

HISTOPATHOLOGY SLIDE SEMINAR

45TH Annual Conference of American Association of Veterinary Laboratory Diagnosticians

> Saturday, October 19, 2002 3:30-6:30

CASES

Part 1: Moderator- A. W. Layton

- 1. S. D. Fitzgerald. Acute lobar pneumonia in a puppy associated with *Bordetella bronchiseptica* and *Mycoplasma* spp. Slide 2561576
- 2. S. D. Fitzgerald. Caprine *Listeria s*epticemia: Comparison of lesions in two *in utero* infected kids. Slide 2566030.
- 3. J. A. Ramos-Vara, I Ganjam, W. Fales. Pulmonary necrobacillosis in white-tailed deer (*Odocoileus virginianus*). Slide 23827-E.
- 4. J. A. Ramos-Vara, M. A. Miller. Metastatic pulmonary adenocarcinoma to the digit in a cat. Slide 818-A.
- 5. M. A. Miller, R. L. Meadows, R. W. Dunstan, J. A. Ramos-Vara. Acantholytic dyskeratotic epidermal nevus with histologic features of Darier's disease in a puppy. Slide 1901-C.
- 6. D. O'Toole, J. P. Dubey. *Neospora*-induced encephalitis in an adult horse from an area of the United States that is naturally devoid of opossums. Slide 01008336.
- 7. D. O'Toole. Chronic hyperplastic and neoplastic cutaneous lesions (Marjolin's ulcer) in hot-branded cattle. Slide 01012724.
- 8. S. D. Grimes. Cerebellar abscess due to *Rhodococcus equi* in an equine foal. Slide 25990-02-1.
- 9. F. Williams, J. A. Ramos-Vara. Undifferentiated round cell tumor and widespread metastasis in a dog. Slide 11586-9.
- G. C. Johnson, W. R. Hause. Symptomatic arachnoid cyst in the cerebrum of a dog. Slide 5292-10.
- 11. S. Rushton, J. Cooley. Atypical interstitial pneumonia in a mixed breed cow. Slide 01-39702.

Part 2: Moderator- S. Grimes

- 12. L. Woods. Cervical vasculitis in emu chicks. Slide D950-3859.
- 13. J. Britt. Proliferative scrotal hemangioma-like lesions in boar. Slide 13333-99.
- H. L. Shivaprasad, R. P. Chin. Lesions of avian encephalomyelitis virus infection in chickens. Slide FO2-580-8.
- 15. H. L. Shivaprasad. Symmetrical encephalomalacia in an eclectus parrot. Slide F01-4625.
- 16. M. M. Sebatian, R. C. Giles, G. R. Rezabek. Mucinous hyperplasia and amyloidosis in the kidneys of a horse. Slide UK-LDDC-2 #16 (2 slides).
- 17. K. L. Diegel, D. J. Patrick, R.W. Dunstan, C. Welti, K. M. Credille. Ichthyosis in two mixed-breed puppies. Slide 2582472-17
- 18. M. Kiupel. Paragonimus kellicotti infection in a red fox. Slide MK
- 19. M. Hoenerhoff, G. Watson, C. Jackson. Enterocolonocecal aganglionosis in a three day old Overo x Overo cross white paint foal. Slide MJH.
- D. J. Patrick, B. A. Steficek, K. J. Williams. Ulcerative, granulomatous and eosinophilic dermatitis in a Holstein cow. Slide 2533121-5
- J. F. Roberts, M. L. Vickers, R. C. Giles, J. M. Donahue and C. Butler. Interstitial pneumonia and esophagitis in a Mojave rattlesnake (*Crotalus scutalatus*) colony. Slide 62533.

Acute lobar pneumonia in a puppy associated with *Bordetella bronchiseptica* and *Mycoplasma* spp.

S.D. Fitzgerald

A 10-week-old female dachshund was presented with a clinical history of acute dyspnea, radiographic evidence of pneumonia and pulmonary edema. On necropsy, the entire left lung was purple, consolidated, and failed to float in formalin. The right lung had approximately 40% of the anterio-ventral lung that was firm, and purple. The bronchial lymph nodes were enlarged and reddened. Histologically, the lungs were diffusely edematous and necrotic; airways and alveoli contained fibrin, numerous neutrophils and macrophages. Scattered colonies of gram-negative bacilli were present in bronchioles. High numbers of *Mycoplasma canis, M. spumans*, and *Bordetella bronchiseptica* were isolated form the lungs. No histologic or virologic evidence of canine distemper virus was present.

Acute bacterial pneumonia in dogs is most frequently associated with *Bordetella, Streptococcus*, or various gram-negative bacteria, however, acute lobar pneumonias are rarely reported. *Mycoplasma canis* is frequently associated with clinical bronchopneumonia in dogs,

and may playa synergistic role with other bacterial agents. In this case, we believe a pre-existing *Mycoplasma* infection predisposed this puppy to a severe fatal *Bordetella* pneumonia, likely complicated by the stress of ownership transfer.

Animal Health Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University, East Lansing, MI

Case #2

Caprine Listeria septicemia: Comparison of lesions in two in utero infected kids

S.D. Fitzgerald

A pair of twin Nubian goat kids were submitted for diagnostic evaluation. One kid was a stillborn male with diffusely atelectatic lungs that failed to float in formalin. The only significant gross finding were dozens of pale 1-3 mm diameter foci scattered throughout the liver. The second kid had lived for 36 hours prior to dying. It's lungs were mottled and firm, with dozens of 2-5 mm diameter foci; similar foci were scattered throughout the liver. Bacteriologic culture

from both kids revealed high numbers of $Listeria\ monocytogenes$ from their livers and lungs. In addition, stomach contents and placenta from the stillborn goat also contained high numbers of L. monocytogenes.

This case represents a late third trimester natural infection by *Listeria*. We can see a progression of septicemic lesions since one twin died *in utero*, while the second lived for 36 hours after birth. Both animals exhibited scattered colonies of small gram positive bacilli within their livers and spleens, but in the stillborn animal there was no significant reaction to the colonies. While in the newborn animal, diffuse suppurative bronchopneumonia, and significant multifocal necrotizing hepatitis with inflammatory infiltrates had developed. Neither animal had lesions in its brain or intestinal tract, which are sites frequently affected by *Listeria* septicemia in neonatal ruminants.

Animal Health Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University, East Lansing, MI

Pulmonary necrobacillosis in a white-tailed deer (Odocoileus virginianus)

J. A. Ramos-Vara (ramosj@missouri.edu), I. Ganjam, W. Fales Veterinary Medical Diagnostic Laboratory, University of Missouri, Columbia, MO 65205, USA

A captive 3-year-old, female white-tailed deer (*Odocoileus virginianus*) developed acute respiratory distress and died within 24 hours. Other animals in the herd developed coughing but clinical signs disappeared shortly after treatment with antibiotics. A field necropsy revealed abundant serofibrinous fluid in the thoracic cavity. The lung was extensively consolidated with multifocal to coalescing areas of caseous necrosis and hemorrhage involving mainly airways but also pulmonary parenchyma. Multifocally, the visceral pleura was covered with thick tan fibrinous exudate. Tracheobronchial lymph nodes were enlarged and wet. The gross pulmonary lesions suggested bacterial (i.e. *Mycobacterium* spp., *Fusobacterium* spp.) or fungal pneumonia.

Microscopically, there are multifocal to confluent areas of coagulative necrosis associated with numerous filamentous bacteria within the pulmonary parenchyma. Necrotic areas are usually closely associated with airways and are infiltrated with degenerated leukocytes with loss of cytologic detail. Within necrotic areas or adjacent to them there are numerous vessels with fibrinocellular thrombi, sometimes containing filamentous bacteria. The wall of some affected vessels is infiltrated by leukocytes and has areas of hyalinosis (fibrinoid necrosis, vasculitis). The endothelium is plump, vacuolated or partially detached. There are also perivascular cuffs of mainly mononuclear leukocytes around some affected vessels. Sometimes thrombotic vessels open into an area of necrosis (suggesting embolic distribution of the lesion). Necrotic areas are usually sharply demarcated from the adjacent parenchyma, which is diffusely infiltrated by macrophages, neutrophils and fewer lymphocytes. Numerous bronchi and bronchioles have disorganized and/or degenerated epithelium. The lumen of affected airways is filled with degenerated leukocytes, desquamated epithelial cells, amorphous material and filamentous bacteria. Congestion, edema and fibrinous exudate are also present in alveoli. Interlobular septa are greatly expanded by mixed inflammatory cells, edema, fibrin and fibrinous lymphatic thrombi. The pleura is multifocally infiltrated by degenerated leukocytes and fibrin. A diagnosis of necrotizing (caseous) bronchopneumonia and fibrinosuppurative pleuritis with intralesional bacteria was made. There was a heavy growth of an anaerobic, gram-negative, nonspore-forming rod, which agglutinated chick red blood cells, and was classified as Fusobacterium necrophorum by the API 20A anaerobe system.

Fusobacterium necrophorum, the causal agent of necrobacillosis, is a common cause of deep stomatitis, laryngitis, liver and foot abscesses in domestic animals, especially cattle, sheep, and pigs. F. necrophorum causes foot abscesses, necrotic stomatitis, navel ill, and liver abscesses in deer, pronghorns, and other wild ungulates. Pulmonary F. necrophorum infection probably disseminates hematogenously from oral, ruminal, or pedal lesions, or develops as aspiration pneumonia. In our case, there was evidence for both routes of infection, with airways more severely affected (consistent with aspiration pneumonia); however, vasculitis and vascular thrombosis was also present in this deer indicating the possibility of septicemia. Interestingly, the necropsy did not reveal gross lesions in the oral cavity, pharynx, rumen, liver, or feet. A small focus of inflammation might have been present in these organs and overlooked during necropsy; alternatively, direct involvement of the lung might have occurred. Pulmonary lesions in this deer resemble Lemierre's syndrome (septic thrombophlebitis caused by F. necrophorum with systemic dissemination) in humans. Pulmonary lesions of necrobacillosis can be easily confused with tuberculosis, especially in the absence of more typical oral or pedal lesions.

References: 1. Abele-Horn M et al. (2001) Lemierre's syndrome with spondylitis and pulmonary and gluteal abscesses associated with Mycoplasma pneumoniae infection. *Eur J Clin Microbiol Infec Dis* 20:263-266. **2.** Edwards JF et al. (2001) Fusobacteriosis in captive wild-caught pronghorns (*Antilocapra americana*) *Vet Pathol* 38:549-552. **3.** Leighton (2001) *Fusobacterium necrophroum* infection. In: *Infectious Diseases of Wild Animals*, Williams ES, Barker IK (eds.), 3rd edit., pp493-496, Iowa State University. **4.** Ramos-Vara JA et al. (1998) Necrotising stomatitis associated with *Fusobacterium necrophroum* in three sows. *Vet Rec* 143:282-283. **5.** Ramos-Vara JA et al. Pulmonary necrobacillosis in a white-tailed deer. *Vet Rec* (in press)

Metastatic pulmonary adenocarcinoma to the digit in a cat

J. A. Ramos-Vara (ramosj@missouri.edu), M. A. Miller. Veterinary Medical Diagnostic Laboratory, University of Missouri, Columbia, MO 65205, USA

A 12-year-old, spayed, female, domestic shorthair cat was presented to the referring veterinarian with a 1-month history of multiple swollen digits in the left front and rear feet. A biopsy of one **digit** was examined. Microscopically, the dermis and soft tissue surrounding P3 are infiltrated by a neoplastic growth consisting of tubules lined by pseudostratified columnar to stratified squamous epithelium. Columnar cells usually have cilia. Some tubules also have goblet cells. The tubular lumina have abundant amorphous, eosinophilic to amphophilic material as well as degenerated cells including leukocytes. This growth invades and expands P3 which is extensively lysed. The growth within P3 has a more squamous appearance than in other areas. The joint space is also infiltrated by carcinoma cells. Neoplastic cells are less frequent in the soft tissue surrounding P2 and do not infiltrate its marrow cavity. This tumor is accompanied by scirrhous reaction and mixed inflammatory infiltrates. The articular cartilage of P3-P2 is multifocally eroded. The overlying epidermis is ulcerated and covered by serocellular crusts. Neoplastic epithelium is immediately under the crust. A diagnosis of metastatic pulmonary carcinoma to the digit was made. Four weeks later the cat was euthanized due to the presence of additional masses in multiple digits. A chest radiograph showed several nodules in the dorsal aspect of the pulmonary field.

The **necropsy** revealed changes mainly in the feet, heart, lung, and pancreas. All four feet had amputated toes (one or more phalanges): right front: second medial digit; right rear: second and third digits; left front: second medial digit; left rear: two middle digits. The surface of the right atrium was rough and tan. The right cranial pulmonary lobe had a 2 x 2 cm raised tan mass that on cut section was well-demarcated from the rest of the parenchyma and had areas of necrosis. A smaller mass was present in the dorsal aspect of the right diaphragmatic lobe. The pancreas had multiple and slightly raised nodules consistent with exocrine nodular hyperplasia.

Microscopically, the **pulmonary nodules** consisted of extensive areas of necrosis with cholesterol clefts, aggregates of lymphocytes, and atypical clusters of epithelial cells, usually forming solid aggregates surrounded by abundant stroma. Numerous vessels associated with bronchi had extensive fibrosis and were infiltrated by atypical epithelial cells forming solid aggregates surrounded by abundant stroma. Atypical epithelial cells were also present in the epicardium and myocardium of the right atrium.

Secondary skin neoplasms result from the metastasis of primary neoplasms in other organs to the skin. Patterns of metastasis are probably the combined result of cell tropism in the primary neoplasm, hemodynamic, immunologic, biochemical, or microenvironmental factors. Secondary skin neoplasms are rare in cats and include mammary carcinoma, gastric carcinoma, and pulmonary carcinoma. Metastatic pulmonary carcinoma usually occurs in old cats (12-year-old average) without sex or breed prelidection. They usually affect multiple digits of multiple paws but occasionally one paw or only one digit can be affected. Other sites (head, abdomen, lip, thigh, lumbar area) can be affected. The pulmonary tumor is usually an adenocarcinoma but some cases have squamous differentiation. The metastatic tumor usually has the same phenotype. In our case, the metastatic site had distinct respiratory epithelial differentiation in contrast to the paucity of typical respiratory epithelium in the pulmonary and cardiac masses. This tumor typically produces bone lysis in the digits.

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Acantholytic dyskeratotic epidermal nevus with histologic features of Darier's disease in a puppy

Margaret A. Miller, Richard L. Meadows, Robert W. Dunstan, José A. Ramos-Vara, Veterinary Medical Diagnostic Laboratory, Veterinary Medical Teaching Hospital, University of Missouri – Columbia and Department of Veterinary Pathology, Texas A & M University

A 2.7 kg, mixed-breed bitch presented at 8 months of age with a plaque on the right ventral hemithorax and a chain of papules along the ipsilateral limb from the truncal lesion to eroded nodules and keratoses on the paw. The owner reported that lesions were present when the dog was obtained at the age of 6 weeks. The keratoses had been debulked, but soon recurred.

The clinical diagnosis was epidermal nevus. Lesions on the thorax and leg were excised with margins using an electro-surgical unit; the keratosis on the paw was debulked; all tissues were submitted in formalin for histologic examination.

Suprabasilar acantholysis and dyskeratosis were the unique histologic features. Acantholysis in epidermis and follicular epithelium resulted in suprabasilar clefts. Dyskeratotic cells were numerous throughout the stratum spinosum and were rounded with intense cytoplasmic eosinophilia; nuclei were sometimes shrunken and basophilic, but frequently were hypochromic with a prominent nucleolus and perinuclear pallor. Neutrophil infiltration was limited to eroded areas. Basal keratinocytes were hyperplastic but well differentiated. Intact epidermis was acanthotic and hypergranulotic with compact orthokeratosis. Crusts of dyskeratotic acantholytic cells, degenerated leukocytes, keratin, and debris covered erosions.

Pemphigus vulgaris was ruled out because it is never linear clinically and acantholysis is generally limited to the first layer of the stratum spinosum and not associated with prominent dyskeratosis. Acantholytic dyskeratosis with suprabasilar clefting is the hallmark of Darier's disease (keratosis follicularis), a human syndrome caused by autosomal dominant mutation of *ATP2A2*, which encodes sarco-/endoplasmic reticulum Ca⁺⁺-ATPase isoform 2 (SERCA2). Lesions usually appear in the first or second decades of life and tend to be generalized and progressive. Grover's disease resembles Darier's disease histologically, but tends to be transient, to appear later, and is not associated with *ATP2A2* mutation. Hailey-Hailey disease (benign familial pemphigus) results from autosomal dominant mutation in *ATP2C1*. Benign familial pemphigus in dogs results in suprabasilar acantholysis mainly in skin over pressure points, ventral chest, and pinna. Dyskeratosis is not prominent.

Acantholytic dyskeratosis is noted in a variety of other cutaneous disorders, including canine erythema multiforme, and may be found focally as an incidental lesion. Viral papilloma was considered because of the dog's age and multiplicity of lesions, but immunohistochemistry for papillomavirus using a genus-specific polyclonal antibody was negative. Squamous cell carcinoma was eliminated from the differential diagnosis because neither atypia nor invasiveness was evident. Warty dyskeratoma and acantholytic acanthoma are usually solitary lesions in old people. Acantholytic actinic keratosis was ruled out because the lesion was probably congenital. An acantholytic dyskeratotic variant of linear epidermal nevus is recognized as a rare congenital or childhood lesion that may be unilateral and distributed along Blaschko's lines (dermatomes). Though localized Darier's disease with unilateral lesions and dermatomal distribution has been described (and attributed to mosaic mutation), we consider epidermal nevus the more appropriate diagnosis in our dog because lesions were congenital, nonprogressive, and unassociated with other manifestations of Darier's disease; furthermore, histologic features were different from those in other recognized dyskeratotic/acantholytic diseases.

The dog returned 3 months after biopsy for CO₂ laser vaporization of remaining abnormal tissue on the footpads. Therapy with a third-generation topical retinoid (adapalene; Differin^R) was instituted twice weekly at the time of bandage changes. Bandages were discontinued after 3 weeks and the owner applies adapalene daily to affected tissue. Although the footpads have not healed completely, no recurrence or development of additional lesions has been noted in the 7 weeks since treatment began and the dog bears weight on the affected leg for the first time.

*Neospora-*induced encephalitis in an adult horse from an area of the United States that is naturally devoid of opossums

D. O'Toole¹ J. P. Dubey²

The most commonly identified etiological agent of equine protozoal myeloencephalitis (EPM) is *Sarcocystis neurona*, for which North and South American opossum species serve as definitive hosts. Less commonly, *Neospora* organisms are found in horses with EPM; a small number of such cases has been reported.

In August 2001, a 14-year old Morgan-cross gelding on a cattle ranch in western Wyoming developed acute-onset incoordination and was euthanized. The ranch is in an area of the state where no opossums occur and, according to the owners, the horse was never off the ranch occurs during his life. Hay fed to the horses was grown locally and was not bought in from out of state. There was a discreet 2.5-cm discolored, hemorrhagic area in white matter at the posterior pole of the right cerebral hemisphere. This corresponded histologically to locally extensive necrotizing eosinophilic granulomatous leukoencephalitis with modest numbers of intralesional tachyzoites. Tachyzoites divided by endodyogeny and were immunohistochemically positive for *Neospora* and negative for *Toxoplasma gondii* and *Sarcocystis neurona*. Microbiological and serological tests for common causes of encephalitis in horses in the western United States were negative. The horse had a serum titer of 1:25 to *Neospora*, and was seronegative to *T. gondii* and *S. neurona*. Five clinically unaffected herdmates had *N. caninum* titers of 1:25 (n = 3) and 1: 100 (n = 2). No further cases of central nervous system disease were recognized in horses on the ranch over the following year. Protozoal abortion was not recognized in either cattle or horses on the ranch. We did not essay isolation of the organism because all pieces of fresh brain were frozen after receipt at the laboratory.

The source of the *Neospora* sp. organism was not established. This is the first report of spontaneous clinical neosporosis in Wyoming in any species, including cattle. Its occurrence in a horse native to Wyoming suggests that the definitive host for this *Neospora* sp. may occur naturally in the state.

The enclosed slide (Case 6-Donal O'Toole-Horse-WSVL01008336) shows affected cerebral cortex and subcortical white matter. There is locally extensive coagulative necrosis with a margin of intense perivascular to interstitial histiocytic-lymphocytic-eosinophilic encephalitis. Organisms are scant in the section. They are most easily identified along viable margins of the necrotic zone, particularly near perivascular cuffs, and in the small areas of starburst necrosis as single zoites.

Citations

- 1. Lindsay DS: 2001, Neosporosis: an emerging protozoal disease of horses. Equine Vet J. 2001 33:116 118.
- 2. Cheadle MA, Lindsay DS, Rowe S et al.: 1999, Prevalence of antibodies to Neospora sp. in horses from Alabama and characterisation of an isolate recovered from a naturally infected horse. Int J Parasitol 29:1537 1543.
- 3. Dubey JP, Liddell S, Mattson D et al: 2001, Characterization of the Oregon isolate of *Neospora hughesi* from a horse. J Parasitol 87:345 353.

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Chronic hyperplastic and neoplastic cutaneous lesions ("Marjolin's ulcer") in hot-branded cattle

D. O'Toole

Linear exophytic cutaneous lesions are chronic sequelae to hot-iron branding in a small proportion of beef cattle in the western US. Some appear to progress to squamous cell carcinoma.

Samples of skin were collected from calves with recent brand lesions (non-exophytic), from adult cattle with typical chronic exophytic hot-brand lesions (brand keratomas), and from cows with large proliferative ulcerated cutaneous lesions at branding sites (squamous cell carcinoma). All three types of lesion are represented on the submitted slide (Case 7 - Donal O'Toole-cow - 01012724).

Acute brand lesions are due to partial thickness coagulative necrosis of epidermis and upper dermis. Lesions corresponded clinically to a third degree burn.

Brand keratomas develop over the subsequent months or years following branding. They follow the contour of the brand and are raised, hairless and remarkably hard. Thick lesions can be as dense as digital horn, and it may be impossible to cut them with a scalpel blade. Histologically, such lesions are attributable to abrupt transition from haired skin of normal thickness to areas of regular epidermal hyperplasia with marked orthokeratotic hyperkeratosis, acanthosis, hypopigmentation, and loss of adnexae. Epithelial atypia is absent. Normal dermal collagen is replaced by mature granulation tissue and distinctive dense pale bundles of collagen that are represented in the middle section on the submitted slide

Squamous cell carcinomas at brand sites are rare. During 13 years in Wyoming I have seen two cases, in cows aged 5 and 13 years. Experienced practitioners confirm their rarity (6 seen in 25 years in practice; Dr. D. Christensen, Powder River Veterinary Clinic, Wyoming). Lesions develop slowly and may recur following surgical excision. Such lesions can be readily distinguished from brand keratomas, since the latter do not ulcerate unless a carcinoma is also present. Lesions may become large and the animal must be euthanized. The presence of large neglected lesions may present a welfare issue, particularly when such animals are presented for salvage slaughter.

Malignancy in brand scars is a rare complication of hot-iron branding in cattle. It may be due to malignant transformation of hyperplastic cutaneous plaques. These lesions have analogies with burn scar carcinomas of people, which are known eponymously as Marjolin's ulcer after the French clinician who recognized an association with old burns.

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Citations:

- 1. Marjolin, J-N: 1828, Ulcère. *In*: Dictionnaire de Médecine 21: 31 50
- 2. Novick M, Gard DA, Hardy SB, Spira M: 1977, Burn scar carcinoma: a review and analysis of 46 cases. J Trauma 17:809 817
- 3. D. O'Toole. JD Fox: 2002, Chronic hyperplastic and neoplastic lesions ("Marjolin's ulcer") at hotbrand sites in adult beef cattle. J Vet Diagn Invest. In press. Publication due January 2003.

Cerebellar abscess due to Rhodococcus equi in an equine foal

Sheila D. Grimes

An eight-week-old, live, male foal with neurological clinical signs was submitted. Head shaking was the primary clinical sign. A 1 cm in diameter region of the cerebellum was adhered to the left side of the skull. A yellowish, granular material was present in the site of adhesion. Other gross lesions included bilateral eyelid abrasions, corneal edema of the left eye and swelling of the left ear. Microscopically, the cerebellum was partially effaced by severe, focally extensive pyogranulomatous inflammation, consisting of numerous neutrophils, macrophages and plasma cells in the area of necrosis. Macrophages were distended by numerous gram-positive coccobacilli. In the adjacent intact cerebellar neuropil, thick perivascular cuffs, gliosis, axonal spheroids and neuronal necrosis were noted. A severe mixed inflammatory infiltrate, consisting of lymphocytes, plasma cells, macrophages and neutrophils, and fibrosis were present in the meninges. Inflammation was also noted in the meninges of the cerebrum, brain stem and cervical spinal cord. The morphologic diagnosis was severe, chronic, focally extensive pyogranulomatous encephalitis with intrahistiocytic bacteria compatible with *Rhodococcus* and a moderate to severe, chronic, widespread lymphoplasmacytic and neutrophilic meningitis. Hypoyon, keratitis and uveitis were also noted. A heavy growth of *Rhodococcus equi* was isolated from the brain.

Rhodococcus equi is an unusual cause of neurological disease in horses. However, there are several reports in the literature of rhodococcal infections of the central nervous system of people, particularly involving immunocompromised AIDs patients. One report describes a traumatic incident which resulted in the infection of the central nervous system of a six-year-old child.

Principally, a cause of bronchopneumonia, enterocolitis and mesenteric lymphadenitis in foals less than six months of age, *Rhodococcus equi* may also result in neurological disease in foals.

Animal Disease Diagnostic Laboratory, Reynoldsburg, OH

Undifferentiated round cell tumor with widespread metastases in a dog

F. Williams III (williamsfre@missouri.edu), J. A. Ramos-Vara Veterinary Medical Diagnostic Lab, University of Missouri

An 8-year-old, neutered male, Labrador retriever dog was presented for necropsy with a history of chronic pain. There was severe muscle atrophy over the left scapula and the left femur. Previous clinical history includes a hyperglobulinemia, normal creatinine kinase levels, and degenerative joint disease. Serum protein electrophoresis showed a polyclonal gammopathy. CSF tap was normal and the patient was treated with prednisone.

On gross examination the right kidney was enlarged 3 times. On cut section, approximately 50% of the renal parenchyma was necrotic and partially liquefied. The caudal portion of the kidney was infiltrated by a white to tan firm mass. The left kidney had multifocal to coalescing subcapsular white nodules over the entire surface. On incision, these nodules extended deep into the renal cortex. Similar white lesions were noted in the epicardium, myocardium, and endocardium, with the near total effacement of the right atrioventricular valve. The lungs were diffusely seeded with white nodules. There were areas of eroded cartilage on the proximal left tibia, head of the left femur, and the left distal humerus. A focal pale area was observed in the distal diaphyseal bone marrow of the left femur.

Microscopically, the renal cortex was diffusely infiltrated by pleomorphic round cells with round to oval, stippled nuclei, variable amounts of eosinophilic cytoplasm, and indistinct cell borders. There were occasional binucleate cells and fewer multinucleate cells. Mitoses were very common (approximately 28 mitotic figures per 10 400x fields). The lung, heart, esophagus, femoral bone marrow, and cerebellum had similar neoplastic growths, although with fewer mitoses. In the heart section, there are multiple areas of myocardial necrosis and collagen fiber replacement associated with the neoplastic infiltration. There was mild hepatic degeneration (steroid type) and chronic synovitis in the left hock and elbow.

Immunohistochemical testing for CD45, CD45RA, immunoglobulin light chains, CD3, CD79a, lysozyme, myeloid-histiocytic marker (Mac 387), desmin, muscle actin, S100 protein, broad spectrum CKs, and low molecular weight CKs antigens were negative. Neoplastic cells were strongly positive for vimentin. A subpopulation of cells (interpreted as interstitial or nonneoplastic) was positive for both NSE and Bla36 antigen.

Evidence of hypergammaglobulinemia and the microscopic appearance of neoplastic cells were suggestive of plasmacytoma, but extensive immunohistochemistry did not confirm this diagnosis. Other rule outs were rhabdoid tumor and melanoma. Rhabdoid tumor is common in young humans and is typically present in the kidney and produces extensive metastases. Immunohistochemically such tumors are positive for vimentin and focally reactive to low molecular CKs, S100, and NSE. Typical paranuclear, vimentin-positive, cytoplasmic inclusions, and centrally located single and large nucleoli (hallmarks for rhabdoid tumors) were not apparent in this case. Melanin pigment, or staining with S100, was not present, which most likely rules out melanoma.

Symptomatic arachnoid cyst in the cerebrum of a dog

*Gayle C. Johnson, Wayne R. Hause

A ten year old neutered male Golden retriever dog was initially presented with seizures of short duration that were controlled with phenobarbital and dexmethasone. Magnetic resonance imaging revealed a welldefined cystic mass in the right frontal cerebrum that was 4.5 cm in length and 3 cm in width. The mass was rounded, did not appear to communicate with the ventricles, and bifurcated anteriorly. The image was of low intensity with T1 and bright with T2, and there was mild enhancement after administration of contrast. The brain was compressed by the cyst, with cingulate gyral herniation, and mild ventricular enlargement. Due to the poor prognosis and development of pacing and drowsiness after 2 months, the patient was euthanized. Histologic specimens revealed that the cyst had a well defined wall comprised of several layers of short fusiform cells that separated its lumen from the parenchyma and ventricles. The wall stained positively for S100 and vimentin antigens, but was negative for GFAP. These findings confirmed that the cyst was of leptomeningeal rather than brain parenchymal origin. Adjacent brain had undergone spongiform change and striking astrogliosis. In veterinary medicine, arachnoid cysts are usually located external to the spinal cord and can be surgically excised to successfully ameliorate clinical signs. This cyst was located at a less common site, and its eventual enlargement resulted in compressive edema and necrosis. Continuity with the leptomeninges was suggested by MRI, but that area was not sampled histologically. Arachnoid cysts are thought to develop by splitting of the arachnoid layer, with CSF entrapment and increased pressure. The immunohistochemistry of the wall distinguishes arachnoid cysts from acquired or quiescent developmental cavitations such as hydranencephaly or porencephaly.

* Person making the presentation. Work from the Veterinary Medical Diagnostic Laboratory, University of Missouri (Johnson) and Associated Veterinary Specialists, Bridgeton Missouri (Hause)

Atypical interstitial pneumonia in a mixed breed cow

Steven Rushton, Jim Cooley

Signalment: 24 month old female Mixed Beef Breed

History: Twelve, one to two years old cattle, were found dead within a four day period out of a herd of forty. The animals were bought at sale as unthrifty animals and are processed and are fed out on pasture. They have been eating some sweet potatoes the whole summer. They were last fed sweet potatoes approximately seven days previously. There was some frothing and obvious respiratory distress among affected animals. Some animals have their necks outstretched and are pulled away from the group.

<u>Gross examination:</u> The lungs are distended and there is marked separation of the interlobular septa by gas bubbles. Similar coalescing gas bubbles occur over the visceral pleura of all lung lobes. The intervening lung parenchyma is purplish-red and has a rubbery consistency. The lungs are easily cut having the consistency of liver. Some fluid is expressed from cut surfaced. Rumen contents are mostly fibrous ingesta with only rare identifiable. bits of sweet potato.

<u>Histological examination:</u> The lung alveolar lumen are frequently flooded by eosinophilic proteinaceous edema fluid intermingled with increased numbers of alveolar histiocytes and occasional clumps of fibrin. Alveolar septa are markedly widened by hyperemic blood vessels, edema, and some fibrin. The alveoli are lined by markedly hyperplastic type 2 pneumocytes that are often cuboidal. Some necrotic cellular debris and occasional neutrophils occur in some sections. Intralobular septa are widely distended mostly with air pockets. Some peripheral edema is present in these air distended spaces which are sometimes marginated by histiocytes.

<u>Morphologic diagnosis</u>: Lung; interstitial pneumonia, exudative and proliferative, subacute, diffuse, severe with interstitial emphysema.

<u>Comments:</u> Growth of appropriate mold on the potatoes and the production of the toxin are likely variable due to environmental conditions. The toxin produced has been identified as 4-ipomeanol. This is absorbed through the rumen into the lungs where further metabolism results in toxic intermediates that damage endothelial cells of blood vessels and the alveolar epithelial lining of the air sacs of the lungs. Damage to the lungs is irreversible.

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Cervical vasculitis in emu chicks

Leslie W. Woods

Four of eight 5-week-old emu chicks died 24-48 hours after placement in an enclosure that was recently treated with a concentrated solution of chlorine bleach in water (1 cup chlorine bleach in one gallon of water). The chicks were immediately placed in the wet enclosure and the owner noted that the chicks drank from puddles of the bleach mixture remaining in the enclosure. Three dead chicks were submitted for necropsy to the California Animal Health and Food Safety Laboratory System at the University of California, Davis. All three chicks had severe uniform subcutaneous hemorrhage and edema of the heads and necks. No skin abrasions or wounds were noted, and no oral or esophageal lesions were seen on the gross examination. The sinuses and tracheas were unremarkable. No other gross lesions were seen in the chicks. Acute vasculitis with accompanying hemorrhage and edema were evident microscopically in the cervical regions of the chicks. No other microscopic changes were seen. Results of heavy metal and anticoagulant screens on tissues were unremarkable.

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Case #13

Proliferative scrotal hemangioma-like lesions in boar

James Britt, DVM, MS

Scrotal skin lesions were submitted from the State Prison Farm from a continuing problem in both younger and older boar. The lesions have a papillomatous epidermal proliferation with a concurrent vascular bed proliferation in a fibrous stroma with lymphocytic inflammation and sometimes eosinophils throughout the dermal vascular buds. The proliferating vascular slits have a bland endothelial lining.

Clinically, the condition appears to be contagious. Tests for papillomavirus by immunohistochemistry and *in situ* hybridization using formalin-fixed tissue (courtesy U. of Saskatoon, Drs. Edward Clark and Beverly Kidney) were negative but two wart vaccines made at different times in our laboratory were reportedly effective and caused the lesions to regress to flat scar plaques. The lesions occur in the white boar (Yorkshire/Landrace) and not in the darker breeds (Duroc).

The dermal vascular component seems similar to bovine cutaneous angiomatosis, scrotal varices tumor in dogs, or pyogenic granuloma (lobular capillary hemangioma) in humans but the proliferative epidermal component is suggestive of papillomas which apparently do not occur in swine, except for a poxviral-induced transmissible genital papilloma of the preputial diverticulum. Scrotal hemangiomas, sometimes described as having a warty surface, have been reported in the scrotum of boars in the older literature and seem to be predominantly in white pigs and can be multiple on one boar and within the herd.

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Lesions of avian encephalomyelitis virus infection in chickens

H. L. Shivaprasad, R. P. Chin

Brain from a 3 week-old chicken. Sixty chicks in a group of 80 had clinical signs of neurological signs such as ataxia, lateral recumbency and opisthotonus, and increased mortality in the flock. Sixty per cent of the birds died by the time the chicks reached five weeks of age. The breeders as well as the chicks had not been vaccinated for any diseases.

Necropsy did not reveal any gross lesions. Histologically there is multifocal severe perivascular cuffing, gliosis and neuronal necrosis (central chromatolysis). In addition there was lymphocytic inflammation in the muscular wall of the proventriculus and in the pancreas. These lesions are consistent with Avian Encephalomyelitis (AE) virus infection. Serologically all the birds were positive for AE virus but negative for Newcastle disease virus.

In addition to the lesions described above other lesions such as myelitis, myocarditis, myositis and lymphocytic inflammation in the wall of the crop/esophagus and gizzard were also observed. These lesions and differential diagnoses for neurological signs in chickens will be discussed.

Case #15

Symmetrical encephalomalacia in an eclectus parrot.

H. L. Shivaprasad

Brain from an approximately two year-old female Eclectus Parrot. Clinical signs of regurgitation, twitching of leg, clenching of feet, seizures, laying on keel, anorexia, etc, of several weeks duration. Increased WBC's, 18.4 thousand (N 9-15), normal uric acid and radiographs. Not responsive to EDTA, Baytril, Calcium, Selenium, vitamin B and fluids. Vitamin B controlled seizures to an extent. Upon necropsy the bird was dehydrated, mildly emaciated and weighed 285 grams. Necropsy of the bird did not reveal any gross lesions. Microscopically there are symmetrical foci of malacia/vacuoles/plaques in the cerebral cortex and cerebellum.

Heart had myocardial degeneration and necrosis of vessels.

Liver and kidney were negative for heavy metals including lead and liver had normal level of vitamin E but high levels of vitamin A.

Mucinous hyperplasia and amyloidosis in the kidney of a horse

Manu M.Sebatian, Ralph C.Giles and Grant R.Rezabek *

Biopsy samples were submitted from a field necropsy of a 12-year –old quarter horse gelding that, died of hemoperitoneum. Kidneys were enlarged to 3 to 4 times normal size.

Microscopic examination of kidneys revealed severe glomerular and tubular change. Diffusely, glomeruli are enlarged, and capillary loops are markedly distended with eosinophilic material and in some, the entire tufts are replaced by this material. Frazer- Lendrum staining of the kidney ruled out that the eosinophilic material is fibrin and staining with Congo red established this to be amyloid. Many of the glomeruli had necrosis of the capillary tufts. Multifocally vessels had fibrinoid necrosis. Diffusely, tubules are ectatic and contained homogenous eosinophilic protein casts, with some tubules containing eosinophilic droplets or crystals resembling hemoglobin casts. In most tubules, lining epithelium is flattened and is undergoing various stages of necrosis and degeneration. Multifocally, interstitium has mild infiltration of lymphocytes and plasma cells with diffuse proliferation of immature fibrous connective tissue. Diffusely renal pelvis has severe glandular (tubular) and papillary hyperplasia of the transitional epithelial mucosa. The glands are cystic and filled with amorphous, pale basophilic to glassy material. Many areas the glandular epithelium are tall, columnar with hyperchromatic nuclei at the base. . Mucinous hyperplasia has been described in species of animals that have gall bladders and the pathogenesis is not well understood. This is the second case of mucinous hyperplasia reported in the kidney of a horse. Amyloidosis of the kidney is the most common and potentially the most serious form of organ involvement. The absence of any lymphoproliferative lesion in the horse suggest this to be AA type of amyloid. The pathogenic relationship between mucinous hyperplasia of the renal pelvis and amyloidosis is unclear.

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Ichthyosis in two mixed-breed puppies

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The ichthyoses (literally "fish scale diseases") are largely heritable and congenital, non-inflamed skin diseases with a unifying feature of orthokeratosis. Although clinically and microscopically heterogeneous, the ichthyoses can be broadly divided into those forms with a unique form of cytolysis present in the upper epidermis known as epidermolysis and those forms that have no epidermolysis. In this report we describe a case of non-epidermolytic ichthyosis in two, mixed- breed, Jack Russell Terrier X Cocker Spaniel puppies.

Skin biopsies obtained from a six month-old, female Jack Russell Terrier mix were submitted to the surgical pathology service at the Michigan State University Animal Health Diagnostic Lab (AHDL) for examination. At birth, both this puppy and a litter mate, also female, had thick tenacious scales covering large areas of skin over their entire bodies with no response to thyroid medication, antibiotic treatments, or anti-seborrheic and antifungal shampoos, according to the clinical history data. Histologic evaluation of skin initially submitted from the first puppy at six months of age, and that of the second puppy obtained during necropsy at seven months of age had similar features characterized by diffuse compact orthokeratosis subtended by nucleated epidermal layers that were only slightly acanthotic. The orthokeratosis extended into the infundibular openings. There was patchy, mild hypergranulosis and no substantive dermal inflammation. Small numbers of Malassezia sp. colonized superficial keratin layers, and bacterial colonies were occasionally associated with the laminated, hyperkeratotic stratum corneum and follicular casts. Because of the morphologic and clinical overlap with a form of non-epidermolytic ichthyosis in humans known as autosomal recessive ichthyosis (lamellar ichthyosis), a condition often found to be due to a mutation in the transglutaminase I gene (an enzyme required for normal cornification), immunohistochemical staining for canine transglutaminase 1 (using monospecific, polyclonal antibodies that are currently under validation) was performed and defined normal expression in relation to control samples.

Cases clinically and histologically identical to those described above have been reported in the Jack Russell Terrier and have been examined by the authors previously. In these cases, the affected dogs were purebred Jack Russell Terriers and, when pedigree information was available, the mode of inheritance was consistent with an autosomal recessive pattern. The presented cases are unusual in clinical presentation (Jack Russell X Cocker Spaniel mix-bred), and suggest that congenital ichthyosis should not be suspect only in purebred puppies, but equally so in mixed-breed dogs, particularly when lineage includes a known affected breed.

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Paragonimus kellicotti infection in a red fox

M. Kiupel, Michigan State University

A red fox (*Vulpes vulpes*) that had been seen for approximately a week in a bison barn and seemed to be depressed, was found dead and was submitted for necropsy on April 22 to the Animal Health Diagnostic Laboratory. This was a male fox that weighed 8.5 pounds and was in poor nutritional and hydration status and moderately autolyzed. The lungs were diffusely dark red, poorly collapsed and frothy fluid floated from cut section. There were two red sharply demarcated firm spherical nodules measuring approximately 1.5-2.0 cm in diameter located in the left caudal lobe of the lungs. When cut open, a clear gelatinous mass exuded from their cavity. Two flukes were recovered from each cavity. The adult flukes were approximately 10 by 6 mm in dimensions, brown, ovoid and shaped like a coffee bean. All other organs were diffusely congested. No other gross lesions were observed.

Sections of lung were examined microscopically. Dilated bronchi containing cross sections of trematodes were characterized by an inner zone of exudate containing parasitic eggs, nuclear debris and blood adjacent to adult flukes. The bronchial wall was thickened by infiltrated mononuclear cells and eosinophils, hypertrophied and hyperplastic bronchial glands and hyperplastic epithelium. In other areas the bronchial epithelium was attenuated and focally eroded. The trematodes were characterized by tegumental spines, vitellaria found within the parenchyma and brown pigment in their intestinal tract. Large numbers of parasitic eggs were randomly distributed throughout the parenchyma and had induced a diffuse interstitial granulomatous inflammation and fibrosis. The eggs were approximately 100 by 50 μm in dimension, unilateral operculated and had a round refractile yellow capsule. Eggs were consistent with trematode eggs and induced mild to moderate granulomatous inflammation. Approximately 60% of the pulmonary parenchyma was effaced by egg granulomas. All other organs appeared microscopically unremarkable.

The lesions in the lungs were consistent with an infection with *Paragonimus kellicotti*. Large number of eggs of *Paragonimus kellicotti*, Hookworm sp., and *Trichuris vulpis* were detected in feces. Large numbers of adult Sarcoptes sp. were detected in samples of skin. Sections of tissue collected at necropsy tested negative for canine parvovirus and canine distemper virus by fluorescent antibody test.

The lung fluke, *Paragonimus sp.*, is the only trematode that has his final habitat in the lungs and the most important species are *P. westermannii* in East Asia and *P. kellicotti* in North America. Mink are considered the final host, but other fish eating carnivores as well as humans, swine and ruminants have been found to be infected. The life cycle is typical of trematodes: The first intermediate host are small aquatic snails and the second intermediate host are freshwater crabs or crayfish. After ingestion of the crabs by the final host, metacecaria migrate from the intestine across the peritoneum and pleura to the lungs. The incidence of *Paragonimus kellicotti* in red foxes in Michigan has been reported between 2-5%. In contrast the incidence in wild mink (*Mustela vison*) in neighboring Ontario has been found to be around 15%. Whereas only mild inflammation in lungs of infected minks indicates that the parasite is well adapted to this host and causing no or only minor clinical disease, in foxes lesions are characterized by extensive necrosis, inflammation and secondary fibroplasia more likely to cause severe clinical disease.

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Enterocolonocecal aganglionosis in a three-day-old Overo x Overo cross white paint foal

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This three day old, female paint foal was an Overo x Overo cross. She was clinically normal for the first 24hrs of life. Shortly thereafter, she became lethargic and depressed, and was not passing fecal material adequately. At necropsy, she had retained meconium in the large colon and cecum.

Multiple sections of jejunum, ileum, large intestine and cecum were submitted to the Animal Health Diagnostic Laboratory at Michigan State University for histopathologic examination. In each, the primary histologic alteration appeared as an absence of small intestinal, large intestinal, and cecal submucosal and myenteric plexus ganglia. There were large amounts of meconium present in the large intestine.

The histologic findings were consistent with aganglionosis, characteristic of the lethal dominant white trait occurring in 25% of Overo x Overo matings. Agenesis of myenteric and submucosal ganglia in these foals leads to dysfunction of normal intestinal peristalsis, resulting in a terminal ileus affecting the small intestine, colon, and rectum. These foals are predominantly white, with a few pigmented dots on the muzzle, abdomen, and hindquarters. Affected foals appear normal at birth but develop signs of colic within 5 to 24 hours, and die within 32-48 hours.

Cutaneous melanoblasts and the myenteric plexus are both derived from the neural crest. This may explain the concurrent lack of cutaneous pigmentation associated with these foals. An additional 25% of these matings results in an unviable embryo that is resorbed in early gestation.

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Ulcerative, granulomatous and eosinophilic dermatitis in a Holstein cow

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A 3-year-old Holstein cow developed dermal eruptions on the face, perineum, and teats. Physical examination revealed pyrexia and tachycardia and dexamethasone was administered. One week prior to development of cutaneous lesions the animal had received ceftiofur sodium (Naxcel®) for a respiratory infection. Due to a lack of improvement and development of anorexia after two days, the owners sent the cow to slaughter. No other animals on the farm were reportedly affected. Two sections of affected skin were submitted for histologic evaluation.

Diffusely within the superficial and mid dermis there was an intense perivascular and periadnexal mixed inflammatory infiltrate. The surface over the majority of the section was ulcerated and covered by a thick serocellular crust. The non-ulcerated epithelium was mildly hyperplastic and a similar but less prominent inflammatory infiltrate was present in the dermis. Scattered necrotic keratinocytes were present within the non-ulcerated epithelium and follicular epithelium. The dermal inflammatory infiltrate was comprised of varying combinations and concentrations of macrophages, lymphocytes, plasma cells, neutrophils, and eosinophils with moderate numbers of scattered multinucleated giant cells. This infiltrate was often present within and obscured apocrine glands and the outer root sheath epithelium. The surface crust was composed of an abundance of degenerate neutrophils admixed with proteinaceous fluid and amorphous cellular debris. The deep dermal arteries and veins were surrounded by smaller nonsuppurative infiltrates.

No evidence was found for an infectious etiology, neoplasia, or an autoimmune reaction. We could not determine a precise cause of these lesions. Our differentials included an immune-mediated drug reaction (eg ceftiofur), the cutaneous manifestation of Hairy vetch (*Vicia villosa* Roth) or possibly citrinin, a bacterial hypersensitivity secondary to a deep folliculitis and furunculosis, or the cutaneous lesions of the syndrome termed "pyrexia with dermatitis in dairy cows". Unfortunately, neither a feed sample nor the carcass were available for further evaluation.

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Acknowledgement: sincere thanks to Dr. Kara Salek and Dr. David Bucholtz from The Veterinary Standard veterinary clinic in Manchester, Michigan for submission of this interesting case and gross photo

Interstitial pneumonia and esophagitis in a Mojave rattlesnake (Crotalus scutalatus) colony

J.F. Roberts, M.L. Vickers, R.C. Giles, J.M. Donahue, and C. Butler

Twelve recently quarantined Mojave rattlesnakes died or were euthanized after developing acute onset of clinical signs associated with interstitial pneumonia and esophagitis. Gross lesions included subserosal and petechial hemorrhage in the oral cavity, proximal esophagus, anterior lung, and ceolomic cavity. Anterior lungs were dark red. Esophageal perforation with massive necrosis was observed in three snakes. Microscopic examination demonstrated peri-esophageal edema and submucosal and perivascular infiltration by heterophils and mononuclear cells in all snakes. Necrotizing esophagitis was observed in six cases. The lungs of nine snakes had interstitial infiltration by heterophils and mononuclear cells and increased interstitial thickness of faveaoli (gas exchange compartments). Epithelial cells lining the airways have formation of syncytia. Faveolar spaces contain conglomerates of degenerating epithelial cells and inflammatory cells mixed with mucus. The oral cavity of some snakes has subepithelial hemorrhage with infilitration by heterophils. The livers of several snakes have multifocal necrosis suggestive of terminal bacterial septicemia. Multiple bacteria species including Salmonell arizona, Morganella morganii, Providencia rettgeri, Bordatella spp, and Corynebacterium spp. were isolated from different snakes. The gastrointestinal tract of some snakes had cestodes of the order Cyclophyllidea, (Oochoristica sp) and encysted spiruids (Physocephalus sp.). Serology for ophidae paramyxovirus was negative on two snakes. Virus isolation of pooled tissues on Vero cells demonstrated cytopathic effect consistent with viral infection. Electron microscopy of Vero cell pellets demonstrated negatively stained virons consistent with reovirus.

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