Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2026-2027

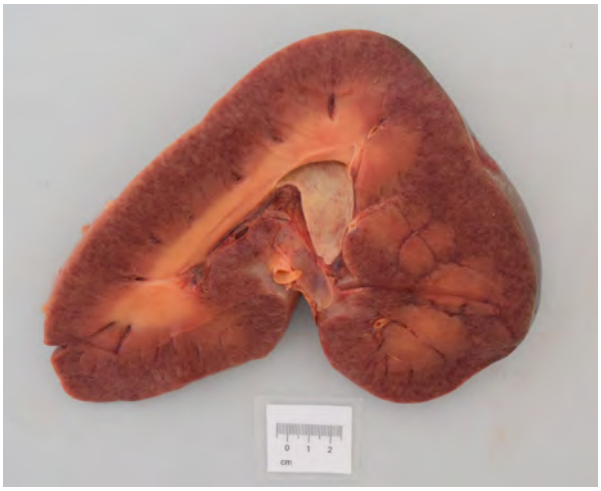
Conference #1 — 19 September 2026

CASE I:

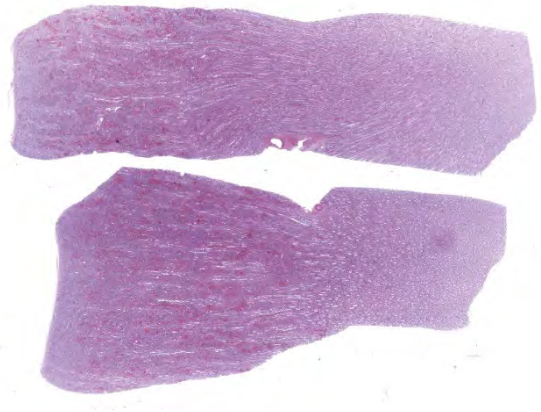
Signalment:
Two months old, male, Selle Français horse (Equus caballus)

History:
On 10.07.2024 the animal presented with acute colic, diarrhea and fever and was admitted to the clinic. Upon arrival, the foal was in a slightly reduced general condition but remained alert and continued nursing from the mare. Its body temperature had dropped to 38.4 °C, but the respiratory rate was increased to 40 breaths/minute. Further clinical examination showed icteric mucous membranes, increased pulmonary sounds bilaterally, mildly increased peristalsis, and profuse diarrhea. The foal did not urinate at all during its stay at the clinic, and no urine could be obtained even after catheterization. Thoracic ultrasound showed bilateral, severe comet trails, lung consolidation and mild pleural effusion. Abdominal ultrasound revealed amotile small intestines filled with gas and fluid, with thickened intestinal walls measuring up to 8 mm. The kidney appeared unremarkable, and the bladder could not be visualized.
Blood analysis revealed a severe azotemia (creatinine 1205 µmol/L) and electrolyte disturbances (Na 120 mmol/L, K 6 mmol/L, Cl 80 mmol/L), indicating severe renal damage. Pronounced hyperbilirubinemia (229.2 µmol/L) indicated hemolysis.
Leptospirosis was suspected and the foal was treated accordingly. The PCR test was positive for pathogenic Leptospira spp., confirming the suspected diagnosis. The condition of the foal worsened dramatically, and it died on 11.07.2024.

Gross Pathology:
The animal was in good body condition based on adequate skeletal muscle mass and adipose tissue stores. The mucous membranes and subcutaneous tissue, as well as the fibrous tissue in the various organs were diffusely discolored yellow. Bilaterally, the tarsocrural joints were markedly filled with yellow, clear fluid (synovia).



1-1. Kidney, foal: The surface of both kidneys were patchy and pale (*Photo courtesy of:* Institute of Animal Pathology, Vetsuisse Faculty – University of Bern www.itpa.vetsuisse.unibe.ch)



1-2. Kidney, foal: Two sections of kidney are submitted for examination. (HE, 6X)

The trachea contained white foam up to the upper third portion. The lung showed multifocal to coalescing, up to 0.3 cm in diameter, dark red petechiae and ecchymosis in all lung lobes, 60 % of the parenchyma was affected. Upon opening the heart, the left ventricle revealed multifocal, up to 0.3 x 0.3 x 0.2 cm in size, subepicardial and subendocardial hemorrhages, in total 20 % of the ventricle was affected.

The abdomen contained 20 ml of yellow, clear fluid. The liver was diffusely pale. Both kidneys adhered to the capsule focally and multifocally the surface of both kidneys were patchy and pale (Figure 1). In the pars glandularis of the stomach, along the marco plicatus was a focal, 14.0 x 7.0 x 0.1 cm in size, acute ulceration. The other examined organs were macroscopically unremarkable.

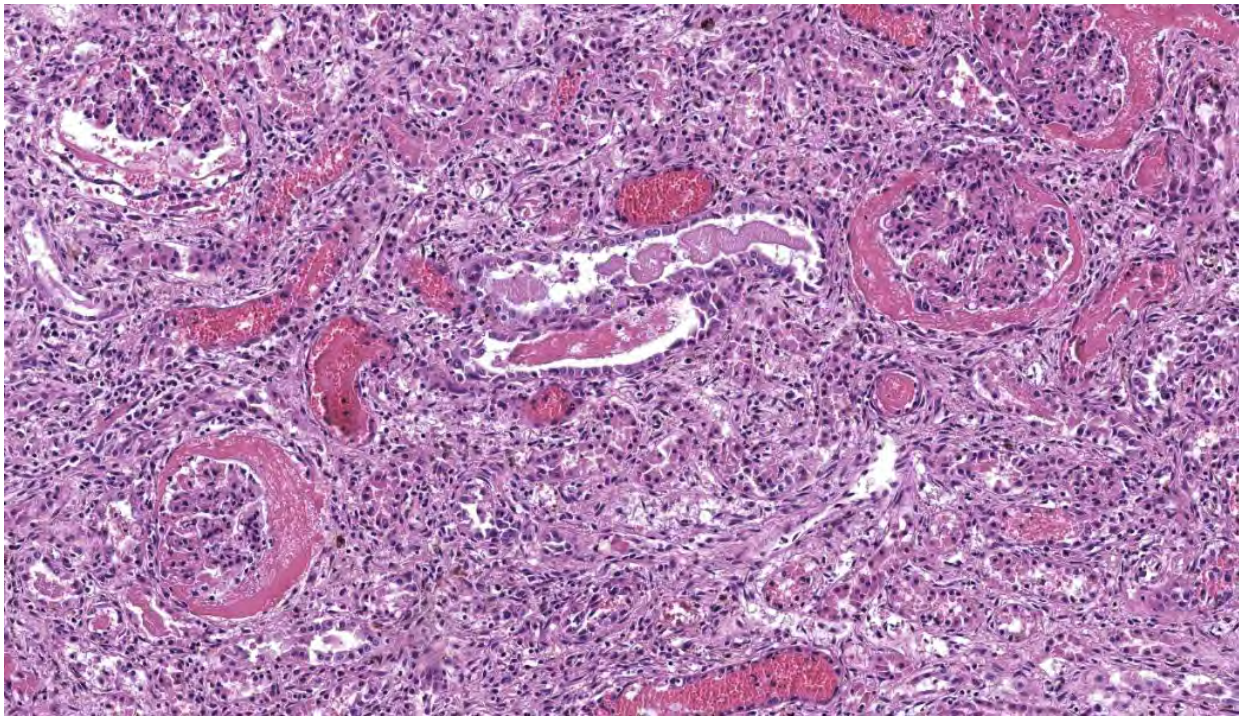
Laboratory Results:
The bacteriological examination was done at the Institute of Veterinary Bacteriology University of Bern.

- RT-PCR for pathogenic leptospires performed on kidney tissue tested positive.
- General cultural examination of the kidney revealed no bacterial growth.

Microscopic Description:
Kidney: Multifocally, up to 70% of the renal corpuscles are affected by a moderate to severe space-occupying accumulation of many extravasated erythrocytes, eosinophilic, fibrillar material (fibrin exudation), and few neutrophils within the urinary space and the mesangium. Few glomeruli are completely replaced by the before mentioned accumulation, partially with loss of continuity of the parietal layer of the Bowman's capsule. Many adjacent tubular structures are mildly dilated and filled with extravasated erythrocytes, eosinophilic, fibrillar material (fibrin), few neutrophils and macrophages. The epithelial cells of some tubules have lost cellular details and exhibit hypereosinophilia, karyorrhexis, and karyolysis (necrosis), with detachment from the basement membrane. Many adjacent blood vessels contain moderate amounts of eosinophilic, fibrillar material, which partially obstruct the lumen (fibrin thrombi). The interstitial space of the cortex is severely infiltrated with neutrophils, macrophages, lymphocytes and plasma cells. Multifocally, there are accumulations of few extravasated erythrocytes (acute hemorrhage). In the medulla, the interstitial inflammatory infiltrate is mild and mainly composed of lymphocytes. In the corticomedullary junction and in the medulla, some tubules contain eosinophilic, homogeneous material (hyaline urinary cast). The kidney is mildly congested.

Contributor's Morphologic Diagnoses:

1. Kidney: Severe, multifocal, acute, exudative glomerulonephritis
2. Kidney: Severe, acute, neutrophilic and histiocytic, tubulointerstitial nephritis with tubular necrosis, intravascular fibrin thrombi, intratubular urinary casts and interstitial hemorrhage



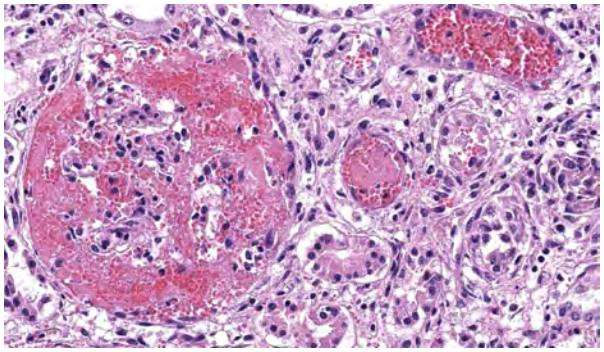
1-3. Kidney, foal: There are changes at all levels of the nephron with glomerular hypercellularity with and fibrin and hemorrhage within Bowman's space and adjacent tubules, and tubular epithelial necrosis and sloughing. There is expansion of the interstitium with loosely packed collagen and fibroblasts.

Contributor's Comment:

Leptospira spp. are obligate aerobic and gram-negative spirochete bacteria divided into distinct serovars,[1] Depending on the level of pathogenicity for animals and humans, they are divided into pathogenic, intermediate, or saprophytic.[2] One serovar is not specific to a single Leptospira species but is adapted to a specific host, known as the maintenance host. For instance, the serogroup bratislava has been associated with horses.[2] The host-adapted serovar may cause disease in its maintenance host or infect incidental hosts, albeit to a lesser extent. The infection may be subclinical, and the host becomes an asymptomatic carrier with persistent spirochetes in the proximal convoluted tubules of the kidneys, or less commonly in the genital tract.[1] The spirochetes are then continuously shed within the urine, allowing the transmission of the disease. Outside of the host, the spirochetes can survive in moist, warm (ideally 28°C), and neutral or mildly alkalinized conditions for weeks or even months.[1]

Leptospirosis is a spirochetal infection caused by pathogenic *Leptospira* spp. In farm and domestic animals, the serovars of *Leptospira interrogans* are an important cause of abortion and stillbirth and might induce an acute or subacute systemic disease (including septicemia, hepatitis, nephritis, meningitis).[1]

When an animal is exposed to *Leptospira* spp. in the environment, usually via urine or body fluid of carriers or contaminated water, the bacterium enters the body via mucous membrane or skin lesion, leading to leptospiremia. The spirochetes reach many different organs via the bloodstream, including the renal interstitial capillaries. There, they migrate through the endothelium into the interstitial spaces, where they reach the tubular lumens via migration through intercellular junctions of tubular epithelial cells. The spirochetes associate



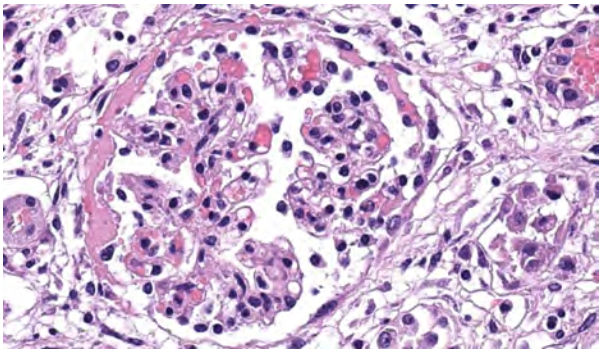
1-4. Kidney, foal: There is necrosis of capillary loops within glomeruli and abundant hemorrhage and polymerized fibrin with Bowman's space. The hemorrhage and fibrin is present in tubules.

with the microvilli of the tubular epithelium and are able to persist in the phagosomes of those cells, especially in the proximal and distal convoluted tubules. Usually, the leptospiremic phase lasts up to 7 days, as the organisms are cleared from most organs thanks to the host immune response (clearing via agglutinating and opsonizing antibodies). However, immunologically privileged sites, such as the proximal convoluted tubules, are spared, and the animal becomes a carrier.[1]

The leptospiremic phase is responsible for the acute or subacute systemic disease, and young animals are more commonly affected. Common clinical and pathological signs include fever, vasculitis (caused by inflammatory cytokine release), hemolytic anemia due to bacterial hemolysins or reaction of antibodies with leptospiral products on erythrocytes, hemoglobinuria, jaundice due to hemolysis or direct liver injury, pulmonary congestion, and occasionally meningitis.[1] Because of the localization and persistence of leptospires in the kidneys, acute tubular injury and interstitial nephritis are one of the main findings. The cause of degeneration and necrosis of the tubular epithelium is multifactorial and comprises direct toxic effects of the leptospires, hypoxia, free hemoglobin, and the concomitant interstitial inflammatory reaction[1].The inflammatory infiltrate might consist of neutrophils in the acute phase, as in our case, but usually macrophages, lymphocytes and plasma cells predominate (chronic lesion). The inflammatory cells are typically localized at the corticodullary junction. Not only the tubules and interstitium can be affected in acute leptospirosis, but also the glomerular structures.

Exudative glomerulonephritis, characterized by the abundant presence of extravasated erythrocytes, fibrin exudation, as well as fewer neutrophils in the urinary space, should be considered suspicious for leptospiral infection, especially in dogs.[3] In the postsepticemic phase, leptospiral infection can manifest itself as abortion, stillbirth or birth of an infected fetus may occur, even weeks to months after infection.[1]

In horses, serologic evidence of *Leptospira* spp. is widespread (reservoir hosts) [4] but the occurrence of acute disease is rare. Different serovars (including *bratislava*, *canicola*, *grippotyphosa*, *hardjo*, *icterohaemorrhagiae*, and particularly *pomona*) have been associated with such acute disease, leading to fever, ano-



1-5. Kidney, foal: In less affected glomeruli, there are fibrin thrombi within glomerular capillaries and only a small amount of hemorrhage and fibrin in Bowman's space. (HE, 1060X).

rexia, acute kidney injury, liver disease accompanied by icterus, epistaxis and acute respiratory distress due to pulmonary hemorrhages.[5] Foals are more susceptible and can develop fatal hepatic and renal diseases. The chronic form of leptospirosis is mostly associated with abortion (associated with serovars *pomona*, *grippotyphosa* and *bratislava*), premature foaling and equine recurrent uveitis.[1] The latter is a complex, multifactorial syndrome characterized by repeated episodes of uveitis, which has been correlated with *Leptospira* spp. (especially serovar *pomona*), even though the exact mechanism remains poorly understood.[6]

In living animals, the diagnosis mostly relies on the evaluation of antibody titers against *Leptospira* spp., using the microscopic agglutination test (MAT) as standard serologic assay, in concordance with clinical symptoms.[7] Indeed, although the polymerase chain reaction (PCR) is a more rapid and sensitive diagnostic method, it is not always reliable due to the intermittent shedding of the leptospires. In the context of pathological examination, leptospiral nucleic acid can be detected by PCR of infected tissue. However, most PCR are designed to detect only pathogenic leptospires and do not allow the identification of the serogroup.[7] Hence, those results should always be interpreted with the clinical and pathological findings. The spirochetes within the cytoplasm and in the lumen of affected tubules can also be identified using a Giemsa or silver stains (low sensitivity), or an immunohistochemistry stain against leptospiral antigens.[7]

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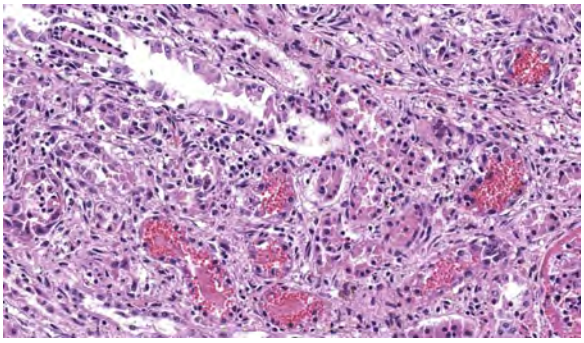
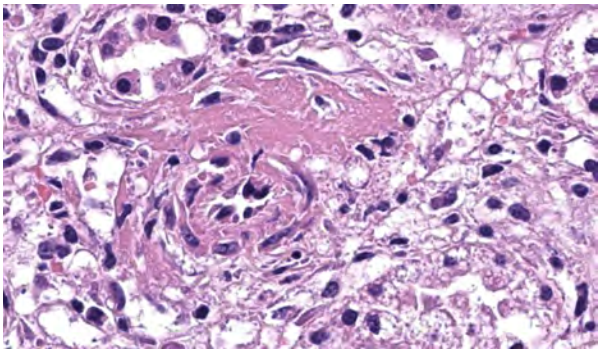


1-6. Kidney, foal: Tubular changes include one or more of the following: Intraluminal hemorrhage and polymerized fibrin, epithelial swelling, necrosis, and sloughing, and aggregates of few neutrophils within the lumen. (HE, 1060X).

JPC Diagnoses:
Kidney: Glomerulonephritis, exudative, subacute, diffuse, marked, with vasculitis and tubular degeneration and necrosis.

JPC Comment:
This week's conference was moderated (in accordance with longstanding JPC/AFIP tradition) by Department chair, COL Sherri Daye. And in line with her own tradition (she is an equestrian extraordinaire among her many talents), horses play a significant role in this week's cases. (See if you can make the connection between Case 4 and equine pathology).

The contributor provides an excellent review of the breadth of disease associated with pathogenic leptospires in horses and other domestic species. While most readers are likely familiar with common forms of glomerulonephritis associated with chronic infectious disease in domestic species, to include membranous, membranoproliferative, and mesangiocapillary (among others), the term "exudative glomerulonephritis" (incorporated into both the contributor's and the JPC's morphologic diagnosis may be unfamiliar and worth a more detailed explanation.



1-7. Kidney, foal: The walls of small vessels are necrotic with extruded fibrin in the wall and adjacent interstitium. (HE, 1506X).

Exudative glomerulonephritis, as the contributor notes, is characterized on light microscopy by the unifying presence of abundant hemorrhage and accompanied fibrin within the urinary space. In acute cases, variable amounts of the following are present and often related to the chronicity and severity of disease: endocapillary capillary hypercellularity (typically by the accumulation of neutrophils), fibrin thrombi within capillary loops, and ultimately segmental to global fibrinoid necrosis of capillary loops. More chronic cases may result in a more generalized hypercellularity of the glomerular tuft, as well as crescent formation.

In both human and veterinary medicine, exudative glomerulonephritis has been most closely associated with various types of infectious disease, and in the human realm, has been referred to as "infection-related glomerulonephritis (IFGN)." The prototypical infection associated with IFGN in humans is post-streptococcal glomerulonephritis which may follow streptococcal pharyngitis or impetigo after a period of 1-4 weeks.[8] Post-streptococcal glomerulonephritis is considered the most common cause of glomerulonephritis in children, with up to 475,000 cases diagnosed per year.[9] (Interestingly, while *Streptococcus equi* infection has been incriminated a number of times in IFGN in humans and obviously results in immune-driven systemic vascular lesions associated with thrombocytopenic purpura in the horse, there are apparently no reports in the veterinary literature of *S. equi* resulting in exudative glomerulonephritis in horses.)

Infectious agents that have been less commonly incriminated in IFGN in humans include *Staphylococcus aureus (*often associated with intravenous drug use), *Bartonella henselae,* and *Coxiella burnetti.* On the other hand, cases of IFGN resulting from spirochetal disease in humans are notably few. Leptospirosis, similar to its effects in most other animal species, results in tubulointerstitial disease in humans (due to its predilection to infect tubular epithelium). Other spirochetes, such as *Treponema pallidum* and *Borrelia burgdorferi* only rarely) result in glomerular disease in humans but typically cause immune-complex glomerulonephritis (ICGN) rather than IFGN (but one case of a human IFGN has been reported in association with *B. burgdorferi* infection.)[10]
In veterinary medicine, it appears that the dog is the outlier when it comes to the renal effects of spirochetal diseases, as dogs famously develop immune-mediated GN with B. burgdorferi[11] and IFGN when infected with leptospires.[3]

References:

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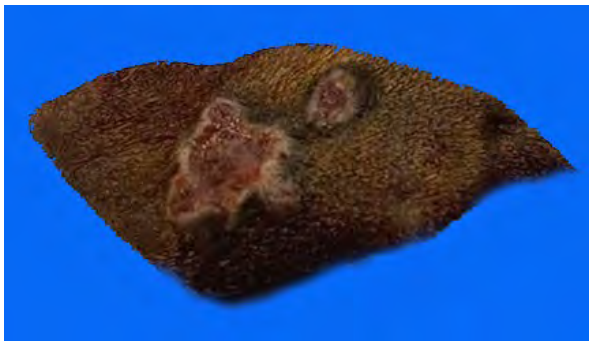
CASE II:

Signalment:
12-year-old, male neutered, Quarter horse, *Equus ferus caballus*

History:
An ulcerated skin lesion, 4 x 3 cm in size, was submitted *in toto* with surrounding haired skin for surgical biopsy from the horse. The horse recovered uneventfully from surgery.

Gross Pathology:
The horse had an ulcerated skin lesion of the left cervical region.



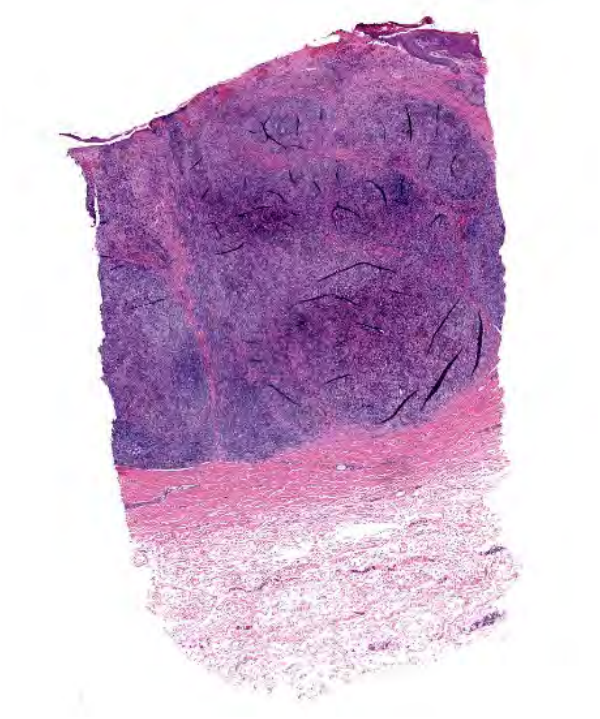
2-1. Skin, horse. There is an ulcerated skin lesion on the neck. (*Photo courtesy of:* New Mexico Department of Agriculture Veterinary Diagnostic Services, www.nmda.nmsu.edu/vds).

Laboratory Results:

A formalin-fixed paraffin-embedded tissue block of the skin lesion was submitted for further speciation of the fungus. Panfungal polymerase chain reaction identified Curvu/aria spicifera with 100% DNA homology with reference strains for this species.

Microscopic Description:

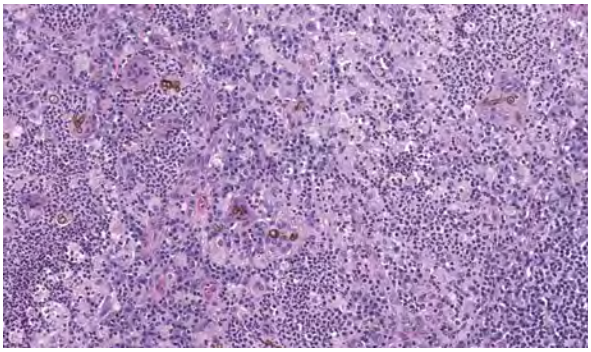
Haired skin: Sections of multifocally ulcerated haired equine skin and subcutis were examined. In the dermis and superficial subcutis, multi nodular and coalescent foci of pyogranulomatous inflammation were associated with pigmented fungi that were usually at the center of the pyogranulomas. The organisms were primarily arranged in pseudohyphae of spherical yeast-like cells that were 8-10µm diameter and protruded from slightly larger (10-15µm diameter) ovoid sclerotia. Germinating buds from the terminal yeasts of the short chains of pseudohyphae were consistent with germ tubes and these were 3-4µm diameter. All stages of the organisms were translucent and uniformly pigmented pale tan, with the melanin pigment confined to retractile fungal cell walls. Degenerate neutrophils were concentrated in the central regions surrounding fungal elements. Langhan's giant cells, admixed with the neutrophilic debris, often contained various fungal elements as well. Smaller numbers of macrophages, neutrophils, lymphocytes and a few additional Langhan's giant cells were located in the tissue and debris surrounding the pyogranulomas and fungi. The ulcers were covered with serocellular debris and degenerate neutrophils. The flanking epidermis was hyperplastic. Within the intact epidermis, deep rete ridges contained a mildly elevated mitotic index of the stratum basale. Hypergranulosis with keratinohyaline granules of the cells of the middle epidermal strata was noted. Laminar hyperkeratosis of the stratum corneum was apparent as well in the remaining epidermis. Within the submitted tissue sections, inflammation and fungi did not extend to margins of the surgical biopsy tissue.



2-2. Skin, horse. The dermis is markedly expanded by poorly formed granulomas. The overlying epidermis is ulcerated with epidermal hyperplasia at the periphery. (HE, 16X)

Contributor's Morphologic Diagnoses:
Haired skin: dermatitis, ulcerative and pyogranulomatous, multinodular and coalescent, chronic, moderate, with pigmented fungal elements, Quarter horse, (*Equus ferus caballus*).

Contributor's Comment:
Many species of pigmented (dematiaceous) fungi are known as plant pathogens and a number of them as opportunistic pathogens in human and animal diseases.[1,2] Pigmented fungi can be identified on a microscopic level in tissues, however identification to a species level requires molecular techniques.[3] Human cases of systemic phaeohyphomycosis are reportedly more common as a result of immune suppression during cancer therapy, renal dialysis and steroid therapy.[4] Superficial phaeohyphomycosis in veterinary species, as with the equine patient in this case, is far more common than systemic disease and immune suppression is not likely involved in the pathogenesis.[5] In one reference, the presence of the fungal granulomas primarily on the head and neck of a series of horses suggests a traumatic event as a common cause of infection.[5] Chromomycosis is a more inclusive term for phaeohyphomycosis and chromoblastomycosis and may indicate either superficial infection or systemic disease.[6]



2-3. Skin, horse. The lesion is composed of poorly formed coalescing pyogranulomas. Pyogranulomas are centered on cross and tangential sections of pigmented yeasts and pseudohyphae. Fungi are often phagocytosed by epithelioid and foreign body-type macrophages, which are admixed with large numbers of largely viable neutrophils with fewer lymphocytes and plasma cells. (HE, 374X)

The description of dematiaceous fungi as primary plant pathogens and occasional opportunistic pathogens of the skin of horses would support the ubiquity of this group of organisms in association with plants and subsequent injuries from affected plant awns and branches.[2]

Dogs, cats, cattle, horses, and goats, as well as humans are affected by cutaneous dematiaceous fungal species.[4,6,7] The identification of pigmented fungal agents to a species level is complicated by the large numbers of pigmented fungi that can infect animals and the histomorphological similarities between species. Molecular diagnostics are needed for speciation when speciation is necessary.[3]

Curvularia species are in the Ascomycota and sexual reproduction involves production of ascospores in the sexual stages. The asexual stages are the survival stages that evolve to escape harsh environmental conditions.[1,2,8] Recent molecular studies have refined speciation of the genus *Curvularia*.[2] The asexual stage of most *Curvularia* species was known as *Bipolaris* until molecular characterization.[1]

A few virulence factors have been described for the pigmented fungi. Melanin is the most universal virulence factor for pigmented fungi[9,10]. As with melanin in animals, it acts as a protection from environmental stressors such as ultraviolet light and host cell oxidative and immune mechanisms. The chemical structures of various melanin molecules varies, however, in fungi, melanin acts as a structural polymer that is linked to chitin in the cell wall.[11] As with the *Curvularia spicifera* in the

horse in this report, the pale tan fungal melanin is confined on a microscopic level to the cell wall.

In many species of fungi, the dormant stages are also considered virulence attributes. In *Curvularia* species and many other diverse groups of fungi, sclerotia form in adverse conditions to protect the organisms from drying, ultraviolet light, tissue cytokines and other noxious influences.[12]. Numerous germ tubes and mycelia were noted in the tissue of the horse in this case, and many originated from the pigmented sclerotia.

Mycoviruses are mostly RNA viruses that act as virulence factors for some endophytic fungi, notably *Curvularia protuberata*, an endophytic fungus of panic grass (*Dichanthelium lanuginosum*). The mycovirus, *Curvularia* thermotolerance virus (CThTV) confers thermotolerance to panic grass when present as an endogenous virus of *C. protuberata*, thus allowing the grass to grow at elevated temperatures.[13] To the author's knowledge, there are no mycoviruses associated with enhanced pathogenicity of chromomycotic agents when infecting animals, however.

Systemic chromomycoses, though rare in animals, most often involve fungal infections of the brain and spinal cord that are invariably fatal.[14] Occasional respiratory manifestations and generalized spread also occur. Most of these infections metastasize from environmental contamination in immune-suppressed humans and animals. Phaeohyphomycoses are considered emerging diseases among humans with chronic immune suppression. Systemic animal chromomycoses are also considered more prevalent with compromise of the immune system. Cutaneous infections in animals are more common and not linked to any depression in immune capabilities.[5]

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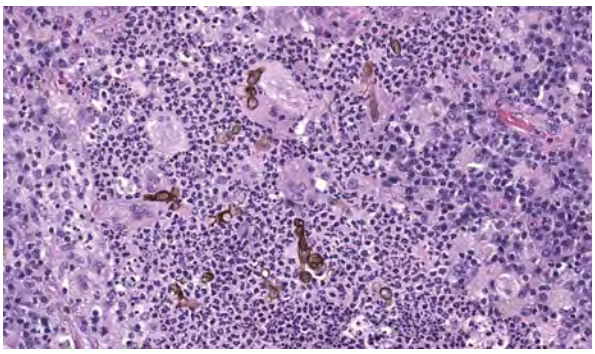
JPC Morphologic Diagnoses:
Haired skin: Dermatitis, pyogranulomatous, chronic, multifocal to coalescing, severe, with pigmented fungal hyphae.

JPC Comment:
The contributor provides an excellent writeup on the breadth of pigmented fungal infections in animal species. These agents have been well represented in the Wednesday Slide Conference over the years, with 14 cases dating back to 1987. In these cases, horses and cats have been overrepresented, with cutaneous and nervous system infections predominating (which is quite representative of the species and system predilection for these agents when infecting mammals). In cats, solitary cutaneous lesions on the face and paws predominate, while multiple lesions on various parts of the body are most often seen in horses.



2-4. Skin, horse. High magnification of dematiaceous yeast and pseudohyphae. (HE, 705X)

As mentioned by the contributor, most infections in domestic species, as opposed to humans, are seen in immunocompetent individuals.[15]

There are a number of additional "virulence factors" described for these pathogens, which assist in protection both in the environment and following infection of animal tissues. The presence of melanin is easily the most well-researched in pathogenic fungi, with *Cryptococcus neoformans* and the various dematiaceous yeasts being the most renowned employers of this compound. In the environment, this compound protects the fungi from the stresses of ultraviolet and electromagnetic radiation, promotes thermotolerance, and assists in protection from unicellular predators, like amoeba.[16] During infection of animal tissue, melanization helps shield *C. neoformans* and dematiaceous fungi from engulfment and killing via the oxidative burst by host macrophages.[16] In addition, melanin likely promotes neurotropism in these fungi[16] - melanin is a very common product of cells derived the neural tube, and its presence likely results in a form of protective mimicry for these fungi when infecting the nervous system.

Additional factors that likely contribute to their pathogenicity both in the environment and within animal tissue include the presence of carotene (also protective from a variant of oxidative stresses), formation of thick cell walls, presence of yeast-like phases (easily the most environmentally sound of the various stages of fungal evolution), adhesion, hydrophobicity, and production of siderophores (a virulence factor best known for its employment by many forms of pathogenic bacteria.[5]

Finally, the confusing terminology associated with dematiaceous fungal infections probably bears some review. A recent review article by Rodrigues *et al.*[17] provides an excellent resource for the terminology of all fungal infections in animal tissues, including those of the pigmented fungi. The term "phaeohyphomycosis" refers to a subset of pigmented fungal infections (including this case), in which the infection is caused by yeast-like cells and hyphae. "Chromoblastomycosis" is also caused by pigmented fungi, predominantly in the form of extremely thick-walled yeast-like cells referred to as "sclerotic bodies" or "Medlar cells". The term "chromomycosis" was historically used to refer to both conditions but has largely fallen out of favor.[17] Budding mycologists may also be confused as to the terms "pseudohyphae" and "hyphae", especially in infections characterized by a yeast form. The prototypical pathogenic yeast infection that produces both pseudohyphae and hyphae, *Candia albicans*, best provides this lesson in morphology, with pseudohyphae having constrictions at the sites of septation, and true hyphae having straight walls over the septations. Agents associated with phaehyphomycosis typically have pigmented hyphae, with no pseudohyphae.[17]

This case also reinforced for all participants the pitfalls of trying to speciate fungi based solely on morphology. In this particular case, participants identified definite constrictions at the sites of septation (see image 2-4), while reports of Curvularia suggest that they only form hyphae, not pseudohyphae. For this reason, plans for definitive speciation (if desired) must include PCR.

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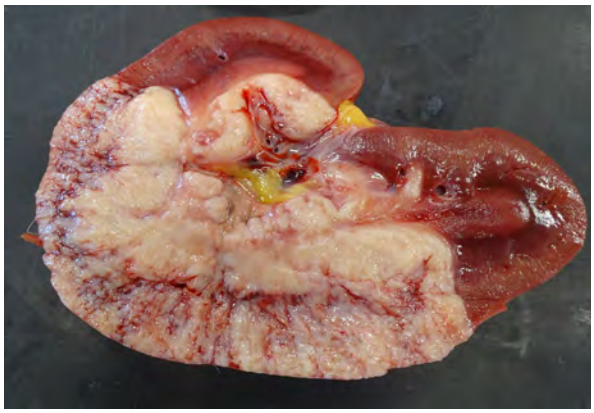
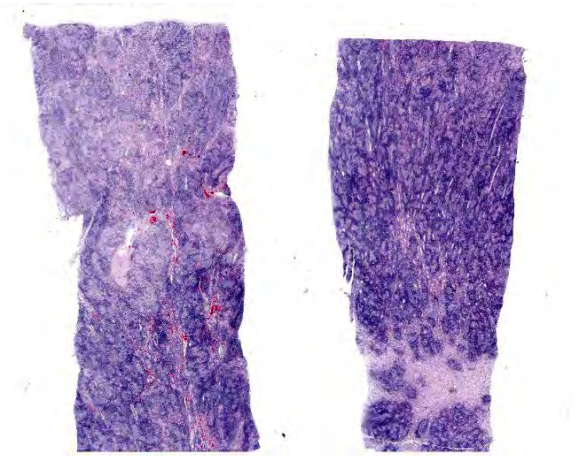
CASE III:

Signalment:
Adult female horse (Equus caballus) 9 years old

History:
A 9-year-old Belgian warm blood mare presented initially with a history of reduced appetite, less energy than usual, and no longer responding when the owners called her. The veterinarian examined her and referred her to the veterinary clinic with a suspected endotoxemia. During the day, she is in the paddock with another pony, and at night, she is kept in the stable. Vaccinations for influenza, tetanus, and EHV-1, as well as deworming, are up to date.
General examination at the veterinary clinic: the animal is lethargic, shows negative menace reflexes, and positive pupillary reflexes. Ultrasound revealed a clearly enlarged left kidney. The walls of the small intestines are thickened. The urinary bladder is large and contains urine with sediment. Blood test results: T /F 8.5, Anemic, Total protein 96, Albumin 28, Triglycerides 2.3, NH3 6. The following day, there was a rapid deterioration in clinical symptoms. The animal was standing with a wide stance, followed later by lateral recumbency. A spinal cord puncture was carried out. Results: cerebrospinal fluid: suspicion of infection with Halicephalobus spp. The animal was euthanized.

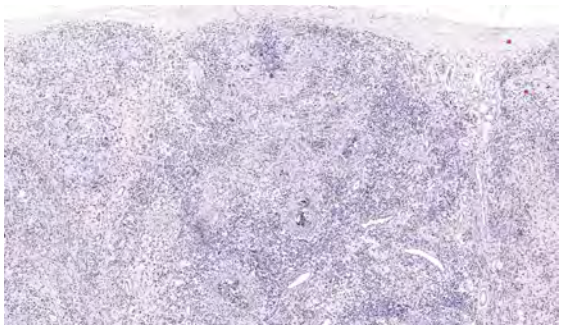


3-1. Kidney, horse. A raised, white to beige, well-demarcated and multilobulated mass effaces approximately 66% of the renal parenchyma. (*Photo courtesy of:* Department of Veterinary Pathology, Ghent University, https: //www.ugent.be/di/di0S/nl).



3-2. Kidney, horse: One section each of the left and right kidney are submitted for examination. At subgross magnification, renal architecture is lost. (HE, 7X)

Gross Pathology:
The carcass was in fair body condition and good postmortem condition. Lungs showed pulmonary congestion and edema with frothy fluid in the trachea. Liver, heart: no gross abnormalities. The left kidney was enlarged. A raised, white to beige, well-demarcated and multilobulated mass was extending through the entire depth of the kidney and obliterating approximately 70% of the renal parenchyma. In the right kidney, there was a focal nodule, (about 2 x 2 cm), with similar appearance to the lesion in the left kidney. Left renal lymph node showed a nodule (about 1 x 0.5 cm), with the same gross appearance as the lesion in



3-3. Kidney, horse. The architecture is effaced by coalescing poorly demarcated areas of granulomatous information which contain cross and tangential sections of adult and larval nematodes. (HE, 90X)

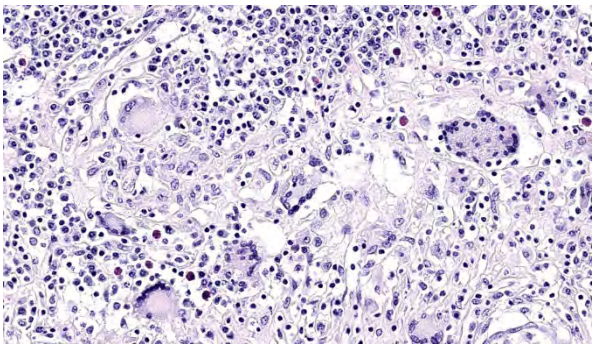
the left kidney. Brain and spinal cord were dissected after fixation: no gross abnormalities. Samples of the kidneys, left renal lymph node, brain and spinal cord were taken for histopathological examination.

Microscopic Description:
Left and right kidney: obliterating approximately 80% of the renal parenchyma within the section are multifocal to coalescing, variably sized, moderately to densely cellular aggregates of inflammatory cells composed predominately of large number of macrophages, giant cells, and lymphocytes and some plasma cells, with a lesser amount of eosinophils, separated by some fibrous tissue. Within these areas, numerous tangential and cross sections through metazoa (adults and larvae) are present. The adult nematodes are approximately 15-20 microns in diameter, and have a thin cuticle, platymyarian-meromyarian musculature, intestinal tract, and characteristic rhabditiform esophagus with a corpus, isthmus and terminal bulb. Multifocally, there are areas where a centrally located, strongly basophilic, granular material has accumulated (dystrophic mineralization).

In addition to nephritis, microscopic examination of the brain and left renal lymph node from this horse identified both meningoencephalitis and lymphadenitis with intralesional rhabditoid nematodes that were consistent with Halicephalobus gingivalis.

Contributor's Morphologic Diagnoses:
Severe chronic granulomatous and eosinophilic nephritis with intralesional Halicephalobus gingivalis.

Contributor's Comment:
Halicephalobus gingivalis, a free living, saprophytic nematode of the order Rhabditidia, family Panagrolaimidae. They are found in water, soil, decaying organic matter, and has been known to parasitize various species including humans, horses, a zebra and a donkey. The life cycle and pathogenesis is still poorly understood. Infection can occur through wounds in oral and nasal mucosal membranes or in skin. Mucosal invasion results in local inflammation, with dissemination throughout, the body possibly via haematogenous or lymphatic spread. The most commonly reported sites of infection in horses are the brain, kidneys, lymph nodes, oral and nasal mucosa, and adrenal glands. H. gingivalis is characterized by its distinct morphology. It has a diameter of approximately 15-25μm, a smooth cuticle and



3-4. Kidney, horse: Areas of granulomatous inflammamtion contain numerous lyphocytes and plasma cells with fewer eosinophils and foreign-body and Langhans'-type giant cells, and loosely arranged fibrous connective tissue which effaces and entraps remnant tubules. (HE, 581X)

platymarian-meromyarian musculature. It shows a rhabditiform oesophagus with a corpus, isthmus and bulb. The gastrointestinal tract is lined by uninucleate cuboidal cells. It has a didelphic reproductive tract with dorsiflexed ovaries. Within well-developed lesions, tangential and cross sections of adults as well as larva are easily visualized, with intermixed 10-l5µm diameter, ovoid, embryonated eggs. Aberrant halicephalobiasis manifests as granulomatous lesions and often carries a high mortality rate in both humans and horses.

Both males and females nematodes exist in the environment, but only female nematodes have been observed within microscopic lesions, suggesting that within a host, reproduction occurs asexually via parthenogenesis.

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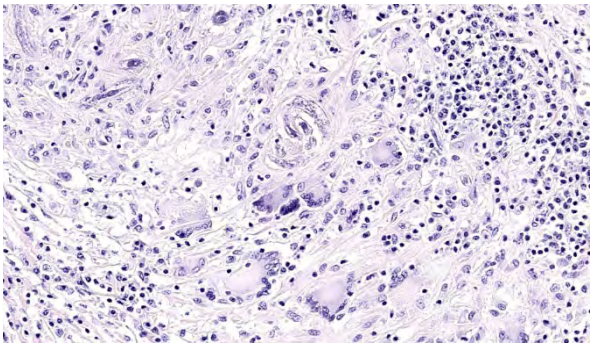
Merelbeke, Belgium
https://www.ugent.be/di/di0S/nl

JPC Diagnoses:
Kidney: Nephritis, granulomatous, chronic, diffuse, severe, with rhabditid adults, larvae, and eggs.



3-5. Kidney, horse: Numerous cross- and tangential sections of larval nematodes are present in áreas of granulomatous inflammation (HE, 490X)

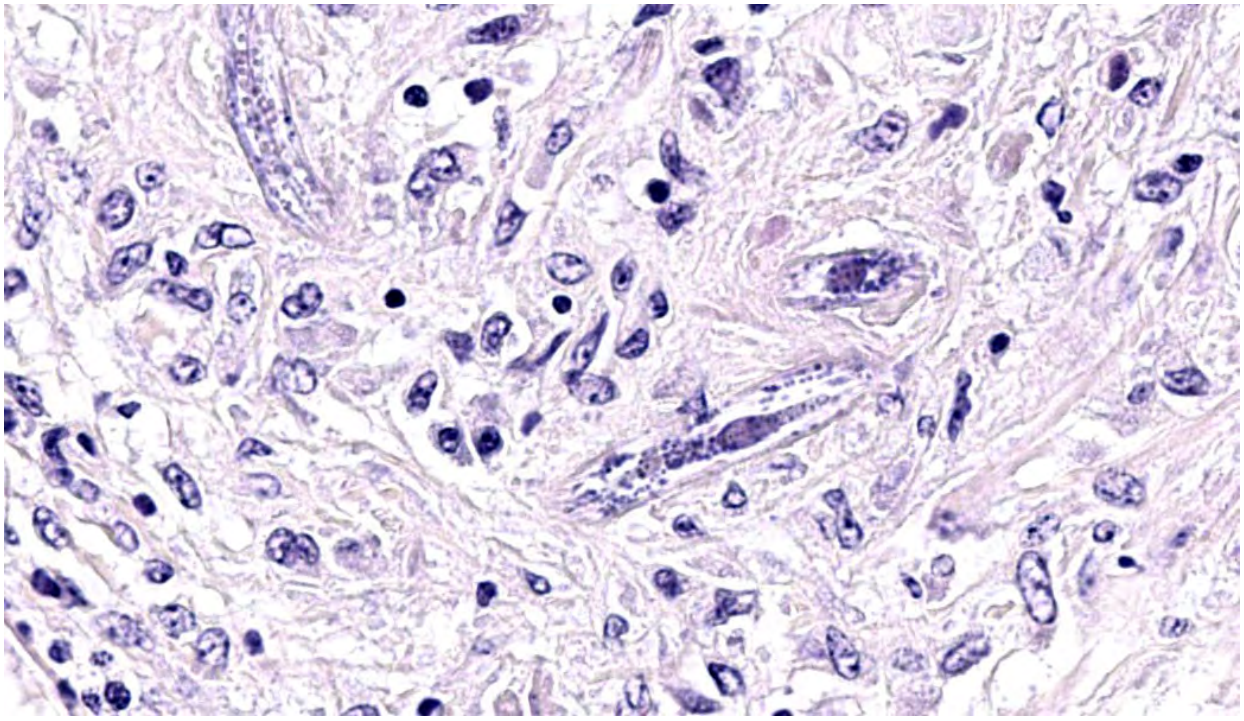
JPC Comment:
Halicephalobus gingivalis is also a frequent visitor to the Wednesday Slide Conference, with sixteen instances since 1990, in which it has appeared most frequently in its current nomenclature (*Halicephalobus gingivalis),* but also in previous scientific names including *Halicephalobus deletrix and Micronema deletrix.*

The contributor provides a concise review of *Halicephalobus gingivalis* infection in the horse, and more basic information may be gained from review of previous iterations in the WSC.

While the majority of publications involve *H. gingivalis* infection in the horse, H. gingivalis appears to be a rare parasite of humans as well with 8 cases reported since 2015.[3,4] It has a worldwide distribution but with reports in humans in Europe, North America, Africa, and Australia. In each case, definitive diagnosis of infection was made at autopsy. In each case, the clinical manifestation was meningoencephalitis with several cases demonstrative meningomyelitis as well.[3] Rarely, nematodes have been found in the lungs and liver as well. Histologic lesions include perivascular acute and chronic granulomatous inflammation, similar to that seen in the horse.[3]

In addition to horses and humans, fatal meningoencephalitis has also been reported in a 7-week-old bovine Holstein calf from a dairy operation. While the source of the infection was not identified, the authors suggested either the umbilicus or milk.[5]

Finally, a few recent reports of *H. gingivalis* infection in horses bear review. Due to the relative rarity of reported cases, many report document the presence of the nematodes in

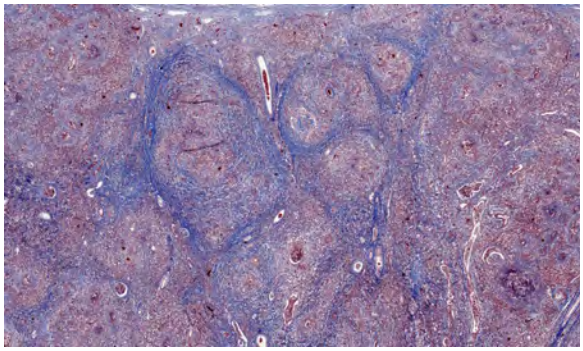


3-6. Kidney, horse: Opportune tangential sections of larva demonstrate a characteristic rhabditoid esophagus with a corpus, isthmus, and bulb. (HE, 1302X)

one or two organs. Some early reports discuss swelling of the jaws as a result of oral migration from the infiltrating nematodes from the gingiva (hence the name *H. gingivalis*) into the underlying maxilla and mandible, resulting in osteomyelitis. A 2024 report chronicled a bone lesion resulting in a comminuted fracture of the tibia[6]. (A characteristic lesion, likely similar to that seen in this case, was present in the left kidney as well.)[6] The pathogenesis of the tibial lesion was not identified, although contamination of a wound in the region could not be excluded.

Differing from the typical report of *H. gingivalis* infection in one or two organs (if one is the brain, the rapidly progressive and devastating effects of neurologic involvement in a horse often results in euthanasia early on in disease progression), a 2025 report[7] describes a "disseminated" infection with *H. gingivalis.* In this case, the agent was found in the heart, kidneys, oral cavity, tongue, left eye, lungs, CNS, adrenal glands, liver, lymph nodes and the spleen (which has not been previously reported). The cause of the prolonged survival (~8 weeks) of this animal following initial diagnosis (following enucleation of an infected eye) may have been facilitated by the administration of corticosteroids and ivermectin, allowing for additional distribution of the parasites via vascular channels before neurologic signs necessitated the animal's euthanasia.[7]

Finally, transplacental transmission and abortion due to *H. gingivalis* was identified in a Connemara mare, who, despite having successful deliveries in previous pregnancies, aborted in two consecutive pregnancies. In both cases, larva of *Halicephalobus gingivalis* were identified within placental tissue. The authors of this study concluded that not all *H.*



3-7. Kidney, horse: A Masson's trichrome demonstrates the abundant fibrous connective tissue surrounding areas of granulomatous inflammation and effacing renal parenchyma. (Masson's trichrome, 46X).

gingivalis infections may result in disseminated or life-threatening infections and that infection may be more widespread than previously thought.[8] A single previous case of verminous mastitis and transmammary H. gingivalis delivery to a foal (who subsequently died) has been reported.[9]

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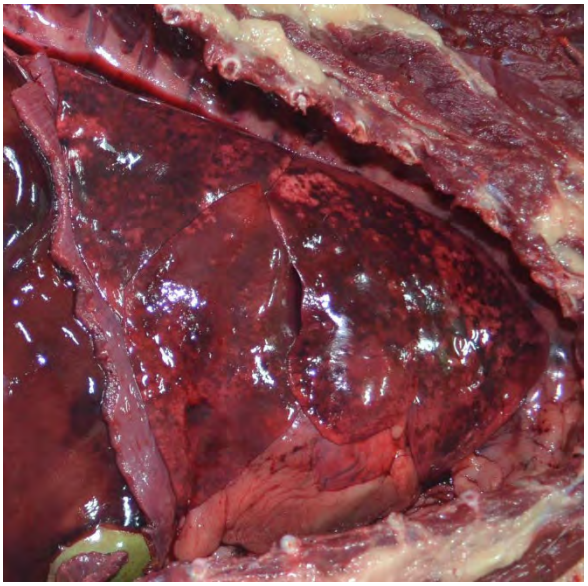
CASE IV:

Signalment:
4-year-old, intact female, Labrador Retriever, domestic dog (Canis lupus familiaris)

History:
The dog, which had a history of allergies and bacterial ear infections, developed "kennel cough" after a visit to a local veterinarian for annual vaccination and a moxidectin injection. Treatment with antihistamines and corticosteroids was administered one day after the beginning of clinical signs. Three days later, the dog developed diarrhea and treatment was interrupted. The cough progressed with presence of mucus. Six days after onset, the dog was lethargic and inappetent, and was brought once again to a veterinary hospital, at which 19 blood work revealed a high white blood cell count. On the morning of the seventh day, the animal died.



4-1. Lung, dog: The lung lobes have multifocal to coalescing dark red to black, variably sized foci widespread throughout the pleural surface. The thoracic cavity has scant amount of red-tinged fluid. (*Photo courtesy of:* Louisiana Animal Disease Diagnostic Laboratory (LADDL), School of Veterinary Medicine, Louisiana State University (LSU) (https://www.vetmed.lsu.edu/laddl/).

Gross Pathology:
The animal was obese, and the body was in moderate autolysis. The thoracic cavity contained approximately 15-20 ml of red-tinged fluid and the parietal pleura lining the intercostal spaces had coalescing dark red areas (hemorrhage). The lungs had bilateral multifocal to coalescing dark red to black, variably sized foci widespread throughout the pleural surface (Figure 1). The caudal aspect of the left cranial lung lobe had a focally extensive gray and firm area that sunk in formalin (consolidation). The trachea was filled with abundant, red-tinged froth and the mucosa was diffusely reddened. The tracheobronchial lymph nodes were enlarged approximately 2X and diffusely dark red, with no corticomedullary distinction.

Laboratory Results:

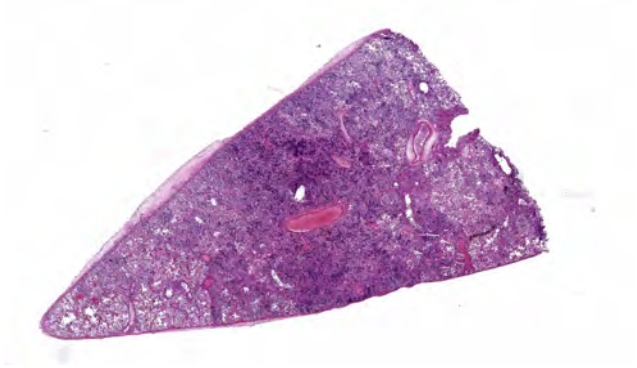
Bacteriology (aerobic culture), Lung:

> Heavy growth of *Streptococcus equi* subsp. *zooepidemicus* and *Escherichia coli*.

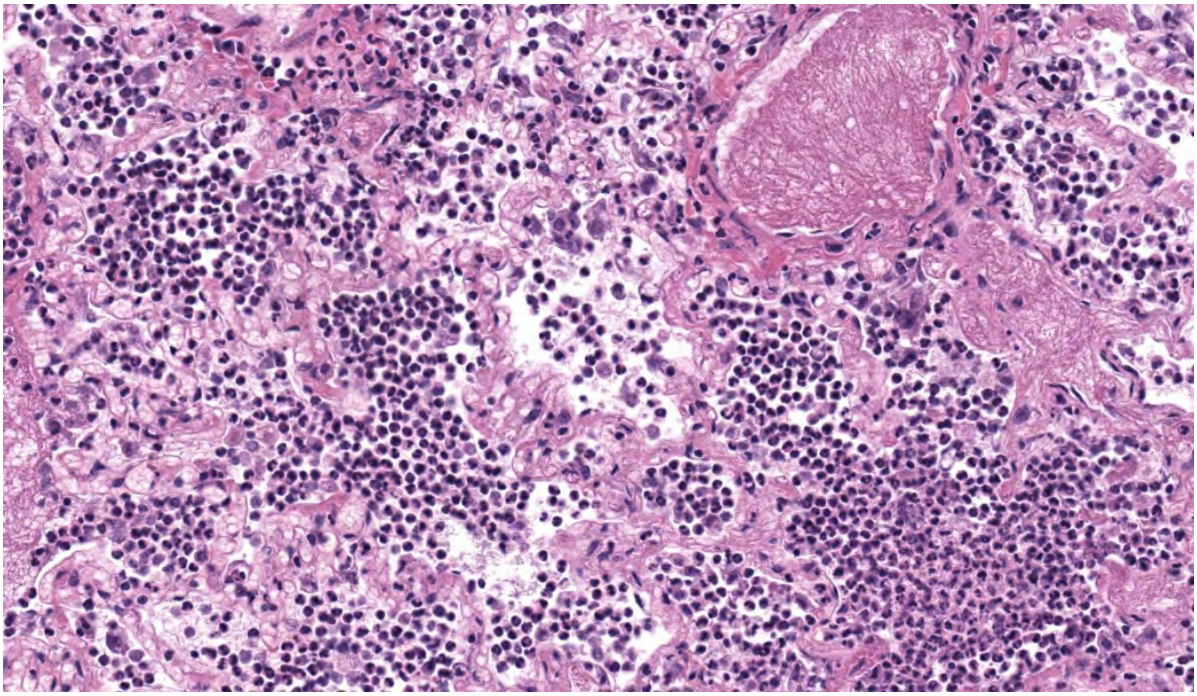
Microscopic Description:
Lung: The alveolar spaces are diffusely flooded by numerous viable and degenerate neutrophils and macrophages, with occasional fibrin exudation and edema fluid. Within alveoli, there are rare colonies of cocci, occasionally organized in short chains; bacteria are also observed within macrophages and adhered to the membrane of inflammatory cells. Multifocal bronchioles are filled with cellular debris and neutrophils. The tunica adventitia and the tunica submucosa of multifocal blood vessels and bronchi are expanded by moderate edema. Occasionally dilated lymphatic vessels contain intraluminal fibrin and few neutrophils. Rare small caliber blood vessels are occluded by fibrin thrombi. The pleura is segmentally expanded by abundant fibrin exudate, edema, and moderate numbers of neutrophils.

Contributor's Morphologic Diagnoses:
Lung: Bronchopneumonia, fibrinosuppurative and hemorrhagic, multifocal to coalescing, marked, acute, with intralesional coccoid bacteria and locally extensive fibrinous pleuritis

Contributor's Comment:
Bacterial pneumonia caused by opportunistic agents is fairly common in dogs. Involved bacteria include generally *Bordetella bronchiseptica*, *Staphylococcus* spp., *Pasteurella multocida*, *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* spp., and *Streptococcus* spp.[4] In a review of 393 cases of streptococcal infections in dogs, several streptococcal species (γ-hemolytic *Streptococcus* spp., β-hemolytic *Streptococcus* spp., *S. canis*, *S. dysgalactiae* subsp. *equisimilis*, and *S. equi* subsp. *zooepidemicus*) were associated with pneumonia.[12] spp., *S. canis*, *S. dysgalactiae* subsp. *equisimilis*, and *S. equi*



4-2. Lung, dog: One section of lung is submitted for examination. The lung is diffusely consolidated with a focal area of pleural expansion by hemorrhage, edema, and small amounts of inflammation. (HE, 18X).



4-3. Lung, dog: Alveolar lumina are filled with viable and degenerate neutrophils, alveolar macrophages, and small amounts of edema and fibrin. Alveolar septa are thickened by congestion, edema and increased numbers of circulating neutrophils. Pulmonary veins occasionally contain non-occlusive fibrin thrombi (top right). (HE, 459X)

Streptococcus equi subsp. *zooepidemicus* (*S. zooepidemicus*) is an opportunistic zoonotic bacterial pathogen capable of causing disease in several animal species.[1,2,5,10,15] These are gram-positive, Lancefield group C, β-hemolytic cocci commonly isolated from the upper respiratory and lower genital tract of horses[9] that can affect different organ systems and express variable clinical presentations, including pneumonia, endometritis, placentitis, meningitis or septicemia.[5,8,14,19] In alpacas and llamas, this bacterium is known to cause sepsis, also called "alpaca fever".[6] In one reported case, cocci were demonstrated within enteric lymphatic vessels of a neonate, suggesting a possible lymphatic dissemination of this agent.[6] *S. zooepidemicus* has also been shown to be transmitted to humans from different animal species such as guinea pigs, horses and dogs, causing severe pneumonia, bacteremia, septic arthritis, and meningitis.[1,10,13,19] *S. zooepidemicus* can also cause pharyngitis, with the potential to trigger acute post-streptococcal glomerulonephritis (APSGN) in humans.[17] In swine, the first documented outbreak of *S. zooepidemicus* in the United States occurred during September and October 2019, with high mortality rates ranging from 10-50% in groups of pigs over the period of 8-10 days at a buying station in Ohio and at an abattoir in Tennessee. Previous outbreaks in pigs were also reported in China, resulting in significant economic losses.[5]

S. zooepidemicus has been associated with severe respiratory disease in dogs for a number of years.[16] However, more recently, its importance has been underscored by fatal outbreaks in kenneled dog populations in several countries.[3,14,18] Hence, the bacterium has been recognized as one of the components of the multifactorial Canine Infectious Respiratory

Disease (CIRD, Kennel Cough), which includes most commonly the bacterium *Bordetella bronchiseptica* and viruses such as Canine Herpes Virus (CHV) and Canine Parainfluenza Virus (CPIV).[14,16] In the present case, it is believed that the dog, which was likely immune-suppressed due to routine treatment with anti-histamines and corticosteroids for allergies, was exposed to a large burden of the bacterium during a visit to the veterinary clinic. No indications of other pathogens related to active disease were observed. While in this case there was heavy growth of both *E. coli* and *S. zooepidemicus* from lung samples, only intralesional gram-positive coccoid bacteria frequently organized in chains a Gram stain of affected lung sections revealed. Therefore, the *E. coli* isolate was interpreted as a contaminant.

The disease caused by *S. zooepidemicus* in dogs frequently has a brisk clinical course and high morbidity, and deaths have been reported to occur as soon as 2 days after exposure.[14] Clinically, the dogs present with severe acute respiratory distress associated with severe, acute fibrinosuppurative, necrotizing and/or hemorrhagic pneumonia, as well as hemothorax.[14,16] The pathogenesis of *S. zooepidemicus* infection in dogs is incompletely understood;[15,16] however, environmental stress, extenuating physical exercise and overcrowding can be determinant aspects in the spread and development of this disease by triggering the release of stress hormones such as cortisol and norepinephrine and consequently reducing resistance to microbial invasion.[11,18]

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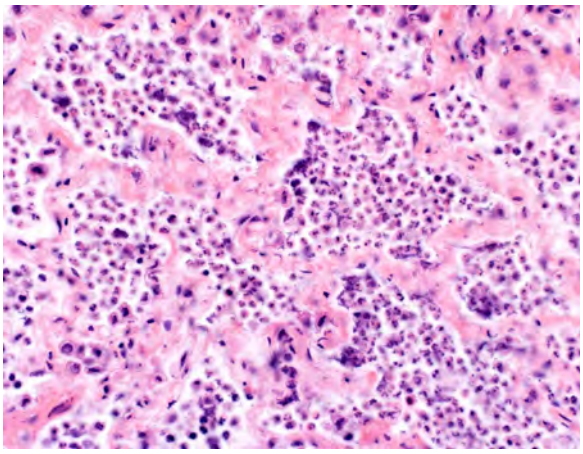
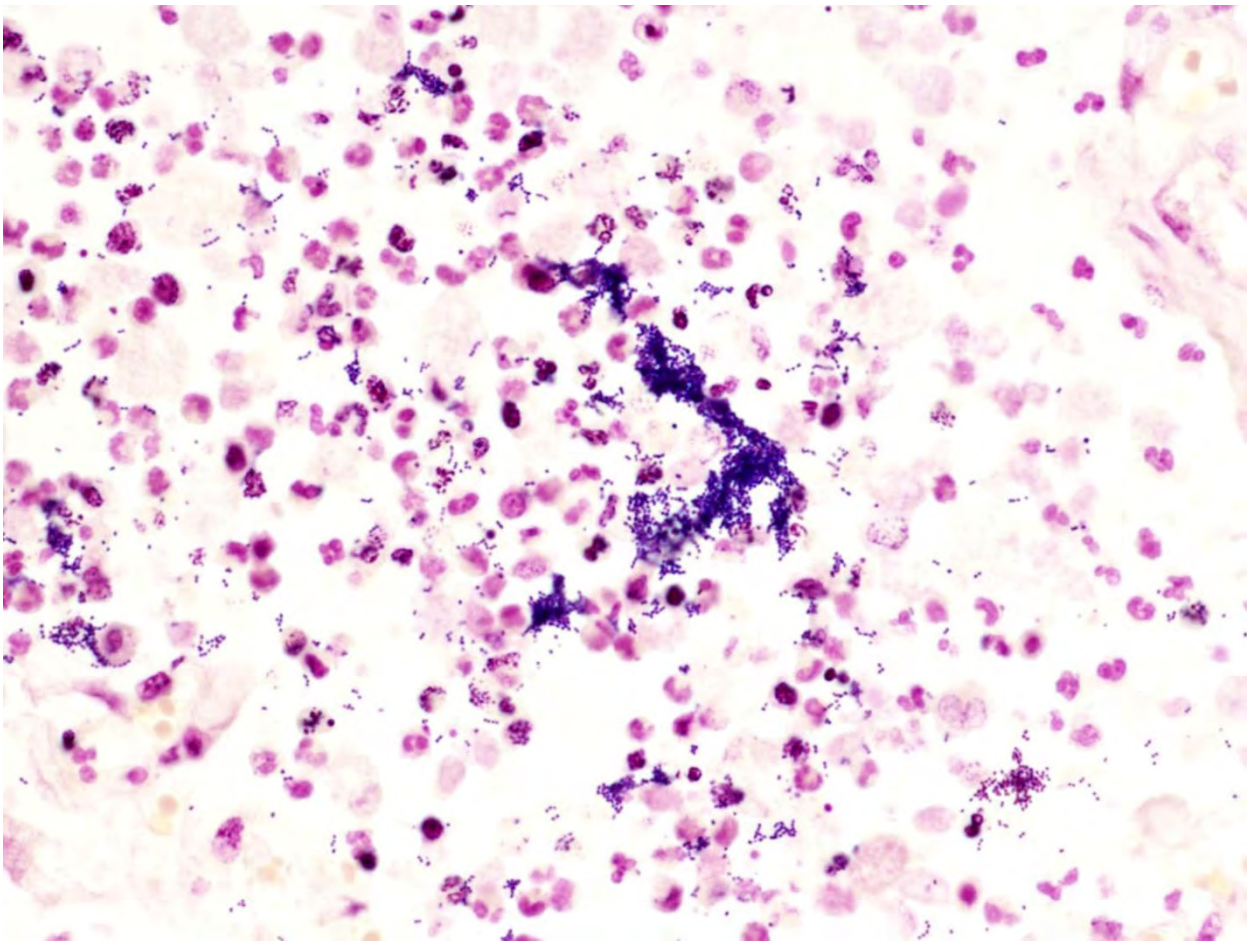
S. zooepidemicus infection in dogs is incompletely understood;[15,16] however, environmental stress, extenuating physical exercise and overcrowding can be determinant aspects in the spread and development of this disease by triggering the release of stress hormones such as cortisol and norepinephrine and consequently reducing resistance to microbial invasion.[11,18] The involvement of stress hormones can also indirectly explain the large numbers of extracellular cocci observed in acutely infected dogs, indicating rapid proliferation and evasion of clearance mechanisms.[18]



4-4. Lung, dog: Multiple alveoli have numerous degenerate neutrophils with fewer histiocytes. There are also frequent cocci, occasionally organized into short chains mixed with the inflammatory cells (HE, 400x). (*Photo courtesy of:* Louisiana Animal Disease Diagnostic Laboratory (LADDL), School of Veterinary Medicine, Louisiana State University (LSU) (http://www.vetmed.lsu.edu/laddl/)



4-5. Lung, dog. A Gram stain characterizes the bacteria as gram-positive (Gram stain, 40x). (HE, 400X). (*Photo courtesy of:* Louisiana Animal Disease Diagnostic Laboratory (LADDL), School of Veterinary Medicine, Louisiana State University (LSU) (http://www.vetmed.lsu.edu/laddl/)

Gross examination of *S. zooepidemicus* infected dogs reveals features similar to the ones observed in this case, such as mottled dark to bright red lungs with variably sized areas of consolidation or alveolar collapse, multifocal areas of hemorrhage in tracheobronchial lymph nodes, and hemothorax.[14,18] Histological features consist of extensive alveolar flooding by neutrophils and macrophages with occasional fibrin (fibrinosuppurative pneumonia), with gram-positive cocci arranged in short chains and occasional clusters within alveoli; these findings are also similar to the ones observed in the present case.[2,16]

Episodes of pneumonia caused by *S. zooepidemicus* in dogs often lead to acute clinical disease with a high mortality rate despite intensive treatment, as even early antimicrobial therapy may not successfully mitigate the inflammatory events that lead to hypotension and multiple organ dysfunction.[15] This can be particularly devastating in sheltered dog populations and, therefore, prevention of spread through adequate management practices is desirable. Survival rates are more likely to improve after follow-up measures, such as designation of intake rows, depopulation programs, and establishment of quarantine facilities are in effect, and these measures can also help prevent further significant respiratory disease outbreaks.[3,7]

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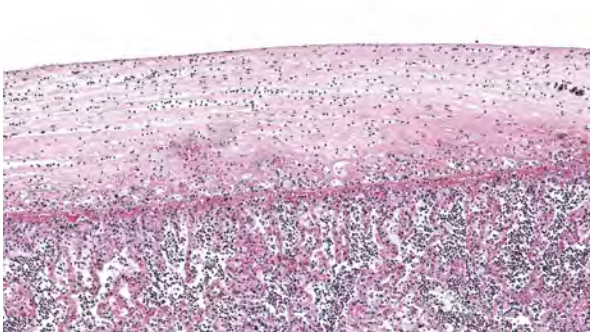
JPC Morphologic Diagnosis: Lung: Bronchopneumonia, fibrinosuppurative and necrotizing, subacute, diffuse, marked, with multifocal pleuritis and intra-alveolar cocci and bacilli.

JPC Comment:
The contributor has provided an excellent review of streptococcocal infections and specifically, *Streptococcus equi* subsp. *zooepidemicus* (*S. zooepidemicus*). The widespread nature of streptococcal diseases in many vertebrate species exemplifies how "big things may arrive in small packages." The small size of streptococci belies the many virulence factors that they possess and their ability to cause severe and life-threatening disease.

The major virulence factors of *Streptococcus zooepidemicus* allow it to escape a variety of the body's attempts at neutralizing this pathogen. Antiphagocytic factors include hyaluronic acid capsule which is identical to that seen in the body, providing a form of molecular mimicry and camouflage.[20] The M-like protein, SzP, helps to prevent opsonization, which significantly reduces phagocytosis by macrophages. An additional M-like protein, SzM, binds plasminogen and allows streptococci to degrade fibrin (a common product of their infection), promoting additional bacterial spread. [20] Streptokinase acts in a similar fashion, cleaving host plasminogen into active plasmin, dissolving thrombi and allowing the bacteria to spread. IgG binding proteins bind to the Fc region of immunoglobulins, allowing S to evade the body's humoral response. [20] Hydrolytic enzymes include C5a peptidases, which destroy this fragment of complement, impairing the recruitment of neutrophils to the site of infection. [20] *S. zooepidemicus* secretes a range of 11 pyrogenic exotoxins which act as superantigens, non-specifically activating and result in a massive release of immune mediators ("cytokine storm") in affected individuals.[15, 20] Lipoteichoic acid (once referred to as the "endotoxin" of streptococci), a component of the wall of these cocci, acts in a similar fashion, and while its release requires the destruction of the bacterium, acts synergistically, with the combination resulting in pyrexia, systemic inflammation, and vascular permeability and is a major driver of "scarlet fever" in humans, as well as necrotizing fasciitis and toxic shock syndrome, among many other syndromes.[20, 21] Finally, streptolysins are potent pore-forming proteins which may resulting in damage to epithelial linings of many tissues, allow dissemination through underlying vasculature, as well as outright resulting in the destruction of inflammatory cells, as well as enhancing production of IL-1, TNF, and IL-6.[15, 20]



4-6. Lung, dog: The pleura is multifocally expanded by edema, fibrin, small amounts of hemorrhage, and low to moderate numbers of neutrophils. (HE, 400X)

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