NHP Secondary Species: Marmosets, tamarins, owl monkeys, squirrel monkeys, and baboons

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2012

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• This is NOT an ACLAM sanctioned presentation
• All information is deemed reliable and correct, but no guarantees on accuracy
• No presented information is known to be specifically included in the ACLAM certification exam

A little perspective….

• Of the ACLAM exam questions that require knowledge of a specific species to answer correctly:
  o Primary species: 60-70%
  o Secondary species: 18-28%
  o Tertiary species: 7-17%

• Nonhuman Primate specific references:

Species

• Give the genus and species for each

Papio hamadryus (baboon)
Saguinus mystax (mustached tamarin)
Saguinus oedipus (cotton top tamarin)
Saimiri sciureus (squirrel monkey)
Callithrix jacchus (common marmoset)
Aotus nancymae (owl monkey)

Taxonomy

Platrrhine | Catarrhine
---|---
South and Central America | Africa and Asia
Flattened muzzle, broad spaced laterally flared nares | Elongated muzzle, narrowly spaced downward facing nares
May have prehensile or pseudoprehensile tails | No prehensile tails (apes do not have a tail)
Arboreal | Terrestrial (mostly)
Require D3 in diet, cannot utilize D2 | Do not require D3 in diet, can utilize D2
Estrus cycle | Menstrual cycle
Diurnal (except owl monkey) | Diurnal
Hemochorial placentation | Hemochorial placentation
No cheek pouches | Cephalothoracic have cheek pouches
No ischial callouses or sex skin | May have ischial callouses and sex skin
Do not have opposable thumbs | All have opposable thumbs
2.1.3.2 or 2.1.3.3 dental formula | 2.1.2.3 dental formula
• Most common NWM species used in research: common marmoset, cotton-top tamarin, owl monkey, squirrel monkey
  • Advantages: reduced cost, shorter generation, ease of handling
  • Disadvantages: more remotely related to humans, restricted availability

Callitrichids (marmosets and tamarins)
• Smallest NWMs, resemble each other
  o Callithrix jacchus and Saguinus oedipus are most commonly used in research
• Anatomy
  o No sexual dimorphism
    • Marmosets
      o 300-500g
      o 7-7.5 inches tall
      o Lifespan: 12 years (wild), 15 years (captivity)
    • Tamarins
      o 400-600g
      o 8-9 inches tall
      o Lifespan: 13.5 years (wild), up to 25 years (captivity)
  o Dental anatomy
    • Marmosets: V-shaped mandible with enlarged, chiseled lower incisors and short canines (for tree gum diet)
    • Tamarins: U-shaped mandible with short incisors, long canines

• Reproduction
  o Generally monogamous
  o Dominant breeding pair
  o Reproductive suppression in subordinates
  o High reproductive capacity!
  o Polyovulatory
    • Non-identical twinning most common
    • Permanent chimerism common due to placental vascular anastomoses and continuous placental hemopoiesis allowing stem cell crossover
      o Freemartinism does not occur (aromatizing enzyme can convert androgens to estrone)
  o Gestation
    • Marmoset: 148 days
    • Tamarin: 183 days
  o Post-partum estrus in marmosets
  o Will breed year-round in captivity
  o Family groups
  o Cooperative rearing

Unique to Callitrichids
• Smaller body size
• Fewer teeth (32 vs. 36 in other NWMs) and specialized lower dentition in marmosets
• Flat nail on big toe, claw-like nails on other digits (tegulae)
• High rate of non-identical twinning, permanent chimeras
• Cutaneous chest or perineal scent glands
• Non-prehensile tail

Callitrichids
• Habitat
  o Entirely arboreal
  o Common marmoset: Brazil
    • Disturbed forest or edge habitat
  o Cotton-top tamarin: Columbia
    • Primary or secondary forest
• Diet
  o Insects, fruit, tree gum/latexes
    • Marmosets rely heavily on tree gum, chew holes in tree bark to access
• Social organization
  o Tamarins: typically multimale-multifemale
  o Marmosets: multimale-multifemale, one male-multifemale, one female-multimale

Callitrichids
• Housing
  o Pairs or family groups
  o Plenty of vertical height, climbing structures, and perches
  o Provide multiple feeding stations above the floor
  o Nest boxes – can be used as transfer/capture boxes
  o Scent marking
  o Easily cold-stressed
  o Diet
    • Susceptible to hypoglycemia
    • Require Vitamin D3 and C in diet

Callicam! http://pin.primate.wisc.edu/callicam/callicam.html
Callitrichids

• Marmoset research models
  o Reproductive biology
  o Chimerism
  o Parkinson’s disease
  o Multiple sclerosis
  o Experimental autoimmune encephalitis (EAE) resembles MS
  o Infectious disease
  o Viral hepatitis
  o HSV-1
  o Toxicology and drug development

• Tamarin research models
  o Chronic colitis
  o Colon cancer
  o Hepatitis A
  o GB Virus B as a model for Hepatitis C

Squirrel Monkeys

• Most commonly used NWM in US biomedical research

  • Anatomy
    o Two main groups, five species
      Saimiri boliviensis, Saimiri sciureus
    o Differentiate by shape of fur over eyes (Roman vs. Gothic arch), some color differentiation
    o Sexual dimorphism – males 650g-1.25kg, females 650-900g
      “Fatting” males
      Canines longer in males
    o Height: 11-12.5 inches
    o Lifespan: up to 20 years
    o High circulating levels of free cortisol

  • Habitat
    o Central and South America
    o Arctoid
    o Eat insects, fruits, seeds, small animals

  • Social Organization
    o Large multi-male/multi-female groups
      Adult females typically unity group although social structure can vary by species

Squirrel Monkeys

• Reproduction
  o Breeding season typically December – March
    Males undergo rapid weight gain prior (“fatting”)
  o Females cycle during breeding season
  o Polygamous
  o Single offspring
  o Gestation: 145 days
  o Males do not participate in infant care

• Housing
  o House in pairs or groups if possible (male pairs may fight)
  o Prone to hypothermia
  o Scent-marking, urine-washing
  o Perch on tail – will develop tail ulcers if perch is not wide
  o Diet
    Prone to hypoglycemia
    Require Vitamin D3 and C in diet

• Research Uses
  o Infectious disease
    Malaria
    Creutzfeldt-Jacob disease
    Chagas disease
  o Addiction
  o Parkinson’s disease
  o Alzheimer’s disease
  o Periodontal disease
  o Steroid resistance
  o Reproduction
    Assisted reproduction technology
    Pelvic organ prolapse

Squirrel Monkeys

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    Assisted reproduction technology
    Pelvic organ prolapse

Owl Monkeys

• Anatomy
  o Single genus with chromosomal/karyotypic variation
  o Eight species – Aotus nancymaae most common in research
  o Males and females similar in size
    Height: 13-14 inches
    Weight: 700g – 1.3kg
  o Lifespan: up to 20 years
  o Nocturnal
    Large globe-like eyes
    Lack tapetum lucidum
    Poor color vision (more rods, less cones)

• Habitat
  o Central and northern South America
  o Arctoid
  o Mainly frugivorous (also eat insects, small animals, leaves)

• Social Organization
  o Male-female pairs or small family groups
Owl Monkeys

- **Reproduction**
  - Non-seasonal breeders in captivity
  - Monogamous
  - Males have low sperm counts
  - Typically singletons
  - Gestation 133 days
  - Males participate heavily in infant care
    - Infants carried by father

- **Housing**
  - Pairs or family groups preferable
  - Prefer warm temps
  - Provide diminished lighting during “dark” cycle, offset from normal day
  - Nest boxes
  - Scent-marking, urine-washing
  - Require Vit. D3 and C in diet

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Baboons

- **Largest OWM**
- Single species (*Papio hamadryas*) with five regional subspecies – *Papio hamadryas hamadryas, anubis, papio, cynocephalus, ursinus* (controversial)

- **Anatomy**
  - Marked sexual dimorphism
    - Males: 25kg, large canines
    - Females: 15kg
  - Immune system similar to humans (same IgG subclasses)

- **Habitat**
  - Sub-Saharan Africa
  - Terrestrial
  - Omnivorous (seeds, leaves, fruit, insects, small animals)

- **Social Organization**
  - Strict social hierarchy (matrilineal dominance hierarchy)
  - Typically multimale-multifemale troops

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Baboons

- **Reproduction**
  - Prominent perineal sex skin
  - Can use to determine stage in menstrual cycle
  - Breed year-round
  - Detect pregnancy with rectal exam or U/S
  - Gestation ~180 days
  - Single births
  - Males may participate in infant care
    - (majority of care by females)

- **Research Uses:**
  - Biomedical devices
  - Cardiovascular
    - Atherosclerosis
  - Osteoporosis
  - Infectious disease
    - Chagas disease
    - Schistosomiasis
  - Reproduction
    - Endometriosis
    - Contraception
    - Premature birth
  - Stroke (focal cerebral ischemia)
  - Transplantation
    - Pancreatic islet transplantation for diabetes

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Blood collection

What is the most common blood collection site in NHPs?

Answer: femoral vein

- NWMs
  - Femoral vein
  - Saphenous
  - Tail vein

- OWMs
  - Femoral vein
  - Saphenous vein
  - Cephalic vein

Guide requirements

- Social housing considered the norm
- Environmental enrichment
- Minimum space requirements

Blood collection

Blood collection sites in NHPs:

- Femoral vein
- Saphenous vein
- Tail vein

Guide for Care and Use of Laboratory Animals, 8th ed. NRC 2011

Measles

- RNA paramyovirus, genus Morbillivirus
- Not a natural infection in NHPs (Anthropozoonosis)
- Aerosol transmission
- Severe disease in New world monkeys (marmosets, owl, squirrel)
  - GI system most affected in NWM, often no rash
  - Fatal gastroenterocolitis in marmosets
  - High mortality
- Causes immunosuppression
- May cause false-negative TB tests
- Modified-live vaccination
  - Interferes with serology, monovalent, expensive
  - False-negative TB test
  - NHPs do not usually mount a response to canine distemper vaccine

Measles

- Maculopapular rash
- Marmoset GI – severe gastroenteritis
- Koplick spots
- Syncitial Cell with inclusions
- Coryza
- Lung with syncitial cells
**Alphaherpesvirinae**

- DNA virus
- Natural host
  - Subclinical or self-limiting infection
  - Oral, genital vesicles
  - Life-long infection with latency in sensory ganglia
  - Periodic reactivation and shedding
- Aberrant host
  - Systemic, often fatal disease

**Alphaherpesviridae**

- Which alphaherpesvirus causes mild or inapparent disease in this monkey?
- And severe, generalized disease in this monkey?

Answer: Herpes T

**Alphaherpesvirus**

- Saimirine herpesvirus 1
  - AKA: Herpesvirus tamarinus, Herpes T
  - Natural host – squirrel monkey
    - Asymptomatic or oral vesicles, ulcers
  - Aberrant host – owl monkey, marmoset, tamarins
    - Generalized disease with depression, vesicular rash, oral vesicles, generalized ulcers and necrosis
    - Death in 24-48h
    - Eosinophilic intranuclear inclusion bodies
  - What is often an early sign of this disease in a marmoset or owl monkey?
    - Extreme pruritus

**Other Alphaherpesviruses**

- Herpes simplex virus (HSV-1, HSV-2)
  - Natural host: humans
  - Human → monkey and monkey → human transmission
  - Aberrant host: Apes, owl monkeys, marmosets, tamarins
    - Can cause lethal disseminated disease
    - Disease in owl monkey may be indistinguishable from Herpes T
  - Cercopithecine herpesvirus 1 (Herpes B)
    - Natural host: macaques
    - Aberrant host: non-macaque species. Severe disease reported in owl monkeys and marmosets
    - Can cause fatal encephalitis in humans
  - What is the take-home message?
    - Do not mix species!

**Saimirine herpesvirus 1**

- AKA: Herpesvirus tamarinus, Herpes T
- Natural host – squirrel monkey
  - Asymptomatic or oral vesicles, ulcers
- Aberrant host – owl monkey, marmoset, tamarins
  - Generalized disease with depression, vesicular rash, oral vesicles, generalized ulcers and necrosis
  - Death in 24-48h
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  - Extreme pruritus

**Herpesvirus Papio 2**

- Papiine herpesvirus 2
- Alphaherpesvirus
- Host: endemic in baboons
- Outbreak of vesicular disease in baboon colony originally attributed to SA8
  - Lesion similar to herpes simplex 2 in humans
    - Predominantly genital vesicles and ulcers
    - Oral ulcers possible
    - Likely venereal transmission
    - Latent with periodic reactivation
    - Possible model for herpes simplex 2 in humans
Gammaherpesvirinae

- Oncogenic
- Usually asymptomatic in immunocompetent natural hosts
- Lymphocryptoviruses (many)
  - Similar to human Epstein-Barr virus
  - Associated with large cell lymphomas in New World Monkeys
- Rhadinoviruses (Herpesvirus aetes, saimiri herpesvirus 2)
  - Common asymptomatic infection in spider and squirrel monkeys
  - Associated with malignant lymphoma or leukemia in aberrant hosts (owl monkey, marmosets, tamarins)

Gammaherpesvirus

- What herpesvirus causes no disease in this monkey but causes lymphomas in owl monkeys and marmosets?
  - Answer: Herpesvirus Ateles
- Rhadinovirus
- Spider monkey is the natural host

What human gammaherpesvirus can cause lymphomas in owl monkeys and marmosets?
  - Answer: Epstein-Barr virus
  - lymphocryptovirus

Parainfluenza viruses

- Paramyxoviridae
- Types 1,2 (SV5, SV41), and 3 associated with disease in NWM
- Not very species specific
  - Transmission can from infected humans
  - Aerosol or contact with secretions
  - Mild to severe upper respiratory disease
  - Multinucleated syncytial cells with INIBs and ICIBs

Monkeypox

- Orthopoxvirus
- NWM, OWM, and apes susceptible
- Zoonotic
- Vesicular exanthema, visceral lesions can occur
- Intracytoplasmic eosinophilic inclusion bodies
- Immunologically related to smallpox and vaccinia
  - Vaccine protective

What animal was associated with a US monkeypox outbreak in 2003?
  - Answer: prairie dogs

Callitrichid hepatitis virus

This monkey developed lethargy and jaundice after being fed newborn mice. What is the likely etiology?

- Answer: Lymphocytic choriomeningitis virus (Callitrichid hepatitis virus)
  - Rapidly progressive viral hepatitis in marmosets and tamarins
  - Rodent reservoir – can spread by feeding non-SPF pinkies

Tuberculosis

- Mycobacterium tuberculosis complex
  - *M. tuberculosis, M. bovis, M. africanum, M. microti, M. canetti
  - M avium – atypical TB
- Tuberculin skin test (TST)
  - 0.1ml (0.05ml in marmosets) intradermal Old Mammalian Tuberculin
  - Observed at 24-48-72h for swelling and erythema, grade 1-5

What technique is shown in the image at left? Why is it used?
  - Abdominal skin TB test. Often used for retesting of a suspected positive
Tuberculosis

- NWMs < OWM

Positive TB test (grade 4) in a marmoset

Acid-fast bacteria on tracheal wash

Name an acid-fast stain: Ziehl-Neelson

Klebsiella

- Gram-negative bacteria
- Associated with significant morbidity and mortality in NHPs
- NWMs susceptible to acute death
- Peritonitis, septicemia, pneumonia, enteritis, air sacculitis
- May be associated with shipping, overcrowding, trauma, maternal neglect

Name this condition in a baboon?
Air sacculitis

What bacteria has been associated with this condition in owl monkeys?
Klebsiella pneumoniae

Pasteurella multocida

- Opportunistic pathogen of owl and squirrel monkeys
- Reported in baboons secondary to surgical procedures, chronic catheters, and chair restraint
- Generally seen in association with shipping or animals in poor condition
- Owl monkeys
  - Pneumonia, meningitis
- Squirrel monkeys
  - Nystagmus, head tilt, circling
  - Meningitis, myocarditis, otitis media
- Baboons
  - Air sac infection, abscesses

Campylobacter

- This spiral or gull-shaped bacteria was cultured from the feces of a tamarin with diarrhea. Identify the bacteria

Campylobacter spp. (jejuni and coli most common)

- Watery or mucohemorrhagic diarrhea
- Asymptomatic carriers common
- Erythromycin the treatment of choice

Yersinia

- Yersinia enterocolitica and pseudotuberculosis seen in outdoor housed marmosets, owl monkeys, squirrel monkeys, OWMs
- Triad of lesions
  - Hepatic and splenic necrosis/abscesses
  - Mesenteric lymphadenopathy
  - Ulcerative enterocolitis
- Squirrel monkeys: cervical lymph nodes enlarged with Yersinia pseudotuberculosis

What technique is used to enhanced Yersinia growth on culture?
Answer: cold enrichment

Enteropathogenic E. coli (EPEC)

- Common cause of diarrhea in marmosets, tamarins, and SIV-infected macaques
- Acute hemorrhagic diarrhea
- Asymptomatic carriers common

Enteropathogenic E. coli (EPEC) on EM

Attaching and effacing E. coli at the brush border, toluidine blue stain
Histoplasmosis

These lesions were observed on a baboon.

On histopathology of the lesions, these organisms were seen with a GMS stain. What is the disease?

Histoplasma capsulatum var. duboisii – reported in baboons.

Trypanosoma cruzi

- Chagas disease
- Natural infection in NWMs
- Trypomastigote in blood
- Amastigote in tissue pseudocysts (skeletal and cardiac muscle)
- Myocarditis = most commonly mentioned lesion in NHPs

Trypanosomal forms (amastigotes) in cardiac muscle

Reduviid (kissing) bug!

Trypanosoma cruzi Enlarged, motiled heart

Hepatocystis kochi

Scattered gray-white foci on baboon liver = mature merocysts

Ruptured cyst in liver causes eosinophilic granuloma

Malaria

- NWMs
  - Plasmodium simium, P. brazilianum
- OWMs
  - P. cynomolgi, P. reui, P. knowlesi, P. gondi
- Man
  - *P. vivax, *P. falciparum, P. malariae, P. ovale
- Lifecycle
  - Hepatic and erythrocytic phases
  - Time to complete erythrocytic cycle characteristic for each species
    - 24, 48, or 72 h
- Clinical signs due to release of organisms from RBCs (schizogony)
  - Typically mild disease in natural hosts
  - P. braziliam more pathogenic in natural hosts
  - Which plasmodium has a quotidian (24h) cycle?
    - P. knowlesi, causes severe disease in rhesus

Pentastomids

- NHPs are intermediate hosts for the nymph form
- Poroccephalus: tend to be found in OWM
- Armillifer: tend to be found in NWM
- Adult forms found in snake

Identify this organism

Answer: pentastomid nymph

Adult worms in snake

Malaria

These organisms were identified on a blood smear from a NHP that had anorexia, fever, and anemia. What is the diagnosis and what is the organism?

Answer: Malaria, *Plasmodium* sp.

Malaria

Malaria

- N W M s
  - Plasmodium simium, *P. brazilianum*
- O W M s
  - P. cynomolgi, P. reui, P. knowlesi, P. gondi
- Man
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Adult worms in snake
Trichosporura leptostoma

- Nematode found in marmosets, tamarins, squirrel monkeys, owl monkeys

In what organ is this nematode usually found?

Answer: inhabits pancreatic ducts
- may cause chronic pancreatitis
- Associated with marmoset wasting syndrome?

What is the intermediate host? Cockroach

Dipetalonema

Identify this parasite which was found in the abdomen of a NWM

Answer: Dipetalonema sp.

Live in serous cavities, may cause fibrinopurulent peritonitis or pleuritis

Smaller worm = male

Acanthocephalans

What is the diagnosis? Prosthennorchi sp. (AKA thorny-headed worm)
- *Prosthennorchi elegans: cecum and colon
- *P. spiralis: terminal ilium

Can this parasite cause clinical signs?
- Yes - mechanical blockage, penetrate mucosal surface which can cause perforation and peritonitis

- Cockroach intermediate host
- Fecal float ineffective for detection, use direct smear or sedimentation

Cryptosporidiosis

- These organisms were identified in the intestine of a neonate.
- Identify the organism
  Cryptosporidium parvum
- Protozoa
- Typically self-limiting in immunocompetent animals
- Diarrhea, dehydration in neonates and immunocompromised
- What is the main form of treatment?
  Supportive care

Toxoplasmosis

- An outdoor housed NWM presented with weakness, neurologic signs and died several days later
- What is the organism?
  Toxoplasma gondii
  - NWM more susceptible than OWM
  - Infected via oocysts shed in feline feces, or eating cysts in meat
  - Tachyzoites are banana-shaped, cysts in tissues

Vitamin D deficiency

- NHPs that receive inadequate sunlight or UVB radiation need Vitamin D supplementation
- Vitamin D3 is the preferred form for diets (New World monkeys utilize D2 poorly)
  - D2 – plant form
  - D3 – animal form

- Deficiency
  - Simian bone disease (rickets) – secondary hyperparathyroidism
  - leads to bone resorption and fibrous replacement
Vitamin C deficiency (Scurvy)
- NHPs must have diets supplemented with Vitamin C
  - What enzyme necessary for Vit. C synthesis do NHPs lack?
  - L-gulonolactone oxidase
- Non-stabilized Vit. C has a shelf life of 3 months
- Associated with cephalohematoma, hyperostosis of the skull in squirrel monkeys
- Other NHPs: gingival bleeding, lameness, bruising, epiphyseal fractures, subperiosteal hemorrhage

Marmoset Wasting Syndrome
A marmoset presented with weight loss, hair loss, muscle atrophy, and colitis. What is the likely diagnosis?
- Is it a disease? Or is it nutrition?
  - Vitamin deficiencies have been implicated (Vit. E, protein)
  - Food allergens
  - Underlying infectious/inflammatory reactions
- Clinical signs
  - Weight loss, skeletal muscle atrophy, hair loss, ventral edema, anemia
- Chronic segmental lymphocytic enterocolitis (CLE)

Cardiomyopathy
What degenerative disease is common in aged owl monkeys and is a major cause of death?
Answer: cardiomyopathy
Also common in some squirrel monkey colonies


Amyloidosis
- Extracellular deposition of amyloid in various body tissues (liver, kidneys, GI, pancreas)
- Secondary or reactive (AA) - associated with chronic inflammatory stimulation
- Typically presents as weight loss and lethargy
  - Hepatomegaly on PE
- May be extensive before clinical signs develop
What stain is used to identify amyloid?
Answer: Congo red
What technique can be used along with Congo red to help with identification?
Answer: polarized light

Chronic colitis
This animal presented with diarrhea and weight loss. A tumor was found in the colon at necropsy.
What is the likely tumor, and what pre-existing condition is it associated with?
Answer: Colonic adenocarcinoma in a cotton-top tamarin, associated with chronic colitis
- Chronic colitis is very common in captive cotton-top tamarins
- Tumors often metastasize

Tooth Root Abscess
- Very common in NWMs, especially squirrel monkeys
- Associated with severe wear and tooth fracture
- Usually presents as swelling under the eye
- Staphylococcus aureus and anaerobes often isolated
- Treatment: pull tooth +/- antibiotics
Hypoglycemia

- NWMs may develop hypoglycemia as a primary disorder
- Weakness, disorientation, lethargy, seizures
- Check glucose in animals that are taking a long time recovering from anesthesia
  - Squirrel monkey < 40 mg/dL
  - Owl monkey < 50 mg/dL
- Treat with oral glucose or IV 5% dextrose

From recent literature....

At the left is an ultrasound image used to measure the biparietal diameter of an owl monkey fetus. What is this measurement used to indicate in NHPs?

Gestational age


From recent literature....

Dyscoria was noted in a female and her two offspring. A third offspring and two of the cagemates were found dead. Oral ulcers with eosinophilic intranuclear inclusion bodies were found on necropsy. What is the diagnosis?

- a. Cytomegalovirus
- b. Herpesvirus simplex
- c. Callitrichid hepatitis virus
- d. Paramyxovirus

Answer: b – Herpesvirus simplex


From recent literature....

- Which NHP parasite can be diagnosed with a fecal antigen-capture assay?
  - o Giardia intestinalis
  - o Trichuris trichiura
  - o Pneumonyssus simicola
  - o Strongyloides cebus

Answer: Giardia


From recent literature....

- Squirrel monkeys have higher circulating levels of which hormone(s) compared to humans?
  - o Cortisol
  - o Testosterone
  - o Insulin
  - o Growth hormone
  - o Thyroxine

Answer: Cortisol and testosterone


From recent literature....

Identify this equipment, often used as a refinement in NHP studies

Answer: Vascular access ports – allow repeated venous sampling, improve safety, and reduce need for chemical restraint

I would like to acknowledge Diane Forsythe and Mary Grant from NIEHS and Susan Spray from Scripts for many of the images used in this presentation.