



WEDNESDAY SLIDE CONFERENCE 2012-2013

Conference 19

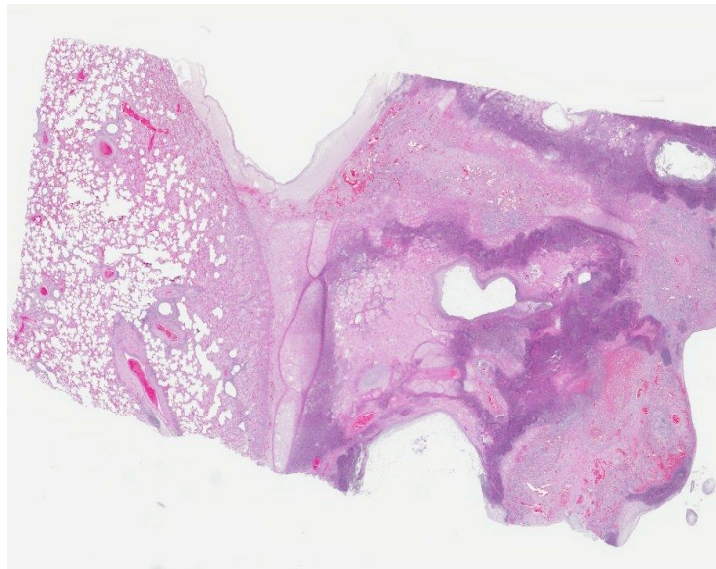
20 March 2013

CASE I: 10-85188 (JPC 3165182).

Signalment: 10-year-old Holstein-Friesian cow from a dairy herd (*Bos Taurus*).

History: This cow presented to the large animal teaching hospital with a history of being off feed and having decreased milk production. A swelling in the

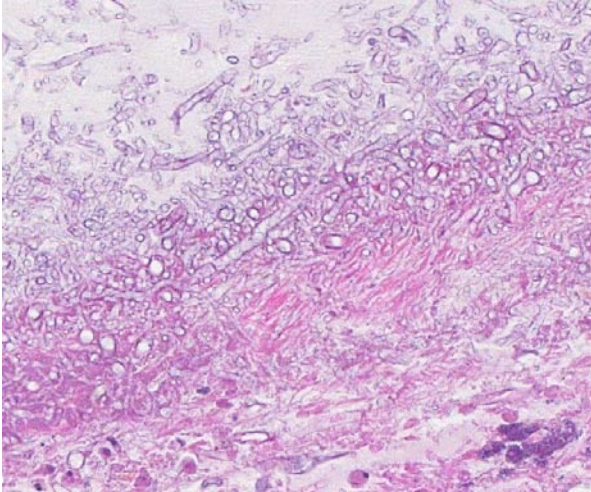
subcutis of her left ventral abdomen was noted. This cow had a history of clinical mastitis in the left front quarter, and was being treated with intravenous antibiotics including sulfadimethoxine and oxytetracycline. Heart sounds were muffled, and multiple “comet tails” were noted on ultrasound examination of the thorax.



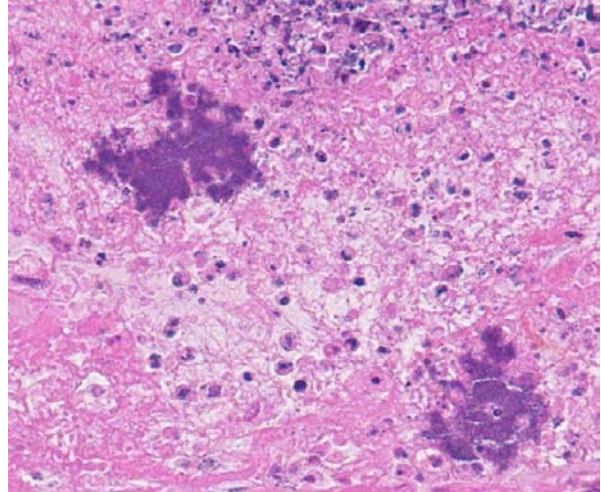
1-1. Lung, ox: Subgross examination of the section of tissue shows confluent areas of necrosis at right delineated by dense basophilic bands of necrotic leukocytes, as well as marked expansion of interlobular connective tissue and lymphatics by marked edema and polymerized fibrin. (HE 0.63X)

Gross Pathologic Findings: There is a moderately increased amount of blood-flecked foam in the distal 1/2 of the trachea and bronchial tree. The lungs contain approximately 100, 0.5 cm to 1 cm, firm, round, red-brown nodules with caseous or purulent centers; these nodules are evenly distributed through all lung lobes. Additionally, there are smaller numbers of subpleural and randomly distributed foci comprising solitary or multiple closely apposed or coalescing, 1 to 2 cm diameter, air-filled bullae surrounded by firm white tissue and lined by green-black, tenacious necrotic material and scattered, variably sized, velvety, white to brown plaques.

Histopathologic Description: Obliterating over 50% of the lung parenchyma in the examined section is a focally extensive, empty space bounded by a dense band of



1-2. Lung, ox: Within necrotic areas, and focally, within the wall of a large vessel, there are numerous clusters of pauciseptate 6-10 μm diameter fungal hyphae with non-parallel walls and bulbous dilations which seen in negative relief. (HE 300X)



1-3. Lung, ox: Also within necrotic areas, there are numerous large colonies of 1-2 μm bacilli, consistent with the *Truperella* cultured at autopsy. (HE 400X)

fungal hyphae embedded in eosinophilic, amorphous to granular necrotic material and fibrin. Fungal hyphae stain relatively poorly with PAS and GMS, and are characterized by nonparallel walls, a lack of septa, irregular, non-dichotomous branching at right angles, and occasional bulbous dilatations. The adjacent pulmonary parenchyma is characterized by lytic or coagulative necrosis, multifocal hemorrhage, granulation tissue, and florid infiltrates of viable and degenerate neutrophils with fewer macrophages, eosinophils, lymphocytes and plasma cells. Within this surrounding tissue are many large colonies of gram positive short rods. Bronchiolar epithelium is multifocally attenuated or eroded, and airway lumina rarely contain proteinaceous material admixed with small numbers of degenerate inflammatory cells. In less affected areas of the lung, alveolar spaces are filled by edema, fibrin, and foamy macrophages and bronchioles are spared.

Contributor's Morphologic Diagnosis:

Pneumonia, necrosuppurative, chronic-active, multifocal, severe, with intralesional fungal hyphae consistent with zygomycetes and gram positive rods. (*Arcanobacterium pyogenes* and *Rhizomucor* spp. [not further classified] were cultured from the lung).

Contributor's Comment: The class *Zygomycetes* is divided into the orders *Mucorales* and *Entomophthorales*. Members of the order *Mucorales* tend to cause disseminated disease characterized by angioinvasion, while members of the *Entomophthorales* tend to cause localized subcutaneous granulomas.² Mucormycosis

generally manifests as subcutaneous, systemic or rhinocerebral infections.² The main portal of entry in bovine mucormycosis is reported to be the gastrointestinal tract; however, a recent report of 194 slaughtered feedlot steers with granulomatous lymphadenitis and intralesional fungal hyphae noted that no evidence of gastrointestinal disease or systemic spread was present in any of the animals, and that other portals of entry could not be completely ruled out.¹ Zygomycetes are cosmopolitan and ubiquitous, and at least one member of the genus *Rhizopus*, *R. pusillis*, is thermophilic.¹ The presence of broad, infrequently septate hyphae with irregular branching is characteristic of these fungi and can be seen in routine H & E stains, but visualization is greatly augmented by the periodic acid-Schiff reaction or Gomori's methanamine silver stain. In the present case, because *Arcanobacterium pyogenes* (but not fungi) were cultured from the mammary gland, it is likely that the bacterial mastitis was the primary source of an embolic pneumonia that was further complicated by aerogenous zygomycete infection. There was no gross or histological evidence of fungal infection in any other tissue, including mammary gland and gastrointestinal tract.

JPC Diagnosis: Lung: Pleuropneumonia, necrosuppurative, chronic, focally extensive, severe, with vasculitis, numerous colonies of bacilli and fungal hyphae.

Conference Comment: The contributor provides a good summary of the fungal aspect of this mixed

infection. Conference participants debated on the bacterial agent; based on the combination of lytic and coagulative necrosis observed, some participants considered *Mannheimia* or *Mycoplasma*. These entities were ruled out, however, as neither of them would be present in large colonies as seen in this slide. Recently *Arcanobacterium pyogenes* (formerly *Actinomyces pyogenes* and *Corynebacterium pyogenes*) has undergone another taxonomic reclassification and subsequent name change and is now known as *Trueperella pyogenes*. Based on phylogenetic and chemotaxonomic differences, the genus *Arcanobacterium* was divided into two genera-- *Arcanobacterium* and a novel genus, *Trueperella*. *T. pyogenes* is the type species for this new genus.⁴ Both genera are in the family *Actinomycetaceae*, a diverse group of gram positive bacteria that also includes the genera *Actinomyces* and *Actinobaculum*.³ *T. pyogenes* is an opportunistic pathogen that clinically causes abscesses, mastitis, suppurative pneumonia, endometritis, pyometra, arthritis and umbilical infections in cattle, sheep and pigs. Its pathogenicity is due to several virulence factors, primarily pyolysin, a hemolytic exotoxin that lyses neutrophils, macrophages and other cell types. Additionally, they produce neuraminidases, adhesins, extracellular matrix-binding proteins and fimbriae. *T. pyogenes* produces proteases as well, but their role in pathogenicity is yet to be determined. Other members of veterinary importance in the family *Actinomycetaceae* include: *Actinomyces bovis* (lumpy jaw in cattle), *Actinomyces species* (pyogranulomatous mastitis in pigs and poll evil and fistulous withers in horses), *Actinomyces viscosus* (cutaneous pyogranulomas in dogs and horses, proliferative pyogranulomatous pleuritis in dogs, abortion in cattle), *Actinobaculum suis* (cystitis and pyelonephritis in pigs), and *Actinomyces hordeovulneris* (cutaneous and visceral abscessation, pleuritis, peritonitis, and arthritis in dogs).³

Contributing Institution: Auburn University
Department of Pathobiology
College of Veterinary Medicine
166 Greene Hall
Auburn, AL 36849

References:

1. Ortega J, et al. Zygomycotic Lymphadenitis in Slaughtered Feedlot Cattle. *Vet Pathol.* 2010;47(1): 108-115.
2. Ginn P, Mansell JEKL, Rakich PM. In: Maxie MG, ed. *Jubb, Kennedy and Palmer's Pathology of*

Domestic Animals. Vol. 1. 5th ed. Philadelphia, PA; Saunders Elsevier: 2007;707-8.

3. Quinn PJ, et al. Actinobacteria. In: *Veterinary Microbiology and Microbial Disease.* 2nd ed. Ames, Iowa: Wiley Blackwell; 2011, Kindle edition, location 6945 of 35051.

4. Yassin AF, Hupfer H, Siering C, Schumann O. Comparative chemotaxonomic and phylogenetic studies on the genus *Arcanobacterium* Collins et al. 1982 emend. Lehnen et al. 2006: proposal for *Trueperella* gen. nov. and emended description of the genus *Arcanobacterium*. *Int J Syst Evol Microbiol.* 2011;61:1265-74.

CASE II: A10-6475 (JPC 3164432).

Signalment: Four-year-old, spayed female domestic medium hair cat (*Felis catus*), feline.

History: The history described facial dermatitis that progressed over a four-month period to generalized erythema and crusting of the pinnae, paws, dorsum, legs, and ventrum. Euthanasia was elected due to progressive deterioration of the cat.

Gross Pathologic Findings: The body was in good postmortem condition. Thick sheets of exfoliated keratin or tan to yellow exudate covered regions of alopecia and erythema on the legs, ventral and lateral abdomen and thorax, dorsum, muzzle, and pinnae. The residual hair coat was easily epilated and often entrapped thick layers of keratin. The cranial mediastinum contained a 5.5 x 3 x 2 cm, pale red to tan mass. The mass contained multiple cystic structures that were separated by soft pale red parenchyma and filled with translucent pale yellow to blood-tinged fluid.

Histopathologic Description: There was severe, diffuse, compact, orthokeratotic to parakeratotic hyperkeratosis that covered the epidermis and extended into most follicular infundibula which often lacked hair shafts. The epidermis was moderately to markedly acanthotic with prominent rete pegs. The epidermis was segmentally eroded to ulcerated and covered by thick serocellular crusts admixed with colonies of gram positive cocci.

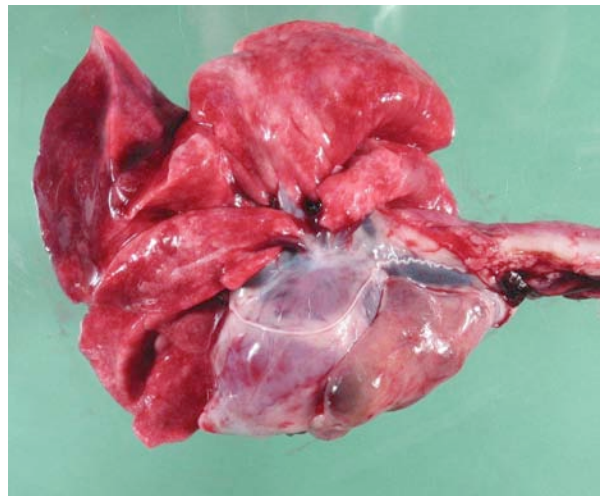


2-1. Thick sheets of exfoliated keratin or tan to yellow exudate covered regions of alopecia and erythema on the legs, ventral and lateral abdomen and thorax, dorsum, muzzle, and pinnae. (Photo courtesy of: The Purdue University Department of Comparative Pathobiology, 725 Harrison St., West Lafayette, IN 47905)

There were scattered individual necrotic keratinocytes in the stratum spinosum, and less frequently in the stratum basale and stratum granulosum. Lymphocytes were multifocally exocytosed into the stratum basale and the deep layers of the stratum spinosum. The dermis was moderately inflamed with a perivascular distribution of mast cells, plasma cells, and fewer lymphocytes. Sebaceous glands were diffusely atrophied.

Morphologic Diagnosis: Skin: Epidermal hyperkeratosis and acanthosis with apoptotic keratinocytes, lymphoplasmacytic perivascular dermatitis, and sebaceous gland atrophy.

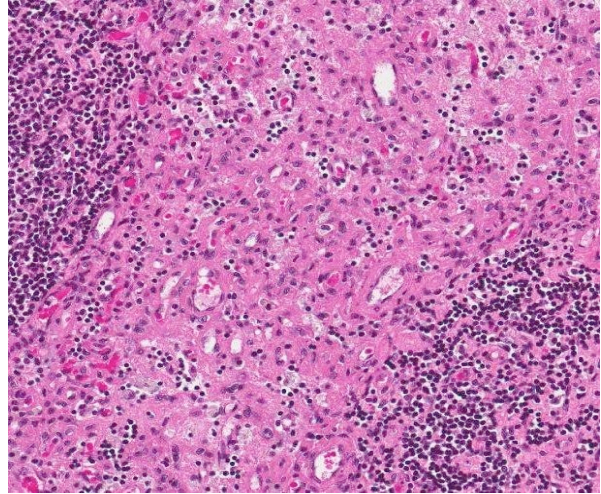
Contributor's Comment: The mediastinal mass was composed of dense aggregates of small to medium-sized lymphocytes that were surrounded by sheets of larger polygonal to round cells with moderate to abundant pale eosinophilic cytoplasm, ovoid to indented hypochromic nuclei, and 0-1 basophilic nucleoli. These larger polygonal cells demonstrated cytoplasmic immunoreactivity for pancytokeratin, facilitating the diagnosis of a thymoma. Thymomas arise from thymic epithelial cells and are classified as lymphocytic, epithelial, or mixed based on the ratio of epithelial cells to lymphocytes.⁴ Thymomas are exceedingly rare in cats and are seen most often in middle-aged to older animals. Several immune mediated conditions in humans, dogs, and cats have been associated with thymomas, including myasthenia gravis, polymyositis, and various dermatoses.⁶



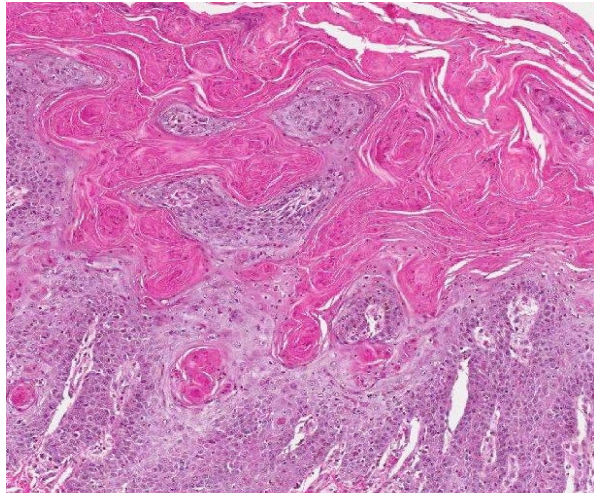
2-2. The cranial mediastinum contained a 5.5 x 3 x 2 cm, pale red to tan mass. The mass contained multiple cystic structures that were separated by soft pale red parenchyma and filled with translucent pale yellow to blood-tinged fluid. (Photo courtesy of: The Purdue University Department of Comparative Pathobiology, 725 Harrison St., West Lafayette, IN 47905)



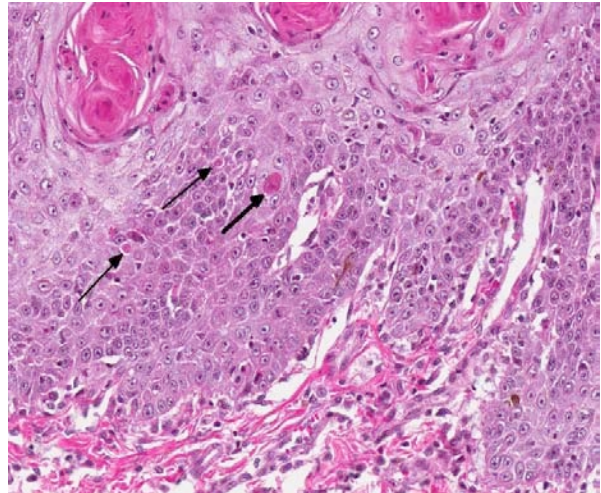
2-3. This slide contains two tissues, a multicystic thymic mass (left), and a section of hyperkeratotic haired skin (right). (HE 0.63X)



2-4. Thymus, cat: The thymic neoplasm is composed of poorly defined sheets of epithelial cells which surround and separate remaining islands of thymic lymphocytes. (HE 280X)



2-5. Haired skin, cat: The epidermis exhibits marked parakeratotic hyperkeratosis which extends down into follicular ostia. There is profound epidermal hyperplasia, acanthosis, and spongiosis, with formation of deep rete ridges and a cell-poor infiltrate at the dermal-epidermal junction. (HE 240X)



2-6. Haired skin: There are necrotic keratinocytes (arrows) at all levels of the epidermis. (HE 360X)

Thymoma-associated exfoliative dermatitis is an uncommon condition that has been reported in cats and rabbits.^{1,5,6} This disorder is thought to be a paraneoplastic syndrome that results from the failure of the neoplastic thymus to eliminate autoreactive T lymphocytes that target epidermal keratinocytes.^{3,5} The association between exfoliative dermatitis and thymomas has been supported clinically by the alleviation of cutaneous lesions following surgical removal of the thymoma.⁵

The cutaneous lesions of erythema and exfoliation of keratin are often first noted on the head, neck, and pinnae, but progressively become more generalized.³

Alopecia is commonly seen as a sequela to the exfoliative dermatitis.³ Clinical differentiation from other exfoliative dermatoses can be achieved by skin biopsies and a diagnosis of thymoma via thoracic radiographs and fine needle aspirates of the mass.³

The typical histopathologic lesions of thymoma-associated exfoliative dermatitis include severe parakeratotic to orthokeratotic hyperkeratosis, acanthosis, mild transepidermal apoptosis, sebaceous gland atrophy, and cell-poor interface dermatitis.^{3,5} An alternative diagnosis to consider is the hyperkeratotic form of erythema multiforme.³ Both conditions can exhibit marked hyperkeratosis

and variable degrees of interface dermatitis, but transepidermal apoptosis is often more severe in erythema multiforme.³

JPC Diagnosis: 1. Thymus: Thymoma.
2. Haired skin, auricular pinna: Epidermal hyperplasia and hyperkeratosis, diffuse, marked, with multifocal keratinocyte necrosis and mild cell-poor lymphoplasmacytic interface dermatitis.

Conference Comment: In an informative summary of this rare condition, the contributor notes that thymoma-associated exfoliative dermatitis is typically characterized by parakeratosis and a cell-poor interface dermatitis; however, in a review of five cats with this paraneoplastic condition, Rottenberg et al also observed examples of cell-rich skin lesions.⁵ Conference participants discussed the use of the terms “cell-poor” and “cell-rich” in defining and categorizing various types of interface dermatitis. Interface dermatitis refers to conditions in which an inflammatory infiltrate abuts and/or obscures the dermoepidermal junction; it is classified based on the dominant inflammatory cell type involved (i.e. neutrophilic, lymphocytic, lymphohistiocytic, etc.), and can be further described as either cell-poor or cell-rich. Cell-poor interface dermatitis is characterized by a sparse infiltrate of inflammatory cells along the dermoepidermal junction, whereas its cell-rich counterpart – also referred to as lichenoid interface dermatitis -- comprises a heavy band-like inflammatory infiltrate which can obscure the epidermal basal layers. In humans, cell-poor interface dermatitis is associated with conditions such as erythema multiforme, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease, graft-versus-host disease, morbilliform viral exanthema, and morbilliform drug reactions. Cell-rich interface dermatitis is observed in cases of idiopathic lichenoid disorders, discoid lupus erythematosus, lichenoid and granulomatous dermatitis, lichenoid purpura, and lichenoid and fixed drug reactions.²

References:

1. Florizoone K. Thymoma-associated Exfoliative Dermatitis in a Rabbit. *Veterinary Dermatology*. 2005;16:281-284.
2. Crowson AN, Magro CM, Mihm Jr MC. Interface Dermatitis. *Archives of Pathology & Laboratory Medicine*. 2008;132(4):652-666.

3. Gross TL, Ihrke PJ, Walder EJ, et al. *Skin Diseases of the Dog and Cat*. 2nd ed. Ames, IA: Blackwell Science Ltd; 2005:68-70, 78-79.
4. Jacobs RM, Messick JB, Valli VE. Tumors of the hemolymphatic system. In: Meuten DJ, ed. *Tumors in Domestic Animals*. 4th ed. Ames, IA: Blackwell Publishing Professional; 2002:165-166.
5. Rottenberg S, Tschärner CV, Rossje RJ. Thymoma-associated Exfoliative Dermatitis in Cats. *Vet Pathol*. 2004;41:429-433.
6. Scott DW, Yager JA, Johnston KM. Exfoliative Dermatitis in Association with Thymoma in Three Cats. *Feline Pract*. 1995;23:8-13.

CASE III: AFIP Case 1 (JPC 4018760).

Signalment: Fetus, female, Thoroughbred, *Equus caballus*, horse.

History: No history was provided.

Gross Pathology: A fetus with a crown-rump length of 61 cm was submitted with attached fetal membranes. There were hundreds of multifocal, white to yellow, irregular, slightly raised, soft, 25mm and 100mm in diameter plaques that often had a ring or pinwheel shape with a clear centre on the skin. The plaques concentrated around the head, particularly around the eyes, and the trunk but also extended along the back, tail, and limbs.

Disseminated throughout the lung lobes were hundreds of 20-50mm diameter, multifocal, firm, off-white to yellow nodules. On the cut section, the nodules were homogenous, off-white and often markedly friable centrally with a thin capsule.

The stroma of the chorioallantois was diffusely variably thickened and expanded by dark red to yellow gelatinous material. The surface of the chorion was mottled with well-demarcated red and tan areas. The chorion was covered by very thin multifocal to coalescing plaques of yellow, friable, foul smelling material. There was abundant, clumped, loosely adhered, tan to yellow material along the amnion, often tracking along blood vessels.



3-1. The equine fetus was covered by numerous multifocal, white to yellow, irregular, slightly raised, soft, 25 and 100mm in diameter plaques, most commonly around the eyes and trunk. (Photo courtesy of: University of Glasgow, School of Veterinary Medicine, Bearsden Rd, Glasgow, UK G611QH, <http://www.gla.ac.uk/schools/vet/>)

Histopathologic Description: Chorioallantois: There is marked, locally extensive necrosis of the chorionic villi that occasionally extends deeply, extending the full thickness of the stroma. Within the affected areas, there is a loss of the normal architecture with extensive areas of necrotic cellular debris, fibrin, and degenerate neutrophils. Layered within the surface debris are numerous 5-10 µm diameter, septate, branching fungal hyphae with non-parallel walls. Large clusters of neutrophils extend deeply into the areas of more viable stroma, and are often admixed with cellular debris and small numbers of lymphocytes, macrophages, and plasma cells. Inflammatory cells expand the walls of deep vessels. Vascular luminal fibrin thrombi are frequent. The allantoic epithelium is multifocally irregularly thickened (proliferation) and is occasionally cystic. Allantoic epithelial cells have abundant often heavily vacuolated cytoplasm. Cellular debris is scattered within the more affected areas.

Haired skin: There is marked diffuse orthokeratotic hyperkeratosis. Embedded within the layers of keratin are aggregates of cellular debris and fungal hyphae as in the placenta. Within the superficial dermis, there is a marked, diffuse infiltrate of lymphocytes and plasma cells.

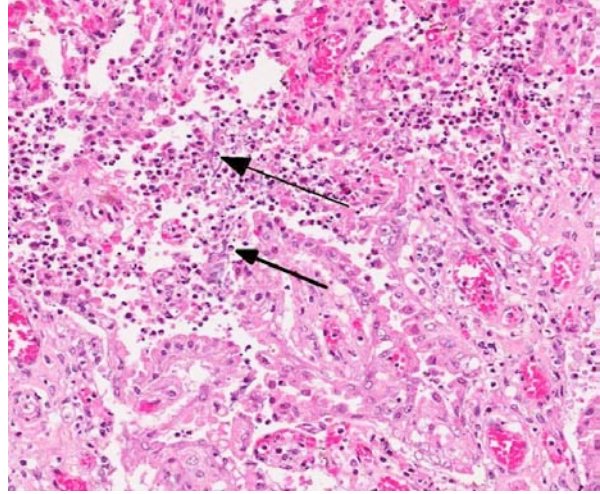
Lung (slide not provided): Randomly scattered throughout the lung are multifocal, nodular areas of inflammation that efface the normal architecture and often engulf adjacent vessels. The centers of the nodules are composed of liquefactive necrosis



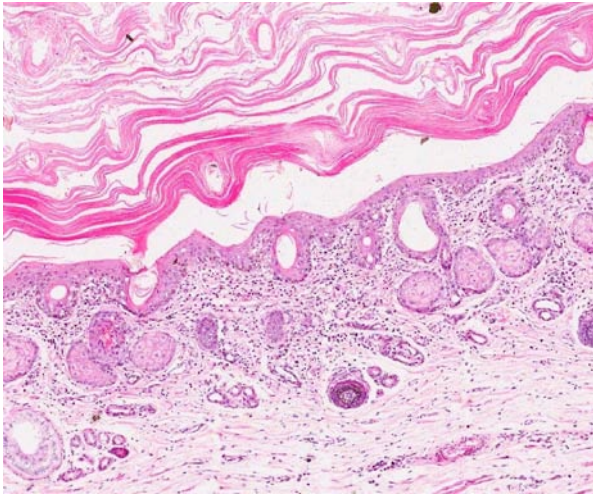
3-2. Disseminated throughout the lung lobes were hundreds of 20-50mm diameter, multifocal, firm, off-white to yellow nodules. (Photo courtesy of: University of Glasgow, School of Veterinary Medicine, Bearsden Rd, Glasgow, UK G611QH, <http://www.gla.ac.uk/schools/vet/>)



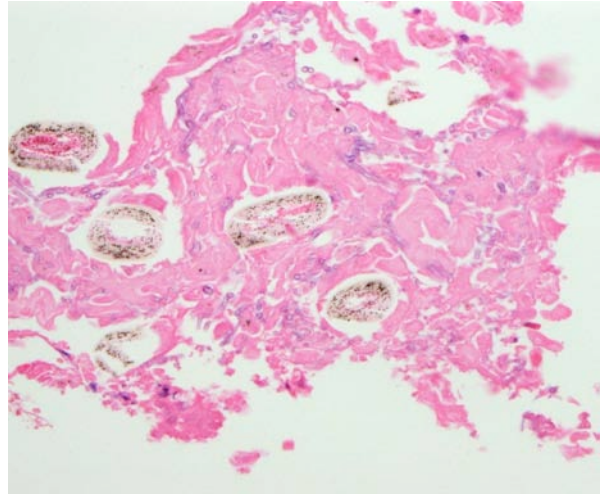
3-3. The chorioallantosis was thickened with a mottled red-tan appearance. The chorion was covered by thin plaques of yellow, friable, foul-smelling material. (Photo courtesy of: University of Glasgow, School of Veterinary Medicine, Bearsden Rd, Glasgow, UK G611QH, <http://www.gla.ac.uk/schools/vet/>)



3-4. Placenta, chorion: Chorionic villi are separated by abundant necrotic debris and aggregates of numerous 4µm wide, pigmented, septate, non-dichotomous, parallel wall, acute angle branching fungal hyphae (arrows). (HE 320X)



3-5. Haired skin: Fetal skin exhibits marked orthokeratotic hyperkeratosis, overlying a markedly inflamed dermis. (HE 240X)



3-6. Embedded within the hyperkeratotic scale overlying the skin are aggregates of cellular debris and fungal hyphae as in the placenta. (Photo courtesy of: University of Glasgow, School of Veterinary Medicine, Bearsden Rd, Glasgow, UK G611QH, <http://www.gla.ac.uk/schools/vet/>)

surrounded by a rim of epithelioid macrophages and multinucleated giant cells admixed with fibrin and hemorrhage. Peripherally, there are moderate numbers of lymphocytes and plasma cells admixed with cellular debris. Entrapped vessels have walls replaced by fibrin and cellular debris. Within the necrotic areas, there are branching clear spaces that are suspicious for fungal hyphae.

Contributor's Morphologic Diagnosis: Placenta: Marked, multifocal to coalescing necrotizing placentitis with intralesional fungal hyphae and vasculitis.

Dermatitis: Marked, multifocal dermatitis with orthokeratotic hyperkeratosis and intralesional fungal hyphae.

Lung: Marked, multifocal granulomatous pneumonia.

Contributor's Comment: Differentials for abortion in horses include a wide variety of maternal, mechanical (vascular), toxic, and infectious causes. Of these causes, placental disease is the most common cause of abortion in horses.² The most common pathogens isolated from the placenta of aborted fetuses are *Streptococcus* spp.,

Leptospira spp., *Escherichia coli*, nocardioform actinomycetes, *Pseudomonas aeruginosa*, *Enterobacter agglomerans*, and *Klebsiella pneumoniae*.²

Mycotic placentitis is less common than bacterial placentitis in horses and typically results in a regionally extensive placentitis centered on the cervical star, reflecting the ascending nature of the infection.^{2,3} Abortion due to mycotic placentitis occurs more commonly in late gestation and results from placental failure.³ Mycotic dermatitis is a common concurrent finding. Pulmonary lesions, as seen in this case, are uncommon and are thought to occur as a result of aspiration of contaminated amniotic fluid. Systemic dissemination is rarely seen in the fetus.⁴ *Aspergillus* spp. are the most common fungal organisms isolated from aborted fetuses.² In this case, the morphology of fungal hyphae is highly suggestive of *Aspergillus* spp.; however, cultures are required for definitive diagnosis.

JPC Diagnosis: 1. Placenta: Placentitis, necrotizing and suppurative, diffuse, moderate, with focal infarction, vasculitis, fibrinoid change, and moderate numbers of fungal hyphae.
2. Haired skin, eyelid: Dermatitis, lymphoplasmacytic, diffuse, mild, with marked epithelial hyperkeratosis and intracorneal fungal hyphae.

Conference Comment: As the contributor states, there are numerous causes of failure of equine pregnancy. In addition to the bacterial and fungal etiologic agents described by the contributor, other infectious causes include viruses such as equine herpesvirus 1 (EHV-1), EHV-3 (equine coital exanthema) and EHV-4, as well as equine viral arteritis virus.¹ EHV-1 is an important cause of abortion; its classic histopathologic lesion is focal necrosis in the liver, and necrosis in other organs is often seen as well. It is often associated with pneumonia, and fibrin casts in the trachea are characteristic of EHV-1 infection. EHV-3 and EHV-4 cause similar lesions, but are not as common. Equine viral arteritis often results in no fetal lesions, as fetal death is likely due to anoxia secondary to myometritis. Bacterial-associated abortion in horses is associated with placentitis, and although fetal sepsis probably plays a major role, macroscopic and microscopic fetal lesions are rare.¹

There are many noninfectious causes of pregnancy failure in horses, some of which include: twinning, umbilical cord anomalies, endometrial fibrosis, premature placental separation, and fetal thyroid hyperplasia and musculoskeletal disease.¹ Twinning results in a decreased surface area of chorionic villi, since villi do not develop in the areas where the two placentas come into contact. In these cases, death is thought to be due to placental insufficiency. Equine umbilical cord anomalies such as excessive or inadequate length and torsion can also result in failure of pregnancy. Endometrial fibrosis, usually a result of past endometriosis, precludes adequate maternofetal interface, thus resulting in either failure of the mare to become pregnant or an inability to carry the fetus to term. Premature placental separation results in a detachment of the caudal part of the chorioallantois from the uterus and a tearing across the body of the placenta instead of at the cervical star. Fetal anomalies are rare in horses; however, in some regions foals abort due to thyroid hyperplasia and musculoskeletal disease, characterized by microscopic thyroid hyperplasia but no macroscopic gland enlargement. Prognathia, flexural deformities, joint laxity, and tendon ruptures can occur in this syndrome.¹

Although not as common, there have also been several abortion storms in mares associated with eastern tent caterpillars (ETC), referred to as mare reproductive loss syndrome (MRLS), the pathogenesis for which has not been fully elucidated. Current hypotheses propose either a bacterial invasion and bacteremia occurrence secondary to injury from ingested ETC-related toxins or from mechanical damage to the gastrointestinal mucosa by setae ("hairs") on the ETC.⁵

Contributing Institution: University of Glasgow
School of Veterinary Medicine
Bearsden Rd
Glasgow, UK G611QH
<http://www.gla.ac.uk/schools/vet/>

References:

1. Foster RA. Femal reproductive system and mammary gland. In: Zachary JF, McGavin MD, eds. *Pathologic Basis of Veterinary Disease*. St. Louis, MO: Elsevier Mosby; 2012:1109-1111.
2. Hong CB, Donahue JM, Giles RC Jr, Petrites-Murphy MB, Poonacha KB, Roberts AW, et al. Equine abortion and stillbirth in central Kentucky

during 1988 and 1989 foaling seasons. *J Vet Diagn Invest.* 1993;(4):560-6.

3. Hong CB, Donahue JM, Giles RC Jr, Petrites-Murphy MB, Poonacha KB, Roberts AW, et al. Etiology and pathology of equine placentitis. *J Vet Diagn Invest.* 1993;(1):56-63.

4. Schlafer DH, Miller RB. Female genital system. In: Maxie MG, ed. *Pathology of Domestic Animals.* 5th ed. Edinburgh, UK: Saunders Elsevier; 2007:508-509.

5. Sebastian MM, Bernard WV, Riddle TW, Latimer CR, Fitzgerald TD, Harrison LR. REVIEW paper: mare reproductive loss syndrome. *Vet Pathol.* 2008;45(5):710-22.

CASE IV: 12-1821 (JPC 4017807).

Signalment: Three-year-old, intact female cat (*Felis catus*).

History: This was a feral cat submitted from a spay-neuter project in southern CA. The history was 'unknown death'. The submitter wished to rule out viral disease and poisons.

Gross Pathology: The carcass was in good post mortem condition but poor body condition, with minimal fat stores, prominent ribs and decreased muscle mass. The most significant lesions were in the lungs. All lung lobes did not collapse and were expanded by multiple coalescing, slightly firm, tan nodules. Tracheobronchial lymph nodes were 4 times normal size. An impression smear of the nodules showed numerous macrophages filled with 2-4 μm yeasts.

All other organs including liver and spleen were considered to be grossly within normal limits.

Laboratory Results: After DNA extraction from the paraffin block, the D1D2 region of the 28S ribosomal RNA gene was amplified by PCR using universal fungal primers. When this PCR amplicon was directly sequenced, the sequence most closely matched that of *Ajellomyces capsulatus* (*Histoplasma capsulatum*) (>99 % sequence identity with GenBank acc # AB176473 and others) when compared with sequences in GenBank.

Histopathologic Description: The architecture of over 80% of the lung in all evaluated sections was distorted by dense sheets of abundant inflammatory infiltrate composed of many epithelioid macrophages that expand the interstitium and fill the alveoli and bronchioles. Mixed with the macrophages were fewer lymphocytes, fibrin and edema residue. Macrophages were commonly distended by 8 to 20 intracytoplasmic yeast bodies that were round, 3 to 4 μm diameter and had a basophilic center surrounded by a 2 μm halo. Multifocally large areas of the lung were replaced by eosinophilic cellular debris, karyorrhectic debris and degenerate cells (necrosis). Small scattered areas were interrupted by hemorrhage.

The tracheobronchial lymph nodes (not submitted) were expanded by sheets of epithelioid macrophages, many of which contained similar yeast bodies. Organisms were further demonstrated by Gomori methenamine silver and periodic acid-Schiff on lung and lymph node. Fewer, scattered macrophages with intracellular yeasts were identified in the liver and spleen with special stains.

Contributor's Morphologic Diagnosis: Bronchopneumonia, histiocytic, focally extensive to coalescing, severe with multifocal necrosis and intralesional, intracytoplasmic yeasts.

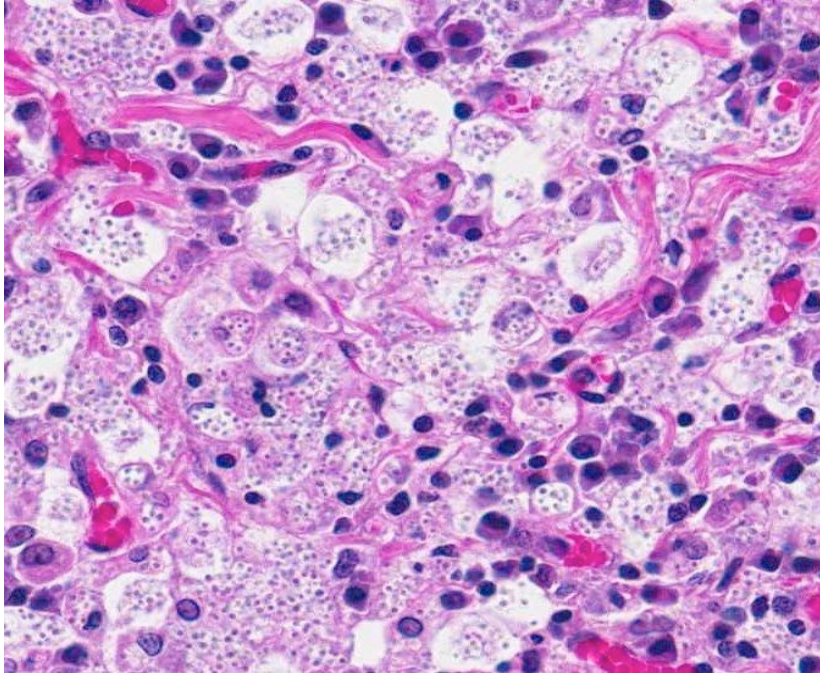
Contributor's Comment: Histoplasmosis is a non-contagious infectious disease of man and animals caused by the dimorphic fungus *Histoplasma capsulatum* var. *capsulatum*.³ It is a soil-born



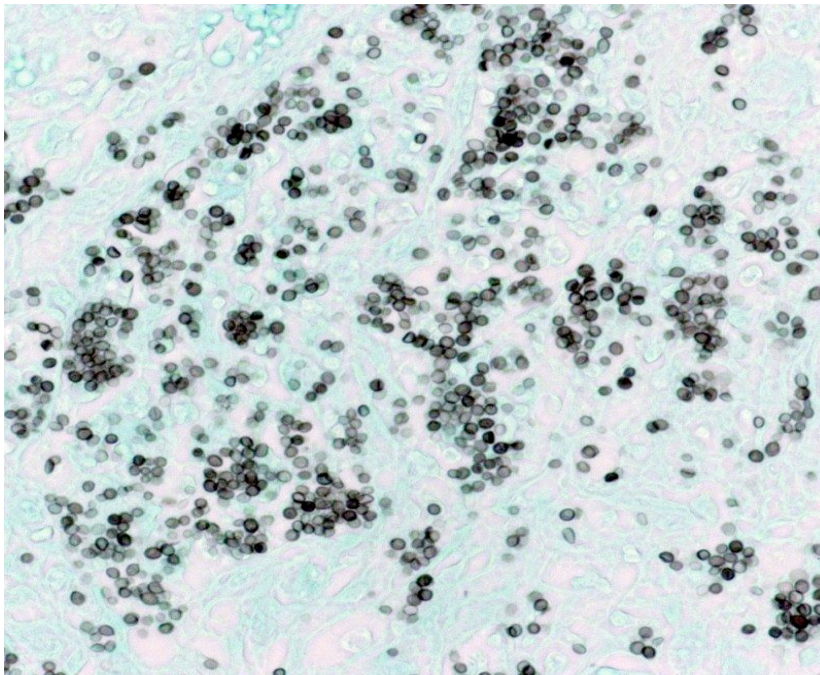
4-1. When the thorax of this cat was opened, lung lobes did not collapse and were expanded by multiple coalescing, slightly firm, tan nodules. (Photo courtesy of the Department of Veterinary Microbiology and Pathology, College of Veterinary Medicine, Washington State University, Pullman, WA 99164-7040 <http://www.vetmed.wsu.edu>)



4-2. Lung, cat: Tracheobronchial lymph nodes were 4 times normal size. (Photo courtesy of the Department of Veterinary Microbiology and Pathology, College of Veterinary Medicine, Washington State University, Pullman, WA 99164-704 <http://www.vetmed.wsu.edu>)



4-3. Lung, cat: Alveoli and airways are filled with innumerable macrophages, which contain multiple intracytoplasmic 4 µm round yeasts, consistent with *Histoplasma capsulatum*. (HE 400X)



4-4. A silver stain demonstrates the numerous yeasts present within macrophages. *H. capsulatum* is also demonstrated well by periodic acid-Schiff stains. (GMS 400X)

infection often associated with exposure to soil contaminated either with bird or bat feces. Although affecting both man and animals, it is not considered a zoonotic disease.⁷ It is distributed world-wide but is considered endemic in the Ohio, Mississippi and St. Lawrence River Valley. However, any area with the right conditions can produce cases, such as the

reported outbreak in dogs and cats in the Rio Grande Valley of Texas.² In that report, exposure was attributed to urbanization of rural land once occupied by chicken farms, and to a local bat cave. Local irrigation made conditions ripe for fungal growth, even in the arid southwest. In endemic areas many people and animals are exposed but few develop clinical disease.⁵ Risk factors include extremes in age and immunosuppression. The travel history was not available for the cat in this report, so it was not determined if the cat traveled from an endemic area or if exposure was local. The FeLV/FIV status of this cat was unknown, but as a feral animal it presumably was at high risk for exposure to immunosuppressive viruses and potentially high doses of infectious agent.

Inoculation is by inhalation of spores from contaminated soil. The spores are then taken up by pulmonary macrophages and spread to local lymph nodes and, often, throughout the body. Respiratory disease is most common, but the frequency of gastrointestinal lesions in animals suggests that oral inoculation is also possible.⁷ Localized infections in the skin and eye are also reported¹; disseminated disease is invariably fatal. Clinical signs include fever, malaise and respiratory distress; hepatic and splenic enlargement are present if the disease is disseminated. Debilitated patients are often anemic and maybe be terminally leukopenic.⁷ Gross lesions are dependent upon the extent of dissemination in the body. The lesions illustrated in the lungs and lymph nodes of this cat are a classic presentation of the respiratory lesions of histoplasmosis in cats.^{1,2} Histologically, the organisms are easily distinguished from other dimorphic fungi (*Cryptococcus neoformans*, *Blastomyces*

dermatitidis and *Coccidioides immitis*) by their size and obligate intracellular location.

The pathogenesis of the disease is best characterized in people.³ Once phagocytized by pulmonary macrophages, the conidia convert to the yeast form and disseminate within the reticuloendothelial system. Dendritic cells present antigen to T lymphocytes and within 2-3 weeks, cell mediated immune responses stimulate cytokine dependent killing of yeast by effector macrophages. In the absence of effective cell-mediated immunity (as in HIV-AIDS patients), fungus disseminates and leads to terminal illness. In the immunocompetent human host infections are most often inapparent, with occasional acute or chronic localized manifestations.⁵ Localized chronic pulmonary infections are often mistaken clinically for neoplasia. The pathogenetic factors that determine inapparent and clinical disease in animals is less well characterized, but presumably involves similar cell mediated immune mechanisms.⁷

Diagnosis can be made by fine needle aspirates or impression smears, confirmed by histopathology and may be verified by culture or PCR. Fungal culture, however, is a risk to laboratory personnel, as the chlamyospores of the mycelial phase are highly infective.⁷

JPC Diagnosis: Lung: Pneumonia, interstitial, granulomatous, multifocal to coalescing, severe with numerous intrahistiocytic yeasts.

Conference Comment: The contributor provides an excellent review of the dimorphic fungus, *Histoplasma capsulatum*. The two forms of dimorphic fungi include the mold form which occurs in the environment and the yeast form which forms in animal tissues.⁴ Several species of dimorphic fungi are opportunistic pathogens in domestic animals, the most common of which are *Histoplasma capsulatum* var. *capsulatum*, *Blastomyces dermatitidis* and *Coccidioides immitis*. Other dimorphic fungi, *Sporothrix schenckii*, *Histoplasma capsulatum* var. *duboisii* and *Histoplasma farciminosum* cause disease less frequently. Another fungal pathogen, *Cryptococcus neoformans*, can also be considered dimorphic, although it rarely appears in its filamentous form, and more often is found in its yeast form. *Candida albicans* can also exist as yeast or hyphae and pseudohyphae; however, its mold form occurs in animal tissues and its yeast form occurs in the

environment.⁴ The included table summarizes differential diagnoses for fungal yeast infections:^{4,6}

	<i>Blastomyces dermatitidis</i>	<i>Coccidioides immitis</i>	<i>Histoplasma capsulatum</i>	<i>Histoplasma farciminosum</i>	<i>Sporothrix schenckii</i>	<i>Cryptococcus neoformans</i>
Disease	Blastomycosis	Coccidioidomycosis	Histoplasmosis	Epizootic lymphangitis	Sporotrichosis	Cryptococcosis
Species most affected	Dogs, humans	Dogs, horses, cats, humans	Dogs, cats, humans	Horses	Horses, cats, dogs, humans	Cats, horses, humans
Organs affected	Lungs, skin, metastasis to other tissues	Lungs, metastasis to bones, skin, and other tissues	Lungs, metastasis to other organs	Skin, lymphatic vessels, lymph nodes	Skin, lymphatic vessels	Nasal cavity, lungs, brain, eye, skin
Tissue morphology	Large (8 to 10 µm), broad-based unipolar budding yeast cells	Large (10 to 80 µm) spherules with numerous 2 to 5 µm endospores	Small (1 to 5 µm) narrow based budding yeast cells <i>var. duboisii</i> are larger (5 to 20 µm)	Small (1 to 5 µm) narrow based budding yeast cells	Small (2 to 5 µm) narrow based budding yeast cells	Small (4 to 8 µm) narrow based budding, thick-walled yeast surrounded by a large 5 to 10 µm gelatinous capsule

Contributing Institution: Department of Veterinary Microbiology and Pathology
College of Veterinary Medicine
Washington State University
Pullman, WA 99164-7040
www.vetmed.wsu.edu

References:

1. Brillhante RSN, Coehlo CGV, Sidrim JJC, et al. Feline histoplasmosis in Brazil: Clinical and laboratory aspects and a comparative approach of published reports. *Mycopathologica*. 2012;173:193-197.
2. Kabali S, Koschmann JR, Robertstad GW, et al. Endemic canine and feline histoplasmosis in El Paso, Texas. *J Med and Vet Mycol*. 1986;24:41-50.
3. Knox KS, Hage CA. Histoplasmosis. *Proc Am Thoracic Soc*. 2010;7:169-172.
4. Quinn PJ, et al. Actinobacteria. In: *Veterinary Microbiology and Microbial Disease*. 2nd ed. Ames, Iowa: Wiley Blackwell; 2011, Kindle edition, location 17002 of 35051.
5. McKinsey DS, McKinsey JP. Pulmonary histoplasmosis. *Sem in Resp and Critical Care Med*. 2011;32:735-744.
6. University of Adelaide Mycology Online. Dimorphic Systemic Mycoses, http://www.mycology.adelaide.edu.au/Mycoses/Dimorphic_systemic/. Accessed online on 28 March 2013.

7. Valli VEO. The hematopoietic system. In: Maxie MG, ed. *Jubb, Kennedy and Palmer's Pathology of Domestic Animals*. 5th ed. Vol. 3. Edinburgh, Scotland: Elsevier; 2007:299-301.