CASE I – 18079-05 (AFIP 3031126).

Signalment: Red fox (Vulpes vulpes), juvenile, female

History: This red fox was found alive at a golf course in late July. It was showing signs of illness: weak, heaving, breathing heavily, not scared of humans. This was the second fox in one week from the same golf course with similar signs. The animal was shot in the head with a .22-caliber rifle and submitted for necropsy.

Gross Pathology: This female red fox was considered to be a young of the year (approximately 3-4-months-old), based on its small size. It was in poor body condition (no fat in subcutis, only a small amount of fat around the base of the heart and in the mesentery). Both lungs were very emphysematous. The mucosa of the caudal region of the trachea was covered by a small to moderate amount of creamy whitish material and contained a few slightly raised plaques, about 2-3 mm in diameter. Almost the entire bronchial tree of both lungs was filled with creamy yellow material suggestive of pus (Fig. 1). The stomach was empty. The large intestine contained a moderate amount of fecal material.

Laboratory Results (clinical pathology, microbiology, PCR, ELISA, etc.): Streptococcus species (group G), was isolated in large numbers from a bronchial swab.

Histopathologic Description: Lesions were confined to the respiratory tract and, in the lungs, were centered around the bronchial tree. Several cross and oblique sections of small nematodes, mixed with numerous ova (often with an operculum evident at both ends), large numbers of macrophages and some neutrophils, rested on the mucosal epithelium of small and large bronchi or were embedded within it. Much of this epithelium was markedly hyperplastic, particularly in the larger bronchi, although areas of epithelial loss were also
evident. The submucosa of the larger intrapulmonary bronchi was infiltrated by numerous plasma cells and some eosinophils. Many ova, several of them degenerated, could be found within bronchioles and alveoli where they were associated with a pyogranulomatous reaction, including multinucleated giant cells that had phagocytized some of these ova. Lesions similar to those within the lungs were in the main bronchi and in the caudal region of the trachea, together with fibrosis, necrosis and fibrin accumulation (tissues not included). The pulmonary nematodes were identified in tissue sections as *Eucoleus aerophilus* (formerly *Capillaria aerophila*).³

**Contributor’s Morphologic Diagnosis:** Severe chronic pyogranulomatous verminous bronchopneumonia

**Contributor’s Comment:** This young red fox had a severe pulmonary parasitic infection, likely complicated by a secondary bacterial infection. The nematode *Eucoleus aerophilus* belongs to the superfamily Trichinelloidea, whose members typically parasitize epithelial surfaces of vertebrates.⁴ *Eucoleus* aerophilus has been reported at a low prevalence in most fecal surveys of dogs and cats and is enzootic in wild foxes in many parts of the world.⁴,⁹ In the three Maritime provinces of Canada (Prince Edward Island, New Brunswick, Nova Scotia), more than 65% of wild red foxes that have been examined were infected by this parasite.⁹ The life cycle of *E. aerophilus* is mainly direct through the fecal-oral route, although earthworms that have ingested the ova with soil can also act as facultative intermediate or, more likely, paratenic hosts.⁴

Clinical signs in infected dogs and cats are generally characterized by a low-grade chronic cough. The disease among foxes raised in earthen runs on fur farms, however, used to be much more severe, with poor growth, decreased fur quality, and substantial mortality from bronchopneumonia, particularly among young animals.⁷ Control of the disease was achieved by shifting the animals to raised cages with wire bottoms. In free-living wild fox, the degree of infection may vary among animals but is probably generally higher in young-of-the-year because of their immature immune system. It is conceivable that, every year, a number of young fox die from pneumonia caused by this parasite, either because their immune system is particularly inefficient or because they are exposed to a very large number of eggs. In this case, secondary infection by *Streptococcus* species group G had likely contributed to the animal’s death. Most bacteria of this group isolated from animals are *S. canis*. This bacterium can be isolated from mucous membranes of asymptomatic domestic carnivores, but it can also cause opportunistic infections, including suppurative bronchopneumonia and septicemia.¹⁰

The nematode *Crenosoma vulpis* is another common pulmonary parasite in the red fox population of the Canadian Maritime provinces and often occurs concurrently with *E. aerophilus*.⁹ This parasite may also be a common cause of respiratory disease in domestic dogs presented with clinical signs of chronic
cough.\textsuperscript{1} \textit{Crenosoma vulpis} has an indirect life cycle, using snails and slugs as intermediate hosts.\textsuperscript{11} \textit{Eucoleus aerophilus} is longer but more slender than \textit{C. vulpis} (Table 1).\textsuperscript{8} Whereas \textit{E. aerophilus} is oviparous, \textit{C. vulpis} is ovoviviparous, and it also tends to inhabit deeper regions of the bronchial tree.\textsuperscript{9} Adults and first stage larvae of \textit{Crenosoma vulpis} were not identified in the lungs of this fox.

Table 1: Comparison of the dimensions of adult specimens of \textit{Eucoleus aerophilus} and \textit{Crenosoma vulpis}.\textsuperscript{8}

<table>
<thead>
<tr>
<th></th>
<th>length</th>
<th>Diameter</th>
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<tr>
<td></td>
<td>Male</td>
<td>female</td>
</tr>
<tr>
<td>\textit{E. aerophilus}</td>
<td>15-25 mm</td>
<td>20-40 mm</td>
</tr>
<tr>
<td>\textit{C. vulpis}</td>
<td>3.5-8 mm</td>
<td>12-16 mm</td>
</tr>
</tbody>
</table>

Other potential nematode parasites of the respiratory system of red fox in this country include \textit{Oslerus (Filaroides) osleri}, \textit{Dirofilaria immitis}, and \textit{Angyostrongylus vasorum}. Infection by \textit{O. osleri} is characterized by the formation of discrete nodules typically found near the bifurcation of the main bronchi, whereas both \textit{D. immitis} and \textit{A. vasorum} are parasites of the pulmonary arterial tree rather than of the airways.\textsuperscript{3} Moreover, the North American distribution of \textit{A. vasorum} is currently confined to the Atlantic Canadian province of Newfoundland.\textsuperscript{2}

\textbf{AFIP Diagnosis:} Lung: Bronchopneumonia, pyogranulomatous and eosinophilic, multifocal, severe, with bronchiolar epithelial hyperplasia, aphasmsids and eggs, etiology consistent with \textit{Eucoleus aerophilus}, red fox (\textit{Vulpes vulpes}), canine.

\textbf{Conference Comment:} The capillarids are a large group of parasites that have been divided into numerous different genera on more than one occasion. The former \textit{Capillaria} affecting dogs and cats is now primarily divided into three genera:\textsuperscript{3} \textit{Eucoleus}, which is found in the airways; \textit{Aonchotheca}, which is found in the intestinal tract; and \textit{Pearsonema}, which is found in the urinary bladder. Other genera of veterinary importance include \textit{Calodium}, which is found in the liver of rats and other mammals.\textsuperscript{3} The division into these genera is not universally accepted as some researchers prefer the previous genus name \textit{Capillaria}.\textsuperscript{6}

The life cycle of \textit{Eucoleus (Capillaria) aerophilus} can be either primarily direct or less commonly indirect involving an earthworm as an intermediate paratenic host. Eggs are deposited in the pseudostratified ciliated epithelium, work their way up the respiratory tree, are swallowed, and are then passed out with the feces.\textsuperscript{4}
Physical characteristics of *E. aerophilus* are similar to those of other aphasmid nematodes.\(^5\) Aphasmids lack a pair of sensory papillae on their caudal end. They lack the prominent lateral cords seen in phasmid nematodes. They have a hypodermal band and one genital tract in the female.\(^5\)

**Contributor:** Department of Pathology and Microbiology, Atlantic Veterinary College, University of Prince Edward Island, Canada

http://www.upei.ca/~avc/index.html

**References:**

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**CASE II – NIAH-No.1 (AFIP 3065665).**

**Signalment:** 9-week-old, female, Leghorn chicken, avian
History: In March 2003, extensive swelling or bulbous protrusions of the integument were noticed in the layer chickens of approximately 11 weeks of age, in a commercial flock. The affected chickens had almost no clinical signs other than the tumors and ate, drank, and walked normally. Approximately 80 of 27,000 (0.3%) chickens in the affected flock were slaughtered because of the tumors. Similar tumors had also occurred in the chickens of another farm originating from the same lot of breeder hens. Both affected flocks had been vaccinated by the wing-web method for fowl pox and Marek's diseases and were sprayed with the infectious bronchitis vaccine at hatching.

Gross Pathologic Findings: The tumors were primarily observed in the head or wing, had a maximum diameter of 10 cm, were usually solitary, soft to firm but not hard, and creamy white to a dull red in color and grew slowly. The overlying skin was wounded in some cases, resulting in ulceration.

Laboratory Results: RT-PCR analyses were performed on the tumor tissues of two affected chickens with a primer pair targeted at the gp85 region of the env gene of subgroups A to E avian leukosis/sarcoma virus (ALSV). Tumor samples were PCR positive. Nucleotide sequence analyses indicated that these viruses belonged to subgroup A of ALSV and had 97.5% nucleotide sequence homology with myeloblastosis-associated virus type 1-like strain 1 of Canadian isolate.

Fifteen of 20 serum samples obtained from 19 weeks of age clinically normal chickens from the affected layer farm were strongly reactive against subgroup A of ALSV, and eight of them were also strongly reactive against subgroup B by an enzyme-linked immunosorbent assay (ELISA).

Histopathologic Description: The tumor was unencapsulated and composed of loose areas with abundant mucinous matrix. Stellate or spindle shaped cells were predominant, whereas mitotic figures were uncommon. Short collagen fibers, which are stained blue by the azan stain and Masson trichrome stain, were observed in the matrix. The mucinous matrix was stained positively with alcian blue pH 2.5 and colloidal iron and showed metachromasia by toluidine blue staining: it was negative with alcian blue pH 1.0, high iron diamine, and periodic acid-Schiff reaction. The positive reactions disappeared after digestion with hyaluronidase. These results demonstrate that the matrix contained hyaluronic acid.

Tumors were specifically stained by a rabbit anti-ALSV serum and two mouse monoclonal antibodies against subgroup A ALSV, and the inner bulb of Herbst corpuscles was strongly stained. Normal cutaneous and subcutaneous tissues of the affected chickens were negative.

Electron microscopy revealed viral particles in the tumor that were 74-97 nm in diameter, had a core (34-46 nm in diameter) and envelopes, and sometimes
showed the budding process. Their ultrastructural characteristics were identical with those of type C retroviruses. 

**Contributor’s Morphologic Diagnosis:** Skin: myxoma, Leghorn, chicken, avian

**Contributor’s Comment:** Generally, neoplastic diseases other than Marek’s disease or lymphoid leukosis are sporadic; however, in the present case, subcutaneous tumors were observed in many layer chickens in a flock. A congenital or genetic disease was suspected at first because a similar disease had occurred in the chickens of another farm originating from the same lot of breeder hens. The results of immunohistochemistry, electron microscopy, RT-PCR analysis, and ELISA indicate that the neoplastic diseases in the present case are associated with subgroup A of ALSV infection. It seems that the virus is exogenous because the ALSV antigen positive area is localized and, in the tumor, it corresponds with the C-type viral particles observed area. Eight of 20 chickens from the affected farm had an antibody to subgroup B; however, it might be a cross-reaction caused by group-specific antigens of ALSV. We conclude that 17 samples had antibodies against subgroup A ALSV. The existence of matrix-inclusion bodies containing ribonucleic acid in the myocardium is further evidence in favor of this viral infection. It is possible that the virus is transmitted vertically from hen to progeny through the egg or horizontally from bird to bird at the breeding site. Chickens inoculated in the wing web with avian sarcoma virus develop sarcomas at the site of inoculation. Epizootic outbreaks of solid tumors have been reported, and the physical transmission of ALSV among newly hatched chickens during the vaccination procedure has been suggested. However, in our case, tumors were observed not only at the site of inoculation, but also in other areas. Further studies are required to elucidate the epizootiology of our case.

The tumor contained large amounts of mucin and involved histologic lesions similar to those previously reported in cases of myxoma in chickens and was therefore diagnosed as myxoma. Myxoma is composed of embryonal connective tissues. Myxoma in the subcutis, spleen, kidney, ovary, and mesentery in chickens has been previously reported. Replication-defective avian retroviruses and Rous sarcoma virus affect mesenchymal cells and cause sarcomas. Various tumors have been reported in chickens inoculated with specific strains of ALSV; for example, strain F-1A of subgroup A has been associated with lymphoid leukosis, erythroblastosis, fibrosarcoma, and hemangioma in inoculated chickens.

Today, it seems that leukosis-free flocks have been established, most commercial flocks consist of genetically resistant lines, the eradication of horizontally transmitted viruses has been accomplished, and, accordingly, there has been a sharp reduction in the incidence of diseases associated with ALSV infection with the exception of subgroup J ALSV. However, in our
unpublished data, layer flocks frequently have ALSV antigens in Japan, and we are concerned about an outbreak of diseases associated with ALSV. The present epizootic outbreak of neoplastic disease is therefore unusual and worthy of study.

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**AFIP Diagnosis:** Feathered skin: Myxoma, leghorn chicken (*Gallus domesticus*), avian.

**Conference Comment:** The contributor gives a good overview of the ALSV-induced myxoma in this flock of commercial chickens.

Viruses of the avian leukosis/sarcoma virus (ALSV) group are members of the *Alpharetrovirus* genus of the family Retroviridae. Other species within this genus include the Rous sarcoma virus and other replication defective viruses that carry various oncogenes. ALSVs are divided into 6 subgroups, A-E and J, based on differences in their viral envelope. Viral replication requires a reverse transcriptase that synthesizes a DNA provirus of the RNA virus. This DNA provirus is then integrated into the host cell genome where viral RNAs are transcribed, which are then translated into precursor and mature viral proteins.

In addition to subgroups, strains of ALSV are generally classified according to the predominant neoplasm they produce, such as lymphoid leukosis virus (LLV), avian erythroblastosis virus (AEV), avian myeloblastosis virus (AMV), and avian sarcoma virus (ASV). Although the oncogenic spectrum of the strains are usually characteristic, they can overlap and are affected by viral origin, dose, and route of inoculation, as well as by host age, genotype, and sex.

Gross and histologic differential diagnoses for neoplasms and lesions that may be caused by ALSV strains include:

- **Lymphoid, erythroid, and myeloid infiltrates**
  - Marek’s disease, lymphoid leukosis virus, and reticuloendotheliosis virus have very similar gross and histologic lesions. They may be differentiated via PCR or serology
  - Erythroblastosis – the liver and bone marrow are usually cherry red
  - Myeloblastosis – the liver is usually pale red and the bone marrow is whitish, grossly the lesions are similar to lymphoid leukosis

- **Myeloctymatosis:** Distinctive character and location, is usually nodular and multiple, occurs on the surface of bone in association with the periosteum and near cartilage

- **Hemangiomia:** Wounds, bleeding from feather follicles, hemorrhages, and sarcomas

- **Renal tumors:** Renal enlargement caused by hematomata, lymphoid leukosis, or accumulation of urates
• Osteopetrosis: Other osteopathies such as rickets, and osteoporosis
• Connective tissue tumors: Granulomas, tuberculosis, pullorum disease

Retrovirus of Animals

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Examples</th>
</tr>
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<tbody>
<tr>
<td>Alpharetrovirus</td>
<td>Avian leukosis viruses, avian carcinoma viruses, avian sarcoma viruses, Rous sarcoma virus, duck spleen necrosis virus</td>
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<tr>
<td>Betaretrovirus</td>
<td>Mouse mammary tumor virus, Jaagsiekte</td>
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<tr>
<td>Gammaretrovirus</td>
<td>Feline leukemia virus, feline sarcoma virus, porcine type C virus, many murine leukemia viruses, many murine sarcoma viruses</td>
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<tr>
<td>Deltaretrovirus</td>
<td>Bovine leukemia virus, human and simian T lymphotropic viruses</td>
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<tr>
<td>Epsilonretrovirus</td>
<td>Walleye dermal sarcoma virus, walleye epidermal hyperplasia viruses</td>
</tr>
<tr>
<td>Lentivirus</td>
<td>Human immunodeficiency virus, simian immunodeficiency viruses, maedi/visna virus, caprine arthritis-encephalitis virus, feline immunodeficiency virus, equine infectious anemia virus, bovine immunodeficiency virus</td>
</tr>
<tr>
<td>Spumavirus</td>
<td>Bovine, feline, simian, and human foamy viruses</td>
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http://niah.naro.affrc.go.jp/index.html

References:
CASE III – 01-5058, 01-5257, 01-5262 (AFIP 3069576).

Signalment: Three young adult (3-year-old) male squirrel monkeys (Saimiri sciureus)

History: Over the course of 8 days, three monkeys presented to the veterinary service center with severe respiratory distress. The animals were sedated for examination and blood collection. Auscultation revealed severe inspiratory strider but normal sounding lung fields. The larynx appeared abnormal in all
three animals but was difficult to completely visualize. One animal died following intubation and the other 2 were euthanized the following day due to poor prognosis.

**Gross Pathology:** Lesions were remarkably similar in all three animals. There was unilateral firm thickening of the left side of the larynx in 2 animals and bilateral swelling in 1. Lungs were normal.

**LABORATORY RESULTS** (clinical pathology, microbiology, PCR, ELISA, etc.):

CBC abnormal findings – elevated WBC (11.7-13.3 K/µl, normal ref range 7.9 +/- 2.8 SD) due to increases in neutrophil counts were noted in all 3 animals.

Clinical chemistry abnormal findings – elevated CPK in all three animals (2928, 5038, and 7752 IU/L, normal CPK ref ranges 562 +/- 1379.8 IU/L).

Cultures were obtained from the laryngeal lesions from 2 of the 3 animals. A pure culture of *Bordetella bronchiseptica* was obtained from both.

**Histopathologic Description:** Tissues from all three monkeys contained similar lesions. The normal histoarchitecture of the larynx is markedly altered by a necrotizing inflammatory process that expands the submucosa and dissects between laryngeal muscle fibers. The inflammation, which consists almost exclusively of viable and degenerate neutrophils within a background of granular eosinophilic and basophilic matrix (fibrinous exudate, necrobiosis, and mucinous degeneration), widely separates and isolates muscle fibers between the intrinsic and extrinsic laryngeal cartilages. Myofiber necrosis in this region is prominent, while extrinsic laryngeal musculature is less severely affected. Multifocally, the overlying mucosa is ulcerated, partially covered by suppurative exudate, and contains expanded pockets of degenerate neutrophils and fibrin. Mucous glands are also disrupted and entrapped within the inflammation. A Gram stain revealed very low numbers of Gram negative coccobacilli, a few of which exhibited filamentous morphology.

**Contributor’s Morphologic Diagnoses:** Larynx: Laryngitis, necrosuppurative, severe, transmural, chronic, with necrotizing myositis and intralesional Gram negative bacteria.

**Contributor’s Comment:** *Bordetella bronchiseptica* can colonize and cause disease in a wide range of mammals and is associated with acute tracheobronchitis in dogs (kennel cough) and cats, atrophic rhinitis in swine, snuffles in rabbits and experimentally can produce acute pneumonias in rats. Members of the *Bordetella* genus include *B. bronchiseptica*, *B. pertussis*, *B. parapertussis*nu and *B. parapertussis*ov and all possess several virulence factors including filamentous hemagglutinin (FHA), fimbriae, pertactin, LPS, dermonecrotic toxin (DNT), tracheal cytotoxin (TCT), and others, but only *B. pertussis* has pertussis toxin. These factors contribute to the organisms’ ability
to colonize respiratory epithelium, but may also contribute to cellular damage and immune regulation. These squirrel monkey cases represent a severe and very interesting manifestation of infection with this agent. Although isolation of this organism from the laryngeal lesions of these three squirrel monkeys does not definitively prove that it was the inciting cause, the lesions are consistent with those that could be produced by a highly pathogenic organism possessing such potent virulence factors.

It is also interesting that all three squirrel monkeys presented with such similar lesions within a relatively short period of time. These monkeys were housed off site in a structure with large garage-like doors that could be opened in warm weather, yet when closed, still had space above and below that would allow access to birds, insects, rodents, and possibly wind blown sticks and leaves. The similarity in age, gender (all young males) and housing of these three animals suggest that an environmental and/or behavioral component may have contributed to their susceptibility. Because many mammals can carry *B. bronchiseptica* in their upper respiratory tracts yet remain asymptomatic, we cannot definitively prove that this organism was the cause of the severe laryngeal lesions. However, pure cultures directly isolated from the lesions of all three animals are supportive that this organism was directly responsible.

Other causes of laryngitis or laryngeal lesions in animals include oral necrobacillosis (calf diphtheria) due to *Fusobacterium necrophorum*, or laryngeal ulcers often seen in feed lot cattle.²

AFIP Diagnosis: Larynx: Laryngitis, necrosuppurative, subacute, focally extensive, severe, with multifocal muscle degeneration, necrosis, hemorrhage, and ulceration, squirrel monkey (*Saimiri sciureus*), primate.

Conference Comment: *Bordetella* spp. are aerobic, non-fermentative, gram-negative coccobacilli. There are six identified species with three of veterinary importance.

*Bordetella* spp. of veterinary importance¹

<table>
<thead>
<tr>
<th><em>B. bronchiseptica</em></th>
<th>Infectious tracheobronchitis (kennel cough) in dogs; atrophic rhinitis in pigs</th>
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</thead>
<tbody>
<tr>
<td><em>B. avium</em></td>
<td>Coryza in turkeys</td>
</tr>
<tr>
<td><em>B. hinzii</em></td>
<td>Commensal in respiratory tract of chickens; opportunistic infections in humans</td>
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*B. bronchiseptica* has several virulence factors that promote colonization and that enable the bacterium to escape destruction in the host. Attachment virulence factors include fimbriae, and two non-fimbrial outer membrane proteins (filamentous hemagglutinin and pertactin). Replication is enhanced by

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² *Fusobacterium necrophorum* is also a Gram-negative, anaerobic, pleomorphic bacillus responsible for bovine, ovine, and porcine diphtheria known as “calf diphtheria.” It is closely related to *Fusobacterium varium* and *Fusobacterium nucleatum*. These bacteria are commonly found in the oral cavity of many mammals and may cause infections in humans and animals, particularly in the respiratory tract. They are often associated with respiratory diseases and can cause severe infections in immunocompromised individuals.
production of hydroxamate siderophores and binding proteins that mobilize iron from transferrin, lactoferrin, and heme. Factors that allow escape from destruction include:

1. Adenylate cyclase toxin/hemolysin (also called cyclosin)
   a. Hemolysin binds to the host cell and facilitates entry of the adenylate cyclase domain.
   b. Adenylate cyclase toxin causes an increase of cAMP intracellularly, which inhibits the respiratory burst of macrophages and prevents phagocytic activity of heterophils.
2. Dermonecrotic toxin (DNT) - Intracellular bacterial toxin released upon lysis of the bacteria; inhibits the Na/K ATPase pump and causes vasoconstriction
3. Lipopolysaccharide - Pyrogentic and mitogenic; causes macrophage chemotaxis and activation; induction of tumor necrosis factor production
4. Tracheal cytotoxin – stimulates nitric oxide production and interferes with mucociliary function
5. Type III secretion products – undefined products; inactivate transcription factor NF-κB and modulate effects on host immune response

_B. bronchiseptica_ infections are often seen in conjunction with other bacterial or viral coinfections. It is generally considered the primary cause of kennel cough in dogs, but canine parainfluenza virus 2, canine adenovirus 2, canine distemper virus, and _Mycoplasma_ spp. have been known to have predisposing roles. Atrophic rhinitis complex generally includes _B. bronchiseptica, Pasteurella multocida, Haemophilus parasuis_, and viral infections including porcine cytomegalovirus. _B. bronchiseptica_ actively promotes colonization of the nasal cavity by _P. multocida_ which in turn produces cytotoxins that inhibit osteoblastic activity and promote osteoclastic reabsorption.

Some sections submitted by the contributor included an adjacent lymph node with multifocal sinus histiocytosis and erythrophagocytosis, interpreted as draining hemorrhage.

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http://med.stanford.edu/compmed/

**References:**
CASE IV - Case 1 (AFIP 3073874).

Signalment: 38-week-old, male, Sprague Dawley rat, *Rattus norvegicus*

History: The rat was euthanized at week 38 of a chronic toxicity study due to a large mass involving the left maxillary region.

Gross Pathologic Findings: A red, firm mass was noted that involved the entire left maxillary region. It was 35 X 25 X 20 mm. The mass appeared the same on the cut surface.

Histopathologic Description: The normal bony architecture of the maxilla is largely replaced by a poorly circumscribed mass that is predominantly composed of epithelial and mesenchymal elements that frequently form variably-sized and shaped tooth-like structures. The epithelial elements of the mass include ameloblasts and odontoblasts that are generally well-differentiated; these cells often palisade along eosinophilic extracellular material with fine, tubular cavities (dentin) or lesser amounts of a more basophilic, hyaline material (enamel). Spindled to stellate mesenchymal cells with an accompanying vascular component (dental pulp) are often present centrally within the abortive tooth-like structures. Multifocally within the mass, odontogenic cells occasionally form cords and nests that are not associated with dental hard substance; these structures sometimes have central cavitations that contain degenerating cells and necrotic debris. There are multifocal areas of necrosis, inflammation, hemorrhage, pigment, and new bone formation within or at the periphery of the mass.

Contributor’s Morphologic Diagnosis: Odontoma

Contributor’s Comment: An odontoma is a dental neoplasm (or hamartoma) in which cellular maturation and differentiation have progressed to the stage of development of both enamel and dentin. Two types are recognized: complex odontoma and compound odontoma. Complex odontomas contain dental pulp, mesenchymal cells, and hard tissue elements, but there is poor differentiation of
the cellular components such that the mass has little resemblance to normal tooth architecture. Compound odontomas have a higher degree of cellular differentiation, and their hard tissue elements resemble abnormally shaped tooth-like structures (denticles). The hard tissue generally appears as dentin (an acellular, smooth, eosinophilic material) with smaller amounts of cementum (resembling bone). Enamel may be completely removed upon decalcification, in which case it will appear as a clear space or cleft in close apposition to the dentin. Incompletely decalcified specimens may have a small amount of enamel that stains basophilic with hematoxylin and eosin. Complex odontomas are rare in all species but are most commonly seen in young horses and young dogs. Compound odontomas generally present as mass-like lesions of the jaw of young canines. Both types of odontomas have been described in the rat. In those species such as the rat where incisors grow continuously throughout the animal’s lifetime, odontoma must be distinguished from dysplasia or a malformation that is congenital or secondary to malocclusion or fracture of the incisor tooth.

Odontomas and other odontogenic tumors have been experimentally induced in rats by carcinogens such as methylnitrosourea and related compounds.

AFIP Diagnosis: Bone, maxilla: Compound odontoma, Sprague-Dawley rat (Rattus norvegicus), rodent.

Conference Comment: Currently there is controversy on the classification of odontomas as either neoplasms or non-neoplastic hamartomas. Odontomas are tumors in which there is a combination of both odontogenic epithelial components and dental matrix structures such as dentin and enamel. The inductive theory of odontogenesis states that the ameloblastic epithelium promotes the surrounding mesenchymal cells to become odontoblasts. These odontoblasts produce dentin, which is necessary for the ameloblasts to form enamel. Neoplasms composed of only epithelium without hard tissues are termed ameloblastomas.

Odontomas can be classified into various types based on their components and organization:

• Complex odontoma – Contains well differentiated dental tissues, including dentin, enamel matrix, odontogenic epithelium, and cementum (horses and rodents) that do not form tooth-like structures
• Compound odontoma – Contains cords of odontogenic epithelium, with intermittent complete odontogenesis forming tooth-like structures (denticles). Occasionally there is bone matrix formation surrounding or adjacent to the denticles.
• Odontoameloblastoma – Contain areas of ameloblastic epithelium that are separate from other areas of complex or compound odontomas.
• Ameloblastic fibro-odontoma\textsuperscript{2} – Contain both dental epithelial tissues (resembling dental lamina) and mesenchymal tissues (resembling dental pulp) that are associated with enamel and dentin.

• Dentinoma\textsuperscript{3} – Contain odontoblasts producing a calcified dentin tissue with no evidence of enamel formation.

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