THANK YOU!

- 2 x 2 slides and accompanying information provided by Diane Forsythe and Mary Grant of NIEHS/NIH
- Thanks to Beth Ford, Scripps Research Institute for organizing and compiling this information into computerized format.
- Thanks to my colleagues at WFUSM for contributing slides
- Disclaimers
  - This is not an ACLAM sanctioned presentation
  - All information is deemed reliable and correct, no warranty for accuracy
  - No information presented is known to be specifically included in ACLAM Board examinations

**Taxonomy**

- **Order** - Primates
- **Suborder** -
  - Prosimii
  - Lemuroidea
  - Lorisoidea
  - Tarsioidea (separate infraorder)
- **Anthropoidea**
  - **Infraorder** -
    - Platyrrini - NWM
    - Family - Callitrichidae, Cebidae
    - Cercopithecidae - OW
      - Superfamily - Cercopithecoidae, Hominoidea
      - Family - Cercopithecidae, Colobinae
      - Macaques, baboons, mangabeys, vervets

**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

**Old World Monkeys - 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 comma-shaped 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

**NHP primary enclosure space requirements**

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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

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

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
- PEG tube (percutaneous endoscopic gastrotomy) with calorically dense diets has been reported to be successful in treating fatal fasters (LAS 38(4), 1999)
- Liver is enlarged with rounded edges, pale and friable, with a diffuse fatty change.
- Focal to extensive areas of fat necrosis.

Fatal Fasting Syndrome
Hepatic lipidosis

- Genus, species?
  - Macaca mulatta
- Common name?
  - Rhesus
Islet amyloidosis

- Islet amyloidosis; amyloidosis of the islets of langerhans
- This lesion is associated with Type 2 diabetes in man and NHP
- What pancreatic lesion would you expect to see in Type 1 diabetes?
  - Loss of beta cells - no amyloid (LAS 1996;46:36)

Type 2 Diabetes

- What macaque has a high incidence of type 2 diabetes?
  - Macaca nigra (Celebes black ape)
- Is the disease in cyno's associated with amyloid deposition in other organs?
  - No
  - (Vet Path 33: 1996)

Insular Amyloidosis

- 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

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

Atherosclerosis and Myocardial Infarction

- 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

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 36d
Sex Skin and Ovarian Morphology

Breast Cancer in Macaques
- Lifetime incidence is around 6%
- Tumors have similar histology to breast cancers in women: Ductal hyperplasia, ductal carcinoma in situ, and invasive ductal carcinoma predominate
- Tumors progress to metastatic disease

Vulvar papilloma
*Macaca fascicularis* papillomavirus
- 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.

Polycystic Ovarian Syndrome
- Clinical signs
  - Hyperandrogenemia
  - Central obesity
  - Insulin resistance
  - Irregular, infrequent menstrual cycles
  - Endometrial hyperplasia
  - Elevated LH (not documented here)
  - Hirsutism (in people)
- Pathology
  - Uterus enlarged, endometrial polyps
  - Ovaries contained many 2-3 mm follicles with any corpora lutea
  - Inducible by in utero androgen exposure in macaques
  - Early origins of polycystic ovary syndrome. Reproduction, Fertility and Development 17:349-360, 2005

Endometriosis
- Implantation of normal endometrial tissue in ectopic locations
- Endometrial epithelium and stroma must be present histologically to differentiate from endometrial carcinoma

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

Kavanagh et al. JMP, 2006
Pentostomes

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

How does the snake become infected?

Gross of Stomach from a Rhesus

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

Nochti nochti

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

Physalopera tumefaciens

- Poorly differentiated mucinous carcinoma; mass without structure
- Carcinomas arise in association with pre existing chronic ulcerative colitis
- These lesions often metastasize

Colonic Adenocarcinoma
Chronic Colitis
Shigelllosis

- Etiology: Shigella flexneri, sonnei
- Confirm Diagnosis: Macconkey, XLD
- Treatment: Enrofloxacin reported to be effective at preventing reactivation
  *(LAS Vol 47#6, Dec 1997)*

Campylobacter (Vibrio) fetus ss jejuni or coli

- Fibrinonecrotic colitis
- Curved gram negative rods with polar flagellum
- Microaerophilic

*Warthin Starry Stain*

Campylobacteriosis

- Colon crypt abscesses and mucosal hyperplasia; involves SI and colon, may see pericholangial hepatitis, organism thought to hide in biliary tract
- Colonizes the mucous coat on surface and in crypts
- Adhesion mediated by adhesins, hemagglutins, flagella

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
  *Whary and Fox, Comp Med 2004*

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
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)

Gastric Infarction in Cyno’s
- Striking and unexpected finding at necropsy
- Gastric necrosis, hemorrhage and edema
- Thrombi in gastric microvasculature
- (Vet Path, 1996)

Yersiniosis
- Colon from rhesus
- Histo: Necrotizing colitis
- Multifocal necrotizing inflammation, primarily multinuclear giant cell response
- Numerous gram negative bacterial colonies
- What is the reservoir for this infection?
  - Wild birds and rodents; feed contamination
  - Ulcers are found over peyers patches
  - Ulcerative diptheric membrane (Shaggy carpet appearance)
  - Y. enterocolitica; Y. pseudotuberculosis
  - What special culture technique can enhance isolation of Yersinia?
    - Cold enrichments (4 degrees C for 4 weeks)

Rhesus esophagus
White floculent material

Candida albicans
- Tongue with PAS stain
- Esophagus with GMS stain
PCB Toxicity (rare)

- 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

Diverticulosis

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

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)

Gluten Enteropathy

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

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

Acanthocephalans

- Thorny Headed Worms
- Intermediate Host
  - Blatella germanica and beetles
  - Prosthennorchis elegans
  - Cecum and Colon
- P. Spirula
  - Terminal Ileum
**Attaching and effacing E. coli**
- H and E of colon
- Tolidine blue stain of colon
- EM; Bacilli attached to shallow cup like projections of enterocyte apical membranes
- Hemorrhagic typhlocolitis
- (LAS, 1996)

**Gastrodiscoides hominus**
- Most common trematode of OWM
- Found in cecum and colon
- Orange red fluck
- Snail is IH; encysts on vegetation

**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 lung

**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

**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 esophagus has double bulb
- What is the pinworm in NWM?
- Trypanoxyuris
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

Hymenolepis nana
dwarf tape worm
- Egg-thick shell, 3 pairs of hooklets, and POLAR FILAMENTS
- Spread by fleas, roaches, beetles
- Both direct and indirect life cycle; only cestode with direct life cycle
- Zoonotic potential because of direct life cycle

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

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

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

Hepatocystis kochi
- 2-4 mm opaque cysts in the liver.
Hepatocystis kochi

- H. simiae (african); H. tawanesensis, H. semnopithecis (asian)
- Liver cyst rupture to release merozoites which infect RBC
- Trophozoites occur in RBC
- Trophozoites in blood smear
- Transmission: midges
- Malarial symptoms?
  - No - schizogony occurs in liver not blood. Heavy parasitemia can alter hemogram since RBC's don't lyse and are counted as nucleated RBC's
- No evidence that it infects humans
- Control can be achieved though the development of infestation free environments by rearing babies in isolation from their mothers, ivermectin may be effective.

Tissues from a Rhesus Monkey

- Brain, meningitis
- Lung, pneumonia
- Abdomen, fibrinopurulent serositis

Streptococcus pneumoniae

- Frribinopurulent serositis
- Diagnosis?
  - What is the reagent used to test for group specific antigens?
  - What is the optochin test? Growth of this organism in culture is inhibited by what specific reagent?
  - Optochin (ethyl hydrocuprein)
  - frribinopurulent serositis 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 the upper respiratory tract, middle ear or orally
  - Pneumonia may be accompanied by meningitis
  - Primary cause of bacterial meningitis; low mortality but high morbidity, usually rapidly progressive, and treatment not certain
  - Vaccination with a human polyvalent vaccine was successful in preventing further cases in an outbreak involving chimpanzees; a polyvalent pneumococcal vaccine was ineffective.

Gram stain of lung impression smear

Streptococcus pneumoniae

Pneumonyssus simicola

- Pulmonary acariasis
- Inhalation is usually symptomatic, but reported to be associated with pneumothorax and pulmonary arteries 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, bululous emphysematous lesions and hemorrhagic lesions may be seen in some cases
- Histologically, localized bronchiolitis, peribronchiolitis, focal lobular pneumonia, alveolar collapse or consolidation and sometimes bronchiectasis
- Macrophages, whose cytoplasm is laden 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

Mycobacterium tuberculosis

- Mycobacterium tuberculosis
- Brain, meningitis
- Lung, pneumonia
- Abdomen, fibrinopurulent serositis
- Pneumonyssus simicola
- Pulmonary acariasis
Mycobacterium tuberculosis

- Histo Lung: necrosis and consolidation
- Tracheal Wash: acid fast organisms
- Lesion: tuberculoid granulomas characterized by caseous centers, giant cells, lymphocytes and epithelioid cells
- Location of acid fast organisms: caseous center

Tuberculosis

- Mycobacterium tuberculosis, M. bovis, M. avium-intracellulare (also many atypical mycobacteria: M. africanum, M. kansasii, M. simiae, M. chelonae)
- Aerobic, slightly curved or straight, occasionally beaded, rods (neither gram-negative or gram-positive)
- 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

Tuberculin Testing and Interpretation

- Read: 24, 48, 72 hrs
- Grade 1-5; 4 and 5 positive
- Meaning of Negative Test
  - 0 (negative) No rxn
  - 1 (negative) Bruise from inoculation; no swelling
  - 2 (negative) Variable erythema; no palpebral swelling
  - 3 (suspect) Variable erythema with minimal swelling, or no erythema and slight swelling
  - 4 (positive) Obvious swelling and dropping of eyelid with variable erythema
  - 5 (positive) Swelling and/or necrosis with eyelid closed

TUBERCULIN SKIN TEST REACTION GRADES

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

Moraxella (Branhamella) catarrhalis: Bloody nose syndrome

- Gram negative diplococci
- Bloody nose syndrome in cynomolgus macaques
- Epistaxis and periorbital edema
- May be associated with low humidity
- Differentiate from viral hemorrhagic syndromes
- Response to penicillin
- Associated with low humidity
- This condition also reported in association with Measles

(LAS vol 49 #1, 1999)
**SPF Levels**

Table 1 SPF level designations:

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<th>STLV</th>
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*SRV: simian retrovirus; STLV: simian T-lymphotropic type I leukemia virus.*

**DNA Viruses**

- **Alpha Herpesviruses**
  - Cercopithecine HV1
  - Cercopithecine HV2
  - Cercopithecine HV 6,7,9
  - Saimiri HV 1
  - Human HV 1.2
  - Human HV 3
- **Beta herpesviruses**
  - Cytomegaloviruses
- **Gamma Herpesviruses**
  - Epstein-Barr V
  - Saimiri HV2
  - Ateline HV2
  - Rhabdovirus

**Pox viruses**

- Monkey pox
- Yaba pox
- Tana pox
- Marmoset pox
- Molluscum contagiosum
- Adenoviruses
- Papaviruses: Polyomavirus macacae (SV40)
- Papillomavirus
- Parovirus
- Hepadnavirus (Hep B)

**B Virus**

Cercopithecine herpesvirus-1 (Herpesvirus simiae)

Herpes B virus, Cercopithecine herpesvirus 1

- Occurs as a common, latent and asymptomatic infection of Asian macaques and has been demonstrated in a number of macaque species. Latent virus found in sensory ganglia. Although rarely responsible for disease in the natural host, inadvertent infection of humans results in a disseminated viral infection characterized by ascending paralysis and high case fatality rate. Infection of nonmacaque species has reportedly produced fatal disease.
- The incidence of infection in immature macaques is low and increases rapidly with sexual maturity, approaching 80-90% in some colonies by 3-4 years of age. The percentage of animals with active oral lesions is much less and found in one study to be 2.3%. The virus is transmitted via biting, sexual behavior and by fomites. Animals remain infected for life and periodically shed the virus in oral and genital secretions.
- Disseminated infection in macaques is rare but when it occurs it is usually fatal.
- Can produce severe symptoms; massive ulceration throughout GI tract
- The pathogenesis is similar to Herpes simplex infection in humans

Herpes B (Cercopithecine Herpesvirus 1)

- Macaques are the natural hosts
- Transmission by bites, wounds, scratches, and splashes
- Venereal transmission in the natural host
- Treatment is possible; acyclovir, gancyclovir, valcyclovir
**Herpesvirus Papio 2 in Baboons**

- Outbreak of vesicular disease in baboon colony originally attributed to SA8 (CHV2)
- Endemic in AGM
- 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

**Simian Varicellovirus Alphaherpesvirinae**

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

**Simian Varicella (CHV 9)**

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**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

**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)
- Beta herpesvirus
Retroperitoneal Fibromatosis Herpes Virus (RFHV)

Rhesus Rhadinovirus (RRV)

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 ludovicianus*
- Recent outbreak associated with what small animal?
- Gambian rats also associated with outbreak in Midwest in June 2003.

BEMP and YABA
- Tumor like lesions
- Histiocytes with eosinophilic ICIB
- ICIB=YABA
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

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

Molluscum contagiosum

- Marked acanthosis with large Basophilic ICIB, more prominent Toward the skin surface
- Molluscum bodies=basophilic structures

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)
RNA Viruses

- Hemorrhagic Fever
  - Simian hemorrhagic fever
  - Flaviviruses
  - Marburg virus
  - Ebola/Ebola-Reston
- Myxoviruses
  - Paramyxoviruses
    - Measles
    - Mumps
  - Respiratory Syncytial (Para)influenza
- Retroviruses
  - Type D-SRV
  - Type C-STLV
  - SIV
  - Foamy virus
  - Rabies - Rhabdovirus
  - Enterovirus or picornavirus - HepA
  - Calicivirus-like - HepE

Parvovirus

<table>
<thead>
<tr>
<th>Family</th>
<th>Genus</th>
<th>Type species</th>
<th>Hosts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parvovirus</td>
<td>Parvovirus</td>
<td>Mouse parvovirus</td>
<td>Murine</td>
</tr>
</tbody>
</table>

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 surfaces of the proximal duodenum; hemorrhagic necrosis of the proximal duodenum
- What is a likely diagnosis?
- Togaviridae; arterivorous
- Not a zoonotic disease; man and NWP not affected

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 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 asymptptomatically 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

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, amphilic 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.

**Pathology, Measles**

- Giant cell pneumonia
- INIB and ICIB within syncitial cells
- Giant cell pneumonia with inclusion bodies

**Measles**

- Etiology: Rubeola virus; paramyxoviridae, morbillivirus
- Reservoir: humans
- Causes immunosuppression
- Can interfere with TB testing

**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)

**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
Two colonies of cynomolgus macaques were tested for SRV at a Japanese primate colony. The findings were:

a. Conventional colony negative, SPF colony negative
b. SPF colony negative, Conventional colony 22.5% positive
c. Conventional colony 76.3% positive, SPF colony 22.5% positive
d. SPF colony 76.3% positive, Conventional colony 92% positive

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

Necrotizing Oral Disease
- ANUG=Acute Necrotizing Ulcerative Gingivitis
- Vincent’s 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 scarring and disfigurement
- Associated with SRV, SIV in NHP and HIV or measles in humans

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 well with H&E and is gram negative; doesn’t stain well with Goodpasture
Echinococcus granulosa

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

Malaria

- A blood smear from a NHP that exhibited anorexia, fever, splenomegaly and anemia

Malaria

- OWM: Plasmodium cynomolgi, P. inui, P. knowlesi, P. gonderi
- NWM: P. b. braziliense, P. simium
- Man: P. vivax, P. falciparum, P. malariae
- Transmitted by anopheline 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 RBCs (schizogony).
- Gross: liver, lungs and spleen are gray and blood is thin

Dermatophytosis

- What is the most common dermatophyte of Old World Monkeys?
  - Microsporum canis

Dermatophytosis

- Microsporum in skin 40X
- Branching septal hyphae-Gridley stain

Chagas Disease

Trypanosoma cruzi

- Submandibular edema
- Pitting edema of extremities
Trypanosoma cruzi

Chronic myocarditis with cystic collections of leishmanial forms 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 amastigote

Cutaneous acariasis
Psorgotes simplex

Chronic dermatitis with cross-section of mites in characteristic location for species
Psorgotes simplex-non-pruritic
DDX-Sarcoptes scabiei-pruritic

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 abscesses and granulomas in a number of tissues

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, opisthotonus
- Usually fatal in 1-19 days due to respiratory paralysis and exhaustion

Histoplasmosis

- Small cutaneous papules and pustules with reddish brown exudate, ulcerations and granulomas
- 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
- GMS stain: Organisms in pairs and connected by narrow stalk and short chains

**Paragonimus westermani**

- X-ray of rhesus thorax
- Gross section with worms in lung
- Adults are plump, brown, ovoid
- What is diagnosis?

**Nocardia asteroides**

- 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

**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

**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?
  - Edesofilaria microfilaria
This is a histo with a fite faraco stain (looks similar to Zell 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

Simian Bone Disease
Nutritional secondary hyperparathyroidism which results in bone resorption and fibrous replacement

- 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

Zinc Toxicity; Copper Deficiency
White rhesus with pigmented eyes-“fading infant”
Excess zinc from chewing on galvanized bars; Zinc chelates copper