### 2007 CL Davis Review NIEHS/NIH Laboratory Animal Medicine Slide Collection

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# THANK YOU!

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  - This is not an ACLAM sanctioned presentation
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# Taxonomy

- Order Primates, then suborders, these into infraorders, and these in superfamilies
- Suborder -
  - Prosimii according to Lab Primates not monophyletic since tarsiers share ancestors with "Anthropoidea"
    - Lemuroidea
    - Lorisoidea
- ➤ Suborder: Strepsirrhini
  - Tarsioidea (separate infraorder) Suborder: Haplorrhini

- Anthropoidea
  - Infraorder Tarsiiformes and Simiiformes
  - Intraorder Simiformes
  - Catarrhini OWM;
    - Family: Cercopithecidae and Hominidae
    - Hominidae Subfamily Hylobatinae and Homininae
      - Genera: Pongo, Homo, Gorilla
    - Family: Cercopithecidae; Subfamily Cercopithecinae and Colobinae
      - Colobinae colobus, leaf monkeys, langurs, proboscis
      - Cercopithecidae Tribe: Cercopithecini and Papionini
      - Macaques, baboons, drills and mandrills, mangabeys, vervets, guenons

Lab Animal Medicine, 2<sup>nd</sup> Ed, "Blue Book"; and The Laboratory Primate, 2005

# Old World Monkeys – Family: Cercopithecidae

- Tend to be large (10-20 kg), diurnal, terrestrial
- Omnivorous, and do not require Vit D3
- Asian macaques and mangabeys tend to be more arboreal, as are colobines who are leaf eaters
- Catarrhines have narrow noses with commashaped nostrils separated by a narrow nasal septum
- Lack prehensile tails, typically have cheek pouches and opposable thumbs, some have ischial callosities, may have sex skin Wagner, WFUSM 2007

# Macaques – General

- Greatest geographic distribution of NHPs
- Characteristics
  - Large cheek pouches
  - Prominent ischial callosities
  - Variable sexual swelling
  - No prehensile tail
  - Marked sexual dimorphism
    Females: 2-6 kg, Males 4-8 kg



# Macaca

- African macaques
  - Barbary macaque, *M. nigra*
- Asian macaques, includes all others
  - M. nemestrina group
    - Includes *M. nemestrina* (pigtail), crested or black ape, *M. nigra*, others
  - M. fascicularis long-tailed, crab eating or cynomolgus macaque.SE Asia, Thailand, Vietnam, Burma, Indonesia, Philippines, Malaysia
  - *M. arctoides*, stumptail
  - M. mulatta, rhesus
  - M. sinica group
    - M. radiata, Bonnet macaque, southern India





# NHP primary enclosure space requirements

Group*	Weight		Floor Area/Animal		Height	
	Пъ	kg	ft²	m <sup>2</sup>	in.	cm
1	~2	<1	1.6	0.15	20	50.8
2	2.2-6.6	1–3	3.0	0.28	30	76.2
3	6.6-22.0	3–10	4.3	0.40	30	76.2
4	22.0-33.0	10–15	6.0	0.56	32	81.28
5	33.0-55.0	15-25	8.0	0.74	35	91.44
6	>55.0	>25	25.1	2.33	84	213.36

Group 1-marmosets, tamarins, and infants (<6 mo. old) of various species.

Group 2---capuchins, squirrel monkeys, and similiar-sized species, and juveniles (6 mo.--3 yr. old) of various species.

Group 3-macaques and African species.

Group 4-male macaques and large African species.

Group 5--baboons and nonbrachiating species > 33.0 lb. (over 15 kg).

Group 6-great apes >55.0 lb. (25 kg) and brachiating species.



# Genus, species?Macaca mulatta

### Common name?

Rhesus







- What is the cause of this condition?
  - Normal sex skin
- Are there any complications associated with this?
  - Yeast infections have been reported in the folds



Do males develop sex skin or is this seen only in females?

# Normal Sex Skin



- What is the genus, species of these monkeys?
  - Macaca nemestrina
- What specific stage of the estrus cycle does maximum turgescence indicate?
  - Ovulation
  - Mean cycle length is 28d in macaques, 36d in baboons



#### Follicular

#### Ovulatory

#### Luteal



Mark Cline, et al

# Changes in sex hormones with natural menopause in cynomolgus monkeys



 Natural menopause described in 7 aged females (~29 yrs) including 2 DM (▲)

- Menopausal changes:
  - Increased FSH
  - Decreased E2 and estrone

# Vulvar papilloma Macaca fascicularis papillomavirus



Wood et al, Vet Pathol. 2004;41(2):108-15

- Describes cervical and vaginal intraepithelial neoplasms with selective staining of lesions demonstrating at least one of three papillomavirus antibodies in all cases
- Neoplasms included benign vaginal papillomas, mild to severe intraepithelial dysplasias, and two invasive cervical carcinomas.
- Common morphologic features included koilocytosis, nuclear atypia, and expansion of the basal epithelium.
- The unique similarities between the observed lesions and those seen in women suggest that macaques may provide a suitable animal model for study of papillomavirus oncogenesis.

# Air sacculitis



- What is this condition?
- What organism commonly causes this condition in owl monkeys?
  - Klebsiella
- Do rhesus monkey have air sacs?
  - Yes

# **Tissues from a Rhesus Monkey**



Brain, meningitis



Lung, pneumonia



Abdomen, fibrinopurulent serositis

# Streptococcus pneumoniae Fribrinopurulent serositis



Gram stain of lung impression smear

What is the reaction used to test for strep capsular antigens?

- Neufeld-Quelling Reaction
- Growth of this organism in culture is inhibited by what specific reagent?
  - Optochin (ethyl hydrocuprein)
- Steptococci are divided in the Lancefield system in 18 distinct antigenic groups based on serologic differences of the cell wall carbohydrates.
  - Most pathogenic are A,B,C,G
- Infections are acquired by aerosol by way of upper respiratory tract, middle ear or orally
  - Stress related events and young age predispose to infection and disease.
- Primary cause of bacterial meningitis; low morbidity but high mortality, usually rapidly progressive, and treatment not effective

Wagner, WFUSM. CLDavis 2007

#### Diagnosis?

# Pulmonary acariasis Pneumonyssus simicola



# Pulmonary acariasis Pneumonyssus simicola

- Infestation is usually asymptomatic, but reported to be assoicated with pneumothorax and pulmonary arteritis in the rhesus monkey
- Gross lesions are located randomly and consist of varying sized pale spots or yellowish gray foci that are usually flat or slightly umbilicated
- The lesions resemble tubercles but are soft rather than firm, bullous emphysematous lesions and hemorrhagic lesions may be seen in some cases
- Histologically; localized bronchiolitis, peribronchiolitis, focal lobular penumonitis, alveolar collapse or consolidation and sometimes bronchiolectasis
- Macrophages, whose cytoplasm is lade with a golden brown to blackish pigment and refractile crystals, are present in and around the lesions and throughout the lung tissue, thought to be breakdown of hosts blood proteins by the mites
- Control can be achieved though the development of infestation free colonies by rearing babies in isolation from their mothers, ivermectin may be effective.
- No evidence that it infects humans
- Pulmonary acariasis can be due to Pneumonyssus simicola and pneumonyssoides in the lung; Rhinophagia in the nasal cavity

# Outdoor Housed Monkey Found Dead



#### Pericardial effusion

 Pale areas myocardium

# Pathology



- Myofiber necrosis with inflammation and edema
- Viral isolation required for definative diagnosis

# Encephalocarditis virus

- Clinical: Sudden death
- Source of Infection: thought to be infected rodents; wild rats tested positive
- Transmission: contaminated food and water; several fatal outbreaks at zoos and research institutions (SFBR 80 dead baboons in 1992)
- Control: rodent control; genetically engineered modified live vaccine
- Mengo virus is a serologically related cardiovirus
- LAS Vol 48 #5 Oct 98

### Mycobacterium tuberculosis







# Mycobacterium tuberculosis



- Histo Lung: necrosis and consolidation
- Tracheal Wash: acid fast organisms
- Lesion: tuberculoid granulomas characterized by caseous centers, giant cells, lymphcytes and epithelioid cells
- Location of acid fast organisms: caseous center Wagner, WFUSM. CLDavis 2007

# Tuberculosis

- Mycobacterium tuberculosis, M. bovis, M. avium-intracelluulare (also many atypical mycobacteria: M. africanum, M, kansasii, M. simiae, M. chelonei)
- Aerobic, slightly curved or straight, occasionally beaded, rods (neither gram-negative or grampositive)
- High lipid content (~ 60%) of the cell wall makes mycobacteria "acid-fast"
  - ability to retain a carbolfuchsin stain despite subsequent treatment with an ethanol-hydrochloric acid mixture

# Diagnosis: M. tuberculosis

- Test Material:
  - Mammalian Old Tuberculin
- MMWR 42#29, 1993
- 1500 units intradermal in palpebrum
- Monkeys with M. avium/intracellulare may be weakly positive with OT but more strongly positive with M. avium
- PCR
- Primagam (IFN-γ)
  - CompMed 2004;54:86





# Pathological Diagnosis

- Acid fast stains (Ziehl-Nielsen, Fite-Faraco Kinyoun's) of impression smears and/or tissues (look for bacilli in the epithelioid and multinucleate giant cells)
- Culture on Lowenstein-Jensen medium; a slow-grower hold cultures for 6-8 weeks
- Others: PCR

# Tuberculin Testing and Interpretation

- Read: 24, 48, 72 hrs
- Grade 1-5; 4 and 5 positive
- Meaning of Negative Test
  - No exposure
  - No time to mount immune response
  - Not able to mount immune response
    - Anergy
    - Immunosuppression; Measles
- Anergic Prediction-Immunization and testing with Tetanus Toxoid (LAS, 1988; LAS, 1991)
- Treatment options
  - isoniazid, rifampin, and ethambutol combination therapy
- Bacteria can become resistant to more than one drug. This is called multidrug-resistant TB, or MDR TB.
  - This is the major reason for <u>not</u> treating NHPs

# TUBERCULIN TEST REACTION GRADES



- 0 (negative) No rxn
  - 1 (negative) Bruise from inoculation; no swelling
- 2 (negative) Variable erythema; no palprebral swelling
- 3 (suspect) Variable erythema with minimal swelling, or no erythema and slight swelling
- 4 (positive) Obvious swelling and drooping of eyelid with variable erythema
   5 (positive) Swelling and/or necrosis with eyelid closed

### Gross of Stomach from a Rhesus



# Nochti nochti

- Gross: gastric papillomas; cauliflower mass
- Trichostrongylid nematode
- Slender bright red 6-9 mm worm in stomach
- Gastric polyps or papillomas contain eggs and parasites



# Physalopera tumefaciens



 Can look like Nochti, Only head in mucosa, Body in gastric lumen

# Monkey Pox



**Eosinophilic ICIB** 

# Monkey Pox

- Orthopox virus; immunologically related to:
  - small pox and vaccinia
- OW and NW and Apes
- Visceral Lesions can occur
- Looks like human small pox; vaccinia protects



# Prairie Dog *Cynomys Iudovicianus*



Recent outbreak associated with what small animal?

### **BEMP and YABA**



#### Tumor like lesions

#### Histiocytes with eosinophilic ICIB=YABA Wagner, WFUSM. CLDavis 2007
#### Zoonotic Potential BEMP and YABA



Wagner, WFUSM. CLDavis 2007

#### Yaba Monkey Virus

- Yaba monkey virus
- Affects Asian and African monkeys
- Rapidly growing subcutaneous nodules up to 4 cm in diameter on head and limbs
- Yaba pox infects histiocytes (unlike other poxviruses) rather than epithelial cells
- Yaba confers immunity to BEMP but BEMP does not confer immunity to Yaba

# BEMP=Benign Epidermal Monkey Pox

- Tanapox virus or
- OrTeCa Pox (Oregon, Texas, California)
- Unrelated to smallpox; Smallpox is orthopox; BEMP and Yaba are Yatapoxvirus.
- Affects Asian monkeys; African sp. carriers?
- Cutaneous lesions; epithelial cells affected
- Spreads less quickly than monkey pox and has smaller cytoplasmic inclusions

#### Molluscum contagiosum



Marked acanthosis with large Basophilic ICIB, more prominent Toward the skin surface

Molluscum bodies=basophilic structures Wagner, WFUSM. CLDavis 2007

#### Molluscum contagiosum

- Molluscipoxvirus
- Affects chimpanzees and humans
- Waxy, firm 3-8 mm epithelial nodules on bridge of nose, eyelid, trunk or groin

#### Dinobdella ferox Nasal Leech



Recovered from the nostril of an old world monkey

#### Dermatophytosis



What is the most common dermatophyte of Old World Monkeys?

Microsporum canis

#### Dermatophytosis



- Microsporum in skin 40X
- Branching septal hyphae-Gridley stain Wagner, WFUSM. CLDavis 2007

Chagas Disease Trypanosoma cruzi







 Pitting edema of extremities

#### Trypanosoma cruzi



Chronic myocarditis with cystic collections of lieshmanial foms in muscle cells.

Skeletal and smooth muscle affected



#### Trypanosoma cruzi Chagas Disease



- Transmitted by "kissing bug"-Triatoma (reduvid)
- Trypanosoma cruzi-flagellate protozoan
- Trypanosomal form found in the blood is the trypomastigote
- Trypanosomal form found in the tissue is the amistigote

#### Cutaneous acariasis Psorgates simplex





Chronic dermatitis with cross section of mites in characteristic location for species

Psoregates simplex-non-pruritic DDX-Sarcoptes scabiei-pruritic



- This is a natural infection in a chimp
- What is the condition?
  - Leprosy
  - Mycobacterium leprae
- Where are lesions usually found?
  - predominantly in the skin and peripheral nerves, particularly in cooler areas (ear, tail, scrotum)



- This is a histo with a fite faraco stain (looks similar to Zeil Neilsen), what is demonstrated with stain?
  - Acid-fast bacilli
  - Histiocytic infiltrate with variable numbers of lymphocytes and plasma cells in skin and nerve (nerve lesions are pathognomonic)
  - What are the natural primate hosts of leprosy?
    - man, chimp and sooty mangaby
- What is the non-primate host
  - 9 banded armadillo, Dasypus novemcinctus LAS 46(3): 341 1996 Wagner, WFUSM. CLDavis 2007

#### Measles







Rash on trunk and face

#### Coryza

Koplick spots seen on tongue or cheek

#### Pathology, Measles



Giant cell pneumonia





INIB and ICIB within syncitial cells

Giant cell pneumonia with inclusion bodies Wagner, WFUSM. CLDavis 2007

#### Measles



- Etiology: Rubeola virus; paramyxoviridae, morbillivirus
- Resevoir: 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**

- 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) Wagner, WFUSM. CLDavis 2007

# Oesophagastumum, Colon



- Nodular worms of OWM
- Transmission is oral with direct life cycle, adults live free in lumen of LI, ingested larvae develop into 4<sup>th</sup> stage in the gut wall and return to lumen
- Usually asymptomatic to diarrhea and anemia

#### Oesophagostomum Nodular Worm



- Dark Nodules in large intestine; contain brown exudate and small white larva
- Most common nematode of OWM
- NWM have similar parasite named Molineus torulosis

#### Acute Gastric Dilatation (Bloat)



Following stomach gas distension, die of respiratory compromise, impaired venous return, and subsequently shock

Stomach markedly distended with gas and brown watery fluid, intestine congested. Subcutaneous emphysema occurs if the stomach ruptures Clostridium perfringens type A may be responsible for gas production

#### Shigellosis





Etiology: Shigella flexneri, sonnei
Confirm Diagnosis: Maconkey, XLD
Treatment: Enrofloxacin reported to be effective at preventing reactivation
(LAS Vol 47#6, Dec 1997) Wagner, WFUSM. CLDavis 2007

# Shigellosis

- Shigella is transmitted from man to NHPs -is not a disease found in wild primates
  - Affects primates only
- Shigella flexneri is most common and most pathogenic - other species can cause enteritis, including S. sonnei, S. boydii, S. dysenteriae
- Gram negative, nonmotile, nonspore-forming pleomorphic rod
- Spreads by fecal-oral route carriers are common with stress precipitating disease in carriers
- Edematous mucopurulent or mucohemorrhagic colitis; thickened colonic mucosa with mucosal fibrinonecrotic to suppurative exudate
  - Limited to colon, may be focal or diffuse
  - Associated with periodontitis –lymphoplasmacytic and PMNs



# Campylobacteriosis



 Colon crypt abscesses and mucosal hyperplasia; involves SI and colon,

- Colonizes the mucous coat on surface and in crypts
- Adhesion mediated by adhesins, hemagglutins, flagella

# Campylobacteriosis

- *C. jejuni* (hipurate +) and *C. coli* (hipurate -), both are urease negative
- Curved gram neg rods, comma- or S-shaped, microaerophilic (best in 5% oxygen)
- Common; acute, recurrent, and chronic carrier states
- Vary from edema with fluid contents to catarrhal enteritis to dysentery
- Colonizes the mucous coat on surface and in crypts, adhesion: mediated by adhesins, hemagglutins, flagella
- Toxin production: fluid secretion, endotoxin and cholera-like entero-toxin binds to GMI ganglioside Wagner, WFUSM, CLDavis 2007

#### Campylobacter fetus ss jejuni or coli



- Curved gram negative rods with polar flagellum
- Microaerophilic
- Warthin Starry Stain

#### Helicobacter pylori



- Gastritis in rhesus, cyno and pig tail
- Usually no clinical signs; occasionally vomiting
- Warthin Starry stain for curved gram negative rods

#### Helicobacter pylori

- What are similarly appearing nonpathogenic organisms also present in the majority of NHP's?
- Gastric spirillum, Gastrospirillum hominis, Helicobacter heilmanni, Helicobacter Heilmanni Like Organisms
- What are the Helicobacter species most commonly identified in the gastric mucosa of NHP's and humans?
- H. pylori and H. heilmanni
- Tissue urease test is used in humans for detection of bacterial urease activity in gastric mucosal biopsy specimens. This is NOT effective for diagnosis of H. pylori in cynos because H. heilmanni also produces urease. H. heilmanni is NOT prevalent in humans but is in NHP's
- (Vet Path; 36, Jan 1999)

# Yersinia - Hemorrhagic erosive typhlytis/colitis



#### Yersiniosis

- What is the resevoir for this infection?
  - Wild birds and rodents; feed contamination
- Outbreaks often associated with wet/winter weather (contact with rodents and birds searching for dry/warm environments) and ingestion of contaminated feed
- Multifocal to diffuse, hemorrhage and necrosis, often transmural, small intest or colon; hepatitis, splenitis, widespread bacteremia
- Ulcerative diptheric membrane (Shaggy carpet appearance)
- Large colonies of gram bacteria in necrotic centers
  - Y. enterocolitica; Y. pseudotuberculosis
- What special culture technique can enhance isolation of Yersinia?
  - Cold enrichments (4 degrees C for 4 weeks)

#### Yersiniosis





- Colon from rhesus
- Histo: Necrotizing colitis
- Multifocal necrotizing inflammation, primarily multinuclear giant cell response
- Numerous gram negative bacterial Wagner, WFUSM. CLDavis 2007

#### Melioidosis (*Burkholderia* [*Psuedomonas*] *pseudomallei*) -Whitmore's disease

- Environmental saprophyte in SE Asia
- Acquire infection by inhalation of dust, ingestion of contaminated water, and contact with contaminated soil especially through skin abrasions
- Can remain clinically latent for years
- Causes absesses and granulomas in a number of tissues
- Report to CDC



#### Simian Varicellovirus Alphaherpesvirinae



- Patas monkey presented with depression and respiratory difficulty
- Face with edema and crusting
- Rash, subcutaneous hemorrhage and petechiation

#### Simian Varicella Virus



- Focal necrosis and hemorrhage in many organs
- Antigenically related to human varicella zoster virus (chicken pox)
- Highly infectious
- Viral latency in the dorsal root ganglia even without clinical signs
   Wagner, WFUSM. CLDavis 2007

#### Simian Varicella Virus



Liver: focal necrosis and INIB
### Simian Varicella Virus Alphaherpes virus

#### Historically

- Cercopithecus herpesvirus 6=Liverpool Vervet (African Green monkey)
- Cercopithecus herpesvirus 7=Delta (Patas and African Greens)
- Cercopithecus herpesvirus 9=Medical Lake Macaque (Macaques)
- Molecular Biology Profiles indicate a single SVV taxonomic group

### B Virus Cercopithecine herpesvirus-1 (Herpesvirus simiae)





### **B** Virus

- Alpha herpesvirus
- Mild or subclinical in macaques
- Can produce severe symptoms; massive ulceration throughout GI tract\*
- Latent virus found in sensory ganglia
- Treatment is possible; acyclovir, gancyclovir, valcyclovir
- Human counterpart: Herpes simplex-NW, Chimps and Gibbons

(\*LAS 1997, O'Sulivan and Jayo)

### Disseminated Herpesvirus Infection

LAS 1997, O'Sulivan and Jayo

## Herpes B –liver necrosis and inclusion bodies



Vet Path 1997;34:405

### Herpes B (Cercopithecine Herpesvirus 1)

- Macaques are the natural hosts
- Transmission by bites, wounds, scratches, and splashes
- Venereal transmission in the natural host





### Herpesvirus Papio 2 in Baboons



- Outbreak of vesicular disease in baboon colony originally attributed to SA8
- Oral and genital mucosa
- Lesions usually resolve spontaneously but may recur
- Can cause scarring which mechanically interferes with breeding
- Venereal transmission reported
- May be good model for H. simplex 2 in humans

### Pentastome larvae Tongue worms



### Pentostomes



- Where are the adult forms found?
  - Armillifer in Python
  - Porocephalus in Boa
- Which Pentostome tends to be found in OWM?
- Armillifer=OW
- Which Pentostome tends to be found in NWM?
- Porocephalus=NW
- Armillifer is more heavily segmented

# How does the snake become infected?



### Tetanus Clostridium tetani



Must diagnose clinically
Can get disease more than once since it is non immunizing disease

- What is the cause of this condition in a young rhesus monkey?
- It is an obligate anaerobe that contaminates wounds
- Can cause post partum infections
- Begins in upper limbs then lower limbs
- Stiff gait, trismus, extensor rigidity, opsithotonus
- Usually fate in 1-19 days due to respiratory paralysis and exhaustion

### Histoplasmosis



- Small cutaneous papules and pustules with reddish brown exudate, ulcerations and gramulomas
- Affects skin, lymph node and bone
- What is the genus and species of the olive baboon?

### Histoplasma capsulatum var dubosi



Histiocytes packed with yeast form of the organism LAS, 1991 GMS stain: Organisms in pairs and connected by narrow stalk and short chains Wagner, WFUSM, CLDavis 2007

### Phytobezoar

- Wood shavings in the stomach of a rhesus monkey
- Trichobezoar can be caused by excessive grooming
- Enrichment objects have been ingested with dire consequences (CT, 1996, traumatic perforation from tire)



CLDavis 2007

### Moraxella (Branhamella) catarrhalis

Gram negative diplococci
Bloody nose syndrome in cynomolgus macaques
Epistaxis and periorbital edema

•May be associated with low humidity

•This condition also reported in association with Measles

•(LAS vol 49 #1, 1999)



### Gastric Infarction in Cyno's





- Striking and unexpected finding at necropsy
- Gastric necrosis, hemorrhage and edema
- Thrombi in gastric microvasculature
- (Vet Path, 1996) Wagner, WFUSM. CLDavis 2007

### Pediculosis





- Nits on hair
  Bodicious longic
- Pedicinus longiceps

### Rhesus esophogus White floculent material



### Candida albicans



#### Tongue with PAS stain

#### Esophagus with GMS stain

### Candida albicans



- Candidiasis
- Septate pseudohyphae and oval budding blastophores in superficial epithelium
- Common in immunosuppressed animals-SRV, SIV

## This tissue is from a cynomolgus that was being used as an animal model. What is the condition?



#### **Atherosclerosis and Myocardial Infarction**

### Acanthocephalans





- Thorny Headed Worms
- Intermediate Host
  - Blatella germanica and beetles
- Prosthenorchis elegans
  - Cecum and Colon
  - P. Spirula
    - Terminal Ileum

### Acanthocephalans

- What form of the parasite is found in the cockroach (IH)?
  - Cystacanth larvae
- Do these parasites usually cause clinical sighs?
  - Yes-Adults often penetrate the mucosa and invade the muscle layers. The attachment sites may perforate
- Would this infection be detected by fecal floatation?
  - No-Eggs are thick walled and embryonated and do not float. Direct smear or sedimentation is necessary for detections

### Attaching and effacing E. coli



Wagner, WFUSM. CLDavis 2007

Hemorrhagic typhlocolitis(LAS, 1996)

### Simian Bone Disease



### Simian Bone Disease

Nutritional secondary hyperparathyroidism which results in bone resorption and fibrous replacemet

- Diet deficient in vitamin D3
- Calcium/Phosphorus imbalance from feeding excessive fruit
- New World Monkeys cannot utilize D2, they need D3 in their diet
- Fat soluble D2 is ergocalciferol; from UV radiation of plant sterols
- D3 is colecalciferol from UV radiation of skin

#### Adenoviral Pancreatitis in a rhesus



Thickened pancreas from rhesus monkey
Nodular lumpy pancreas looks like neoplasm

### Simian Adenovirus 23



- Histology: INIC vary from small eosinophilic to large basophilic/smudgy looking
- EM: Paracrystalline array of virus
- (LAS, 1991)

#### Strongyloidiasis



- Lung with pulmonary hemorrhage
- Small intestine with hemorrhagic enterocolitis
- What is the etiologic diagnosis?
- Strongyloidiasis (threadworm); nematode
- Larva rather than eggs are passed in the feces; sometimes a severe inflammatory response to the larva

### Strongyloidiasis



- Strongyloides cebus in NWP; S. fullerborni in OWM; S. stercoralis in apes and man
- Transmission oral and skin penetration
- Autoinfection; the third stage larva pass out through the anus and penetrate perianal skin
- What causes pulmonary lesions?
- Migrating larvae cause hemorrhage in the Wagner, WFUSM. CLDavis 2007

### Strongyloidiasis

Larva are passed in the feces; NOT eggs

- Adult females burrow into the mucosa of the proximal small intestine, forming tunnels in which ova are deposited. Larva hatch and break out of the tunnels into the lumen. In hyperinfection the first stage larva develop rapidly to third stage rhabditiform larva and penetrate bowel before being passed out in the feces. This process may affect the full thickness of the colon and sometimes the ileum.
- Only the females are parasitic

### Simian Hemorrhagic Fever



- Several rhesus monkeys died with hemorrhage
- Petecchial hemorrhage on mucosal and serosal surfaces of the duodenum; hemorrhagic necrosis of the proximal duodenum with sharp demarcation at pylorus
- Splenomegaly with purple mottled hemorrhagic surface
- What is a likely diagnosis?
- Togaviridae; arteriovirus
- Wagner, WFUSM. CLDavis 2007 Not a zoonotic disease; man and NWP not affected

### Simian Hemorrhagic Fever



- Splenomegaly with purple mottled surface; the spleenic lymphoid follicles are ringed with a zone of bright red hemorrhage. The white pulp is greatly reduced.
- Patas and possibly other african species carry this disease asymptomatically and are persistently viremic
- Hepatic necrosis with Councilman's bodies is NOT a feature of SHF, unlike other hemorrhagic fevers
- Must report to CDC special pathogens branch
- Culture in MA-104 cells

### Balantidiasis-Balantidium coli



- Isolated from the colon of a chimp
- Reported in chimps, OWM and NWM
- Diagnosis: identification of trophozoites in wet mount of feces or impression smear of colonic mucosa
- Has macro and micro nuclei



### Amyloidosis



### Large intestine -Severe, diffuse amyloidosis



- Deposition of SAA in multiple tissues associated with numerous chronic inflammatory diseases
- Rhesus are most commonly affected
- Chronic diarrhea, weight loss, hepatomegaly, osteoarthritis
- Amyloid deposition in the spleen, lymph nodes, liver, lamina propria of GI tract
- Stains with Congo Red
- Rx: DMSO and small-molecule drugs that prevent SAP from binding to amyloid deposits
#### Hepatic Lipidosis



# Fatal Fasting Syndrome of Obese Macaques

- Anorexia and acute weight loss from any cause in obese monkeys; affected animals still have abundant fat deposits
- Clinical Findings: Anorexia, lethargy, azotemia or sudden death in obese macaques
- Control: Avoid feeding to levels conducive to obesity



- Liver is enlarged with rounded edges, pale and friable, with a diffuse fatty change.
- focal to extensive areas of fat necrosis.

#### Panniculus - Diffuse fat necrosis "Fatal fasting syndrome of obese macaques"



# Fatal Fasting Syndrome

#### Treatment:

- PEG tube (percutaneous endoscopic gastrotomy) has been reported to be successful in treating fatal fasters with calorically dense diets (LAS 38(4), 1999)
- Naso and orogastric tubes are used for short term administration of liquid diets. These rarely supply the caloric and protein requirements needed to reverse lipid accumulation
- Hepatic lipidosis in humans, dogs and mice causes hepatomegaly without clinical disease
- In macaques, cows and cats, hepatocyte lipid accumulation can lead to clinical disease
  - In these species, obesity and weight loss seem to be important predisposing factors in the development of hepatic lipidosis
- Kidneys also pale, renal tubular epithelium fattty vacuolar changes and often azotemia Wagner, WFUSM. CLDavis 2007

# Correlation between Leptin and Bodyweight in Monkeys



Wagner et al. ILAR

Wagner, WFUSM. CLDavis 2007

### Changes in Glucose and Insulin Responses to a IV GTT



Wagner et al. ILAR J, 2006

#### **Insular Amyloidosis**





#### Immunostain

- What is the material in the abnormal islet?
  - Amyloid Immunostaining for IAPP (Vet Pathol 1996;33:479)
- What special stain is used for amyloid identification?
  - Congo Red
- What technique can be used along with Congo Red to assist in identification of amyloid?
  - Polarized light

#### Mycobacterium avium, M. intracellulare





- Gross ileum, thick ruggose lesions
- Histo, H&E, diffuse histiocytic infiltrate in lamina propria
- Histo, Zeil Neilson: macrophages packed with organisms
- Giant cells are NOT usually features of these lesions

#### Endometriosis



- Implantation of normal
- Implantation of normal endometrial tissue in ectopic locations
- Endometrial epithelium and stroma present
- Rx?
  - Leuprolide

### Immunodeficiency Syndromes

- Simian Immunodeficiency Viruses
  - Lentiviruses with antigenic and pathologic similarities to HIV
  - Not common as a cause of naturally occurring disease
- Simian Retroviruses 1 and 2
  - Type D retroviruses
  - Called "Simian AIDS", produces a chronic wasting disease, with immunosuppression, noma, and retroperitoneal and subcutaneous fibromatosis
- Simian T-Lymphotropic Virus I
  - Retrovirus with almost complete homology to HTLV-I
  - No natural disease has been associated with it
- Simian Foamy Virus
  - Spumavirus subgroup of retroviruses
  - Prevalent in many NHPs, different serotypes but all seem to be nonpathogenic in host but cytotoxic in cell cultures
  - Humans have seroconverted with no signs Wagner, WFUSM. CLDavis 2007

#### **Retroperitoneal Fibromatosis**



- Fibrous proliferation around the mesenteric root beneath the serosal surface
- Can be localized or generalized, eventually the entire GI tract can become encased
- Associated with SRV 2
- Can cause intestinal obstruction

#### **Retroperitoneal Fibromatosis**



- Simian RF is a vascular fibroproliferative neoplasm which has many morphological and histological similarities to Kaposi sarcoma of humans
- Kaposi sarcoma herpesvirus-related sequences found in RF macaque tissue
- RF associated herpesvirus of rhesus macaques is a gammaherpesvirus closely related to human herpesvirus-8
   Wagner, WFUSM. CLDavis 2007

# Cytomegalosvirus







- An SRV positive rhesus presented with CNS and respiratory tract signs and orchitis
- Disease only in fetuses and immunodeficient animals
- Large basophilic INIB and granular eosinophilic ICIB in mesenchymal cells (not surface epithelium like other herpes viruses)
- Betaherpesvirus

Mesenteric LN – Lymphadenopathy in a SRV+, M avium + NHP

# Mycobacterium avium, M. intracellulare





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   Wagner, WFUSM. CLDavis 2007

### **Necrotizing Oral Disease**





- ANUG=Acute
  Necrotizing Ulcerative
  Gingivitis
  - Vincents Stomatitis
  - Necrosis and ulceration of the interdental papillae accompanied by bleeding
- Noma=Greek-to devour
  - Acute gangrenous process of oral cavity involving gingiva, cheeks, lips leading to bone denudation and sequestrum formation
  - Severe oral facial scaring and disfigurement

# NOMA



Necrotizing lesion affecting mucous membranes and bony structures of the upper dental arcade

- Associated with SRV type 2 and HIV or measles in humans
- Mixed bacterial infection
- Poor response once osteomyelitis present

Submandibular salivary glands: Multifocal lymphoid hyperplasia Simian type D Retrovirus 1 or 2



#### Gastrodiscoides hominus



#### Diverticulosis



- Usually no clinical signs
- Gross: saccular protrusions along taenia coli, muscular hypertrophy
- May be come impacted and inflamed
- Etiology unknown; not common

#### Vitamin C deficiency OWM



- Those species requiring vitamin C in the diet lack what enzyme?
  - L-gulonolactone oxidase (necessary for ascorbic acid formation)
- How does this disease present in OWM?
  - Gingival hemorrhage, loose teeth
  - Rubperiosteal hemorrhage, abnormal ossification of bones
  - Epiphyseal fractures and anemia

# Vitamin C deficiency in NWM



- What is this condition in the squirrel monkey
  - Cephalohematoma; hyperostosis of the skull
- What is the cause ?
  - Vitamin C deficiency

#### Nocardia asteroides



Lung tissue gram stain



Acid fast organisms

- Monkey presented with dyspnea, cough and weight loss
- Acid fast stain
- Aerobic, gram positive, partially acid fast filamentous organism

Often associated with cellular deficiency Wagner, WFUSM. CLDavis 2007

#### Dipetalonema gracile (peritoneal)



- Filarid parasite
- Microfilaria are found circulating in the blood and can be identified by the pattern of acid phosphatase staining
- Transmitted by blood sucking insects: midge, mosquito Wagner, WFUSM. CLDavis 2007

#### Dipetalonema gracile



- Male is smaller than female
- D. perstans, D. streptocerca, D. rodhaini are zoonotic (LAS 46(3),96)
- What are the genus/species most commonly found
  - D. gracile (peritoneal)
  - Tetrapetalonema (SQ)
- Granulomas and arterial thickening in the spleen have been reported in Cyno's infected with what species?
  - Edesonfilaria microfilarias

# Liver, Cyno: Edesonfilaria



#### **PCB** Toxicity



- A rhesus presented with photophobia, patchy hairloss and diarrhea. On necropsy the stomach looked like this. What has been reported to cause this condition?
  - PCB toxicity resulting from ingestion of concrete sealant and percutaneous absorption of compounds containing PCB's.
- Histopathology: meibomian gland ductal squamous metaplasia; stomach ulcers and hemorrhage, epithelial hyperplasia, cystic dilation, fibroplasia of GI mucosa
   Wagner, WFUSM. CLDavis 2007

#### Enterobius vermicularis



- This was found on an anal tape test from a chimp. What is the genus and species?
- An oxyurid nematode (pinworm) causes proctitis in chimps
- Male has spicules on end and esophogus has double bulb
- What is the pinworm in NWM?
  - Trypanoxyuris

#### **Gluten Enteropathy**



- Histology of the SI of a rhesus that presented with progressive weight loss in spite of increased appetite and diarrhea. What is the cause of this?
- Gluten sensitive enteropathy (celiac sprue in humans)
- Villous atrophy of duodenum and jejunum, crypt hyperplasia and plasmacytic-lymphocytic infiltrate of lamina propria (SI look like colon) (LAS 1988;38:592)
   Wagner, WFUSM. CLDavis 2007

#### **Gluten Enteropathy**



- Histology of intestine after dietary intervention
- Gluten is a water insoluble protein found in certain cereal grans, particularly wheat, barley and rye
- Carbohydrate and fat malabsorption respond to gluten exclusion
   Wagner, WFUSM. CLDavis 2007

# Entamoeba histolytica (sarcodine protozoa)







- Gross: Colitis
- Histology: classic flask shaped ulcers
- Trophozoites seen in mucosa, submucosa and may invade
   lymphatics or vessels to form amoebic abscess
   Wagner, WFUSM. CLDavis 2007

# A fatal disease occurred in a colony of these animals



#### Simian Ebola-like filovirus



- Histology liver: ICIB
- EM of virus particle
- What is the disease?
  - Simian Ebola-like filovirus (Ebola-Reston)
  - This virus is antigenically distinct from African filoviruses

#### Simian Ebola-like filovirus

- Transmission: aerosol and contact
- Fatal disease in Philippine cynomolgus. 5-10% seropositivity in rhesus, african green, and cynomolgus imported Philippines, Indonesia, China, Mauritius
- Humans can become infected but do not become ill
- Clinical signs for NHP: fever, weight loss, anorexia, hemorrhage, rash, diarrhea, maculopapular rash, splenomegaly, widespread petecchial hemorrhages, interstitial pneumonia

#### Simian Ebola-like filovirus

- Pathology: lymphoid necrosis, massive fibrin deposition in spleen, hepatic necrosis, interstitial nephritis, amophilic cytoplasmic inclusion bodies in hepatocytes, extensive viral replication in tissue macrophages and interstitial fibroblasts.
- Much of the necrosis may be secondary to ischemia
- Cells in affected areas often contain ICIB. This is one of the most important lesions to differential Ebola from SHF or Marburg.
### Rodentolepis nana (Hymenolepsis nana) dwarf tape worm



- Egg-thick shell, 3 pairs of hooklets, and POLAR FILAMENTS
- Spread by fleas, roaches, beetles
- Direct or indirect life cycle?
  - Both; only cestode with direct life cycle
  - Zoonotic potential because of direct life cycle Wagner, WFUSM, CLDavis 2007

### Toxoplasma gondii



#### Hepatic necrosis



### PAS liver



Brain Giemsa-Trophs

- Outdoor monkey died with CNS signs
- Sporozoan protozoan
- NWM more susceptible than OWM

### Toxoplasma gondii

### Transmission:

 food contaminated by cat feces or ingestion of meat containing cysts (many NHP catch and eat rodents)

- Necrosis and inflammation of liver, spleen, lymph nodes, heart, lung, adrenal, intestine, muscle, brain
- Individual organisms, trophozoites, (banana shaped); cyst in tissues
- Sabin-Feldman Dye Test
- Toxoplasmosis stains with what?
  - H&E and is gram negative
  - Doesn't stain well with Goodpasture

# Larval Cestodes



Pseudophyllidean
cestodes in the family
diphyllobthriidae which
form spargana
(pleurocercoid larvae)

- Cyclophyllidean cestodes form cysticercoid larvae, coenurus larvae or hydatid larvae are found in various tissues
- Transmission of eggs or infected intermediate host (often an arthropod) Wagner, WFUSM. CLDavis 2007

### Coenurus serialis (Multiceps)



# Cysticercus cellulose beef tapeworm





# Echinococcus granulosa



- Hydatid disease
- Adult in canine species
- Entire abdoman seeded
- "Hydatid sand"

# Zinc Toxicity; Copper Deficiency



White rhesus with pigmented eyes-"fading infant" Excess zinc from chewing on galvanized bars; Zinc chelates copper Wagner, WFUSM. CLDavis 2007

### Malaria



A blood smear from a NHP that exhibited anorexia, fever, splenomegaly and anemia Wagner, WFUSM. CLDavis 2007

## Malaria

- OWM: Plasmodium cynomolgi, P. inui, P. knowlesi, P. gonderi
- NWM: P. brazilianum, P. simium
- Man: P. vivax, P. falciparium, P. malariae
- Transmitted by anopheles mosquito in wild
- Transmitted at birth or by percutaneous inoculation in the laboratory
- The periodic clinical signs are a result of the release of organisms from RBC's (schizogony).
- Gross: liver, lungs and spleen are gray and blood is thin

# Hepatocystis kochi





Trophozoites in blood smear

- H. simiae (african); H. taiwanesnsis, H. semnopitheci (asian)
- Liver cyst rupture to release merozoites which infect RBC
- Trophozoites occur in RBC; Transmission: midges
- Malarial symptoms?
  - No schizogency occurs in liver not blood. Heavy parasitemia can alter hemogram since RBC's don't lyse and are counted as nucleated RBC's

## Hepatocystis kochi



2-4 mm opaque cysts in the liver from what?

Ruptured cyst result in eosinophilic granulomas which resove into small circular scars in the liver

# Strabismus and Anisocoria

