The Armed Forces Institute of Pathology
Department of Veterinary Pathology

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Conference 6

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Moderator:

Dr. Anthony Confer, DVM, PhD, Diplomate ACVP

CASE I – 03032021 (AFIP 2890683).

Signalment: Tissues from a 2.5-year-old, Hereford cow (*Bos taurus*)

History: Patient presented with a 6-8 month duration of upper respiratory noise and a 2 week history of bloody nasal discharge. Physical examination reveals normal temperature and pulse, increased respiration, inspiratory stridor with multiple 0.5-2.0cm in diameter, tan firm sessile to polypoid masses present in both nares.

Gross Pathology: The patient is in excellent nutritional condition. Significant gross findings were limited to the nasal mucosa. The nasal mucosa of the bilateral nasal passages were expanded by multifocal and coalescing, raised, 0.5cm-2.0cm in diameter, granular to smooth, firm nodules that are present beginning 3cm caudal to the opening of the nares extending 15cm back into the nasal passage.

Laboratory Results: Fungal culture of gross lesions: *Pseudoallescheria boydii*
Bacterial culture of gross lesions: Small number of contaminants (*Streptococcus sp.*, *Bacillus sp.*)
BVD immunohistochemistry (ear notch): negative

Contributor's Morphologic Diagnosis: Granulomatous rhinitis, multifocal, severe with intralesional fungal organisms identified at culture as *Pseudoallescheria boydii*.

Contributor's Comment: In March to April of 2003, several individual cattle from geographically isolated herds across the state of Oklahoma presented with nearly identical clinical signs and gross lesions consistent with nasal granulomas. Cultures from the lesions revealed either *Pseudoallescheria boydii* or *Bipolaris sp*. Interestingly, similar fungal organisms were incidentally present within an ear notch skin sample (granulomatous dermatitis) obtained for BVD immunohistochemistry in this patient.

Although uncommon, *Pseudoallescheria boydii* typically causes localized infections in cutaneous and subcutaneous connective tissues. Within lesions, the organism is often arranged as densely entangled hyphae (2-5µm) and swollen cells (15-25 µm) that can be grossly evident as tissue grains or granules. Within the nasal mucosa of this cow, the organisms were disseminated, and even when visualized with silver stains, did not form entangled hyphae. In fact, hyphae were inconspicuous compared to the variably-sized spherical swollen cells.

Other than the cutaneous and subcutaneous mycetomas, *Pseudoallescheria boydii* has also been implicated in bovine abortions.

AFIP Diagnosis: Nasal mucosa: Rhinitis, eosinophilic and granulomatous, diffuse, severe, with numerous fungal conidia and few hyphae, Hereford cow (*Bos Taurus*), bovine.

Conference Comment: This case, as published in the November 2007 issue of Veterinary Pathology, gives a good overview of *Pseudoallescheria boydii*.[9]

P. boydii are 5-8µm septate hyphae that form 6-30µm terminal round conidia with a discrete outer wall. They may exhibit narrow- or broad-based budding. GMS is preferred over PAS for demonstrating the hyphae and conidia. The case presented in conference is unusual in that it consists of numerous 6-30µm round, occasionally budding conidia, with relatively few hyphae. In some slides, the conidia are light brown in H&E sections.

P. boydii are ubiquitous within the environment. However, infections by this fungus are extremely rare and primarily reported in immunocompromised patients. In this case, there was no evidence the cow was immunocompromised. In animals, *P. boydii* primarily causes trauma-induced eumycotic mycetomas. It has rarely been associated with equine and bovine abortions, pneumonia in a calf, granulomatous rhinitis and onychomycosis in the horse, and eumycotic mycetoma and keratomycosis in the dog and horse. Unlike in dogs, nasal infections of cattle with *P. boydii* do not typically invade the underlying bone.

Gross differentials for rhinitis in cattle include atopic rhinitis, neoplasia (e.g. lymphoma, squamous cell carcinoma), foreign body, actinobacilloisis, actinomycosis, and other fungal diseases (e.g. rhinosporidiosis, aspergillosis and phycomycosis). *P. boydii* differs from *Aspergillus* sp. and *Fusarium* sp. by an absence of both angioinvasion and dichotomous branching.

Treatment of *P. boydii* is difficult and requires antifungal-susceptibility testing since the organism exhibits some level of inherent resistance to most antifungal agents.

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CASE II – UFSM-2 (AFIP 2897020).

Signalment: 6-month-old, female, Charolais, bovine

History: This calf belonged to a group of 210 beef calves with ages varying from 6-8 months. They were weaned at 3 months of age and placed in a pasture of 4 hectacres. This pasture was very wet and had accumulated water in several places. At one end of the pasture there was a feed trough where the calves had *ad libitum* access to corn silage and to concentrate (wheat bran) at the proportion of 1%/bw/day. During mid-fall of 2003 (3 months after being introduced onto the 4 ha.) 20 calves developed a respiratory disease with clinical signs including cough, rectal temperature of 40ºC-41ºC, serous nasal discharge, tachypnea, dyspnea, labored breathing through the mouth, and anorexia with weight loss. Four calves died after a clinical course of disease of 5-8 days. The remaining 16 sick calves were treated with Doramectin 1%, and recovered slowly.

Gross Pathology: The carcass was thin and dehydrated. The lungs had large, red-gray, firm, slightly depressed, patchy areas of consolidation, mainly in the dorsocaudal

lobes. Alternating with the consolidated depressed areas there were pink-white bulging, emphysematous areas of the lung parenchyma. The lumen of the trachea and major bronchi contained large tangles of numerous slender, white, 5-8 cm, nematodes mixed with a mucinous, foamy exudate. These parasites had morphology compatible with *Dictyocaulus* spp. The areas of consolidation could be appreciated on the cut surface of the lungs. At the cut surface multiple 1 mm in diameter, yellow foci could be observed randomly distributed in the lung parenchyma, and the parasites could be seen in the luminae of bronchi. There was an excess of 50 ml of yellow turbid fluid in the pericardial sac. Moderate dilatation was observed in the right ventricle of the heart, and a slight nutmeg pattern was seen in the liver. Large numbers of *Haemonchus contortus* were found in the abomasum and moderate numbers of *Oesophagostumum* spp. were found in the large intestine.

Laboratory Results: The parasite found in the airways was identified as the trichostrongilid nematode, *Dictyocaulus viviparous*

Contributor's Morphologic Diagnosis:
1) Interstitial pneumonia, proliferative, with nematodes and larvae consistent with *Dictyocaulus viviparus*, Charolais, bovine.
2) Bronchitis and bronchiolitis, chronic, suppurative, with epithelial hyperplasia and bronchiolitis obliterans, Charolais, bovine.
3) Heart, dilatation of the right ventricale (*Cor pulmonmale*), Charolais, bovine (slides not included).
4) Nutmeg liver, Charolais, bovine (slides not included).

Etiologic diagnosis: Parasitic bronchitis and pneumonia

Etiology: *Dictyocaulus viviparus*

Contributor's Comment: The lesions present in the submitted slides are consistent with a patent infection of *Dictyocaulus viviparus* in cattle. Except for the aberrant migration of *Ascaris suum* larvae in the bovine lung, *D. viviparous* is the only lung worm in this animal species.[8] Bovine dictyocaulosis occurs worldwide but is seen more frequently in areas of high rainfall and intense irrigation.[7] In the southern hemisphere it occurs mainly after weaning in calves less than one-year-old, during the fall (as was the case of the present outbreak) or winter and even in the first months of spring.[7] The adult *D. viviparus* may reach 8 cm in length, and is a nematode which has a direct life cycle.[3] The female worms lay eggs in the trachea and bronchi of affected animals. The eggs hatch rapidly and first stage larvae are coughed up, swallowed, and shed in the feces. In the pasture, depending on the climate, the larvae can develop within 7 days in to infective third stage larvae. Upon being ingested with the grass by cattle, they penetrate the small-intestinal wall and gain access to the mesenteric lymph nodes were they molt to the L4 stage; these are taken by blood and lymph to the lungs, where they locate in the pulmonary capillaries of the ventral portions of the caudal lobes.[3,8]

Approximately seven days after ingestion, penetration of the alveoli occurs, and from there the larvae reach the bronchioles where the final molt (L5) takes place; during further development the young adults move up to the bronchi. The prepatent period is 3-4 weeks.

The lesions produced by *D. viviparus* depend on the susceptibility of the host and on the number of invading larvae. There are two main manifestations of clinical disease caused by *D. viviparus.* The primary infection occurs in calves younger than 1-year-old, and even older cattle previously unexposed to *D. viviparus,* that come into contact with heavily parasitized pastures for the first time. And, this was the case for the calves of this report. The second manifestation is referred to as **reinfection syndrome**. This condition occurs 14-16 days after immune, adult cattle that have been infected previously with *D. viviparus*, are placed on heavily contaminated pasture. Clinical signs include respiratory distress, marked coughing, increased respiratory rate, projectile diarrhea, dramatic milk yield drop, and harsh respiratory sounds. This second manifestation being the function of an allergic reaction.[1,3]

The primary infection can be subdivided into a **penetration phase** (1-7 days), a **prepatent phase** (approximately 7 to 25 days after infection), a **patent phase** (approximately 25 to 55 days after infection), and a **postpatent phase** (approximately 55 to 90 days after infection). The penetration phase is usually not associated with clinical signs.[3] As the larvae reach the alveoli in the prepatent phase there is coughing, increased respiratory rate, but death is infrequent unless complications occur. In this phase no adult worm can be found in the airways; even though *D. viviparus* larvae can be seen in the smears of expectorated mucous, they are not detectable in the feces. In the patent phase clinical signs are marked and include coughing, increased respiratory rate, labored breathing, decreased intake of food and water, loss of condition, harsh respiratory sounds, crackling sounds in the lung, and subcutaneous emphysema. Deaths are frequent in this phase and lesions observed at necropsy include bronchitis, bronchiolitis, parasitic pneumonia with consolidation and collapse of the lung lobes, and the presence of hyaline membranes. Secondary bacterial bronchopneumonia is seen in some cases.[1,7] As is the

case in this report, adult worms, larvae, and eggs are observed in the airways. Many larvae are passed in the feces and can be detected by the Baermann technique. Recovery occurs in the late patent phase, with gradual waning of the clinical signs leading to a recovery over several months time. However, deaths may occur in 25% of cases due to complications such as sudden exacerbation of dyspnea at days 45-60, after secondary bacterial infection.[1,8] Lesions in these fatal cases include pulmonary edema, hyaline membranes, alveolar epithelial hyperplasia, and interstititial emphysema.

In the case reported here, *Cor pulmonale* was observed to be associated with hydropericardium and nutmeg liver. This was interpreted as being caused by impediment of blood transit through the lung, and thus congestive heart failure.

The diagnosis of this case was straightforward since the epidemiology, clinical signs, typical lesions, and the presence of large characteristic worms permitted a definite diagnosis. All things considered, if an animal with the above discussed symptoms was examined superficially, without necropsy and discovery of nematodes, ARDS would be a definite differential.

AFIP Diagnosis: 1. Lung: Bronchitis and bronchiolitis, chronic, multifocal to coalescing, moderate, with multifocal bronchiolitis obliterans, adult and larval nematodes and ova, etiology consistent with *Dictyocaulus viviparus*, Charolais (*Bos taurus*), bovine.
2. Lung: Pneumonia, interstitial, acute, diffuse, severe with fibrin.
3. Lung: Bronchopneumonia, suppurative, multifocal, marked.

Conference Comment: The contributor gives an excellent overview of the life cycle of *Dictyocaulus viviparus*, and the various stages of infection.
Reinfection is necessary to maintain immunity as a de-

Lungworms of selected domestic and wild mammals:

- *Aelurostrongylus abstrusus* – cats; catarrhal bronchiolitis, submucosal gland hyperplasia, granulomatous alveolitis, alveolar fibrosis
- *Eucoleus aerophilus (Capillaria aerophila)* – dogs, cats, foxes; dogs and cats usually have very mild infection
- *Crenosoma vulpis* – foxes, occasionally dogs; eosinophilic catarrhal bronchitis and bronchiolitis
- *Filaroides hirthi, Andersonstrongylus milksi (Angiostrongylus milksi, F. milksi)* – dogs, mink; pyogranulomatous, eosinophilic pneumonia
- *Oslerus* (*Filaroides*) *osleri* – wild canids; single/multiple 1-10mm diameter, firm, gray-pink, sessile or polypoid, submucosal nodules in trachea and bronchi, usually at tracheal bifurcation
- *Angiostrongylus vasorum* – dogs, foxes; inhabits pulmonary artery and right ventricle
- *Dictyocaulus filaria* – sheep and goats; catarrhal and eosinophilic bronchitis and bronchiolitis
- *Dictyocaulus viviparus* – cattle; pneumonia, bronchitis, pulmonary edema and emphysema
- *Dictyocaulus arnfieldi* – horses, donkeys; obstructive or eosinophilic bronchitis, edema, atelectasis
- *Muellerius capillaris* – sheep and goats; small subpleural nodules; alveolar fibrosis +/- granulomatous inflammation
- *Protostrongylus rufescens* – sheep and goats; lambs and kids; adults live in bronchioles; results in pulmonary nodules and eosinophilic bronchiolitis.
- *Metastrongylus apri* – pigs; growth retardation, bronchitis, catarrhal inflammation

crease in the immune response is seen in as little as 100 days following infection. A hypersensitivity reaction seen in animals with the reinfection syndrome caused by *D. viviparus*, can have clinical signs and lesions indistinguishable from acute bovine pulmonary edema (ABPE).[8]

In the case presented at this conference there appears to be a more acute interstitial component underlying the verminous pneumonia with features of acute respiratory distress syndrome (ARDS). In addition, the multifocal suppurative bronchopneumonia may be the result of a secondary bacterial infection, which is not uncommon in these cases.

Bronchiolitis obliterans is a lesion of chronic bronchiolar damage that consists of either fibrous polyps occluding the bronchiolar lumen or intraluminal aggregates of inflammatory cells that obstruct the airways.[2] It can occur following a variety of pneumonias caused by agents such as bovine respiratory syncytial virus (BRSV), bovine parainfluenza virus 3 (BPIV-3), infectious bovine rhinotracheitis (IBD), *D. viviparus*, bacteria, toxic gases, and hypersensitivity reactions.[2]

Histologic features of metastrongyles include a body cavity, intestine lined by few multinucleated cells with microvilli, accessory hypodermal chords, coelomyarian musculature, and, in females, a uterus with larvae or embryonated eggs.[4]

We are grateful to Dr. Chris Gardiner, AFIP consultant in veterinary parasitology, for his review and comments on this interesting case.

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CASE III – 02B5194 (AFIP 2839228).

Signalment: A 10-year-old, male, Labrador retriever

History: The dog had recently become ataxic, nonresponsive to the owner, uncomfortable when lying down, and had watery diarrhea for several days before presentation. Radiographs revealed diffuse calcification throughout the small intestine, enlarged liver, and diffuse spondylosis of the thoracic and lumbar vertebral columns. An ultrasound revealed multiple hypoechoic nodular masses in the liver and diffuse hyperechogenicity of the submucosa of the small intestine. Because of the grave prognosis, owner elected euthanasia. Biopsy specimens of liver, spleen, and small intestine were collected.

Gross Pathology: Received for biopsy was a 10 cm segment of small intestine. The wall was firm and thickened and had multiple, 1-3 mm, white, raised foci on the serosal surface. The entire circumference of the submucosa was prominent, gritty and white.

Laboratory Results: CBC and serum chemistry panel revealed anemia, elevated liver enzymes (AST, ALP, ALT, and total bilirubin), hypoalbuminemia, hyperglobulinemia, and hypocholesterolemia.

Contributor's Morphologic Diagnosis: Small intestine: Enteritis, granulomatous, eosinophilic, transmural, chronic, severe, with large numbers of intralesional, mineralized and unmineralized trematode eggs (*Heterobilharzia americana*)

Contributor's Comment: *Heterobilharzia americana* (Digenea: Schistosomatidae) is a blood trematode that causes canine schistosomiasis in North America. Natural *H. americana* infection has been reported in bobcat, armadillo, beaver, dogs, coyote, a captive born Brazilian tapir, mountain lion, mink, nutria, opossums, raccoons,

red wolves, swamp rabbits, white-tailed deer, etc. Geographically the natural infection is essentially limited to the southern Atlantic Coast states (Florida, Georgia, North Carolina, South Carolina) and Gulf Coast states (Texas, Louisiana, Mississippi), although it has been reported in Kansas.

Members of this family, Schistosomatidae, are the only trematodes that live in the blood stream of warm-blooded hosts. They are dioecious, the male bearing the female in the ventral gynaecophoric canal. There are no metacercaria. The cercariae become fork-tailed and penetrate directly through the skin of the host. In the eggs there are no opercula. The intermediate hosts are snails of the genera *Fossaria cubensis (Lymnaea cubensis)* and *Pseudosuccinea columella*. The adult worms reside in the mesenteric veins. The eggs laid in the mesenteric veins produce enzymes to erode through submucosa and mucosa of the intestine to reach the intestinal lumen. Some of the eggs are carried by the venous flow to the liver, spleen, and other organs such as the lungs and brain. Once the eggs containing mature miracidia leave the host, they must reach water of low osmotic pressure in order to hatch. The miracidia swim actively until they find snails of the right species. They bore into them and become mother sporocysts that produce daughter sporocysts that in turn produce cercariae. A single miracidium can produce several thousand cercariae. They leave the snail, swim in the water, and enter the host by penetrating through the skin and into the lymphatics.

Clinical signs of canine *H. americana* infection include dermatitis due to skin penetration, coughing, chronic intermittent mucoid to hemorrhagic diarrhea, and anorexia. Significant clinical pathology findings include anemia, hyperglobulinemia, hypoalbuminenia, eosinophilia, and hypercalcemia in some cases. No hypercalcemia or eosinophilia was noted in this particular case, however. Although the pathogenesis of hypercalcemia in schistosomiasis is not fully understood, a recent report described hypercalcemia with elevated parathyroid hormone-related protein (PTHrP) in canine schistosomiasis. Fecal floatation is usually ineffective in the diagnosis of *H. americana* infection. Saline sedimentation or a miracidia hatch is necessary to diagnose the infection. Incidentally, the liver (not submitted) of the current case had eosinophilic granulomatous hepatitis with numerous intralesional trematode eggs.

AFIP Diagnosis: Small intestine: Enteritis, granulomatous, submucosal, circumferential, multifocal to coalescing and multifocally transmural, severe, with myriad schistosome eggs, Labrador retriever (*Canis familiaris*), canine.

Conference Comment: *Heterobilharzia americana* and *Schistomatium douthitti* are the two species of schistosomes that infect mammals in the United States of America.[7] Although typically limited to the southern Atlantic and Gulf of Mexico coastal states, *H. americana* infection in Kansas has been reported, presumably linked to the importation of infected raccoons into the state during the mid-20th century.[7]

The most tissue damage occurs during oviposition and extrusion of the eggs through the tissue. The ideal movement of eggs to the outside world includes penetration of the mesenteric vessels, lamina propria and exit into the intestinal lumen, through secretions produced by the miracidium as well as through mechanical disruption.[6] When the eggs migrate in the wrong direction or get swept into the portal or systemic circulation, they can induce a granulomatous reaction in a variety of organs (lymph node, liver, lungs, etc.), depending on where they lodge.[6]

The eggs within tissue usually invoke a hypersensitivity reaction, resulting in a granulomatous response that is followed by degeneration or mineralization of the schistosome eggs and eventual fibrosis.[6] The mineralization of the schistosome eggs in this case is unusual in its extent.

Although hypercalcemia was not seen in this case, it has been associated with chronic granulomatous inflammation.[8] Activated macrophages produce calcitriol that is not regulated by parathyroid hormone, calcitriol, or calcium levels.[8] Causes of hypercalcemia are listed below:

- Neoplasia (lymphoma, multiple myeloma, adenocarcinoma of the apocrine gland of the anal sac, tumors metastatic to bone)
- Primary hyperparathyroidism (hyperplasia, adenoma, adenocarcinoma) - elevated levels of circulating parathormone cause increased intestinal absorption of calcium and phosphorus as well as increased renal activation of vitamin D
- Granulomatous inflammation (canine blastomycosis, bovine paratuberculosis, schistosomiasis)
- Hypoadrenocorticism (increased tubular resorption of calcium)
- Osteolytic lesions of bone
- Immobilization
- Metabolic acidosis
- Renal failure in horses (rarely canine renal failure associated with familial disease)

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CASE IV - 1-777-05 (AFIP 2977999).

Signalment: 3-day-old, male, beef calf, black Angus

History: Diarrhea affecting multiple calves at 3-7 days of age. Calves are unresponsive to treatment and die 1-2 days after onset of clinical signs.

Gross Pathology: Segmental, dark red, small intestine with semifluid bloody content

Laboratory Results:
Serum IgG(1) >2000 mg%
E coli K99 negative
Gram stains of intestinal contents reveals moderate bacilli
Clostridium perfringens cultured anaerobically. *C. perfringens* PCR genotyping:

Alpha	Beta	Epsilon	Iota	Beta2	Enterotoxin
POS	POS	NEG	NEG	NEG	NEG

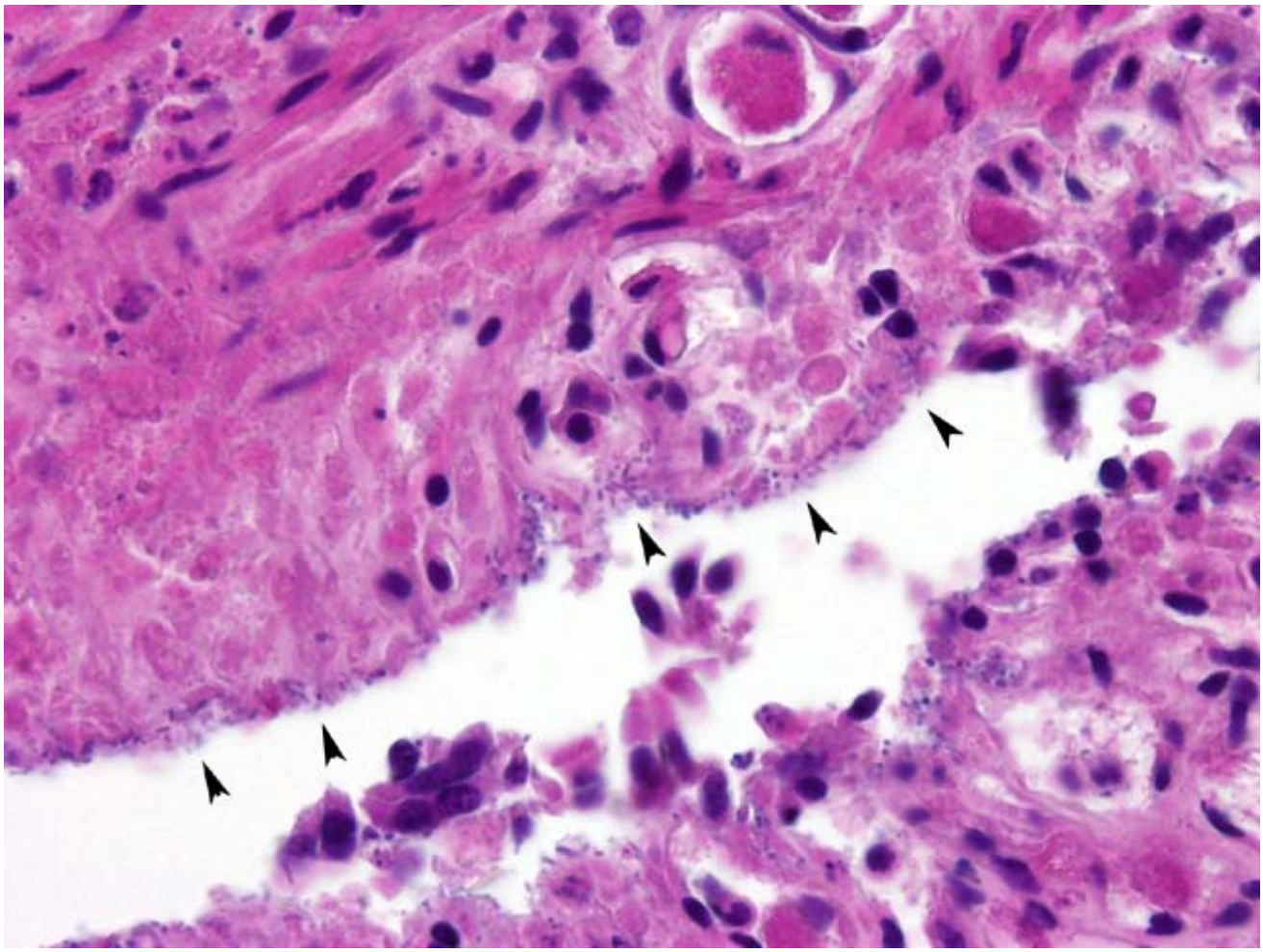
Contributor's Morphologic Diagnosis: Small Intestine: Enteritis, necrotizing, acute, segmental, marked, with bacilli

Contributor's Comment: This is a typical case of neonatal hemorrhagic enterotoxemia (necrotic enteritis) due to *Clostridium perfringens* type C, as determined by PCR genotyping. This is a disease of neonatal calves, lambs, foals and piglets.[3] *Clostridium perfringens* types A and C are increasingly common in poultry, due to reduced use of antibiotic growth promoters.[4] Clinical signs include hemorrhagic diarrhea, dehydration, anemia and weakness. Although sporadic in occurrence, this disease has a high morbidity and mortality despite treatment. Disease is primarily due to elaboration of cytotoxic beta-toxin. This toxin is readily degraded by trypsin. The trypsin inhibitors in colostrum, effective in facilitating absorption of intact maternal immunoglobulins, also inhibit the degradation of beta-toxin in neonates.[5] Death can be due to dehydration and fluid/acid-base derangement or due to secondary gram-negative septicemia/endotoxemia. This case presented with a mild interstitial pneumonia suggestive of bacteremia/endotoxemia and had adequate passive transfer of maternal antibody, both typical ancillary findings. Vaccination for *C. perfringens* type C and D is readily available and widely used.

AFIP Diagnosis: Small intestine, villi: Necrosis, diffuse, with fibrin thrombi, and myriad mixed bacilli, Angus (*Bos taurus*), bovine.

Conference Comment: The five types of *Clostridium perfringens* are differentiated by their production of one or more of the four types of antigenic exotoxins.[1] Diagnosis depends on demonstration of the toxin with the presence of hemorrhagic and necrotizing enteritis.[3] Bacterial **colonization (fig. 4-1)** alone will not produce disease or determine a diagnosis. Disease production is dependent on toxin type and the toxin's effect on tissue, either through local toxin inducing necrotizing effects, secretory effects of locally acting enterotoxins, or systemic effects of absorbed (entero)toxins.[1]

Alpha toxin is a lecithinase (phospholipase) that damages cell membranes causing necrosis or lysis of erythrocytes, platelets, leukocytes, and endothelial cells. Beta toxin is a trypsin labile, pore forming toxin that causes necrosis, decreases mobility of intestinal villi, and enhances bacterial attachment to the villi. The Epsilon toxin is produced



4-1 Small intestine, Black Angus calf. The necrotic, denuded villi are lined by a dense layer of bacilli that are 3-7 um long by 1-2 um wide (arrowheads). (H&E 600X)

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as a prototoxin and activated by enzymatic digestion (i.e, by trypsin in the intestine), and causes necrosis. Iota toxin increases capillary permeability and is also produced as a prototoxin that is activated by proteolytic enzymes.[1]

Another *Clostridium perfringens* toxin identified as ß2 has been described in recent literature. Despite its name, ß2 toxin is unrelated to the Beta toxin.[1] The gene cpb2 codes for ß2-toxin, but not all cpb2 positive strains of *C. perfringens* produce the ß2 toxin *in vitro*.[6] It has been implicated in enteric disease in swine and typhlocolitis in horses.[1]

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Clostridium perfringens – Types, toxins and diseases

Type	Toxin				Diseases
	Alpha	Beta	Epsilon	Iota	
A	+ +	-	-	-	• Gas gangrene • Food Borne Illness humans • Necrotic enteritis - Chickens • Gastroenteritis - Ferrets • Yellow lamb disease - enterotoxemia, western US • Colitis X in horses - unproven association
B	+	+ +	+	-	• Lamb dysentery • Hemorrhagic enteritis - calves, foals, guinea pigs - UK, S. Africa, Middle East
C	+	+ +	-	-	• Enterotoxic hemorrhagic enteritis - neonatal lambs, goats, cattle, pigs • Struck - Adult sheep, UK
D	+	-	+ +	-	• Overeating disease/ pulpy kidney - Sheep, cattle, goats • Focal symmetric encephalomalacia - Sheep
E	+	-	-	+ +	• Enterotoxemia – calves, lambs. guinea pigs, rabbits

Table adapted from Brown et al.[1] & Jones et al.[7]

Notes: