Pathology of the Domestic Ferret

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PURPOSE

The purpose of this 2-hour block of instruction is to gain knowledge and experience in the gross diagnosis of diseases of the domestic ferret (*Mustela putorius furo).* Of course, the study of disease in this species far exceeds what can be presented in a two-hour block of time, but I will attempt to cover a number of diseases of interest. In some cases, inclusion or exclusion from this collection was the result of the availability of high-quality photographs. I am a firm believer that one can learn far more from one excellent photograph of a single entity, than from many poor ones. If the only available image is of poor quality, the image won't leave a lasting impression, and the student learns nothing.

I have included a brief morphologic or etiologic diagnosis for each entity. The formulation of concise, accurate morphologic diagnoses is a major pursuit of every good pathologist, especially those who seek certification in this specialty. The formulation of a good morphologic diagnosis is a learned skill; for those seeking additional experience in this endeavor, I would suggest attendance at the annual AFIP Descriptive Pathology Course in Washington D.C.

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Slide No.	Organ	Condition	Morphologic Diagnosis	Notes

1		INTRODUCTION		
2		Photograph Credits		
3	Presentation	Normal	Normal	Normal fitch ferret Males average 2.5 lbs, females 1.25 lbs. Most ferrets are already neutered and descented.
4			**Nervous System**	
5	Presentation	Canine distemper	Cachexia	Ferret distemper is highly infectious and 100% fatal in this species
6	Presentation		Cachexia, diarrhea	Diarrhea is commonly seen in affected animals. Note nasal hyperkeratosis.
7	Conjunctiva		Diffuse mucopurulent conjunctivitis	Clinical signs resemble distemper in other species; photophobia and mucupurulent conjunctivitis and rhinitis are early presenting signs.
8	Nasal planum		Diffuse mild nasal hyperkeratosis with mucopurulent rhinitis	Hardpad disease (hyperkeratosis of the nasal planum and foodpads is a pathognomonic sign of distemper in ferrets.)
9	Footpads		Diffuse mild footpad hyperkeratosis	
10	Footpad (mink)		Diffuse severe footpad hyperkeratosis	
11	Lung		Diffuse fibrinosuppurative bronchopneumonia	Pneumonia is a result of immunosuppression and is the most common cause of death in affected animals.
12	Urinary bladder		Numerous intracytoplasmic and intranuclear epithelial inclusions	Inclusions can be found in many epithelial tissues in affected animals. Urinary bladder, lung, and Biliary tract are good sites to sample.

13	Footpad		Diffuse severe footpad hyperkeratosis with numerous intracytoplasmic viral inclusions	Intracytoplasmic and intranuclear inclusions may be found in in apparently unaffected skin. IFA is even more sensitive, if available.
14	Lung		Diffuse necrotizing bronchointerstitial pneumonia	Immunohistochemistry for morbillivirus antigen shows the extent of infection in affected lungs
15	Presentation	Rabies	Aggression	Furious and mad forms of rabies are seen in ferrets
16	Cerebrum		Intracytoplasmic viral inclusions (Negri bodies) in cerebral neurons in a mink	Less than 60 cases of rabies in ferrets have been recorded, making it one of the most rarely affected domestic species
17	Vaccine box			Ferrets require annual IM vaccination; treated like dogs and cats in bite incidents (10-day quarantine in US)
18	Presentation	Neural tube	Multiple defects including cleft palate, iniencephaly, craniorachischisis, and exenteration	Neural tube defects occur with highest incidence in litters from color-diluted sires.
19	Neural tube	Skull, vertebral column	Diffuse craniorachischisis with iniencephaly	Iniencephaly is a malformation/fusion of cervical veterbrae resulting a “star-gazing” appearance.
20			Diffuse craniorachischisis with iniencephaly	In affected animals neural defects (as seen here) may include agenesis of cerebral hemispheres and spinal cord.
21	**Gastrointestinal System**			
22	Teeth	Broken teeth	Bilateral mandibular canine fractures	The pulp cavity of the ferret tooth is relatively shallow and becomes less prominent with

				age – ferrets can tolerate more significant loss of the crown without a requirement for endodontic therapy.
23	Teeth	Periodontal disease	Diffuse moderate dental calculus	Ferrets are similar to other domestic animals with regard to frequency of periodontal disease, which may be worsened in animals on bland diets.
24			Severe dental calculus with periodontitis and root abscess	
25	Oral cavity	Mucocele	Oral mucocele	Mucoceles are occasionally seen in ferrets, likely as a result of chewing foreign objects
26	Head, subcutis	Zygomatic salivary duct	Zygomatic salivary gland mucocele	Rupture of the duct of the zygomatic salivary gland often results in mucoceles on top of the head. Long-term drainage is usually required.
27				
28				
29	Esophagus	Megaesophagus	Megaesophagus with marked intrathoracic dilation	This disease of young, male ferrets has not yet been linked to other conditions.
30	Lungs	Aspiration pneumonia	Multifocal to coalescing gangrenous pneumonia	Aspiration is the eventual cause of death of most animals with megaesophagus. Look for fungal infections in the ulcerated esophagus as well.
31	Esophagus	Myofasciitis (Disseminated idiopathic myositis)	Multifocal severe neutrophilic esophagitis	Myofasciitis is an idiopathic fatal condition of young ferrets resulting in characteristic neutrophilic inflammation in the esophagus, heart, skeletal muscle, and lymph nodes.
32			Esophagus, muscularis and serosa: Esophagitis, neutrophilic focally extensive, severe.	
33	Hind legs		Diffuse severe hindlimb muscle atrophy (normal on left)	Affected skeletal muscles show marked wasting, and occasionally may have neutrophilic inflammation as

				well.
34	Stomach	*Helicobacter mustelae*	Diffuse m0derate atrophic gastritis with melena	Clinical signs and gross lesions of this common infection of middle-aged and older ferrets are usually tenuous.
35			Ultrastructural appearance of spiral bacteria	*H. mustelae* are spiral-shaped bacteria that live in the mucous layer overlying the gastric mucosa.
36			Multifocal to coalescing lymphoplasmacytic gastritis	Evidence of *Helicobacter* infection is commonly seen in clinically normal animals as well.
37			Small numbers of argyrophilic bacteria (Warthin-Starry 4.0)	Organisms are best demonstrated in the pylorus with a silver stain.
38	Stomach	Gastric ulcers	Diffuse pyloric ulcers with melena	The presence of digested blood in the stomach is positive proof of gastric ulcers.
39	Gastric contents		Tarry stools	The presence of tarry, unformed stools is a sign of a potentially life-threatening condition.
40	Stomach		Focal pyloric ulcer with hemorrhage	Large pyloric ulcers can result in fatal gastric bleeds in 5 mins.
41	Stomach		Pinpoint pyloric ulcers; perforating pyloric ulcer	Numerous small bleeding points in the pyloric stomach is far more common than large focal ulcers.
42	Feces	Epizootic catarrhal enteritis		The first name of the disease was the “Green Slime”. One still hears this type of feces referred to as “the greenies” today.
43	Cadaver		Diffuse serous atrophy	Affected animals rapidly lose condition. Note colon filled

			of fat	with green, loose feces.
44	Small intestine		Diffuse lymphocytic and atrophic enteritis with maldigested feces	The affected section of intestine ahs a thinned, congested wall and contains birdseed-like feces.
45			Normal ferret jejunum	The normal ferret jejunum has long, plush villi.
46			Focal villar tip enteric necrosis	The acute lesion of ECE is necrosis of enterocytes at the villar tips.
47			Diffuse lymphoplasmacytic enteritis with villar atrophy, fusion, and blunting	Following necrosis of villar tip enterocytes, villar shortening and re-epithelialization may result in marked decreases in absorptive surface area and diarrhea.
48			FeCoV antigen in villar tip enterocytes	Ferret enteric coronavirus, a group A coronavirus, characteristically infects villar tip enterocytes.
49			Coronavirus particles in enterocyte SER	Transmission EM of coronaviral particles in enterocyte ER; coronaviral particles in feces
50	Presentation	Inflammatory bowel disease		IBD is rapidly becoming one of the most common diagnoses in ferrets today; while virtually unheard of a decade ago.
51	Feces		“Birdseed” feces	This type of feces is commonly seen in IBD and other malabsorptive disorders – “seeds” represent undigested globules of fat and protein
52	Small intestine		Diffuse lymphocytic enteritis with villar fusion and blunting.	The key to diagnosis of the lymphocytic form is villar blunting and presence of increased numbers of intra-

				epithelial lymphocytes (IELs)
53	Small intestine, lymph node	IBD (eosinophilic gastroenteritis)	Diffuse eosinophilic enteritis; diffuse eosinophilic lymphadenitis with Splendore-Hoeppli material	Eosinophilic gastroenteritis is a more severe clinical form of IBD but also responds to immunosuppression and dietary changes.
54	Colon	*Lawsonia intracellulare*	Diffuse proliferative colitis (serosal view)	*L. intracellulare* is a pathogen in a number of species, but the ferret is the only species in which the colon is affected.
55			Multifocal to coalescing proliferative colitis ("adenomatosis")	Marked proliferation of immature mucosa form "glandular" mucosal thickenings. Fine bleeding points result in hematochezia
56	Feces		Blood and mucous in feces	Affected animals pass frequent small bowel moves with tenesmus and frank blood.
57	Colon		Diffuse proliferative and lymphocytic colitis; argyrophilic bacteria in apical cytoplasm (Warthin-Starry 4.0)	Note the proliferation of immature, non-mucous-containing colonic epithelium. In silver stains, massive numbers of bacilli are present in apical cytoplasm of colonic epithelium
58	Small intestine	*Giardia lamblia*	Low and high magnifications of trophozoites attached to the luminal surface.	*Giardia* trophozoites and cysts can be recovered from the feces of clinically normal animals as well.
59	Small intestine	*Eimeria, Isospora sp*	Diffuse lymphocytic enteritis with villar blunting	Coccidia is occasionally seen as a facility outbreak as a result of poor sanitation. Infections in very young and very old animals may be fatal.
60			Abundant intraepithelial schizonts	Almost every epithelial cell in this segment of gut has a schizont, which often excyst at

			and gamonts	the same time, resulting in large stretches denuded of epithelium.
61	Small intestine	Rotavirus	Focally extense superficial and necrotizing enteritis	Common in ferret kits at 2-3 weeks of age, histologic lesions are mild and consist of vacuolation and necrosis of villar tip enterocytes. Disease in adults is subclinical.
62	Presentation	Gastrointestinal foreign bodies		Most common cause of severe GI distress in ferrets less than 1 year of age.
63	Small intestine		Focally extensive necrotizing enteritis with rubber foreign boy and proximal dilatation	Rubber, latex, and cloth are most common in ferrets. Cloth foreign bodies are most often seen in older ferrets due to boredom.
64	Stomach	Trichobezoars		GI signs minimal until well-formed. Assume shape of the stomach.
65	Oral cavity	Foreign bodies	Foreign object between maxillary dental arcade; electrical cord burn with oronasal fistula	Ferrets often explore their environment with their mouth, leading to misadventure.
66	Liver, intestinal tract	*Mycobacterium avium*	Multifocal to coalescing granulomatous hepatitis and enteritis	Ferrets are susceptible to a wide range of mycobacteria including *M. avium,* which affects the gastrointestinal tract, *M. bovis* (in feral ferrets in New Zealand) and *M. genovense.*
67	Stomach	*Clostridium perfringens type A*	Diffuse necrotizing gastritis	Outbreaks of black-footed ferret kits occurred at the National Zoo in the 1990's.
68	Rectum	Prolapsed rectum	Rectal prolapsed	Rectal prolapse may be seen in concert with loose stools of any

				cause.
69	Mandible	Oral squamous cell carcinoma	Mandibular squamous cell carcinoma	Oral squamous cell carcinoma is the most common neoplasm of the ferret oral cavity, and is often mistaken in early stages for periodontal disease.
70	Intestine	Intestinal T-cell lymphoma	Diffuse intestinal lymphoma	Lymphoma is the most common neoplasm of the GI tract, with both T- and B-cell lymphoma reported.
71	Ileum	Intestinal adenocarcinoma	Intestinal adenocarcinoma	Adenocarcinomas of the stomach and intestine have a characteristic “napkin ring” appearance with proximal dilatation.
72	Anal sac	Squamous cell carcinoma of the anal sac	Anal sac squamous cell carcinoma	SCC arising from the anal sac is a rare neoplasm in the ferret.
73		**Hepatobiliary and Exocrine Pancreas**		
74	Liver	Hepatic lipidosis	Diffuse hepatic lipidosis	Hepatic lipidosis is a common physiologic finding in anorexia and often results in elevated ALT and alkaline phosphatase.
75	Pancreas	Pancreastic exocrine hyperplasia	Multifocal pancreatic exocrine hyperplasia	Exocrine pancreatic hyperplasia is a common aging finding; nodules are the same color as the surrounding pancreas.
76	Liver	Hepatocellular carcinoma	Hepatocellular carcinoma	These slow-growing neoplasms eventually result in liver failure.
77 78	Liver	Biliary cystadenocarcinoma	Biliary cystadenocarcinoma	These slow-growing tumors often look benign histologically, but eventually replace hepatic lobes and cross over into other lobes.
79		**Endocrine System**		

80	Presentation	Islet cell tumor		Signs of hypoglycemia in ferrets include “trances”, ptyalism, and coma.
81	Pancreas		Pancreatic islet cell tumor	Islet cell tumors, the most common neoplasm in ferrets, are generally red or pink in colors (due to vascularity).
82		Normal pancreas		Ferrets, as obligate carnivores, have large pancreases, with two distinct lobes.
83		Islet cell tumor	Encapsulated and unencapsulated islet cell tumors	All islet cell tumors are potentially malignant whether encapsulated or not.
84	Presentation	Adrenal-associated endocrinopathy	Bilaterally symmetrical truncal alopecia	Hair loss is the most common presenting sign for adrenal disease in ferrets. Other causes of hair loss are extremely uncommon in ferrets.
85			Severe diffuse alopecia	Alopecia is the result of estrogen effect on hair follicles.
86	Diagram		Diagram of pituitary-gonadal-adrenal interaction	Adrenocortical disease in ferrets is due to interruption of the pituitary-gonadal axis and the effects of unremittent LH production on receptors in the adrenal cortex
87	Pop Quiz			Can you spot the adrenal ferret?
88	Vulva		Diffuse vulvar hypertrophy	Estrogen receptors on vulvar fibroblasts results in 200x increase in size in young ferrets in heat, or 50% of spayed ferrets with adrenal disease.
89	Adrenal glands		Normal anatomy of ferret adrenal glands	The right adrenal gland is located under the caudate liver lobe and on top of the posterior vena cava, making for

				tricky surgical removal.
90	Adrenal glands		Adrenocortical hyperplasia, adenoma, adenocarcinoma	Histologic features of proliferative adrenal lesions in ferrets. Regardless of type, a good prognosis is usually warranted if early treatment is accomplished.
91	Adrenal gland	Teratoma	Adrenal teratoma	Teratomas are rarely seen in ferret adrenal glands and often appear as mineralized densities on radiographs.
92	Pancreas	Diabetes mellitus	Diffuse islet cell glycogenosis	While spontaneous cases do arise, many are the result of long-term prednisone use
93	**Hematolymphatic System**			
94	Spleen	Splenomegaly	Diffuse splenic extramedullary hematopoiesis	Splenic hematopoiesis is a common finding in middle-aged and older ferrets, and is a stereotypical response to chronic inflammation
95	Spleen	Splenomegaly	Diffuse splenic extramedullary hematopoiesis	95% of enlarged spleens are the result of extramedullary hematopoiesis; the remainder are due to neoplasia
96	Thymus, liver, spleen	Lymphoblastic lymphoma	Thymic, hepatic, and splenic lymphoma with splenic infarction	Lymphoblastic (juvenile) lymphoma generally affects ferrets less than 2 years of age; tumors are predominantly visceral.
97	Cervical lymph nodes	Lymphocytic lymphoma	Nodal lymphoma	Lymphocytic lymphoma generally affects animals over 5 years of age, results in married enlargement of lymph nodes, and neoplastic cells are mature lymphocytes.
98	Cytologic	Lymphocytic leukemia		Look for monomorphic populations on cytologic

	preparation			aspirates in order when diagnosing lymphoma.
99	Spleen	Lymphoblastic leukemia	Splenic lymphoma with focal infarct and splenic rupture	Infiltration of splenic sinusoids by neoplastic cells often results in stasis and splenic infarction.
100	Abdominal viscera	Aleutian disease	Bilateral glomerulonephritis, splenomegaly with infarct, ecchymotic gastric serosal hemorrhage, and hematuria	The basic mechanism of Aleutian Disease is the precipitation of antigen-antibody complexes in basement membranes throughout the body.
101	Illustration		Viral particles and crystallographic reconstruction	Due to its configuration, the Aleutian disease parvovirus results in the formation of abundant non-neutralizing antibodies.
102	Kidneys		Diffuse membranous glomerulonephritis	Renal glomeruli are the largest vascular bed in the body – making the kidneys the target organ in Aleutian disease in ferrets.
103	Urinary bladder		Hematuria with serosal hemorrhage	Excessive levels of antigen-antibody complexes result in clotting deficiencies in terminal disease.
104	Kidney		Diffuse membranous glomerulonephritis; plasmacytic infiltrates in numerous tissues	Plasmacytic infiltrates in numerous organs is characteristic for Aleutian disease. Don't confuse aging changes in glomeruli for glomerulonephritis – look for proteinaceous casts in tubules as well.
105	Test kit			While in-house testing kits are available, CIEP is still the "gold standard" test for this disease.

106	Abdominal viscera	Coronavirus-associated systemic granulomatous disease	Multifocal granulomatous peritonitis, mesenteric lymphadenitis, and colitis	Within the last five years, a number of cases of systemic granulomatous disease have been diagnosed in young ferrets, with lesions resembling the “dry” form of feline infectious peritonitis. Feline enteric coronavirus (FeCoV) antigen, a Group A coronavirus, has been recovered from the lesions.
107	Spleen		Multifocal to coalescing granulomatous splenitis	
108	Liver		Multifocal to coalescing granulomatous hepatitis with thrombophlebitis	
109	Spleen	Hemangiosarcoma	Splenic hemangiosarcoma	Hemangiosarcoma in the spleen may be surgically excised if detected early; in other viscera it has a poor prognosis.
110	Abdominal cavity		Mesenteric hemangiosarcoma	
111	Skin		Cutaneous hemangiosarcoma	Skin tumors warrant a good prognosis.
112			**Urinary Tract**	
113	Kidney	Bacterial urinary tract infections	Hydronephrosis	Female ferrets are prone to urinary tract infections, with bacteria able to reach he kidney in as little as two weeks. Blockage of the ureter by cellular debris may result in hydronephrosis.
114	Prostate	Cystic prostatic disease	Squamous metaplasia of prostatic glandular epithelium with cyst formation	Estrogen secretion by functional adrenocortical lesions results in squamous metaplasia of the prostatic epithelium.
115	Radiograph		Focally extensive prostatic cysts with suppurative inflammation	Large prostatic cysts in male ferrets results in dysuria and post-renal azotemia, and may ultimately result in total urinary obstruction.

116	Prostate			The presence of keratin debris within prostatic cysts often incites a profound suppurative inflammatory response.
117	Radiograph	Urolithiasis	Struvite uroliths	Urolithiasis is less commonly seen today as a result of decreased usage of plant proteins in ferret chows. Today, dysuria is more commonly associated with prostatic disease.
118	Kidney	Renal cysts	Multiple renal cortical cysts	Renal cysts are seen in up to 33% of animals at necropsy, and are rarely considered of clinical importance.
119		Renal cyst	Focally extensive renal cyst	Cysts may attain a large size, but due to the toughness of the renal capsule, rarely rupture
120		Polycystic kidney disease	Multiple renal cortical and medullary cysts with nephrosclerosis	Autosomal recessive PKD is seen in ferrets as in many other species and results in death in young animals.
121		Chronic interstitial nephritis	Diffuse chronic interstitial nephritis	CIN is a common finding in older ferrets.
122		**Reproductive System**		
123	Skin, vulva	Estrus-associated bone marrow suppression	Multifocal to coalescing cutaneous hemorrhage, melena, and vulvar swelling	Ferrets are induced ovulators, so estrus production continues for a prolonged period. Bone marrow suppression may affect any one or all three lines of marrow cells (RBC, WBC, platelets) resulting in severe anemia, hemorrhage, or secondary bacterial infections. Approximately 50% of unbred jills die as a result of unterminated estrus.
124			Focally extensive cutanesous ecchymosis with vulvar swelling	
125	Digits		Severe anemia	

126	Lungs		Diffuse purulent pleuritis	
127	Mammary glands	Mastitis	Diffuse suppurative mastitis	Coliforms and *Staphylococcus* are common causes. Kits must be weaned or moved to another jill.
128		**Cardiovascular System**		
129	Heart	Dilatative cardiomyopathy	Bilateral ventricular dilatation with chronic passive hepatic congestion	Dilatative cardiomyopathy is the most common form of CMP in ferrets. Many older ferrets have evidence of CMP at necropsy. The cardinal histologic lesion is myofiber loss and replacement by fibrosis; in acute stages, lymphocytic inflammation may be present in the myocardium.
130			Cardiomyopathy with marked pleural effusion	
131			Multifocal to coalescing myocardial fibrosis with myofiber loss (HE)	
132			Multifocal to coalescing myocardial fibrosis with myofiber loss (Masson's trichrome))	
133	Heart	*Dirofilaria immitis*	Cardiac dirofilariasis	Ferrets in heartworm=endemic areas should be on prevention.
134		**Respiratory System**		
135	Lung	Aspiration pneumonia	Multifocal to coalescing gangrenous pneumonia	Aspiration pneumonia is often seen in animals that have been force fed by syringe, or occasionally in animals receiving liquid antibiotics.
136	Lung	Endogenous lipid pneumonia	Multifocal to coalescing subpleural histiocytosis	Endogenous lipid pneumonia is a common incidental finding in furbearing animals.
137	Conjunctiva	Influenza	Diffuse mild serous conjunctivitis	Ferrets are the animals model for Type A and B influenza; the natural disease is self-limiting

138	Lung	Systemic fungal infection	Multifocal to coalescing granulomatous pneumonia	Systemic infections with *Blastomyces, Cryptococcus* and *Histoplasma* are occasionally seen in ferrets.
139	Lung	*Mycobacterium genavense*	Diffuse granulomatous pneumonia	In recent years, a number of atypical bacterial species have been reported in ferrets, including *M. genavense, M. abscessus, M. celatum, and M. microti*
140		**Musculoskeletal System**		
141	Tip of tail	Chordoma	Caudal vertebral chordoma	Chordomas are the most common neoplasm of the musculoskeletal system. They are slow-growing, invasive tumors of little metastatic potential, but if they arise anywhere other than the tail, a poor prognosis is warranted.
142				
143	Radiograph		Cervical vertebral chordoma	Chordoma has been reported a number of times in the cervical vetebrae of the ferret with uniformly poor results.
144	Cervical vertebra			Chordomas are extremely infiltrative neoplasms which predispose to pathologic fractures and para- or tetraparesis.
145	Skull	Osteoma	Cranial osteoma	Osteomas are slow-growing benign bone tumors which often arise on the skull or other flat bones.
146	Skull, X-ray			
147			Maxillary osteoma	Surgical excision Is generally curative, however, this practitioner was hesitant in attempting removal.
148	Leg, vertebra	Osteosarcoma	Femoral, vertebral	Osteosarcomas may be seen on either flat or long bones, with

			osteosarcoma	no predilection for each. There has been no reports of metastasis of osteosarcoma in the ferret.
149	Eye, orbit	*Actinomyces sp.*	Focally extensive granulomatous orbital cellulitis and osteomyelitis	*Actinomyces* has been reported in a number of cases of deep-seated infection in the skull of ferrets.
150		**Integumentary System**		
151	External ear canal	*Otodectes cynotis*	Aural otodectiasis	Ear mites are a common infection in ferrets and easily treated with cleansing and ivemectin.
152	Facial skin	*Ixodes hexagonus*	Dermal ixodiasis	Ticks are occasionally seen in animals housed outdoors, usually in poor conditions.
153	Haired skin	*Demodex sp.*	Follicular demodicosis	*Demodex* mites are commonly found in normal ferrets, and may be seen in increased numbers in immunosuppressed individuals.
154	Foot	Sebaceous epithelioma	Cutaneous sebaceous epithelioma	Sebaceous epitheliomas and other variants of sebaceous adenomas are the most common neoplasm of the skin and invariably benign.
155	Haired skin			Although they look ugly both grossly and histologically, sebaceous epithelioma is still invariably benign.
156	Haired skin	Mast cell tumor	Cutaneous mast cell tumor	Mast cell tumors are also invariably benign, although they may appear either singly or multiply.
157	Prepuce	Apocrine cysts	Preputial apocrine cysts	Apocrine cysts, and neoplasms, are most common on the face, neck, prepuce, and perineum.
158		Apocrine gland	Preputial apocrine	

		adenocarcinoma	adenocarcinoma	Neoplasms on the prepuce or perineum have a high incidence of malignancy, and are the site of most malignancies in ferret skin.
159	Ear	Leiomyosarcoma	Cutaneous leiomyosarcoma	Smooth muscle tumors are commonly seen, especially in the dorsal neck and back, where they arise from hair follicles (piloleiomyomas).
160	Haired skin	Vaccine-related sarcoma	Cutaneous fibrosarcoma	Vaccine-related sarcomas are rarely reported in ferrets. Inflammatory lesions due to deposition of vaccine in the dermis are more common.
161	Haired skin, face	Peripheral nerve sheath tumor	Malignant peripheral nerve sheath tumor	Peripheral nerve sheath tumors in the ferret are most commonly seen on the face.
162				Recurrence of previously excised tumor but much more aggressive (as is often the case following surgical intervention.
163			**Nervous System**	
164	Cerebrum	Meningioma	Cerebral meningioma	Lymphoma is the most common neoplasm in the brain of the ferret.
165	Eyes	Cataracts	Bilateral lenticular cataracts	A common finding in older ferrets, there is no known cause for cataracts.
166	Eyes	Glaucoma	Unilateral bupthalmia	Both secondary and primary glaucoma have been seen in the ferret.
167	Retina	Peripheral retinal atrophy	Diffuse loss of inner nuclear and plexiform layers	This condition is common in oder ferrets, whose owners often do not know that they are blind. Histologically, It is

				similar to RP in humans.
168	Eye	Lymphoma	Retroorbital lymphoma	Lymphoma is the most common cause of bulging eyes in ferrets.

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(*Mustela putorius furo*)

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Nervous System

Canine Distemper

Synopsis: Canine distemper is the most serious disease in ferrets. Essentially 100% fatal, the morbillivirus that causes canine distemper results in an accelerated syndrome that closely mimics signs seen in canids and other susceptible species. Disease progression ranges from 12 days in ferret-adapted strains to approximately 42 in wild canine strains. The disease is profoundly immunosuppressive, with animals that survive this stage of the disease succumbing to neurologic dysfunction within several weeks. This disease n the U.S. is primarily seen in young kits from pet stores. Treatment is not recommended. Currently, there is one approved distemper vaccine for ferrets (Fervac-D, United Vaccines); however, many commercial modified live canine vaccines are used in ferrets. Recombinant vaccines using a canarypox vector are being developed for use in ferrets and exotic mammals.

Gross lesions. Similar to those seen in the dog. Photophobia, oculonasal discharge, hyperkeratosis of the planum nasale and footpads, a papular rash beginning on the chin and progressing to a generalized form, bronchopneumonia.

Microscopic lesions. Brightly eosinophilic, 2-5 um intracytoplasmic and intranuclear inclusions may be seen in a wide variety of epithelial cells, neurons, and occasionally in white blood cells and megakaryocytes. (The urinary bladder, renal pelvis, and biliary epithelium in my places are the most productive places to look for inclusions.) Additionally, multinucleate cells may be found in any of these sites. A non-suppurative encephalitis with demyelination may be seen in animals with neurologic disease. The presence of suppurative bronchopneumonia in a young ferret is suggestive of this disease.

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Rabies.

Synopsis: Ferrets, as well as any other mammal, are susceptible to rabies. Ferrets, however, have a low recorded incidence of rabies, with less than 25 confirmed cases since 1954. The disease can result in both furious (less common) and dumb forms, and often presents as a progressive hindlimb paralysis. Researchers have shown that ferrets inoculated IM with virulent rabies virus do not secrete the virus in their saliva. Currently, there is one approved killed rabies vaccine available for use in the ferret (Imrab, Rhone-Merieux).

Gross lesions. None.

Microscopic lesions. Intracytoplasmic eosinophilic viral inclusions (Negri bodies) may be demonstrated on HE stains or on standard fluorescent antibody tests.

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Niezgoda M, et al. Viral excretion in domestic ferrets inoculated with a raccoon rabies isolate. *Am J Vet Res* 59(12) 1629-1632.

Rupprecht CE et al. Evaluation of an inactivated rabies virus vaccine in domestic ferrets. *JAVMA* 196:1614-1616, 1990.

Neural Tube Defects

Synopsis: NTD's are one of the most common birth defects in ferret kits. They may range from simple cranioschisis (external opening of the skull), to spina bifida, to craniorachischisis (opening of the skull and vertebral column with loss of cerebral tissue). Many variants are seen. Additionally, growth retardation and other birth defects (kidney defects appear commonly) may be seen in the fetus.

Gross lesions. Agenesis of skin and musculature overlying various segments of the skull and/or spinal cord, with variable loss os neural tissue.

Microscopic lesions. Additionally, there may be fusion or other deformation of the vertebrae. With cranioschisis or craniorachischisis, there is often agenesis of the cerebrum and cerebellum, with a rudimentary medulla (cerebrovasculosa) remaining.

Additional references.

Williams BH et al.. Iniencephaly and other neural tube defects in a litter of ferrets (Mustela putorius furo). *Vet Pathol* 31(2): 260-262, 1994.

Gastrointestinal System

Dental Disease

Synopsis: Broken teeth are common in older ferrets, most commonly affected are the upper canines. While few broken teeth result in clinical debility, exposure of the pulp requires extraction or root canal procedures. Accumulation of dental calculi is common in older ferrets on semi-moist or moist diets. Tooth root abscesses are occasionally seen in ferrets. Dental malformations, including supernumerary teeth or decrease numbers of adult teeth have also been documented.

Gross lesions. Discoloration of broken teeth suggests devitalization. Draining tracts may be seen, especially in the area of the zygomatic arch with tooth root abscesses.

Microscopic lesions: N/A

Additional references:

Andrews PL, Illman O. Some observations of anatomical abnormalities and disease states in a population of 350 ferrets (Mustela furo). IZ. VersuchsteirkdI 21:346, 1979.

Berkovitz BK. Supernumerary deciduous incisors and the order of eruption of the incisor teeth in the albino ferret. *J. Zool*., 155:445, 1968

Verstraete FJM. Advances in Diagnosis and Treatment of Small Exotic Mammal Dental Disease. *Sem In Avian and Exot Pet Med* 12(1):37-48, 2003.

Megaesophagus

Synopsis: The cause of megaesophagus is currently unknown in the ferret. It presents similarly to megaesophagus in the dog and cat. Occasionally, secondary *Candida* infections may be seen. The condition occurs in middle-aged to older ferrets, and treatment is usually ineffective. In 2009, the first case of myasthenia gravis was identified in a ferret with mild megaesophagus.

Gross lesions: Marked dilation of the intrathoracic esophagus. Ulcerations may be present anywhere along the length. Evidence of bronchopneumonia may be present due to aspiration.

Microscopic lesions. Often none. In chronic cases, there may be discernable atrophy of the muscular layers. In other cases, there may be hyperkeratosis of the lining epithelium, and the presence of numerous yeast within the mucosa, inciting a lymphocytic and neutrophilic inflammatory response.

Additional references:

Blanco MC et al. Megaesophagus in nine ferrets. *JAVMA* 205:444-447, 1995.

Couturier J, Huynh M, Boussarie D, Cauzinille L, Shelton GD. Autoimmune myasthenia gravis in a ferret. J Am Vet Med Assoc. 2009 Dec 15;235(12):1462-6.

Myofasciitis

Synopsis. Myofasciitis is an inflammatory condition of uncertain etiology in ferrets that exhibits characteristic microscopic lesions in young ferrets in the esophagus, heart, and skeletal muscles. Presumed to be of immune-mediated origin, this condition results in neutrophilic infiltrates which efface esophageal muscle, cardiac muscle, and skeletal muscle. Clinical signs are non-descript and include persistent high fever, leukocytosis (which is occasionally extreme), hindlimb weakness, paresthesia, occasional abscessation of one or more peripheral nodes (often in the hindlegs), wasting, difficulty swallowing, and ultimately death. Animals may also exhibit hyperesthesia. Treatment regimens including antibiotics, antivirals, and anti-inflammatorys may slow down the progression of disease, but are not curative.

Gross lesions: While morbidity is low in affected facilities, mortality of this condition is high. Gross lesions include whitish swellings of the esophagus, cardiac muscle, and various skeletal mucles, including the diaphragm, and pronounced muscle wasting.

Microscopic lesions: Inflammation in affected organs is neutrophilic in nature, and the neutrophils are generally viable. In the esophagus, the inflammatory infiltrate is largely confined to the muscular and serosal layers. The combination of neutrophilic inflammation in the heart and esophagus (and ultimately other thoracic organs) is unique to this condition in the ferret.

Additional references:

Garner MM et al. Myofasciitis in the domestic ferret. *Vet Pathol* Jan 2007, 44(1) 25-38.

Helicobacter mustelae

Synopsis. This bacterium, recently discovered by James Fox et al. at MIT, causes disease in significant numbers of ferrets over the age of four years. The bacterium causes gastric disease via two mechanisms - a) the stimulation of a marked lymphoplasmacytic inflammatory response, resulting in loss of glandular epithelium, most prominently in the pylorus, and 2) the ability to increase the pH of the stomach. Animals over the age of 3 years rarely do not show evidence of *Helicobacter* infection.

Gastric ulcers are also commonly seen in animals with severe Helicobacter infection. (see below) Recent evidence that *H. mustelae*-infected ferrets have elevated levels of gastrin suggests a possible relationship with peptic ulcer disease.

Gross lesions: There are often no gross lesions in uncomplicated cases of gastric *Helicobacter*. Advanced cases may be coupled with gastric ulcers. In these cases, the gastric mucosa is often lined by moderate amounts of digested blood; gastric ulcers are often fine bleeding points concentrated in the pylorus.

Microscopic lesions: Warthin-Starry 4.0 is the stain of choice to demonstrate the presence of the bacteria in the superficial mucus and in extracellular locations within the gastric glands. The pyloric stomach is the preferred biopsy site, although low numbers of bacilli may also be seen in the fundus and duodenum in severely infected animals.

Additional references.

Batchelder M, et al. Natural and experimental Helicobacter mustelae reinfection following successful antimicrobial eradication in ferrets. *Helicobacter*. 1996 Mar; 1(1): 34-42.

Fox JG, et al. *Helicobacter mustelae*-associated gastritis in ferrets. An animal model of *Helicobacter pylori* gastritis in humans. *Gastroenterology* 99:352-361-1990.

Fox JG et al. Gastric colonization of the ferret with *Helicobacter* species: Natural and experimental infections. *Rev Infect Dis 13(suppl 8)*:S671-680, 1991.

Fox JG et al. Role of gastric H in isolation of *Helicobacter mustelae* from the feces of ferrets. *Gastroenterology* 104:86-92, 1993.

Gottfried MR et al. *Helicobacter pylori*-like microorganisms and chronic active gastritis in ferrets. *Am J Gastroenterol* 85:813-818, 1990.

Otto G et al. Eradication of *Helicobacter mustelae* from the ferret stomach: an animal model of *Helicobacter pylori* chemotherapy. *Antimicrob Agents Chemother* 34:1232-1236, 1990.

Perkins SE et al. Helicobacter mustelae-associated hypergastrinemia in ferrets. AJVR 57(2):147-150, 1996.

Gastric ulcers

Synopsis. Ferret, like other mustelids, are extremely susceptible to stress-related gastric ulcers. This is a common finding in animals with other systemic diseases and often contribute to debility in older animals. They are often seen in association with gastric *Helicobacter mustelae* infection, however, a definitive cause-and-effect relationship has not been proven in this species. vessels.

Gross lesions: Two distinct forms of gastric ulceration may be seen in the ferret. The most common form is the presence of digested blood within the stomach lumen. Ulcers are pinpoint, extremely difficult to see, and are present in the highest numbers in the pyloric region of the stomach. The second, less common form, is he presence of a single, focally extensive, ulcer in the pyloric stomach. These large ulcers may result in sudden death due to erosion into the submucosal blood vessels.

Microscopic lesions. Microscopically, ulcers appear as full-thickness areas of glandular necrosis and loss which are well-demarcated from the surrounding tissue. Bleeding ulcers may be covered with a layer of brown hemoglobin pigment.

Additional references.

Hudson M et al. A ferret model of acute multifocal gastrointestinal infarction. *Gastroenterology* 102:1591-1596.

Inflammatory Bowel Disease

Synopsis. Inflammatory bowel disease is extremely common in middle aged and older ferrets. IBD in the ferret generally falls into one of two categories: the lymphocytic/plasmacytic form, and the eosinophilic form (also known as eosinophilic gastroenteritis.

The cause of inflammatory bowel disease in the ferret, as in other species is mulitfactorial. The nature of the antigens precipitating a chronic, uncontrolled inflammatory reaction in the intestine is largely unknown in the ferrets, but strong evidence exists that infection by *Helicobacter mustelae* and ferret coronavirus may eventually result in the development of this condition. Dietary antigens have not been investigated in this condition, although dietary modification commonly is effective in amerliorating clinical signs.

The lymphocytic form is more commonly seen and presents with milder clinical signs. The severity of histologic lesions, however, rarely equates with the severity of clinical disease. The more severe form, eosinophilic gastroenteritis was first described by James Fox et. al of MIT in 1992. Although the etiology of this disease is likewise unknown, presumed cases have been treated successfully with ivermectin, suggesting some form of parasitic origin. The wasting disease is most commonly seen in young male ferrets under 14 months of age. Peripheral eosinophilia may be seen in affected animals. Unlike the lymphocytic form, lesions of eosiniphilic IBD may be present in a wide range of abdominal organs, including the liver, spleen, and mesenteric lymph nodes.

Gross lesions: None.

Microscopic lesions. Small to moderate numbers of of lymphocytes, plasma cells, and eosinophils are commonly seen in the small intestine of the ferret. Lymphocytic forms of inflammatory bowel disease are associated with intramucosal lymphocytes (intraepithelial lymphocytes- IELs), and evidence villar atrophy, blunting, and fusion.

With EE, Eosinophilic infiltrates may be seen in the small intestine - a diffuse mucosal infiltrate and an eosinophilic vasculitis may be present. Additionally, prominent eosinophilic infiltrates may be seen in the mesenteric lymph nodes, liver, pancreas, or any other abdominal organ (and have rarely been reported in the thorax

as well.). Aggregates of Splendore-Hoeppli material may be seen within the lymph nodes and rarely in the liver in areas of accumulated eosinophils, but are rarely seen in the gut.

Additional references.

Blomme, EA et al. Hypereosinophilic Syndrome with Hodgkin's-like Lymphoma in the Ferret. *J Comp Pathol* 120:211-217, 1999.

Fox JG et. al. Eosinophilic gastroenteritis with Splendore-Hoeppli material in the ferret (Mustela putorius furo). *Vet Pathol* 29:21-26, 1992.

Palley LS, Fox JG. Eosinophilic gastroenteritis in the ferret. *In* Kirk RW, Bonagura JD (eds.): Current Veterinary Therapy XI. Philadelphia, WB Saunders, 1992, pp. 1182-1184.

Proliferative colitis

Synopsis. Proliferative colitis is an uncommon disease which is usually seen in male ferrets under one year of age. The disease is sporadic, with only one or two animals in a large colony being affected. Clinical signs include tenesmus and production of small, frequent bowel movements which often contain frank blood and mucus. The disease is caused by a campylobacter-like organism (recently reclassified as a species of *Desulfovibrio*) which results in asymmetrical proliferation of immature epithelium, causing marked thickening of the wall. This condition is subject to periodic periods of recrudescence, often during times of stress. If untreated, it may be fatal.

Gross lesions. There is noticeable thickening of the colonic wall, which becomes opaque (normally you can see fecal material through the colonic wall).. The mucosa is prominently "cobblestoned."

Microscopic lesions. The mucosa is multifocally thickened up to five times normal by a proliferation of immature epithelial cells with vesicular nuclei and a moderate amount of basophilic cytoplasm Scattered islands of normal goblet cell may be present, but there is an overall marked decrease in goblet cells. Silver stains will demonstrate the presence of the bacteria in the apical cytoplasm of epithelial cells.

Additional references:

Finkler MR. Ferret colitis. *In* Kirk RW et al. (eds.). Current Veterinary Therapy XI. Philadelphia, WB Saunders, 1992, pp. 1180-1181.

Fox JG et al. Proliferative colitis in ferrets. *AM J Vet Res* 43:858-864, 1982

Fox JG, Lawson GH. Campylobacter-like omega intracellular antigen in proliferative colitis of ferrets. *Lab Anim Sci* 38:34-36, 1988.

Fox JG et al. Proliferative colitis in ferrets: Epithelial dysplasia and translocation. *Vet Pathol* 26:5150517, 1989.

Fox JG et al. Intracellular Campylobacter-like organism from ferrets and hamsters with proliferative bowel disease is a Desulfovibrio sp. *J Clin Microbiol* 32:1229-1237, 1994.

Krueger KL et al. Treatment of proliferative colitis in ferrets. *JAVMA* 194:1435-1436, 1989.

Intestinal parasites

Synopsis. With the exception of coccidia, intestinal parasites are uncommon in ferrets. *Toxocara cati, Toxascaris leonina, Ancylostoma* sp., *Dipylidium caninum, and Giardia* sp. have all been reported in ferrets. Three species of coccidia have been seen in ferrets: *Eimeria furo, Eimeria ictidea,* and *Isospora laidlawii.* While most coccidial infections are subclinical, lethal coccidial infections are occasionally seen in young kits. Ferrets have been experimentally infected with a number of intestinal parasites, including *Strongyloides stercoralis.*

Gross lesions. Generally none, although digested blood may be present in the GI tract of kits severely affected with coccidial infections.

Microscopic lesions. Numbers of parasites range from very low to extremely high in severe infections where almost every enterocyte contains merozoites. All stages of the parasite, including micro- and macrogametocytes can be seen. Meronts contain up to 16 merozoites. Coccidial infections have also been seen in the hepatobiliary system.

Abe N et al. Zoonotic genotype of *Giardia intestinalis* detected in a ferret. *J Parasitol* 2005 Feb;91(1):179-82.

Bell, JA. Parasites of domesticated pet ferrets. *Comp Cont Educ Pract Vet* 16(5):617-622, 1994.

Williams, BH et al. Biliary coccidiosis in a ferret (Mustela putorius furo). *Vet Pathol* 33(4):437-439, 1996.

Epizootic catarrhal enteritis

Synopsis. ECE is a coronaviral disease of ferrets which causes epizootics of high morbidity (up to 100%), but low mortality. The ferret enteric coronavirus (FECV) is a novel group A coronavirus based on phylogenetic analysis of partial amino acid sequences of the polymerase, spike, and membrane proteins, and full sequence of the nucleocapsid protein. The diarrhea is rapidly dehydrating and most mortalities occur in older animals with concurrent illness. Symptoms include vomiting and passage of a dark green stool with abundant mucus. During the recovery phase, stools assume a "birdseed" like appearance.

Gross lesions. Generally none. The intestine may be flaccid with a moderate amount of watery ingesta.

Microscopic lesions. Sections should be taken from 3-4 different areas of the jejunum, as well as the remainder of the gastrointestinal tract. Early lesions include vacuolar degeneration and necrosis of apical enterocytes, with resultant marked villar atrophy, fusion and blunting. Later in the course of disease, there is a marked lymphocytic enteritis with large numbers of lymphocytes among mucosal epithelial cells.

Additional references:

Williams BH, Kiupel M, West KH, Raymond JT, Grant CK, Glickman LT: Coronavirus-associated epizootic catarrhal enteritis in ferrets. J Am Vet Med Assoc 217(4):526-30, 2000

Wise AG, Kiupel M, Maes RK. Molecular characterization of a novel coronavirus associated with epizootic catarrhal enteritis (ECE) in ferrets. Virology. 2006 May 25;349(1):164-74.

Rotavirus

Synopsis: Rotaviruses are occasionally seen in ferrets, but only cause significant disease isn kits less than 3 weeks of age. Rotaviruses infecting ferrets are considered to be in the “atypical” group of rotaviruses, probably group C rotaviruses. “Atypical” rotaviruses have not been cultivated successfully in cell culture. Enzootic infections are commonly seen at large commercial ferretries. A 1983 outbreak in Finland killed thousands of ferret kits.

Gross lesions. Lesions are limited to the gastrointestinal tract, wth yellow-green liquid feces distending the colon. Fecal soilin may be seen in affected kits.

Microscopic lesions: Lesions are limited to valuolation and necrosis of villar tip enterocytes and mild villar atrophy. Fuchsin-positive inclusions have been reported.

Additional references:

Torres-Medina A. Isolation of an atypical rotavirus causing diarrhea in neonatal ferrets. *Lab Anim Sci* Apr 1987 37(2): 167-171.

Gastrointestinal foreign bodies

Synopsis. Gastrointestinal foreign bodies are commonly seen in young or bored, cage-bound ferrets. Ferrets commonly ingest latex, plastic, and foam rubber. Ferrets may also ingest towels or other forms of bedding. Anorexia and passage of abnormal stools are common presenting signs; abdominal pain is not commonly seen.

Gross lesions. A focal area of intestinal distention with or without hemorrhage may be seen. In many cases, the wall of the intestine at the site of the blockage is thinner than that of the adjacent intestine due to continuous peristaltic movements at the site of blockage. Intestinal perforation may rarely be seen.

Microscopic lesions. Ulceration, necrosis and thinning of the muscular layers at the site of blockage. Marked attenuation of villi and granulation tissue may be seen in longstanding blockages.

Additional references.

Mullen HS et al. Gastrointestinal foreign body in ferrets: 25 cases (1986-1990) *J Amer Anim Hosp Assoc* 28:13-19, 1992.

Clostridium perfringens

Synopsis. Clostridium perfringens type A has been reported in black-footed ferret kits.

Gross lesions: Gastric bloat, multifocal intestinal hemorrhage.

Microscopic lesions. Typical of clostridial infections. Marked coagulative necrosis of the intestinal mucosa with numerous adherent 2X6-8 um bacilli.

Additional references.

Schulman FY et al. Gastroenteritis associated with Clostridium perfringens type A in black-footed ferrets (Mustela nigripes). *Vet Pathol* 30:308-310, 1993.

Mycobacterium avium-intracellulare

Synopsis: This is a rare condition in ferrets which is most commonly seen in the gastrointestinal tract and mesenteric lymph nodes, although accumulation of macrophages containing the organism may be seen in any organ.

Gross lesions. Mesenteric lymphadenopathy is the most common gross lesion.

Microscopic lesion. The presence of large foamy macrophages with a grayish granular cytoplasm are suggestive of this disease - acid-fast stains reveal numerous bacilli within macrophages.

Additional references.

Saunders GK, Thomsen BV: Lymphoma and Mycobacterium avium infectioun in a ferret (Mustela putorius furo). *J. Vet Diag Invest* 18(5): 513-515.

Schultheiss PC, Dolginow SZ. Granulomatous enteritis caused by *Mycobacterium avium* in a ferret. *JAVMA* 204:1217-1218, 1994.

Neoplasia

Synopsis. The most common gastrointestinal neoplasm is, as in several other organ systems, lymphosarcoma. The lymphoblastic form of lymphosarcoma is the most common form in the intestine. (See hematopoietic system for a more detailed description of this condition.) The first KIT-positive gastrointestinal stromal tumor was reported in 2009.

Additional references.

Fox JG, et al. Helicobacter mustelae-associated gastric adenocarcinoma in ferrets (Mustela putorius furo). Vet Pathol. 1997 May; 34(3): 225-229.

Girard-Luc A, Prata D, Huet H, Lagadic M, Bernex F.A KIT-positive gastrointestinal stromal tumor in a ferret (Mustela putorius furo). J Vet Diagn Invest. 2009 Nov;21(6):915-7.

Endocrine System

Islet cell tumors

Islet cell neoplasms are the most common neoplasm of this species. These neoplasms generally result in hypoglycemia as a result of inappropriate secretion of insulin. Clinical signs include lethargy, stupor, ptyalism, and ataxia, and may progress to coma and death. Non-functional islet cell tumors are commonly seen in older animals at necropsy. While all islet cell tumors are potentially malignant, metastasis is rare, as opposed to islet cell neoplasms in the dog and cat.

Gross lesions. Islet cell tumors are reddish-brown, well-defined nodules which range in size from 2mm-1 cm. They are firmer than the surrounding pancreatic tissue and may be multiple. These neoplasms must be differentiated grossly from foci of pancreatic exocrine hyperplasia, a common benign age-related finding. (Foci of exocrine hyperplasia are generally the same color and consistency of the surrounding tissue, and may be numerous). Small reddish brown nodules may also be present in the mesentery adjacent to the pancreas.

Microscopic lesions. Similar to islet cell neoplasms in other species. These tumors are most commonly unencapsulated, and resemble normal, albeit greatly enlarged islets of Langerhans. Identical foci may be present in the surrounding mesentery. Metastasis to visceral organs is rare. These neoplasms stain strongly for insulin with scattered glucagon staining.

Additional references.

Andrews GA, et al. Immunohistochemistry of pancreatic islet cell tumors in the ferret (Mustela putorius furo). Vet Pathol. 1997 Sep; 34(5): 387-393.

Caplan ER, et al. Diagnosis and treatment of insulin-secreting pancreatic islet cell tumors in ferrets: 57 cases (1986-1994). J Am Vet Med Assoc. 1996 Nov 15; 209(10): 1741-1745.

Chen S. Pancreatic endocrinopathies in ferrets. *Vet Clin N Am Exot Anim Pract* 2008 Jan 11(1): 107-123.

Lloyd CG, Lewis WG.Two cases of pancreatic neoplasia in British ferrets (Mustela putorius furo). J Small Anim Pract. 2004 Nov;45(11):558-62

Marini RP et al. Functional islet cell tumor in six ferrets. *JAVMA* 202:430-433, 1993.

Weiss CA et al. Insulinoma in the ferret: clinical findings and treatment comparison of 66 cases. *JAAHA* 34(6):471-475, 1998.

Adrenal-associated endocrinopathy

Synopsis. AAE is a common endocrine disorder of middle aged to older ferrets. The syndrome is the result of proliferative lesions in the adrenal cortex which secrete excess amounts of estrogenic hormones. As a result of this excess estrogens, affected ferrets exhibit a range of cutaneous, behavioral, and reproductive signs. While technically a form of hyperadrenocorticism, AAE should not be confused with Cushing's disease, or hypercortisolism. Only rarely are cortisol levels elevated in these patients. Interestingly, unlike dogs and cats, metastasis occurs extremely late in the course of disease with adrenocortical carcinoma, and early removal of affected adrenals carries a fair prognosis. A 2008 report states that type of neoplasm, left vs. right adrenal gland, or

complete versus partial removal had no effect on survival time. Recently, cutaneous neoplasms with histologic and immunohistochemical features of adrenocortical tumors have been identified in the skin of unrelated animals; however the significance of these tumors has yet to be clarified.

Gross lesions. Bilaterally symmetrical alopecia beginning over the tailhead and progressing forwards over the flanks and abdomen is strongly suggestive of AAE. Additionally, the presence of an enlarged vulva in a spayed female also strongly suggests AAE. These clinical signs may be the result of any of the three types of proliferative adrenocortical lesions - hyperplasia, adenoma, or carcinoma. The normal length of the ferrets adrenal gland ranges from 3-5 mm; glands exceeding 5 mm often contain proliferative lesions. Diameters exceeding 1 cm is highly suggestive of adrenocortical carcinoma in the ferret.

Microscopic lesions. Proliferative lesions of the ferret adrenal cortex fall into three categories - hyperplasia, adenoma, and carcinoma. In a recent retrospective of 104 proliferative adrenocortical lesions archived at the AFIP, hyperplasia and carcinoma were present in 45% of cases each, while adenoma was present in 10%. The presence of necrosis, cellular atypia, and a mitotic rate greater than 1/10 hpf are strong indicators of malignancy. The presence of a single nodule in the adrenal cortex without factors associated with malignancy indicates adenoma, while the presence of multiple nodules is evidence of nodular cortical hyperplasia. Many neoplasms have a prominent spindle cell component which is primarily a proliferation of smooth muscle and has no prognostic significance. Extracapsular extension of proliferative cortical tissue may be seen in all three lesions, and does not occur indicate one lesion over another. Anaplastic carcinomas with large lakes of mucin have been identified as a distinct variant (2003) and are considered to be an aggressive form with the highest metastatic potential. A recent article (Protain et al.) suggests that an increased level of cornified preputial epithelial cells may be identified cytologically in male ferrets with increased levels of hydroxyprogesterone, but not with androsteniadone or estrogen.

Additional references:

Bielinska M, Kiiveri S, Parviainen H, Mannisto S, Heikinheimo M, Wilson DB. Gonadectomy-induced adrenocortical neoplasia in the domestic ferret (Mustela putorius furo) and laboratory mouse. Vet Pathol. 2006 Mar;43(2):97-117.

Bielinska M et al. Review paper: origin and molecular pathology of adrenocortical neoplasms. Vet Pathol. 2009 Mar;46(2):194-210.

Gliatto JM et al. A light microscopical, ultrastructural and immunohistochemical study of spindle-cell adrenocortical tumors of ferrets. J Comp Pathol 113(2) 175-183, 1995

Gould WJ et al. Evaluation of urinary cortisol:creatinine ratios for the diagnosis of hyperadrenocorticism associated with adrenal gland tumors in ferrets. *JAVMA* 206:42-46, 1995.

Neuwirth L, et al. Adrenal ultrasonography correlated with histopathology in ferrets. Vet Radiol Ultrasound. 1997 Jan; 38(1): 69-74.

Peterson RA 2nd, Kiupel M, Capen CC. Adrenal cortical carcinomas with myxoid differentiation in the domestic ferret (Mustela putorius furo). Vet Pathol.;40(2):136-42, 2003.

Peterson RA 2nd, Kiupel M, Bielinska M, Kiiveri S, Heikinheimo M, Capen CC, Wilson DB. Transcription factor GATA-4 is a marker of anaplasia in adrenocortical neoplasms of the domestic ferret (Mustela putorius furo). Vet Pathol. 2004 Jul;41(4):446-9.

Protain HJ et al. Assessment of cytologic evaluation of preputial epithelial cells as a diagnostic test for detection of adrenocortical disease in castrated ferrets. Am J Vet Res. 2009 May;70(5):619-23.

Ramer JC et al. Effects of melatonin administration on the clinical course of adrenocortical disease in domestic ferrets. *J Am Vet Med Assoc* 2006 Dec 229(11) 1743-1748.

Rosenthal KL: Hyperadrenocorticism associated with adrenocortical tumor or nodular hyperplasia in ferrets: 50 cases (1987-1991). *JAVMA* 203:271-275, 1993.

Rosenthal KL et al. Questions about assays used for estradiol 1-17 beta (letter). *JAVMA* 204:1001-1002, 1994.

Simone-Frielicher, E. Adrenal gland disease in ferrets. Vet Clin North Am Small Anim Pract. 2008 Jan, 11(1): 125-137.

Scott DW et al. Figurate erythema resembling erythema annulare centrifugum in a ferret with adrenocortical adenocarcinoma-associated alopecia. *Vet Dermatol* 5:111-115, 1994.

Smith M et al. Subcutaneous neoplasms of the ventral abdomen with features of adrenocortical tumors in two ferrets. *Vet Pathol* 2007 Nov 44(6): 951-955.

Swiderski JK et al. Long-term outcome of domestic ferrets treated surgically for hyperadrenocorticism: 130 cases (1996-2004)

Wagner RA, Dorn DP. Evaluation of serum estradiol concentrations in alopecic ferrets with adrenal gland tumors. *JAVMA* 205:703-707, 1994.

Weiss CA, et al. Clinical aspects and surgical treatment of hyperadrenocorticism in the domestic ferret: 94 cases (1994-1996). *J Am Anim Hosp Assoc*. 1997 Nov; 33(6): 487-493.

Wheler CL, et al. Ferret adrenal-associated endocrinopathy. *Can Vet J*. 1998 Mar; 39(3): 175-176.

Diabetes mellitus

Synopsis. Diabetes mellitus, is a poorly-defined, uncommon disease which has been reported in both the domestic and the black-footed ferret. Blood glucose levels in affected ferrets generally range into the 500's, but levels as high as 725 g/dl have been reported. Polydipsia, polyuria, glucosuria, and loss of body condition have been reported in affected ferrets.

Gross lesions. None.

Microscopic lesions. Glycogenic vacuolation of the islets of Langerhans is the most consistent and noteworthy histologic lesion. Glycogen accumulation may also be seen in renal tubular epithelium. In several cases in the AFIP archive, lenticular cataracts have been noted.

Additional references:

Benoit-Biancamano MO, Morin M, Langlois I. Histopathologic lesions of diabetes mellitus in a domestic ferret. *Can Vet J*. 2005 Oct;46(10):895-7.

Chen S. Pancreatic endocrinopathies in ferrets. *Vet Clin N Am Exot Anim Pract* 2008 Jan 11(1): 107-123.

Thyroid Disease

Synopsis. Thyroid abnormalities are extremely rare in the ferret. One case of thyroid adenocarcinoma has been documented in the ferret. In over 2500 cases on archive in the Registry of Veterinary Pathology at the AFIP, not one thyroid lesion has been catalogued.

A single case report of pseudohypoparathyroidism has been published (2003). The disease manifested initially as a seizure disorder, and lab tests showed low serum calcium, high serum phosphorus, and extremely high serum parathyroid hormone concentrations. The animal improved after treatment with dihydrotachysterol, a Vitamin D analog.

Additional references:

Heard, DJ et al. Thyroid and adrenal function tests in adult male ferrets. AJVR 51(1):32-35, 1990.

Wills TB et al. Thyroid follicular adenocarcinoma in a ferret. *Vet Clin Pathol* 2005 Dec;34(4):405-8.

Wilson GH, Greene CE, Greenacre CB: Suspected pseudohypoparathyroidism in a domestic ferret. J Am Vet Med Assoc.: 222(8):1093-6, 2003

Hematolymphatic System

Splenomegaly

Synopsis. The cause of this extremely common finding in ferrets is yet unknown; many theories abound. This condition is most commonly seen in middle-aged to older ferrets, but may be seen in ferrets as young as six

months. As the incidence of neoplasia in enlarged spleens is somewhat less than 10%, this change most likely represents a response to chronic inflammatory disease (Bruce Williams, personal opinion). The previously reported syndrome of hypersplenism in a ferret is most likely not a distinct entity in this species. Marked enlargement of the spleen for any reason increases the spleen's phagocytic capability, resulting in increased RBC breakdown. Additionally, anemia of chronic disease may complicate many cases of splenomegaly. Lymphosarcoma is by far the most common splenic neoplasm, with hemangiosarcoma being rarely seen.

Gross lesions. Enlarged spleens may range up to 10 cm. in length. While most spleens are diffusely enlarged, a small percentage of spleens will contain single or multiple discrete nodules, which are more likely to represent splenic neoplasms.

Microscopic lesions. 95% of cases consist of a combination of marked congestion and extramedullary hematopoiesis, representing erythrocytic, leukocytic, and megakaryocytic lines. Florid EMH may resemble lymphosarcoma in that a large percentage of the cells within the red pulp may have a markedly increased nuclear/cytoplasmic ratio and a high mitotic rate, but represent the immature forms of the various cell lines. The marked variation in cell size, and the presence of islands of erythrocytic precursors and megakaryocytes contrasts well with the monomorphic population of cells seen in most cases of lymphosarcoma.

Large areas of coagulative necrosis, often bordered by a combination of viable and degenerate neutrophils and various amounts of granulation tissue may be seen in grossly enlarged spleens. As enlarged spleens are prone to rupture, various signs of splenic trauma, including hematoma, siderotic plaques, and large areas of parenchymal fibrosis are commonly seen.

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Ferguson DC. Idiopathic hypersplenism in a ferret. *JAVMA* 186:693-695, 1985.

Lymphosarcoma

Synopsis. Lymphosarcoma is the most common malignancy in the domestic ferret. These neoplasms most commonly arise spontaneously, however, a recent article documents horizontal transmission of malignant lymphoma in ferrets using cell or cell-free inoculum. This finding, coupled with the occasionally clustering of lymphomas in a single facility, has prompted speculation that lymphosarcoma in the ferret may be the result of a retroviral infection. A viral agent has not, as of yet, been isolated from cases of lymphosarcoma in the ferret.

Several variants of lymphoma exist in the ferret. The most commonly seen form, in which the neoplastic cell is a mature, well-differentiated lymphocyte occurs in older ferrets, primarily resulting in peripheral lymphadenopathy, with visceral spread and subsequent organ failure late in the course of disease. A second form occurs primarily in young ferrets less than two years of age. This form, in which the neoplastic cell is a large blastic lymphocyte, is characterized by early visceral neoplasms, often with the production of a large thymic mass. An enlarging thymic neoplasm often results in compression of the lung lobes, dyspnea, and pleural effusion, and may often be misdiagnosed as pneumonia or heart disease by veterinarians with little experience in this species. A third, uncommon form, in which combinations of peripheral lymphadenopathy and visceral neoplasms and numerous bizarre lymphoblasts may be seen, is known as the immunoblastic polymorphous variant.

Gross lesions. Adult (lymphocytic) form - diffuse lymphadenopathy. Splenic white pulp may be greatly expanded and grossly visible on cut section. In later stages, firm white nodules may be seen in a number of visceral organs, including the liver and kidney, and the spleen may be diffuse enlarged. Juvenile (lymphoblastic) form - The presence of a thymic mass is strongly suggestive of this condition. Diffuse hepatosplenomegaly is often seen due to massive infiltration of these organs also. Neoplastic cells may be seen in any organ, including the bone marrow.

Microscopic lesions. In the adult form, biopsy of lymph nodes reveals diffuse effacement of the normal architecture by an infiltrate of small non-cleaved lymphocytes which breach the capsule and extend into the surrounding tissue. (However, extension into surrounding tissue may also be seen in cortical hyperplasia of the mesenteric nodes due to the attenuated and occasionally absent capsule seen in these nodes.) The mesenteric lymph nodes have been reported to be the most common site; however, this diagnosis may be difficult due to the routine presence of marked hyperplasia in these nodes. The presence of tingible body macrophages scattered throughout the node ("starry-sky" effect) is commonly seen in this form. In the liver, neoplastic infiltrates are primarily seen

extending from portal areas, which in the spleen, the earliest sign of lymphosarcoma is an expansion of the well-differentiated lymphocytes in the mantle of the periarteriolar lymphoid sheaths. Mitotic rates generally average 1-2/hpf. In a recent article, 21/23 cases of the adult form could be diagnosed by cytology.

In the juvenile form, examination of infiltrated organs often reveals effacement of normal architecture by a monomorphic population of large cleaved and non-cleaved lymphoblasts, which may be admixed with smaller, more well-differentiated cells. In the liver, neoplastic cells are more commonly seen as discrete nodules distending sinusoids and replacing hepatocytes, while in the spleen, the periarteriolar lymphoid sheath is totally replaced and expanded by a monomorphic lymphoblast population. Discrete nodules of blastic lymphocytes may be seen in any visceral organ; infiltration of lymph nodes is a late finding. The mitotic rate of the lymphoblastic cells is generally high, ranging up to 6/hpf. A recent immunophenotypic characterization of thymic lymphomas of young ferrets revealed that 9/10 were C3+ (T cell origin) and 1/10 was CD 79+ (B cell origin).

Finally, the distribution of the immunoblastic polymorphous variant resembles that of the lymphocytic form. However, scattered through infiltrated nodes is a subpopulation of atypical large cleaved, often multinucleate lymphocytes which may range up to 50 or 60 um in diameter. Occasionally, Reed-Sternberg-like cells may be present, and this form has been referred to as “Hodgkin-like lymphoma” in a recent article. Bizarre-looking lymphocytes in this condition may be misinterpreted as megakaryocytes, however, use of immunohistochemical techniques such as Factor VII antigen, CD3 and BLA-36 (a lymphocyte marker) may be used to distinguish between the two cell lines in the spleen and bone marrow. The mitotic index in this form of lymphoma is also high. In this form, the presence of only a single affected lymph node has also been reported.

A common request for pathologists working with ferrets is evaluation of splenic aspirates from animals with enlarged spleens. This task is fraught with pitfalls. As a general rule: extramedullary hematopoiesis will be seen in the VAST majority of cases. Evidence of erythrocytic precursors and abundant peripheral blood should lead the prudent pathologist to a diagnosis of EMH. Cases of splenic lymphosarcoma may be identified on splenic cytology by the presence of a monomorphic population of cells with large nuclei, prominent nucleoli, an absence of erythrocytic precursors, and minimal blood elements. Additionally, mitotic figures should be present.

Additional references.

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Boone, LI et al. Large granular lymphocyte leukemia in a ferret. *Vet Clin Pathol* 24(1) 6-10, 1995.

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Erdman, SE et al. Clinical and pathologic findings in ferrets with lymphoma: 60 cases (1982-1994). JAVMA 208(8): 1285-1289, 1996.

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Li X, et al. Cutaneous lymphoma in a ferret (Mustela putorius furo). *Vet Pathol* 32:55-56, 1995.

Rosenbaum MR, et al. Cutaneous epitheliotropic lymphoma in a ferret. *J Am Vet Med Assoc.* 1996 Oct 15; 209(8): 1441-1444.

Aleutian Disease

Synopsis. Aleutian disease is caused by the same parvovirus that causes Aleutian disease in mink; however, the disease is quite different between these two species. In mink, AD results in rapidly life-threatening immune- mediated glomerulonephritis, vasculitis, and hypergammaglobulinemia. In ferrets, there are notable similarities, including a hypergammaglobulinemia, and in late stages of the disease, an immune complex glomerulonephritis; however, the disease is much more insidious, with a progression of as long as 2 years. Ferrets in the late stages of disease will be hyperproteinemic (8-9 mg/dl, with >20% of this total being comprised of

gammaglobulins. Serologic testing is available through United Vaccines (Madison, WI) or the Research Animal Diagnostic Laboratory in the Department of Comparative Medicine, Massachusetts Institute of Technology.

Gross lesions. Gross lesions are seen only late in the course of disease. Splenomegaly and lymphadenopathy are the most common gross lesions with this disease; splenic infarction as a result of marked splenomegaly may complicate the clinical and pathologic picture.. Enlarged, brown-tan kidneys may be present. In terminal cases, clotting abnormalities resulting from vasculitis and the marked hypergammaglobulinemia may result in petechial hemorrhage and hematuria.

Microscopic lesions. Several characteristic microscopic findings are seen in ferret AD as well as in the mink disease. Prominent plasmacytic infiltrates are seen in numerous organs, most prominently in the renal interstitium, hepatic portal areas, and in the splenic red pulp, where an almost pure population of plasma cells expands the red pulp. Additionally, there may be marked plasmacytosis of numerous lymph nodes and the bone marrow.. In most cases, there will be marked membranous glomerulonephritis and numerous ectatic protein-filled tubules as a result. (Note: Glomerulosclerosis is commonly seen in chronic interstitial nephritis in this species - but there is little evidence of tubular protein casts or plasmacytic infiltrate in uncomplicated CIN). Vasculitis may be seen in almost any organ.

Additional references:

Alexandersen S et al. Acute interstitial pneumonia in mink kits inoculated with defined isolates of Aleutian mink disease parvovirus. *Vet Pathol* 31:216-228, 1994.

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Wolfensohn SE, Lloyd MH. Aleutian disease in laboratory ferrets (letter). *Vet Rec* 134:1001, 1995.

Coronavirus-Associated Granulomatous Disease

Synopsis. In 2006, a group of European pathologist published the irst report of a novel granulomoatus disease in ferrets resembling the dry form of feline infectious peritonitis, and their identification of Group A coronaviral antigen within the lesion. Subsequent investigations in the United States have identified that the antigen is of the ferret coronovairus known to cause epizootic catarrhal enteritis, as well as identifying coronaviral particles in macrophages from affected ferrets.

Gross lesions: The disease grossly resembles the dry form of feline infectious peritonitis, with non-caseating granulomas affecting the mesentery, peritonitis, and a variety of abdominal and less commonly thoracic organs.

Microscopic lesions: Areas of granulomatous inflammation are composed primarily of histiocytes with lesser numbers of lymphocytes and plasma cells and rare multinucleate giant cells. The arrangement of inflammatory lesions are not overtly vascular in origin. Innumohistochemistry for Group A coronavirus will be multifocally and weakly positive throughout the lesion. Affected animals may show mild anemia, thrombocytopenia, and hypergamaglobulinemia as a clinically diagnostic feature.

Additional references:

Garner MM: Clinicopathologic features of a systemic coronavirus-associated disease resembling feline infectious peritonitis in the domestic ferret (Muatela putorius) *Vet Pathol* 2008 March, 45(2): 236-246.

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J. Martinez et al. Identification of group 1 coronavirus antigen in multisystemic granulomatous lesions in ferrets (Mustela putorius furo.) *J Comp Path* (138(1): 54-58, 2008.

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Urinary System

Bacterial Urinary Tract Infections

Synopsis. Bacterial urinary tract infections are commonly seen in female ferrets, and uncommonly seen in male ferrets. The most common causative agent in the ferret is *E. coli*, with *Staphylococcus aureus* being isolated out of a significant number of cases. Bladder infections are often subclinical in female ferrets, and ascending infections resulting in pyelonephritis are not uncommon. Renal failure may result from severe pyelonephritis in this species.

Gross lesions. Often none. Hydronephrosis and hydroureter may be present in long-standing or resolved infections.

Microscopic lesions. Ulcerative cystitis and/or a suppurative tubulointerstitial nephritis. Bacteria are rarely seen.

Prostatic Squamous Metaplasia

Synopsis. Squamous metaplasia of the prostate has only recently been recognized as a common cause of dysuria and urethral blockage in the ferret. The squamous change in the prostate is the result of excess estrogens liberated from proliferative adrenal lesions (see adrenal-associated endocrinopathy, above). Accumulation of secretory material and lamellated keratin results in the formation of multiple prostatic cysts. Impingement of the prostatic cysts upon the prostatic urethra results in dysuria, and finally complete urinary blockage in male ferrets. The bladder of blocked ferrets may be manually expressed, but ferrets cannot void on their own. In earlier literature, due to the close association with the bladder, the condition was referred to as the "triple bladder syndrome". Surgery is directed toward removal of prostatic cysts and the affected adrenal.

Gross lesions. Single to multiple, variably-sized fluctuant cysts are present near the bladder trigone. The cysts are thick-walled, and firm on palpation. Identification of an enlarged adrenal gland or an adrenal neoplasm is often possible in these animals.

Microscopic lesions. Multiple cysts or fragments of cysts are often available for examination. Atrophic prostate glands (as a result of the effects of circulating estrogens) are often present at the periphery of the cysts, although in advanced cases, they may be lined by squamous, rather than glandular epithelium). The wall consists of multiple layers of squamous epithelium, surrounded by variable amounts of immature fibrous connective tissue. The lumenal contents of the cyst may vary from lamellated keratin and keratin debris, to abundant purulent inflammation (in which case there is often a combination of chronic-active inflammation and granulation tissue in the cyst wall and prostate (overeager manual expression of the bladder?).

Additional references:

Coleman GD et al. Cystic prostatic disease associated with adrenocortical lesions in the ferret (Mustela putorius furo). Vet Pathol, 35(6):547-549, 1998.

Nolte DM, Carberry CA, Gannon KM, Boren FC: Temporary tube cystostomy as a treatment for urinary obstruction secondary to adrenal disease in four ferrets. J Am Anim Hosp Assoc. 38(6):527-32, 2002.

Urolithiasis

Synopsis. Numerous references refer to the formation of struvite uroliths in ferrets; however, the actual incidence is probably overestimated, especially in light of recent findings of prostatic squamous metaplasia. Male

ferret are more likely to develop uroliths than females; however, the syndrome has not been well characterized, and dietary influences have not been explored, although high ash cat foods are frequently blamed. Clinical signs include frequent licking of the genital area, dysuria, anuria, and occasionally, hematuria. Reportedly, pregnancy may increase the incidence of urolithiasis in pregnant jills due to the effects of estrogen on the ferret's handling of calcium and phosphorus. Cystine crystals have also been reported.

Gross lesions. Struvite uroliths often have a corrugated surface. Single or multiple uroliths may be present in the bladder, or rarely in the renal pelvis. Reports of struvite "sand" as may be seen in the feline urologic syndrome" are anecdotal.

Microscopic lesions. Similar to that seen in urolithiasis in other animals.

Additional references.

Dutton, MA. Treatment of cystine bladder urolith in a ferret (Mustela putorius furo). *Exotic Pet Pract* 1(8):7, 1996.

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Palmore WP, Bartos KD. Food intake and struvite crystalluria in ferrets. *Vet Res Commun* 11:519-526, 1987.

Renal Cysts

Synopsis. Renal cysts are common incidental findings in the ferret. Although often submitted for histologic evaluation, they are of little clinical significance and have no effect on renal function. Rare cases of true polycystic disease may be seen in this species. Polycystic kidneys are enlarged, may be felt on external palpation, and may cause renal failure.

Gross lesions. Single or multiple cysts may be present in the cortex of one or both kidneys. When viewed from the capsular surface, they are thin, bulge slightly, and are fluid filled. Cysts may range up to 1 centimeter in diameter. Polycystic kidneys may be markedly enlarged and fill the posterior abdomen. They are composed of variable numbers of cysts with little intervening fibrous connective tissue.

Microscopic lesions. In benign cysts, there may be little or no fibrosis surrounding the cyst, or the cyst may have a thick wall of fibrous connective tissue throughout which are scattered numerous atrophic glomeruli and tubules. In a reported case of polycystic disease in a ferret, the kidney contained multiple fluid-filled cysts in both the cortex and medulla which were lined by cuboidal epithelium. The cysts were separated by abundant fibrous connective tissue which contained moderate numbers of lymphocytes.

Additional references.

Dillberger JE. Polycystic kidneys in a ferret. *JAVMA* 186:74, 1985.

Jackson CN et al. Cystic renal disease in the domestic ferret**.** Comp Med. 2008 Apr;58(2):161-7

Chronic Interstitial Nephritis

Synopsis. Chronic interstitial nephritis is a common finding in ferrets. Early lesions can be seen as early as 2 years, and advanced cases resulting in renal failure may occur as early as 4.5 years. The progression of the disease is most akin to that seen in older cats. Ferrets are generally maintained on a high protein diet with protein levels in excess of 34%. This is generally accomplished by feeding premium kitten chows or specially formulated ferret chows. Due to the prevalence of chronic interstitial nephritis in older ferrets, lowering of protein levels after three years of age is reached is generally advocated by most practitioners.

Gross lesions. Kidneys are generally pitted and large focal depressions may be seen in the outer cortex as a result of scarring. "Peeling" the renal capsule is recommended during the ferret necropsy. Severely affected kidneys may be asymmetric with respect to size.

Microscopic lesions. The pattern of microscopic changes associated with chronic interstitial nephritis in the ferret is unique. At low magnification, there are linear bands of fibrosis which extend from the capsule inward. Glomerular and tubular changes are most commonly seen in these areas of fibrosis. There is periglomerular and glomerular fibrosis resulting in glomerulosclerosis. The interstitium is expanded by fibrous connective tissue throughout which is scattered moderate numbers of lymphocytes and plasma cells. Tubules within these radiating streaks of fibrosis exhibit variable degrees of atrophy. Pathologists with little experience with ferret tissues may be tempted to diagnose chronic infarction. As the disease progresses, there is a diffuse glomerulosclerosis throughout the cortex, as glomeruli outside of the areas of interstitial fibrosis are affected. Areas of fibrosis tend to coalesce into large areas devoid of functional glomeruli and tubules.

Reproductive System

Estrus-associated Aplastic Anemia

Synopsis. Ferrets are induced ovulators - intact females remain in estrus until mated, spayed, or are cycled out by injections of human chorionic gonadotropin. 50% of unmated jills will develop marked bone marrow suppression as a result of high levels of circulating estrogens. All three bone marrow cell lines are affected - erythrocytes, leukocytes, and megakaryocytes. Initially, there is a mild thrombocytosis and leukocytosis, but the condition soon progresses to a non-regenerative anemia, leukopenia, and thrombocytopenia. The anemia may remain non-regenerative anemia up to 4 months past ovariohysterectomy in affected animals. In addition to thrombocytopenia, a liver-associated clotting abnormality may also be present. Hemorrhage is reported to be the most common cause of death. Similar signs may be caused by exogenous estrogen administration, but are not seen in cases of adrenal-associated endocrinopathy.

Gross lesions. Female ferrets in estrus have prominently swollen vulvas. Signs of hyperestrogenism include pale mucus membranes, alopecia, melena, thin watery blood, hemorrhages throughout the body, hematuria, pyometra, bronchopneumonia, and vaginitis.

Microscopic lesions. Diagnosis of aplastic anemia is most commonly made on the combination of a low PCV (<20%) in a jill in estrus. The most characteristic lesion in affected jills is hypocellularity of the bone marrow. There is also no evidence of splenic hematopoiesis; small amounts of EMH may be seen in the liver. There may be evidence of hemorrhage (hemosiderin-laden macrophages, erythrophagocytosis) in lymph nodes and the spleen. Suppurative metritis or pneumonia may be seen as a result of the marked leukopenia.

Additional references.

Bernard SL et al. Estrogen-induced bone marrow depression in ferrets. *AJVR* 44: 657-661, 1982.

Manning D, Bell J. Lack of detectable blood groups in domestic ferrets: Implications for transfusion. *JAVMA* 197:84-86, 1990.

Mead RA et al. Optimal dose of human chorionic gonadotrophin for inducing ovulation in the ferret. *Zoo Biol* 7:263-267, 1988.

Mastitis

Synopsis. Mastitis is occasionally seen in pregnant jills in the first few weeks of lactation. Hemolytic *E. coli* is the most commonly isolated organism, and results in a syndrome of gangrenous mastitis. If untreated, jills rapidly become septic and/or endotoxemic. *Staph aureus* is occasionally cultured from cases of mastitis and produces a more suppurative, less necrotic form of mastitis.

Gross lesions. Affected teats are swollen, necrotic, black, firm, and non-painful. In *Staph aureus* mastitis, the mammary glands are hot, painful, and reddish in color; purulent exudate may be expressed from the lactiferous ducts.

Microscopic lesions. The primary lesion in *E. coli* mastitis is diffuse severe coagulative necrosis which extends into the adjacent adipose tissue and muscle. There are large pockets of hemorrhage and edema in the affected glands; numerous bacteria may be seen. Areas of infarctions are well-demarcated by a line of degenerate neutrophils and cellular debris, and vascular thrombosis may be seen. Other signs of sepsis, or endotoxemia, including margination of neutrophils in the pulmonary capillaries and hypertrophy of Kupffer cells in the hepatic sinusoids may be seen, as well as colonies of gram-negative bacilli in numerous tissues.

In staphyloccoccal mastitis, there is less evidence of infarction. A purulent galactophoritis and mastitis is present. Staphylococci are often prominent.

Additional references.

Liberson AJ et al. Mastitis caused by hemolytic *Escherichia coli* in the ferret. *JAVMA* 183:1179-1181, 1983.

Cardiovascular System

Cardiomyopathy

Synopsis. Cardiomyopathy is a common disease in the American lines of ferrets, which has a presumed genetic basis. Several forms of this condition may be seen - dilatative, hypertrophic, and a restrictive form in which there is marked replacement of myocardium by fibrous connective tissue, with minimal change in chamber area. Signs of cardiomyopathy may be seen as early as 1 year of age in severely affected animals, but are more common between 5 and 7 years of age.

Gross lesions. Gross lesions are similar to those seen in other domestic species. In subclinical cases, a congested, occasionally nodular liver may be the only gross lesion as a result of chronic passive congestion in this organ. The heart may appear enlarged, and the right ventricle may appear thin or flabby. With progressively severe cases, there is often an accumulation of a serosanguinous ascitic transudate in the abdominal cavity, the pleural cavity, or both. In severe cases, the lungs are atelectatic and compressed by the presence of a globose heart and abundant pleural effusion. In cases in which the heart is not enlarged, examination of the left ventricular free wall and the interventricular septum may reveal marked thickening and impingement upon the ventricular lumen. Rarely, the presence of fibrous connective tissue may be seen upon close inspection of the cardiac wall, and occasionally, due a previous ischemic event, a focally extensive area of the ventricular wall may be translucent and paper thin as a result of total loss of myocytes in this area ad replacement by fibrous connective tissue.

Microscopic lesions. Early lesions consist of an increase in fibrous connective tissue around myocardial vessels which extends into the interstitium. As the condition progresses, there is atrophy and loss of myocytes. Focal areas of myocyte degeneration may be present, with an infiltrate of moderate numbers of macrophages, lymphocytes, plasma cells, and rare neutrophils. In some cases of cardiomyopathy, there may be marked focal malalignment of myocytes, suggesting orientation in several different planes.

Centrilobular fibrosis, edema, micronodular hemosiderosis, and loss of subcapsular hepatocytes with resulting fibrosis all attest to chronic hepatic congestion, which is a common finding in cardiac disease in the ferret. In contrast, the presence of chronic signs of left-sided heart failure are relatively uncommon. In terminal stages of the disease, there may be necrosis of centrilobular hepatocytes due to stasis and hypoxia. The presence of marked myocardial fibrosis with or without inflammation, and evidence of chronic systemic congestion are highly suggestive of cardiomyopathy in this species.

Additional references.

Greenlee PG, Stephens E. Meningeal cryptococcosis and congestive cardiomyopathy in a ferret. *JAVMA* 184:840-841, 1984.

Lipman NS et al. Clinical, functional, and pathologic changes associated with a case of dilatative cardiomyopathy in a ferret. *Lab Anim Sci* 37:210-212, 1987.

Wagner RA. Ferret cardiology. *Vet Clin North Am Exot Anim Pract.* 2009 Jan;12(1):115-34, vii.

Dirofilariasis

Synopsis. Ferrets are also susceptible to heartworm infection, but due to the fact that most ferrets are kept indoors, cases are still uncommon. Ferrets in heartworm endemic areas are usually maintained on monthly ivermectin at approximately 0.2 mg/kg. (Note: in my experience, the vast majority of cases of dirofilariasis in ferrets come from Florida.) Due to the small size of the ferret heart, as few as two heartworms may result in fatal cardiac insufficiency. The small numbers of heartworms in these animals also necessitates the use of occult heartworm tests due to the low levels of circulating microfilaremia. A recent report of transvenous removal of adult heartworms identified biliverdinuria as a potential presenting sign.

Gross lesions. Lesions of heartworm disease in the ferret are essentially the same as cardiomyopathy (see above), as infection commonly results in heart failure in this species. Aberrant cerebral heartworm migration has been noted in this species. The presence of heartworms within the right ventricles and pulmonary artery can be construed as the cause of death in any ferret in which it is observed.

Microscopic lesions. Microscopic lesions are as expected with heart failure (see above).

Additional references.

McCall JW. Dirofilariasis in the domestic ferret. *Clin Tech Small Anim Pract* 13(2):109-112, 1998.

Moreland AF et al. Dirofilariasis in a ferret. *JAVMA* 188:864, 1986.

Bradbury C, Saunders AB, Heatley JJ, Gregory CR, Wilcox AL, Russell KE Transvenous heartwormextraction in a ferret with caval syndrome.J Am Anim Hosp Assoc. 2010 Jan-Feb;46(1):31-5.

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Respiratory System

Endogenous lipid pneumonia

Synopsis. This condition, also known as "foam cell foci" or "subpleural histiocytosis" is a common incidental finding in mustelids at necropsy and is of no clinical significance. It is often mistaken at necropsy by practitioners as a dissemination neoplasm. The cause of this finding, and the origin of the lipid, is not known.

Gross lesions. Multiple to coalescing white to yellow foci are present within the subpleural pulmonary parenchyma. A transverse cut through one of these foci will reveal its superficial nature.

Microscopic lesions. The basic lesion is simply an aggregate of lipid-laden macrophages in the alveoli immediately subjacent to the pleura. As the lesion increases in size, it may include moderate numbers of lymphocytes and cholesterol clefts.

Aspiration pneumonia

Synopsis. By far, the most common cause of pneumonia in the ferret is aspiration, either of orally administered medicants or of vomitus. Ferrets often resist liquid oral medication by fighting and squirming during administration, and often involuntarily inhale part of the medication.

Gross lesions. In cases of aspiration pneumonia, there may be consolidation of the cranioventral lung lobes, either unilaterally or bilaterally. The severity of lesions seen with aspiration of vomitus is proportionate to the length

of time since the event. In most cases, aspiration occurs as a terminal event, so minimal gross lesions are seen. In long-standing cases, gangrenous, cavitated lesions may be seen in the pulmonary parenchyma.

Microscopic findings. The primary lesion in aspiration pneumonia is in the small airways. Bronchioles contain a mixture of viable and degenerate neutrophils, sloughed epithelial cells, and variable amounts of eosinophilic proteinaceous material (which may be admixed with food particles when vomitus is aspirated). Often, there is an accumulation of foamy macrophages in the surrounding alveoli. In long-standing cases, there may be a pronounced granulomatous response, with numerous foreign body and multinucleate giant cells admixed with lymphocytes, plasma cells, and cholesterol clefts. Occasionally, you may find eosinophilic crystalline proteins within the cytoplasm of macrophages. In cases of aspiration of vomitus, the lesion is characterized by extensive necrosis of the airway and surrounding alveoli, with sloughing of the bronchiolar epithelium and coagulative necrosis of the adjacent alveolar septa. Colonies of gram-negative bacilli or mixed colonies may be seen in cases of aspiration of vomitus.

Influenza

Synopsis. Ferrets are the only domestic animal species which is susceptible to the human influenza viruses. For this reason, they are a) often used as animal models in influenza research, and b) often infected by their human owners. The disease is quite similar to that in humans, with clinical signs being photophobia, a catarrhal nasal discharge, sneezing, coughing, pyrexia, anorexia, and malaise. A 2008 report details the clinical signs and pathologic lesions associated with experimental infection of ferrets with H5N1 avian influenza.

Gross lesions. Lesions are generally minimal, with congestion and exudation of the nasal mucosa and mild reddening of the tracheal mucosa.

Microscopic lesions. There is mild subacute inflammation and occasional necrosis of the nasal mucosa. A recent article (Patterson et al.) described the microscopic lesions of patchy bronchointerstitial pneumonia with necrotizing bronchiolitis in naturally occurring type A influenza in a ferret colony.

Additional references.

Cardona CJ. Avian influenza in birds and mammals. *Comp Immunol Microbiol Infect Dis.* Epub May 14 2008. (Epub ahead of print).

Glathe, H. Enteral influenza infection of ferret. Archiv fur experimentelle Veterinarmedizin 38(5):771-777, 1984.

Patterson AR et al:Naturally occurring influenza infection in a ferret (Mustela putorius furo) colony. J Vet Diagn Invest. 2009 Jul;21(4):527-30.

Renegar KB: Influenza virus infections and immunity: A review of human and animal models. *Lab Anim Sci* 42:222-232, 1992.

Smith H, Sweet C. Lessons for human influenza from pathogenicity studies in ferrets. *Rev Infect Dis* 10:56-75, 1988.

Systemic fungal infections

Synopsis. Dimorphic fungal infections are an emerging disease in the ferret, and the disease is very similar to that seen in other species. *Blastomyces dermatititidis, Cryptococcus neoforomans, Cryptococcus gatti, and Histoplasma capsulatum* have all been reported in the domestic ferret. As a general rule, these infections primarily affect the respiratory tract, expecially the lungs, but occasionally are seen as infections in multiple organs. Treatment is almost always unsuccessful.

Gross Lesions: Gross lesions include granulomas in the lung and other organs. Depending on the type of dimorphic fungi, fibrosis may or may not be present – *Blastomyces* tends to cause fibrotic lesions, while *Cryptococcus* tends to have lesions with little inflammation and a poor attempt by the body to wall off the developing granulomas.

Microscopic Lesions: Infections with dimorphic fungi are usually typical pyogranulomas or pyogranulomatous inflammation; little inflammation may be seen in some cases of cryptococcosis.

References: Eshar D, Mayer J, Parry NM, Williams-Fritze MJ, Bradway DS Disseminated, histologically confirmed Cryptococcus spp infection in a domestic ferret. J Am Vet Med Assoc. 2010 Apr 1;236(7):770-4.

Musculoskeletal System

Chordoma

Synopsis. Chordomas are the most common neoplasm of the musculoskeletal system of the ferret. They arise in or adjacent to vertebra from remnants of primitive notochord, and are most commonly seen at the tip of the tail. Chordomas have also been documented in cervical spine. Early reports mischaracterized this neoplasm as a chondrosarcoma, and this mistake is still repeated by pathologists who are unfamiliar with ferret tissue. Chordomas are considered potentially malignant, however, metastasis has not been seen in neoplasms arising in the tail. Cutaneous metastasis was reported in one chordoma from the cervical spine.

Gross lesions. Chordomas are most commonly seen as club-like swellings at the tip o the tail which involve the last caudal vertebra. Cervical chordomas present as lytic neoplasms in the neck of animals with posterior paresis. Physical exam shows a markedly decreased range of motion and pain upon movement of the neck.

Microscopic lesions. Chordomas are locally aggressive neoplasms which often infiltrate vertebral bodies. The neoplasm is composed of foamy "physaliferous cells" which are separated by a moderate amount of myxomatous matrix. There are multifocal areas of well-differentiated cartilage and bone within these neoplasms.

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Integumentary System

Ectoparasites

Synopsis. Ferrets are commonly infected with two types of ectoparasites: ear mites (*Otodectes cynotis*) and fleas (*Ctenocephalides sp.*) Most young ferrets and many older ones have clinical cases of ear mite infection which require periodic treatment. Grossly, ferrets with ear mites have copious amounts of a thick brown-black wax. However, swabs from the ears should be examined microscopically for the presence of adult mites or their eggs, as ferrets without mites may also have large accumulations of wax due to neglectful owners.

Sarcoptic mange has been reported in ferrets. This disease comes in two distinct forms in ferrets - a very pruritic whole-body form, and a variably pruritic form localized to the feet. Grossly this form is characterized by swollen feet, evident of self-mutilation, and nail loss. Histologically, the disease is similar to that in the dog, with marked ulceration and hyperkeratosis of the skin and a few cross sections of mites in the epidermis or deep under the overlying crust.

Demodectic mange is generally seen in older or immunosuppressed ferrets. Skin scrapings may demonstrate the presence of nymphs or adults. Skin biopsies reveal moderate hyperkeratosis and the presence of a few cigar-shaped mites within the hair follicles.

Additional references: Oxenham M. Flea control in ferrets. *Vet Rec* 138(15):372, 1996.

Neoplasia

Synopsis. By far, the most common skin problem in ferrets is neoplasia. The incidence of cutaneous neoplasia increases with age in this species. While there are a wide range of cutaneous neoplasms that have been documented in the ferret, the two most common types of neoplasms seen in the skin of the ferret are 1) sebaceous epithelioma and 2) mast cell tumor.

Sebaceous epitheliomas appear as warty, verrucous lesions which may arise anywhere on the animals body, but have a predilection for the head and neck. Microscopic examination reveals an unencapsulated neoplasm composed of basal cells, of which a small percentage exhibit sebaceous and or squamous differentiation. Although early reports referred to these neoplasms as "basosquamosebaceous carcinomas", they possess no features of malignancy, and evidence of metastasis has not been seen.

Mast cell tumors are also common skin tumors in ferrets. Gross, they most often appear as flat, alopecic, hyperkeratotic plaques which are variably pruritic. Microscopic examination reveals a well-demarcated, unencapsulated neoplasm which is generally confined to the superficial dermis, and is composed of well-differentiated mast cells. Low numbers of eosinophils are scattered through the neoplasm, but vasculitis and collagen degradation is hardly ever seen. Metachromatic stains such as toluidine blue or Giemsa reveal few cytoplasmic granules, so the diagnosis is primarily made (and rightly so) on the HE section.

Dermal leiomyomas/leiomyosarcomas are commonly seen in the skin of ferrets, and most commonly arise from smooth muscle associated with hair follicles (piloleimyomas). The skin of the back and neck are most commonly affected, but they may be seen anywhere on the body. These neoplasms are well encapsulated and have no metastatic potential; although cellular atypia and a moderate mitotic rate may be seen. Surgical excision is generally curative.

Vaccination-site fibrosarcomas have been recently described in the ferrets (2003). The presence of macrophages containing basophilic granular material (interpreted as vaccine material) or peripheral lymphocytic aggregates were described in these tumors and may vbe valuable in differentiating them from piloleiomyomas.

Additional references.

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Tunev SS, Wells MG: Cutaneous melanoma in a ferret (Mustela putorius furo). Vet Pathol 39(1):141-3, 2002

Dermatomycosis

Synopsis. This is an uncommon disease in ferrets, but is occasionally seen in mink. Most cases occur either in very young animals kept in poor conditions, or in older, immunosuppressed animals. Both *Microsporum canis* and *Trichophyton mentagrophytes* have been seen in ferrets.

Gross lesions. Dermatophytosis is similar to that seen in other domestic species - animals have areas of crusting alopecia with brittle hair and numerous broken hair shafts. In immunosuppressed animals, the rash can become generalized (at which time it must be differentiated from that seen with canine distemper infection).

Microscopic lesions. Biopsies from affected sites are generally covered with a thick layer of keratin debris, degenerate neutrophils, and entrapped fungal arthrospores and hyphae. There is ulceration of the skin, and follicles often contain numerous fungal arthrospores which occasionally invade the hair shaft. Many follicles may not contain

a hair shaft, only lamellar keratin debris. There is generally a neutrophilic or lymphoplasmacytic dermal infiltrate in perivascular and periadnexal areas.

Additional references:

Hagen KW et al. Dermatoycoses in fur animals: chinchila, ferret, mink, and rabbit. Vet Med Small Anim Clin 67(1): 43-48, 1972.

Miscellaneous skin disorders

1. Bacterial skin disease. Due to the nature of ferret skin, bacterial skin disease is fairly uncommon. Traumatic wounds, or poor husbandry are generally required for bacterial skin disease to occur in this species. King et al. described a case of superficial spreading pyoderma in the ferret following fire ant bites.
2. Pemphigus foliaceous. A recent submission to the AFIP (1999) for consultation of skin from a ferret with generalized eruptions revealed classic vesicular lesions consistent with pemphigus foliaceous in other species; i.e., intracorneal pustules containing rafts of acantholytic cells, a thickened epidermis, and prominent superficial lymphocytic and eosinophilic dermatitis. This disease has not been previously described in the ferret literature.

Additional references.

King, WW. Superficial spreading pyoderma and ulcerative dermatitis in a ferret. *Veterinary Dermatology* 7(1):43-47, 1996.

Special Senses

Cataracts

Synopsis. There are several reports of cataracts in individual animals and breeding colonies. While many causes have been postulated, no definitive cause has been isolated. Cases in individual animals are considered to be spontaneous. Cataractous change may also be seen in the lenses of diabetic animals, however, since the lifespan of diabetic ferrets is generally short, grossly visible cataracts generally have not formed.

Gross lesions. Cataracts in ferrets generally involve both the cortex and nucleus of the lens.

Microscopic lesions. The microscopic appearance e of cataracts in ferrets is similar to that in other domestic species, with formation of balloon cells in the outer cortex, initially, progressing toward the nucleus. Morgagnian change has not been described in ferrets.

Additional references.

Miller PE et al. Cataracts in a Laboratory Colony of Ferrets. *Lab Anim. Sci* 43:562-566, 1993.

Glaucoma

Synopsis. Glaucoma is an uncommon finding in ferrets. The diseases manifests in ferrets much as it does in other species – initial pain, blepharospasm, loss of vision, and eventually progression to bupthalmos with prolonged intraocular pressure. Most casse of glaucoma are secondary to anterior uvieitis or lens displacement. Primary glaucoma due to goniodysgenesis have been reported, but are extremely rare.

Gross lesions: Bupthalmos may be accompanied by lenticular displacement or retinal detachment.

Microscopic lesions. Evidence of intraocular inflammation, lenticular degeneration and retinal degeneration may be seen in affected animals.

Additional references.

Good KL. Ocular disorders of pet ferrets. *Vet Clin North Am Exot Anim Pract*. 2002 May;5(2):325-39.

Moniani-Ferreira F, Mattos BC, Russ HH. Reference values for selected ophthalmic diagnostic tests of the ferret (Mustela putorius furo). *Vet Ophthalmol*. 2006 Jul-Aug;9(4):209-13.

Neoplasia (other than previously described)

Synopsis. Numerous neoplasms have been described in the ferret, most of which are similar both grossly and histologically to those seen in other animals. Neoplasms easily represent up to 60% of total surgical biopsies of ferrets, with the balance being islet cell tumors, adrenal neoplasms, chordomas, and the skin tumors already mentioned. While the following is by no means an exhaustive list of the remaining, it represents those which I personally, feel are most commonly seen and most significant in this species.

Reproductive. Tumors of smooth muscle are the most common neoplasm of this system, and are also seen in the endocrine system (generally arising in the adrenal gland) and rarely in the gastrointestinal system and subcutaneous tissue. Low grade leiomyosarcomas, demonstrating an infiltrative nature, moderate atypia, and a moderate mitotic rate are more common than leiomyomas in this species. Additionally, leiomyosarcomas have been reported as occurring "free-floating" in the abdomen. As the majority of these tumors are attached to the adrenal gland, ovary, or testis, and are removed due to the organomegaly that they cause, the prognosis is generally good. Metastasis of leiomyosarcoma has not been seen.

Testicular neoplasms - Interstitial cell tumors are the most common neoplasm of the ferret testicle, but combinations of two or more neoplasms are not uncommon. (Indeed, one of my own ferrets, obtained as a 4-year-old cryptorchid had **FOUR** neoplasms in the same testicle - interstitial cell tumor, seminoma, Sertoli cell tumor, and a carcinoma of the rete testis). This illustrates the importance of removing cryptorchid testicles in this species - you can always find at least one neoplasm and often more in retained testicles.

Ovarian neoplasms - Tumors of germ cell or stromal cell origins are most commonly seen, epithelial neoplasms are rare. One teratoma has been reported.

Gastrointestinal system. The second most commonly seen neoplasm of the gastrointestinal system (after lymphosarcoma) are tumors of smooth muscle origin, arising from the muscular layers of the GI tract. Low-grade leiomyosarcomas are most commonly seen. Mesotheliomas are occasionally seen in the peritoneum and serosal surfaces of ferrets. They are locally aggressive, result in marked abdominal effusion, and warrant a poor prognosis. Pancreatic exocrine adenocarcinomas are occasionally seen in the pancreas - these neoplasms are locally aggressive with a moderate metastatic potential, most commonly to the liver. Intestinal adenocarcinomas are rare locally aggressive neoplasms Gastric carcinoma has been experimentally reproduced in the presence of *Helicobacter mustelae* with a carcinogenic compound. Primary hepatic neoplasms are uncommon in ferrets, with biliary cystadenocarcinomas being the most commonly seen. These neoplasms have a bland histologic appearance, and may be easily misdiagnosed microscopically as hepatic cysts or cystadenomas. If left to progress, they often replace large areas of hepatictissue nad may bridge to additional lobes. Hepatic carcinomas are more commonly seen than benign neoplasms and warrant a poor long-term prognosis.

Musculoskeletal system - Osteomas are generally seen arising from flat bones. They are expansile neoplasms composed of trabecular of well-differentiated bone lined by osteoblasts and a few osteoclasts. The trabeculae are wide and there is little intervening space. Marrow is not seen. Osteosarcomas are far less commonly

seen, and appear to be equally divided between long bones and flat bones. Rhabdomyosarcomas are also uncommon neoplasms of ferrets.

Integumentary system. Apocrine cysts are a common finding in ferrets. They most commonly occur around the head, neck, prepuce, and vulva, due to the large numbers of scent glands in these regions. Apocrine gland cystadenomas and carcinomas are not uncommon and have a similar distribution. Apocrine gland carcinomas are locally aggressive neoplasms with a moderate potential for metastasis. Hemangiomas and low-grade hemangiosarcomas are occasionally seen; metastasis has not been reported. Squamous cell carcinoma has been reported several times in the ferret and has a predilection for the face, where it is locally destructive with a low metastatic potential.

Urinary system. Transitional cell carcinoma and renal adenocarcinoma has been rarely reported in the ferret. Renal tubular cell neoplasms are the most common tumor in the black-foorted ferret, but rarely metastasize.

Hematolymphatic system. Cranial mediastinal thymomas were resported in 2 5-year-old ferrets and should be considered in the differential diagnosis for thoracic neoplasia.

Nervous system. One case of a granular cell tumour has been reported in the prosencephalon of a ferret, and one granular cell tumor has been submitted to the AFIP. In this case, the granular cells stained positively for glial fibrillary acidic protein, suggesting astrocytic origin.

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Jones Y, Wise A, Maes R, Kiupel M. Pelioid hepatocellular carcinoma in a domesticated ferret (Mustela putorius furo)**.** *J Vet Diagn Invest.* 2006 Mar;18(2):228-31.

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Lloyd MH, et al. Synovial sarcoma in a ferret. Vet Rec. 1996 Dec 21; 139(25): 627-628.

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Rice LE et al. Pyloric adenocarcinoma in a ferret. *JAVMA* 200:1117-1118, 1992.

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