents of disease in reptiles as listed in the contributor's comments. Future investigations of diseases in reptiles will no doubt increase the list of susceptible hosts.

In addition to the hepatocellular eosinophilic intranuclear inclusion bodies, several participants observed occasional, rarely intraheterophilic, gram-variable bacilli.

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

Suggested reading.

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2. Jacobson ER, Gaskin JM, Roelke M, et al: Conjunctivitis, tracheitis and pneumonia associated with herpesvirus infection in green sea turtles. J. Am. Vet. Med. Assoc. 189: 1020-1023, 1986.

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Slide 100 (AFIP 2288053)

History. This tissue is from a 10-month-old, female, Channel Catfish, Ictalurus punctatus. Heavy mortality occurred in 15 of 32 ponds on a commercial catfish farm in southern Georgia commencing in the fall of 88 and extending through the spring of 89. Heaviest mortality occurred during February and March. Highest mortality in the ponds was 99% (282,000 of 284,000) fingerlings and 100% (all 6,000) brood fish. Affected fish were weak, anorectic, and gasping.

Gross Pathology. Gill filaments are markedly swollen and mottled various

shades of pale to bright red.

Diagnosis. Gill: Branchitis, granulomatous, diffuse, severe, with epithelial and mucous cell hyperplasia, secondary lamellar fusion, and protozoal cysts, catfish (Ictalurus Punctatus), piscine.

Contributor's Comment and Conference Note. Visits were made to the farm during February, March, and April of 1989. Numerous dead fish were observed around the edges of many ponds on each visit. Common names for this disease are "proliferative gill disease" and "hyperplastic gill disease". Controversy surrounds identity of the infective agent. Historically, Henneguya exilis kudo has been linked to this disease. Recently, a relationship between Shaerospora ictalaria n. sp. has been suggested. The disease has been transmitted under experimental conditions only by exposure of naive catfish to pond mud from "diseased" ponds. A secondary host is suspected. The specimen submitted was obtained in late February 1990 from one of the ponds that had experienced granulomatous branchitis. Overall, myxozoan-associated granulomatous branchitis was mild during fall 1989 through spring 1990 on this farm. This specimen has typical gill lesions with numerous interstitial multicellular organisms. No myxozoan spores were observed in this specimen but some catfish collected from this farm in 1989 and 1990 have had Henneguya exilis cysts.

This farm was established recently and production began in 1987. Ponds that had the heaviest mortality were "new ponds" that were stocked the prior summer. Outbreaks of the disease are most common in ponds in the first year of production hence the disease is also called "new pond" disease.

Proliferative gill disease (PGD) has historically been associated with the presence of the myxobolid Henneguya exilis kudo (1-4); however, there is recent evidence suggesting this may not accurately reflect the etiopathogenesis since H. exilis has been observed in catfish without signs of PGD (5). Henneguya exilis also has not been demonstrated in specific-pathogen-free catfish with experimentally induced PGD (6). Recently, a possible relationship between Sphaerospora ictaluri and PGD in the absence of environmental contaminants which may cause gill tissue damage has been suggested (7). Evidence suggests that PGD can be transmitted to catfish from water or mud from infected ponds, but not from infected catfish to uninfected catfish (6,8,9). This suggests an intermediate host may exist. Results of recent work (currently in press) by the contributor with well-water raised channel catfish fry suggest a triactinomyxoid myxozoan Aurantiactinomyon sp. as producing lesions consistent with PGD and further suggest an oligochate, Dero obtusa, present in pond mud is involved in the transmission.

Although special stains failed to demonstrate paired blue polar capsules (features consistent with those described for mature myxozoan spores), serial sections contained numerous basophilic aggregates composed of multiple small (approximately 1 μ) round organisms frequently surrounded by mononuclear cells which may represent immature myxozoan spores.

Contributor. Veterinary Diagnostic & Investigational Lab., P.O. Box 1389, Rt.

7, Brighton Road, Tifton, GA 31793.

Suggested reading.

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2. Bowser PR, and Conroy JD: Histopathology of gill lesions in channel catfish associated with Henneguya. Journal of Wildlife Diseases 21: 177-179, 1985.

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Slide 101 (AFIP 2292826)

History. Tissue from one of several captive tiger snakes (Notechis scutatus) which regurgitated two days after feeding. The problem was first noted in one of the snakes and then apparently spread to reptiles in contact with the initial case.

Gross Pathology. Poor nutritional status is evidenced by dorsal muscle wasting with spinal prominence. There was mild gastric mucosal thickening with accentuation of longitudinal rugae; a small amount of mucus was present on the gastric mucosa.

Diagnosis. Stomach: Gastritis, hyperplastic, chronic, diffuse, moderate to severe, with myriads of epithelial cell-associated protozoal organisms, etiology--consistent with Cryptosporidia sp., tiger snake (Notechis scutatus), reptile.

Contributor's Comment and Conference Note. The gastric mucosa is

thickened; numerous protozoal organisms (Cryptosporidium sp., presumptive) line the microvillous border of surface, pit and glandular epithelium; surface epithelium in some focal areas is hyperplastic, in some focal areas it has undergone cuboidal metaplasia; there has been almost total replacement of glandular granular cells by mucous neck cells as well as by surface type epithelium; there is cystic dilatation of gastric glands; moderate lamina proprial edema and fibrosis; mild to moderate patchy infiltrates of inflammatory cells, mainly plasma cells but also lymphocytes and heterophils. Occasional coccidia were also present in surface lining cells.

Cryptosporidiosis has been identified in at least 12 different hosts. Although cryptosporidial infection occurs most commonly in the intestine, it has been observed in the stomachs of mice and snakes, the bursa of Fabricius in chickens, the bile and pancreatic ducts of the rhesus monkeys, and the airways of turkeys.

The infection causes diarrhea in a variety of hosts, and there is a demonstrable intestinal lesion in pigs, lambs, calves and foals. Gastric cryptosporidiosis is an insidious disease of mature snakes characterized by a slowly progressing hypertrophic gastritis. Affected snakes are usually adults, but juveniles have been found with typical clinical signs and lesions.

The most common lesion in snakes is hyperplasia of mucous neck cells of the gastric glands with replacement of the granular cells that line the deeper portions of the gastric glands. The net effect is marked narrowing of the gastric lumen, excess mucus production and inadequate secretion of gastric enzymes and hydrogen ions.

Snakes with Cryptosporidiosis have a palpably firm stomach that may cause the surrounding body wall to bulge. These snakes will often regurgitate within several days of feeding. The intestinal longitudinal rugae are thickened and there is frequently an abnormal amount of mucus adherent to the mucosa.

Electron microscopy typically demonstrates the cryptosporidial organism attached to the glycocalyx of epithelial cells. Macrogametes are characterized ultrastructurally by the presence of dark staining polysaccharide granules. The membrane surrounding the parasite appears to be fused with the host cell membrane at one point, forming a specialized attachment zone.

Contributor. University of Melbourne, Veterinary Clinical Centre, Werribee, Victoria, 3030, Australia.

Suggested reading.

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6. Fox JG, et al: Lab. Animal Med., 1984, p. 635.
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Slide 102 (AFIP 2292188)

History. During the first 6 months of 1990 an unusually high number of stranded bottlenose dolphins were sighted or were found dead in the Mobile Bay area. This young male, bottlenose dolphin, Tursiops truncatus was found dead and submitted for necropsy.

Gross Pathology and Laboratory Results. The dolphin measured 118 cm. No adipose tissue was present. The lungs were diffusely mottled with irregular areas of dark red discoloration visible from the pleural and cut surfaces.

Salmonella sp. (serotype typhimurium) was isolated from the lung. Pseudomonas sp. and Vibrio sp. were isolated from the lung, spleen, and intestine.

Diagnosis. Lung: Bronchitis, subacute, multifocal, mild, with intraluminal metastrongyles and associated bronchiectasis, Atlantic bottlenose dolphin (Tursiops truncatus), cetacean.

Contributor's Comment and Conference Note. Other tissues were unremarkable except for focal bacterial colonization in blood vessels of kidney, adrenal gland and liver. Lung was dissected and intact nematode parasites were removed from bronchi. The parasites were identified as Halocercus sp. Little is known about the transmission of these nematodes. The reported presence of mature parasites in neonatal dolphins suggests the infection may be transplacentally transmitted and may be a contributory factor in neonatal mortality of cetaceans. Vibrio sp., Pseudomonas sp. and Salmonella sp. are often isolated from lungs of stranded cetaceans with pneumonia. Salmonella septicemia has been observed to produce an acute serofibrinous pneumonia with small numbers of inflammatory cells.

Conference participants agreed the morphologic characteristics of the intrabronchial parasites were consistent with a metastrongyle, most likely Halocercus sp.

Parasitic infections are recognized as a major cause of disease in aquatic mammals. In addition to infection with Halocercus lagenorhynchi(1) and other Halocercus sp., verminous pneumonia has been reported in the pilot whale with Sternurus sp. (5). The harbor porpoise (Phocaena phocaena) is frequently infected with the lungworm Pseudolius inflexus (6,7). Hepatic trematodiasis in cetaceans is reported with the families Fasciolidae and Opisthorchidae (8,9). The trematodes Braunina cordiformis and Pholeter gastrophilus have been observed within the stomach (8,10). Braunina cordiformis frequently causes a small focus of gastritis at its site of attachment. Harpactius pulex, a copepod, has been found associated with cutaneous ulcerations of a dolphin (T. truncatus) and a manatee (Trichechus manatus

latirostris).

Filarial infection in pinnipeds has been reported with both Dipetalonema spirocauda and Dirofilaria immitis (3). Infection with the dog heartworm D. immitis is apparently uncommon in feral animals but has been reported in harbor seals and sea lions maintained in captivity in endemic areas (3).

Bacterial pneumonia is reported as one of the most common diseases encountered in aquatic mammals (3). Staphylococcal lung infections appear to be most common, although Streptococcus sp. and Pseudomonas sp. are also reported in captive cetaceans (3).

Contributor. College of Veterinary Medicine, Auburn University, Auburn, AL 36849.

Suggested reading.

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Slide 103 (AFIP 2186867)

History. This 2-year-old, intact male, Siamese cat had been missing for 2 days prior to submission to the referring veterinarian. On presentation the cat was severely dehydrated and rectal temperature was 106 degrees F. Treatment with fluids

and antibiotics resulted in fever reduction, however, the cat died 3 days later.

Gross Pathology. Submandibular and mesenteric lymph nodes were enlarged (3x normal size) and were mottled tannish-grey to red on capsular and cut surfaces. Numerous 1-2 mm, tannish-white circular foci were present on capsular and cut surfaces of liver and spleen.

Diagnosis. Lymph node, mesenteric (per contributor): Lymphadenitis, necrotizing, diffuse, severe, with perinodal steatitis, necrotizing vasculitis and thrombosis, Siamese, feline.

Contributor's Comment and Conference Note. Additional histopathology lesions included multifocal necrotizing hepatitis and splenitis. Definitive diagnosis in this case was based on positive culture of Francisella tularensis from liver, spleen and lymph node. Additional history revealed that the cat had caught and eaten wild cottontail rabbits in the past with the most recent such incident occurring 1 week prior to death. Tularemia is enzootic in wild rodents and rabbits in the United States. Francisella tularensis may be transmitted from wild animal reservoirs by ingestion, inhalation, inoculation by biting insects and ticks, or by direct penetration of skin and mucous membranes. This cat was assumed to have become infected by ingestion of wild cottontail rabbits.

Francisella tularensis is most commonly seen in rodents and lagomorphs. This highly infectious disease is ubiquitous in the United States (2). Several endemic foci in Canada have been reported in several mammalian species, and in birds, reptiles, amphibians, fish and arthropods (1,4). While the gross lesions in rodents and lagomorphs are fairly characteristic, with splenomegaly and focal necrosis in liver, spleen, lymph nodes and bone marrow, it is nonspecific in birds (4) (As a result, the disease is probably overlooked unless a specific test on cultures are performed).

An outbreak of tularemia in farm raised ranch mink has been reported after adding 2 infected wild rabbits to the mink ration (2).

Contributor. Murray State University, Breathitt Veterinary Center, P.O. Box 2000, North Drive, Hopkinsville, KY 42240.

Suggested reading.

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205-206, 1985.

Slide 104 (AFIP 2130815)
History. This 6-month-old beef calf died with respiratory disease symptoms.

Gross Pathology and Laboratory Results. There was anteroventral consolidation involving 25-35% of the lungs. Multifocal round to irregular erosions/ulcerations were present in the oral cavity and esophagus (0.5-1 cm diameter). The larger lesions were centrally ulcerated and had slightly elevated margins.

Pasteurella haemolytica was isolated from the lung. Non-cytopathic BVD virus was isolated from pooled tissues. Fluorescent antibody testing of the esophagus for BVD virus was negative. Negative-stained preparations of esophageal lesions were examined by EM. No viral particles were found.

Diagnosis. Esophagus: Esophagitis, subacute, focal, mild, with epithelial cell ballooning degeneration and intracytoplasmic inclusion bodies, breed unspecified, bovine.

Contributor's Comment and Conference Note. Although virus was not demonstrated by electron microscopy, the esophageal lesions are diagnostic for bovine papular stomatitis (BPS). Differential diagnoses for esophageal ulcers also include BVD virus infection and systemic IBR virus infection. Esophageal lesions due to BVD virus infection are usually linear to irregular and not round. Microscopically, BVD virus ulcerations are due to epithelial necrosis, are non-proliferative, and do not produce inclusion bodies. FA testing is often positive with BVD virus-induced esophagitis. IBR virus-induced esophageal ulcers are grossly similar in size and shape to BPS. Microscopically, IBR virus ulcers are necrotizing with a prominent leukocytic reaction at the base of the ulcers and amphophilic intranuclear inclusions are often present in necrotic epithelial cells.

Foot and mouth disease and vesicular stomatitis are diseases that primarily produce oral lesions but occasionally produce necrotizing esophageal lesions without inclusion bodies.

Bovine papular stomatitis is generally a disease of minor significance. Although this animal also had pneumonic pasteurellosis and BVD virus infection, none of the ulcers was morphologically compatible with BVD virus induced lesions. The susceptibility of animals to BPS may be increased by concomitant diseases.

Several sections contained focal erosions and variable numbers of lymphocytes and plasma cells within the lamina propria/submucosa.

Bovine papular stomatitis usually occurs in younger animals. The papules may persist for several weeks before spontaneous recovery occurs. The papules vary in size from a few millimeters up to a centimeter in diameter, have a pale center and a hyperemic rim. These occur on the muzzle, tongue and may extend into the esophagus, reticulum, rumen and omasum. The lesions seldom ulcerate or become superinfected.

Contributor. Department of Veterinary Science, SDSU, P. O. Box 2175, Brookings, SD 57007.

Suggested reading.

1. Jubb RVF, Kennedy PC, Palmer N: Pathology of Domestic Animals, 3rd ed., Vol 2, pg. 12-14 and 90-100.

2. Griesemer RA, and Cole CR: Bovine papular stomatitis. III. Histopathology. Am. J. Vet. Res. 22: 482-486, 1961.

Slide 105 (AFIP 2289185)

History. This is a surgical sample from an extensively bosselated growth involving the glans penis of an intact male 10-year-old, German Shepherd-Collie not known to roam. This exophytic mass surrounded the dorsal and lateral portions of the glans and was highly vascular. Resection involved stripping away the mass from the underlying venous sinuses and sliding posterior preputial mucosa forward for coverage. The dog was normal and well healed at suture removal 2 weeks later but has been lost to further follow-up.

Gross Pathology and Laboratory Results. Multiple pieces of multinodular growth were received, measuring in aggregate 5x2.5x2cm. The outer surfaces were rather smooth underlain by a deep collagenous core. The urethra was not involved.

Preoperative blood work was normal.

Diagnosis. Glans penis, per contributor: Transmissible venereal tumor, German Shepherd dog-Collie mix, canine.

Contributor's Comment and Conference Note. This submucosal round cell tumor is composed of broad sheets forming exophytic papillary fronds with occasional nests in venous or lymphatic channels. Tumor cells are typically round to polyhedral with indistinct wispy eosinophilic cytoplasm and large nuclei with a prominent central to eccentric nucleolus and distinct marginated chromatin. Mitotic activity is brisk with some tingible debris and scattered aggregates of lymphocytes and plasma cells. The vascular stroma is irregular.

Recently, a veterinary oncologist advocated the use of vincristine to cure these tumors, but the historically high rate of spontaneous regression and surgical cures warrants caution in interpreting this therapeutic efficacy. Metastases are infrequent and seem to relate more to host immunological status than cellular morphology.

The exact cell of origin of the transmissible venereal tumor (TVT) is not known. It has been described as a tumor of lymphocytes, histiocytes, reticular cells, and mature end cells of the reticuloendothelial series. There are significant and constant karyotypic differences between normal dog cells and the tumor cells. The normal chromosome count for the dog is 78; all but two are acrocentric chromosomes. In TVT, there are usually 58-59 chromosomes, of which 13-17 are metacentric and 42 are acrocentric. TVT is most common during the years of greatest sexual activity (transmitted to the genitals by coitus). The tumor may be

solitary or multiple, cauliflower-like, pedunculated, nodular, papillary or multilobulated. Ultrastructurally, there are no features specific for TVT cells; however, numerous cytoplasmic interdigitations with neighboring cells are usually evident. Growth is initially rapid and later slows with immune inhibition. Metastasis is uncommon. Spontaneous regression is common with associated multifocal necrosis, infiltration of lymphocytes, probable cell mediated tumor lysis, and decreased numbers of tumor cells. Fibrosis and collagen deposition may be apparent in terminal stages of regression.

Contributor. Los Angeles County Comparative and Veterinary Services, 12824 Erickson Avenue, Downey, CA 90242.

Suggested reading.

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2. Epstein R, and Bennet B: Histocompatibility typing and course of canine venereal tumors transplanted into unmodified random dogs. Cancer Res 34: 788-793, 1974.

3. Vincristine treatment of transmissible venereal tumor. J. Am. Vet. Med. Assoc. 181: 163-164, 1982.

4. Cockrill JM, and Beasley JN: Ultrastructural characteristics of canine transmissible venereal tumor at various stages of growth and regression. Am. J. Vet. Res. 36: 677-681, 1975.

5. Hill DL, Yang TJ, Wachtel A: Canine transmissible venereal sarcoma: tumor cell and infiltrating ultrastructure in different growth stages. Vet. Pathol. 21: 39-45, 1984.

Slide 106 (AFIP 2085247)

History. This 9½-year-old male Beagle was clinically diagnosed as having hypothyroidism approximately 2 years prior to death. At this time, the dog was obese, had a poor hair coat and appeared to be quite lethargic. The dog was found dead in its kennel.

Gross Pathology and Laboratory Results. The right thyroid gland was approximately 2-3 times normal size and had a multinodular appearance. The gland was brown and soft. The left thyroid gland could not be located. The coronary arteries had numerous multifocal, yellowish-white gritty deposits which were present within the vessel wall. The aorta, pulmonary, carotid, and renal arteries were unremarkable on gross examination, although the mesenteric artery had numerous similar appearing plaques in the vessel wall.

Dog 3IA - Years of Age

	4	6	7	8	9	Normal Values
Cholesterol mg%	160	350	622	500+	500+	110-260
RBC X 106/mm3	7.8	6.2	4.9	4.6	4.9	6 - 8

Diagnosis. Heart, coronary arteries: Atherosclerosis, segmental to circumferential, with mineralization, diffuse, moderate, Beagle, canine.

Contributor's Comment and Conference Note. The cause of death of this dog was cardiac failure resulting from myocardial infarction secondary to the severe atherosclerosis in the coronary arteries. This dog had a long history of hypercholesterolemia resulting from hypothyroidism. The hypothyroidism resulted from congenital aplasia of the left thyroid gland and effacement of the right thyroid by an apparently nonfunctional follicular adenoma. Histologic examination of both the heart and kidneys showed multiple ischemic infarcts of various ages associated with vessels showing marked atheromatous change.

In dogs, hypercholesterolemia is primarily related to hypothyroidism and in most dogs with atherosclerosis there is a history of hypercholesterolemia and/or hypothyroidism. It is unusual for severe atherosclerosis to occur in dogs, and clinical consequences are rare.

Atherosclerosis has been reported to occur in nonhuman primates, aged swine, birds, dogs and ruminants. In swine, the lesion is most severe in older animals (8-14 yrs). Affected vessels include the aorta and its branches, extramural coronary arteries and intracranial (but extracerebral) arteries. In dogs, lesions affect extracerebral as well as coronary and renal arteries and are most pronounced in the tunica media and intima. Atherosclerotic lesions in birds have been reported in several species to include pigeon, turkey, chicken and parrot.

In humans, the atheromatous plaque is considered the fundamental lesion of atherosclerosis. Histologically plaques are composed of three components: (1) cells, including smooth muscle cells, macrophages, and other leukocytes; (2) connective tissue, including collagen, elastic fibers, and proteoglycans; and (3) intracellular and extracellular lipid deposits. The proportion of these three components may vary giving rise to a spectrum of lesions. Typically they are composed of a superficial fibrous "cap", a cellular area beneath and adjacent to the cap, and a deeper necrotic "core".

Contributor. Lovelace Inhalation Toxicology Research Institute, P. O. Box 5890, Albuquerque, NM 87185.

Suggested reading.

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Edition, Academic Press, Orlando, Vol. 3, pp 39, 1985.
2. Patterson JS, Rusley MS, and Zachary JF: "Neurologic manifestations of cerebrovascular atherosclerosis associated with primary hypothyroidism in a dog." J. Am. Vet. Med. Assoc. 186(5) : 499-503, 1985.
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Slide 107 (AFIP 2286510)

History. This 56-day-old male miniature swine (Hanford-Hormel Strain) was part of a nutritional study.

Gross Pathology. 1. A firm, black/gray, smooth nodular mass, 2.5 cm in diameter, located beneath the skin of lower eyelid. The cut surface was black, smooth and firm. 2. A mass, 2.0 cm in diameter, was located on the left temporal region. 3. Multiple black/gray spots (0.1 to 0.4 cm in diameter) in lungs, stomach and cecum.

Diagnosis. Haired skin: Melanoma, Hanford-Hormel strain, miniature swine, porcine.

Contributor's Comment and Conference Note. Microscopic examination revealed heavily pigmented cells (melanocytes/melanophages) in the hyperplastic epidermis, dermoepidermal junction and dermis. The cells were pleomorphic, mostly large, epithelioid and spindle-like. Some cells were multinucleated or vacuolated. The nuclei varied in size and shape and were mostly basophilic, vesicular, vacuolated or contained pigment. Mitotic figures were infrequent. In the dermis, invasion/permeation of multiple lymphatics, blood vessels and nerve sheaths by these cells was apparent. The pigment was dark brown and was confirmed to be melanin by Fontana stain. Similar lesions were observed in the lymph nodes contained in the grossly observed mass (2.0 cm in diameter) located on the left temporal region and as multiple black/gray spots (0.1 to 0.4 cm in diameter) in the lungs, stomach and cecum of the piglet. The left lower eye-lid skin lesion was considered primary malignant melanoma with systemic metastases in the lymph nodes, lungs, stomach and cecum.

Melanocytic growths in swine usually occur congenitally or in the Duroc-Jersey and, the Hormel and Sinclair miniature swine. Melanomas are occasionally seen in other swine breeds and appear to represent the same disease as in the miniature swine. There is no sex predilection. They primarily originate in the skin, but may also arise in internal organs. In the Duroc-Jersey breed, the flank has been reported to be the most common site. There is no site predilection in Hormel and Sinclair breeds. Genetic factors appear to be important in swine since the occurrence can be increased by selective breeding. Melanomas in swine have a high prevalence

of spontaneous regression that is thought to result from the cytotoxic effects of tumor-specific T lymphocytes that infiltrate these tumors. Regression does not always occur however, and young adult swine may develop lesions of sufficient size to cause organ dysfunction.

Contributor. Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 "C" Street, SW, Washington, DC 20204.

Suggested reading.

Jubb, Kennedy and Palmer: Pathology of Domestic Animals (Academic Press, Inc.) 3rd ed., Vol 1, 513, 1985.

Slide 108 (AFIP 2285061)

History. This 10-year-old, male castrated mixed-breed dog had a four month history of chronic, severely hyperkeratotic, erosive to ulcerative, oozing and crusting skin lesions, which were located on the head, involving the muzzle and periorbital areas, distal extremities, pronounced at the paws and all pressure points, lateral thorax and all mucocutaneous junctions. The lesions were painful.

The dog presented with generalized muscle atrophy and weight loss. The mucous membranes were pale and a grade IV/VI systolic heart murmur could be identified.

Gross Pathology and Laboratory Results. Clinical laboratory findings showed:

- a mild to moderate regenerative, normochromic, microcytic anemia with mild poikilocytosis, polychromasia, a few schistocytes and target cells
- a mild lymphopenia and an increased number of band neutrophils
- a slight elevation of total protein with a pronounced hypoalbuminemia
- a severe elevation of alkaline phosphatase and lipase.

Blood glucose levels were in the normal range

Moderate to severe chronic diffuse hyperplastic superficial lymphocytic and plasmacytic dermatitis with

- marked parakeratotic hyperkeratosis,
- severe superficial intra- and intercellular epidermal edema and multifocal vesicles,
- epidermal microabscesses, erosions and ulcers and serocellular crusts,
- multifocal folliculitis and furunculosis.

Diagnoses. 1. Haired skin: Dermatitis, subacute, diffuse, moderate, with marked parakeratotic hyperkeratosis, acanthosis and intraepidermal edema, mixed breed, canine. 2. Haired skin: Epidermitis, suppurative, multifocal, moderate, with gram-positive cocci.

Contributor's Comment and Conference Note. Severe pronounced intra- and

intercellular edema in the upper levels of the epidermis (stratum malpighii, granulosum) associated with pronounced parakeratotic hyperkeratosis are typical histological changes seen in necrolytic migratory erythema (NME) in man. This disease is considered a paraneoplastic dermatosis observed with hyperglucagonemia due to pancreatic alpha-cell tumors. Cases of NME not associated with pancreatic tumors have also been described with hepatic cirrhosis, chronic pancreatitis or intestinal disorders with malabsorption syndrome.

Typical distribution of the skin lesions is face, involving lips and periorbital area; distal extremities; genital area; perineum and lower abdomen. Often the skin lesions tend to precede the determination of the tumor.

A few cases in dogs with skin lesions consistent with NME have been reported with coexistent diabetes mellitus (described as an ulcerative dermatosis associated with diabetes mellitus) and coexistent with hepatic cirrhosis (described as hepatocutaneous syndrome). Although in some of these cases slightly elevated plasma glucagon levels could be measured, none of these dogs showed any evidence of a pancreatic tumor. However, all dogs presented with pronounced hepatic cirrhosis which led to the name hepatocutaneous syndrome. This 10-year-old dog showed a severe micronodular hepatic cirrhosis at necropsy.

Elevation of plasma glucagon levels are described in connection with chronic liver changes due to reduced metabolism of glucagon - particularly of its biologically active fraction (3,500 dalton) - by the injured liver tissue.

The precise pathogenesis of NME and its direct connection with a hyperglucagonemia is still not known. The suspected cause of the skin lesions is the consistently present hypoalbuminemia and hypoaminoacidemia.

Increased concentration of total serum protein in the present case was due to an increase in serum globulins, which was probably in response to the secondary bacterial infection (microbiology result: Staph. intermedius).

Important clinical differential diagnoses are: pemphigus foliaceous, lupus erythematosus, zinc-responsive dermatosis, generic dog-food disease, erythema multiforme, essential fatty acid deficiency.

Conference participants agreed the histomorphological lesions and clinical history are consistent with those described for necrolytic migratory erythema (hepatocutaneous syndrome).

Contributor. Department of Pathology, Cornell University, New York State College of Veterinary Medicine, Ithaca, NY 14853-6401.

Suggested reading.

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2. Doyle JA, Schroeter AL, Rogers III RS: Hyperglucagoaemia and necrolytic migratory erythema in cirrhosis possible pseudoglucagonoma syndrome. Br. J. Dermatol. 100: 581587, 1979.

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Slide 109 (AFIP 2288674)

History. These tissues are from a 1.5-year-old male Siamese cat and a 5-year-old spayed female mixbreed dog. Both animals presented with a deep dermal/subcutaneous well-circumscribed mass which was firm and nonpainful. Both had been previously vaccinated (approx. 1 month) in the area where the mass subsequently developed.

Gross Pathology. There was a tan/white well-defined, but not encapsulated mass in the deep dermis and panniculus.

Diagnosis. Subcutis (per contributor): Panniculitis, necrotizing and granulomatous, focal, severe, with lymphoid follicle formation and intralesional foreign material, mixed breed, canine (Siamese, feline).

Contributor's Comment and Conference Note. Injection site reactions are not well described in the veterinary literature. During the rabies epizootic of 1988-90 in Pennsylvania, increased numbers of injection site reactions were seen in cats and dogs vaccinated in the subcutis with rabies vaccine. The histologic appearance of those lesions was essentially identical to those presented here. There is central necrosis, surrounded by variable numbers of macrophages, lymphocytes, plasma cells, and eosinophils. Often, there is the formation of peripheral lymphoid follicles. Globular material, which is interpreted to be vaccine or carrier, is usually found in the center of the lesion, free, or within macrophage cytoplasm.

The low magnification view of this lesion is reminiscent of a lymph node with central necrosis and inflammation, and thus may lead to a misdiagnosis of necrotizing lymphadenitis.

Although the majority of injection site reactions at our institution have been associated with rabies vaccine, we have seen this sort of reaction secondary to other vaccines.

Conference participants agreed the histomorphological lesions and clinical history are consistent with those described in the literature for injection site necrotizing and granulomatous panniculitis.

Contributor. Laboratory of Pathology, School of Veterinary Medicine, University of Pennsylvania, 3800 Spruce Street, Philadelphia, PA 19104.

Suggested reading.

1. Hendrick M, Dunagan C: Focal necrotizing granulomatous panniculitis associated with subcutaneous injection of rabies vaccine (a review of 10 cases). J. Am. Vet. Med. Assoc. 198: 304-305, 1991.

2. Wilcock BP, Yager JA: Focal cutaneous vasculitis and alopecia at sites of rabies vaccination in dogs. J. Am. Vet. Med. Assoc. 188: 1174-1177, 1986.

Slide 110 (AFIP 2218359)

History. This 6-year-old neutered female Jack Russell terrier was initially presented with pruritic scaly collarettes on lateral thorax which had been noticed about 10 months previously. The lesions were unresponsive to topical and parenteral antibiotics and steroids and did not regress once formed. A pinch biopsy showed sparse histiocytic lymphocytic infiltration of basal epidermis. Three months later the dog was presented with multiple skin plaques over chest and sternum with paravulval nodule (approximately 0.7 cm diameter).

Gross Pathology. Multiple, slightly raised poorly-circumscribed plaques; some red but others pale and scaly. On gross section pale cream slight thickening of skin. Para-vulval tumor similar (0.75 cm diameter) with cream uniform appearance and poorly-defined borders.

Diagnosis. Haired skin: Lymphosarcoma, epitheliotropic, Jack Russell terrier, canine.

Contributor's Comment and Conference Note. Irregularly thickened skin plaques with hyperkeratotic surface and thickened epidermis with variable parakeratosis. There are focal hemorrhages beneath the epidermis at several sites. At the peripheral zones the epidermis is infiltrated by irregularly ovoid or more pleomorphic cells and at several sites there are clusters of similar cells within epidermal spaces constituting Pautrier-like foci. The central part of the lesion comprises dense aggregates of neoplastic cells, often with misshapen or indented nuclei and prominent nucleoli. The neoplastic cells extend deeply into the dermis and around hair follicles, obliterating adnexae. There is a sharp cut-off at the level of subcutaneous fat although a few deep blood vessels contain neoplastic cells.

This is interpreted as a cutaneous lymphoma resembling human mycosis fungoides.

Most human reports regard mycosis fungoides and Sezary syndrome as variants of cutaneous T cell lymphoma. Where the cutaneous lymphoma is accompanied by leukemia the condition is classified as Sezary syndrome. Mycosis fungoides is regarded as a T cell lymphoma arising in the skin and lymphoid tissue and is slowly progressive. In man, the T cell lineage of the tumor cells can be demonstrated by monoclonal antibody techniques but this is not as yet widely available for canines.

The presence of intracutaneous foci of tumor cells, Pautrier microabscesses and lymphocytic-histiocytic cells with bizarre nuclei, distinguish this from other cutaneous lymphomas.

This case was reviewed by the Department of Dermatopathology. The presence of lymphoid nests involving both the epidermis and hair follicles was felt to be suggestive of mycosis fungoides in human beings. Reported cases of mycosis fungoides in animals have been in middle-aged to older dogs and cats with no sex predilection. The three well-defined stages described in humans have not been documented in all animals as those affected have been presented for veterinary care in the plaque or tumor stages. Also, verification that it is actually a T-lymphocyte neoplasia has not been accomplished in all affected animals. Ultrastructurally, the abnormal T-lymphocytes are similar though distinguishable from histiocytes. Their nuclei have bizarre convolutions, and their cytoplasm contain a moderate amount of free glycogen, few mitochondria, and scanty endoplasmic reticulum. The differential diagnosis should include, in addition to other skin tumors, pagetoid reticulosis, pemphigus vulgaris, bullous pemphigoid, lupus erythematosus, and cutaneous inflammation.

Contributor. Department of Veterinary Pathology, R.(D).S.V.S., University of Edinburgh, Summerhall, Edinburgh EH9 IQH.

Suggested reading.

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716-724, 1978.
2. Zenoble RD, and George JW: Mycosis fungoides-like disease in a dog. J. Am. Anim. Hosp. Assoc. 16: 203-208, 1980.
3. Thrall MA, Macy DW, Snyder SP, and Hall RL: Cutaneous lymphosarcoma and leukemia in a dog resembling Sezary syndrome in man. Vet. Pathol. 21: 182-186, 1984.
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Slide 111, L22 (AFIP 2289155)

History. This male thoroughbred foal was born one month early and had breathing problems.

Gross Pathology and Laboratory Results. Both kidneys were enlarged and had severe perirenal edema. Cut sections revealed pale radiating streaks. The liver was yellow. The amniotic membrane was green due to fetal diarrhea.

Fetal serum had 1:102,400 titer for Leptospira pomona. Direct fluorescent antibody technique on the kidney and placenta was positive for Leptospira sp. Leptospira interrogan serogroup pomona serovar Kennewicki was isolated from the kidney.

Diagnosis. Kidney: Nephritis, pyogranulomatous, multifocal to coalescing, moderate, Thoroughbred, equine.

Contributor's Comment and Conference Note. Numerous spirochetes were demonstrated in the lumina of renal tubules by Warthin-Starry silver stain.

Conference participants agreed that the clinical history and the light microscopic lesions were consistent with a leptospiral nephritis. Silver stains confirmed the presence of tubular intraluminal and intraepithelial silver-positive bacteria with leptospiral morphology.

After infection with Leptospirosis sp., a bacteremia may follow with localization of the spirochetes in the kidneys, liver and pregnant uterus. In cattle, sheep and horses icterus is observed during the bacteremic phase. This is mainly due to intravascular hemolysis caused by a hemolysin. Later, the red cell hemolysis continues as an antibody mediated injury. Although renal injury may be severe, resultant mortality is uncommon except in dogs infected with L. canicola. Localization of leptospires in the pregnant uterus frequently results in abortion in

ruminants and swine.

Contributor. Livestock Disease Diagnostic Center, 1429 Newtown Pike, University of Kentucky, Lexington, KY 40511.

Suggested reading.

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Slide 112 (AFIP 2185693)

History. This is tissue from a 2-year-old, male Sprague-Dawley rat (Rattus) that had a distended abdomen and an enlarged scrotum.

Gross Pathology. The abdomen contained 350 ml of clear red fluid that did not clot within the abdominal cavity. The serosal surface of the liver, kidney, urinary bladder, and epididymis were covered by red to gray, firm, friable, finely-granular masses.

Diagnosis. Testicle, epididymis: Mesothelioma, Sprague-Dawley rat, rodent.

Contributor's Comment and Conference Note. The visceral and parietal vaginal tunic has a focally invasive, well-demarcated, non-encapsulated mass. The mass is arranged into solid papillary structures that are supported by dense

fibrovascular stroma. Papillae are covered by cuboidal to polyhedral cells that have large vesicular nuclei and prominent nucleoli. The cells have a moderate amount of cytoplasm and indiscrete cell borders. Sometimes the cells form rosettes on the serosal surface. The mass is focally necrotic and has a patchy inflammatory cell infiltrate composed of lymphocytes, neutrophils, macrophages, and mast cells. Mitoses range from 1 to 3 per high-power field.

Mesotheliomas are rare in all species. The overall incidence of this tumor at MSDRL is 0.02 percent (12/76,308).

Spontaneous mesotheliomas have been reported in the rat and are most commonly associated with the peritoneal cavity. Asbestos can induce this tumor in experimental animals.

Mesotheliomas must be differentiated from chronic proliferative inflammation and metastatic carcinoma from other organs.

Conference participants agreed that the histomorphological features of the neoplasm were consistent with mesothelioma. Of the various currently recognized patterns, fibrous, adenoid and papillary, this case most resembled a papillary mesothelioma. They have been induced with a high incidence in chickens with avian leukosis virus (1). In calves, they are found commonly as a congenital tumor (2). Occasionally they occur in older cattle. The neoplasm has also been reported in the dog, cat, horse and pig. There is no breed or sex prevalence in any species (2).

In humans, mesothelioma has long been associated with asbestos exposure, where it is probably a cocarcinogen with other factors such as cigarette smoke. An association between asbestos and mesotheliomas has not been convincingly demonstrated in animals.

Contributor. Merck Sharp & Dohme, Department of Safety Assessment, West Point, PA 19486.

Suggested reading.

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Slide 113, L23, L24 (AFIP 2075745)

History. Queen gave birth to three kittens on Monday and three more the following Wednesday. All three kittens born on Wednesday died. Prior to death, owner noticed abdominal distension and the kittens cried as if in pain. On clinical examination, there were colic type symptoms and the kittens cried extensively. A postmortem examination was performed on one kitten shortly after death and formalin fixed heart and liver were submitted to TVMDL.

Gross Pathology. Lesions were limited to the heart and liver. The pericardial sac contained 3 ml of yellow gelatinous fluid. The myocardium was mottled. The liver was mottled but not reported to be enlarged.

Diagnosis. Heart, myocardium: Myocarditis, necrotizing, subacute, multifocal, moderate, with protozoal zoites, Manx, feline.

Contributor's Comment and Conference Note. Additional lesions in this kitten consisted of a severe necrotizing hepatitis with organisms consistent with Toxoplasma gondii. It is of interest that a litter mate of this kitten died at 10 weeks of age with predominantly respiratory symptoms. Heart, lung, and liver were submitted from this older kitten and lesions consistent with toxoplasmosis were observed in all tissues. Although congenital infection has been suspected in kittens based largely on epidemiological findings, this was not documented in experimental transmission studies (1). In this report, transmission via the queen's milk or salivary secretions was deemed a possibility.

Conference participants agreed that the multifocal areas of myocardial necrosis were attributable to the presence of protozoal zoites. Although a definitive diagnosis would require a positive peroxidase-antiperoxidase test using antibodies to Toxoplasma gondii, the ultrastructural morphology of the organisms is consistent with that described for T. gondii (J.P. Dubey, personal communication).

Contributor. Texas Veterinary Medical Diagnostic Lab., P.O. Box 3200, Amarillo, TX 79116-3200.

Suggested reading.

1. Migaki G, et al: Toxoplasmosis in a California sea lion (Zalophus californianus). Am. J. Vet. Res. 38(1): 135-136, 1977.

2. Dubey JP, Hoover EA: Attempted transmission of Toxoplasma gondii infection from pregnant cats to their kittens. J. Am. Vet. Med. Assoc. 170: 538-540, 1977.

3. Nichols BA, O'Conner GR: Penetration of mouse peritoneal macrophages by the protozoon Toxoplasma gondii. Lab. Invest. 44: 324-335, 1981.

4. Parker GA, Langloss JM, Dubey JP, Hoover EA: Pathogenesis of acute toxoplasmosis in specific-pathogen-free cats. Vet. Pathol. 18: 786-803, 1981.

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8. Dubey JP, and Thulliez: Serologic diagnosis of toxoplasmosis in cats fed Toxoplasma gondii tissue cysts. J. Am. Vet. Med. Assoc. 194(9): 1297-1299, 1989.

9. Frenkel JK: Toxoplasmosis in human beings. J. Am. Vet. Med. Assoc. 196(2): 240-248, 1989.

10. Pratt PW (ed.): Feline Medicine, 1st Ed., Am. Vet. Public., Inc., pp. 133-137, 1983.

11. Stalheim OHV, et al: Update on bovine toxoplasmosis and sarcocystis, with emphasis on their role in bovine abortions. J. Am. Vet. Med. Assoc. 176(4): 299-302, 1980.

12. Werk R: How does Toxoplasma gondii enter host cells? Review Infectious Diseases 7(4): 499-457, 1985.

13. Dubey JP, Carpenter JL, Spear CA, Topper MJ, and Uggia A: Newly recognized fatal protozoan disease of dogs. J. Am. Vet. Med. Assoc. 192(9): 1269-1285, 1988.

14. Dressen DW: Toxoplasma gondii infections in wildlife. J. Am. Vet. Med. Assoc. 196(2): 274-276, 1989.

15. Dubey JP, Hattal AL, Lindsay DS, and Topper MJ: Neonatal neosporum caninum infection in dogs: isolation of the causative agent and experimental infection. J. Am. Vet. Med. Assoc. 193(10): 1259-1263, 1988.

16. Mills J: Pneumocystis carinii and Toxoplasma gondii infections in patients with AIDS. Review Infectious Diseases. 8(6): 18001-1011, 1896.

Slide 114 (AFIP 2289149)

History. This 26-year-old gelding pony was presented to the local veterinarian for clinical signs of acute neurologic disease, characterized by head pressing, and circling to the left. The pony had been given an anthelmintic two days before onset of clinical signs. The pony was later euthanatized and presented for necropsy.

Gross Pathology. No significant lesions were evident on gross postmortem examination.

Diagnosis. Brain, meninges and cerebrum: Meningoencephalitis, multifocal, mild, breed unspecified, equine.

Contributor's Comment and Conference Note. Various sections of the brain were submitted. Moderate to moderately severe leptomeningeal and perivascular accumulations of lymphocytes, plasma cells, eosinophils, and macrophages were evident. Variable numbers of elongated, slender, basophilic parasitic organisms were found within many of the inflammatory foci. The organisms measured approximately 290 um X 11 um in size, and contained elongated uteri, many of which contained eggs.

Nematodes of the genus Halicephalobus have been considered saprophytic and found in decaying humus. Recently, this nematode has been considered a facultative parasite in humans and horses. Tissues most commonly affected in the horse include brain, kidney, oral/nasal tissue, lymph nodes, lung, spinal cord, and adrenal gland. Heart, liver, stomach, ganglion, and bone have also been reported to be affected in the horse.

It was interesting to note that the pony in this case had been treated with an anthelmintic two days before onset of clinical signs. Parasite death induced by the anthelmintic may have caused an increase in the inflammatory

response to the nematodes.

The morphologic characteristics of the perivascular nematodes were consistent with those described for Halicephalobus deletrix. Recently a similar nematode parasite has been described in a case of verminous mastitis in a Paso Firo mare (12). The nematode was identified as a member of the genus Cephalobus, family Cephalobidae. Morphologically the Cephalobus species was described as having a blunt posterior end in tissue sections, whereas Halicephalobus deletrix is described as having a pointed posterior end. This report suggests that not all histiotropic infections of horses by rhabditoid nematodes are caused by Halicephalobus deletrix.

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

Suggested reading.

1. Spalding MG, Greiner EC, Green SL: Halicephalobus (Micronema) deletrix infection in two half-sibling foals. J. Am. Vet. Med. Assoc. 196: 1127-1129, 1990.

2. Cho DY, Hubbard RM, McCoy DJ, Stewart TB: Micronema granuloma in the gingiva of a horse. J. Am. Vet. Med. Assoc. 187: 505-507, 1985.

3. Binford CH, et al: Pathology of Tropical and Extraordinary Diseases, Vol. 2. pp 468-470, 1976.

4. Chitwood M: Identification of parasitic metazoa in tissue section. Exp. Parasit. 32: 407-519, 1972.

5. Ferris DH, et al: Micronema deletrix in equine brain. Am. J. Vet. Res. 33: 33-38, 1972.

6. Frauenfelden HC, et al: Cerbrospinal nematodiasis caused by a filariid in a horse. J. Am. Vet. Med. Assoc. 177: 359-362, 1980.

7. Jubb and Kennedy. Pathology of Domestic Animals, 3rd ed, vol 1. pp 311-313, 1985.

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9. Powers RD, et al: Micronema deletrix in the central nervous system of a horse. J. Am. Vet. Med. Assoc. 170: 175-177, 1977.

10. Rubin HL, et al: Equine infection with Micronema deletrix. J. Am. Vet. Med. Assoc. 165: 256-258, 1974.

11. Thompson RG: Special Veterinary Pathology. BC Decker Inc. pp 552-553, 1988. Originals by L. McKinney (1984)) and T. Lipscomb (1987).

12. Greiner EC, et al: Verminous mastitis in a mare caused by a free-living nematode. J . Parasitol. 77: 320-327, 1991.

Slide 115, L25 (AFIP 2288076)

History. This 4-year-old Dorset ewe was an NIH flock member for her entire adult life and was group housed in an outdoor pen. She had chronic epiphora of the left eye, and recently was noticed to have difficulty breathing. Nasal polyps were

noted on a clinical examination and a biopsy was submitted. Later, the sheep was euthanatized and her head submitted for necropsy.

Gross Pathology. The left caudal nasal cavity is completely filled by a soft, tan and white, verrucous mass which has enveloped nasoturbinates. The caudal nasal septum is distorted and deviates to the right. The mass extends into the left frontal sinus, right nasal cavity, right frontal sinuses, and nasal pharynx. The right retropharyngeal lymph node is mildly enlarged.

Diagnosis. Nasal turbinate (per contributor): Adenocarcinoma, tubulopapillary, Dorset, ovine.

Contributor's Comment and Conference Note. The NIH Animal Center in Poolesville, Maryland, houses nearly 350 adult Dorset sheep which are received as young adults from a contract farm in Virginia. Nasal neoplasms in our flock are not common but do occur regularly at a low frequency - every year, one or two cases are recognized clinically; however, complete necropsies with examination of the nasal cavity are very rarely performed, so the true incidence is unknown. In this ewe, no metastases were present in the retropharyngeal lymph nodes, and no viral particles were found with electron microscopy.

Conference participants agreed the histomorphological features of the mass were consistent with those described for nasal adenocarcinoma.

Adenocarcinoma is the most common type of nasal epithelial tumor in sheep. An as yet unproven infectious etiology has been suspected due to the epizootiologic pattern of occurrence. The neoplasms in sheep have been reported from North and South America, Europe, Japan and Africa. In cattle, undifferentiated carcinoma, adenocarcinoma and squamous cell carcinomas have been reported in the nasal sinuses. The cells of origin are most likely from Bowman's gland and other epithelia in the olfactory mucosa of the ethinoturbinate bone.

Contributor. National Institutes of Health, Comparative Pathology 28A/111, 9000 Rockville Pike, Bethesda, MD 20892.

Suggested reading.

1. Duncan JR, Tyler DE, Van Der Maaten MJ, and Anderson JR: Enzootic nasal adenocarcinoma in sheep. J. Am. Vet. Med. Assoc. 151(6): 732-734, 1967.

2. McConnell EE, van Rensburg IBJ, and van Wyk JA: A case of adenocarcinoma of the olfactory mucosa in a sheep of possible infectious origin. J. S. Afr. Vet. Med. Assoc. 41(1): 9-12, 1970.

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5. Yonemichi H, Ohgi T, Fujimoto Y, et al: Intranasal tumor of the ethmoid

olfactory mucosa in sheep. Am. J. Vet. Res. 39(10): 1599-1606, 1978.

Slide 116 (AFIP 2291782)

History. Starting from the first to second day of life this 3-day-old "Weisses Alpenschaf" lamb developed blisters at the nostrils and at the coronary bands of several claws followed by exungulation. Several cases were observed in this particular flock of sheep within the last two years. The affected lambs had to be euthanatized because of loss of claws and because of inappetence and weight loss.

Gross Pathology and Laboratory Results. Blisters which were partly blood filled as well as erosions were seen at the nose, lips, oral mucosa, surface of the tongue, oesophagus, coronary bands, scrotum, skin (ear, inguinal region).

Hematology and clinical chemistry normal.

Bacteriology: negative.

Virology: negative (electron microscopy).

Immunohistology: no immune complex deposits.

Diagnoses. 1. Tongue: Glossitis, ulcerative, subacute, multifocal, moderate, with subepidermal cleft, "Weisses Alpenschaf", breed, ovine. 2. Mucocutaneous junction: Chylitis, acute, focally extensive, moderate, with subepidermal cleft.

Contributor's Comment and Conference Note. This is an inherited disease with probably autosomal recessive inheritance. Epidermolysis bullosa is a mechanobullous disease occurring in humans, calves, dogs and sheep. The dystrophic type is characterized by subepidermal cleft formation, the basement membrane being at the roof of the blister, and by scarring. In humans with E. bullosa there seems to be an underlying defect of collagen type VII, the major structural protein of the anchoring fibrils. Our data suggest the disease in sheep might have the same biochemical characteristics (absence or defect of collagen VII, reduction of anchoring fibrils).

The natural incidence of E. bullosa in sheep of this breed is very low. By inbreeding experiments the contributor was able to reproduce the disease.

Epidermolysis is a lesion common to a group of inherited diseases whose common feature is the formation of bullous lesions following minor trauma. In dogs, it is commonly reported in collies, shelties and occasionally their crossbreeds and is similar to epidermolysis bullosa simplex in humans. Cutaneous lesions usually develop prior to 6 months of age. Well developed vesicles or bullae typically do not form in this thin canine skin. The microscopic lesion is a subepidermal vesicular dermatitis secondary to hydropic degeneration of basal keratinocytes. The floor of the vesicle is formed by an intact PAS positive basement membrane. The lesion is similar to that of lupus erythematosus but lacks a lichenoid component. In the dog, the differential diagnosis would include bacterial folliculitis-furunculosis, dermatophytosis, demodecosis, atopy, pemphigus foliaceous and erythematosus, and zinc responsive dermatitis.

Suffolk and South Dorset Down breeds of sheep are frequently affected.

The condition resembles both the dominant and recessive forms of dystrophic epidermolysis bullosa of humans in that the subepidermal cleft forms beneath the basement zone. Unlike dogs, sheep develop lesions in the oral cavity. Lesions also develop at the coronary bands. The disease is fatal.

Contributor. Institut für Veterinärpathologie, University of Zürich, Winterthurerstr. 268 CH-8057 Zürich.

Suggested reading.

1. Ehrensperger F, Hauser B, and Wild P: Epidermolysis bullosa in sheep. Tierarztl. Umschau 42(9): 697-700, 1987.

2. Bruckner-Tuderman L, Rüegger S, Odermatt B, Mitsuhashi Y, Schnyder UW: Lack of type VII collagen in unaffected skin of patients with severe recessive dystrophic epidermolysis bullosa. Dermatologica 176: 57-64, 1988.

Slide 117 (AFIP 2291784)

History. This 6-year-old Holstein-Fresian cow had a history of progressive depression and anorexia over 1 week when it was presented to the clinician. An acute mastitis was diagnosed in one quarter and treated with several antibiotics. Since the cow did not respond to this treatment it was slaughtered one week later.

Gross Pathology and Laboratory Results. The parenchyma of the affected quarter was markedly swollen and indurated. It was of reddish color and had many necrotic areas with a diameter of 1-2 mm.

Nocardia asteroides could be isolated from the affected tissue.

Diagnosis. Mammary gland: Mastitis, granulomatous and necrotizing, diffuse, moderate, Holstein-Fresian breed, bovine.

Contributor's Comment and Conference Note. Although Nocardia is a known cause of mastitis in cattle, we rarely see mastitis from nocardial infection and usually only a single animal is affected within a herd. This animal, however, is 1 of 7 cows submitted within a single year. All 7 cows developed an acute mastitis shortly after parturition and were treated parenterally as well as intramammarily with various antibiotics for several days. There was always a marked swelling and induration, the cows did not respond to therapy and lost weight. Within 14 days of the onset of the disease all cows were euthanatized and submitted for necropsy. An etiological diagnosis of Nocardia mastitis was based on the histological appearance - granulomatous to necrotizing mastitis with gram-positive, slender, branching bacteria on Brown-Brenn stained sections - and confirmed culturally.

Conference participants agreed the clinical history and histomorphologic light microscopic features were consistent with a Nocardial asteroides mastitis. Special stains confirmed the presence of numerous gram-positive, PAS-positive, silver positive and acid fast negative branching filamentous organisms associated with the lesions.

Nocardiosis in the cow can cause an iatrogenically induced granulomatous mastitis resulting from introducing the organism through the teat canal during mastitis treatment. It may also occur spontaneously, the organisms originating from the soil. The disease is characterized by discharging sinuses from the mammary gland through the skin. Cryptococcal mastitis, caused by Cryptococcus neoformans may have the same yellow gelatinous material. Other causes of bovine granulomatous mastitis include Mycobacterium sp. and Candida sp.

Contributor. Institute of Veterinary Pathology, Winterthurerstr. 260, 8057 Zurich, Switzerland.

Suggested reading.

Sears PM: Nocardial mastitis in cattle: Diagnosis, treatment, and prevention. Comp. Cont. Educ. 8: F41-F45, 1986.

Slide 118, L26 (AFIP 2286502)

History. This 36-hour-old female llama (Llama glama) was presented at 6 hours of age with a congenital tibial fracture. Therapy consisted of external fracture fixation, plasma, antibiotics and an enema. During hospitalization the animal did not urinate or defecate. Clinical signs prior to death included abdominal distension and respiratory distress.

Gross Pathology and Laboratory Results. Necropsy revealed moderate ascites. Petechial, ecchymotic and paint brush serosal hemorrhages covered the stomach wall which also was crepitant on palpation. The gastric mucosa (all 3 compartments) was hyperemic and petechiated with adherent blood clots. The cut surface of the gastric wall was emphysematous. The duodenum was distended with fluid and gas, and ecchymotic mucosal hemorrhages were seen. The small intestine was twisted on the mesenteric root. The jejunum was dark red and distended with gas. The spiral colon had a similar appearance. The lungs had a diffuse patchy pattern of consolidation.

Microbiology-Clostridium perfringens, in significant numbers, was cultured from the stomach and spiral colon. No significant anaerobic growth was obtained from the jejunum. Clostridial FA evaluation of stomach was negative for C. chauvoei, C. novyi and C. septicum.

Diagnosis. Stomach: Gastritis, hemorrhagic and emphysematous, acute, diffuse, moderate, Llama (Llama glama), camelid.

Contributor's Comment and Conference Note. The gastric mucosa has variably sized intraepithelial bullae, some contain degenerating keratinocytes and neutrophils, while others are empty or distended by serum proteins. Some necrosis is evident. The submucosa has a honeycomb pattern consistent with emphysema. Hemorrhages are seen in all layers of the stomach wall.

Clostridia are believed to have caused these lesions since time between death

and necropsy was less than 2 hrs, a heavy growth of C. perfringens was obtained from the stomach but not from the jejunum and gastric emphysema was severe enough to float stomach sections in formalin.

Since this case, another neonatal llama (40 hrs. old) with clostridial gastritis has been seen. This llama had severe mural gastric hemorrhages and a fibrinonecrotic gastric mucosa with emphysema. The small intestine and spiral colon were purple and filled with bloody contents. A mixed population of Clostridia sp, including a 4 + growth of C. perfringens, were grown from the stomach mucosa. Necropsy was done within 1 hour of death.

Conference participants agreed the clinical history and histomorphologic light microscopic lesions were consistent with those described for hemorrhagic and emphysematous gastritis in llamas.

Also discussed were the unique anatomic features of the family Camelidae (camels, Guanoco, Llama, Alpaca, Vicoruna). The stomach is three chambered and ruminating. Camelidae differ from all other mammals by having oval instead of circular red blood corpuscles. Members of the Camelus and Llama run with a swinging stride, as both genera front and hind legs move in unison on each side of the body. They eat primarily grasses, though camels when hungry, will eat a wide variety of food. They have a habit of spitting stomach contents at annoying objects, including zoo visitors.

Contributor. Department of Veterinary Pathology, College of Veterinary Medicine, University of Minnesota, St. Paul, MN 55108.

Suggested reading.

1. Fowler ME: Medicine and Surgery of South American Camelids, 1st Edition, Iowa State University Press, Ames, Iowa, 1989, pp 118-120.

2. Ellis RP, et al: An overview of Clostridium perfringens type A Enterotoxemia in Alpacas and Llamas. American Association of Small Ruminant Practitioners, Symposium on Diseases of Small Ruminants, Corvallis, Oregon, 1990, pp 2-3.

Slide 119 (AFIP 2285556)

History. This male, 108-week-old B6C3F1 mouse is from a 2-year carcinogenesis bioassay.

Gross Pathology. Liver, right lateral lobe. Irregularly shaped, 25x23x14 mm, yellow-brown mass.

Diagnosis. Liver: Hepatocellular carcinoma, B6C3F1 mouse, rodent.

Contributor's Comment and Conference Note. This case is a typical example of the hepatocellular carcinomas commonly seen as incidental lesions in aging mice. The section is from an irregularly-shaped, 25 x 23 x 14 mm, firm, yellow-brown liver mass. This mass is comprised of closely packed, indistinct lobules of neoplastic cells

arranged in sheets and multicell-layered acinar-like structures and trabeculae. The acinar-like structures often have prominent clear lumina while the trabeculae are often separated by endothelium-lined blood-filled channels. The neoplastic cells are quite pleomorphic. In some areas, cells are small with scant basophilic cytoplasm and hyperchromatic to vesicular oval nuclei. In other areas, cells are large, polygonal to oval and contain abundant eosinophilic cytoplasm with or without vacuolization and basophilic stippling. Nuclei are often very large, vesicular and may exhibit bizarre outlines and/or cytoplasmic pseudo-inclusions. Binucleate and multinucleate cells are rare, but mitotic figures are common in some areas. There are small foci of coagulative necrosis and single cell necrosis scattered throughout as well as a large central area of infarction with cavitation. Not all these histologic features are evident in every slide.

Conference participants agreed the histomorphologic characteristics were consistent with a hepatocellular carcinoma. This case was reviewed by both the Department of Veterinary Pathology and the Department of Hepatic Pathology.

Contributor. National Institute of Environmental Health Sciences/National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

Suggested reading.

1. Frith CH, Ward JM: Color Atlas of Neoplastic and Non-Neoplastic Lesions in Aging Mice, pp. 12-13, Elsevier, Amsterdam, 1988

2. Maronpot RR, Haseman JK, Boorman GA, et al: Liver lesions in B6C3Fl mice: The National Toxicology Program, experience and position. Arch. Toxicol. Suppl. 10: 10-26, 1987.

3. Turusov VI, Takayama S: Tumours of the liver. In: Pathology of Tumours in Laboratory Animals, Vol. II, The Mouse, (ed) VI Turusov, pp. 193-271, IARC, Lyon, France, 1979.

Slide 120 (AFIP 2293544)

History. This 1-year-old male Syrian hamster died during a chronic study.

Gross Pathology. As an incidental finding, a clear, straw-colored, fluid-filled and raised cyst measuring about 7 mm in diameter was found in the left lobe of the liver.

Diagnosis. Liver: Cestode larva, with fibrous encapsulation and chronic inflammation, Syrian hamster (Mesocricetus auratus), rodent.

Contributor's Comment and Conference Note. Syrian hamsters were obtained from an outside supplier and used in a chronic study. Presence of a single clear cyst was found in the liver of about 10% of the animals (from control and treated groups). Upon excision, a tapeworm (10-20 cm long) everted from the lumen. Microscopically, the metazoan parasite was characterized by the absence of body cavity and digestive tract and by the presence of numerous calcareous corpuscles, a

thick layered cuticle with a basement membrane and evidence of body segmentation. These histological features lead us to the identification of a Strobilocercus larvae (Cestodes).[2-4] Specific identification by Dr. Marion Georgi of Cornell University (U.S.A.) on formol fixed tissue of an intact specimen revealed the presence of a strobilocercus (sometimes called Cysticercus fasciolaris) of Taenia taeniaeformis (synonym: Hydatigera taeniaeformis), adult tapeworm of cat. The parasite was encysted in an about 100 micron thick fibrous capsule which compressed the surrounding hepatic parenchyma. Rare mixed inflammatory cells were present in this capsule and, focally, one or two rows of macrophages lined the cystic cavity. Foci of lymphocytes, plasma cells and hemosiderin laden macrophages were also noted at the periphery of the capsule.

Rodents are intermediate hosts of Taenia taeniaeformis and infestation of rat or mouse colonies are well documented; however, hepatic cyst containing the strobilocercus of this parasite has been reported only once in hamsters.[1] Host connective tissue capsules can give rise to sarcoma.[6] The origin of this infestation was not determined. However, as this metacestode doesn't occur in our colony of rats or mice, infestation of these hamsters was considered to have occurred prior to arrival at our facility.

Conference participants agreed that the light microscopic appearance of the intrahepatic metazoon parasite was consistent with a cestode strobilocercus.

Cestodes are characterized by a body filled with parenchyma and lacking an intestinal tract. Calcareous corpuscles (mineralized spherules that are usually similar in size) are present in all cestodes. All cestodes are bisexual. Larva vary in form and may be cystic or solid.

Contributor. Laboratories PFIZER - Centre de Recherche, BP 159, 37401 Amboise Cedex (France).

Suggested reading.

1. Bunte RM: Diseases of hamsters. POLA - 1988 - US Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD 21701-5011.

2. Chitwood M, Lichtenfels JR: Identification of parasitic metazoa in tissue sections. Experiment. Parasitol. 32: 407-519, 1972.

3. Davis JA, Donkaewbua S, Wagner JE, White RG: Cysticercus fasciolaris infection in a breeding colony of mice. Lab. Anim. Sci. 39: 250-252, 1989.

4. Georgi ME, Georgi JR: Histopathological diagnosis. In: Parasitology for Veterinarians. Georgi JR, W.B. Saunders Company, 4th edition, Philadelphia, Chapt. 14, 1985, pp. 301-330.

5. Kohn FD, Barthold SW: Biology and diseases of rats. In: Laboratory Animals Medicine. Eds. JG Fox, BJ Cohen & FM Loew. Academic Press Inc., Orlando, Chapt. 4, 1984, pp. 91-122.

6. Tucek PC, Woodward JC, Moreland AF: Fibrosarcoma associated with Cysticercus fasciolaris. Lab. Anim. Sci. 23: 401-407, 1973.

Slide 121 (AFIP 2236853)

History. This tissue is from an aging Skh: hairless (Skh-l) mouse which served as a control animal in a dermatotoxicology study.

Gross Pathology. Alopecia universalis.

Diagnoses. 1. Skin, hair follicles and sebaceous glands: Ectasia and dilatation, diffuse, moderate, Skh-l mouse, rodent. 2. Skin: Dermatitis, granulomatous, multifocal, mild.

Contributor's Comment and Conference Note. Marked cystic dilatation of pilosebaceous units is a spontaneous aging change in Skh: hairless mice. Rupture of cystic follicles with the release of highly irritating sebum and keratin into the dermis is associated with granulomatous inflammation of the skin.

Conference participants agreed that the clinical history and histomorphologic changes observed microscopically were consistent with those described for aging Skh-l hairless mice. These cysts reportedly form from remnants of the external root sheath after the first pilage is shed. In 20 to 30 week animals, the cysts are large, usually in a double row, often with fat cells interspersed. As the animals age, the cysts get larger with thin walls that often rupture, provoking a granulomatous reaction containing lymphocytes, macrophages, mast cells and polymorphonuclear leukocytes. Despite extension of cyst contents into the dermis, the inflammatory response is usually mild even in 1-year-old mice.

Contributor. Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, OH 45239.

Suggested reading.

Kligman LH, Akin FJ, and Kligman AM: Prevention of ultraviolet damage to the dermis of hairless mice by sunscreens. J. Invest. Derm. 78: 181-189, 1982.

Slide 122 (AFIP 2145835)

History. This tissue is from a 104-week-old, male, Sprague-Dawley rat that was a control animal in a carcinogenesis study.

Gross Pathology and Laboratory Results. The spleen and mandibular, cervical and mediastinal lymph nodes were enlarged. The liver was mottled, and the bone marrow was greenish-red and gelatinous.

Hematology	145441	Median Value
WBC (XI03/ul)	505	(10.4)
Abs. Neutrophils (XI03/ul)	498	(5.4)
Abs. Lymphocytes (XI03/ul)	15.2	(3.6)
Abs. Monocytes (X103/ul)	0	(1.2)
Abs. Eosinophils (X103/ul)	0	(0.1)

Diagnosis. Liver: Myeloid leukemia, Sprague-Dawley rat, rodent.

Contributor's Comment and Conference Note. Hepatic sinusoids are widened, hepatic cords are compressed, and lobular architecture is diffusely disrupted by a heterogeneous population of granulocytes which are tightly-packed into solid sheets. Individual cells have scant to moderate, amphophilic, granular cytoplasm, large round to segmented nuclei that have a diffuse chromatin pattern, and inconspicuous nucleoli. Mitoses are 0-6/hpf, averaging 3/hpf. There is mild to moderate centrilobular hemorrhage and edema. Centrilobular hepatocytes are intensely eosinophilic and have a finely vacuolated cytoplasm. Portal triads have mild to moderate biliary hyperplasia.

Peripheral blood smear best characterized the leukemic cells as metamelocytes and myelocytes; however, a few myeloblasts and promyelocytes were present. Neoplastic cells similar to those in the liver were also observed in the bone marrow, spleen, kidneys, lungs, and noted lymph nodes.

A relatively high natural incidence of hemopoietic tumors may be found in the following rat breeds: granulocytic leukemia occurs in WN rats over 18 months of age, mononuclear leukemia is present in aged Fischer rats, and acute stem cell leukemia is common in young Sprague-Dawley rats. The incidence of acute myeloid leukemia in aged, male, Sprague-Dawley rats at Merck Sharp & Dohme is low (historical control is 0.1 percent). Granulocytic leukemia can be induced experimentally by oral administration of N,N'-2,7,-fluorenylbisacetamide in rats.

This case was reviewed by both the Department of Veterinary Pathology and the Department of Hemolymphatic Pathology. Conference participants agreed the diffuse sinusoidal infiltrate was most consistent with a leukemic process. The tumor cells have a blastic appearance with prominent central nucleoli, many cells had an irregular nuclear shape suggestive of monocytoid differentiation supporting a myelomonocytic leukemia over a lymphoid neoplasm. Immunohistochemical stains for LCA, UCH-1 and L-26 were inconclusive. Many neoplastic cells stained positively with Leder stains.

The moderator added that in mice, marked hepatic extramedullary hematopoiesis is not uncommonly observed in association with inflammatory skin lesions and would have to be considered as a differential diagnosis in these animals. Several sections also contained a thrombus within a large vein.

Contributor. Merck Sharp & Dohme, Research Laboratories (WP44-1), West Point, PA 19486.

Suggested reading.

1. Brunning RD: Acute myeloid leukemias. The Hematopoietic System. 34th ACVP Meeting. pp. 135-140, 1983.

2. Benirschke K, Garner FM, and Jones TC: Pathology of Laboratory Animals. Vol. II, Springer-Verlag, New York, 1978, pp. 1117.

3. Takayama S, and Fujiwara M: Hematogenous development of rat mature granulocytic leukemia--distribution of leukemic foci in vertebral bodies. Acta. Pathol. Jpn. 28: 663-668, 1978.

Slide 123 (AFIP 2287591)

History. This 3-year-old, female, German Shepherd dog suffered diarrhea and weight loss for one month prior to euthanasia. During the last week it developed stationary nystagmus and hind limb paralysis.

Gross Pathology and Laboratory Results. There was discospondylitis of the T6-T7 vertebrae with necrotic debris extending into the spinal canal. The kidneys each had friable tissue in the renal pelvis with yellowish exudate. Multiple infarcts were visible in the spleen. Sublumbar lymph nodes were enlarged. A 1 cm diameter abscess was ventral to the sixth lumbar vertebra.

A pure culture of Aspergillus terreus was obtained from a sublumbar abscess.

Diagnosis. Vertebrae and intervertebral disc: Osteomyelitis, pyogranulomatous and necrotizing, diffuse, severe, with associated fungal hyphae, German Shepherd Dog, canine.

Contributor's Comment and Conference Note. Multisystemic disease due to Aspergillus terreus has been reported in dogs in Australia and the U.S.A. (2,3). Similar disease can also result from A. deflectus (1). This uncommon condition is seen predominantly in German Shepherds. Inflammation is suppurative to granulomatous and commonly involves kidneys, spleen, bone, intervertebral discs, heart, and bone marrow (3). Fungal invasion of vascular walls and thrombosis are also common findings. The dog in this case had all of these lesions as well as pyogranulomatous inflammation of sublumbar lymph nodes and liver. In the tissue provided, the organisms were most numerous in the necrotic marrow and in the disc. Most of the fungi were not visible on H&E stained slides, but were well demonstrated using a GMS stain. The organism did not stain with PAS.

The histomorphologic lesions were described by the conference participants. Uniform, irregular branching septate fungal hyphae with terminal and intercalated swellings or "spores" were visible with silver stains in areas of severe necrotizing pyogranulomatous osteomyelitis. Conference participants agreed these morphological characteristics are most consistent with Aspergillus terreus; however, definitive lateral spores were not evident. Pseudocellescheria boydii may have similar morphology and cannot be ruled out based on histomorphological appearance in tissue sections alone. Cultural studies or immunofluorescence would be required for a definitive diagnosis.

Contributor. Colorado State University, College of Veterinary Medicine and Biological Sciences, Department of Pathology, Fort Collins, CO 80523.

Suggested reading.

1. Jang SS, Dorr TE, Biberstein EL, Wong A: Aspergillus deflectus infection in four dogs. J. Med. Vet. Mycol. 24: 95104, 1986.

2. Kabay MJ, Robinson WF, Huxtable CRR, McAleer R: The pathology of disseminated Aspergillus terreus infection in dogs. Vet. Path. 22: 540-547, 1985.

3. Neer TM: Disseminated aspergillosis. Comp. Cont. Ed. 10: 465-471, 1988.

Slide 124 (AFIP 2288227)

History. This 10-year-old, mixed breed dog had a 3 to 4 month history of coughing. Radiographs revealed a mass in either the caudal mediastinum or caudal lung lobe. There was no evidence of metastases in other lung field regions.

Gross Pathology and Laboratory Results. At the time of surgical exploration, a 10 cm oval mass was found in the caudal lung lobe. It was pale yellow in color with dark brown colored areas. The mass was extremely firm and on cross section there were numerous necrotic areas.

The lobectomy sample was submitted for evaluation. Cytology aspirates suggested a papillary adenocarcinoma.

Diagnosis. Lung: Pneumonia, histiocytic, diffuse, severe, with cholesterol clefts, hemorrhage, bronchiolitis obliterans and type II pneumocyte hyperplasia and atypia, mixed breed, canine.

Contributor's Comment and Conference Note. Some portions of the lung were markedly atelectatic with peribronchiolar and interstitial smooth muscle hyperplasia, airway and alveolar collapse, mild alveolar hemorrhage and a marked alveolar histiocytosis with the foamy macrophages also containing intracytoplasmic hemosiderin. Other regions had alveolar dilatation with focally severe fibroplasia of the interstitium often enveloping cholesterol clefts. Within the regions of fibroplasia, within dilated alveoli, and extending from the bronchiolar epithelium were multiple polyp-like masses of obliterative bronchiolitis with the luminal exudate composed of foamy hemosiderin-tinted macrophages with interspersed cholesterol clefts. Some alveolar lumina contained stream-like mucin also containing foamy macrophages. In one region a large bronchiole was markedly dilated with luminal hemorrhage, cholesterol clefts and macrophages. Toward its more peripheral aspect the lumen became progressively obliterated with the exudate compressing and focally necrotizing the lining epithelium. Occasionally free within alveoli were clusters of atypical epithelial cells with variably-sized nuclei, occasional prominent nucleoli, and aberrant nucleus to cytoplasmic ratios. Mitoses were rarely seen in these cells. Also present in some interstitial regions were foci of intense neutrophilic inflammation. The pleura was thickened and had a somewhat polypoid appearance. A second portion of lung contained a papillary neoplasm (not submitted) which obliterated pulmonary architecture, and within which were foci of necrosis, distorted vasculature, cholesterol clefts, seroproteinaceous exudate, and accompanying macrophages and neutrophils. There was minimal atypia with the neoplastic cells arranged in papillary projections supported by scant collagenous cores. The cells appeared to have microvillous borders but no evidence of cilia. It was felt to be most consistent with a Clara cell or bronchiolar adenocarcinoma.

Endogenous lipid pneumonia is also termed "golden pneumonia" or "cholesterol pneumonia" and is usually seen distal to major airway obstruction. The accumulation of foamy macrophages is characteristic within alveolar spaces and occasionally the interstitium. As macrophages deteriorate they release cholesterol and other lipids resulting in the formation of cholesterol clefts which are the hallmarks

of an endogenous lipid pneumonia. The presence of clusters of tumor cells would support the pathogenesis of airway obstruction.

Most conference participants believed the histomorphological lesions were consistent with a diffuse histiocytic pneumonia with extensive bronchiolitis obliterans and cholesterol clefts. Several sections contained papillary clusters of atypical cells within alveoli that may represent metastatic foci of neoplastic cells; however a definitive diagnosis of Clara cell carcinoma was not possible based solely on the tissues submitted.

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

Suggested reading.

1. Katzenstein A-L A, Askin FB: Miscellaneous II. Nonspecific Inflammatory and Destructive Diseases. In: Surgical Pathology of Non-Neoplastic Lung Diseases. Vol 13, 2nd Edition, Major Problems in Pathology, Philadelphia, W.B. Saunders, 1990, pp. 540-545.

2. Dungworth DL: The Respiratory System. In: Jubb KVF, Kennedy PC, and Palmer N, Pathology of Domestic Animals, Third Edition, Academic Press, New York, 1985, pp. 472-473.

Slide 125 (AFIP 2287100)

History. This 4-year-old female spayed Dachshund was owned by an individual in the United States foreign service. She spent some time in Belgium and Tunisia. The dog became lethargic 4-5 months after moving from Tunisia to the United States. Six months after the lethargy signs began, she developed a truncal alopecia. A local veterinarian examined the dog which was found to have pale mucous membranes and a generalized alopecia with an ulcerative periorbital dermatitis. A skin biopsy was taken. Due to the biopsy results, as well as significant abnormalities on the urinalysis and chemistry profile, the animal was euthanatized.

Gross Pathology and Laboratory Results. Examination of the skin revealed a diffuse, mostly truncal seborrhea sicca with alopecia. Periorbital alopecia and erosions were seen bilaterally. Generalized lymphadenopathy, splenomegaly and focal acute enterocolitis were noted.

This dog had a hematocrit of 17% that proved to be a non-regenerative Coomb's positive anemia. She was also isothenuric, having a 4+ proteinuria with a urine protein/creatinine ratio of 23. Hypoalbuminemia (1.2 gm/dl) and hypergammaglobulinemia (8.2 gm/dl) were also noted.

Diagnoses. 1. Skin: Dermatitis, lymphoplasmacytic and histiocytic, multifocal, mild, with intrahistiocytic protozoal organisms, Dachshund, canine. 2. Lymph node (unknown site): Lymphadenitis, histiocytic, diffuse, mild, with plasmacytosis and intrahistiocytic protozoal organisms. 3. Kidney: Glomerulonephritis, membranous, global, diffuse, moderate. 4. Kidney: Nephritis,

interstitial, lymphoplasmacytic and histiocytic, multifocal, chronic, with intrahistiocytic protozoal organisms .

Contributor's Comment and Conference Note. Impression smears of the spleen, liver and lymph nodes revealed characteristic organisms also seen in the skin biopsy. Organisms were seen histologically in a wide variety of organs including skin, lymph nodes, kidney, spleen, liver, small and large intestines, skeletal muscle, meibomian glands, bone marrow and heart. Kupffer cell hyperplasia and myeloid hyperplasia of the bone marrow were marked in this case. In the vertebrate host, the parasite is in the amastigote stage, appearing round to oval, approximately 2-3 microns in diameter and containing a nucleus and a smaller kinetoplast. Leishmania are strict intracellular parasites found mostly in macrophages in which they multiply by binary fission. Heavily parasitized host cells rupture and fresh cells are then invaded.

Canids are thought to be a reservoir for various leishmanial species in Old World leishmaniasis. Visceral leishmaniasis produces similar lesions in humans and dogs. The patient exhibits macrophage hyperplasia, with chronic parasitism and secondary infections. In humans, while antibody is produced in large quantities, it is not protective and may even contribute to the pathogenesis of hemolytic anemia, glomerulonephritis or amyloidosis. The pattern of disease in humans and probably dogs is partly determined by the species of parasite, its tropism for skin or viscera, differences in immunogenicity and the host's cell-mediated immunity response.

Conference participants agreed the light microscopic appearance of the intrahistiocytic protozoal organisms was consistent with those described for Leishmania sp.

Of interest was the diffuse thickening of glomerular capillary walls and widening of mesangia which is consistent with a membranous glomerulonephritis.

Contributor. Division of Comparative Medicine, Department of Pathology, Johns Hopkins University, Baltimore, MD 21205.

Suggested reading.

1. Bryceson ADM: Leishmaniasis. In: Textbook of Medicine. Wyndaarden JB and Smith LH (eds). WB Saunders Co., Philadelphia, PA pp 1731-1739, 1982.

2. Elbihari S, et al: Leishmania infecting man and wild animals in Saudi Arabia. Canine cutaneous leishmaniasis in the Eastern Province. Transactions of the Royal Society of Tropical Medicine and Hygiene 81: 925-927, 1987.

3. Kirmse P, et al: Canine leishmaniasis in Morocco with special reference to infantile Kala-azar. Transactions of the Royal Society of Tropical Medicine and Hygiene 81: 212-213, 1987.

4. Muller GH, Kirk RW, Scott DW: Cutaneous parasitology. In: Small Animal Dermatology, 3rd edition, WB Saunders Co., Philadelphia, PA pp 301-304, 1983.

Slide 126 (AFIP 2296428)

History. European wild horse, male, adult of unknown age. It became

emaciated. Depression, anorexia, liquid stool with mucus were seen. The animal did not respond to the treatment for gastroenteritis.

Gross Pathology and Laboratory Results. Bloody liquid about 500 ml in the peritoneal cavity, adhesion of the stomach to the surrounding tissue infiltrated with solid masses of differentiation, a large mass was present in the cardia. The mass looked like a cauliflower, its surface was rough, dirty brown in color. Ulcers were seen in the mucous membrane. The consistency of the mass was firm, with a base connected to the stomach wall of 5 cm in thickness. There were blood clots near the mass. Hyperemic and hemorrhagic foci were seen in the fundus of stomach. There were also numerous masses seen on the serosa of stomach, pancreas, esophagus, liver, lung, spleen and omentum.

Total count of leukocyte: 17200/mm,^{3} Polymorphonuclean: 76%, occult blood (+ +) parasite egg and pyocyte (-).

Diagnosis. Stomach: Squamous cell carcinoma, breed unspecified, equine.

Contributor's Comment and Conference Note. The tumors in the stomach wall and metastatic foci were atypical squamous cell carcinoma.

Conference participants agreed the histomorphological lesions were consistent with those described for equine gastric squamous cell carcinoma.

Contributor. Veterinary College, Beijing Agricultural University, Beijing 100094, People's Republic of China.

Suggested reading.

Barker JK, Van Drummel AA: The alimentary system. In: Jubb KVF, Kennedy PC and Palmer N eds. Pathology of Domestic Animals 3rd ed. New York, Academic Press, 1985, pp 50-51.