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1425 Porter Street
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CASE I – 03 R 732 (AFIP 2944354).

Signalment: 1 year old, female, Prkdc.Scid mouse.

History: The mouse was inoculated subcutaneously in its left hind footpad with 10 million stationary phase *Leishmania amazonensis* promastigotes (MHOM/BR/00/LTB0016). Approximately 10 months post-infection, while the left hind footpad only displayed minimal swelling, there was macroscopic evidence of pronounced, soft and non-ulcerated tumefactions (~ 0.25 to 1cm in length and/or thickness) at the level of the ipsilateral and contralateral limbs, and on the head. At that time point, the mouse was sacrificed and its tissues processed for histology.

Gross Pathology: The swellings of the limbs and head consisted of white, soft, subcutaneous nodules that appeared like adipose tissue.

Contributor's Morphologic Diagnoses: Dermatitis and panniculitis, pyogranulomatous, diffuse, chronic, severe.
Rhinitis, granulomatous, diffuse, chronic, moderate.

Contributor's Comment: *Leishmania amazonensis*, a member of the *L. mexicana* complex, is prevalent in South America. Transmission occurs through the bite of phlebotomine sand flies of the genus *Lutzomyia* with *Lu. flaviscutellata* being considered as the main sand fly vector. The reservoir includes forest rodents and marsupials. Human infection with *L. amazonensis* is not frequent and estimated to represent approximately 3% of the cases in the Amazon region.[1] Infection of the

host with *L. amazonensis* usually results in localized to diffuse cutaneous lesions that sometimes spread to mucous membranes and occasionally to viscera.[1] Mouse models of *L. amazonensis* infection are considered as good models of diffuse cutaneous leishmaniasis and mucocutaneous leishmaniasis. After infection with *L. amazonensis*, most inbred strains of mice develop chronic cutaneous lesions that are characterized by a diffuse infiltrate of heavily parasitized macrophages, rare lymphocytes and scattered areas of necrosis.[2] In the macrophages, *L. amazonensis* amastigotes reside within large parasitophorous vacuoles, which result from the fusion of the phagosome with late endosomes/lysosomes.[2,3] The amastigotes are usually arranged along the periphery of the parasitophorous vacuole, and it is thought that the proteophosphoglycans that they secrete are responsible for the characteristic enlargement of the parasitophorous vacuole.[2] While inflammation, and in particular $CD4^+$ T cells, have been shown to participate in the pathology and the development of cutaneous metastases after *L. amazonensis* infection, metastases have recently been reported in SCID mice, indicating that functional T and B cells are not necessary for the spread of the infection to distant cutaneous sites.[4] This is consistent with what is observed in patients co-infected with *Leishmania* spp. and HIV, who can develop atypical disseminated cutaneous lesions.

AFIP Diagnosis: Head, multiple cross sections: Dermatitis and panniculitis, histiocytic and neutrophilic, chronic, diffuse, severe, with mild rhinitis and myriad intrahistiocytic protozoal amastigotes, Prkdc.Scid mouse, rodent.

Conference Comment: *Leishmania* sp. are protozoans in the order Kinetoplastida, family Trypanosomatidae.[5] Leishmaniasis is endemic in Mediterranean countries, and in some parts of Africa, India, and Central and South America. Leishmaniasis occurs rarely in animals in the United States except in endemic areas in Oklahoma, Texas, and Ohio. It has also been reported in Foxhounds in the eastern coastal states. The disease occurs in 3 forms – cutaneous, mucocutaneous, and visceral. Amastigotes are most commonly identified within macrophages, but can occasionally be found within other leukocytes, endothelial cells, or fibroblasts. Additionally, free organisms may be found within the interstitium of necrotic areas.[5,6,7]

Two forms are involved in the life cycle of *Leishmania*: the promastigote, which develops extracellulary in the sandfly vector, and the amastigotes, which multiply intracellularly in host macrophages. Promastigotes released into the host dermis by infected sandflies are phagocytosed by macrophages. The acidity within phagolysosomes induces them to transform into amastigotes. The amastigotes are protected from the intravacuolar acid by a proton-transporting ATPase, which

maintains the intracellular parasite pH at 6.5. The amastigotes proliferate within macrophages causing them to rupture and release progeny amastigotes that infect additional cells. Additionally, *Leishmania* organisms possess two surface glycoconjugates, which appear to be important in their virulence – lipophosphoglycans and gp63. Lipophosphoglycan is a glycolipid that forms a sense glycocalyx causing C3b deposition on the parasite surface (complement activation). On the other hand, lipophosphoglycan inhibits complement action by preventing insertion of the membrane attack complex (C5-C9) into the parasite membrane. The C3b binds to Mac-1 and CR1 on macrophages resulting in phagocytosis of the organisms. Lipophosphoglycans protect amastigotes once within macrophages by inhibiting lysosomal enzymes and scavenging oxygen free radicals. The second glycoconjugate, gp63, is a zinc-dependent metalloproteinase that cleaves complement and some lysosomal enzymes in addition to binding fibronectin receptors on macrophages facilitating adhesion of promastigotes.[8]

Humoral immune responses are non-protective and detrimental. T_H2 cytokines (e.g. IL-4, IL-13, IL-10) prevent effective killing of *Leishmania* by inhibiting activation of macrophages. Massive antibody production leads to organ damage by immune complex deposition. A cell-mediated (T_H1) immune response is protective and genetically predetermined.[8,9]

Many conference participants considered *Histoplasma* as a differential for this case. *Histoplasma* organisms are also typically found in macrophages, are similar in size to *Leishmania* and may illicit an intense histiocytic to granulomatous response; however, the yeast lack a kinetoplast and stain with PAS and GMS stains. *Leishmani*a amastigotes contain a round, eccentric nucleus with a rod-shaped kinetoplast that lies perpendicular to the nucleus. In Giemsa stained sections, amastigotes have pale blue cytoplasm, a red nucleus, and purple kinetoplasts.[5]

Other differentials include:

Trypanosoma cruzi – kinetoplast is parallel to the nucleus
Toxoplasma gondii – 2-5 um tachyzoites, no kinetoplast
Neospora caninum – 4-7 um tachyzoites, no kinetoplast
Sporothrix schenkii – 4-10 um, oval to cigar shaped, no kinetoplast
Blastomyces dermatitidis – 10-20 um, broad-based budding, no kinetoplast

Contributor: http://www.vetmed.iastate.edu/departments/vetpath/

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CASE II – 05-4288533 (AFIP 3032023).

Signalment: 4 week old, female, Saanen goat, Caprine. *Capra hircus*.

History: On a Saanen goat farm outside Melbourne Australia with 20 milking goats, four 6 week old female kids became anorexic, lethargic, tachypneic and dyspneic over 2 to 3 days. One goat was killed and examined and three other kids were treated with 8mg/kg Engemycin 100 (oxytetracycline 100mg/mL) (Intervet) for 10 days and recovered and returned to the herd. The following week, another kid developed multi-focal arthritis and with treatment recovered.

Gross Pathology: At necropsy this goat had a marked diffuse mucopurulent pleuritis and pericarditis and no other significant gross pathological findings.

Laboratory Results: From the pleural swab, on horse blood agar, chocolate blood agar and CNA plates a pure colony of small slimy green mucoid alpha haemolytic colonies grew within 48 hours. Other bacteria were not isolated. Isolates were positive for casein reduction, sensitivity to digitonin, reduction of Tetrazolium chloride, glucose metabolism and arginine metabolism and liquefaction of coagulated serum. Bacterial DNA was extracted from two isolates and a 1400 base pair region of the 16S ribosomal gene was amplified by PCR using universal bacterial primers. Polymerase chain reaction amplicons were purified using Magnasil magnetic beads (Promega) following the supplied protocol. The PCR amplicons were sequenced using the Big Dye Terminator V3.1 sequencing kit (Applied Biosystems) with one of the 16S PCR primers and also an internal primer to obtain a continuous sequence of 800 base pairs on an ABI Prism 310 genetic analyser. Sequence reactions were cleaned and purified using Magnasil Green (Promega) and were analysed on the Ribosomal Database Project website (http://rdp.cme.msu.edu) maintained at the Michigan State University, USA. 16S RNA sequence analysis of both isolates was consistent with members of the *Mycoplasma mycoides* cluster. The sequence of one isolate was most consistent with *M. mycoides* subsp *mycoides* large colony (LC) type Y goat strain with 95.9% sequence homology. The second isolate was most consistent with *M. mycoides* subsp *mycoides* LC type Y goat strain with 85.7% homology.[1]

Histopathologic Description: The pleura and interlobular connective tissue septa of the lung were thickened by edema fluid, fibrin and moderate numbers of loosely packed neutrophils. Macrophages, lymphocytes, neutrophils and necrotic cells partially distended lymphatics and thin walled blood vessels. The lung parenchyma was collapsed and consolidated. Individual lobules had bronchial and bronchiolar intraluminal plugs of neutrophils and debris which less frequently extended into alveoli, which had thickened septal walls. The pericardium was markedly and diffusely thickened by fibrin and edema fluid, together with moderate numbers of lymphocytes. Also in the pericardium there were neutrophils and fragmented karyorrhectic debris with multi-focal areas of necrosis.[1]

Contributor's Morphologic Diagnoses: Subacute diffuse moderate suppurative bronchopneumonia and pleuritis.

Contributor's Comment: The isolation of a *Mycoplasma* spp. from a goat lung has always been a dilemma as it is important to distinguish *Mycoplasma capricolum* subsp. *capripneumoniae*, the cause of contagious caprine pleuropneumonia, from other *Mycoplasma* spp. Contagious caprine pleuropneumonia, a condition with high morbidity and mortality that causes severe fibrinous pleuropneumonia has never been reported in Australia.[2] The Mycoides cluster is a group of closely related mycoplasmas consisting of several ruminant pathogens. The cluster is divided into two subgroups, Mycoides subgroup, that includes *M. mycoides* subsp.

mycoides large colony (LC); *M. mycoides* subsp. *mycoides* small colony (SC); and *M. mycoides* subsp. *capri* and the capricolum subgroup, that includes *M. capricolum* subsp. *capricolum; M. capricolum* subsp. *capripneumoinae and M.* sp. Group 7 of Leach.[2,3] *M. mycoides* subsp. *mycoides* small colony (SC) is the cause of contagious bovine pleuropneumonia, a severe fibrinous pleuropneumonia of cattle that results in pronounced interlobular edema and intralymphatic thrombosis, this agent is also exotic to Australia.[5] *Mycoplasmas* have previously been isolated from Australian goats both with and without clinical disease.[4] Mycoplasmal pneumonia needs to be differentiated from other causes of bacterial bronchopneumonia in goats, including *Pasteurella multocida* and *Mannheima haemolytica*.[6]

Contagious caprine pleuropneumonia is an exotic disease in most countries and until recently the classification and diagnosis of *M. capricolum* subsp. *capripneumoniae* and the distinction from other pathogenic Mycoplasmas of goats was difficult due to the limited number of biochemical and physiological properties that could be used to differentiate the species. The development and recent advances in molecular techniques and sequence analysis has provided a useful complement or alternative to conventional methods for disease diagnosis and phylogenetic studies.[3] The histological findings of this case are similar to a previous Australian case of *M. mycoides* subsp. *mycoides* LC.[4] However, while *M. capricolum* subsp. *capripneumoniae* causes only pleuropneumonia, *M. mycoides* subsp. *mycoides* LC can result in septicemia, mastitis, keratitis, arthritis or genital lesions.[2] Recently, *M. mycoides* subsp. *mycoides* large colony (LC) was isolated from an Australian goat with mastitis (unpublished). *M. mycoides* subsp. *mycoides* LC, has been isolated from the ears of clinically normal Australian goats and ear mites may aid the spread of the organism.[7]

AFIP Diagnoses: Lung: Bronchopneumonia, chronic-active, multifocal, moderate, with marked fibrinous pleuritis, Saanen goat (*Capra hircus*), caprine.

Conference Comment: The contributor provides a concise and thorough overview of *Mycoplasma* spp. in goats and emphasizes the importance of distinguishing *M. capricolum* subsp. *capripneumoniae*, the cause of contagious caprine pleuropneumonia (CCPP), from other *Mycoplasma* spp.

Mycoplasmas are the smallest prokaryotes capable of self-replication and lack cell walls resulting in extreme pleomorphism. Most pathogenic mycoplasmas are host and site specific. Additionally most pathogenic mycoplasmas parasitize joints and mucous membranes and are almost always associated with respiratory, urogenital, mammary, or ocular infections.[6,8]

Infections with *M. capricolum* subsp. *capripneumoniae* are limited to the thoracic cavity and always result in only pleuropneumonia while infection with the other mycoplasmas results in polysystemic infections. Other mycoplasmas can cause histopathologic pulmonary lesions similar to *M. capricolum* subsp. *capripneumoniae* (*Mycoplasma* biotype F38) in goats, but are not considered to cause CCPP. The pathogenesis of CCPP is thought to involve a cross-reaction between IgG antibodies against mycoplasmal antigens and ciliary proteins causing inflammation and ciliary disfunction.[9] CCPP is the caprine counterpart of contagious bovine pleuropneumonia. In contrast to contagious bovine pleuropneumonia, prominent interstitial edema and formation of pulmonary sequestra are not prominent features of CCPP.[6,9, 10]

Some diseases of veterinary significance caused by common *Mycoplasma* spp. infections in livestock are listed in the table below:[8,9]

***MYCOPLASMA* SPP.**	**DISEASE**	**SPECIES AFFECTED**
Mycoplasma mycoides subsp. *mycoides* SC	Contagious bovine pleuropneumonia	Cattle
Mycoplasma bovis	Mastitis, arthritis, pneumonia	Cattle
Mycoplasma mycoides subsp. *mycoides* LC	Pneumonia, arthritis, mastitis, septicemia	Goats, sheep
Mycoplasma capricolum subsp. *capripneumoniae*	Contagious caprine pleuropnemonia	Goats
Mycoplasma agalactiae	Mastitis (contagious agalactia), arthritis, pneumonia, kertoconjunctivits, vulvovaginitis	Goats, sheep
Mycoplasma capricolum subsp. *capricolum*	Septicemia, mastitis, polyarthritis, pneumonia	Goats, sheep
Mycoplasma mycoides subsp. *capri*	Septicemia, pleuropneumonia, arthritis, mastitis	Goats
Mycoplasma hyopneumoniae	Enzootic pneumonia of swine	Pigs
Mycoplasma hyorhinis	Pneumonia, arthritis, polyserositis	Pigs
Mycoplasma hyosynoviae	Polyarthritis	Pigs

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CASE III – AFIP case 1 (AFIP 3026272).

Signalment: 1-year-old, intact male, domestic short-haired cat (*Felis catus*).

History: Owner has lost 5-6 cats over the past 6 months. The cats lose weight despite normal eating habits and activity. The owner finds the cats dead without other signs. Owner is concerned about possible toxicity.

Gross Pathology: The patient is in poor nutritional condition. Mucous membranes and subcutaneous tissues are mildly pale and icteric. The spleen is enlarged 3-5 times normal with widely scattered, 2-3 mm white foci throughout the splenic capsule and cut surface. Mesenteric and submandibular lymph nodes are 2-5 times expected size; their cut surfaces bulge slightly and have scattered, discrete white foci similar to that seen in the spleen. The lungs fail to collapse entirely, are mildly firm, and diffusely reddened. Sections of spleen and lymph node are collected fresh and submitted for bacterial culture.

Histopathologic Description: Spleen: The spleen exhibits multifocal, individual to coalescing foci of inflammation and necrosis particularly centered upon and effacing the white pulp. The foci are relatively abruptly demarcated from adjacent red pulp. The necroinflammatory foci consist of an admixture of intact and degenerate neutrophils and macrophages admixed with conspicuous cellular debris and fibrin.

Contributor's Morphologic Diagnosis: Spleen: Acute, multifocal, severe, necrosuppurative splenitis.

Contributor's Comment: Tularemia is caused by a small pleomorphic, strictly aerobic, Gram-negative coccobacillus *Francisella tularensis*. Humans and animals become infected by either direct contact with infected animals (usually lagomorphs or rodents) or by arthropod bites, particularly fleas, flies and ticks that have fed on infected animals. Ticks can maintain infection throughout their life cycle.[1]

After *F. tularensis* enters the host, the organism multiplies and disseminates by invading vascular endothelium or by spreading along superficial or deep lymphatics.[2] If bacteremia develops, the organisms are removed by the mononuclear-phagocytic system; however, *Francisella* can survive and multiply within macrophages (facultative intracellular pathogen).[1,2] Ensuing lesions are characteristic (Figures 1-4 Case 028A), but not specific, and consist of yellow/white foci of necrosis within the spleen, liver and lungs. Lymph nodes are often extremely enlarged and contain foci of necrosis and other lymphoid tissue (Peyer's patches, tonsils) can also be involved. Clinical signs can range from asymptomatic infection to fulminant fatal disease; salient features include fever, lethargy, depression, lymphadenopathy, hepatosplenomegaly, oral or lingual ulcers, and icterus.[2]

The diagnosis of tularemia in cats can be challenging because neither the clinical signs, gross, nor microscopic lesions are specific. In cats, important etiological differentials include: plague (*Yersinia pestis*), pseudotuberculosis (*Yersinia pseudotuberculosis*), and feline infectious peritonitis virus (feline coronavirus) infection.[3] Confirmatory diagnosis can be achieved through serology, culture, PCR, fluorescent-antibody or immunohistochemical staining methods on infected tissues.[1,2,3]

AFIP Diagnosis: Spleen: Splenitis, necrotizing, acute, multifocal to coalescing, severe, with lymphoid depletion and fibrin thrombi, cat (*Felis catus*), feline.

Conference Comment: Tularemia (deer fly fever, rabbit fever) is a zoonotic disease with worldwide distribution, affecting more than 100 species of wild and domestic mammals, birds, fish, and reptiles. The primary reservoir in the U.S. is the wild rabbit. There are two main biovars:[1,3,4]

1. *F. tularensis* subsp. *tularensis* (type A) is highly virulent; associated with a tick-rabbit cycle; occurs only in North America; produces classic disease in humans
2. *F. tularensis* subsp. *holarctica* (Type B) is less virulent; associated with rodents, ticks, mosquitoes, mud, and water; and occurs throughout the Northern Hemisphere

Both strains have been isolated from cats in the United States. Ticks and the deerfly (*Chrysops discalis*) are important vectors in North America.

The most common modes of transmission of *F. tularensis* to humans are via an arthropod bite or direct contact with infected tissues. Cat-associated cases usually involve people being scratched or bitten by cats that have a history of hunting or eating wild animals, especially rabbits. The infectious dose for humans is as few as 10 to 50 organisms inhaled as an aerosol or injected intradermally. Therefore, isolation of *F. tularensis* and necropsies of animals with suspected tularemia should be performed with adequate biosafety equipment.[1,2,4]

Differential diagnoses considered in this case included infections caused by *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Toxoplasma gondii*, feline infectious peritonitis virus and feline virulent systemic calicivirus.

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CASE IV – 050780-18 (AFIP 3027308).

Signalment: Adult, female, strain 13 breeder guinea pig, approximately 7-8 months old.

History:* This adult female strain 13 breeder guinea pig was born at the USAMRIID colony in November 2004 and paired with boar #FA61. On July 3, 2005 the animal presented clinically for listlessness. During physical examination the attending veterinarian noted pain upon abdominal palpation, distended abdomen, bloody vaginal discharge, and pododermatitis of the forefeet. The clinical differential diagnosis was dystocia. Because of progressively worse clinical signs, the animal was euthanized with carbon dioxide on the same day and immediately necropsied.

Gross Pathology: This adult female guinea pig was in good flesh and had abundant subcutaneous and cavitary fat. Externally, the abdomen was slightly distended, and there was mild excoriation of the dorsal surface of both front feet. Frank blood stained the perineum and external genitalia (vaginal labia). On internal examination, the right horn of the uterus was markedly enlarged approximately five times normal size (2 cm in diameter) as compared to the left uterine horn. There was multifocal coalescing hemorrhage and diffuse congestion of the right uterine horn visible from the serosal surface. Filling the lumen of the right uterine horn and attached to the wall of the uterus was a hemorrhagic mass of dense fibrovascular tissue admixed with hemorrhagic clots. The left uterine horn was slightly congested and enlarged. Recognizable fetuses were not observed in the lumen of either uterine horn. The mesenteric lymph nodes were enlarged approximately three times normal size. The spleen was slightly enlarged and congested.
Gross Diagnoses:
1. Uterus, right horn: Endometritis, hemorrhagic, with retained placenta.
2. Uterus, left horn: Congestion, diffuse, mild.
3. Lymph nodes, mesenteric: Lymphadenopathy, moderate.
4. Spleen: Congestion, diffuse, acute, mild.

Laboratory Results: *Proteus mirabilis* and *Citrobacter freundii* were cultured from the uterine contents. *Proteus mirabilis* and *Escherichia coli* were cultured from the heart blood.

Histopathologic Description: Diffusely and transmurally, the uterine wall is expanded up to twice normal thickness by abundant hemorrhage, fibrin, and edema. The endometrial and myometrial vasculature is markedly congested, and occasionally endometrial vessels are occluded by fibrin thrombi. There is

multifocally extensive attenuation, erosion, and ulceration of the mucosal epithelium with loss of endometrial glands, and replacement by hemorrhage, fibrin, and necrotic cellular debris admixed with low numbers of degenerate heterophils. Multifocally, remaining endometrial glands are mildly ectatic, lined by degenerate and necrotic glandular epithelial cells, and contain few degenerate heterophils and necrotic cellular debris. Multifocally, the mucosal and glandular epithelium is infiltrated and disrupted by small colonies of bacilli; the bacteria measure approximately 1 – 2 μm in length.

Partially filling the enlarged uterine lumen, and multifocally attached to the endometrium in some histologic sections, there is a dense, highly cellular fibrovascular mass (retained placenta) covered by a single layer of columnar epithelial cells (yolk sac epithelium). The retained placenta is composed of loosely arranged fibroblasts in a collagenous matrix separated by hemorrhage, fibrin and edema; multifocally degenerate and necrotic yolk sac epithelial cells that are occasionally disrupted and replaced by small colonies of bacilli; variably sized and congested yolk sac vessels; and a labyrinth of anastomosing columns of polygonal cells with large amounts of microvacuolated cytoplasm and prominent oval nuclei (syncytiotrophoblasts) separated by vascular channels and capillaries.

Tissue Gram stains of serial sections of the uterus by the Lillietwort method demonstrates numerous, small to medium gram-negative bacilli within the uterine lumen, endometrium, and necrotic retained placenta; few, scattered gram-positive cocci are also present.

Contributor's Morphologic Diagnoses: 1. Uterus, right horn; and placenta: Endometritis and placentitis, necrotizing and hemorrhagic, subacute, diffuse, moderate to marked, with congestion, edema, retained placental tissue, and many small to medium Gram-negative bacilli.
2. Uterus, left horn: Endometritis, suppurative, subacute, diffuse, mild to moderate, with congestion, small fragment of retained placenta, and small to medium Gram-negative bacilli (slides not submitted).
3. Kidney: Pyelonephritis, chronic-active, multifocal, mild to moderate, with tubular degeneration, mineralization, necrosis, and dilatation, neutrophilic tubulitis, and scattered cellular and hyaline casts (slides not submitted).
4. Urinary bladder: Cystitis, heterophilic, chronic-active, multifocal, minimal to mild, with scattered small bacilli (slides not submitted).

Contributor's Comment:** The clinical signs, necropsy lesions, histopathologic findings, and tissue Gram stains indicate bacterial endometritis and retained placenta as the cause of the pain and listlessness in this adult female breeder guinea pig. The gross findings of an intraluminal hemorrhagic mass in the uterus,

confirmed histologically as a necrotic placenta, suggests pregnancy and abortion during the period just before euthanasia, although no fetuses were identified grossly or histologically in the uterus, and neither aborted fetuses nor dead pups were observed in the cage. We cannot explain the absence of dead pups or fetuses, although we speculate the aborted young may have been consumed by other adult animals in the cage; guinea pigs, both males and females, are known to consume the placenta after expulsion, and we suppose that any aborted fetuses may have met the same fate.[5]

The underlying pathogenesis for the retained placenta and bacterial endometritis is uncertain in this case. The animal had concurrent chronic-active pyelonephritis and chronic-active cystitis with intralesional bacteria (slides not submitted), indicating an ascending urinary tract infection. The bacterial infection in the uterus and placenta may have originated from a chronic, subclinical, ascending urinary tract infection, causing abortion and retention of the placenta. Alternatively, the retained placenta, and subsequent secondary bacterial infection of the reproductive tract may have resulted from uterine inertia as a result of dystocia. Primiparous guinea pig sows not bred before 7 to 8 months are at significant risk for dystocia because the pelvic symphysis may not separate adequately during parturition, resulting in dystocia and uterine inertia.[5] Unfortunately, the clinical history in this case was incomplete, and we are uncertain if this older female guinea pig was a primiparous or multiparous breeder.

The microbial culture results from the uterine contents and heart blood, and the histomorphology of the infectious organisms in the uterus and retained placenta indicate a mixed bacterial infection. The isolation of *Proteus mirabilis* from both the uterine contents and heart blood suggests this bacterium may have been the primary offending pathogen, although we cannot exclude contribution of the other isolated bacteria.
A wide variety of causes for dystocia, abortion, and stillbirths are described for the guinea pig. Reported causes of abortion and stillbirths include nutritional deficiencies, pregnancy toxemia, *Bordetella, Salmonella, Streptococcus*, cytomegalovirus infections, asphyxia at birth, toxoplasmosis, erysipelas, and dystocia.[2] In addition to delayed breeding of primiparous sows after 6 months of age, other reported non-infectious causes of dystocia in the guinea pig include obesity and large fetuses.[5]

Proteus organisms are Gram-negative rods, 0.5 μm wide by 1.0 to 3.0 μm long, and are easily demonstrable in the feces of animals, but are rarely found in large numbers except when the normal intestinal microflora is deranged. *Proteus* sp., as well as other endogenous bacteria of the bowel and skin such as *E. coli*, staphylococci, streptococci, *Enterobacter*, and *Pseudomonas* are frequently involved in urinary tract infections.[4] These organisms establish infection in the

lower urinary tract (i.e. urethra and urinary bladder) and often ascend to the renal pelvis and parenchyma causing pyelonephritis. Like animals, 95 percent of human cases of acute pyelonephritis are secondary to ascending bacterial infection emanating from a primary infection in the urinary bladder.[1] We are uncertain if *Proteus* sp. was the cause of the ascending urinary tract infection in this guinea pig, as the urine was not cultured.

The guinea pig placenta shares multiple similarities to that of humans and is considered a favorite among pharmacologists and toxicologists when studying placental pathology. Unlike other laboratory rodents, the guinea pig has a rather long gestation period (up to 70 days); it is hardy, patient, and easily bred; it has an endocrine pregnancy control similar to that of the human; and it has a discoidal, hemomonochorial placenta with a fetal/maternal transport barrier which is very similar to that of the human placenta.[3]

* Research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the *Guide for the Care and Use of Laboratory Animals*, National Research Council, 1996. The facility where this research was conducted is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

**Opinions, interpretations, conclusions, and recommendations are those of the author(s) and are not necessarily endorsed by the U.S. Army.

AFIP Diagnosis: Uterus: Metritis, subacute, diffuse, mild with hemorrhage, congestion, edema, colonies of bacilli, and retained placenta, strain 13 breeder guinea pig, rodent.

Conference Comment: The pregnant uterus and its contents, the placenta, and developing embryo or fetus are more prone to infection than the non-gravid uterus. Reasons for this include the following:

1. The gravid uterus is under the influence of persistent rather than cyclic progesterone stimulation.
2. The chorionic epithelium of the placenta secretes substances that predispose the gravid uterus to certain types of infection.
3. The placenta and embryo/fetus are immunologically-privileged sites and are not protected from infection by the maternal immune system.

There are two basic sources of infection of the gravid uterus: the maternal blood (hematogenous route) and the maternal cervix and vagina (ascending infection). Certain infections persist in a latent state and become activated during pregnancy

and invade the gravid uterus and conceptus resulting in abortion and stillbirth. Microbiologic agents associated with abortion and stillbirth in domestic species include bacteria, fungi, protozoa, rickettsia, chlaymydia, and viruses.[6]

Additionally, nonspecific endometritis is common in the postpartum uterus. This is especially common as a complication of abnormal deliveries, such as abortion, retained placenta, dystocia, twinning, and traumatic injuries of the reproductive tract. In these cases, delayed involution of the uterus, coupled with the accumulation of necrotic placental and endometrial debris in the presence of an open cervix promotes establishment of infection that may progress to pyometra. Bacteria isolated from nonspecific endometritis in domestic animal species include: *E. coli*, *Proteus*, *Actinomyces pyogenes*, β-hemolytic streptococci, *Klebsiella*, *Clostridium*, *Fusobacterium*, and *Bacteroides*.[6]

The pathogenesis of retained placentas is multifactorial and may involve infectious diseases of the placenta, abnormal gestation periods, hormonal imbalances, and mechanical factors.[6]

As pointed out by the contributor, guinea pigs have a discoidal, labyrinthine, hemo-monochorial placenta that represents the chorioallantoic main placenta. Additionally, guinea pigs have a separate subplacenta and yolk sac placenta. The subplacenta is a specialized segment of the chorioallantoic placenta that connects the main placenta with the junctional zone and serves as a source of trophoblast invasion into the endometrium. Throughout pregnancy subplacental syncytiotrophoblasts produce large amounts of glycoprotein secretory granules that are secreted into the maternal blood lacunae where they accumulate and are released during degeneration of the subplacenta. The secretion of the granules may assist in separation of the placenta of in postpartum removal of cellular debris and wound healing. The yolk sac placenta participates in the selective absorption and transfer of maternal immunoglobulins for fetal immunoprotection and occurs in mice, rats, rabbits, and guinea pigs.[3]

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