The Armed Forces Institute of Pathology
Department of Veterinary Pathology
WEDNESDAY SLIDE CONFERENCE
2002-2003

CONFERENCE 7
30 October 2002

Conference Moderator: LTC Dana Scott, DVM, Diplomate, ACVP
Chief, Animal Medicine, DODVSA, OTSG
Falls Church, VA 22041-3258

CASE I – 02-0406 (AFIP 2839501)

Signalment: 2-year-old, female, cynomolgus macaque (*Macaca fascicularis*), nonhuman primate

History: This monkey was on a skin allograft transplantation protocol investigating various immunomodulating therapies for transition to renal allograft transplantation. It was treated with Thymoglobulin and then tried on an experimental intramuscular formulation of Rapamycin (immunosuppressive drug) given at 1-2 mg/kg/day for only 10 days, then switched to an oral formulation of Rapamycin (RAPA) at 0.5 mg/kg/day because of injection site reactions. RAPA blood levels sent for analysis the week prior. Euthanized with IV Pentobarbital euthanasia solution following skin graft rejection, weight loss, leukopenia, and general malaise ("lethargic & sick"). Request to check lung and gastrointestinal system (for vascular toxicity seen with PO formulation), liver, thymus, lymph nodes, injection sites, and other routine organs.
     Initial planned therapy for CG2X Skin graft. Thymoglobulin 20mg/kg IV, days 0, 1, 3, 5, 7. Rapamycin 2mg/kg IM, days 3, 4, 5, 6, 7, and then 1mg/kg IM for days, 8-30. Bone marrow transplant 6x10^9/kg on day 7.

Gross Pathology: This young cynomolgus macaque is in fair nutritional condition with small amounts of subcutaneous and visceral fat stores, a stomach full of food and fruit, abundant cecal digesta, and formed feces in the colon. Weight is 2.22 kg at necropsy. There is a chest tattoo "CG2X". There are four skin graft sites over the dorsal lumbar area; the two cranial transplants are excised. The right caudal allograft is rejected (necrotic-lost). The left caudal autograft is viable. The left leg has multifocal caseous abscesses (injection sites of RAPA). The thymus is small (stress–immunosuppression). The gallbladder (gross photo taken) has a thick wall (increased 2X over normal) and the serosa is red (rule/out congestion, edema, hemorrhage). It contains normal green bile and the mucosa appears normal. The lungs have multifocal to coalescing red consolidations in the dorsal lobes with white miliary foci (rule/out pneumonia). The spleen has multifocal, 2-4 mm, white foci (rule/out septic emboli from abscesses). The

left auricle (atrium) has a 3mm, white-yellow focus. The vagina has a pigmented (black) focus on the bladder (ventral) side. The stomach has a focal serosal hemorrhagic area at the esophageal entry and a focal mucosal erosion. There are no other gross lesions noted.

Laboratory Results: Elevated Rapamycin levels over the 10 ng/ml level desired, WBC below 2,000/µl, and negative serology for retroviruses.

Contributor's Morphologic Diagnoses: 1. Spleen, white pulp: Lymphoid depletion, diffuse, severe.
2. Spleen: Necrosis, multifocal, with numerous eosinophilic intranuclear inclusion bodies, karyomegaly, and cytomegaly.
(slides not submitted)
3. Heart, myocardium/endocardium of atrium & ventricle (slide 45): Myoendocarditis, necrotizing, acute, multifocal, moderate, with eosinophilic intranuclear inclusion bodies and karyocytomegaly.
4. Skeletal muscle with sciatic nerve (slides 43-44): Myositis, necrotizing, subacute to chronic, multifocal, marked, with encapsulating fibroplasia and mild fibrosis, mineralization, and central bands of coagulative necrosis of myofibers in bundles (drug/RAPA injection site reaction).
5. Lung: Necrotizing vasculitis, acute, multifocal, marked, with hemorrhage, fibrin aggregates (deposition), moderate histiocytic and neutrophilic interstitial pneumonia or alveolitis, and subpleural organized thrombi.
6. Thymus, thymocytes: Lymphoid depletion, diffuse, severe, with remnant epithelial cells.
7. Lymph nodes, multiple sites: Lymphoid depletion, diffuse, severe, and mild sinus hemosiderosis.
8. Gallbladder, serosa: Hemorrhage and edema, diffuse, marked to severe. Liver, sublobular and hepatic veins: Perivascular hemorrhage, multifocal, moderate.
9. Bone marrow: Elevated myeloid:erythroid ratio (2:1); adequate megakaryocytes, numerous eosinophils.
10. Haired skin, skin graft (slide 41) from dorsal back: Fibroplasia, focal, two sites, mild, consistent with interface/suture reaction at the site of a healed autograft; haired skin, skin graft (slide 42) from dorsal back: Dermatitis, ulcerative and necrotizing, subacute, focally extensive, marked, with epidermal degeneration & necrosis, dermal and adnexal necrosis (loss with suppurative interface), and fibroplasia (granulation tissue), consistent with a rejected allograft and wound healing.
11. Brown & white adipose tissue, multiple sites: Fat atrophy, serous, diffuse, mild to moderate.
12. Kidneys, ureter, aorta/pulmonary artery, pancreas, haired skin, mammary gland & nipple, ovaries, oviducts (multiple paratubal cysts), uterus/cervix, vagina (focal melanosis of outer tunica muscularis around inflamed glandular ductules), adrenal glands, salivary glands, stomach, small and large intestine (low cecal numbers of *Balantidium coli*), urinary bladder, trachea (focal parathyroid cysts), Thyroid/parathyroid glands, pituitary gland, cervical spinal cord, brain, and eyes: No significant lesions noted.

Contributor's Comment: This monkey was markedly immunosuppressed as evident by the severe lymphoid depletion diffusely in the spleen and other lymphoid organs. The necrosis in the spleen and heart is multifocal (disseminated), although some slides/sections of spleen may only have a focal distribution. The inclusion bodies in the enlarged nucleus vary in size, color, and shape, but many are eosinophilic to magenta and surrounded by a clear halo with marginated chromatin (owl's eye cells). The primary differential diagnosis for the necrosis in the spleen and the heart with prominent intranuclear inclusion bodies +/- karyomegaly is: disseminated cytomegalovirus and/or adenovirus. Electron microscopic analysis of the splenic lesion demonstrated characteristic intranuclear and cytoplasmic herpesvirus particles.

Cytomegalovirus (CMV) is the most common and single most important viral pathogen in human organ transplant recipients. CMV is a highly cell associated betaherpesvirus that is a common infection that remains latent (circulating white blood cells, bone marrow, etc.) in immunocompetent individuals. It can cause severe systemic infection in immunosuppressed animals, such as with SIV/HIV and transplant patients. Disseminated CMV infection in humans (cytomegalic inclusion disease) can cause lesions in the lungs, liver, gastrointestinal tract (esophagus, colon), salivary glands, kidneys, pancreas, thyroid gland, adrenal glands, eyes, and brain. Interestingly, in this case, the prominent gross and microscopic lesions were in the heart and spleen (both reported sites in nonhuman primates). Immunohistochemical studies with rhesus CMV infection in the spleen have shown antigen expression in splenic cells (to include endothelial cells and tissue macrophages) in perifollicular (mantle and marginal-zone) areas and the red pulp. Additionally, in other organs, epithelial cells have shown RhCMV antigen; and along with endothelial cells, the multifunctional "pericyte" is also identified as a cellular site of virus antigen localization.

The net effect of the overall immunosuppressive drug regimen on the CMV pathogenesis is important. The drug Rapamycin is reported to have no ability to reactivate latent CMV; however, once there is active, replicating virus present, Rapamycin will amplify the infection by inhibiting antiviral (critical CMV-specific cytotoxic T-cell) response. The greatest problems in human and animal model transplant patients has been in those treated with antilymphocyte antibodies (like Thymoglobulin in this case) followed by Cyclosporine or Tacrolimus (or a similar drug like Sirolimus/Rapamycin in this case).

Primary CMV (seronegative/naïve recipient with an infected allograft from a seropositive donor), reactivated CMV (seropositive), and CMV superinfection (seropositive/seropositive) are reported in human transplant recipients. We could not perform a sera comparison of the donor to this recipient; therefore, we did not determine the pattern of infection (primary, reactivated, or superinfection) in this case.

AFIP Diagnoses: 1. Spleen: Splenitis, necrotizing, acute, multifocal, mild, with cytomegaly, and eosinophilic intranuclear inclusion bodies, Cynomolgus macaque (*Macaca fasicularis*), nonhuman primate.
2. Spleen, white pulp: Lymphoid depletion, diffuse, severe.

Conference Comment: A betaherpesvirus, cytomegalovirus is an enveloped, 150-200 nm in diameter, linear, double stranded DNA virus that has an icosahedral nucleocapsid. It is transmitted through direct contact. CMV replicates slowly, often producing greatly enlarged (cytomegalic) cells. Latent infection with cytomegalovirus results in intermittent or continuous viral excretion. Although the viral inclusion bodies are predominantly intranuclear, intracytoplasmic inclusions do occur.

Contributor: Walter Reed Army Institute of Research/Naval Medical Research Center, 503 Robert Grant Avenue, Silver Spring, MD, 20910-7500

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CASE II - 415 (AFIP 2839955)

Signalment: Approximately 3-year-old, male, Cynomolgus macaque, (*Macaca fasicularis*), primate

History: This stock monkey, maintained in a barrier facility, developed an acute rectal prolapse without any preceding gastrointestinal symptoms and was euthanized the following day.

Gross Pathology: Rectum: prolapsed (~10 mm), swollen, hyperemic, dry and crusty mucosal surface.

Laboratory Results: None.

Contributor's Morphologic Diagnoses: 1. Rectum: Prolapse and acute severe necrosuppurative proctitis with edema and hemorrhage. (Not included)
2. Cecum & Colon: Intestinal spirochetosis, Cynomolgus macaque, primate, etiology consistent with *Brachyspira sp*. (*B. pilosicoli*)

Contributor's Comment: Necropsy and microscopic findings support the clinical history of rectal prolapse, but the cause of this condition was not established. Giardiasis has been identified as the cause of rectal prolapse in squirrel monkeys. (1) However, the characteristic trophozoites were not found in the present case. Instead, diffuse (cecum) and segmental (colon) bacterial colonization of the superficial and glandular mucosae was evident in the large intestine. The spirochete-like bacteria created a thick basophilic (H&E stain) fringe at the microvillous brush border. Transmission electron microscopic examination demonstrated the bacteria attached to the brush border of cecal enterocytes by their polar ends with occasional invagination into the terminal web of the cells. The compact mat of bacteria effaced the microvilli and there was rarefication of the terminal-web microfilaments. The lamina propria of the cecum also contained minimal edema and a mild mononuclear cell infiltrate (lymphocytes, plasma cells, and macrophages) with a few eosinophils. The significance and/or contribution of large intestine spirochete infestations in the pathogenesis of rectal prolapse has yet to be determined.

Large intestine spirochetosis is an emerging cause of colitis of humans and animals, characterized by spirochete attachment and damage to epithelial cells and invasion of the cecal and colonic mucosae (2). *Brachyspira* (formerly *Serpulina*) *pilosicoli* has been identified as the primary etiologic agent of intestinal spirochetosis (2). Lesions indicative of intestinal spirochetosis have been seen in a wide range of hosts, including humans (3-7), non-human primates (7-11), pigs (12, 13), dogs (14, 15), opossums (16), guinea pigs (17), birds (18-20). Transmission across species has been shown in pigs, chickens, and laboratory mice inoculated with *B. pilosicoli* strains from humans, monkeys, pigs, dogs, and birds (21, 23, 24). Thus, *B. pilosicoli* is a potential zoonotic agent capable of being transmitted from animals to humans. It has been suggested that opossums and wild birds could be natural reservoirs for the disease (2).

All species affected with *B. pilosicoli* have lesions limited to the large intestine (2). Colonization of the mucosa by spirochetes is visible on routine histopathological examination as a thickened brush border, which stains blue with H&E and Giemsa, red with periodic acid-Schiff, and black with Warthin-Starry stains (2). However, confirmation of *B. pilosicoli* is accomplished by immunohistochemical staining with a *Brachyspira spp.*-specific mouse monoclonal antibody, fluorescent rRNA in situ hybridization, or 16s ribosomal RNA-sequence specific PCR amplification (11, 18, 25). The initial step in the pathogenesis of intestinal spirochetosis appears to be chemotaxis of spirochetes toward mucin (22, 26). Epithelial cell attachment may involve the interaction between a specific spirochete ligand (adhesin) and a host-cell receptor (23, 24). However, attachment of *B. pilosicoli* to exposed lamina propria in the large intestine of humans (7), pigs (2), and dogs (27) has also been described. The bacteria attach by their polar ends to the brush border of surface colonic enterocytes in a picket-fence fashion, causing displacement or effacement of microvilli and rarefaction of the terminal-web microfilaments (28). *B. pilosicoli* causes damage and penetrates the epithelium at the extrusion zone between crypt units. Spirochetes have been found attached to the intercellular junctions between enterocytes (21, 23) and penetration may involve dissociation of these complexes by a serine protease present in the outer membrane of the spirochete (24). After translocating across the epithelium, *B. pilosicoli*

spread extracellularly in the lamina propria, are phagocytosed by macrophages, and enter submucosal blood capillaries in humans (7, 29), non-human primates (7), pigs (25), dogs (14, 27), opossums (16) and chicks (23). Translocation of *B. pilosicoli* to extraintestinal sites (mesenteric lymph nodes and pericardial sac) has also been documented (2). After epithelial cell attachment is no longer seen, *B. pilosicoli* persist in the lumina of the crypts and intercellularly within goblet cells of the cecum and colon (18, 25). Repair of the superficial epithelial damage is characterized by hyperplasia of the crypt epithelium with goblet cell depletion and increased mononuclear cells in the lamina propria (12, 26).

Intestinal spirochetosis was found in 42% of clinically normal rhesus monkeys (*Masaca mulatta*) (28), in 57/59 wild caught baboons (*Papio* spp.) (10), in 11/14 wild-caught vervet monkeys (*Cercopithecus aethiops*) (9), in seven colony-raised rhesus (11), and in two crab eating macaques (*Macaca fascicularis*) (11). A majority of the monkeys with intestinal spirochetosis show no clinical signs or gross lesions indicative of intestinal disease. Histological lesions are limited to focal or diffuse thickening of the brush border of the surface epithelium that extends to the neck of the crypts in the cecum, colon, and rectum. Inflammation of the large bowel varies, but it is usually minimal or absent. Some monkeys have inflammatory cell infiltrates in the lamina propria similar to those seen in ulcerative colitis in humans (11). Concurrent infection with adherent flagellated bacteria and spirochetes (*Brachyspira aalborgi*) is present in most monkeys (7-9, 11, 30). *Brachyspira aalborgi* is closely related to *B. pilosicoli* and is also found in human beings (4-6) and opossums (16) with intestinal spirochetosis. Unclassified flagellated bacteria have also been seen along with spirochetes in humans (7, 8) and opossums (16) with intestinal spirochetosis. Uncovering the role of *B. aalborgi* and flagellated bacteria in intestinal spirochetosis may provide insight into the molecular mechanisms of this emerging infectious disease (2).

AFIP Diagnosis: Large intestine, luminal enterocytes: Myriad apically attached elongate bacteria, etiology consistent with *Brachyspira pilosicoli*, cynomolgus macaque (*Macaca fasicularis*), nonhuman primate.

Conference Comment: The contributor has provided a concise summary of spirochetosis in nonhuman primates. In piglets, *B. pilosicoli* (porcine intestinal spirochetosis) causes mild diarrhea and catarrhal, erosive or ulcerative typhlocolitis. However, piglets infected with *B. hyodysenteriae* (swine dysentery), have severe diarrhea and mucohemorrhagic colitis. Spirochetosis is also an important condition in birds, particularly turkeys, chickens and pheasants, where *Borrelia anserina* causes septicemia, mucohemorrhagic enteritis, hepatomegaly, splenomegaly and pale kidneys.

Rectal prolapse in nonhuman primates used in research is often associated with stress, diarrhea, *Enterobius* sp. (pinworms), or straining to defecate.

In addition to the intestinal spirochetes, some sections also contain rare protozoal organisms, which are consistent with *Balantidium* sp.

Contributor: Schering Plough Research Institute, PO Box 32, 144 Rt. 94 Lafayette, NJ 07848

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CASE III – 00-718 (AFIP 2840293)

Signalment: 1.5-year-old, intact female, American Eskimo dog, *Canis familiaris*, canine

History: The dog presented with a four to five day history of severe vomiting, melena and lethargy. The owner reported that the dog had always been considerably smaller than the other littermates. Recently the dog had demonstrated significant weight loss. Following clinical work-up renal failure was diagnosed. The dog showed no response to symptomatic treatment and the owner elected euthanasia.

Gross Pathology: All of the subcutaneous tissues were moderately edematous. A mild serosanguineous effusion was present within the thorax and abdomen. Both kidneys were small and firmer than normal with an irregularly pitted cortical surface. The renal capsule was removed with great difficulty. On hemi-section, the pitted areas in the cortex corresponded to areas of cortical thinning and bands of white tissue, which extended into the medulla. Both renal cortices also contained numerous, 2 to 8 mm diameter fluid filled cysts. A large (2.3x1.1x0.8cm) thrombus was present in the left renal vein. The left atrial endocardium was covered by 2 to 4 mm, raised, white, irregular plaques.

Laboratory Results:
Complete blood count: Normocytic, normochromic anemia.
Chemistry screen: BUN: 255 mg/dL; Creatinine: 8.4 mg/dL; Phosphorus: 28.4 mg/dL;
        Albumin: 2.1 g/dL.
Urinalysis: Urine specific gravity: 1.011; Protein: 3+; trace glucose.
Urine protein:creatinine ratio: 19.6
Abdominal ultrasound: Small irregular kidneys bilaterally

Contributor's Morphologic Diagnosis: Severe diffuse membranoproliferative glomerulonephritis with segmental glomerulosclerosis, and chronic diffuse tubulointerstitial nephritis. (Hereditary Nephritis/Alport's Syndrome)

Contributor's Comment: Both kidneys demonstrate similar changes on histology. The tubular interstitium is multifocally expanded and replaced by fibrous connective tissue and an infiltrate of inflammatory cells. The severity of the interstitial change varies from mild, with minimal separation of the tubules, to severe with contraction of the cortex and complete loss of the normal renal architecture. The inflammatory cell infiltrate is composed of a mixture of lymphocytes and plasma cells. Many tubules are

slightly dilated with attenuation of the renal tubular epithelium. Tubules frequently contain eosinophilic granular material (protein casts). Glomeruli have a thickened, irregular to undulating Bowman's capsule, which is lined by hypertrophic and hyperplastic parietal cells. The glomerular tufts are segmentally to globally thickened by bright eosinophilic matrix. Many glomerular tufts are contracted. The periglomerular urinary space frequently contains eosinophilic granular material (protein fluid).

Because of the severe proteinuria, and the suspicion of a hereditary glomerulopathy, samples from one kidney were submitted to the Texas Renal Disease Laboratory at the Texas A & M College of Veterinary Medicine for electron microscopy and immunofluorescence. On electron microscopy, the glomeruli had collapsed capillary loops with undulating, irregularly thickened basement membranes. The basement membranes exhibited severe diffuse laminar splitting. The lamina densa was rarefied. The visceral epithelial cells were hypertrophied and had diffuse foot process fusion. On immunofluorescence, the thickened Bowman's capsules exhibited mild segmental labeling for IgM. This labeling was believed to be due to immunoglobulin loss secondary to the loss of glomerular permselectivity. Based on the clinical findings and the distinctive changes in the glomerular basement membranes, a diagnosis of hereditary nephritis of Alport's syndrome was made.

Hereditary nephritis (HN) is caused by an inherited defect in the basement membrane (type IV) collagen, which results in progressive glomerulonephritis and typically renal failure. Natural occurrence of the disease is reported in humans and dogs. A transgenic mouse model (COL4A3 mutant) also exists. The most common form of inheritance in humans and dogs is X-linked dominant, with any one of a number of reported mutations occurring in the COL4A5 gene. A smaller number of cases is due to autosomal recessive inheritance and typically involves a mutation in the COL4A3 or COL4A4 genes. A rare autosomal dominant form of the disease has been reported in humans, however, a specific mutation has not been described. These mutations alter the structure of any one of 6 genetically distinct type IV collagen chains (α1(IV) through α6(IV)) and affect the formation of the triple helical molecule.

Clinically, the first sign of disease is proteinuria without azotemia. Humans frequently have evidence of microscopic hematuria, however, this has not been a prominent finding in dogs. Proteinuria develops in dogs between 3 to 8 months of age. At this time, minimal thickening of the glomerular tufts may be detected by light microscopy. The majority of the kidney architecture is within normal limits. On electron microscopy, there is a characteristic thickening of the glomerular basement membrane with splitting of the lamina densa into 2 or more layers. These changes, while diffuse, are typically mild. As the disease progresses there is increased thickening and splitting of the glomerular basement membrane with fusion of the epithelial cell foot processes. Extensive interstitial fibrosis with mild lymphoplasmacytic/histiocytic tubulointerstitial nephritis develops secondarily, with eventual progression to an end stage kidney. Most dogs reach this stage by 8 to 27 months of age. Males are typically more severely affected than females, with a more rapid onset and progression of renal disease.

Canine breeds affected by HN include Samoyeds, English cocker spaniels and miniature bull terriers. A group of mixed breed dogs near Navasota, Texas has also recently been documented to suffer from this disease. X-linked dominant inheritance is reported in Samoyeds and a specific G to T transversion at exon 35 of the COL4A5

gene has been identified. Bull terriers and the Navasota dogs also demonstrate X-linked dominant inheritance; English cocker spaniels show autosomal recessive inheritance. The exact mutations in the latter 3 breeds have not been identified.

While the light microscopic findings in this case are non-specific, the thickening and splitting of the glomerular basement membrane seen via electron microscopy is characteristic of HN in dogs and man. Because the dog in this case is female, the suspected mode of inheritance is autosomal recessive. Definitive diagnosis of HN would require the identification of the specific genetic mutation. We believe this case represents a new genetic form of HN in the dog.

AFIP Diagnosis: Kidney: Glomerulonephritis, membranoproliferative, global, diffuse, severe, with nephron loss, severe interstitial fibrosis, and minimal lymphoplasmacytic interstitial nephritis, American Eskimo dog, canine.

Conference Comment: The contributor has provided a complete summary of canine hereditary nephropathy. This case was reviewed in consultation with the Department of Nephropathology, Armed Forces Institute of Pathology, which concurred that the glomerular changes were consistent with HN/Alport's syndrome. Conference participants discussed the necessity of electron microscopy to diagnose HN/Alport's syndrome.

The basement membrane lesions seen in HN can be compared to those seen in immune-mediated glomerulonephritis. The pathogenesis of immune-mediated glomerulonephritis involves antigen-antibody complexes located subendothelially or within the glomerular basement membrane. These antigen-antibody complexes incite complement fixation and leukocyte infiltration. Neutrophils and monocytes initiate an acute inflammatory response causing glomerular damage. In addition to the renal lesions described by the contributor, some sections also contain a focal cortical abscess.

Contributor: The University of Pennsylvania, School of Veterinary Medicine, Laboratory of Pathology and Toxicology, 3800 Spruce Street, Philadelphia, PA, 19104

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CASE IV - A230 (AFIP 2839022)

Signalment: Goslings of two flocks, three to four weeks of age (*Anser domesticus*)

History: In spring 2001, increased mortality of 3-4 weeks-old goslings was observed in two flocks (flock I and II) in Southern Germany. The flocks were about 300 km apart but had received goslings from the same hatchery. Clinically, animals showed apathy and anorexia and died within 3-4 days. Goslings of both flocks were submitted for necropsy.

Gross Pathology: Three animals (flock I) showed severe haemorrhagic typhlitis and swelling of spleen and kidneys, whereas in later cases visceral gout was the main finding. Animals (flock II), examined within the first week of the disease course, showed fibrinous to haemorrhagic enteritis. In animals, examined at a later time, congestion of lungs and liver, a pale myocardium and urate depositions in the kidneys were observed.

Laboratory Results: Flock I: Microbiological examination led to the isolation of variable numbers of *Klebsiella, E.coli* (ß-haemolytic) and *Staphylococcus* sp. Three animals developed a moderate to severe intestinal coccidiosis two weeks after the beginning of the disease process.
Flock II: Cultures of various organs yielded non-specific growth. *Chlamydia* were not identified (ELISA). Two goslings showed mild intestinal coccidiosis.
Transmission electron microscopy of liver and kidney of one gosling of flock I revealed icosahedral viral particles with 45 nm in diameter (compatible with papovaviridae).
PCR, detecting a polyomavirus-specific 144 bp fragment, yielded a positive result in the kidney and liver of one gosling of each flock.

Contributor's Morphologic Diagnosis: Kidney: Tubulonephrosis, necrotizing, multifocal, severe, with haemorrhages and focal tubular accumulation of urate crystals; goose (*Anser domesticus*), avian. Consistent with haemorrhagic nephritis enteritis of geese. Etiology: Goose hemorrhagic polyomavirus (GHPV).

Contributor's Comment: Additionally, necropsied goslings showed degeneration of intestinal crypt epithelium and haemorrhage. Histologically, the tubular lesions in the kidney were difficult to distinguish from autolytic changes. Therefore, molecular biological examination (PCR) was performed which identified polyomavirus-specific sequences. Transmission electron microscopy on formalin-fixed renal tissue of one gosling was not sufficient for the detection of polyomaviral particles in tubular epithelial nuclei.

Hemorrhagic nephritis enteritis of geese (HNEG) was first described in Hungary in 1969. The disease spread through goose breeding areas of Germany and France with an epizootic pattern. HNEG is characterized by high morbidity and high mortality in geese 4 to 10 weeks of age. Sudden death is the most common outcome, generally preceeded by coma. The acute course is associated with diarrhea, dyspnoea and nervous signs. At necropsy, oedema and petechia in the subcutis, ascites, haemorrhagic enteritis and nephritis are common findings. Hepatomegaly, splenomegaly, hydropericardium and pulmonary edema are occasionally seen. Histopathological finding in kidneys are represented by oedema and detachment of the tubular epithelium from the basement membrane. In progredient cases, cells are replaced by granulation tissue. Secretion of uric acid is disturbed and kidney and/or visceral gout can develop.

In 2000, a novel polyomavirus was isolated from geese and was identified as goose hemorrhagic polyomavirus (GHPV). GHPV belongs to the family *Papovaviridae,* which consists of two genera: papillomavirus and polyomavirus. Members of the family are highly species-specific. Polyomaviruses are non-enveloped 40-50 nm icosahedral virions, containing a 4.8 to 5.5 kbp circular double-stranded DNA. In mammalian hosts, polyomaviruses predominantly cause inapparent infections, whereas in birds, the infection leads to severe disease. The prototype of avian polyomavirus is the budgeriar fledgling disease virus. It is responsible for abdominal distention, reddening of the skin and sudden death. Furthermore, it induces a chronic disorder of feather formation known as "French molt". At necropsy, hydropericardium, enlarged heart and liver and swollen and congested kidneys are often seen. Histopathologically, large pale basophilic intranuclear inclusion bodies are typical for polyomavirus infections.

The transmission of GHPV is still unknown, but transmission from subclinically infected parents to breeding stock via the hatching egg is considered. This is supported by the fact that in the present case, the two flocks have received goslings from the same hatchery.

AFIP Diagnosis: Kidney: Nephritis, tubulointerstitial, necrotizing, acute, multifocal, moderate, with mild hemorrhage, goose (*Anser domesticus*), avian.

Conference Comment: Large amphophilic to basophilic intranuclear inclusion bodies can commonly be found in most avian polyomavirus infections. In contrast, goose hemorrhagic polyomavirus is the only known polyomavirus that does not produce viral inclusion bodies. This absence of inclusions is similar to lymphotropic papovavirus infections.

Polyomaviruses also cause disease in many mammalian hosts, including nonhuman primates, hamsters, rodents, cattle and rabbits. In addition to the renal lesions, many sections demonstrate a mild airsacculitis.

Contributor: Institut fuer Veterinaer-Pathologie, Justus-Liebig-Universitaet Giessen, Frankfurter Str. 96, 35392 Giessen, Germany

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Kathleen A. Ryan, DVM
Major, Veterinary Corps, U.S. Army
Wednesday Slide Conference Coordinator
Department of Veterinary Pathology
Armed Forces Institute of Pathology
Registry of Veterinary Pathology*