61th AAVLD Diagnostic Pathology Slide Seminar



American Association of Veterinary Laboratory
Diagnosticians
Kansas City, Missouri
Saturday, October 20, 2018
3:30-6:00 PM

61th AAVLD Diagnostic Pathology Slide Seminar

Case #	Species	Organ/Tissue	Diagnosis/Cause
1	Goat	Skin	Epidermolysis bullosa
2	Bovine	Skin	Post-tattooing aural fibropapillomas
3	Bison	Skin	Pseudocowpox virus
4	Camel	Skin	Idiopathic nasal hyperkeratotic dermatosis
5	Dog	Nasal turbinate	Nasal rhinosporidiosis
6	Pig	Lung	Metastrongylus apri & Pasturellosis
7	Dog	Lung	Paraquat toxicity
8	Dog	Lung	Pneumocystis-associated pneumonia
9	Bird	Infraorbital sinus	Mycoplasma gallisepticum & Avibacterium spp.
10	Cat	Eye	Ocular cytauxzoonosis
11	Deer	Brain	Sarcocystis-associated encephalitis
12	Dog	Brain	Disseminated protothecosis
13	Dog	Brain	Intravascular lymphoma
14	Dog	Spinal cord	Histiocytic sarcoma
15	Dog	Ganglia	Dysautonomia
16	Pig	Vessels	Porcine circovirus-3-associated arteritis

^{*}Note: All case presentations are under consideration for the <u>2018 Diagnostic Pathology Slide Seminar Resident/Graduate Student Award.</u>

Case 1 Epidermolysis bullosa in a 1-day old goat

Wallaya Manatchaiworakul, Michelle Magagna, Williams Kurt, and Erica Noland Michigan State University Veterinary Diagnostic Laboratory, Lansing, MI

Signalment and History: A 1-day-old male, Nigerian Dwarf goat was born with patchy areas of alopecia and the distal aspects of all four limbs were ulcerated. A female twin to this affected goat had no clinical signs of disease. One other kid from this 304 head herd was previously born with similar lesions.

Gross Findings: The skin of all distal limbs had multiple large regions of epithelial ulceration. There was also regionally extensive to patchy areas of hair loss along the entire limbs, and multiple additional areas of patchy hair loss over the dorsum, flank, and head.

Histopathologic Findings: In the sections of haired skin, there is multifocal subbasilar cleft formation or full thickness epithelial loss. Subbasilar clefts occasionally contain mild accumulations of neutrophils and karyorrhectic debris. In some areas of epithelial loss, there are multifocal colonies of coccoid bacteria scattered along the exposed surface and low numbers of interstitial degenerative neutrophils within the superficial dermal stroma. The dermis within these regions was often devoid of adnexa. A section of the tongue had similar subbasilar clefts.

Morphologic diagnosis: Haired skin and tongue: Multifocal subbasilar cleft formation and epithelial ulceration

Additional Testing: In sections of the above described haired skin specimens specially stained with Periodic acid-Schiff (PAS), there is a PAS-positive basement membrane at the bottom of subepidermal blisters or lining portions of skin with epithelial ulceration.

Comments: Findings in this case are consistent with epidermolysis bullosa (EB). EB is a rare group of inherited mechanobullous diseases that affect both nonhuman mammals and humans alike. Lesions are characterized by blistering and ulceration of the skin and mucous membranes following mild mechanical trauma. Such blistering and ulceration of the skin and mucous membranes is due to mutations in genes responsible for structural proteins of the basement membrane zone or of the cytoskeleton of keratinocytes within the stratum basale of the epidermis.

Based on level of skin cleavage on ultrastructural examination, EB can be divided into three main subtypes. These main subtypes include EB simplex (EBS), junctional EB (JEB), and dystrophic EB (DEB). EBS is characterized by intraepidermal clefting via cytolysis of basal keratinocytes, while clefting within the lamina lucida of the basement membrane zone is characteristic of JEB and clefting below the lamina densa of the basement membrane zone is characteristic of DEB.

DEB has been previously reported in goats. In this case, given the presence of a PAS-positive basement membrane at the bottom of the blisters on histochemical staining, lesions in this case most likely either represents a form of EBS or JEB. To the authors' knowledge, this is the first report of non-dystrophic form of EB in goats. Because this is a heritable disease, mating of carrier animals should be avoided to prevent future animal suffering and loss.

- 1. Capt A, Spirito F, Guaguere E, et al. Inherited junctional epidermolysis bullosa in the German pointer: establishment of a large animal model. J Invest Dermatol. 2005;124(3): 530–535.
- 2. Mauldin EA and Peters-Kennedy J. Integumentary System. In: Maxie MG, ed. Jubb, Kennedy, and Palmer's pathology of domestic animals. 6th ed. St. Louis, MO: Elsevier; 2016: 533-536.
- 3. Niskanen J, Dillard K, Arumilli M, et al. Nonsense variant in COL7A1 causes recessive dystrophic epidermolysis bullosa in Central Asian Shepherd dogs. PLoS One. 2017;12(5).
- 4. Olivry T, Linder KE, Wang P, et al. Deficient plakophilin-1 expression due to a mutation in PKP1 causes ectodermal dysplasia-skin fragility syndrome in Chesapeake Bay retriever dogs. PLoS ONE. 2012:7(2)
- 5. Riet-Correa F and Medeiros GX. Epidermolysis bullosa in animals: a review. Vet Dermatol. 2015;26:3-13.

Case 2 Outbreak of post-tattooing aural fibropapillomas in a group of 14 beef calves

Raisa Glabman, Dodd Sledge, Dalen Agnew, Daniel Grooms, Erica Noland Michigan State University Veterinary Diagnostic Lab, Lansing, MI

Signalment and History: Within 2 months after ear tattooing at a 4H event, this 4-month-old black Angus steer developed markedly raised, smooth surfaced, and superficially crusted dermal lesions, which were strictly confined to and covered the entire tattooed regions.

Histopathological Findings: In a biopsy from the ear, the dermis is expanded by a moderately cellular proliferation of plump spindle cells haphazardly arranged in sheets and bundles supported by moderate collagenous stoma. These spindle cells have indistinct borders, a moderate amount of pale eosinophilic cytoplasm, and oval to elongate vesiculate nuclei with 1-2 distinct nucleoli and mild anisokaryosis. There are 4 mitotic figures per 10 high power (400x) fields. Within the superficial to mid dermis admixed with the spindle cell population, there are occasional mild perivascular infiltrates of histiocytes and fewer lymphocytes, plasma cells, and neutrophils. The overlying epidermis is moderately hyperplastic, covered by thick layers of compact ortho- to parakeratotic hyperkeratosis, and forms numerous long, broad rete pets that interdigitate with the expansile spindle cell population. In segmental regions, the stratum granulosum is prominent and contains many large and irregularly shaped keratohyalin granules. Few keratinocytes within the stratum spinosum, stratum granulosum, and extending into the stratum corneum are rounded, and have abundnant lightly basophilic cytoplasm and large, vesiculate to open faced nuclei.

Additional Findings: Immunohistochemistry demonstrated strong nuclear immunoreactivity for papillomavirus antigen in scattered cells in the stratum granulosum and corneum.

Diagnosis: Bovine aural fibropapilloma

Comment: While the histopathologic findings in this case are classic for a papillomavirus associated fibropapilloma, this case is particularly interesting from an epidemiologic perspective as it raises questions about the source of infection and the pathogenesis of the lesion. In humans, tattoo-associated verruca vulgaris have been described, with latency periods ranging from 2-12 months. Proposed pathogeneses include inoculation of virus through contaminated ink or tattoo instruments, contamination of the tattoo site from the artist's saliva, or irritation of pre-existing regions of subclinical or latent papillomavirus infection. Upon further investigation in the current bovine case, at least 14 of the 107 calves that were tattooed on the same day developed similar lesions confined to and covering the entire tattooed regions. For disinfection, 1:3 sodium hypochlorite to water was applied to the ear prior to tattooing and to the head gate, numbers, and tattooer between animals, and hands were disinfected; however, the ink roller was not disinfected between animals. We hypothesize that the act of tattooing served to inoculate papillomavirus into the epidermis and dermis, and that the ink or the ink roller may have been a source of contamination.

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- 2. Wanat KA, Tyring S, Rady P, Kovarik CL. Human papillomavirus type 27 associated with multiple verruca within a tattoo: report of a case and review of the literature. *Int J Derm* 2014; 53: 882–884.

Case 3 First report of *Pseudocowpox virus* infection in an American bison (*Bison bison*)

Vinay Shivanna, Giselle Cino, Chanran Ganta, Douglas Marthaler Kansas State Veterinary Diagnostic Laboratory, Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas

Signalment and History: A 7-year-old female bison was euthanized for declining condition and sores on vulva and udder.

Gross findings: There were multifocal raised, keratinized plaques (0.5–2cm) covering the skin of the ventral tail, perineum, caudoventral abdomen, udder, both inguinal recesses, and the medial aspects of both thighs. Distal to the thighs, the plaques became gradually fewer and smaller in size (0.2–0.5cm). Smaller papules (0.2–0.5cm) also covered both axillae and the hind limbs distal to the thigh. No gross lesions were present in reminder of the tissues examined.

Microscopic findings: Multiple sections of the keratinized skin plaques examined consistently showed moderate epidermal hyperplasia with elongated rete pegs and marked parakeratotic hyperkeratosis with crusts of degenerate neutrophils and cell debris. Multifocally, few epithelial cells within the stratum spinosum and stratum corneum have undergone ballooning degeneration and occasionally contain eosinophilic intracytoplasmic inclusion bodies (3-5µm Bollinger body).

Ancillary testing: Parapoxvirus was confirmed by qPCR (Ct 18.6) on skin, by negative stain ElectronMicroscopic examination of skin suspension, and by metagenomic analysis. Skin samples were negative for BVDV by real-time PCR and immunohistochemistry. Sequencing and phylogenetic analysis based on *B2L* envelope gene showed that the bison parapox shared 100% identity with bovine pseudocowpox virus.

Diagnosis: Dermatitis, proliferative and erosive, multifocally extensive, severe with ballooning degeneration and occasional intracytoplasmic eosinophilic inclusion bodies and crusting.

Comments: The gross and histologic lesions are characteristic of poxvirus infection². Further molecular analysis characterized the virus as pseudocowpox virus. The genus *Parapoxvirus* (family *Poxviridae*), characterized by ovoid virion structure is composed of *Pseudocowpox virus*, *Orf virus*, *Bovine popular stomatitis virus* and *Parapoxvirus of Red deer in New Zealand*. Pseudocowpox virus infection in bovine is generally a mild, self-limiting infection with papules and scabs on teats or udder¹. The occurrence of a severe pseudocowpox virus (in the absence of BVDV) that probably led to deterioration in the health of bison is of a concern. Parapoxviruses are zoonotic, causing cutaneous papules in humans. Identification of new susceptible hosts sheds light on the viral evolution and might have economic significance to bison industry.

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- 2 Mauldin EA, Peters-Kennedy J: Chapter 6 Integumentary System Maxie, M. Grant *Jubb, Kennedy & Palmer's Pathology of Domestic Animals: Volume 1 (Sixth Edition)*: W.B. Saunders; 2016: 509-736.e501.

Case 4 A Case of Camelid Dermatosis

Loni Schumacher¹ and Adam Copeland²

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Signalment and History: An 11-year-old female alpaca had a history of oral lesions of one year. Lesions developed in the corner of the mouth and recently progressed to ulcers, scabs, and discoloration involving all lip margins. A complete biopsy punch was submitted for further examination.

Microscopic Description: There is marked, diffuse, hyperplasia of the epidermis with prominent rete ridges, thickening of the stratum spinosum (acanthosis), and mild intercellular edema. Scattered throughout the layers of the epidermis are few, individualized, apoptotic keratinocytes that are shrunken with pyknotic nuclei and have bright eosinophilic cytoplasm often surrounded by one or two lymphocytes (satellitosis). The basement membrane contains segmental areas of vacuolation (subepidermal vacuolation). Multifocally infiltrating the superficial dermis, extending along the dermoepidermal junction, and surrounding superficial dermal blood vessels and adnexa are low numbers of lymphocytes, plasma cells, fewer neutrophils, and rare eosinophils. Adhered serocellular crusts approximately 3-4 mm thick are composed of compact lamellations of keratin with or without retained nuclei (parakeratotic and orthokeratotic hyperkeratosis), keratin lakes, neutrophils, and enmeshed coccobacilli bacteria colonies.

Diagnosis: Lymphoplasmacytic superficial dermatitis, moderate, chronic, with marked acanthosis, parakeratotic and orthokeratotic hyperkeratosis, and serocellular crusts

Comments: Microscopic lesions are suggestive of idiopathic nasal/perioral hyperkeratotic dermatosis or 'munge'. This is a poorly understood condition, which primarily affects younger camelids¹; however, all ages are susceptible. Nasal, perioral, periaural, and/or periocular areas can be affected with occasional involvement along the bridge of the nose². A more generalized condition is referred to as idiopathic necrolytic hyperkeratosis (INNH or 'generalized munge'). Lesions consist of thick, adhered crusts of parakeratotic and orthokeratotic hyperkeratosis, along with epidermal necrosis, edema, and mixed perivascular inflammation². In this case, there were also features of an autoimmune disease; however, lesions were chronic and there was a large amount of superficial bacteria. Differentials include infectious causes of dermatitis, arthropod/insect bites, or zinc-responsive—all of which, according to some², are thought to trigger this disorder. Regardless of the cause, spontaneous regression may occur but often treatment with antibiotics, topical antiseptics, glucocorticoids, and zinc are used in various combinations³. Interestingly, follow-up revealed marked improvement after several days of scrubbing affected areas with povidone iodine spray.

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- 2. Scott DW, Vogel JW, Fleis RI, Miller WH, Jr., Smith MC. Skin Diseases in the Alpaca (Vicugna pacos): A Literature Review and Retrospective Analysis of 68 Cases (Cornell University 1997-2006). *Vet Dermatol*. 2011;22(1):2-16.
- 3. Fowler ME. Medicine and Surgery of South American Camelids: Llama, Alpaca, Vicuna, Guanaco: Iowa State University Press.; 1998.

Case 5 Nasal Rhinosporidiosis in a Dog

Ryan Taylor, Wes Baumgartner,

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Clinical History: This is a seven year old, female spayed German shepherd that presented to the Mississippi State University College of Veterinary Medicine for an approximately two month duration of sneezing blood. A CT revealed a focal, soft tissue mass within the right nasal passage. Rhinoscopy revealed a reddened bulbous, soft tissue, multilobulated mass with small, well-demarcated, white nodules.

Histopathology:

Right nasal mass: The nasal turbinates are diffusely and irregularly expanded by intense inflammation in association with a fungal organism, resulting in loss of bony tissues. Large numbers of endosporulating sporangia ranging from 10-500 microns wide are scattered throughout the stroma; juvenile sporangia have central nuclei with amphophilic granular material. With maturity, immature endospores accumulate and the sporangial wall changes from hyaline pink to light blue. Mature sporangia exhibit progressive endospore maturation with centrally located mature, botryoid endospores. Many sporangia are ruptured, and are surrounded by many neutrophils and large macrophages. Intervening stroma is populated by large numbers of plasmacytes, lymphocytes and neutrophils, all in a densely collagenous matrix with many small caliber blood vessels. The epithelium is hyperplastic, stratified, and squamous. Mature sporangia are seen to discharge endospores onto the surface.

Morphologic Diagnoses:

Right nasal cavity: Rhinitis, pyogranulomatous, with mesomycetozoan sporangia (consistent with *Rhinosporidium seeberi*), chronic, locally extensive, severe

Discussion:

The morphological characteristics of this organisms are consistent with *Rhinosporitium seeberi*. It is endemic in India, Sri Lanka, Argentina, and found sporadically in other parts of the world. In the United States, *R. seeberi* is usually found in the southern states in aquatic environments. This is a rare cause of rhinitis in dogs, and infection has been reported in other vertebrates, including humans. It is thought to be an aquatic protistan (mesomycetozoea), but classification is controversial. Infection is thought to occur after traumatized mucus membranes come in contact with stagnant water infected with endospores. Disease in humans is reported in arid regions, suggestion possible airborne spore transmission. Surgical removal of the polyps are the treatment of choice. The prognosis for canine rhinosporidiosis is very good if the nasal polyp can be completely excised. In this case, the lesion was debulked, and the patient was placed on dapsone. Three month post-surgery, there has been no relapse in clinical signs and no evidence of regrowth.

References:

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Case 6 Pleuropneumonia in a Pig

Chris L. Siepker, Corrie Brown

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SIGNALMENT: Nine-month-old, black and tan, Berkshire barrow

History: One pig out of nine on pasture died following an episode of acute respiratory distress. **Gross Necropsy Findings:** Covering the visceral organs of the pleural cavity was 250 ml of a dark, serosanguinous fluid. The right caudodorsal lung lobe was extensively distended, firm, and mottled pale tan to dark red with hemorrhage. On cut surface there were large, coalescing areas of necrosis, characterized by pallor, firm parenchyma and hemorrhage. The interlobular septa were multifocally expanded by a pale tan, gelatinous material. Pale tan to yellow, friable, fibrin tags were multifocally adhered between the visceral and parietal pleurae on all lung lobes. The left caudodorsal lung lobe was soft, spongey, and diffusely dark red. Within the bronchioles and bronchi were large numbers of slender. 1 cm in length, pale tan adult nematodes, entrapped within mats of thick mucus. The tracheobronchial lymph nodes were markedly enlarged (up to 4 cm x 4 cm x 2 cm) and mottled dark red to pale tan. Extending from the carina to the larynx was abundant, off-white to pink foam. Externally, large numbers of live, 2-3 mm long, dark brown to black, sucking louse were present on the skin of the pig. Coiled within the papillae at the base of the tongue were numerous 0.5 cm to 1 cm, thin, pale tan nematodes. **Histopathology Findings:** The visceral pleura of the lungs was extensively elevated by haphazardly arranged strands of fibrin, degenerative neutrophils and some hemorrhage. In some sections, the alveoli, bronchioles, and bronchi are infiltrated by large numbers of inflammatory cells and necrosis. Alveoli are filled with abundant viable and degenerative neutrophils with variable amounts of fibrin. Wellcircumscribed areas of necrosis coalesce, comprised of strands of eosinophilic fibrin and neutrophils with elongate to streaming nuclei. Within mats of fibrin are bacteria, comprised of 1-3 um, gramnegative coccobacilli. Bronchioles and bronchi contain large numbers of adult nematode parasites. Nematode larvae and eggs are scattered within the surrounding alveoli.

Final diagnosis: Fibrinonecrotic pleuropneumonia, suppurative, subacute, regionally extensive, severe, with bacteria and intrabronchial nematode parasites

Ancillary diagnostics: Pasteurella multocida was cultured from both fresh lung tissue and a tracheobronchial lymph node. Fresh lung tissue was positive for *Mycoplasma* spp. (Ct of 21) and negative for Porcine Reproductive and Respiratory Syndrome virus (PRRSV) by PCR. Parasites identified on fecal floatation include; *Trichuris suis*, *Eimeria* spp., *Metastrongylus* spp., and *Trichostrongylus spp.*

Comments: Pasteurella multocida is often considered a "secondary" invader or component of the porcine respiratory disease complex (PRDC). P. multocida is often found in conjunction with other respiratory pathogens, such as PRRSV and/or Mycoplasma hyopneumoniae, the causative agent of enzootic pneumonia. In this case large numbers of bacteria were seen adjacent to areas of necrosis, consistent with P. multocida. P. multocida often results in a dry pleuritis with fibrinous adhesions, compared to Actinobacillus pleuropneumoniae which is considered to produce lesions which are more wet or moist. Additionally, there were large numbers of parasites within the bronchioles, consistent with Metastrongylus spp. which would have further exacerbated respiratory disease in this pig. M. apri is the most common lungworm seen in swine throughout the world, and most commonly are found in the diaphragmatic lung lobes. Numerous other ecto-and endoparasites (Haematopinus suis, Trichuris suis, Gongylonema spp., and Balantidium coli) were observed in this pig.

References:

¹Zimmerman J, Karriker L, Ramirez A. *Diseases of Swine*. 10th ed. 2121 State Avenue, Ames, Iowa 50014, USA: Blackwell Publishing, 2012.

Case 7 Paraquat Toxicity in a Dog

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Signalment and History: A 2.5 year old, female German Shorthair Pointer presented to the VHC for inappetence and vomiting. Radiographs were performed revealing subcutaneous emphysema, pneumomediastinum, and pneumothorax. The animal became increasingly dyspneic and was euthanized the following week due to poor prognosis.

Gross Findings: Approximately 15 mL of clear, serous fluid was collected from the pleural cavity. The lungs were diffusely and moderately edematous, oozing abundant serosanguinous fluid on cut section. Regionally extensive, multifocal to coalescing pulmonary hemorrhage affected 80% of the lung. The caudal third of the trachea and main bronchi contained a moderate amount of red-tinged froth.

Microscopic findings: Lung: Diffusely, most alveoli are prominently conspicuous due to thickened walls, lined either by numerous plump cuboidal epithelium (type II pneumocyte hyperplasia) or deeply eosinophilic, fibrillary material (adherent fibrinous exudate). Much of the pulmonary interstitium is expanded by scant fibrous connective tissue. Many alveoli are partially filled with hemorrhage and multifocally, alveoli appear fused forming larger, ectatic alveolar spaces (alveolar emphysema). Throughout, mixtures of edematous, fibrin-rich fluid fills alveolar spaces mixed with moderate numbers of alveolar macrophages, fewer multinucleated giants cells, lymphocytes and plasma cells and rare neutrophils. The peribronchial and bronchiolar connective tissue is distended by edema and/or hemorrhage. The pulmonary vasculature is diffusely and markedly congested. The visceral pleura is often lined by plump, cuboidal mesothelial cells (reactive mesothelium).

Diagnosis: Lung: Pneumonia, interstitial, fibrinonecrotizing, subacute to chronic, diffuse, severe with type II pneumocyte hyperplasia, hyaline membranes, hemorrhage, edema, and reactive visceral pleural mesothelium.

Comment: The animal came from a farm where the use of Paraquat was used by the land-lord. A sample of serum was submitted to Iowa State University for GCMS screen yielding negative. Due to the rapid excretion of the toxin (almost 100% within 24 h through urine) and the timeframe in which the animal had been hospitalized after presumptively being exposed to the herbicide, it is to be expected to be negative. Nevertheless, the morphological changes are consistent with the pneumotoxicant. Paraquat, a quaternary hydrogen compound, is a highly toxic herbicide, banned in 32 countries in the world that may cause fatal, acute diffuse alveolar damage if inhaled or ingested. The toxin alters the redox cycling of the type I pneumocytes, causing oxidant injury through the depletion of NADPH and glutathione and resulting in severe necrotizing interstitial pneumonia with prominent type II pneumocyte proliferation in subacute to chronic cases.

References

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Case 8 Pneumocystis-associated pneumonia in a cavalier King Charles spaniel dog

Gordon Ehrensing, Kurt Williams, and Dodd Sledge Michigan State University Veterinary Diagnostic Laboratory, Lansing, MI

Signalment and History: A 3-year-old female spayed cavalier King Charles spaniel dog had a greater than 1 month history of progressive respiratory disease characterized by persistent tachypnea and dyspnea. Thoracic radiographs revealed a diffuse interstitial pulmonary pattern. Clinical signs did not improve following medical management including antibiotics, and euthanasia was elected.

Gross Findings: The lungs were diffusely rubbery to firm, non-collapsed, and had distinct rib impressions. All lobes were mottled pink to red and were extensively stippled by numerous pinpoint to 1 mm, minimally raised tan foci. There is a large volume of foam throughout the trachea.

Histopathologic Findings: Throughout the lungs, there is extensive filling of alveolar spaces by abundant eosinophilic flocculent proteinaceous material and numerous large foamy alveolar macrophages. Alveoli are lined by plump cuboidal type II pneumocytes. Septae are markedly expanded by fibrosis, edema fluid, fibrin, and multifocal aggregates of lymphocytes, fewer plasma cells, and occasional degenerate neutrophils. Peribronchial lymphoid aggregates are prominent. Pleural surfaces are mildly expanded by fibrin, additional loose aggregates of lymphocytes, and dilated lymphatic vessels. Within the mediastinal lymph nodes, sinuses are expanded by moderate numbers of foamy macrophages, fewer neutrophils, and edema fluid.

Additional Testing: Additional sections stained with Grocott-Gömöri's methenamine silver (GMS) stain highlight the thick wall of myriad 5-8 µm in diameter intracellular and extracellular ovoid fungal cysts within alveoli.

Comments: The gross and histologic findings including the histologic identification of GMS-positive intra-alveolar fungal cysts were consistent with pulmonary pneumocystosis in this dog. *Pneumocystis* spp. are yeast-like ascomycete fungi which classically produce pneumonia in immunocompromised people and animals. The binomial name *P. carinii* is frequently over-applied in veterinary medicine to any case of pneumocystosis. *Pneumocystis* spp. are stenoxenous organisms, and five species have been formally characterized to date in humans and rodents. In addition to its pulmonary form, extrapulmonary pneumocystosis affecting a variety of organs has been reported in humans as well as in one dog. Several breeds of dog, including the cavalier King Charles spaniel (CKCS), appear predisposed. Hereditary deficiencies in immunoglobulin levels have been described in CKCS which suggest a breed-specific humoral impairment predisposes these animals to spontaneous infection by several pathologic organisms.

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Case 9

Infraorbital swelling caused by Mycoplasma gallisepticum and Avibacterium spp. coinfection in peafowl (Pavo cristatus)

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Signalment and History: A flock of peafowl in Oklahoma had experienced chronic respiratory disease for several months. Seven peafowl were maintained on a farm that also had 35 backyard chickens. Wild birds such as corvids, sparrows, doves, and robins were frequently noticed on the farm. Four peafowl were reported to have swellings beneath one or both eyes, resulting in impairment of vision. One peacock had died due to progression of disease. Delayed and decreased egg production were noted in the peahens. Infraorbital swellings from two peafowl were removed and submitted to OADDL for testing.

Gross Findings: At surgery, the infraorbital cystic swelling was noted to contain tan-yellow, inspissated exudate. The exudate was arranged in concentric laminations on cut surfaces.

Histopathologic Findings: The provided tissue represents a swollen infraorbital sinus from a peahen that was removed by surgery. Microscopically, the tissue is consistent with a distended and fibrotic cyst that contains exfoliated epithelial cells interspersed with cellular debris, macrophages, degenerate heterophils, and colonies of coccobacilli. Loss of cilia, epithelial attenuation, and squamous metaplasia are observed in most of the lining mucosa. A small area of remaining respiratory epithelium shows goblet cell hyperplasia and hypersecretion. The wall of the cyst is thick and composed of mature fibrous tissue with scattered lymphocytes, plasma cells, and heterophils.

Diagnosis: Marked, chronic-active, diffuse, heterophilic and mixed-cell sinusitis with associated fibrosis, intralesional bacteria and mucosal squamous metaplasia.

Additional Findings: The exudate from the infraorbital cyst was positive by polymerase chain reaction for *Mycoplasma gallisepticum*. A heavy growth of *Avibacterium* spp. was also isolated from the exudate by culture, and the 16S rDNA sequencing revealed 99% homology to multiple *Avibacterium* spp., including *A. paragallinarum*.

Comments: The lesions in this case are consistent with chronic-active sinusitis associated with *Mycoplasma gallisepticum* and *Avibacterium* spp. coinfection. Infection of *M. gallisepticum* can cause significant respiratory disease in birds and is well-documented in chickens and turkey. *M. gallisepticum* may predispose the birds to other infections and plays a role in the development of polymicrobial, chronic respiratory disease. Infection of *A. paragallinarum*, the etiology of an acute upper respiratory disease, Infectious Coryza, is also well-recognized in chickens. Both pathogens have been associated with growth retardation, mortality, and economic loss in poultry, but they are seldom reported in peafowl.¹⁻²

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Case 10 Ocular Cytauxzoonosis in a Domestic Cat (Felis catus), Manhattan KS

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Signalment and History: An approximately 1 year old, 1.9 kg, intact female, domestic shorthair cat presented to necropsy after a 2 day history of jaundice and respiratory distress.

Gross Pathology: The cat was in good body condition with adequate muscling, subcutaneous and intraabdominal fat. The sclera, adipose and subcutaneous tissue were diffusely icteric. The thoracic cavity contained 30 mL of serosanguinous fluid. The lungs were wet, heavy, mottled pink with disseminated petechial hemorrhages. The submandibular, retropharyngeal, tracheal, bronchial, and mesenteric lymph nodes were enlarged and dark red. The spleen was dark red, oozed dark red fluid on cut section, and moderately enlarged (9.1 g, 4.8% body weight). The liver had a prominent reticular pattern and had mottled dark red spots that were more prominent in the periphery of all lobes. Both kidneys had randomly distributed capsular, cortical, and medullary petechial hemorrhages. The urinary bladder mucosa also had mild, multifocal petechial hemorrhages. A 10 cm segment of large colon contained red tinged feces and mildly congested mucosa. Both ovaries were small and inactive.

Histopathology: Within, the periocular fat, extraocular muscles, third eyelid, conjunctival, scleral, choroidal, retinal, ciliary body, and iridial blood vessels, there are intrahistiocytic schizonts. The bulbar conjunctiva, third eyelid, and uvea additionally have mild to moderate perivascular mononuclear inflammation that disseminates through the connective stoma and contains occasional intrahistiocytic schizonts and a few organisms escaping from ruptured macrophages. The bulbar apposing surface and submucosa of the third eyelid was most severely affected; it is additionally infiltrated by extensive, mononuclear inflammation with prominent lymphoid follicles.

Diagnosis: Eye: Intravascular and perivascular histiocytosis with intrahistiocytic *Cytauxzoon felis* and mild to moderate, mononuclear conjunctivitis and uveitis

Comments: Domestic cats are an aberrant host for *Cytauxzoon felis*, a tick-borne (*Amblyomma americanum*), hematogenous, protozoan parasite common in the Southeast and South-central United States. During acute infection, sporozoites replicate within monocytes and macrophages, and form schizonts. The unchecked schizont proliferation results in profound macrophages distention and accumulation in peripheral vasculature where they cause systemic, vascular obstruction and perivascular inflammation.

Occluded alveolar, hepatic, renal, and splenic circulation is the most common cause of patient morbidity; however schizonts can infect any vascularized tissue. In this cat, the eye demonstrated the remarkable extent of *C. felis* infiltration; however, collateral retinal and ciliary arterial circulation protected the eye from ischemic necrosis. Ocular *C. felis* infection can result in markedly dilated iridal stromal vessels, bulbar conjunctival and retinal hemorrhage, and vascular congestion that is visible during ophthalmic examination.

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Case 11 Sarcocystis Induced Abortion in a Mule Deer Fetus

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SIGNALMENT and HISTORY: This full-term, stillborn, male, fetus, mule deer (*Odocoileus hemionus*) was part of a mule deer mortality study conducted by the University of Nebraska-Lincoln in conjunction with the Nebraska Game and Parks Commission. The stillborn fetus was found on June 5, 2018. The fetus had a twin that appeared healthy.

GROSS NECROPSY FINDINGS: The crown to rump length was 54 cm. The hooves were covered in eponychium. The lungs were firm and rubbery and sank in 10% neutral buffered formalin. The abomasum contained gelatinous, red to yellow, serosanguinous fluid.

HISTOPATHOLOGIC FINDINGS: Brain: Occasional, loose aggregates of lymphocytes, macrophages, and neutrophils are scattered within the choroid plexus and leptomeninges. Scattered throughout the brain, but most concentrated in the brainstem, are frequent nodules of microglia, astrocytes, and lymphocytes associated with necrotic neuroparenchyma. Moderate numbers of lymphocytes and macrophages surround blood vessels throughout the neuroparenchyma. Occasional endothelial cells of multiple small blood vessels contain 15-25-µm diameter schizonts with numerous basophilic, radially arranged merozoites with a single nucleus. The schizonts often bulge into blood vessel lumens. Similar foci of inflammatory cells with associated schizonts are scattered throughout the myocardium.

FINAL DIAGNOSIS: Brain: Necrotizing lymphohistiocytic meningoencephalitis and myocarditis, multifocal, subacute, severe, with intraendothelial protozoal schizonts consistent with *Sarcocystis* sp.

COMMENTS: Sarcocystis spp. are protozoal organisms that have been linked to abortions, stillbirths, and neonatal deaths in intermediate hosts, including cattle, goats, sheep, pigs, and occasionally, deer. The prevalence of *Sarcocystis*-induced disease in free-ranging deer populations, and the resulting population impacts, are unknown. The parasite has an obligatory two-host life cycle. Sexual reproduction occurs in the intestines of carnivorous definitive hosts, including dogs, coyotes, foxes, wolves, and raccoons. Oocysts are then defecated into the environment, where they are ingested by herbivore intermediate hosts, in which asexual phases of replication occur in muscle or nervous tissue. Traditionally, infections with Sarcocystis spp. in intermediate hosts are not considered pathogenic, and typically manifest as thin-walled cysts ("sarcocysts") embedded in skeletal and cardiac muscle. Heavy infections can result in weight loss, anemia, abortion, or death. The pathogenesis of Sarcocystis-induced abortion is not definitively known, but proposed causes include maternal anemia resulting in fetal hypoxia, premature induction of parturition induced by maternal production of PGF_{2a} from damaged endothelial cells, thrombosed vessels, necrotizing endometritis, or necrotizing inflammation of the fetus. Multifocal necrosis surrounded by mononuclear cells may be seen in affected organs. Microscopic lesions must be differentiated from other protozoal causes of abortion, including Toxoplasma gondii and Neospora spp., which can be difficult based solely on microscopic lesions. Microscopic schizonts with radially-oriented merozoites and tropism for endothelial cells led to the presumptive diagnosis of Sarcocystis-induced abortion in this case. Immunohistochemistry for Sarcocystis spp. was negative, posing a diagnostic challenge. Diagnosis of Sarcocystis sp. was confirmed with polymerase chain reaction and genetic sequencing. This organism was most similar to S. grueneri in reindeer from Norway (95.5% similarity). The population-level impacts of Sarcosystis infection in wild cervids are not currently known; however, increased vigilance among wild populations may bring awareness to this and other infectious causes of mortality and low recruitment in cervids.

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Case 12 Disseminated Protothecosis in a Dog

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SIGNALMENT: 5-year-old male neutered Pomeranian

History: This dog presented to MSU-CVM Neurology service approximately 1 month ago prior for seizures, ataxia and right head turn. MRI at that time showed obstructive hydrocephalus secondary to a narrowing at the mesencephalic aqueduct. After immunosuppressive therapy, the neurologic signs were not alleviated despite initial improvement. The patient died suddenly after being walked outside during hospitalization.

Gross Necropsy Findings: There is mild cerebellar herniation through the foramen magnum. The lateral ventricles are moderately dilated and the ventricular surfaces are roughened with multiple 0.1-0.3 cm raised tan plaques. Widely disseminated white pinpoint foci are present throughout the liver, kidneys, and the myocardium.

Histopathology Findings (Brain section): The lateral ventricle is moderately dilated. Chronic inflammation effaces the periventricular neuropil, ependyma and choroid plexus; in addition the leptomeninges, and random areas in the neuropil are similarly affected. Epithelioid macrophages form nodules with occasional necrotic centers that contain small numbers of eosinophils, fewer lymphocytes, and many algal organisms. Sporangia are round to oval and 8-20 um wide with a clear 2 um thick wall, and basophilic internal material or multiple (2-8) wedge-shaped endospores; they are often extracellular and rarely intrahistiocytic. The associated neuropil is hypercellular with gliosis, many rod cells, and neuronal satellitosis. Perivascular cuffs of epithelioid macrophages and fewer lymphocytes are evident. **Final Diagnosis:** Meningoencephalitis and ependymitis, granulomatous and necrotizing, severe, with intralesional algal organisms (*Prototheca sp.*)

Comments: *Prototheca* sp. is a ubiquitous, saprophytic, unicellular algal organism that is commonly isolated from sewage and animal waste. The organism is closely related to *Chorella* sp, and both genera replicate via endosporulation. The two known pathogenic species are *Prototheca zopfii* and *P. wickerhamii*, and disease has been reported in variety of mammalian species including cattle, dogs, cats, and humans. Animal exposure to the organism is usually due to contamination of water, soil or food. *Prototheca* typically does not infect animals, save in cases of immunosuppression. Organisms can infect the skin or gut mucosa through wounds, and in permissive hosts can spread throughout the body.

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Case 13 Intravascular Lymphoma in a Cocker Spaniel Dog

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Signalment and History: A 7-year-old castrated male Cocker Spaniel dog was euthanized following a 5-month history of progressive paraparesis and seizures.

Clinical MRI Findings: Brain MRI revealed multifocal asymmetric intra-axial ill-defined lesions which were T2 hyperintense and some of which displayed susceptibility artifacts on T2*-weighted images (consistent with hemorrhage). Two separate T2 hyperintense intramedullary lesions were associated with the spinal cord, one located at T10-11 and one at L1-2.

Gross Findings: A 1x1 cm area of hemorrhage was on the surface of the left frontal cortex and a 1.2x1 cm area of hemorrhage with multifocal 2 mm yellow-white specks was in the left ventral piriform lobe. The heart was diffusely pale tan and the epicardial vessels were congested.

Microscopic Findings: Small to medium sized vessels in the cerebral piriform lobe, hippocampus, and thalamus are filled with intraluminal, pleomorphic, neoplastic round cells with round nuclei, clumped chromatin, and moderate amounts of eosinophilic cytoplasm, consistent with lymphocytes. Nuclei are occasionally indented. There are 0-2 mitotic figures per 400X field. Vessel walls in the piriform lobe are often expanded by bright eosinophilic homogenous material (hyalinosis), or disrupted by fibrin and karyorrhectic debris (necrosis). Hemorrhage, numerous large astrocytes with vesicular nuclei, and glial cells surround affected vessels. There is vacuolation and cavitation of the surrounding neuropil.

Additional Findings: Neoplastic lymphocytes have intermediate to strong cytoplasmic and occasionally strong membranous immunoreactivity to CD3 monoclonal antibody. Vessels throughout the myocardium, renal cortex, and cervical and lumbar spinal cord contain neoplastic intraluminal lymphocytes.

Final Diagnosis: Cerebrum, spinal cord, heart, kidney. Intravascular T cell Lymphoma **Comment:** Intravascular lymphoma is a rare, progressive, fatal disease characterized by large, pleomorphic neoplastic lymphocytes proliferating within vessels, without a primary extravascular mass or leukemia. Intravascular lymphoma has been described in humans, dogs, cats, and a horse. In dogs, lymphocytes are most often T cells or non-T, non-B cells of undetermined lineage, and the central nervous system and lungs are most commonly affected. Dogs are most often presented with neurologic disease, and death or euthanasia generally occurs after 4-6 weeks. The prolonged clinical course in this dog was unusual. Vascular occlusion, necrosis, and subsequent hemorrhage and infarction have been described; and in this case were the cause of the MRI findings and cerebral hemorrhage seen grossly. The pathogenesis and source of neoplastic lymphocytes is unknown. In humans, neoplastic cells have been reported to lack the β_2 -integrin CD11a/CD18 (lymphocyte function antigen-1) or the common β_1 -integrin subunit (CD29), which both facilitate firm adhesion to the endothelium. Deficiencies in either molecule may explain the failure of diapedesis in this disease; however, similar deficiencies have not been reported in dogs.

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Case 14

Histiocytic sarcoma rising from the dorsal root ganglia in 2 locations of the spinal column of a dog

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Signalment and History: A 12 year old, female spayed Labrador Retriever mix presented to the Oklahoma State University Teaching Hospital for hindlimb paralysis of 9 days duration. The referring veterinarian prescribed a muscle relaxer, steroid, antibiotics and a gastric protectant, but the patient did not improve and was brought to the OSU VTH. On physical exam the patient was bradycardic, with a respiratory rate of 108 and SPO2 of 90-94. The patient exhibited bilateral hindlimb paralysis with no evidence of deep pain perception. Hindlimb reflexes were normal, but abdominal palpation revealed a large flaccid bladder. Radiographs showed moderate spondylosis of T2-T3 and T9-T13. The patient declined rapidly and humane euthanasia was elected.

Gross Findings: The hindlimb muscles were diffusely and moderately atrophied, but internal organs were otherwise within normal limits. Upon dissection of the spinal column, there were two (2) multifocal, oblong, pale to tan, multi-lobulated masses extending from the dorsal root ganglia which expanded the epidural space at the level of T3-T4 and the cauda equina. Each mass corresponded to a focally extensive region of grossly visible spinal cord compression.

Histopathologic Findings: The ganglia and adjacent epidural connective tissue overlying the spinal cord at the level of T3-T4 and the cauda equina was effaced by large sheets of neoplastic cells that vary from spindloid to polygonal in shape and were supported by a thin fibrovascular stroma. The cells were highly pleomorphic, with abundant amounts of eosinophilic cytoplasm. Nuclei were round to ovoid, with vesiculate chromatin, karyomegaly, and numerous multinucleated cells. Mitoses averaged 3-4 per single high powered field (400x). This neoplasm expanded to the point of compressing a focally extensive region of the spinal cord, which contained a large number of markedly dilated and brightly eosinophilic axons (spheroids), as well as numerous dilated myelin sheaths that contain large foamy gitter cells (digestion chambers). Within the gray matter, small numbers of scattered neurons are shrunken, with hypereosinophilic cytoplasm and condensed nuclei (neuronal necrosis).

Diagnosis: Multicentric epidural histiocytic sarcoma with myelin and axon (Wallerian) degeneration **Additional Findings:** Neoplastic cells stain diffusely positive with CD18 (histiocyte marker) and Iba1 (ionized calcium binding adaptor molecule 1; microglia/macrophage marker), and stain negative for S-100 and GFAP (neural tissue markers).

Comments: These results indicate a rare tumor composed of neoplastic cells of the macrophage lineage that we suspect arose from resident macrophages or microglia within the dorsal root ganglia. The expansile growth of this neoplasm directly caused compression and Wallerian degeneration of the spinal cord, resulting in the clinical sign of hindlimb paralysis.

Case 15 Dysautonomia in a Mixed breed Dog

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Signalment: An 11-week-old, male intact, mixed breed dog.

History: The dog was presented to the KSU Veterinary Health Center for weight loss, anorexia, vomiting, regurgitation, tenesmus, and lethargy. Referral radiographs revealed megaesophagus. Physical exam findings included non-responsive mydriatic pupils, poor anal tone, moderately distended urinary bladder, and crusting around the nose. Due to poor prognosis, the animal was humanely euthanized.

Gross necropsy findings: There was marked dilation of the esophagus up to approximately 2 cm in diameter, beginning at the tracheal bifurcation and extending to the stomach. The colon contained a large amount of feces. The lungs were diffusely and moderately edematous and congested.

Histopathology findings: Autonomic ganglia: Multifocally, neurons show characteristics of degeneration, necrosis and loss, with some or all of the following features: increased cytoplasmic eosinophilia, rounded cell body with loss of Nissl substance, variable vacuolation of cytoplasm with central chromatolysis, karyolysis, and paracentral or peripheral pyknotic nuclei. There are occasional aggregates of lymphocytes and macrophages that surround neurons with evidence of neuronal phagocytosis.

Final diagnosis: Autonomic ganglia: Neuronal degeneration, necrosis, and loss, moderate, multifocal. Condition: Canine dysautonomia

Comments: Dysautonomia is an idiopathic disorder that occurs in a number of species including dogs, cats, and horses. Cases have been described worldwide, however increased numbers of cases have been described in the Midwestern United States, particularly Kansas and Missouri.² Histopathologic changes include extensive chromatolysis and death of ganglion cells in various ganglia and central nervous system.^{1,2} In the dog the most commonly affected ganglia include the pelvic, mesenteric, and ciliary ganglia.¹ Clinical signs vary but are related to dysfunction of the sympathetic and parasympathetic nervous system as evidenced by the commonly observed clinical signs which include vomiting, regurgitation, decreased anal tone, mydriasis, decreased to absent pupillary light reflexes, and dysuria.² Findings at gross necropsy are related to similar dysfunction and include megaesophagus, fecal impaction, and aspiration pneumonia.² Interestingly, most affected animals tend to be young. In a review of dysautonomia, Harkin et al found a median age affected of 18 months with 77% (50/65) under 3 years of age and other studies cited in this review found mean ages of 14 and 18 months.² The cause of dysautonomia is unknown in dogs, but exposure to the outdoors/rural lifestyle, scavenging behavior, or toxins have been discussed as risk factors or potential causes. In horses and cats, *Clostridium botulinum type C* has been suggested as a potential causative agent.¹

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Case 16 Systemic Arteritis Associated with PCV3 Infection in Post-Weaning Pigs

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Signalment and History: Clinical cases of poor performance and non-specific symptoms such as, anorexia, weight loss, and occasionally respiratory disease in post-weaning pigs were sporadically reported in different swine herds.

Gross Findings: Necropsy performed on the farm reported no significant gross lesions.

Histopathologic findings: Histopathologic examination showed systemic lymphoplasmacytic and histiocytic arteritis most remarkably observed in the myocardium, spleen, kidney, and mesenteric vasculature. In affected vessels the inflammatory infiltrate was mainly distributed in the walls of blood vessels and perivascular areas, often with thickening of the tunica intima characterized by edema and focal hyperplasia.

Diagnosis: Lymphoplasmacytic and histiocytic arteritis in multiple organs, subacute, multifocal, severe.

Additional Findings: PCR for porcine circovirus 3 (PCV3) was positive with Ct values of 22-23. In situ hybridization (ISH) for the viral mRNA targeting ORF2 gene (open reading frame 2, encoding the viral capsid) showed co-localization of the probe to the lesions. Additionally, PCV3 was detected by ISH in lymphoid follicles of lymph nodes and in the white pulp of the spleen. Interestingly, lymphoid depletion, a classical lesion of PCV2 cases, was not consistently observed.

Comment: While a variety of endemic and opportunistic pathogens were occasionally detected by PCR and aerobic bacterial culture, myocarditis, systemic arteritis, and sometimes interstitial pneumonia were consistently observed, likely suggesting a viral etiology. Several important differential viral etiologies including PCV2, influenza A virus, porcine reproductive and respiratory syndrome virus, classical swine fever virus, pestivirus, foot-and-mouth disease virus, porcine parvovirus, West Nile virus and encephalomyocarditis virus were ruled out. Further studies using PCV3 specific PCR have indicated that this virus has been endemically distributed in the US swine population. Similar to diagnosing PCV2 cases, the diagnosis of PCV3-associated syndromes may require a combination of the following findings: (i) a comprehensive clinical evaluation of the herd, (ii) histological lesions, and (iii) detection of the virus. To date, experimental inoculation trying to reproduce clinical signs and lesions associated with PCV3 infection has not been reported. The presence of PCV3 mRNA associated with systemic arteritis and myocarditis however demonstrate the ability of this virus to replicate and amplify in a variety of tissues, and its potential role as a cause of clinical disease. Differentiation of PCV3- and PCV2-associated lesions has important management implications as there is no commercial vaccine for PCV3 and this agent continues to be detected across the globe. Furthermore, this serves as continued evidence for the importance of surveillance and characterization of pathogenesis for this agent.