NONHUMAN PRIMATE PATHOLOGY

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Goals of this talk
- Present an overview of the ‘natural’ disease entities of NHPs-specially Macaques spp.
- Discuss ‘most important’ disease entities in more detail
- Discuss ‘not so important’ disease entities as appropriate
- Make a case that the disease processes in NHP are similar to other higher order mammals
Now for the punch line(s)...

- The response to an ‘insult’ in NHP is almost exactly similar to those in other higher order mammals…a granuloma is a granuloma.
- Beware of ‘unique’ anatomic features and corresponding pathology. Eg., cheek pouch infection (airsacculitis) ; diverticulosis;
- If you are unable to get a Stromberg style “shoot from the hip” answer, go to your basics…again, a granuloma is a ....

Now for the punch line(s) (cont.)...

- Even if you don't learn anything in the next 2 hours, KNOW THE FOLLOWING:
  - Assure yourself of minimum protective conditions while doing a monkey necropsy
  - Know "THE" B virus
    - Very high mortality rate in humans (88%)
    - Asymptomatic carriers can shed virus
  - Know TB
  - Know SIV + opportunistic infections (especially histopath); have Bruce’s “CAN diagnosis(es)”
  - Know the invading bugs- sal, shi, yer, Entomeba
  - Know Endometritis
  - Know Bloat
  - Know-Know-Know ---- you get the idea!!!

Catarrhine (down-nosed) or Old World Monkeys
Platyrrhine (flat-nosed) or New World Monkeys

- Family Aotidae
  - night monkeys
- Family Alouatta
  - howler monkeys
- Family Ateles geoffroyi
  - Central American spider monkey
- Family Callithrix jacchus
  - white-tufted-ear marmoset
- Family Callibius moloch
  - dusky titi
- Genus Cacajao (uakaris)
- Family Leontopithecus rosalia
  - golden lion tamarin
- Family Cebus capucinus
  - capuchin monkey
- Family Saimiri sciureus
  - South American squirrel monkey
- Callithrix pygmaea
  - pygmy marmoset
- Genus Pithecia (saki monkeys)

BACTERIAL DISEASES

- Mycobacterium tuberculosis
- Streptococcus pneumoniae
- Klebsiella pneumoniae
- Mycobacterium leprae
- Staphylococcus aureus
- Shigellosis
- Yersiniosis
- Salmonella
- Campylobacteriosis
- Listeriosis
- Escherichia coli
- Bordetella bronchiseptica
- Clostridium tetani

* Gram-positive
* Gram-negative

Tuberculosis

* M. tuberculosis and M. bovis
Human lung histology

Central necrosis

Langhans-type giant cells
IMMUNODEFICIENCY-ASSOCIATED MYCOBACTERIOSIS

- Mycobacterium avium paratuberculosis (Johne's Disease)

*Streptococcus pneumoniae*
(Diplococcus pneumoniae, Pneumococcus pneumoniae)
Leprosy - Hansen's disease
*Mycobacterium leprae*

*Staphylococcus aureus*
Bacterial Enteritides
- *Salmonella*
- *Shigella*
- *Yersinia*
- *Campylobacter*
- *E. Coli*
- *Entamoeba histolytica* (parasite)

Shigellosis
*Shigella flexneri*  *Shigella sonnei*

Gram negative, aerobic, invasive
Yersiniosis

Yersinia pseudotuberculosis  Yersinia enterocolitica

*from squirrel
Yersiniosis Histopathology

Common histopathology:
- Leukocytosis
- Hyponatremia
- Hypochloremia
- Preterminal azotemia
- Hyperfibrinogenemia

Hepatic microabscess

• Yersinia colonies
Campylobacteriosis
*Campylobacter fetus ss. Jejuni*
*Campylobacter fetus ss. coli*

Listeriosis
*Listeria monocytogenes*
Escherichia coli

- **ETEC: Enterotoxigenic E. coli**
  - Adhesins to bind enterocytes
  - Proteinaceous enterotoxins – LT and ST
  - Non-invasive

- **EPEC: Enteropathogenic E. coli**
  - Lack fimbriae, ST and LT enterotoxins
  - Shiga toxin
  - Actin rearrangement
  - Associated with ulcerative colitis in cotton top tamarins and marmosets

Escherichia coli (cont.)

- **EHEC: Enterohemorrhagic E. coli**
  - Hemolytic-uremic syndrome and sudden kidney failure
  - Fimbriae
  - Shiga toxin

- **EAEC: Enteroaggregative E. coli**
  - Aggregative fimbriae
  - Hemolysin and ST enterotoxin

- **EIEC: Enteroinvasive E. coli**
  - Resembles Shigella
*Bordetella bronchiseptica*

*Tetanus*

*Clostridium tetani*
Common Viral Diseases in NHPs

**DNA Viruses**

- Herpes viruses
  - Herpes B
  - Herpes Simplex virus
  - Herpesvirus saimiri
  - Epstein-Barr Virus
  - Simian Varicella Virus
- Papilloma virus
- Adenovirus
- Simian virus 40 (SV-40)
- SRV-2

**Pox viruses**

- Monkeypox
- Yabapox

**B Virus**

- Images of B virus-infected tissue samples
Herpes Simplex Virus

Herpes saimiri

*from marmoset
Herpes Virus Saimiri

*from marmoset

Herpes Virus Saimiri

Epstein-Barr Virus

N872
Benign Epidermal Monkey Pox (BEMP)

RNA VIRUSES

- Simian hemorrhagic fever viruses
- Measles virus
- Simian T-lymphotropic virus I
- Simian T-cell leukemia virus (STLV-1)
- Yellow Fever virus
- SIV
- Rabies
- Lymphocytic choriomeningitis virus (LCMV)
- Hepatitis A virus
- Encephalomyocarditis virus (EMCV)
- Simian Foamy Virus
Measles Virus Histology

NHP Measles Vaccine
- Discontinuation of ATTENUVAX® Measles vaccine by Merck & Co. routinely used for NHPs
- Other options to consider:
  - M-M-R® II Vaccine
    - Live virus human vaccine for Measles, Mumps and Rubella
    - Highly immunogenic and generally well tolerated in humans
  - Vanguard® Canine Distemper-Measles Vaccine
    - Canine Distemper-Adenovirus Type 2-Measles-Parainfluenza Vaccine
    - High degree of epitopic homology between MV, CDV, and RPV
    - Contains Adenovirus which can interfere with vaccine research
  - Rinderpest Vaccine
    - Single vaccinia virus recombinants expressing the H and F genes of RPV.
    - Provides partial protection; multiple vaccinations required

Simian Immunodeficiency Virus
- Classification:
  - Family: Retroviridae
  - Genus: Lentivirinae
  - Species: SIVmac, SIVcyn, SIVmne, SIVsm, SIVagm, SIVmnd, SIVcmz, SIVsyk
- Very similar to HIV in humans
- Species effected: Old World NHPs
- Clinical Signs:
  - Animals become immunosuppressed and are susceptible to opportunistic infections
  - Infection by cytomegalovirus, adenovirus, papovavirus, Pneumocystis carinii, Mycobacterium avium complex, Cryptococcus neoformans, Toxoplasma gondii, and Candida
- Chronic diarrhea and wasting
- Disseminated cutaneous eruption on the trunk, groin, medial thighs and face
  - with resolution in 1-7 weeks
- Generalized lymphadenopathy and/or splenomegaly
- Pathology:
  - Lesions independent of immunosuppression in a variety of organ systems: skin, GI tract, cardiopulmonary, nervous and lymphoid systems
SIV (cont’d)

- **Diagnosis of Simian Type D Retrovirus-Induced AIDS**
  - Generalized lymphadenopathy and/or splenomegaly accompanied by at least four of the following clinical and laboratory findings:
    - Weight loss (>10%)
    - Fever (>103°F)
    - Persistent refractory diarrhea
    - Chronic infections unresponsive to therapy
    - Opportunistic infections
    - Neosporosis (M. ortii)
    - Retroperitoneal or SQ fibromatosis
  - Hematologic abnormalities:
    - Anemia (PCV <30%)
    - Neutropenia (<1700)
    - Lymphopenia (<1600)
    - Thrombocytopenia (<50,000)
    - Pancytopenia
    - Bone marrow hyperplasia
    - Characteristic lymph node lesions

Where Does HIV Come From?

[Image of a diagram showing the relationship between various simian viruses and HIV.]

Opportunistic Infections associated with SIV

*Pneumocystis carinii*
Pneumocystis carinii

Opportunistic Infections associated with SIV

Retroperitoneal Fibromatosis

Lymphocryptovirus-induced hairy leukoplakia

Simian/Human Immunodeficiency Virus (SHIV)

- Although SIV causes AIDS-like disease in monkeys, immune reactive epitopes of SIV env are different from HIV-1 → diminishes predictive value of SIV model
- SHIV is molecular hybrid of SIV and HIV-1, replacing env, tat, and rev genes of SIV-mac239 with HIV-1 counterparts
- Combines SIV's replicative ability in macaques with ability to encode HIV-1 envelope proteins → more valid model for assessing HIV vaccine efficacy

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Recent Detection of Simian Foamy Virus in Bushmeat

- April 2010: Two strains of HIV-like virus detected in bushmeat from two mangabeys and chimpanzees
- Can infect humans but long-term effects unknown
- Bushmeat trade a threat to public health and wildlife populations

Simian T-Cell Leukemia Virus I (STLV-I)

Simian Hemorrhagic Fever Virus
Ebola Virus

Marburg Virus

Lymphocytic Choriomeningitis Virus (LCMV)

* Marmoset
Family Adenoviridae

Fungal Diseases

- Histoplasmosis
- Histoplasma capsulatum var duboisi
- Candida albicans
- Pneumocystis carinii
- Miscellaneous fungal infections
Candidiasis, moniliasis, or “Thrush”
*Candida albicans*

Miscellaneous Fungal infection in NHP
*Coccidioides immitis*  
*Pyogranulomatous panniculitis*
Parasitic Diseases

- **Internal Parasites:**
  - Plasmodium (Malaria)
  - Entamoeba histolytica
  - Acantocephala (Thorny-headed worms)
  - Respiratory mites
  - Pentastomes
  - Cestodes

- **External Parasites:**
  - Lice
  - Cutaneous mites
  - Hepatocystis kochi
  - Balantidium coli
  - Sarcocystis spp.
  - Cryptosporidium sp.
  - Trichomonas sp.
  - Nochtia nochtii

Malaria

- *Plasmodium cynomolgi*
- *P. inui*
- *P. knowlesi*
- *P. gonderi*
- *P. brasilianim*
- *P. coatneyi*
Entamoeba histolytica
(amebiasis)
Acantocephala
(Thorny-headed Worms)

*Prosthenorchis elegans  Prosthenorchis spirula

*White-footed Tamarin
Respiratory Mites

Pneumonyssus simicola, Pneumonyssoides sp., Rhinophaga sp.
Pentastomes (Pentastomiasis)

*Armillifer porocephalus*
Cestodes (Cestodiasis)

- Adults
  - Cyclophyllidean

- Larvae
  - Cyclophyllidean
    - cysticercoid, cysticercus, coenurus, hydatid;
  - Pseudophyllidean
    - spargana

Cysticercus cellulosae

- Cysticercus cellulosae
Cestodiasis

*from Greater galago

**Hepatocystis kochi**

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**Cryptosporidium sp.**

**Trichomonas spp.**
**Nochtia nocti**

**External Parasites: Lice**
External Parasites: Cutaneous Mites

- *Sarcoptes sp.*
- *Demodex sp.*
- *Psorergates sp.*

Systemic Pathology

- Periodontal Disease
  - Gingival Hyperplasia
  - Acute Gastric Dilation/ Bloat
  - Gastric Infarction
  - Diverticulosis
- Arterio-venus fistula
- Generalized amyloidosis
- Insular amyloidosis
- Endometriosis

Periodontal Disease
Gingival Hyperplasia

Acute Gastric Dilatation (Bloat)
Generalized Amyloidosis
Nutritional & Metabolic Diseases

- Vitamin C deficiency (scurvy)
- Fat necrosis
- Fatal fatty liver syndrome
- Simian Bone Disease (Vitamin D₃ deficiency in NWM)
- Anemia of owl monkeys
- Chronic colitis of macaques
- Hypoglycemia

Vitamin C Deficiency
Scurvy

*squirrel monkey*
Fatty Liver Syndrome Or Fatal Fasting Syndrome Of Obese Macaques
Vitamin D3 Deficiency In New World Monkeys, Simian Bone Disease

*scritton top tamarin*
Anemia Of Owl Monkeys

*owl monkey
Hypoglycemia

- blood glucose < 40 mg/dl
- Squirrel monkeys predisposed
  - high metabolic rate
  - limited glycogen reserves
  - low body fat
  - limited ability to utilize ketones & fatty acids

Thank You!!!