CASE I: UKLDDC7501 (JPC 2985450).

Signalment: 1 year old male domestic shorthair, Felis domesticus, feline.

History: The cat presented with a 1 month history of ataxia, head tilt, and aggression towards other animals and people. Prior to death, the cat was capable of eating and drinking.

Gross Pathology: The animal presented in good body condition and postmortem preservation. The only significant gross finding was a 1.2 cm in diameter well demarcated light brown mass in the rostral portion of the left cerebral hemisphere.

Laboratory Results: Pathogenic bacteria, viruses, and fungi were not isolated from the brain, lungs, liver, kidneys, or intestines.

Contributor’s Histopathologic Description: Located within the cerebral neuropil is an expansile, well demarcated area consisting of large numbers of neutrophils, macrophages, and lymphocytes, small amounts of fibrous connective tissue, and variably sized areas of necrosis. Intermixed throughout the lesion are low numbers of 7-2 micrometer round to oval yeast bodies which have thick cell walls, moderate amounts of poorly staining cytoplasm, and round 3-15 micrometer homologous staining nuclei. Some of the yeast bodies display broad based budding. Multiple blood vessels in the neuropil adjacent to the lesion are surrounded by low to moderate numbers of lymphocytes and macrophages. The overlying meninges contain low to moderate numbers of lymphocytes, macrophages and neutrophils, and small amounts of fibrillar acidophilic proteinaceous material.

Contributor’s Morphologic Diagnosis: Severe chronic focal necrotizing pyogranulomatous encephalitis with intralesional yeast. Moderate chronic multifocal meningoencephalitis.

Contributor’s Comment: Blastomycosis was diagnosed based on the morphological characteristics of the yeast. Blastomycosis is most frequently reported in canids and humans, though cases in other domesticated and non-domesticated species are occasionally seen. The dimorphic fungi are not commonly isolated from the environment, but are thought to survive in manure and in soil containing decaying vegetation and high moisture content. Disease is thought to be initiated by inhalation of B. dermatitidis conidia. At body temperatures, conidia transform to the yeast phase which may disseminate and elicit pyogranulomatous inflammatory responses in the lungs, bones, liver, spleen, lymph nodes, skin, eyes, urogenital tract, and brain. This case is remarkable as the cat presented with neurologic signs accompanied with a distinct cerebral lesion suggestive of neoplasia. Lesions consistent with B. dermatitidis were not seen in other organs or tissues.

JPC Diagnosis: Cerebrum: Meningoencephalitis, pyogranulomatous, multifocal, severe, with lymphocytic perivascular cuffing and budding yeasts.

Conference Comment: The three clinical forms of blastomycosis are primary pulmonary infection, most common in domestic animals, disseminated disease, as in this case, and local cutaneous infection secondary to direct tissue
inoculation, which is rare. *B. dermatitidis* has several virulence factors. Blastomyces Adhesion 1 (BAD-1) is a surface protein which mediates adhesion to host cells and modulates immune response, and alpha-glucan protects against killing by macrophages. The adhesion molecules bind to CD14 and complement receptor 3 (CR3) on macrophages and induces activation; however, *Blastomyces* is not readily phagocytized. *Blastomyces* initially causes a neutrophilic response, but with the onset of cell mediated immunity, a granulomatous response predominates. Differential diagnosis for this case includes *Cryptococcus* spp., which often cause a gelatinous toruloma in the brain, and *Aspergillus* spp., which often causes severe necrotizing vasculitis.3,5

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**References:**  

**CASE II:** V07-14306 (JPC 3106650).

**Signalment:** One year old female Border collie (*Canis familiaris*).

**History:** This dog experienced chronic diarrhea that was often hemorrhagic, coupled with wasting. She was treated with various agents for giardiasis. She responded to treatment, then the diarrhea/wasting recurred. The dog was not brought in for further treatment. She was presented to the veterinarian several weeks later, and was extremely emaciated and anorexic, with severe, watery diarrhea. Euthanasia was elected rather than further treatment. Another dog (11 months old) in the household had similar symptoms.

**Gross Pathology:** This young female Border collie was extremely thin, with no subcutaneous or internal body fat present. Terminal weight was 19.2 lbs. There was fecal pasting around the anus. The portal vein was markedly distended caudal to the liver and readily visible as it coursed caudad. The liver had a greenish tinge to the serosal surface and an accentuated lobular pattern, and was very firm on palpation. The heart was enlarged and rounded, with a developing double apex, and both ventricular walls were thin. The small intestine was distended with gas, and contents had a foul odor. There were aggregates of yellowish-brown mucoid material attached to mucosal surfaces in a random distribution.

**Laboratory Results:** Parasitology - fecal samples from both dogs were positive for *Heterobilharzia americana* trematode eggs on fecal sedimentation test (Dr. Jack Malone, Louisiana State University, performed assay).

**Contributor’s Histopathologic Description:** Liver sections had severe and striking periportal fibrosis coupled with a mixed inflammatory infiltrate. Numerous trematode eggs were seen in portal regions; these had commonly induced a fibrotic response. Mixed inflammatory infiltrates composed of lymphocytes, plasma cells, and occasional
eosinophils were seen, primarily in portal triads. There were also copious aggregates of brownish-black pigment granules deposited throughout the liver, most common in the portal triads. The small intestine (multiple sections) had copious numbers of trematode eggs embedded in the mucosa, submucosa, and extending into the muscularis in some areas (i.e., transmural distribution); these were surrounded by varying amounts of reactive fibroplasia and mixed inflammatory infiltrate forming microgranulomas.

**Contributor’s Morphologic Diagnosis:** Liver: hepatitis, chronic, portal, nonsuppurative due to *Heterobilharzia americana.*

**Small intestine:** Enteritis, chronic, nonsuppurative, transmural, due to *Heterobilharzia americana.*

**Contributor’s Comment:** This was a case of disseminated trematode infection due to *Heterobilharzia americana,* a schistosome trematode found in the southern US. Primary hosts include rabbits, raccoons and bobcats, all of which occur in the San Juan River Valley of northwestern New Mexico (i.e., "four corners" region of US). The fluke has essentially the same life cycle as *Fasciola hepatica* (also present in this area), and uses the same lymnaeid snail as part of its indirect life cycle.

In addition to the lesions in the tissues submitted, there were disseminated granulomas surrounding eggs in the pancreas, lung, lymph node, and kidney; the small intestine and liver were most severely affected. The trematode is in the family Shistosomatidae; these parasites are of relatively low importance in North America. In addition to this trematode in dogs, there is a dermatitis of humans (i.e., "swimmer's itch") that is caused by a cercariae of wild waterfowl (*Trichobilharzia, Austrobilharzia, and Bilharziella*).¹

The miracidium hatches very soon after the egg comes in contact with water, and then enters a freshwater snail (*Lymnaea cubensis*), in which cercariae develop in daughter sporocysts. Activity by these snails is dependent upon ambient temperatures between ranges of 10°C-29°C. If the ambient temperatures are within this range, development in the snail is completed within 30 days. Upon emergence from the snail, the cercariae penetrate the skin of the host (i.e., dog, rabbit, raccoon, bobcat, or nutria), and migrate by way of the lungs to the liver. After a period of development in the liver, mature males and females make their way to the mesenteric vein and mate. These adults do not reproduce in mammalian hosts, and but may live there for 4-10 years, producing thousands of eggs during that time.⁶ Eggs laid in the terminal branches of the mesenteric veins passively work through the bowel wall via a mechanism of proteolytic enzymes that are emitted through an ultramicroscopic pore in the eggshell. They then progress to the gut lumen and escape in the feces. If feces are deposited in water, the process starts over again. The eggs evoke a granulomatous reaction that eventually prevents their egress, and favors their carriage to other organs with consequent production of widely disseminated granulomas.

It is of interest that fluke infestations, which are most often associated as problems in animals in a wet climate, can occur in a "high desert" climate and geographical environment such as the American Southwest. In the area involved, there is both flood irrigation and excessive water runoff situations during a summer wet or "monsoon" season. During these times, the necessary elements for this infection (as well as fascioliasis in cattle) are present, especially along the river bottoms or "bosque" zones. Of further interest is the involvement of the lymnaeid snail that is "double dipping" in trematode infections in several species with two different trematode parasites.

**JPC Diagnosis:** 1. Liver: Hepatitis, portal, granulomatous, diffuse, moderate, with numerous trematode eggs and nodular hemosiderosis. 2. Small intestine: Enteritis, granulomatous, multifocal, moderate, with numerous mucosal and submucosal trematode eggs and intravascular adult schistosomes.

**Conference Comment:** As mentioned by the contributor, cercariae penetrate the skin and leave seldom seen petechiae with a marked leukocytic inflammatory response to the parasite. The cercariae develop into schistosomula and migrate through dermal vessels to the lungs, where a heavy parasite load can result in pneumonia. After migration to the liver, hepatic cirrhosis can result following healing of the granulomatous response to the eggs, leading to liver failure and gastrointestinal malabsorption. Common laboratory abnormalities reflect hepatic failure, widespread granulomatous disease, and parasitism, and include hypoalbuminemia, hyperglobulinemia, hypercalcemia, azotemia, anemia, and eosinophilia. Anemia reflects both enteric blood loss and chronic inflammatory disease. A reported sequel to schistosomiasis is membranoproliferative glomerulonephritis, due to the accumulation of antigen-antibody complexes within the glomerular capillary wall, which stimulates an inflammatory
cascade leading to varying degrees of glomerular cell proliferation and basement membrane thickening. Clinical pathology abnormalities common in cases of glomerulonephritis include renal proteinuria, hypoalbuminemia, azotemia, and anemia. Diarrhea is a typical clinical finding attributed to rupture of enteric mucosal vessels and a type I hypersensitivity reaction that results in enteric ganglionitis. Small granulomas, called pseudotubercles, form in deeper tissues in chronic disease when endophlebitis precludes escape of the eggs into the intestinal lumen, as discussed by the contributor. Pseudotubercles are initially primarily eosinophilic and later progress to traditional granulomas. With chronicity, degenerate eggs often mineralize or become coated with Splendore-Hoeppli material. Adult schistosomes elicit eosinophilic endophlebitis, intimal proliferation, and thrombosis in mesenteric and portal veins, as demonstrated in this case. Adults feed on erythrocytes and regurgitate hematin pigment, which was also evident in this case. Due to slide variation, not all sections of small intestine featured adult schistosomes in mesenteric vessels.

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References:

CASE III: A10-536 (JPC 4001074).

Signalment: 4 ½ year old male rhesus macaque (Macaca mulatta)

History: This rhesus macaque was inoculated with SIVmac251as part of an experimental single-cycle SIV vaccination trial and had undergone routine phlebotomies. Twenty months post inoculation, the animal developed chronic weight loss (25% weight loss over four months.) The animal was also reported to have anorexia and chronic diarrhea. On clinical examination, the animal was in poor body condition and was observed to have pale mucous membranes as well as a large palpable abdominal mass. Due to suspicion of progression to simian acquired immune deficiency syndrome, the animal was humanely euthanized.

Gross Pathology: A large, roughly oval, firm, encapsulated mass was adhered to the serosal surface of the mid-distal colon. On cut surface, the mass was friable, with interlacing patterns of pale tan to white. The mucosa of the colon was thickened and pale with an irregular cobblestone appearance. The mucosa of the duodenum and most of the jejunum was also thickened with prominent lacteals. The right lung lobes were atelectatic with multifocal to coalescing white fibrotic areas and firm white raised nodules on the tissue margins. A large thrombus partially obstructed a pulmonary artery. The left lung lobes were red and diffusely edematous. There were no gross lesions noted on examination of the central nervous system.

Contributor’s Histopathologic Description: Colon: Replacing and disrupting the muscular layers and submucosa of the colon is a large region of liquefactive necrosis that is characterized by innumerable degenerative neutrophils, large numbers of macrophages, fewer plasma cells, and lymphocytes admixed with fibrin, cellular and karyorhectic
debris (necrosis). Interspersed with the inflammation and necrosis are marked numbers of 2-3 um, pale basophilic, round to oval, protozoal organisms that have apically oriented nuclei. Large numbers of viable and non-viable organisms are also noted within macrophages. Numerous colonic crypts also contain protozoal organisms similar to those described above. Inflammatory cells breach the colonic basement membrane in multiple places and to varying degrees separate and surround colonic crypts. Endothelial cells of the vasculature within the abscesses are plump, branched, and reactive. The serosa is proliferative and thickened with abundant fibroplasia, edema, and scattered numbers of inflammatory cells in similar proportions to those noted above. Submucosal lymphoid aggregates are often disrupted by the inflammation and there are several ectopic lymphoid follicles close to the serosa. There are small numbers of epithelial associated bacteria noted along the lumen surface of the colonic epithelium (Brachyspira sp.).

**Contributor’s Morphologic Diagnosis:** Colon: Locally extensive, severe, chronic, necrosuppurative, and histiocytic abscessation with intralesional protozoal organisms consistent with *Spironucleus* spp.

**Contributor’s Comment:** The genus *Spironucleus* is composed of flagellated protists of the phylum *Sarcomastigophora* and is closely related to other flagellates of the genera *Giardia* and *Hexamita*. Being of the order Diplomonadida, this organism is bilaterally symmetrical with two karyomastigonts and flagella that are typically not appreciated using light microscopy. It lacks an undulating membrane. This genus inhabits the gastrointestinal tract of a variety of animal hosts including birds, fish, mice, and non-human primates. *Spironucleus* can remain as a normal commensal in the intestine but also possesses the capacity to invade the intestinal epithelium and localize to other organ systems. Following ingestion, *Spironucleus* transforms from a resistant non-motile cyst into a motile trophozoite (flagellated form). Currently, the taxonomy of the closely related genera of flagellates is being elucidated through the use of small subunit ribosomal DNA (SSU rDNA) sequencing and *Spironucleus* can be broken out into three separate clades. The first and most primitive clade likely originated in marine environments. The second clade was isolated from freshwater Ide and Angelfish while the third clade was isolated from terrestrial animals. The three clades are likely only distantly related to one another.

In fish, *Spironucleus salmonicida* causes significant mortality in farmed salmon. *Spironucleus vortens* is a fresh water species that causes disease in the ornamental fish industry and is highly suspected to be one of the potential causative agents of hole-in-the-head disease in cichlids.

In birds, *Spironucleus meleagridis* was first isolated from turkeys and described and named by McNeil, Hinhsha and Kofoid in 1941 but was later found to infect many species of birds. Infection with *Spironucleus meleagridis* is reported to cause infectious catarhial enteritis in turkeys and other fowl including Chukar partridges and ring-necked pheasants and is also associated with significant morbidity and mortality. Cysts of *S. meleagridis* are found most frequently in thick mucus and are less frequently found in feces. This mechanism may enhance transmission and survival of the organism in the environment.

In laboratory rodents, *Spironucleus muris* (and potentially other *Spironucleus* species) is a commensal organism of the small intestine of rats, mice, and hamsters but can cause significant disease in immunocompromised animals (i.e. disease, environmental stress, very young animals). In severe outbreaks, there can be up to 50% mortality particularly in young mice that clinically have depression, diarrhea, and weight loss. The organism primarily colonizes the duodenal crypts and may cause an acute or chronic form of disease.

In non-human primates, a flagellated organism (*Octomitus pithici*) was described in the feces of nonhuman primates as early as 1929 by DaCunha and Muniz. More recently, phylogenetic analysis was performed on an unknown diplomonad isolated from two rhesus macaques immunocompromised from simian acquired immune deficiency syndrome (SAIDS). The organism was most closely related to *Spironucleus meleagridis*. Further investigation and screening of both SIV infected and uninfected rhesus macaques revealed that the organism was prevalent in the colony and most likely a commensal organism in normal macaques. It is suspected that the organism invades the colonic mucosa in immunocompromised animals, striking the gastrointestinal associated lymphatic tissue and disseminating either to regional lymph nodes or systemically via the lymphatics or vasculature. We suspect that in the present case, the abscess originated in a colonic lymph node following invasion from the colon. Lesions associated with *Spironucleus* were not seen in other tissues.
The bacteria noted along the epithelial border are consistent with *Brachyspira* sp. (*B. pilsicoli* is the most common). This is a common, often incidental finding in the large intestine of macaque species. The role that this bacterium plays in colonic inflammation is currently unknown; however, since it can be found in the colon of almost all macaque species, its role in causing disease is likely negligible.

**JPC Diagnosis:** Colon: Coli*ti*ts, necrosuppurative, transmural, diffuse, severe, with innumerable protozoan trophozoites.

**Conference Comment:** Pathologic infection with commensal organisms or parasites that would otherwise be cleared by an immunocompetent animal is common in non-human primates with SIV, and often results in death. Because the lentivirus depletes CD4+ T cells, infected non-human primates commonly develop opportunistic infections with *Pneumocystis carinii*, *Mycobacterium avium-intracellulare* and *M. tuberculosis*, *Cryptosporidium* spp., cytomegalovirus (CMV), adenovirus, papovavirus (SV40), *Cryptococcus neoformans*, *Toxoplasma gondii*, *Candida albicans* and *Plasmodium*.

In SIV-infected monkeys, lymphadenopathy and splenomegaly due to lymphoid hyperplasia is present in early stages of disease with lymphoid atrophy (depletion) in later stages, and thymic atrophy occurs in young animals. Histologically, there is giant cell (syncitial) interstitial pneumonia, granulomatous and giant cell lymphadenitis and splenitis, giant cell meningoencephalomyelitis, non-septic vegetative valvular endocarditis, glomerulosclerosis, and syncitial giant cells may also be present in lymph nodes, kidney, and the gastrointestinal tract.

Other lentiviruses of veterinary importance include equine infectious anemia virus in horses, Maedi-visna virus which produces ovine progressive pneumonia in sheep, caprine arthritis-encephalitis virus in goats, feline immunodeficiency virus in wild and domestic felids, and bovine immunodeficiency-like virus in cattle.

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CASE IV: G8229 (JPC 4003619).

Signalment: 16-year-old male intact mandrill (Mandrillus sphinx) non-human primate.

History: The animal lived in a zoological garden as the alpha male of a mandrill group. At the age of ten years, the animal developed multifocal ulcerative and nodular, pruritic lesions of the facial skin, at the nasal mucocutaneous junctions as well as on the oral and nasal mucosa. The course of disease was undulating with periods of improvement alternating with phases of deterioration with expansion of the cutaneous and mucosal wounds associated with inappetence, apathy, and stridors. Skin biopsies taken one years after the onset of clinical signs revealed a granulomatous inflammation with evidence of fungal structures. Although the etiological agent could not be classified, an aspergillosis, a mucormycosis, and a trichophytosis were ruled out on the basis of the histomorphology of the fungal elements. During the course of disease, different sole and combined antifungal therapeutic approaches were applied. However, permanent recovery could not be achieved. Due to worsening of the skin lesions, the development of new ulcers in the left gluteal region, and increasing psychosocial stress within the group, the mandrill was finally euthanized for animal welfare reasons. The mandrill was serologically positive for simian immunodeficiency virus (SIV) and negative for simian t-cell leukemia virus (STLV) and herpes B.

Gross Pathology: At necropsy, the mandrill was in good nutritional condition. The skin on the bridge of the nose revealed a severe multifocal to confluent ulcerative dermatitis with marked, partly nodular thickening of the subcutis and superficial crust formation. The ulcerative lesions extended to the corners of the mouth and also involved the anterior nasal and oral mucosa. A focally extensive ulcerative and proliferative skin lesion (ca. 8 x 5 cm) was also present between the anus and the left ischial tuberosity. The mandibular and left inguinal lymph nodes were moderately enlarged.

Laboratory Results: Immunohistochemistry using a polyclonal anti-Candida albicans-antibody revealed a positive reaction of the fungal organisms. Fungal culture of the skin revealed fast-growing, light green yeast colonies on a chromogene medium. Microscopically, the colony material consisted of gram positive, narrow-budding, round yeasts with a size of 2-5 μm. On the species level, the isolated yeast was identified as Candida albicans using MALDI-TOF MS. The etiology was confirmed by a PCR with Candida albicans-specific primers targeting the gene for the integrin like protein alpha INT1, which was positive on the fungal culture material.

Contributor’s Histopathologic Description: At microscopic examination, the dermis and subcutis of the nasal skin respectively the propria of the oral mucosa contained multifocal to coalescing nodular inflammatory foci beneath an extensively ulcerated squamous epithelium. The nodules were composed of abundant macrophages, eosinophils, multinucleated giant cells, viable and degenerate neutrophils, and fewer lymphocytes and plasma cells and were separated by strands of mature collagenous connective tissue. In addition, a few fibroblasts aligned along the periphery of the inflammatory cell infiltrates. Multinucleated giant cells were primarily Langhans type, with occasional foreign-body type, and contained up to 20 nuclei. There were multifocal slight hemorrhages. Multifocally within giant cells but also located in the extracellular space, there were faintly stained fungal organisms represented by round, thick-walled, yeast-like bodies as well as short hyphae. The fungal elements were strongly positive with Grocott stain and with PAS reaction (Figure 2B). They were only weakly stained by Congo red. Hyphae were characterized by rare, irregular branching, infrequent septation, thin, non-pigmented walls, and occasional bulbous dilations. The yeast-like bodies measured between 5 and 10 μm, were sometimes surrounded by a clear halo and sporadically seemed to form pseudohyphae. There was no evidence of angioinvasion.
Contributor’s Morphologic Diagnosis: Mucocutaneous junction: dermatitis/panniculitis and stomatitis, granulomatous and eosinophilic, chronic, multifocal to coalescing, marked, with multifocal ulceration, hemorrhages, and numerous intrallesional fungal organisms (short hyphae and yeast-like bodies), mandrill, nonhuman primate.

Contributor’s Comment: Candidiasis is caused by yeasts of the genus Candida, usually C. albicans, and is the most frequently occurring mycotic disease in nonhuman primates. Candida spp. are ubiquitous dimorphic fungi that normally inhabit the alimentary and genital mucosa as well as the skin of mammalian animals and humans. They represent opportunistic pathogens as disease generally only develops when the host resistance is lowered due to pre-existing disease (metabolic disorders, hematologic malignancies etc.), retrovirus infection, immunosuppressive drugs, or penetrating trauma or burns. Further risk factors include stress, cachexia, nutritional deficiencies, and immunologic defects. Candida infections most often cause localized or systemic suppurative to necrotizing, ulcerative mucosal lesions with pseudomembrane formation, but they are also rarely associated with chronic deep cutaneous granulomatous lesions with evidence of giant cells. In humans, chronic mucocutaneous candidiasis (CMC) is defined as the inability to clear fungal infections leading to persistent and recurring infections of skin and mucous membranes with yeasts, mostly Candida albicans. Although CMCs can arise from a variety of clinical conditions (HIV infection, steroid therapy etc.), they also may present as primary, hereditary immunodeficiencies due to impaired cell-mediated immunity against Candida species, mainly reflecting defects in the T017 response. Obvious predisposing immunosuppressive factors to facilitate tissue invasion of the opportunistic fungi could not be identified in the present case. As mandrills are natural and asymptomatic carriers of SIV, the SIV infection of the animal did probably not represent an immunocompromising factor. However, it cannot be excluded that a possible immunosuppressive factor could have been social stress due to the mandrill’s role as the alpha male of the group at a rather young age. The presence of a primary immunodeficiency with general increased susceptibility for mucocutaneous candidiasis is also not unlikely and might also explain the poor success of the antymycotic therapy. Other common etiologies for fungal infections of the skin in nonhuman primates include dermatophytes (Microsporum canis, Trichophyton mentagrophytes), Histoplasma capsulatum var. duboisii, Sporothrix schenckii, and Coccidioides immitis. While dermatophytes usually cause a mild superficial inflammatory response with hyperkeratosis and alopecia, infections with Histoplasma capsulatum var. duboisii, Sporothrix schenckii, and Coccidioides immitis may lead to ulcerative and granulomatous dermatitis. Further descriptions of cutaneous mycoses in nonhuman primates include cutaneous zygomycosis characterized by necrotizing dermatitis and panniculitis in two adult female rhesus monkeys following extensive fight wound trauma and a focal fungal granuloma in the skin of the nose caused by Madurella mycetomatis in a female adult mandrill.

JPC Diagnosis: Mucous membrane: Stomatitis, granulomatous, multifocal to coalescing, severe, with ulceration and numerous intracellular yeasts, pseudohyphae, and hyphae.

Conference Comment: Candida persists in the oropharyngeal cavity in the yeast form by ligand-receptor interactions. Yeast ligands include mannose, C3d receptors, and mannoproteins; and host receptors include fibrinogen, fibronectin, thrombin, collagen, laminin, and vitronectin-binding proteins. Candida yeast mainly bind mannose receptors, while Candida hyphae primarily bind complement receptor 3 (CR3) and theFc-gamma receptor. Binding induces the yeast form to switch to the invasive filamentous form, which proliferates at normal body temperatures. Candida spp. produce a large number of functionally distinct adhesins that are important determinants of virulence; they also produce enzymes, including aspartyl proteinases, which degrade extracellular matrix proteins; catalases, which resist oxidative killing by phagocytes; and adenosine which blocks neutrophil oxygen radical production and degranulation.

Candidiasis is mainly a disease of keratinized epithelium in young animals, especially pigs, calves, and foals and typically presents as a superficial infection that produces relatively mild lesions in skin and mucous membranes that grossly appear as white pseudomembranes which, when removed, reveal ulcerated or erythematous tissue underneath. In birds it is a common infection in the mouth, esophagus, crop, and proventriculus. In piglets, lesions present in the oral cavity (“thrush”), esophagus, and gastric squamous mucosa. In calves, lesions are present in the ventral sac of the rumen, omasum, or reticulum following prolonged antibiotic therapy, and in foals, gastrointestinal candidiasis involves the squamous epithelium and is associated with ulceration adjacent to the margo plicatus.

In adult ruminants, Candida is one of several angioinvasive fungi that can produce mycotic abomasitis or rumentits and subsequent fungal hepatitis. The feeding of a high carbohydrate diet increases volatile fatty acids, leads to the
disruption of normal rumen flora and proliferation of *Streptococcus bovis*, with subsequent lactic acid production. Ruminal acidosis results in mucosal ulceration allowing fungal hyphae to penetrate the mucosa, invade the vasculature, cause thrombosis, infarction, and acute necrosis. Subsequent hematogenous or direct spread leads to dissemination via portal vasculature to the liver.\(^{14}\)

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