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Conference Moderator: LTC Todd O. Johnson, DVM, Diplomate ACVP
Department of Veterinary Pathology
Armed Forces Institute of Pathology
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CASE I – N05-169-6 (AFIP 2988200)

Signalment: A 3-year old female intact, Yorkshire, Sus scrofa, porcine

History: Animal was found dead in its pen on a dirt lot. Diarrhea was noticed in other pigs and one died approximately 1 week earlier.

Gross Pathology: A mature intact female Yorkshire hog was presented for necropsy in good body condition. External examination revealed numerous bright red rhomboid lesions located in the skin of the ventral neck, ventral abdomen, snout and all four limbs. The inguinal lymph nodes were palpable and enlarged 2 to 3 times normal size (5x8cm). A thick, red mucoid exudate exuded from both nostrils and a small quantity of tan mucoid exudate was present in the vaginal opening. Both the thoracic and abdominal cavities contained excessive amounts of serosanguineous fluid. The spleen was markedly enlarged and dark red. The liver was black and mottled. The omentum was attached to the abdominal wall by yellow strands of fibrin. The jejunum was moderately distended with gas and there were scattered 2 to 5 cm red foci in the mucosa of the jejunum and colon as well as on the serosa of the spiral colon. The joint capsules of the carpal joints were thickened and contained a serosanguineous fluid.

Laboratory Results: Microbiological examination: Heart Blood, no pathogen detected; Joint swab, *Erysipelothrix rhusiopathiae* growth was heavy.

Histopathologic Description: Sections of the skin show areas of necrosis involving the basal portion of the epidermis and upper dermis. Minimal neutrophilic infiltrates are present in the necrotic areas. The epidermis is thickened near areas of necrosis and some sections show mild hyperkeratosis, small foci of ulceration and

separation of the epidermis and dermis. There is marked capillary congestion and some arterioles show myodegeneration and perivascular infiltrates of neutrophils and fibrin. Some vessels contain fibrinous and cellular thrombi. Occasional colonies of rod-shaped bacteria are present in perivascular areas. Postmortem autolytic changes prohibited definitive microscopic evaluation of visceral organs.

Contributor's Morphologic Diagnosis: Dermatitis, necrotizing, ulcerative, mild to moderate, multifocal, with vasculitis, marked capillary congestion and vascular thrombosis, skin, porcine, due to *Erysipelas rhusiopathiae*

Contributor's Comment: *Erysipelothrix rhusiopathiae* is of wide geographic distribution and outbreaks occur in a wide range of animals including pigs, lambs, and birds. Under natural conditions, erysipelas is transmitted by ingestion of the organisms, contamination of skin lesions, or by the bites of infected flies. Erysipelas occurs in humans mainly as an occupational disease of meat and poultry plant workers, veterinarians, and rendering-plant workers (2).

In swine, the disease is an acute highly fatal septicemia or a chronic disease characterized by endocarditis, polyarthritis and skin necrosis. The organism can persist for months in tissues of diseased pigs and these animals become the primary source of infection for healthy swine. Healthy swine may be carriers and shed organisms in feces (1). While the disease can be a highly fatal septicemia, recovery can occur after treatment with appropriate antibiotics. Thus the disease in sows can be controlled in modern commercial farrow-to-finish operations when proper vaccination protocols are followed (3).

The pathogenesis of the early septicemic phase of the disease involves changes in capillaries and venules in visceral organs and synovial tissues. Thirty-six hours after subcutaneous exposure to virulent *E. rhusiopathiae*, there is swelling of endothelial cells, adherence of monocytes to vascular walls and wide spread thrombosis. This disseminated coagulopathy leads to fibrinous thrombosis, diapedesis and vascular invasion by bacteria. Lesions in skeletal muscle are associated with vascular lesions and consist of segmented hyaline necrosis of muscle fibers that may be followed by fibrosis, calcification and regeneration. Lesions in the central nervous system consist of vascular damage leading to degeneration of neurons and malacic changes in the cerebrum, brain stem and spinal cord. (2)

The most common lesion in chronic swine erysipelas is a proliferative, non-suppurative arthritis, occurring mainly in the hock, stifle, elbow and carpal joints. Vegetative valvular endocarditis is a less common finding.

AFIP Diagnosis: Haired skin and subcutis: Vasculitis, acute, multifocal, moderate, with fibrin thrombi and superficial dermal necrosis, Yorkshire, porcine.

Conference Comment: The contributor provides an excellent review of swine erysipelas lesions and pathogenesis. Conference attendees debated the presence of superficial dermal necrosis and bacteria within dermal vessels.

Erysipelothrix rhusiopathiae is a Gram-positive, non spore forming, facultative anaerobic bacillus with a worldwide distribution. Swine are the most important reservoir and approximately 30-50% of healthy swine harbor the organism in their tonsils or lymphoid tissue, periodically shedding the bacteria in their feces. Young pigs (3 months -1 year) and pregnant sows are most susceptible.

As the contributor noted, there are two forms of disease: the acute febrile septicemic form and the chronic form. Clinical findings for the acute septicemic form include pyrexia, depression, lethargy, anorexia, lameness, abortion, stillbirth and purple discoloration of the skin. Chronic cases may develop the classic "diamond skin" lesions, lameness and swollen joints as well as signs of cardiac insufficiency and decreased growth rate. Typical necropsy findings for acute disease include: pink to purple congested skin; edematous, congested lungs; petechiae and ecchymoses of the epicardium, atrial myocardium, renal cortex; hemorrhagic gastritis; and congestion of the liver and spleen. Chronic disease may result in slightly raised, necrotic diamond shaped skin lesions; arthritis and synovitis with serosanguineous effusion into joint cavities; hyperemic and proliferative synovial membranes and joint capsules; articular cartilage erosion; ankylosis; spondylitis; and vegetative valvular and mural endocarditis.

In this case, the cutaneous vasculitis with fibrin thrombi and dermal necrosis strongly supports the diagnosis. Attendees also considered porcine dermatitis and nephropathy syndrome (PDNS) in the differential diagnosis. PDNS is believed to be caused by coinfection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus 2 (PCV2). The cutaneous lesion of PDNS consists of severe necrotizing vasculitis affecting the dermis and subcutis, with epidermal necrosis, ulceration and dermal hemorrhage (4).

In sheep, erysipelas is almost always a percutaneous infection with the bacteria gaining entry through the umbilicus, docking and castration wounds, shear wounds, cuts, and abrasions. Lesions may be confined to the skin or localize in the joints resulting in fibrinopurulent polyarthritis and osteomyelitis (1). Additionally, calves also develop polyarthritis and marine mammals develop an acute septicemia with lesions similar to swine erysipelas. Turkeys can develop acute and chronic forms of disease with hemorrhage, splenomegaly, polyarthritis, and endocarditis. In humans, *E. rhusiopathiae* causes erysipeloid, a localized skin lesion found in

people who handle infected shellfish or turkeys. Conversely, human erysipelas is an infectious skin disease caused by *Streptococcus pyogenes* and is characterized by a rapidly spreading rash than can develop a “butterfly” shaped erythematous lesion on the face (5).

Contributor: Department of Pathobiology, College of Veterinary Medicine, Nursing and Allied Health, Tuskegee University, Tuskegee, AL 36088

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CASE II – P05-5907 (AFIP 2991567)

Signalment: Five year-old, female, Holstein Friesian cow.

History: This animal was losing weight and had malaise in October 2004. On 11-26-2004 it was taken into the clinic at the Faculty of Veterinary Medicine with polyuria and polydipsia. Later, in June 2005, over a period of a week, problems reoccurred with reduced appetite, malaise and dehydration. The clinicians suspected *Quercus* poisoning.

Gross Pathology: The animal was in poor body condition. The carcass exuded a uremic fetor. In the heart, two large valvular cysts were present on the left atrioventricular valve. Both kidneys showed irregularity of the external surface and adhesion of the renal capsule. On cut section multiple areas of firm pale tissue (fibrosis) were observed. The abomasal mucosa was thickened, with an irregular multinodular surface (hyperplasia).

Laboratory Results: Blood urea was measured at 50 mmol/l in June 2005.

Histopathologic Description: Abomasum. The tunica mucosa is markedly hyperplastic, with large numbers of mucus producing epithelial cells (mucoid hyperplasia) and absence of chief cells. There is an increase in the number of mitotic figures in the abomasal gland epithelium. In the abomasal lumen and sometimes in the glands multiple cross sections and occasional longitudinal sections of nematodal organisms are present. These nematodes are round in cross section, and they have a cuticle with external cuticular ridges. Usually a single, roughly circular section through the intestinal canal is seen, with a wall consisting of a single layer of columnar cells (morphologically consistent with *Ostertagia* sp. larvae). In some specimens a uterus can be seen (females), in others a vas deferens is present (males). The lamina propria contains moderate multifocal infiltrates of mainly eosinophils, lymphocytes and plasma cells and forming of lymphoid follicles.

Contributor's Morphologic Diagnosis: Chronic marked nodular hyperplastic abomasitis with intralesional nematodal parasites morphologically resembling *Ostertagia* sp. larvae (ostertagiosis).

Contributor's Comment: *Ostertagia ostertagi* is perhaps the most common cause of parasitic gastritis in cattle. Ostertagiosis is characterized by weight loss and diarrhea and typically affects young cattle during their first grazing season. Pathological changes are maximal when the parasites are emerging from the gastric glands. Parietal cells, which produce hydrochloric acid, are replaced by rapidly dividing, undifferentiated, non-acid-secreting cells. The end result is a thickened hyperplastic gastric mucosa, creating macroscopically visible nodules where the parasites are located. These nodules can coalesce, giving the mucosa the aspect reminiscent of Moroccan leather.¹

This case is somewhat atypical in that the animal is a five year-old cow. Moreover, there was concomitant renal failure with a marked chronic interstitial nephritis and protein-losing nephropathy. Both the renal and the abomasal lesions may have contributed to the illness of the animal. Perhaps the animal's immune reactions to the *Ostertagia* larvae were depressed due to the chronic renal disease.

AFIP Diagnosis: Abomasum: Mucous neck cell hyperplasia, diffuse, moderate, with mild, subacute, eosinophilic abomasitis and trichostrongylid nematodes, etiology consistent with *Ostertagia* sp., Holstein Friesian, bovine.

Conference Comment: Conference attendees discussed the anatomical location of the section and the diffuse absence of parietal cells. Some felt the section may be from the pyloric region of the abomasum and that the complete lack of parietal

cells was, in part, due to anatomic location. All agreed there was diffuse mucous neck cell hyperplasia and eosinophilic abomasitis.

Ostertagia spp. infection has been called the most important parasitism in grazing sheep and cattle in temperate climate zones throughout the world. It results in tremendous production loss, as well as clinical manifestations of anorexia, diarrhea, wasting, and some deaths.

The life cycle is direct with eggs being consumed with fecally contaminated feed. In the rumen the L3 larvae exsheath, penetrate the abomasal glands and undergo two molts to the L5 stage. L5 larvae emerge and mature on the mucosa approximately three weeks following ingestion (Type I ostertagiasis). During larval development there is interstitial inflammation and mucous neck cell hyperplasia which replace parietal cells. Parietal cells produce hydrochloric acid (HCl) and their loss results in a decreased hydrochloric acid production and a subsequent increase in abomasal pH. Under basic conditions, pepsinogen, produced by chief cells, is not converted to pepsin which results in decreased protein digestion. Increased plasma pepsinogen levels result from leaky intercellular junctions allowing backflow of pepsinogen between poorly differentiated mucous neck cells. Increased blood gastrin levels may have a central effect on the satiety center resulting in decreased appetite and motility. Diarrhea is probably the result of the elevation in abomasal pH. Plasma proteins are lost into the gastrointestinal tract contributing to weight loss and hypoproteinemia. Some larvae may persist in mucosal glands in a stage of arrested development (hypobiosis) for up to four months before the synchronous maturation, emergence and molting to the L5 stage (Type II ostertagiasis) (2).

Typical necropsy findings include thickened abomasum with multifocal to coalescing nodules containing larval or adult nematodes (6-15mm long), multifocal erosions, erythema, catarrhal exudate and foul smelling abomasal contents. Additional findings include subcutaneous and mesenteric edema, ascites, liver atrophy and a dilated gallbladder due to inanition.

Typical light microscopic findings include mucous neck cell hyperplasia, decreased parietal cells and lymphoid nodules within the mucosa. The lamina propria may be infiltrated by variable numbers of eosinophils, neutrophils, lymphocytes, plasma cells and globule leukocytes.

Ostertagia spp. are trichostrongyle nematodes with evenly-spaced, external longitudinal cuticular ridges, platymyarian musculature and a large intestine composed of few multinucleated cells.

The mnemonic "HOT" is useful for remembering the most important abomasal nematodes:

"H": *Haemonchus contortus* in sheep and goats and *H. placei* in cattle, also known as the "barber pole worm".

"O": *Ostertagia* spp.

"T": *Trichostrongylus axei* infects cattle, sheep, and goats

All of these are trichostrongyles; the key to identifying *Ostertagia* spp. in histologic section is the evenly-spaced external cuticular ridges.

This case was reviewed in consultation with Dr. Chris Gardiner, AFIP consultant in veterinary parasitology. We are grateful to Dr. Gardiner for his comments on this classic case.

Contributor: University of Utrecht, Faculty of Veterinary Medicine
Department of Pathobiology, Pathology Division
Faculty website: www.vet.uu.nl

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CASE III – B05-425 (AFIP 2985163)

Signalment: 31-year-old, neutered male with body weight of 2.1 kilograms, Capuchin monkey, *Cebus* species

History: A 31-year-old capuchin monkey was presented to the University of Georgia Veterinary Teaching Hospital's Exotic animal service. Animal was bright, alert, responsive but in very poor body condition (Score: 1.5/5) weighing about 2.1kg (Gross photo: 1). Animal had decreased appetite, lethargy, and infrequent shivering or shaking of the body. A well circumscribed movable mass of approximately 4x3cm was palpated in the ventral neck. Ultrasonography revealed extensive cystic changes in the liver and both kidneys. Fine needle aspirates of these masses failed to indicate neoplastic disease and these cystic changes were considered to be benign geriatric changes. The entire mass from the ventral neck

area was surgically excised. The excised mass was submitted in formalin for histopathologic examination.

Gross Pathology: The mass was firm, solid, tan, and measured about 3.0 X2.0 cm (Gross photo: 2).

Laboratory Results: Blood chemistry and urinalysis showed evidence of mild renal insufficiency. Creatinine was mildly elevated (1.4mg/dL), mild proteinuria (26 mg/dL) and low urine specific gravity (1.010) suggested a mild renal insufficiency. Thoracic radiographs, other biochemistry parameters and hematology were unremarkable.

Histopathologic Description: Thick fibro-vascular bands of varying size are compressing and separating numerous cords and follicles lined with epithelial cells. The cells are cuboidal to polygonal, with indistinct borders and scant amphophilic to basophilic cytoplasm. Nuclei are oval to elongated, hypo- to hyperchromatic with inconspicuous nucleoli. Cellular and nuclear polymorphism is moderate and mitoses average 24 per 10 HPFs. There are multifocal variably sized necrotic areas and hemosiderin laden macrophages throughout the tumor. Approximately ¼ of all follicles are filled with blood and cellular debris, while a few of them are filled with colloid. Immunohistochemically the neoplasm was positive for thyroglobulin and cytokeratins AE1/AE3 (IHC photos: 1 & 2).

Contributor's Morphologic Diagnosis: Thyroid gland – Follicular adenocarcinoma

Contributor's Comment: Reported frequency of thyroid neoplasia in new-world primates is very low. A review of the literature revealed only 2 cases of thyroid cystadenoma in black-tailed marmosets (1). One case of nodular thyroid hyperplasia in a cynomolgus monkey has been described (2). Other endocrine tumors described in new-world primates include pituitary adenomas, pheochromocytoma, adrenal ganglioneuroma, adrenal cortical adenoma, parathyroid chief-cell adenoma and pancreatic islets-cell adenoma. To our best knowledge this is the first case of thyroid gland adenocarcinoma described in a new-world primate.

AFIP Diagnosis: Thyroid gland: Medullary thyroid carcinoma, Capuchin monkey, primate.

Conference Comment: Conference attendees debated several features of this neoplasm including the presence or absence of capsular invasion or penetration; the homogenous, eosinophilic, acellular material which often separates cells; and whether or not the neoplastic cells could be of medullary (C-cell) origin.

We chose to run several immunohistochemical stains to further characterize the neoplasm and a Congo red stain to see if stromal amyloid was present. In our lab the neoplastic cells are negative for both thyroglobulin and thyroid transcription factor-1 (TTF-1) and positive for calcitonin, chromogranin, and synaptophysin. The Congo red stain results are equivocal. Additionally, the case was reviewed by pathologists in the Department of Endocrine and Otorhinolaryngic Pathology. Based on the morphologic features and immunohistochemical staining characteristics, we favor a diagnosis of medullary thyroid (C-cell) carcinoma.

As noted in the contributor's description, this neoplasm was characterized by a pleomorphic polygonal cell population with a high mitotic rate, but neither capsular penetration nor vascular invasion was present in our sections. Attendees discussed the importance of clear capsular or vascular invasion in the diagnosis of malignancy in human thyroid follicular tumors. However, the same criteria do not apply for human medullary tumors; in fact, most human medullary carcinomas are nonencapsulated. There are insufficient reports of thyroid neoplasia in non-human primates to judge the significance of encapsulation in this case. Some attendees felt the homogenous, eosinophilic, acellular material may represent amyloid. Stromal amyloid deposits are common in C cell neoplasms of humans and animals (3).

Medullary carcinomas occur commonly in many strains of rats and their incidence increases with the age of the population. C-cell neoplasms also commonly occur in bulls, where they are known as ultimobranchial neoplasms (3).

Calcitonin-secreting C-cells originate from neural crest cells and migrate into the 5th (ultimobranchial) pharyngeal pouch. The ultimobranchial body migrates and fuses with the midline primordium that forms the thyroid gland in mammals. In submammalian species the ultimobranchial gland remains separate.

Ultimobranchial tumors may derive from:

1. Undifferentiated stem cell remnants of the ultimobranchial bodies (negative for calcitonin, somatostatin, and neurotensin)
2. Parafollicular C-cells (positive for calcitonin, somatostatin, and neurotensin)

In rats, the chronic administration of vitamin D3 has been reported to increase the frequency of medullary carcinomas (3). Likewise, there is a suggested relationship between long-term excess dietary Ca^{2+} and a high incidence of ultimobranchial tumors in bulls.

Typical clinical findings of C-cell carcinoma include normal or slightly lowered levels of circulating calcium; palpable nodules in the anteroventral cervical region of bulls and horses and; in bulls, an increased incidence of vertebral osteosclerosis with

ankylosing spondylosis deformans, osteophytes, vertebral fractures and degenerative osteoarthritis.

Grossly, C-cell carcinomas are firm, multinodular uni- or bilateral tumors that typically involve the entire gland. They can be yellow, tan or white with lobules separated by dense, white fibrous connective tissue. Additionally, they can be hemorrhagic and have areas of necrosis.

Microscopically, they are usually infiltrative neoplasms which may be solidly cellular or form small nests, occasional ducts, follicles or cysts with variable amounts of stromal amyloid. The neoplastic cells are polygonal to spindle with eosinophilic, finely granular cytoplasm and vesicular, oval to elongate nuclei with a variable mitotic rate. Calcitonin is the most reliable immunohistochemical marker for canine and bovine C-cells. Metastasis is usually to the cranial cervical lymph nodes with pulmonary metastasis occurring less frequently.

The differential diagnosis includes follicular adenomas or carcinomas of the thyroid gland, parathyroid adenomas or carcinomas, and chemodectoma (carotid body tumors, aortic body tumors).

The ultimobranial (C-cell) tumors of aged bulls may present as part of a multiple endocrine neoplasia (MEN) syndrome and include pheochromocytomas or pituitary adenomas. An autosomal dominant pattern is suggested for development in Guernsey bulls.

Interestingly, in humans approximately 15-20% of C-cell carcinomas are part of an inherited syndrome of multiple endocrine neoplasia (MEN). Forms of familial medullary thyroid carcinoma syndromes include:

- Medullary carcinoma.
- MEN IIA characterized by C-cell hyperplasia-medullary carcinoma, adrenal medullary hyperplasia-pheochromocytoma and parathyroid hyperplasia-adenoma.
- MEN IIB characterized by C-cell hyperplasia-medullary carcinoma, adrenal medullary hyperplasia-pheochromocytoma, gastrointestinal and ocular ganglioneuromas and skeletal abnormalities (3).

Additional information on multiple endocrine neoplasia syndromes in animals can be found in two fairly recent Veterinary Pathology articles (4, 5):

Contributor: Department of Pathology, College of Veterinary Medicine, DW Brooks Drive, UGA, Athens, GA 30602

<http://www.vet.uga.edu/vpp/index.html>

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CASE IV – NADC APHIS-1 2005 (AFIP 2984288)

Signalment: 6-8 month old, female, Dorset cross, *Ovis aries*, ovine

History: The animal was inoculated intravenously with a previously untested blood stabilate collected from a sheep infected with *Ehrlichia ruminantium* (Gardel strain). During the following 6 weeks this animal and all similarly inoculated sheep were clinically normal and were negative by PCR for *E. ruminantium* on multiple blood samples. Due to the apparent failure of the blood stabilate, the sheep was then re-inoculated intravenously with a bovine blood stabilate infected with the same Gardel strain of *E. ruminantium*. Eleven days after the second inoculation the animal's temperature increased to 39.5C and the fever persisted until the animal died on day 17. The animal was also observed circling in the pen on days 13 through 16 after the second inoculation.

Gross Pathology: There was mild cerebral, pulmonary and perirenal edema along with a mild generalized lymphadenopathy.

Laboratory Results: *E. ruminantium* was identified by PCR on multiple blood samples following the second inoculation.

Histopathologic Description: Cerebrum. Within the meninges and neuropil many blood vessels are markedly congested, contain increased numbers of leukocytes

and are surrounded by abundant clear space. There is perivascular hemorrhage surrounding fewer vessels. Infrequently within the cytoplasm and adjacent to the nucleus of endothelial cells are 2 to 10 micron, oval, amphophilic colonies or morulae containing numerous 1-2 micron round organisms. There are increased numbers of glial cells with many glial cells and neurons partially to completely surrounded by clear space.

Contributor's Morphologic Diagnosis: Cerebral edema, mild, diffuse, with intraendothelial rickettsia consistent with *Ehrlichia ruminantium*.

Contributor's Comment: Heartwater is caused by the endotheliotropic organism *E. ruminantium*, formerly named *Cowdria ruminantium*, which infects sheep, goats, cattle, and some species of wild ruminants.¹ The disease is transmitted by multiple species of *Amblyomma* ticks and is present in sub-Saharan Africa and in the Caribbean Islands.¹ The most important vectors are *A. variegatum* (Sub-Saharan Africa and Caribbean) and *A. hebraeum* (southern Africa).¹ Because the agent is infectious but not contagious, introduction of infected ticks and subclinically infected animals are the most likely mechanisms for introducing heartwater into new geographical areas.²

Heartwater is a large potential threat to United States livestock. In the US, there are susceptible domestic and wild host species (white-tailed deer), and two experimentally proven vectors, *A. maculatum* and *A. cajennense*, that are present in many areas of the US.^{2,3} Exotic *Amblyomma* ticks, which could potentially be infected with *E. ruminantium*, have frequently been found on reptiles imported into the US.⁴ Cattle egrets, which are hosts for immature *Amblyomma* ticks and are known to fly from the Caribbean to the US, are another possible mechanism for introducing the disease.²

Peracute and acute disease with high mortality rates are common in naïve susceptible animals, but clinical signs and mortality can be variable dependent on the virulence of the isolate and host factors (species, breed, and age of the animal).⁵ Interestingly, calves less than 3 weeks of age and lambs less than 1 week of age are innately resistant to disease and this resistance is not related to maternal immunity.⁵

Fever, depression, anorexia, dyspnea, numerous central nervous system signs such as ataxia, and sudden death with few clinical signs are commonly seen in heartwater.² Diarrhea may also be a prominent sign in cattle.² Typical gross lesions are pulmonary edema, hydropericardium, hydrothorax, cerebral edema, lymph node edema, and splenomegaly.¹ Not all lesions are usually present in one animal and some animals have minimal lesions.¹ Microscopically, edema, hemorrhage and vascular congestion may be present in multiple tissues.⁶ Colonies of organisms

within capillary endothelial cells are most easily observed in the brain, lung and kidney.¹ Additional lesions that may be present in the brain include focal areas of malacia, lymphocytic perivascular cuffs, and glial nodules.^{1,6} The precise mechanism by which *E. ruminantium* causes increased vascular permeability is unclear.¹

Laboratory diagnosis is by PCR, histopathology and brain smears. Brain smears are the traditional method of testing in which a 3 to 4 cubic millimeter portion of cerebral gray matter is crushed between two slides, and then smeared to create alternating thick and thin areas on the slide.¹ The slide is stained with Giemsa stain and thinly stretched capillaries are examined for colonies of organisms.¹

AFIP Diagnosis: Brain, cerebrum: Congestion and edema, diffuse, mild, with intraendothelial rickettsia, etiology consistent with *Ehrlichia ruminantium*, Dorset cross, ovine.

Conference Comment: The contributor provides an excellent review of heartwater disease caused by *Ehrlichia ruminantium*, formerly *Cowdria ruminantium*. Conference attendees were able to locate the organism within endothelial cells but had difficulty characterizing its morphologic features. All agreed that cerebral edema was a feature and that increased clear space surrounding vessels was not an artifact. Cerebral edema was characterized by increased clear space surrounding vessels with thin fibrous connective tissue tags spanning the perivascular space.

E. ruminantium is a Gram-negative, pleomorphic rickettsia, and colonies containing from one or two to several thousand individual organisms are found in the cytoplasm of endothelial cells. Most organisms are coccoid, except for colonies containing very large organisms in which pleomorphic forms may be seen (1).

E. ruminantium belongs to the family Anaplasmataceae and therefore grows in an intravacuolar compartment, bound by a lipid bilayer membrane, within the cytoplasm of infected host cells. Conversely, species in the family rickettsiaceae grow freely in the cytoplasm of their eukaryotic host cells (1).

The susceptibility of different breeds of cattle varies with Zebu breeds (*Bos indicus*) being more resistant than European breeds (*Bos taurus*). Sheep are more susceptible than cattle and Angora goats are particularly susceptible (1).

The pathogenesis of heartwater is not well understood. Initial replication of the organism seems to take place in the reticuloendothelial cells and macrophages of the regional lymph nodes followed by dissemination via the bloodstream and endothelial cell invasion in various organs and tissues. Increased vascular


permeability with transudation is responsible for effusion into body cavities and tissue edema (1). A toxin has been suggested as the cause of brain edema resulting in increased cerebrospinal fluid pressure and the subsequent development of neurogenic myocardial degeneration and pulmonary edema (7).

Contributor: National Animal Disease Center, 2300 Dayton Ave., Box 70, Ames, IA 50010

www.nadc.ars.usda.gov

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Signature Authenticated by Approve 
Approved by: Carl I Shaia,
: Thursday, 29 December, 2005 at 6:16:

Carl I. Shaia, DVM
Major, Veterinary Corps, U.S. Army
Wednesday Slide Conference Coordinator
Department of Veterinary Pathology
Armed Forces Institute of Pathology
Registry of Veterinary Pathology*

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