



What's your Diagnosis?

Presented by Beth Ford, DVM, MPVH, DACLAM
The Scripps Research Institute
For
(Seminar name??)
(Location????)



CASE #1

Mouse

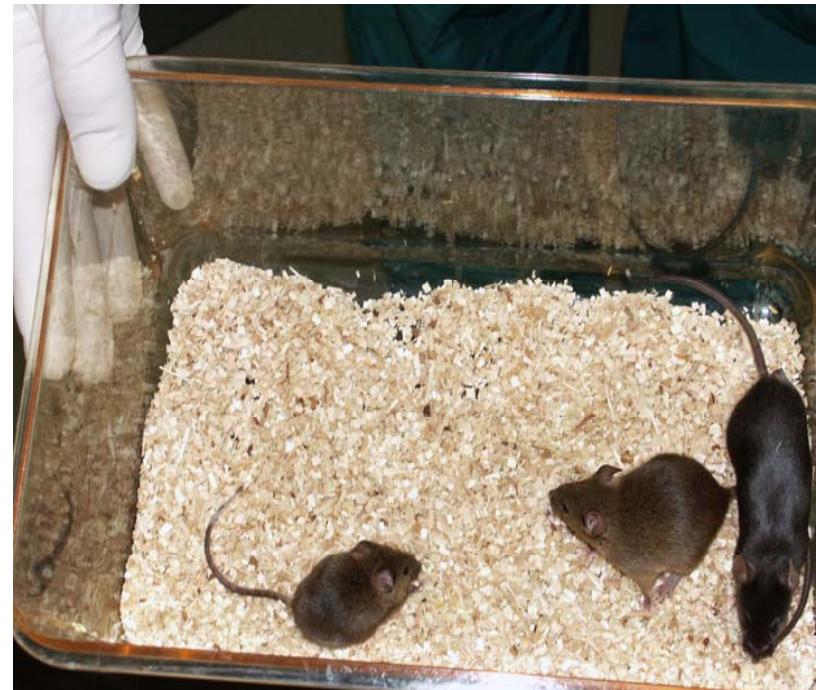


Weanlings from same litter



Weanlings from same litter

- Is there a problem?
 - Yes, one animal is smaller than the others
- Observation of behavior reveals:
 - Lethargy
- Physical examination reveals:
 - Dehydration (tenting of skin)
 - Emaciation
- And....



What is your Diagnosis?



Incisor Malocclusion



- “Mal” = not or none
- “Occlusion” = close or shut
- Common disorder of many strains of laboratory mice
- Occurs when mandibular and maxillary teeth are not normally aligned

Incisor Malocclusion



- Rodent incisors are “open-rooted” and grow throughout life
- Gnawing behavior keeps normally aligned teeth at a normal length



Incisor Malocclusion



- Treatment consists of a regularly scheduled trimming of teeth using blunt scissors
 - Wear eye protection!!
- Undiagnosed or untreated malocclusion may result in oral or facial abscesses and osteomyelitis or death
- Reserve treatment for valuable mice—it is labor intensive!



CASE #2 - #4

Rodent Skin Conditions

Black Mice from an Approved Vendor



- Mice received approximately 4 weeks ago
- Many began showing signs of alopecia dorsally approximately 2 weeks after arrival



Black Mice from an Approved Vendor



- Approximately 1 week ago, the alopecic areas began to ulcerate
- A skin scraping did not reveal any ectoparasites

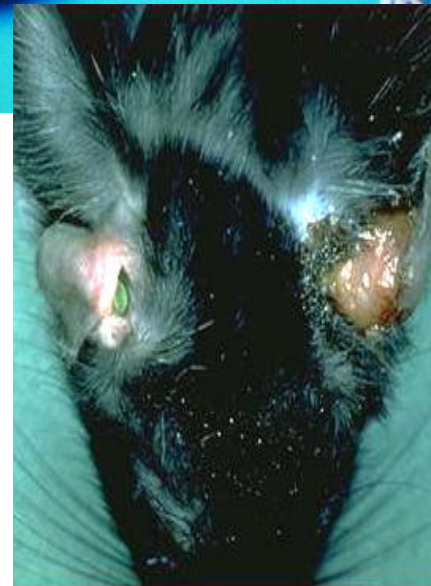
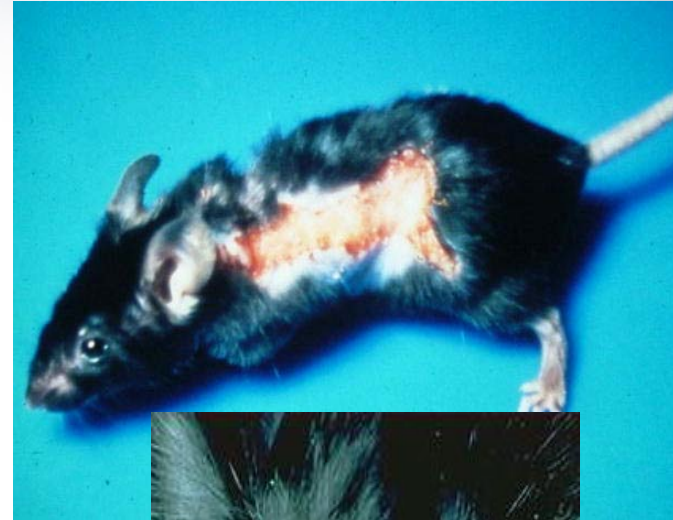
Black Mice from an Approved Vendor



- Some lesions responded to a topical application of triple antibiotic ointment
- Some animals did not respond to treatment and had to be euthanized



What's Your Diagnosis?



Ulcerative Dermatitis



- Seen in most black mouse strains with females affected 5 times more often than males
- In the C57Bl/6 line, males and females are affected equally

Chronic Ulcerative Dermatitis



- Cause is unknown
- Microbiological assessments have revealed a variety of bacteria that are considered to be secondary opportunists
- Seasonal fluctuation in incidence suggests environmental factors may play a role
 - Significant seasonal changes in temperature and humidity

Chronic Ulcerative Dermatitis



- Some evidence that incidence is related to diet
 - Mice on ad libitum diets are more susceptible than mice on restricted diets
 - Specific dietary factors have not been identified
- Acariasis has not been incriminated





CASE #3

Rodent Skin Conditions



Cage with Adult Male Mice



- 3 of 4 mice have multiple wounds on dorsum and tail and a rough hair coat
- One mouse has no lesions and a smooth and shiny coat

What's your Diagnosis?



Skin Trauma



- Skin lesions caused by fighting
- Fighting is not limited extensively to males
 - Though they do tend to be more aggressive
- Single animal free of lesions is probably the aggressor
 - Removal of this animal usually ends the fighting





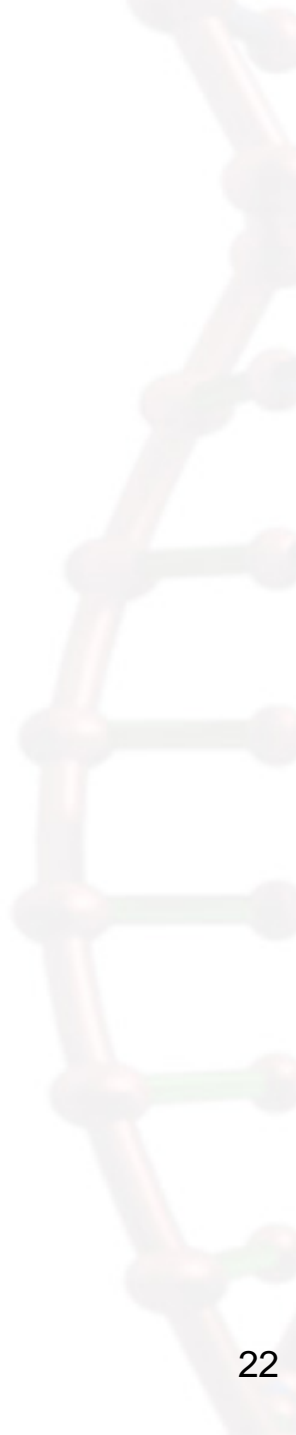
- Fighting may resume if one of the previously submissive animals becomes the dominant aggressor
- Placement of nesting material may decrease intra-cage aggression
- There is some strain predilection





Case #4

Rodent Skin conditions



Multiple cages of Mice



- Numerous cages of mice are reported to have significant losses of fur on their bodies and faces
- There is no sign of ulceration but some of the animals have minor redness of the bare skin
- Other animals have no redness
- All the animals appear bright, alert and responsive

What's your Diagnosis?



Barbering



- A social dominance behavior in mice
- Both sexes engage in this activity
- Chronic barbering may result in poorly formed or pigmented club hairs

Barbering

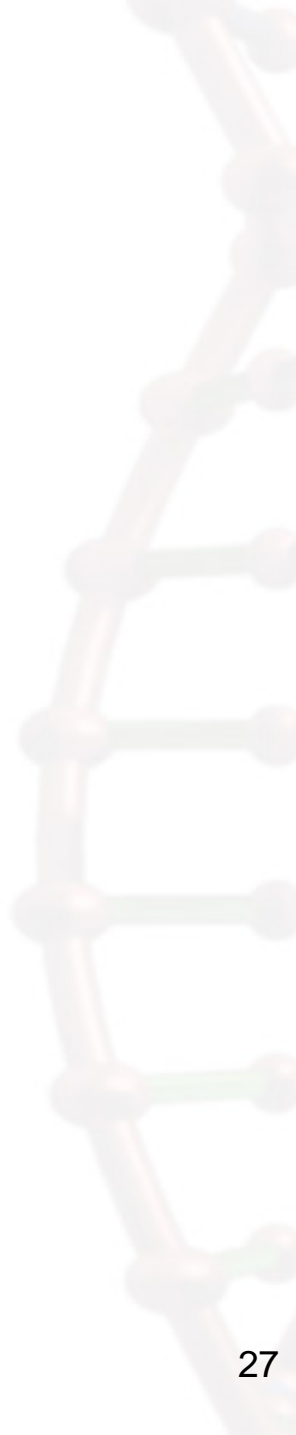


- Other causes of alopecia in mice
 - Abrasion against cage surface
 - Improperly diluted disinfectants
 - Clipping hair prior to application of experimental compounds
- Differential Diagnoses:
 - Dermatophytosis
 - Ectoparasitism
 - Idiopathic Hair Loss



Case #5

Rat



Experimental Colony of Rats



- Animal Care Technician reports hearing numerous sneezes in a rat room of 32 recently received rats
- Approximately 40 sneezes/minute are heard
- Some animals have porphyrin staining around their eyes and external nares



Experimental Colony of Rats



- Two days later, the sneezing has subsided, but many of the animals show signs of photophobia
- Some animals show signs of swelling in the ventral cervical area



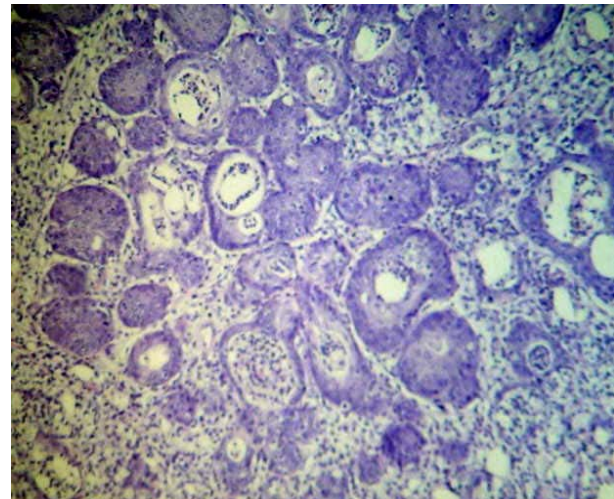
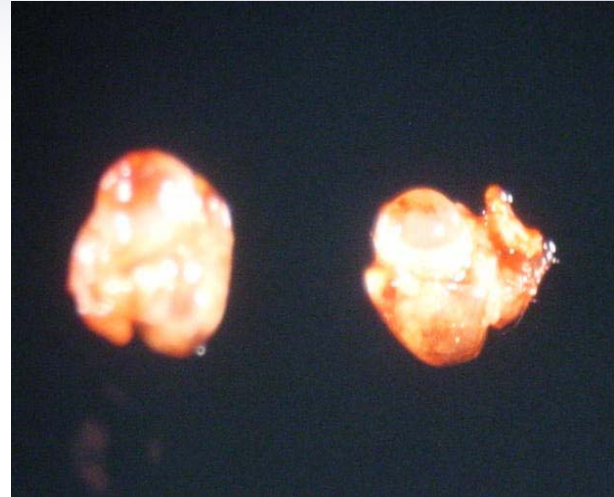
- Other animals show exophthalmos/megaloglobus



Necropsies are performed on rats with most significant clinical signs



- The Harderian glands are mottled, discolored and swollen
- Histologically they show squamous metaplasia and mononuclear cell infiltration



Necropsy and Histopathology



- The cornea shows signs of keratitis
- The salivary glands (not shown) are edematous and markedly enlarged
 - Histologically: marked necrosis of ductal and acinar epithelial cells, effacement of the normal architecture

Other Pathology

- Tracheitis, focal bronchitis and bronchiolitis
 - Characterized by mononuclear and polymorphonuclear cell infiltration

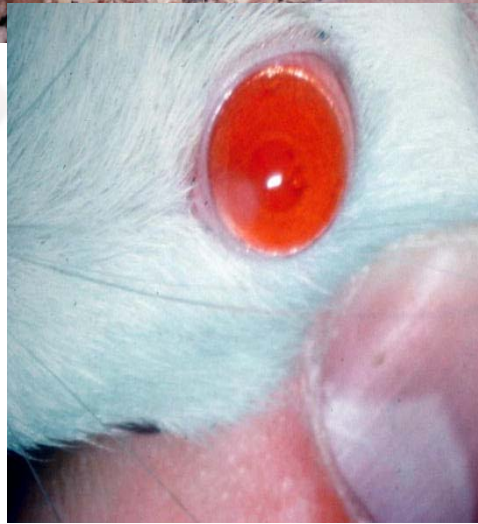
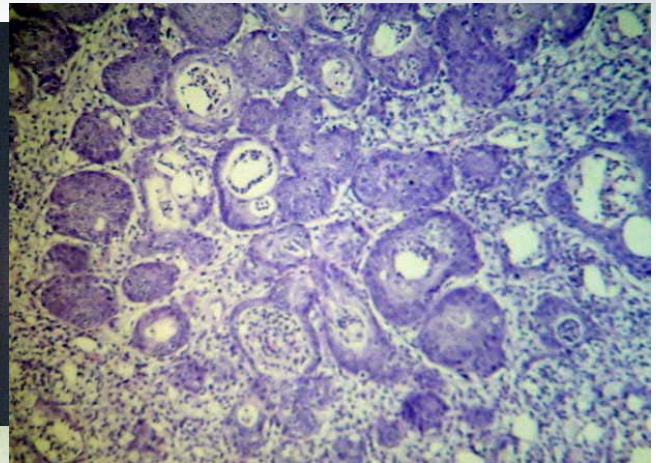


Meanwhile.....



- Numerous other rats in the animal facility are beginning to show similar clinical signs
- Within 3 weeks all rat holding rooms contain rats with clinical signs
 - Very contagious!!!!

What's Your Diagnosis?



Differential Diagnoses



- Sialodacryoadenitis-SDAV
- Mycoplasma pulmonis
- Sendai Virus
- Subcutaneous edema associated with Pseudomonas aeruginosa infections
- High Environmental Ammonia Levels
- Stress Associated Chromodacryorrhea

Sialodacryoadenitis-SDAV



- Corona Virus –enveloped RNA
- High morbidity and negligible mortality
- Permanent ocular damage may occur
 - From dacryoadenitis and impaired Harderian gland function
- Significant depletion of Epidermal Growth Factor in affected salivary glands
 - May have significant effects on certain types of research

Treatment



- None
- Disease is self limiting
 - there is no carrier state
- Suspend breeding for 6 weeks to “burn out” the disease
- Previous infection will provide protection for up to 15 months
- Glands will return to normal



Case #6

Rabbit



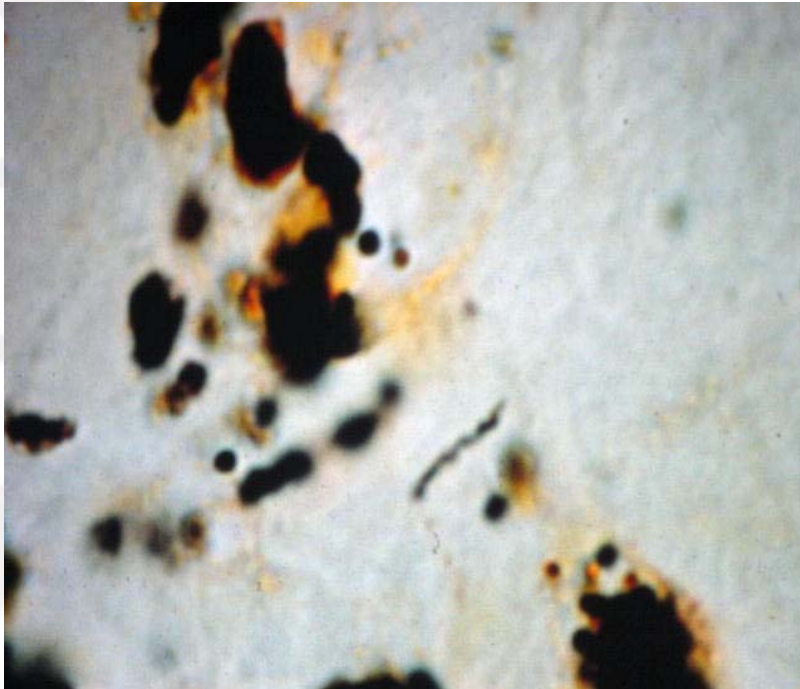


- A rabbit in a breeding colony was reported one week ago to have areas of erythema and edema around the nostrils and mouth
- These subtle lesions quickly became ulcerations and then progressed to scales and crusts

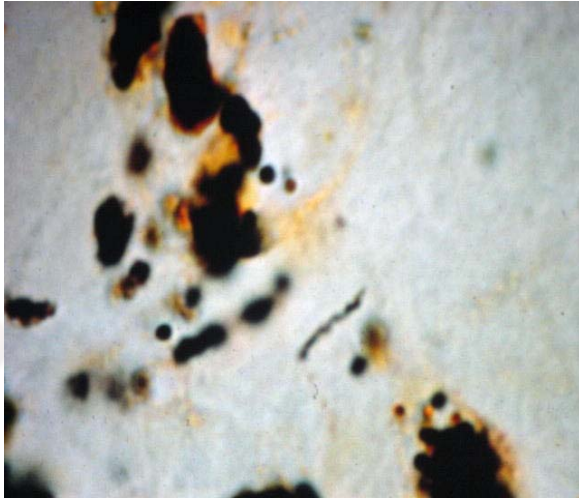




- A smear of the affected tissue was stained with Warthin-Starry silver stain and revealed the characteristic spiral morphology of spirochete bacteria



What's your diagnosis?



Rabbit Syphilis



- Venereal Spirochetosis or Treponematoses due to *Treponema cuniculi*
- *T. cuniculi* usually infects by penetration of intact or damaged mucus membranes
 - Does not require venereal transmission
 - Facial lesions can often occur without genital involvement
- Serology tests have been developed and are useful in enzootically infected colonies

Research Implications

- *T. cuniculi* resembles *T. pallidum*; the cause of human syphilis
- In the 1920s studies were undertaken to determine if humans inoculated with *T. cuniculi* could mount an antibody response
 - This did not occur
 - If it had, a vaccine against syphilis may have resulted



Treatment for Rabbit Syphilis



- Penicillin is drug of choice
- Three injections of 42,000-84,000 IU/kg given 7 days apart

- Lesions heal with in 2 weeks

Prevent infection or re-infection by keeping a closed colony

If new animals are necessary, examination for lesions and serologically testing should occur prior to introduction to colony





Case #7

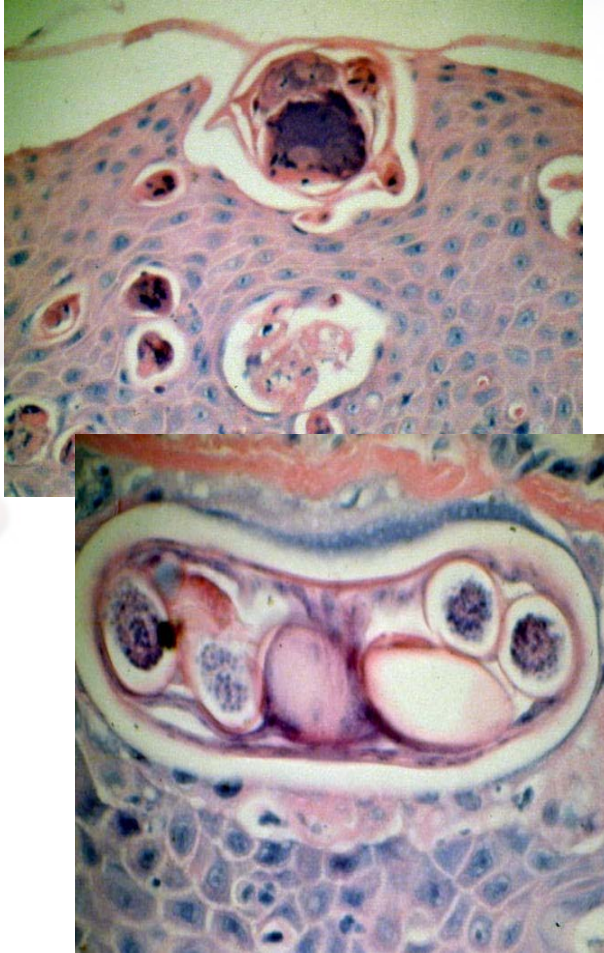
Xenopus Frog





- A xenopus frog was observed to have rough thickened pitted appearance to the skin on its dorsal surface with large patches sloughing
- The frog was euthanized and a necropsy was performed





- Necropsy revealed epithelial erosion and ulceration, hyperkeratosis, vacuolation and mixed inflammatory cell infiltrate
- There was evidence of visceral septicemia
- Sections of the skin revealed the organisms shown here



This egg was seen on a wet mount



What's your diagnosis?



- *Differential Diagnoses List:*
 - *Pseudocapillaria xenopi*
 - *Rhabdias*
 - *Foleyella*
- Table on next slide indicates methods to differentiate

Nematode	Clinical signs	Diagnostic Methods	Egg/adult characteristics
<i>P.Xenopi</i>	Rough, thick skin 2° bacterial/ fungal infection	Wet mount preps and skin scraping	Bipolar eggs
<i>Rhabdias</i>	Pneumonia	Fecal examination and tracheal wash	Larvated eggs
<i>Foleyella</i>	Asymptomatic, weakness or malaise	Fresh blood smear	Only one seen in blood

Pseudocapillaria xenopi



- Treatment:
 - Levamasole medicated tank water for 4 days and then retreat 10-14 days later
 - Levamasole does not kill embryonated larvae

Ineffective Treatments



- Thiabendazol
 - Was extremely irritating to skin when placed in water
- Ivermectin
 - Worked well orally and by injection into dorsal lymph sac
 - 2 treatments; 10-14 days apart
 - Recurred 1-3 months later
 - Not soluble for practical application in water

Another potential benefit of levamasole treatment:



- immune stimulating properties
 - cutaneous nematodiasis is often accompanied by 2^o infections with *aeromonas* or *citrobacter freundii*....
- **Reference:**
 - Iglauer et al, Anthelmintic Treatment to Eradicate Cutaneous Capillariasis in a Colony of South African Clawed Frogs (*xenopus laevis*), pp. 477-482.
 - LAS, vol 47, No. 5, October 1997



CASE # 8

Guinea Pig





- Adult guinea pig presents with cervical enlargement
- Palpation reveals bilateral masses that are freely moveable, firm to soft
- The animal is euthanized and a necropsy is performed



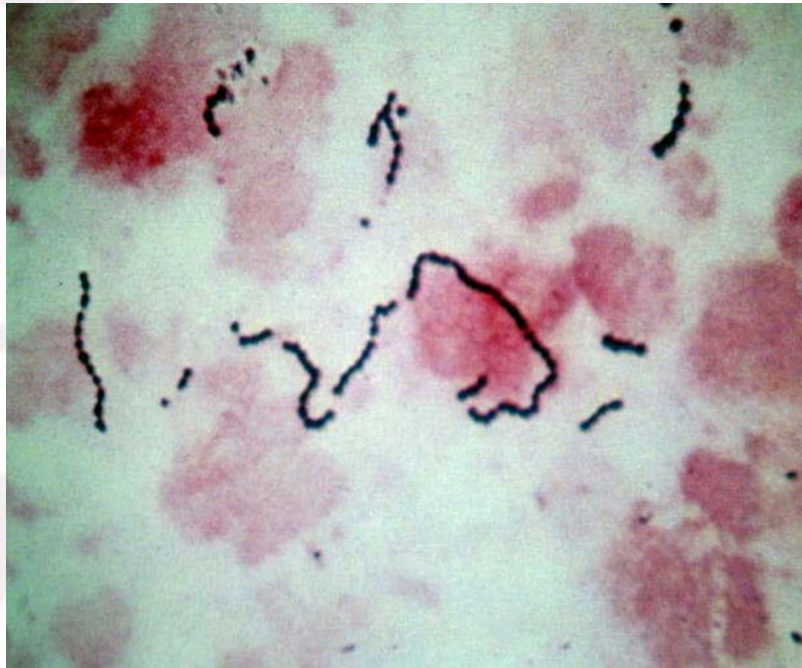
Gross Necropsy



- The bilateral masses are identified as abscessed cervical lymph nodes and contain thick purulent exudate

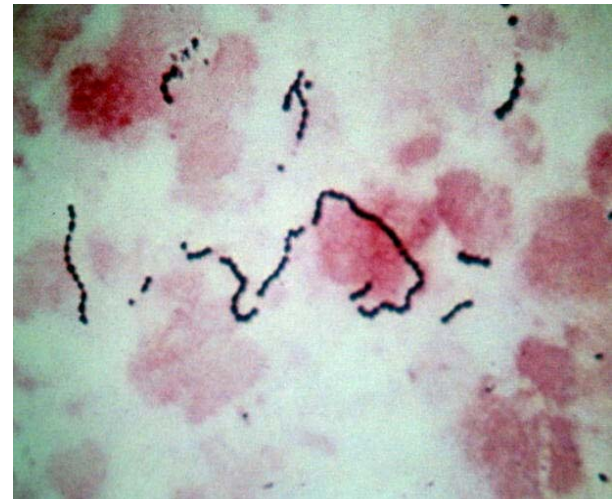


Impression smear



- A smear of the tissue reveals chains of gram positive cocci
- A culture of the tissue produces beta-hemolysis on a blood agar plate

What's your Diagnosis?



Streptococcal Lymphadenitis

“Lumps”



- *Streptococcus zooepidemicus*
 - Gram-positive encapsulated coccus of Lancefield's Group C
- Is associated with suppurative lymphadenitis in Guinea pigs
- *S. zooepidemicus* is normal flora in GP conjunctiva and nasal cavity
 - Enters through mucosal abrasions in oral cavity
 - Stress increases susceptibility to infection

Treatment and Prevention



- Complete surgical excision of affected lymph nodes is most effective
 - Surgically draining abscess with copious flushing may also be done
 - Systemic antibiotic therapy with TMS or enrofloxacin post operatively
- Prevent cervical lymphadenitis by keeping GPs in clean, stress-free environment
 - Isolate affected animals from others until abscesses are healed



Case #9

Guinea Pig





- A group of young guinea pigs presented with reduced appetite and decreased activity
- Most of the animals had no definitive physical signs



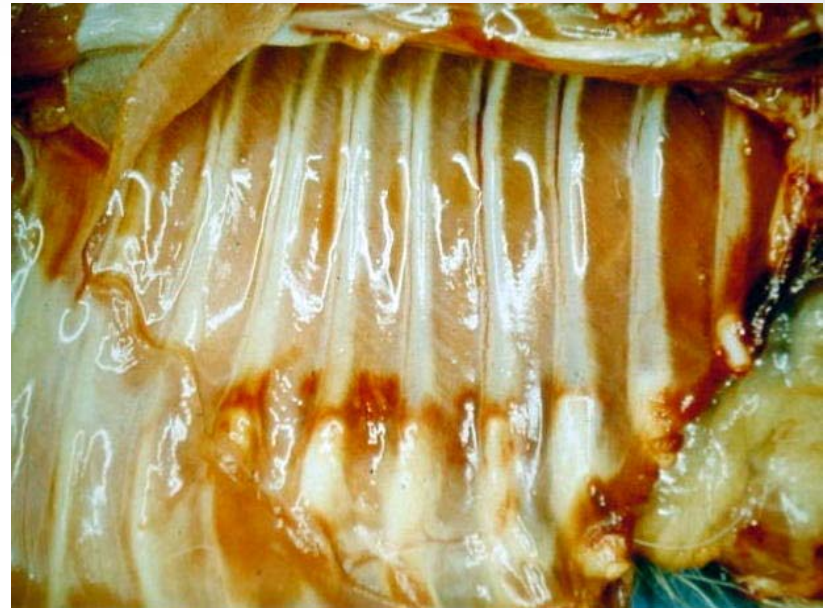
- One guinea pig had a rough hair coat and diarrhea.
- It was exhibiting teeth grinding and swollen rear limbs.
- There was vocalization and struggling during palpation indicative of pain.
- A radiograph showed enlarged costochondral junctions
- The animal was euthanized for necropsy



Necropsy



- Initial observation included
 - muscular hemorrhage
 - fracture of the femur



- The costochondral junctions were enlarged and there were periosteal hemorrhages

What's your diagnosis?



Vitamin C Deficiency

Scurvy



- Signs of scurvy can occur in as little as 2 weeks of ascorbic acid deprivation
- Guinea pigs can't convert glucose to ascorbic acid due to lack of L-gulonolactone oxidase enzyme.
- Require 15-25mgs Vitamin C per day to prevent scurvy
- Pregnant animals require 30 mgs per day

Vitamin C Deficiency

Scurvy



- Diagnosis of Vitamin C deficiency is based on history, clinical signs and radiographic findings
- Serum ascorbic acid levels can confirm the diagnosis
- Positive response to treatment is often most practical means of confirmation

Vitamin C Deficiency

Scurvy



- Treatment:
 - Parenteral administration of 50 mgs ascorbic acid subcutaneously or
 - 50 mgs vitamin C orally at same dosage
- After recovery, supplement vitamin C daily with fresh cabbage, kale or oranges OR
- Use good quality guinea pig chow; NOT rabbit chow
 - Rabbit chow formulation is inappropriate for guinea pigs



Case #10

Non Human Primate





- During the annual physical examination procedures of a rhesus macaque colony, the following abnormalities are noted in juveniles:
 - Weight loss and joint tenderness
 - Subtle lameness
- Other animals in the colony show a pattern of clinical signs of a possible disease condition



- Many of the other animals have:
 - scruffy hair coats
 - gingival swelling and loose teeth
 - hyperemia and hemorrhage of the gums
 - subcutaneous petechial hemorrhages
- Blood work on affected individuals reveals a macrocytic anemia



What's Your Diagnosis?



- Differential Diagnoses list:
 - Vitamin C deficiency
 - Undetermined toxin
 - Parasitic infestation
 - Other nutritional toxicities or deficiencies

Vitamin C Deficiency



- Deficiency of Vitamin C results in the inability of animals to produce hydroxyproline and intracellular cement, which are required for maintaining the integrity of blood vessels, bone and a variety of other tissues





- Because of the lack of cellular L-gulono-lactone oxidase, humans and nonhuman primates, with the exception of some prosimians, require dietary vitamin C.



A Historical Perspective Case



- A young squirrel monkey presents with an enlarged misshapen head
- Palpation reveals a smooth, irregular mass confluent with the skull with no appreciable margins



A Historical Perspective Case



- A quick visual survey of the squirrel monkey colony reveals occasional other monkeys that have misshapen heads



A Historical Perspective Case



- A squirrel monkey with a misshapen head is euthanized for an unrelated study and a necropsy is performed.
- A striking finding is hyperostosis of the skull
- This is due to periosteal elevation that occurred when the monkey was young and deficient in vitamin C

Cephalohematoma

- The periosteal elevation is a result of hemorrhage from fragile capillaries in the inner layer of the periosteum.
- Growing bones are sites where collagen turnover and blood vessel formation are most rapid and thus most vulnerable to ascorbic acid deficiency
- Later ossification followed by remodeling toward normal structure results in this “turban head” presentation



Vitamin C Deficiency



- Treatment consists of ascorbic acid injections; 25 mg/kg given IM BID for 5 days
- Vitamin C deficiency can be avoided by feeding appropriate feed, and paying attention to storage conditions and shelf life

More details on vitamin C



- L –Ascorbic acid (vitamin C) is an essential cofactor for many enzyme oxidation processes.
- Ascorbate serves as an important tissue antioxidant. Scurvy , a dietary deficiency of the vitamin C manifests in the musculoskeletal system by joint pain and tenderness, reluctance to move, lameness or abnormal locomotion, muscle wasting, subperiosteal hemorrhages and epiphyseal fractures.
- Juvenile animals are most susceptible.
- Chronic ascorbate deficiency is characterized by gingival swelling, hyperemia, injury and hemorrhage as well as by periodontal bone resorption, epiphyseal injury and fracture of long bones.

These species do not need dietary Vitamin C



- (*Tupaia glus* (Tree Shrew), *Nycticebus coucang* (Slow Loris))
 - The tree shrew was recently reclassified from a primate to an insectivore
- Both these species have the enzyme L-gulonolactone oxidase. All other NHP require it in the diet.



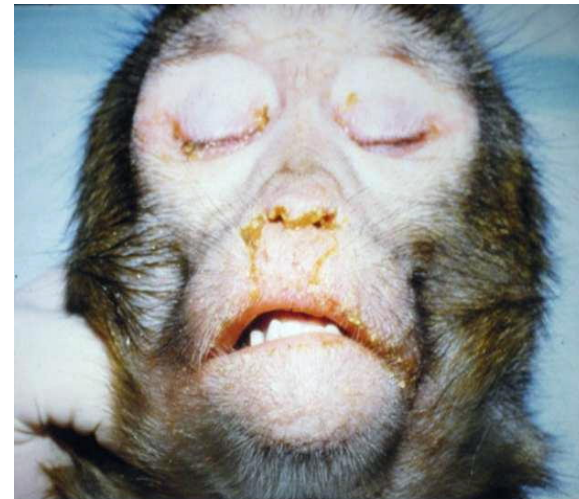
Case #11

Non Human Primate





- Numerous animals in a colony are reported to be coughing and lethargic
- A rhesus with severe signs is presented with a rash on its face and body
- Conjunctivitis and coryza are also seen

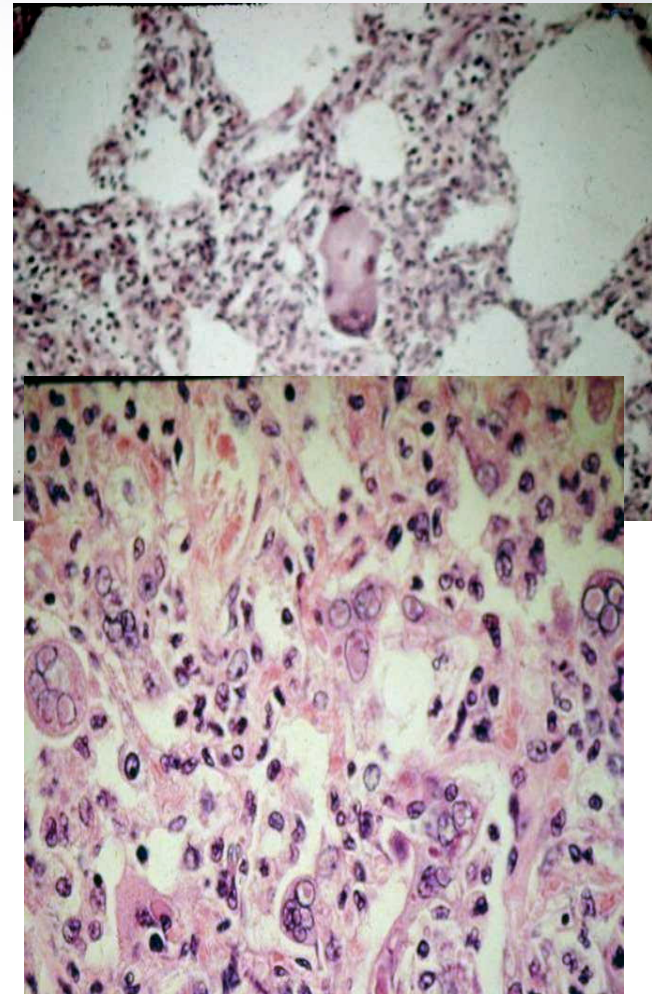
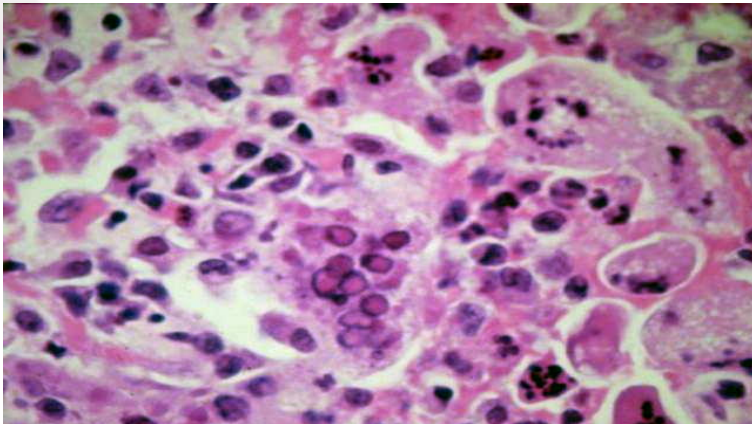




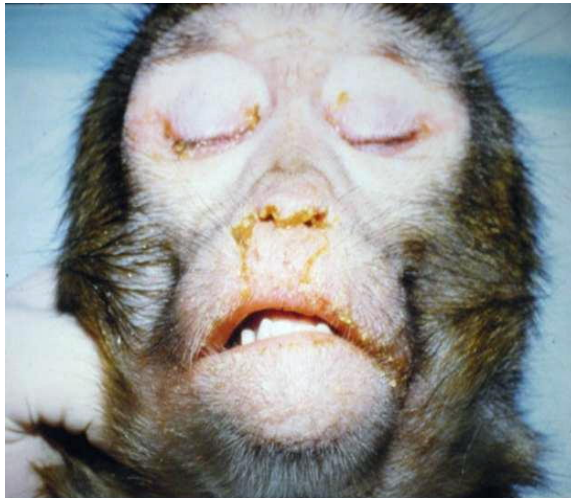
- Physical examination reveals white spots on its tongue and cheek
- Harsh respiratory sounds
- A necropsy is performed on one of the most severely affected animals and histopathology evaluated

Histopathology

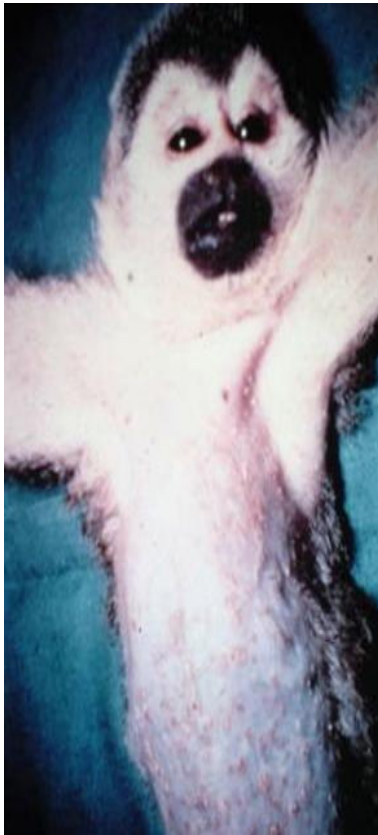
- Clockwise from upper right
 - Giant cell pneumonia
 - INIB and ICIB are seen within syncytial cells
 - Giant cell pneumonia with inclusion bodies



What's your Diagnosis?



Measles



- Etiology: Rubeola virus; paramyxoviridae, morbillivirus
- Reservoir: humans
- Causes immunosuppression
- Can interfere with TB testing
- The GI system tends to be the most severely affected in NWM; can cause Fatal gastroenterocolitis in marmosets and owl monkeys



Measles



- Prevention: vaccination
 - Live attenuated measles virus vaccine
 - Canine distemper virus vaccine
 - Canine distemper/measles combo vaccine
- Nonhuman Primates do not usually develop measurable response from the canine distemper vaccine
- Established guidelines to determine immunity to measles in humans
 - Birth before 1957 (least reliable)
 - Documentation of 2 doses of measles vaccine after 12 months of age
 - Seropositivity
 - (LAS Vol 49#1; February 1999)



The End

