Biology and Diseases of the Laboratory Ferret

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Who am I? Allison Rogala, DVM, DACLAM

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References
• Laboratory Animal Medicine, 3rd Edition, Edited by Fox, Anderson, Otto, Pritchett-Corning, Whary
• Biology and Diseases of the Ferret, 3rd Edition, Edited by Fox and Marini

Species Categories
Based on mean importance ratings from the Role Delineation Study. The suggested species were classified as priority, secondary, and tertiary. Refer to the table above.

<table>
<thead>
<tr>
<th>Category</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Mouse (Mus musculus)</td>
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<tr>
<td>Primary</td>
<td>Rat (Rattus norvegicus)</td>
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<tr>
<td>Primary</td>
<td>Rabbit (Oryctolagus cuniculus)</td>
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<tr>
<td>Primary</td>
<td>Macaques (Macaca spp.)</td>
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<tr>
<td>Primary</td>
<td>Dog (Canis familiaris)</td>
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<tr>
<td>Primary</td>
<td>Pig (Sus scrofa)</td>
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<tr>
<td>Secondary</td>
<td>Zebrafish (Danio rerio)</td>
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<tr>
<td>Secondary</td>
<td>African clawed frog (Xenopus laevis and Xenopus tropicalis)</td>
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<tr>
<td>Secondary</td>
<td>Cat (Felis domestica)</td>
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<tr>
<td>Secondary</td>
<td>Guinea pig (Cavia porcellus)</td>
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<tr>
<td>Secondary</td>
<td>Ferret (Mustela putorius furo)</td>
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<tr>
<td>Secondary</td>
<td>Squirrel monkey (Saimiri sciureus)</td>
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<tr>
<td>Secondary</td>
<td>Sheep (Ovis aries)</td>
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<td>Secondary</td>
<td>Syrian hamster (Mesocricetus auratus)</td>
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<td>Secondary</td>
<td>Baboon (Papio spp.)</td>
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<tr>
<td>Secondary</td>
<td>Marmoset/tamarins (Callitrichidae)</td>
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<tr>
<td>Secondary</td>
<td>Gerbil (Meriones spp.)</td>
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<td>Secondary</td>
<td>Goat (Capra hircus)</td>
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<tr>
<td>Tertiary</td>
<td>Other rodents</td>
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<tr>
<td>Tertiary</td>
<td>Chicken (Gallus domestica)</td>
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<td>Tertiary</td>
<td>Other nonhuman primates</td>
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<tr>
<td>Tertiary</td>
<td>Other mammals</td>
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<tr>
<td>Tertiary</td>
<td>Other birds</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Invertebrates</td>
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</tbody>
</table>

“what level of detail do I need to know?”

Tertiary species
Secondary species: Ferrets
Primary species
Taxonomy

- Mustelidae
  - Mustelinae is the subfamily
    - Genus Mustela (weasels, mink, ferrets)
      - 5 subgenera
        - Mustela (weasels)
        - Lutreola (European mink)
        - Vison (American mink)
        - Putorius (Ferrets)
        - Grammogale (South American Weasels)
  - Genus Martes (martens)

Other Members

- Smallest member (25g): Least weasel, Mustela nivalis
- Largest member (45kg): Sea otter, Enhydra lutris

Mustela putorius furo

- Ferrets
- “European polecat”
- Domesticated over 2000 years ago; bred for rabbiting (rabbit hunting) in North Africa
- Mustela nigripes (North American black-footed ferret) is closest relative
  - Early use in England and the US was rodent control
  - Also used for “ferret-legging” or ‘Put’em Down’

Use in Research

- Human influenza
- Reye’s syndrome
- SARS coronavirus
- Cystic fibrosis
- Helicobacter-induced GI diseases
- Neural development
- Drug induced emesis
- Visual cortex development

Use/Availability in Research

- Readily available commercially
- Coat colors include: albino, sable (fitch), Siamese, silver mitt, Siamese-silver mitt
- Fitch or wild coat color is most common
- Anecdotal from BB: 75% of US ferrets with a blaze or white head= Waardenburg syndrome & deafness
- Albino ferrets have impaired motion perception and contrast sensitivity

Laboratory Management and Husbandry

- Housing
  - Guide for the Care and Use of Laboratory Animal Housing Standard (pg 59)
  - Cat or rabbit caging widely used
  - Cages with grid floor spacing must be less than 1 inch apart.

<table>
<thead>
<tr>
<th>Weight of Animal</th>
<th>Floor Area/Animal (ft²)</th>
<th>Height (inches)</th>
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</thead>
<tbody>
<tr>
<td>&lt; 4 kg</td>
<td>3.0</td>
<td>24</td>
</tr>
<tr>
<td>&gt; 4 kg</td>
<td>4.0</td>
<td>24</td>
</tr>
</tbody>
</table>
Housing and Husbandry of Ferrets

• Question

Temperature requirements for ferrets are similar to what other lab animal species?

Housing and Husbandry of Ferrets (Answer)

• Rabbits

Temperature requirements:

61-72 F (Page 44 of the Guide)

Blue book, page 578 recommends 41-18 C (39.2-64.4 F)

Ferrets < 6 weeks should be housed at >15 C

Kits under this age required a heat source if separated from the dam

They tolerate low temperatures well and high temperatures poorly.

Temps >30 C (86 F) cannot be tolerated.

Study Table 14.1 on page 579

• WHY are they heat intolerant?

Light Cycles

• Non-breeding: 12:12h

• Lighting can be altered to control breeding cycles

• Breeding/lactating: 16h of light daily

• Breeding or long term (beyond 6 months):
  • "winter light"
  • 6 weeks of year
  • 14h of DARK

• Help maintain physiologic normalcy

Air Circulation

• 10-15 air changes per hour

• Use non-recirculated air:
  • Strong ferret odor
  • Susceptibility of ferrets to human respiratory infections
  • DO NOT overlap with rodents
  • Rodents instinctive fear of ferrets
  • Ferret scent can disrupt breeding & physiology

Ferret Caging

• Females may be single or co-housed but may become pseudopregnant

• Males >12 weeks should be single housed

• Enrichment program:
  • Co-housing
  • Nesting material
  • Extra paper for hiding
Ferret Caging

- Considerations of metal caging
  - Avoid sharp edges → broken teeth
  - Zinc toxicosis < metal leaching during steam sterilization
- Litter box
  - Avoid clay litters → dust → upper respiratory infections

Ferret Enrichment

- Isolation can result in hyperactivity
- Socially-reared ferrets superior in maze learning
- Prefer prey-like interactions

Question

• Research with the black-footed ferret has demonstrated that enrichment lowers ______ _______ ______ in juvenile males.

Answer

• Fecal glucocorticoid metabolites (FGM)
• Enrichment had NO effect on FGM in juvenile females and adult males.
• Page 580 in LAM 3rd edition; Published by Poessel et. al., 2011.
Ferret Biology—Unique Anatomic/Physiologic Characteristics

1. Long, narrow thorax
2. Proportionately long trachea
3. Total lung capacity 3x that for an animal its size
4. High degree of bronchial branching and extensive bronchial submucosal glands
5. Paired common carotid arteries arise from brachiocephalic trunk (or innominate artery)
6. Simple monogastric stomach
7. Short alimentary tract (3h transit time)
8. Paired anal scent glands
9. No cecum
10. Heat intolerant

Extramedullary hematopoesis common
- Splenomegaly (rule out: infectious, neoplastic, isoflurane administration)
- No naturally occurring antibodies against unmatched erythrocyte antigens

Ferret Biodata

- Table 14.2, LAM BB 3rd edition, page 581
- Life span is 6-8 years
- Weaning: 6-8 weeks
- Newborn kits: 6-12 g at birth; grow to ~400 g by weaning
- Length of breeding life: 2-5 years
- Litter size: 8 average
- Eyes open: 34 days
- Gestation: 42 days
- Sexually intact adults are subject to seasonal fluctuations of body fat of 30-40%
- Dental formula: 2(I3/3, C1/2, P4/3, M1/2)

Question

- What is a male ferret called and how much does it weigh?
- What is a female ferret called and how much does it weigh?

Answer

- A male ferret is called a hob and weighs 1-2 kg.
- A female ferret is called a jill and weighs 0.5-1kg.
- Young are called kits.

Photo: imgur.com
Ferret Nutrition

- Commercial diets available, featuring high protein (up to 50%) and low carbohydrate (<10%)
- Strict carnivores
- Short digestive tract and rapid GI transit time require that protein be readily digestible
- Adult ferrets drink 75-100 ml of water daily.

Ferret Reproduction

- Table 14.7, LAM BB 3rd edition, page 585
- Question
  - Ferrets are ________ breeders and ________ ovulators.

Ferret Reproduction

- Answer:
  - Ferrets are SEASONAL breeders and INDUCED ovulators. Page 584, LAM BB, 3rd edition

Ferret Repro Data

- Minimum breeding age: 8-12 mos (M); 4-5 mos (F)
- Estrous cycle: Monoestrus, March-August
- Induced ovulators
- Age at puberty
  - Female (750-1500g): 6-12 mos
  - Male (1500-2500 g): 6-12 mos

Ferret Repro Data

- Question
  - ________ ________ is the hallmark of estrus in jills.
Ferret Repro Data

• Answer
  • VULVAR SWELLING is the hallmark of estrus in jills.
  • Females are brought to male ~14 D after vulvar enlargement.
  • Left together ~2 days.

Ferret Husbandry—Pregnancy

• Jills within 2 weeks of parturition should be singly housed
• Rabbit nest boxes, cat litter pans work well and should have bedding.
  • Should be at least 6 inches deep.
• Parturition occurs rapidly with few impending signs
• Jills that pass their due date without delivery should be palpated. Kits remaining beyond the 43rd day typically die.
• Dystocia is common and jills tolerate C-sections well.
• Oxytocin may be used.
• Crossfostering has been successful.

Ferret Husbandry—Newborns

• Altricial and covered in lanugo hair
• 3 days: albinos retain white hair; pigmented ferrets acquire gray coat
• Completely dependent upon jill for first 3 weeks of life.
• Sexing—anogenital distance
• Developmental landmarks
  • Hear: 32 days
  • Open eyes: 34 days
  • 1st Teeth erupt: 14 days
Diseases of Ferrets

- Infectious Diseases
- Metabolic and Nutritional Diseases
- Traumatic Disorders
- Iatrogenic Disorders
- Neoplastic Diseases
- Miscellaneous Diseases

Legal Information

- Legal in 48 states other than CA and HI
- Classified as a pet in 1999 Rabies Compendium NASPHV
- Treatment after bite incidents may vary by locality
  - Most enforce 10-day quarantine
  - Some localities may enforce euthanasia and testing

Case 1 Lesions

- Erythematous, pruritic rash on chin and ventral neck

Additional lesions

- Mucopurulent ocular discharge
- Hyperkeratosis of footpad

Histopathology

- Bladder with eosinophilic inclusions
- Both intracytoplasmic and intranuclear INIC and ICC bodies in respiratory epithelial cells and macrophages.
What’s Your Diagnosis? (WYD)

Answer

• Distemper

Canine Distemper Virus

• CD or CDV
• Paramyxoviridae
  • Genus: *Morbillivirus*
  • Related to measles and rinderpest
  • Several strains, including ferret-adapted CDV that differ in incubation, C/S and duration
• MOST SERIOUS VIRAL INFECTION OF FERRETS
  • Almost 100% mortality
  • Vaccine and husbandry are imperative

Canine Distemper Virus

• Catarrhal phase
  • 7-10 days post-infection
  • Fever, rash, footpad hyperkeratosis (inconsistent), serous to mucopurulent ocular/nasal discharge
  • Erythematous, pruritic rash spreads from chin to inguinal region
  • CD-mediated immunity response similar to measles in humans
• CNS phase
  • Ataxia, tremors, paralysis
  • Death in 12-16 days (ferret strain) and within 35 days (canine strain)

Canine Distemper Vaccine --Transmission

• Unvaccinated dogs and other canids, mustelids, procyonids serve as reservoirs
• Virus shed from infected hosts from all orifices, urine, feces and sloughed skin.
• Viremia detectable 48 hours post-infection and PERSISTS until ferret dies or mounts neutralizing antibody response.

Canine Distemper Virus—Necropsy and Diagnosis

• Eosinophilic inclusion bodies in tracheal, bronchial and bladder epithelium
• Presumptive DX based on C/S, ? Vax history, exposure
• Fluorescent antibody test on peripheral blood on conjunctival scraping
• RT-PCR used to detect experimental infection
• DDX: B. bronchiseptica, Influenza
INIC and ICIC bodies in respiratory epithelial cells and macrophages.

Canine Distemper Virus-Prevention

- Humane euthanasia of affected animals recommended due to lack of literature on animal survival.
- Modified Live Vaccine of chicken embryo tissue culture origin (CETCO)
  - SQ or IM
  - Vaccinate kits every 2-3 weeks starting at weeks of age until 14 weeks of age.
  - Fervac-D or Purevax Ferret Distemper
  - Vaccine reactions have been noted

Case 2

- Clinical Signs
  - Progressive weight loss
  - Melena
  - Ataxia
  - Tremors

Lesions

- Splenomegaly
- Glomerulonephritis

Histopathology

Non-suppurative meningitis with plasma cell cuffing

Clinical Pathology

Hypergammaglobulinemia
Aleutian Disease

- Aleutian Mink Disease (ADV)
- Parvovirus
  - Genus: Amdoparvovirus
  - Species: Carnivore amdoparvovirus 1
  - Mink-derived strains are more virulent to mink than are ferret-derived strains
  - Most common strain in ferrets is ADV-F.
  - Transmission may be direct or via aerosol of urine, saliva, blood, feces and fomites.

Lesions are typically immune-mediated with elevation of gammaglobulins of >20% of the total proteins.

C/S include: weight loss, malaise, cachexia, ataxia, tremors.

DX: Presumptive based on HGG and chronic weight loss. Confirmed by IFA or CIEP (counterimmunoelectrophoresis).

DDX: Neurotropic form of CD, chronic wasting diseases such as neoplasia, malabsorption/maldigestion, bacterial enteritis.

Antigen antibody complexes are formed in large numbers which are deposited in vascular basement membranes throughout body.
Widespread vasculitis including glomerulonephritis and interstitial pneumonia.
• What human orthomyxovirus is zoonotic and pathogenic to ferrets?

Answer
• Human influenza viruses A and B
• Pathogenicity of type B is low.
• Ferrets are also susceptible to avian, phocine, equine and swine influenza.
• C/S appear 48 hours post-infection and include anorexia, fever, sneezing and serous nasal discharge.
• Transmission is aerosol and direct contact.
• TX: Antibiotic, antivirals

Since ferrets are warm-blooded...

• What other viral disease are they susceptible to?

Rabies
• Rhabdovirus
  • Genus: Lyssavirus
  • Infrequently reported in ferrets.
  • Treatment and Control: USDA-approved, killed rabies vaccine given at SQ at ages 3 months, 1 year and annually thereafter.
• DDx: Neurotropic form of CD
• DX: IFA of brain tissue

• What is the causative agent of “green slime disease” in ferrets?

Answer
• Coronavirus
• Or Epizootic Catarrhal Enteritis (ECE)
  • Genus: Alphacoronavirus
  • High morbidity and low mortality.
  • Shed in feces and saliva. Highly infectious.
  • C/S: Decreased appetite, diarrhea and vomiting; diarrhea is green and mucoid.
  • DX: Hx, C/S; DDx: Intestinal biopsy and histopath; RT-PCR on feces.
Ferret Enteric Coronavirus

Diagnosis:
- Clinical signs and history
- Histology
- IHC
- Clinical pathology not specific

Ferret Systemic Coronavirus
Ferret Systemic Coronavirus (FRSCV)

- Ferret Systemic Coronavirus Disease (FSCD)
- Systemic, granulomatous disease
- Behaves similar to Feline Infectious Peritonitis (FIP)
- Affects animals under 1 year of age
- C/S are non-specific (lethargy, anorexia, vomiting, diarrhea, weight loss)
- Dx: Histology
- Predominant necropsy findings are enlarge mesenteric lymph nodes
- Pyogranulomatous inflammation

Case 3

- Chronic gastritis

Histopathology

- Normal pyloric junction in adult ferret, HE, 10X
- Pyloric junction in 4-year old ferret, HE, 10X

Histopathology--Special staining

Helicobacter mustelae

Clinical signs:
- Typically asymptomatic
- Vomiting, melena, chronic weight loss, low hematocrit

Diagnosis:
- Endoscopic visualization of gastric/duodenal ulcers
- Biopsy

Treatment:
- Triple therapy: amoxicillin, metronidazole, bismuth subsalicylate
- Ranitidine bismuth and clarithromycin

DDx:
- Gastric foreign body

What’s the etiologic agent?
- What’s the stain?
- Ubiquitous or not?
**Helicobacter mustelae**

- Every ferret with chronic gastritis is *H. mustelae* positive
- Nearly 100% prevalence in exposed weanlings
- “Ferret is the only domesticated animal to date that has naturally occurring helicobacter associated ulcer disease.”
- Infected ferrets may also be susceptible to gastric cancer

**Case 4**

- Chronic diarrhea (green and/or bloody)
- Lethargy
- Anorexia
- Marked weight loss
- Dehydration
- Rectal prolapse

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**Necropsy**

*Segmented thickened colon*

**Histopathology**

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**Special Staining**

Intracytoplasmic organisms in hyperplastic epithelial cells

**What is the etiologic agent?**
Proliferative Bowel Disease

Necropsy Findings:
• Segmented, thickened lower bowel
• Histo: marked mucosal proliferation and intracytoplasmic *L. intracellularis* w/ Silver Stain

Clinical signs:
• Large bowel diarrhea
  - May be blood tinged, mucous, often green
• Rectal prolapse may occur
• Lethargy, anorexia, dehydration

Case 5
• Diarrhea, dehydration and lethargy in a four month old ferret

Etiologies?

Enteric Coccidiosis

• *Isospora laidlawi*
• *Eimeria furonis*
• *Eimeria ictidea*

Infection occurs after ingestion of sporulated oocysts.
Usually subclinical in ferrets.
Dx: Fecal flotation or direct wet mount of feces
Tx: Good husbandry, Sufadimethoxine, Coccidiostat

Coccidiosis

• Schizonts and gametocytes of *E. furonis*
• Generally asymptomatic and minimal gross lesions
Tuberculosis
- *Mycobacterium bovis, avium, tuberculosis, celatum*
- Aerobic, gram-positive, non-branching, non-sporeforming, ACID FAST rods
- Ferrets may be more susceptible than other species

Clostridium perfringens
- *Clostridium perfringens* type A (Clostridium welchii)
- Ubiquitous organism in intestines of all humans and animals.
- Acute abdominal distension, dyspnea, cyanosis in weaning ferrets. May be found dead and bloated.
- DX: Isolation of toxins from ingest; Mouse protection assay.

Case 6
- Bilaterally symmetrical alopecia

Additional clinical signs
- Vulvar swelling

Most likely diagnosis?

Adrenal gland tumor or Adrenal-associated Endocrinopathy
- Second most common type of neoplasia in ferrets
- Thought to be cause by early spay/neutering
- Artificially prolonged photoperiod (indoor housing) may also contribute
- In males, enlarged prostate may result in urinary blockage
- Animals are NOT cushingoid!!!
Adrenal-associated Endocrinopathy

Treatment
- Surgical excision or debulking
- Right adrenal difficult to remove (attached to vena cava)
- Medical management
  - Palliative only
  - Leuprolide acetate
  - Deslorelin acetate
  - Melatonin

Case 7 Signs
- Vomiting
- Ataxia
- Weakness
- Pawing at mouth
- Posterior paresis
- Collapse

Necropsy/Histopath

Insulinoma
- Islet Cell Tumor
- Causes hypoglycemia
- Manage with prednisone and/or diazoxide
- Dietary modification
- Surgical debulking may reduce clinical signs transiently
Islet Cell Tumor

Most common ferret tumor
Arise from Islet of Langerhans
• Clinical signs: hypoglycemia, lethargy, stupor, ptyalism, ataxia, hindlimb paresis, salivation, seizures, coma, death
• Inappropriate secretion of insulin resulting in “trances”

Islet Cell Tumor

• Most tumors secrete insulin
• Diagnosis: history, clinical signs, blood glucose test
  • - 60-80 g/dl – questionable, <60 positive

Diagnosis based on histopathology?

Lymphoma

• Most common in young animals (<2 years, very aggressive)
• Common forms are multicentric and gastrointestinal lymphoma
• Possibly retroviral involvement
• H. mustelae involved with specific gastric lymphoma
• Difficult to Dx; C/S include weight loss, anorexia, lethargy, splenic or liver enlargement.
• Treat with chemotherapy (L-asparaginase/cyclophosphamide/prednisone)

Lymphoma

• Neoplastic lymphocytes
WYD?

• What is this common tumor of ferrets that typically occurs on the tail, but can also occur in the cervical region present like a lymphoma?

Chordoma

• Notochord remnants
• Not epithelial
• Masses on tail that may cause ulceration of overlying skin.
• Slow-growing.
• Metastasis has been documented.

Chordoma

• Neural tube defects
• Gastrochisis
• Cleft palate
• Corneal dermoids
• Cataracts
• Supernumerary incisors

Congenital Lesions

Cataracts

• Common cause of disease in aging ferrets.
• Dilatative form most common
• C/S: Lethargy, weight loss, anorexia and signs of CHF.
• DDx: Radiographs
• Tx: Medial therapy (support care, diuretics, inotropics)
• Long-term prognosis is guarded/poor.

Cardiomyopathy
Cardiomyopathy

Ectoparasites

- Ticks (*Ixodes* sp)
- Ear mites (*Otodectes cyanotis*)
- Fleas (*Ctenocephalides* sp.)
- Sarcoptic mange has been reported
  - Very pruritic, whole body form
  - Variable pruritic form localised to the feet
- Demodectic mange in old or immunosuppressed ferrets
- Biopsy moderate hyperkeratosis and mites

Ectoparasites (Earmites: *Otodectes cyanotes*)

Ectoparasites: Demodex sp.

Dirofilariasis

- Susceptible to natural and experimental infection with *Dirofilaria immitis*.
- Monthly heartworm preventative. In endemic areas, animals should be treated year round.

Hyperestrogenism

- Induced ovulators
- May remain in persistent estrus if not bred or if estrus not terminated chemically or via O VH.
- >1 month may develop estrogen-induced anemia.
- Also causes BM suppression.
- C/S: vulvar enlargement, bilaterally symmetrical alopecia of tail and abdomen, weakness, lethargy.
- Avoid by O VH of non-breeders, use vasectomized hobs, Tx animal 10 days after estrus start. 
Eosinophilic Gastroenteritis

- Eosinophilic gastroenteritis, idiopathic disorder
- Splendore-Hoeppli material in inflamed lymph nodes
- Originates from Igs of host-derived inflammatory cells. Named after Splendore, an Italian physician and Hoeppli, a German parasitologist.

http://www.yamagiku.co.jp/pathology/case/case045.htm

The End