CASE 1 – H06/344/110 #2 (AFIP 3041763).

**Signalment:** 13-year-old, female, Freiberger horse (*Equus caballus*)

**History:** The horse had colic for 6 days. The horse showed obstipation at the flexura pelvis. Its colon was displaced to the right at the flexura urethra vesicae. The horse showed slight icterus. With ultrasound examination the liver was in conspicuous. The clinicians suspected a primary or secondary hepatopathy.

**Gross Pathology:** The liver showed severe atrophy of the Lobus hepatis dexter; the whole liver was mildly more friable and was marbled dark and pale brown; on cut section, pus was coming out of the bile ducts; several small (up to 0.5 cm in diameter) white, hard superficial nodules were present (calcifications). In the stomach, few *Gasterophilus intestinalis* were present on the pars non-glandularis. Th e wall of the ileum was mildly thickened (up to 1 cm thick). The left colon ascendens ventralis contained large amounts of mucus and dry, dark green, fibrous content (impaction); the mucosa was mildly edematous.

**Laboratory Results:** The blood values showed elevated liver enzymes.

In the liver, a high content of *Pasteurella* sp, and of a mixed flora were isolated (Institut für Veterinär-Bakteriologie of the University of Bern).

**Histopathologic Description:**
Liver: Multifocally in the lumen of the bile ducts, in the portal triads and in the surrounding liver parenchyma, there are many degenerate neutrophils and cell debris. The bile ducts are surrounded by moderate to large amounts of connective tissue and many lymphocytes, macrophages, plasma cells and degenerate neutrophils. Multifocally the bile ducts are increased in size and in number (bile duct hyperplasia). They are lined by columnar epithelial cells. Epithelial cells show rare pyknotic nuclei or karyorrhexis and karyolysis. Many epithelial cells are plump and contain large amounts of amorphous cytoplasmic and plump, vesiculated, pale basophilic nuclei. Multifocally there are a lot of bile plugs. There is mild lymphangiectasia and perportal edema. Multifocally there is a mild infiltration of the liver capsule with few lymphocytes and plasma cells.

**Contributor’s Morphologic Diagnosis:**
Liver: Cholangiohepatitis, suppurative, multifocal to coalescing, severe, chronic
Atrophy of the Lobus hepatis dexter
Colon ascendens ventralis, left: Impaction
Contributor’s Comment: Cholangiohepatitis is a sporadic, but common disease of adult horses. Generally, the disease process is initiated by an ascending biliary tract infection due to a gram negative rod. In the chronic state cholesterol gallstones can develop, causing obstruction of the biliary tree and leading to icterus and colic. Cholangiohepatitis may also occur secondarily to cholecystitis.

The exact etiology and pathogenesis of cholangiohepatitis in large animals is unknown. The early stages of the disease are often associated with periportal inflammation as well as cholestasis in the bile ducts. In suppurative cholangiohepatitis, the bacterial infection may be distributed through portal circulation or extend through the bile ducts. In non-suppurative cholangiohepatitis, disease progression is more likely due to an immune-mediated processes.

Because the hepatocytes are replaced more rapidly than they can be replaced, fibrosis begins to bridge the affected areas of the liver. As the fibrosis becomes more extensive, cholestasis and failure of hepatic function may occur. The bile ducts and bile duct epithelium undergo proliferation, which may impair bile excretion.

On necropsy, the liver will appear firm, pale brown to green, with prominent irregular markings on the cut surface.

Histopathologically, two forms are described. A suppurative form in which there is extensive neutrophilia in the periportal area. The neutrophils often contain bacteria. Biliary hyperplasia, loss of hepatocytes, and fibrosis are also evident in the periportal areas. A non-suppurative form occurs in which the primary cellularity is composed of mononuclear cells, primarily lymphocytes, and plasma cells.

Early in the disease, clinical signs are referable to the inflammatory processes occurring in the liver. These inflammatory signs include fever and hepatomegaly, and may lead to colic and biliary obstruction. Anorexia follows in cases which present for colic. Biliary obstruction may then lead to icterus and hepatic photosensitization. Hepatic encephalopathy and related signs are rare except in cases of chronic hepatic fibrosis.

Clinical pathologic changes include significantly elevated GGT (600-2500 U/L), slight elevations in AST and SDH relative to the GGT levels, elevated bile acids, leukocytosis with neutrophilia, hyperfibrinogenemia and hyperproteinemia; coagulation parameters should be within normal range.

AFIP Diagnosis: Liver: Cholangiohepatitis, chronic-active, diffuse, severe, with bile duct hyperplasia, diffuse bridging fibrosis, and cholestasis, Freiberger horse (Equus caballus), equine.

Conference Comment: The contributor gives an excellent overview of cholangiohepatitis in horses. Cholangiohepatitis in horses has been reported to occur as a primary disease, or secondarily due to cholelithiasis, duodenal inflammation, intestinal obstruction, neoplasia, parasitism, and certain toxins such as pyrrolizidine alfalfa and those of Trifolium hybridum (alsike clover).

Suppurative cholangiohepatitis in horses is most commonly associated with cholelithiasis, which is thought to result from ascending infections from the small intestine. CHolangiohepatitis an d/or pancreatitis secondary to reflux of duodenal contents may occur acutely as in cases of duodenal obstruction or more chronically, due to either intermittent or continuous reflux of duodenal contents. The bacteria most commonly associated with cholelithiasis and cholangiohepatitis in horses are Escherichia coli, Salmonella sp., Aeromonas sp., and Citrobacter sp.

Whether choleliths occur prior to or following the development of cholangiohepatitis has not been determined. The pathogenesis of cholelith formation is not clear, although most choleliths are reported to contain a mix ed amount of bilirubin, bile pigments, cholesterol, and esters of cholic and carboxylic acid, calcium phosphate, and sodium taurodeoxycholate.

In cattle and sheep, cholangiohepatitis has been reported to occur due to sporidesmin, a fungal toxin produced by Pithomyces chartarum, and liver flukes such as Fasciola hepatica.

Contributor: Institute of Animal Pathology, University of Berne, Vet suisse Faculty, Länggassstrasse 122, P.C. 8466 CH - 3001 Berne http://www.vetmed.unibe.ch/content/tierpathologie/index_ger.html

References:
1. Boute M: Cholangiohepatitis and pancreatitis secondarily to severe gastroduodenal ulceration in a foal. Can
are coalescing in areas replacing large portions of the hepatic parenchyma. There are a few tan masses in the liver measuring 2-4 mm in diameter. Bilaterally, the cortex of the kidneys is light tan and contains many small cysts. The lungs are edematous and there is pink foam in the trachea. The left AV valve of the heart has mild, irregular thickening of the valve leaflet (endocardiosis).

Laboratory Results: Tumor cells were positive for chromogranin A, neuron specific enolase (NSE) and synaptophysin. Tumor cells were negative for GFAP, VIP, somatostatin, S-100, cytokeratin, NFP and substance P.

Contributor’s Morphologic Diagnosis:
Adrenal gland:
1) Pheochromocytoma
2) Myelolipoma (not in all sections)

Contributor’s Comment: Pheochromocytomas are neuroendocrine neoplasms derived from chromaffin cells of the adrenal medulla and are most common in dogs, cattle and rats. T he adre nal medulla deri ves f rom the neural crest and consists of three types of cells: Chromaffin, neuronal (ganglion-like), and sustentacular cells. Chromaffin a nd ganglion-like c ells are descented f rom a common s yrn pathoadrenal neu roblastic p recursor, e xpress neuronal cytoskeletal proteins an d exhibit cat echolaminergic p roperties.

CASE II – A03-255 (AFIP 2890562).

Signalment: 17-year-old, male, Cotton-top tamarin (Saguinus oedipus), nonhuman primate

History: T his elderly tam arin wa s wea k, lethargic and ataxic. He was dyspneic under ketamine anesthesia. On auscultation there was a cardiac arrhythmia and a systolic ejection murmur that was loudest on the left and an EKG demonstrated occasional sipped beats a nd a bnormal QRS complexes. An ultrasound revealed cystic areas in the liver and increased mineralization in the right renal calyces. A mass was palpated in the right cranial abdomen. The animal was euthanized due to a poor prognosis.

Gross Pathology: In the region of the right adrenal gland is a large tan and red mass (Fig. 2-1) approximately 1.5 cm in diameter. The mass has a slightly irregular surface and is compressing the subjacent renal parenchyma. In the left adrenal gland is a focal tan, round approximately 4 mm in diameter. There are numerous cysts in the liver, especially in regions near the diaphragm, filled with clear liquid. The cystic regions are coalescing in areas replacing large portions of the hepatic parenchyma. There are a few tan masses in the liver measuring 2-4 mm in diameter. Bilaterally, the cortex of the kidneys is light tan and contains many small cysts. The lungs are edematous and there is pink foam in the trachea. The left AV valve of the heart has mild, irregular thickening of the valve leaflet (endocardiosis).
A diagnosis of a malignant pheochromocytoma in domestic animals is based on invasion of the capsule and adjacent structures (e.g. vena cava) and/or metastasis. In humans, both capsular and vascular invasion may be encountered in benign lesions. Therefore, a diagnosis of malignancy is based exclusively on the presence of metastases. The metastases may involve regional lymph nodes, as well as more distant sites in cluding liver, lung, spleen and bone. There are only a few reports of malignant pheochromocytomas with multiple metastases in domestic animals.

Functional pheochromocytomas have been reported infrequently in animals. These tumors may occasionally be associated with clinical signs as a result of the continuous or episodic secretion of one or more of the catecholamines: epinephrine, nor epinephrine or dopamine. Elevations of blood pressure induced by the sudden release of catecholamines from the adrenal medulla may precipitate acute congestive heart failure, pulmonary edema, myocardial infarction, ventricular fibrillation and cerebral hemorrhage. In this case, clinical cardiac abnormalities and histologic findings of myocardial fibrosis (slide not submitted) might suggest catecholamine production by the tumor. Human pheochromocytomas are known to produce sustained hypertension in one-third of cases and experimental catecholamine administration induces myofibrillar degeneration and interstitial fibrosis in animals. However, plasma catecholamine levels and urinary excretion of catecholamines and their metabolites were not measured in this case.

In nonhuman pri mates adrenal gland tumors are rare. Recognized tumors include: myelolipomas, pheochromocytomas, cortical adenomas, cortical adenocarcinomas, paragangliomas, melanocytomas, and hemangioma/angiomatous tumors. In New World monkeys, myelolipomas are recognized. Melanocytomas, which are common in Old World primates, have been reported in the ring-tailed lemur (Lemur catta), rhesus monkey (Macaca mulatta) and cynomolgus monkey (Macaca fascicularis). In humans, pheochromocytoma is an uncommon neoplasm and is usually a benign gland tumor affecting one or both adrenals.

At the New England Primate Research Center, myelolipomas and pheochromocytomas are the two most common recognized neoplasms in the adrenal glands of aged Cotton-top tamarins. In humans, most pheochromocytomas occur sporadically in adults with a slight female preponderance. About 10% occur in seveal combinations, usually autosomal dominant, familial adrenal syndromes in cluding the multiple endocrine neoplasia (MEN) syndromes, type I (von Hippel-Lindau disease) and type II (Sturge-Weber syndrome). In the familial syndromes, most of the tumors develop in childhood with a strong male preponderance. Most of the tumors in the syndromes are bilateral (70%), but in the nonfamilial setting only 10-15% are bilateral.

In some sections of adrenal from this animal, a myelolipoma was also recognized. Myelolipomas are benign lesions commonly encountered in the adrenal glands of cattle and nonhuman primates and infrequently in other animals. They are composed of accumulations of fat cells and hemopoietic tissue, resembling both lymphoid and myeloid elements. Areas of mineralization or bone formation may occur. Although the origin of these lesions is uncertain, they appear to develop by metaplastic transformation of cells in the adrenal cortex or cells lining adrenal sinuoids.

AFIP Diagnosis: Adrenal gland: Pheochromocytoma, Cotton-top tamarin (Saguinus oedipus), primate (Fig. 2-2-3).

Conference Comment: The contributor gives an excellent overview of pheochromocytomas and their origin. They occur most often in cattle, dogs and some laboratory rats. In dogs, Boxers appear to be overrepresented, and F344 rats with severe chronic pressure or aggressive glomerulonephritis. Humans have been found to have an increased incidence. In bulls and humans, pheochromocytomas are rare. Pheochromocytomas have been associated with calcitonin secreting C-cells of the thyroid gland.

Tumor development within the adrenal medulla has been associated with multiple factors, including genetics, dietary factors, chronic high levels of growth hormone or prolactin associated with pituitary tumors, and autonomic nervous system stimulation.

In dogs, caval thrombi occur more frequently with pheochromocytomas than adrenal cortical tumors. The caval thrombus primarily develops as an intraluminal extension from the phrenicocoabdominal veins rather than by direct invasion of the vena cava.

In rats, the three types of chromaffin cells: epinephrine cells, norepinephrine cells, and small granule-containing
cells, unlike human chromaffin cells, which contain both epinephrine and nor epinephrine granules within a single cell. Either epinephrine or norepinephrine secreting cells, or both may be found within a pheochromocytoma. Ultrastructurally, norepinephrine granules have an eccentrically placed, small, electron dense core that is surrounded by a wide submembranous space. Epinephrine granules have a coarse granular core that is less dense than that of norepinephrine granules, and has a narrower submembranous space. In dogs, norepinephrine appears to be the principle catecholamine secreted by pheochromocytomas.


References:
CASE III – 040739-16 (AFIP 3073369).

Signalment: 4-year-old, female, cynomolgus macaque (*Macaca fascicularis*).

History: Animal caretakers observed a 4-year-old, female, cynomolgus macaque (*Macaca fascicularis*), a colony animal, as being in estrous and not eating well. During physical examination by the laboratory animal veterinarian, the animal was lethargic, dehydrated, and there was a moderate amount of perineal bloody discharge. Initial treatment included oral non-steroidal anti-inflammatory (aspirin) and oral electrolyte replacement. There was no clinical improvement and the regimen was changed to intramuscular flunixin meglumine, and 300 ml of subcutaneous fluids. The animal’s physical condition continued to deteriorate and she became unresponsive and hypothermic. Additionally, increased capillary refill time, bilateral nystagmus, mucoid diarrhea, persistent bleeding from the perineum and significant abdominal pain were observed. The macaque was treated for shock and suspected sepsis using intravenous fluids with 2.75% dextrose and continued intramuscular enrofloxacin and flunixin meglumine. Despite these aggressive therapies, the animal succumbed and a complete necropsy was performed.

Gross Pathology: Gross necropsy findings included moderate bloody discharge from the vulva. The mucous membranes of the lips, mouth, conjunctiva, and sclera were diffusely pale white. The urinary bladder was diffusely green to black, distended, and contained a mixture of dark red to greenish black fluid. The urinary bladder contains a mixture of clotted blood and bloody urine.

3-1. Urinary bladder, cynomolgus macaque. The urinary bladder contains a mixture of clotted blood and bloody urine.

3-2. Urinary bladder, cynomolgus macaque. The mucosa and muscular wall are necrotic and friable.

Gross photographs courtesy of U.S. Army Medical Research Institute of Infectious Diseases Fort Detrick, MD 21702-5011
granular to clumped (clotted blood and bloody urine) (Fig. 3-1). The mucosa and muscular wall of the urinary bladder were friable and easily torn (necrotic) (Fig. 3-2). The hemorrhagic contents from the urinary bladder and the heart blood were sampled at necropsy for microbial culture; the heart blood was ex tremely thin and watery during collection.

**Laboratory Results:** Sections were stained by the Gram-Twort staining method. De-paraffinized sections were immersed in crystal violet for 1 minute and stained with Lugol’s iodine and neutral red/fast green. Gram-positive organisms stain blue to black and Gram-negative organisms stain pink to red.

Heart blood culture: No growth after 72 hours

Urine culture: *Corynebacterium* sp.

**Histopathologic Description:** Within the section of urinary bladder there is transmural necrohemorrhagic to fibrinosuppurative cystitis that is diffuse and severe (Fig. 3-3). The urinary bladder mucosa is replaced by a fibrinonecrotic (diphtheritic) membrane or pseudomembrane, composed of abundant fibrin, hemorrhage, necrotic transitional epithelial cells, degenerate neutrophils, and many coryneform bacteria (Fig. 3-4). The wall of the urinary bladder (submucosa, muscular tunica, and serosa) is expanded three to four times its normal thickness by abundant fibrin, edema, hemorrhage, and viable and degenerate neutrophils. Blood vessels are congested and there is multifocal necrotizing vasculitis with disruption of architecture in some/all vessel tunics (intima, media, and adventitia) and multifocally blood vessels contain fibrin thrombi.

Additional significant histologic findings in the cynomolgus macaque included acute to subacute fibrinous polyserositis that included the urinary bladder, stomach, pancreas and mesentery. The inflammatory lesions on the serosal surfaces of the viscera were attributed to leakage of the contents from the necrotic urinary bladder into the abdomen (peritonitis).

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3-3. Urinary bladder, cynomolgus macaque. Diffusely, there is transmural hemorrhage and loss of urothelium. (HE 20X).

3-4. Urinary bladder, cynomolgus macaque. Multifocally within areas of hemorrhage and necrosis there are large colonies of bacteria. (HE 100X).

3-5. Urinary bladder, cynomolgus macaque. Pleomorphic short rods are Gram-positive. (Gram-Twort method, 400X).

*Photomicrographs 3-4 and 3-5 courtesy of U.S. Army Medical Research Institute of Infectious Diseases Fort Detrick, MD 21702-5011*
**Contributor’s Morphologic Diagnoses:**
1. Urinary bladder: Cystitis, necrohemorrhagic, transmural, subacut, diffuse, severe, with fibrinonecrotic membrane, hemorrhage, edema, necrotising, aspiritis, thrombi, structural loss (perforation), and many Gram positive coryneform bacteria (Fig. 3-5).
2. Urinary bladder, serosa and mesentery: Serositis and peritonitis, necrotizing, subacute, diffuse, severe, with neutrophilic and histiocytic inflammation, marked mesothelial cell hypertrophy and phlebitis, hemorrhage, fibrin and edema.

**Contributor’s Comment:** Corynebacterial infections in domestic animals are important causes of disease, morbidity, and death in humans and various wild and domestic animal species. *Corynebacterium diphtheriae* causes diphtheria in humans, a highly contagious upper respiratory tract disease characterized by a pseudomembrane within the tonsil, pharynx, and nose. However, many nontypeable coryneform bacteria are a component of the bacterial flora in the skin and mucous membranes, ubiquitous environmental organisms, and potential opportunistic pathogens. With a few exceptions, the opportunistic infections caused by non-typeable coryneform bacteria are characterized by necrotizing tissue lesions with suppurative inflammation in the affected host.

Of the non-typeable coryneform bacteria, several members of the *Corynebacteria renale* group, including *C. renale* (I), *C. pilosum* (II), and *C. cystitidis* (III), are opportunistic urinary tract pathogens in domestic animals and natural causes of cystitis, ureteritis, and ascending pyelonephritis in cattle. This condition in the bovine is commonly known as bacillary pyelonephritis. Animals may become predisposed to bacillary pyelonephritis through physical or chemical damage to the lower genitourinary tract caused by dystocia, urinary bladder paralysis, and urinary catheterization. Urinary tract infections are more common in females. These predisposing factors disrupt the host’s natural defenses, such as the mucosal barrier, and may allow initial colonization of tissue with coryneform bacteria. Hemorrhagic urethritis, cystitis, and pyelonephritis develop as a result of ascending urinary tract infection.

This case displayed similarities to corynebacterial urinary tract infections in other animal species, including natural and experimental infections in cattle, goats, mice and rats. With *C. renale* group bacteria in cattle in particular may affect all or part of the urinary tract. In the urinary bladder, typical lesions include mucosal thickening from infiltrating leukocytes and hemorrhage, vasculitis and fibrin thrombi, mucosal necrosis, ulceration and perforation, hemorrhage; and replacement of the mucosa by a fibrinonecrotic (diphtheritic) membrane. Several bacterial virulence factors may predispose animals to infection and progression of necrohemorrhagic lesions.

### Table of common pathogenic Corynebacteriae adapted from Jones et al. and Quinn et al.

<table>
<thead>
<tr>
<th>Organism Principal Species</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Corynebacterium diphtheriae</em> Human</td>
<td>Diphtheria</td>
</tr>
<tr>
<td><em>C. renale</em> (Type I) Bovine</td>
<td>&quot;Bacillary&quot; pyelonephritis, ureteritis, cystitis, may be recovered from healthy individuals</td>
</tr>
<tr>
<td><em>C. cystitidis</em> (Type II) Bovine</td>
<td>Hemorrhagic cystitis and pyelonephritis</td>
</tr>
<tr>
<td><em>C. pilosum</em> (Type III) Bovine</td>
<td>Cystitis and pyelonephritis</td>
</tr>
<tr>
<td><em>C. pseudotuberculosis</em> Ovine and caprine</td>
<td>Caseous lymphadenitis, produces phospholipase D exotoxin</td>
</tr>
<tr>
<td>Equine</td>
<td>Ulcerative lymphangitis and pectoral abscesses</td>
</tr>
<tr>
<td><em>C. bovis</em> Bovine</td>
<td>Mastitis (rare), found in teat canal of 20% of apparently healthy dairy cows</td>
</tr>
<tr>
<td><em>C. kutscheri</em> Rodents</td>
<td>Pseudotuberculosis</td>
</tr>
<tr>
<td><em>C. ulcerans</em> n-human primates, and many other species</td>
<td>Bite wounds and abscesses</td>
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</table>
urinary system lesions due to *C. renale* group organisms. *Corynebacteria renale* group organisms possess pili, allowing attachment to the urogenital mucosa and facilitating ascension of microbes into the bladder and kidneys. The bacteria produce urease and hydrolyze urea, which may be contributory to extensive ulceration of the mucosa and necrosis in the affected tissues. 5,8,9,14 Thus, high protein diets and subsequently elevated urinary urea levels may predispose animals to disease because of the ability to hydrolyze urea. 9

Host factors may also predispose animals to infection. In cattle, females are more predisposed to infection than males due to anatomic structure, hormonal influences, and risks associated with pregnancy or iatrogenic procedures; infection in bulls is rare. 8 Females have short urethras, which decreases the anatomic barrier bacteria must overcome to reach the urinary bladder and kidneys, and urethral trauma associated with dystocia or castration may serve as initiating events for infection. 8,10,14 Hormone-induced changes in female animals may serve as predisposing factors; high estrogen levels may affect the functional integrity of the epithelium in the urethra and urinary bladder; culture with high estrogen levels that graze pastures are reportedly prone to infection with *C. renale*. 8,9 In some animal species, such as the sow, estrogen causes an elevation in the urine pH, which may produce an alkaline environment optimal for expression of bacterial pili and enhanced microbial survival and proliferation. 8,9 S. pneumoniae and experimentally induced *C. renale* infections in animals are frequently associated with alkaline urine, although the mechanisms are effective in post infection bacterial hydrolysis of urea and production of ammonia rather than preexisting alkaluria. 5,8,14

In this case, the histopathologic findings of necrotizing and hemorrhagic cystitis, and the microcolony culture results from the contents of the urinary bladder support the underlying cause of death as complications from infection by non-diphtheritic coryneform bacteria. The signalment, clinical history, pathological findings and a n m i c r o b i a l culture results in this case of necrohemorrhagic cystitis show similiar histology to spontaneous and ex perimentally induced corynebacterial urinary tract disease observed in several animal species. The perineal bleeding was presumed to be normal estrous bleeding, therefore, diagnosis and treatment were delayed in this case. Severe urinary tract infection due to corynebacteria should be included in the clinical differential diagnosis for protracted perineal bleeding in macaques.

**AFIP Diagnosis:** Urinary bladder (per cocontributor): Cystitis, necrohemorrhagic, transmural, with fibrin, edema, and large colonies of bacilli, cyanotic.

**Conference Comment:** The contributor gives an extensive overview of *Corynebacterium* infections, th eir pathogenesis and virulence factors. Although members of the *Corynebacterium renale* group are commonly associated with cystitis and pyelonephritis in cows, they are not generally associated with cases of non-hum an primates. 14

In sheep, ulcerative postrichia of wethers (also known as sheath rot or pizzle rot) 6, is a disease that occurs due to the presence of a transmissible urea-hydrolyzing bacterium and the excretion of urine rich in urea. 5 The lesions begin as an ulceration of the prepuce that may progress to destruction of the urethral process and ulceration of the glans penis. 5 *C. renale*, *Rhodococcus equi*, and *C. hofmannii* have all been isolated from infections. 5

In dogs and cats *Corynebacterium urealyticum*, a urease-producing bacteria, is associated with alkaline urine of pH > 8 and struvite and calcium phosphate precipitations that form encrustations along the bladder wall. 1,11 *Staphylococcus* sp and some strains of *Proteus mirabilis* are more commonly associated with alkaline urine and struvite production in dogs, but do not produce the mucosal encrustations seen with *C. urealyticum*. 1

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Research at USAMRIID is conducted in compliance with the Animal Welfare Act and other principles stated in the Guide for the Care and Use of Laboratory Animals, National Research Council, 1996. USAMRIID is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

**References:**


4. Hayashi A, Yanagawa R, Kida H: Adhesion of *Corynebacterium renale* and *Corynebacterium pilosum* to the Mac OG Macaques (Macaca fascicularis), primate.

CASE IV – G7344 (AFIP 3034502).

Signalment: 5-year-old, intact male, rhesus m acaque (Macaca mulatta), non-human primate.

History: This monkey was inoculated with simian immunodeficiency virus (SIVmac239) on 25/08/05 via the tonsillar route. Th ere was a high virus load after two weeks post infection. Twenty-five weeks after the tonsillar challenge the animal showed a pustular skin rash, deteriorating general condition and reduced appetite. The monkey was euthanized on 15/02/06 due to a poor prognosis.

Gross Pathology: At necropsy the rhesus macaque was in a good nutritional condition. Th e skin was covered with multiple single to coalescing umbilicated pustules. Pustules were preferentially found within the inguinal region, the lips, the hands and feet but they also affected the tongue, the gingiva and the oropharyngeal mucosa. The skin pustules were umbilicated, covered with a central invaginated crust and surrounded by peripheral hyperemia.

Further findings included a severe, necrotising pneumonitis and splenitis, a generalized hyperplasia of the lymph nodes and severe follicular hyperplasia of the spleen.

Laboratory Results: Immunohistochemistry: Herpes simplex Type 1 and 2: negative

Histopathologic Description: At microscopic examination the skin and the mucous membranes revealed focal areas with epidermal vesiculation, epidermal acanthosis, acantholysis and ballooning degeneration as well as full thickness dermal necrosis and ulceration. A mixed inflammatory infiltrate composed of neutrophilic and eosinophilic granulocytes, few histiocytes and lymphocytes accompanied the process. In some locations hair follicles and sebaceous glands were involved in the dermal process. Intact affected cells of the vesicle base or margin contained single round to oval intracytoplasmatic inclusion bodies identical with Guarnieri bodies. The Guarnieri bodies were eosinophilic and lay close to the nuclei of infected cells. They were randomly distributed within the altered epithelium. Rare syn cyti a formations were found close to the basal epithelial layer. At the skin of soles and palms the lesion was arrested in the vesicular stage, covered with a thick intact epidermal cell layer (not included in all sections).

Transmission electron microscopy of skin samples revealed single orthopox like particles in the cytoplasm of keratinocytes.

Monkey pox virus was diagnosed by PCR and cell culture.

Contributor’s Morphologic Diagnosis: Tongue: Dermatitis, erosive-ulcerative, subacute, multifocal, severe, with single intracytoplasmatic eosinophilic inclusions, rhesus macaque (Macaca mulatta), non-human primate.

Skin: Dermatitis, proliferative, pustular, subacute, multi-
Today we gained experience with the outcome of the disease in immunocompromised monkeys. This accidental case of monkeypox in a non-immunocompromised animal described here showed that the disease outcome was characterized by severe vesicular exanthema. The skin rash was accompanied by severe respiratory tract involvement and progression of the disease was fatal. Till now it is not clear how transmission occurred in this case. Diagnosis was complicated due to the minimal content of inclusion bodies indicative for poxvirus infection. By electron microscopy typical orthopox-like viral particles were demonstrable. An Eczema herpeticatum was considered as differential diagnosis, but immunohistochemistry for Herpes simplex type 1 and 2 was negative.

AFIP Diagnosis:
1. Glabrous skin: Dermatitis, vesiculopustular, focally extensive, marked, with acanthosis and ballooning degeneration, rhesus macaque (Macaca mulatta), primate (Fig. 4-1).
2. Hairy skin: Dermatitis, necroulcerative, neutrophilic and eosinophilic, focally extensive, severe with ballooning degeneration.
3. Tongue: Glossitis, necroulcerative, neutrophilic and eosinophilic, multifocal, marked, with ballooning degeneration and intralesional cocci (Fig. 4-2 and 4-3).

Conference Comment: In 2003, several people in the Midwestern United States were diagnosed with monkeypox virus infection. All affected individuals were associated with exposure to captive prairie dogs that had been housed with Gambian giant pouched rats (Cricetomys sp.), rope squirrels (Funisciurus spp.), and/or dormice.
(Graphiurus sp.) that originated from Ghana.\textsuperscript{2,4} As of 30 July 2003, 72 human cases had been reported of human monkeypox virus infection.\textsuperscript{2} Affected individuals included veterinarians, pet store personnel, an animal distributor, and children and parents that bought the infected rodents.\textsuperscript{2}

Ultrastructurally, orthopoxviruses are 37.5 X 200 nm particles, located free in the cytoplasm, composed of an outer membrane enclosing a characteristic dumbbell-shaped inner electron lucent core that is bounded by two lateral bodies.\textsuperscript{4}

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References:
Orthopoxvirus diseases of animals. Table extracted from Ginn et al.3

<table>
<thead>
<tr>
<th>Orthopoxvirus</th>
<th>Key points</th>
</tr>
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<tbody>
<tr>
<td>Camelpox virus</td>
<td>Dromedary camels; clinically identical to camel contagious ec-thyma (parapox)</td>
</tr>
<tr>
<td>Cowpox virus</td>
<td>Cutaneous and occasionally respiratory lesions in domestic cats; on face and forepaws; affects wild and domestic Felidae, cattle, dogs, rodents, humans; not endemic in cattle, and infections in cattle are uncommon; wild rodents are the reservoir; severe fatal pneumonia in elephants</td>
</tr>
<tr>
<td>Ectromelia virus (mousepox virus)8</td>
<td>Limb amputation in surviving mice; systemic infection</td>
</tr>
<tr>
<td>Monkeypox virus</td>
<td>Rodents, New Wold monkeys, and great apes; systemic disease</td>
</tr>
<tr>
<td>Buffalopox virus</td>
<td>Affects waterbuffalo in India; Zebu cattle apparently refractory to infection; closely related to Vaccinia virus</td>
</tr>
<tr>
<td>Uasin Gishu disease virus (unassigned)</td>
<td>Horsepox became naturally extinct in 19th century; recent uncharacterized orthopox viruses isolated from horses with equine papular dermatitis, and in equines with Uasin Gishu disease in Kenya; are found closely related to Vaccinia virus and cowpox virus</td>
</tr>
<tr>
<td>Vaccinia virus</td>
<td>Does not cause natural infection in domestic animals</td>
</tr>
<tr>
<td>Variola virus (human smallpox)</td>
<td>Affects humans and non-human primates; irradiated?</td>
</tr>
</tbody>
</table>