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**CUTANEOUS DEMODICOSIS AND UV-INDUCED SKIN NEOPLASIA IN TWO GOELDI’S MONKEYS (*CALLIMICO GOELDII*)**

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**ABSTRACT:** Two nonrelated Goeldi’s monkeys (*Callimico goeldii*) from the same enclosure developed multifocal alopecia with hyperkeratotic to ulcerative skin lesions on the lower abdomen and inner thighs. Necropsy samples of the first animal showed hyperplastic dermatitis together with in situ carcinoma and intralesional Demodex organisms. The second monkey developed similar lesions 2.5 yr later. Skin scrapings and biopsies also revealed Demodex mites within hyperplastic dermatitis. Long-term treatment with ivermectin, imidacloprid-moxidectin, and sarolaner resolved the demodicosis but skin lesions progressed to actinic keratosis and carcinoma. **Both cutaneous neoplasia and demodicosis are rarely described in New World monkeys and these are the first reported cases in Goeldi’s monkeys. Since the animals had access to ultraviolet (UV) light, as recommended for indoor-housed callitrichids, the skin tumors were likely UV-induced and the mites have settled particularly within impaired regions. Thus, apparent demodicosis can indicate cutaneous immunosuppression and might alert caretakers to adjust the UV regime.**

**Study Design**: Case series: one female and one male Goeldi’s monkey from the same enclosure at a German zoo

**Goal:** This report describes concurrent cutaneous demodicosis and skin neoplasia in a pair of Goeldi’s monkeys that were housed mainly indoors within the same enclosure.

**Key Points:**

* At the age of 12.5 yr, the female monkey showed multifocal nonpruritic alopecia, followed by erythema, epidermal plaque formation with scaling, erosion, and ulceration on the skin of the lower abdomen, groin, and inner thighs
  + Because of the rapid progression of the skin lesions and deterioration of general condition
* At the age of 17 yr, the male monkey developed similar skin lesions on the ventral abdomen and inner thighs
  + Due to poor prognosis, the animal was euthanized 5 mo after the onset of symptoms and sent to necropsy
* Spontaneous SCC is a fairly common neoplasm in nonhuman primates, most frequently located in the oral cavity, integument (perineal, especially in female baboons), esophagus, and cervix-uterus
* The localization of the lesions as well as their histological appearance with gradual progression from epithelial hyperplasia to precancerous actinic keratosis to in situ carcinoma to SCC is strongly suggestive of cumulative exposure of UV radiation as the underlying cause
* UVB is recommended for captive callitrichids that are housed indoors or in temperate climate zones in order to prevent vitamin D deficiency and related metabolic bone disease, such as rickets in juveniles or osteomalacia in adults
  + UVB radiation intensity of the applied UV lamp at the distance (35 cm) in which the animals preferably ‘‘sunbathed’’ can reach up to 980 microW/cm^2, depending on the age of the light bulb.
  + Maximum intensities of 80-120 microW/cm^2 at distance of 100 cm regarded as sufficient for rickets prevention
* UV-induced immunosuppression by impairment of antigen-presenting cell function and induction of immunosuppressive cytokine production may have facilitated additional Demodex infiltration
  + Cutaneous demodicosis is generally rare in non-human primates and has been reported in captive-bred squirrel monkeys, tamarins, and rhesus macaques with mites being predominantly present on appendages, head and neck, or perineal regions
  + The mites spend their entire life span on the host with a life cycle of approximately 18–24 days and feed on serum, sebum, and white blood cells, while the persistent infestation is usually regulated by the host’s immune system
  + Thus, Demodex infestations are often unapparent and subclinical, sometimes even without concomitant inflammation, especially in immunocompetent hosts

**TLDR:**

* UV light for indoor-housed callitrichids must be applied carefully and radiation intensities should be measured at areas where the animals preferably ‘‘sunbathe’’ to adjust the appropriate distance to the lamp and avoid excessive exposure
  + Moreover, an apparent mite infestation can be indicative of immunologically impaired skin functions and might be regarded as an early warning signal to adjust the UV regime

**Related Articles**

*None on the current ACZM reading list*

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**SEROLOGICAL DIAGNOSIS OF *BAYLISASCARIS PROCYONIS* IN PRIMATES USING A HUMAN ELISA TEST**

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**ABSTRACT:** The usefulness of a human enzyme-linked immunosorbent assay (ELISA) for serological diagnosis of Baylisascaris procyonis larva migrans was assessed in nonhuman primates (NHP). The test was originally developed as an assay performed on human samples at Purdue University. **Six participating zoos submitted 258 NHP serum samples, spanning these major phylogenetic groups: 1) great apes (n = 84), 2) lesser apes (n = 17), 3) Old World monkeys (n = 84), 4) New World monkeys (n = 20), and 5) prosimians (n = 53).** Sera were tested in duplicate using a microtiter-well ELISA with *B. procyonis* larval excretory-secretory proteins as antigen, and serum from an experimentally infected baboon (*Papio anubis*) served as positive control. **The ELISA clearly identified seropositive animals in all zoos.** With putative cutoffs of optical density (OD) measured at 405 nm (OD 405) of <0.150= negative, 0.150–0.250= indeterminate, and .0.250 = positive, **149 of 258 (57.8%) were clearly negative** (mean OD 0.046), **and 78 of 258 (30.2%) were clearly positive** (mean OD 0.657, range 0.253–1.773), the rest being indeterminate. Of these, 15 were high positive with OD 1.095–1.773 (mean 1.314). **Positive animals were seen from all zoos; 76 (97.4%) were great apes, lesser apes, or Old World monkeys**. **The four highest ODs were in a siamang (*Symphalangus syndactylus*), lion-tailed macaque (*Macaca silenus*), Sumatran orangutan (*Pongo abelii*), and western lowland gorilla (*Gorilla gorilla gorilla*), all from different zoos.** **Prosimians had a mean OD of 0.039 and New World monkeys 0.021, indicating that human reagents either did not work for these groups or few infected animals were represented. These results indicate that the human ELISA for B. procyonis works well for at least higher phylogeny NHP and that serologic evidence of infection is surprisingly common, correlating with what is known for exposure to this parasite in zoos.**

**Study Design:** Sera were obtained from potentially exposed (or infected) individuals either

1. When taken for routine diagnostic purposes and stored temporarily or historically in serum banks (within the last 20 yr)
2. Prospectively from animals showing clinical signs suggestive of Baylisascaris NLM

**Goal:** Determine the seroprevalence of *B. procyonis* in zoo primates, as well as shed light on whether human reagents and cutoff values for the serologic test in humans could also apply to NHPs

**Key Points:**

* *Baylisascaris procyonis*, the raccoon ascarid, is a common intestinal parasite of raccoons that has emerged as an increasingly well recognized helminthic disease of both animals and humans, in which it causes various forms of larva migrans or baylisascariasis
* Raccoons utilize preferred communal defecation sites termed latrines
  + In zoos, raccoon latrines are typically found in stored hay and straw used to feed or bed animals, in stored grain or other food items, on walkways or sidewalks near enclosures, or within enclosures themselves
  + They are also found frequently on rooftops of buildings and on tops of other enclosures, where the feces and infective eggs can fall into the exhibits below
* Clinically, baylisascariasis is characterized by aggressive larval migration and invasion of the central nervous system (CNS), causing a form of the disease termed neural larva migrans (NLM) or Baylisascaris encephalitis
  + The parasite has produced fatal or severe NLM in more than 150 species of paratenic host animals, both birds and mammals, in North America and is a well- recognized zoonosis
* Baylisascaris larva migrans is difficult to diagnose clinically
  + Because B. procyonis does not complete its life cycle in paratenic hosts, eggs and larvae are not shed in their feces, negating diagnosis by fecal examination
  + In these animals, depending on dose, hematologic and biochemistry values are often within normal limits, although affected animals may have a cerebrospinal fluid (CSF) eosinophilic pleocytosis
  + Finding larvae in brain biopsies or through advanced imaging (CT or MRI) is usually unrewarding and often impractical in NHPs, although MRI lesions in deep white matter are suggestive
  + In addition to clinical signs and epidemiologic associations, antemortem diagnosis is strongly dependent on finding anti–*B. procyonis* antibodies in serum and CSF, at least in humans
  + Polymerase chain reaction (PCR) assays have been developed, but are only useful on tissues, feces, or soil that contain larvae or eggs
    - Larvae are rarely present in the blood in cases of NLM, so PCR may only be practical to confirm infection post-mortem or in biopsies if larvae are found in brain or other tissues
* NHPs are highly susceptible to Baylisascaris larva migrans and, to date, at least 31 NHP species have been identified with proven or suspected Baylisascaris NLM by postmortem examination (most cases), biopsy, positive serology, or a combination of methods, including results from this study
  + Great apes, lesser apes, and Old World monkeys were more likely to be positive, at 44.0%, 52.9%, and 35.7%, respectively, by human ELISA for B. procyonis
* Prosimians and New World monkeys had substantially lower mean ODs, and further investigation of these groups is warranted
  + The results could indicate that human reagents either did not work for these ‘‘lower’’ primate groups or that too few infected animals were represented
  + This could also be influenced by age, as these species have shorter life spans than other NHPs and, thus, less time to be exposed
  + Other factors likely include behavioral and dietary differences between primate groups, which might influence their direct exposure to raccoon latrines or contaminated materials and ingestion of infective eggs
* Variations seen between zoos would be related to local raccoon numbers and B. procyonis prevalence, as well as particular facility designs and management
* NHP behavior should also be considered, in that strictly arboreal primates might be less likely to encounter raccoon feces
* Some of the variation seen between zoos could also be due to confounding factors, such as having fewer apes and Old World monkeys (or more prosimians and New World monkeys) at certain institutions
* Almost certainly, increased seroprevalence is related to exhibit design and husbandry, in relation to NHP access to raccoon latrines or contaminated materials
  + For example, all seven lion-tailed macaques from one zoo had high ODs (0.853–1.642, mean 1.279) indicating a probable common source of infection in this group
  + At another zoo, latrines were discovered on the ledge of an exhibit housing colobus monkeys, of which 9 of 11 (81.8%) were seropositive
    - Mitigation of this risk would include raccoon control and cleaning up latrines at least weekly, before the eggs become infective (as early as 11–14 days after shedding)
* Diet was also thought to be a factor that could potentially influence Baylisascaris seroprevalence, as folivorous or frugivorous animals may be more likely to forage on vegetation that may be contaminated with raccoon feces
  + However, no significant difference was observed between frugivores and folivores, insectivores, or omnivores, perhaps related to sample size
* Animals with clinical signs were more likely to be seropositive, with ODs ranging from 0.005 to 1.581
  + However, the individual with the highest OD (1.773) and many other seropositive NHPs were asymptomatic (OD range 0.001– 1.773)
* Seropositive animals with no clinical signs are medically termed ‘‘covert’’ infections (i.e., covert Baylisascaris or baylisascariasis, similar to covert toxocariasis in humans)
* A common misconception concerning Baylisascaris is that the larvae are neurotropic and always cause clinical NLM
  + They are not neurotropic (i.e., they do not have a predilection for the brain), but some (estimated at 5%–7%) enter the CNS as a result of dissemination
  + The other 93%–95% of larvae migrate and encapsulate in various noncritical tissues, where they cause little to no recognizable harm or clinical signs but are still present to stimulate positive serologic responses
  + Therefore, finding asymptomatic animals with anti-Baylisascaris antibodies is not unusual and reflects being exposed to smaller inocula of eggs without CNS migration, having fewer numbers of larvae entering larger brains, where they may be better tolerated, or both conditions
* Similar to humans, low levels of infection occur more commonly in NHPs and other animals than is recognized and that most infections will not result in clinical signs.
  + Therefore, a positive or negative OD has to be interpreted with caution in light of clinical findings and history
  + Additionally, the ELISA used in this study detected immunoglobulin G antibodies, indicating only that the animal was infected at some point in time

**TLDR:**

* The results of this study indicate that serologic evidence of Baylisascaris infection is surprisingly common in NHPs in zoos
* The human ELISA for *B. procyonis* works well in at least higher phylogeny NHP, but must be interpreted in light of the aforementioned caveats

**Related Articles**

*None on the current ACZM reading list*

Long, Mackenzie E., Shannon GM Kirejczyk, and Elizabeth Howerth. "Pathology in Practice." *Journal of the American Veterinary Medical Association* 256.6 (2020): 661-663.

Case summary - Disseminated toxoplasmosis in a captive squirrel monkey.

* **History:**
  + 6yo F squirrel monkey (*Saimiri sciureus*).
  + Peracute episode of respiratory disease, blood tinged foam from nostrils and hypothermia, sudden death.
  + Housed with 2 conspecifics in a zoo, conspecifics no clinical signs.
* **Gross Findings:**
  + Good body condition.
  + Mild serosanguineous fluid bilaterally around nares and within thorax.
  + Tracheal bifurcation filled with red-tinged fluid.
  + Lungs diffusely mottled pink to red and very wet.
  + Spleen markedly enlarged and friable.
  + Liver pale brown with reticular pattern, numerous pinpoint hemorrhages.
* **Cytologic Findings:**
  + Impression smears of lungs showed macrophages containing round to elongated 2-5 micrometer long organisms with small basophilic nuclei.
* **Histopathologic Findings:**
  + Alveolar septa diffusely infiltrated by macrophages, lymphocytes, plasma cells, neutrophils with foci of lytic necrosis containing round to elongated protozoal tachyzoites with a small, basophilic nucleus.
  + Edema, fibrin, hemorrhage within alveoli.
  + Intracytoplasmic tachyzoites or clusters of ~20 tachyzoites.
  + Splenic red pulp diffusely engorged, foci of lytic necrosis with extra and intrahistiocytic protozoal tachyzoites.
  + Protozoal tachyzoites also found within the liver.
  + LN between duodenum and pancreas contained a large foci of lytic necrosis with low numbers of tachyzoites.
  + Small foci of lytic necrosis in the left basal ganglion of the brain with tachyzoites and hemorrhage.
* Morphologic diagnosis – Severe, acute, multifocal necrotizing pneumonitis, splenitis, hepatitis, encephalitis, and mesenteric lymphadenitis with protozoal tachyzoites, consistent with disseminated *T. gondii* infection.
* *T. gondii* – Obligate intracellular, apicomplexan protozoan.
  + Prevalence 30-50% in human population worldwide.
  + Felidae only definitive host in which the parasite undergoes sexual replication in the intestinal epithelial cells to form oocysts.
  + Oocysts then shed in feces, contaminate water or food, facilitate ingestion by IM hosts.
  + Upon ingestion of a sporulated oocyst, sporozoites emerge and disseminate from the intestinal tract to other tissues by a hematogenous route/lymphatics.
  + Sporozoites invade any cell type by direct penetration or phagocytosis.
  + Multiple to form a pseudocyst (termed tachyzoites), and continue to replicate by endodygeny until the cell ruptures.
  + Released tachyzoites invade additional cells.
  + In the DH – Asexual stages can occur or the bradyzoites may enter intestinal tissues and undergo the sexual stage of development to form zygotes that develop into oocysts.
* Ddx – *Sarcocystis spp, Neospora spp.*
* CS – Systemic illness including malaise, hypothermia, resp distress.
* Most common gross and histo findings in fatal toxoplasmosis cases in New World primates include pulmonary congestion and edema, interstitial pneumonia, splenomegaly, necrotic splenitis, multifocal necrotic hepatitis, and mesenteric lymphadenitis.
* For definitive dx, immunohistochemical analysis of tissue sections for *T. gondii* antigen is recommended.
* Bacilli found in the colon may have been incidental or contributed to GI inflammation and dissemination of *T. gondii* from the intestines.
* No specific tx, control measures include prevention of environmental contamination and exclusion of vector spp from animal enclosures.

Ceccolini, M. E., Macgregor, S. K., Spiro, S., Irving, J., Hedley, J., Williams, J., & Guthrie, A. (2020). Yersinia pseudotuberculosis infections in primates, artiodactyls, and birds within a zoological facility in the united kingdom. *Journal of Zoo and Wildlife Medicine*, *51*(3), 527-538.

Infection with Yersinia pseudotuberculosis can be difficult to diagnose and treat successfully. **Twenty-four cases from the Zoological Society of London (ZSL) London Zoo and ZSL Whipsnade Zoo were identified between 2001 and 2019. Husbandry, medical, and postmortem records for six primates, 10 artiodactyls, and eight birds were reviewed to identify common clinical signs and gross lesions**. Most cases occurred during the winter; however, an outbreak in four primates occurred during the summer following a period of stress associated with increased ambient noise and activity. Common clinical signs included lethargy (6/6 primates, 4/10 artiodactyls, 4/8 birds) or death without premonitory signs (3/10 artiodactyls, 4/8 birds). **Once clinical signs were observed, disease progressed quickly. Poor condition was common in mammals (6/6 primates, 9/10 artiodactyls), but often went undetected** until postmortem examination. **Neurological signs occurred in three of six primates.** Diarrhea and anorexia were uncommon in all animals. **Hepatitis was observed in all groups** (4/6 primates, 2/10 artiodactyls, 4/8 birds), **mesenteric lymphadenomegaly was common in mammals** (4/6 primates, 8/10 artiodactyls), **and gastroenteritis was common in artiodactyls** (7/10). **Erythematous, punctate rashes, which have only been reported with yersiniosis in humans, were present in three of six primates. Bacterial cultures from the liver in primates and birds or enlarged mesenteric lymph nodes in artiodactyls were often diagnostic. All isolates were susceptible to marbofloxacin, oxytetracycline, streptomycin, ceftazidime, amoxicillin clavulanic acid, trimethoprim sulfamethoxazole, azithromycin, and doxycycline, and resistant to clindamycin.** Histopathology and Perl's Prussian blue stains were performed on available liver samples (n = 18). **Intracellular hemosiderin was present in 17 of 18 cases.** Additional research is needed to determine if there is a relationship between hemosiderosis and yersiniosis.

**Introduction:**

* *Yersinia pseudotuberculosis* - zoonotic, gram-negative, facultative, anaerobic coccobacillus, ubiquitous, 14 serotypes (not host-specific)
  + Psychrophile (prefers 4-20C, survives as low as -20C)
  + Wild rodents and bird reservoirs - transmission fecal oral (contaminated water/food)
  + Occurrence of dz is sporadic to epizootic
* CS: lethargy, hyporexia, dehydration, poor condition, diarrhea, abortion, peracute death with no premonitory signs
  + Subclinical cases documented in cervids, primates, carnivores, rodents, and birds
  + Pathogenicity related to host immunocompetency, virulence factors, environmental conditions (cold, wet weather)
  + Availability of excess iron believed to promote growth - hemosiderosis associated with increased susceptibility in humans, mice, and birds
  + Mammals: often primary GI disease (ulcerative enteritis, mesenteric lymphadenomegaly, and hepatitis)
  + Birds: lymphoreticular, hepatitis, splenitis
* Diagnosis is challenging antemortem; culture, PCR on feces, serum, or tissues, growth often suppressed by GI bacteria, can improve with cold enrichment but can take up to 6 weeks

**M+M:**

* Post-mortem records, histopath on archived liver samples in formalin, Perl’s Prussian Blue (PPB) stain for hemosiderosis, culture and gram stain from archived isolates

**Results:**

* 6 primates: white-faced saki monkey, silvery marmosets
  + Cluster of cases in August, housed together, underconditioned, near construction
  + Acute death within 24 hours or lethargy, ataxia, paraplegia, hyporexia and death in 5-9 days
  + Multifocal nodular abscesses in livers, lung, enlarged mesenteric lymph nodes, petechial hemorrhages in skin, GI
  + Yptb isolated from liver, heart, brain, kidney, spleen, lung, GI, feces
* 10 artiodactyls: Chinese water deer, axis deer, fallow deer, gemsbok, impala, scimitar-horned oryx
  + Death within 24 hr, poor BCS, lethargy, diarrhea, enlarged mesenteric lymph nodes, hemorrhage in GI, necrotizing gastroenteritis, hepatic abscesses, some comorbidities
  + Yptb isolated from mesenteric lymph nodes, liver, abdomen, spleen, GI, heart, pharyngeal abscess, and feces
* 8 birds: toco toucan, Fisher’s turacos, Von der Decken’s hornbill, Sulawesi hornbill, tarictic hornbills
  + Acute death within 24 hours, 1 case survived 3 days.
  + Hepatic abscesses, splenomegaly +/- nodules and necrosis, effusion, nodules in air sacs, bacterial colonies visible in multiple organs
  + Yptb isolated from liver, spleen, lung, choana, coelom, cloaca, heart, and feces
* Various treatment attempted: TMS, meloxicam, Clavamox, marbofloxacin single dose, long-acting oxytetracycline, doxycycline
  + Asymptomatic conspecifics moved to a new enclosure and treated remained clinically normal
  + Some animals died up to 6 weeks after finishing antibiotic courses
  + Antibiotics may have been discontinued prior to resolution or infection or continued exposure, insufficient plasma antimicrobial levels, or inadequate tissue penetration
* All isolates in the study were susceptible to marbofloxacin, oxytetracycline, streptomycin, ceftazidime, clavamox, and TMS
  + All isolates were resistant to clindamycin
* Hemosiderosis may have predisposed animals to yersiniosis (positive in 94% of cases) or developed secondary to hepatic injury by Yptb
* Most cases during late autumn, winter, early spring, cold and rainy, sporadic and associated with stressors, poor condition, or comorbidities
* Atypical findings: absence of gross GI ulceration in all cases, neurologic signs and dermal hemorrhages in primates
* Isolation from feces was rarely successful in primates, but was successful in birds

**Discussion/Conclusions**

* Yersiniosis should be treated early, with appropriate antibiotics, and for an extended period
* Immunosuppression from env stressors including inclement weather is a risk factor
* Hepatic hemosiderosis was common in affected animals
* Poor condition, lethargy, and death without premonitory signs was frequent, diarrhea and anorexia were not commonly observed.
* Most animals died or were euthanized within 24 hr of onset of clinical signs
* Gross hepatic abscesses and mesenteric lymphadenopathy should increase suspicion, absence of ulcerative enteritis should not rule it out
* Culture from liver in primates and birds or enlarged lymph nodes in artiodactyls were diagnostic
* Fecal cultures should be considered for surveillance in birds

Pathology in Practice

JAVMA 2018;253(4):423-426

Case:

* 7 mo old female common marmoset
* Sudden onset lethargy, inappetence progression to disorientation, trembling, ataxia
* Died 72 hours after initial onset, conspecific male in the house died with similar CS shortly after
* Gross: erythematous, raised, mildly crusted facial lesions around mouth and on lips; few 1-2 mm round vesicles on caudodorsal tongue; pulmonary edema
* Histo: epidermal ulceration, necrosis, ballooning degeneration of keratinocytes, rare syncytia, lymphoplasmacytic perivascular cuffing in cerebrum and cerebellum, amphophilic to eosinophilic intranuclear inclusions in keratinocytes, glial cells, neurons, and Purkinje cells
* Ancillary testing: ulcerated facial lesions PCR positive for herpes simplex virus type 1 (*Human herpesvirus 1* [**HHV-1**]); cerebrum, cerebellum, and tongue positive on IHC (not spleen or liver).

Key Points:

* Several primate alphaherpesviruses cross interspecies barriers causing fatal encephalitis in nonnatural hosts
  + *Cercopithecine herpesvirus 1* (herpesvirus simiae; monkey B virus; *Macacine alphaherpesvirus 1*): carried by macaques, zoonotic threat to humans
* HHV-1:
  + human reservoir: vesiculoulcerative lesions around mucocutaneous membranes, similar clinical signs in Old World primates,
  + acutely lethal in New World NHP: oral/facial lesions, neurologic signs +/- conjunctivitis, lymphadenitis
    - Nonsuppurative meningoencephalitis with mononuclear cell expansion of Virchow-Robin spaces, extending into meninges +/- vasculitis
    - Intranuclear herpetic inclusion bodies in neurons, glial cells, and basal keratinocytes bordering necrotic areas +/- adrenocortical cells and neurons of myenteric plexus
    - Syncytia characteristic
  + Clinical course 1-10 days (mean 3 days)
  + Definitive diagnosis: PCR, IHC, virus isolation, IFA
* Domestic rabbits also susceptible to HHV-1 through zooanthroponosis, often confined to nervous system (lymphoplasmacytic viral encephalitis)

Conclusion: veterinarians treating marmosets, other nonhuman primates, and rabbits should be aware of the risk of HHV-1 transmission through human contact.



Long-term surveillance of langur alphaherpesvirus in a zoo population of silvered langurs (*Trachypithecus cristatus*).

Gustavsen, K. A., Raphael, B. L., Wildes, M. J., McAloose, D., McCann, C. M., Hilliard, J. K., & Calle, P. P.

*Journal of Zoo and Wildlife Medicine*, 2018;49(2):345-354.

Langur alphaherpesvirus (HVL), a provisionally named alphaherpesvirus in the Simplexvirus genus, was ﬁrst identiﬁed in 1991 at the Bronx Zoo in wild-origin silvered langurs (Trachypithecus cristatus) and their descendants. HVL is closely related to B virus (Macacine alphaherpesvirus 1) based on serologic and genetic data, but its natural history and zoonotic potential remain unknown. A cohort study was undertaken to describe the epidemiology, clinical impact, and potential management implications of this virus in a naturally infected, zoobased population of silvered langurs. **Opportunistic surveillance sampling from 1991 through 2015 resulted in 235 serum samples and 225 conjunctival and buccal mucosal swabs from 75 individuals.** A total of 43 individuals (57.3%) were seropositive for HVL within this period. Seroprevalence increased signiﬁcantly with age, and indirect evidence suggested a peak in transmission at the onset of sexual maturity**.** These ﬁndings were similar to the behavior of other simplexviruses in their adapted hosts. Yearly cumulative incidence declined signiﬁcantly through the study period, with zero or one new case detected each year from 2007 through 2015. The density of this population decreased within the study period for management reasons unrelated to HVL infection, and a change in age distribution or less-frequent contacts may have contributed to low transmission. In addition, clinical signs of simplexvirus infection were rare, and virus isolation was negative on all mucosal swabs, suggesting that viral shedding was infrequent. Yearly period seroprevalence remained relatively constant with a median of 45.8%, likely because of the extended survival of infected individuals within the population. Maintenance of a naturally occurring, novel virus with unknown zoonotic potential in a zoo population for over 25 yr highlights the importance of biosecurity and biosafety for management of silvered langurs and all primate species.

**Background:**

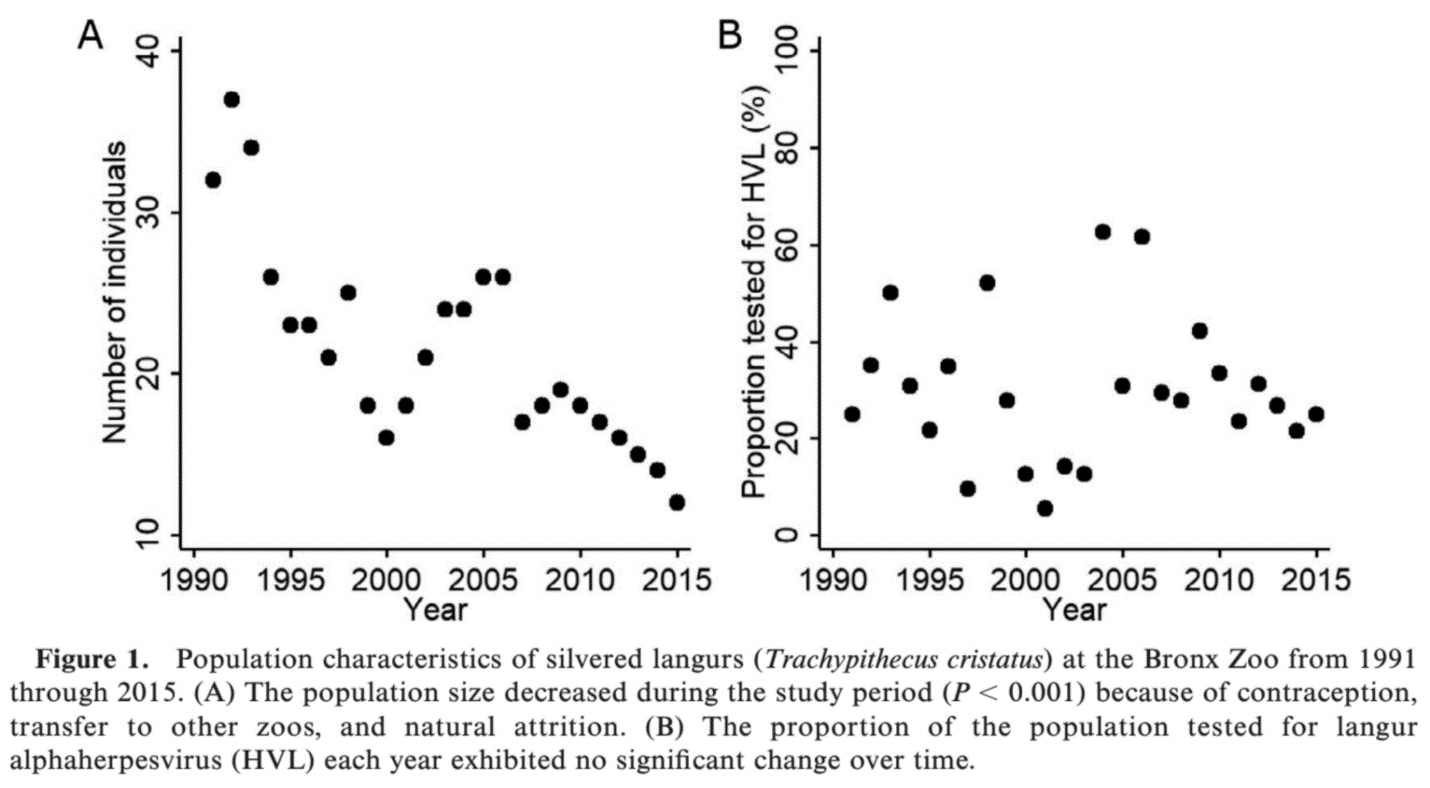
* *Simplexvirus* genus - Alphaherpesviruses: inapparent or mild mucosal lesions in natural host
  + Juvenile, immunosuppressed, or atypical host: severe systemic disease, malaise, conjunctivitis, rhinitis, mucosal/mucocutaneous ulcerations, ataxia, seizures
  + Latent in sensory ganglia, titers persist for life but may wax and wane
* B virus - *Macacine alphaherpesvirus 1; Cercopithecine herpesvirus 1* - endemic in Macaques, encephalomyelitis in humans with historic 80% mortality rate
  + Peaks at the onset of sexual maturity, likely from social stress and increased contact
* HVL - langur alphaherpesvirus, novel simplexvirus in silvered langurs at the Bronx Zoo
  + Close serologic and virologic relation to B virus so theoretic zoonotic risk
  + Population has 8 wild-origin founders - 1 was seropositive shortly after importation
* **Cumulative incidence**: number of incident cases detected each year as a % of the at-risk population that year (not seropositive in any previous year)
* **Period prevalence**: total number of seropositive individuals in the population each year as a % of number of known seropositive or seronegative status that year

**Key Points:**

* Virus isolation negative on all surveillance mucosal swabs
* Entire study period: 57.3% seropositive, none reverted to consistent seronegative status
  + Median age at serologic diagnosis: 5 years
  + Proportion of seropositive increased with age to a constant 85-100% 10 yr or older
* Cumulative incidence declined over time, 1 or less per year after 2007
  + Decreasing population density vs infrequent shedding
  + Transferred near sexual maturity for SSP, may be removed just prior to seroconversion
* Period prevalence had no change over time - likely extended survival of seropositive individuals
* Clinical cases are rare: 3 cases with severe oropharyngeal ulceration or fibrinonecrotic plaques +/- pneumonia in young adults, only 1 positive on VI
  + No oral mucosal or mucocutaneous vesicles were documented
* Silvered langurs appear to be an adapted host: predominantly asymptomatic, increase in seroprevalence with age

**Take Home:**

* Langur alphaherpesvirus (HVL) is a naturally occurring, endemic infection in silvered langurs with unknown zoonotic potential. Maintained in Bronx Zoo population for 25 years
* Close serological and virological relationship with B virus (*Macacine alphaherpesvirus*) suggests potential severity of cross-species simplexvirus infections and justifies heightened biosecurity.



Chang, Ai-Mei, Chen-Chih Chen, and Michael A. Huffman. "Entamoeba spp. in wild formosan rock macaques (Macaca cyclopis) in an area with frequent human-macaque contact." *Journal of wildlife diseases* 55.3 (2019): 608-618.

ABSTRACT: **Entamoeba is a genus of gastrointestinal protozoon that is transmitted through contaminated food and water**. This protozoon is commonly found in human and nonhuman primates. Contact between humans and Formosan rock macaques (Macaca cyclopis) has become more frequent due to food provisioning; accordingly, concerns regarding zoonotic pathogen transmission through the fecal-oral route have increased. For example, surveillance of intestinal parasites in wild Formosan rock macaques indicated that **Entamoeba infection was the most prevalent type of intestinal parasite infection**. The morphologies of pathogenic and nonpathogenic species are difficult to distinguish. In this study, we **collected fecal samples** from wild Formosan rock macaques in the Shoushan National Nature Park (Kaohsiung, Taiwan) and a**dopted both morphologic and molecular methods for Entamoeba species identification**. In total, we collected 208 fecal samples with a **57.7%** (120/208, 95% confidence interval: 50.9–60.4%) **prevalence of Entamoeba infection**. Four Entamoeba species were identified: three nonpathogenic species, Entamoeba coli (19%), Entamoeba chattoni (50%), and Entamoeba hartmanni (11%), and one potentially pathogenic species, Entamoeba nuttalli (20%). Our study revealed the risk of zoonotic transmission of these Entamoeba species to humans. To address relevant public health and wildlife conservation concerns, further research is required to fully understand the virulence of E. nuttalli isolated from Formosan rock macaques.

BACKGROUND:

* E. histiolytica causes hemorrhagic dysentery, liver ulcers, extra-intestinal lesions, death
* Amoebiasis second leading cause of death by parasites in humans
* Morphologically E. histolytica, E. nuttalli, E. dispar are indistinguishable

STUDY DESIGN: Fecal samples collected from unidentified individuals over 1 year in the national park. Performed sedimentation technique for microscopic ID and evaluated molecular PCR

RESULTS:

* Sequenced and banked for the four identified *Enamoeba* species
* Created phylogenetic trees compared to sequences from GeneBank
* Human isolations were mixed with NHP isolations in various subclades—indicate possibility of transmission

DISCUSSION:

* High prevalence of Entamoeba infection in NHPs; most common protozoal infection in NHPs
* Drinking water may be contaminated

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Woolf, Danielle, et al. "Leptospira species status of captive nonhuman primates and free-ranging rodents at the barranquilla zoo, colombia, 2013." *Journal of Zoo and Wildlife Medicine* 51.4 (2021): 780-788.

Abstract: Leptospirosis is a zoonotic disease with worldwide distribution caused by pathogenic Leptospira spp. **Pathogenic Leptospira spp. are shed in urine of infected hosts** and transmitted via ingestion of contaminated food or water, inoculation, inhalation of aerosolized urine, and absorption through mucous membranes. **Leptospirosis is of particular concern in tropical and subtropical regions** such as Barranquilla, Colombia. Recent reports indicate that in Barranquilla, rodents, dogs, and humans have a high leptospiral seroprevalence; and amongst zoo mammals, nonhuman primates have a high prevalence of Leptospira spp. infection. We therefore sought to determine whether primates in captivity at the Barranquilla Zoo were exposed to Leptospira spp. and whether there was a probable causal transmission link between the primates and peridomestic rodents. **Samples were collected from 29 captive nonhuman primates, 15 free-ranging rats (Rattus rattus), and 10 freeranging squirrels (Sciurus granatensis). Serum samples from primates, rats, and squirrels were evaluated via microagglutination test (MAT) vs 24 reference Leptospira serovars.** Blood and urine from the primates and kidney tissue from the rats and squirrels were cultured in Ellinghausen-McCullough-Johnson-Harris (EMJH) medium and polymerase chain reaction (PCR) of lipL32 was performed to determine whether active infection was present**. Leptospiral seroprevalence was found to be 66.7% (10/15) in rats, 60% (6/10) in squirrels, and 6.9% (2/29) in neotropical primates.** Ateles hybridus and Ateles fusciceps had positive titers to serogroups Cynopteri and Ictohaemorrhagiae, respectively. Of the rodents that had antibodies against Leptospira spp., 90% of the rats and 66.7% of the squirrels corresponded to the serovar australis. Interestingly, **all animals were culture and PCR negative, indicating Leptospira spp. exposure in the absence of current infection**. While their status as maintenance hosts needs to be investigated further, this is the first study to show leptospiral seropositivity in red-tailed squirrels (S. granatensis).

Intro

* Leptospirosis is the world’s most widely distributed zoonosis
* Leptospirosis is caused by pathogenic serovars of a bacterial spirochete of the genus Leptospira.
* Pathogenic Leptospira spp. are shed in urine of infected hosts
* Rodents have been recognized to be the most important and widely distributed reservoirs or maintenance hosts of leptospiral infection
* Leptospirosis is of particular concern in tropical/subtropical regions
* This paper sought to determine whether primates in captivity at the Barranquilla Zoo were exposed to Leptospira spp. and whether there was a probable causal transmission link between the primates and peridomestic rodents

M&M

* Samples were collected from 29 captive nonhuman primates, 15 free-ranging rats, and 10 free-ranging squirrels
* Serum samples from primates, rats, and squirrels were evaluated via microagglutination test (MAT) vs 24 reference Leptospira serovars.
* Blood and urine from the primates and kidney tissue from the rats and squirrels were cultured and PCR performed to determine whether active infection was present

Results and discussion

* Leptospiral seroprevalence was found to be 66.7% (10/15) in rats, 60% (6/10) in squirrels, and 6.9% (2/29) in neotropical primates
  + The 2 NHP’s that were positive received untreated drinking water, other primates in the zoo received treated drinking water
* All animals were culture and PCR negative, indicating Leptospira spp. exposure in the absence of current infection
* Overall, 81.3% (13/16) of the rodents sampled (black rats and red-tailed squirrels combined), were seropositive against serovar australis. None of the captive nonhuman primates that were sampled were seropositive for serovar australis
* Given the distribution of Leptospira spp. serovars and the spectrum of maintenance reservoirs is very broad and heterogeneous, the results presented here need further evaluation to determine whether what is being observed is due to cross-reactivity and/or coinfection with less common serovars that may be circulating
* First study to show seropositivity in red tailed squirrels

**PREVALENCE OF LAWSONIA INTRACELLULARIS INFECTION IN NONHUMAN PRIMATES AND PEST RODENTS IN A ZOOLOGICAL COLLECTION**

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**Abstract**: In 2016 and 2017, Lawsonia intracellularis was isolated from several pileated gibbons (Hylobates pileatus) presenting with diarrhea in Mulhouse Zoo (eastern France). To this day, infection with this bacterium has rarely been described in nonhuman primates (NHP) in captivity or in the wild and there are no data about the prevalence or transmission of the disease. This study focuses on finding the prevalence of this infection amongst Mulhouse Zoo’s NHP collection and trying to identify a source of contamination responsible for this epizooty. Forty-eight real-time PCR were conducted on feces from all NHP species in the zoo and on small mammals trapped in the NHP housing structures. No NHP was experiencing symptoms at the time of the study, however test results showed that Lawsonia intracellularis can be found in 61.76% (21/34) of the group total (n ¼ 34) and the prevalence even increases to 92.3% (12/13) in the Lemuriform infraorder (n ¼ 13). In small mammals (n ¼ 14), prevalence of the bacterium is 57.17% (8/14) including 77.78% in rodents (7/9). The results of this study show that several NHP species are healthy carriers and some species of small mammals can be considered as a potential source of contamination. Because of the difficulty encountered trying to isolate the bacterium, it is plausible that infections caused by Lawsonia intracellularis have been underdiagnosed to this day, and that it could be an emerging disease in Europe. Therefore, using real-time PCR to search for this bacterium seems essential in case of diarrhea occurring in nonhuman primates. Moreover, even though further studies on contamination sources need to be conducted, the issue of the presence of rodents in NHP housing structures has to be taken very seriously and tackled with the utmost care.

**Summary**:

Intro:

* Lawsonia intracellularis
  + curved gram-negative bacillus
  + obligate intracellular enteropathogen
  + causative agent for proliferative enteropathy
    - primarily recognized in pigs, chickens, horses
  + replicates in cytoplasm of intestinal epithelial crypt cells without killing them
  + hard to isolate - possess an immunomodulatory mechanism, can facilitate infection by other pathogens (Campylobacter, parvovirus)
  + L. intracellularis identified in macaque and ostriches, disease might be endemic in rabbits, Virginia possums, and coyotes which may serve as a reservoir
  + interspecies transmissions of same strain possible
  + bacteria can survive for up to 2 wk under strict microaerophilic and thermal conditions
  + several means of transmission -direct contact, via feces, via mechanical vectors (clothing, shoes, cleaning supplies), via biological vectors (rodents, shrews, small birds, ants [Formicidae]), via interspecies transmission
* Objective - determine prevalence of infection in different NHP species at the zoo and try to identify how it transmitted to animals (focus on biologic vectors)

M+M:

* Pooled fecal samples from NHP and rodents trapped tested by PCR
* 34 groups of NHP from 31 different species tested

Results/Discussion:

* 21 groups (~62%) were positive
* Differences between and among infraorders also noticed
  + higher prevalence being found in Lemuriform infraorder than in Simiiform infraorder
  + prevalence percentages of Platyrrhine and Catarrhine micro-orders were not significantly different
* PCR still strongly positive in animals following previous outbreak, indicating a persistent carrier state
* ~57% of rodents tested positive
  + No common shrews were positive

Conclusions:

* percentage of asymptomatic carriers among NHP higher than expected
* rodents may be important source of infection
* Lawsonia should be on ddx list of diarrhea in NHP and investigated via PCR on feces

**Use of a human indirect immunofluorescence antibody assay for Balamuthia mandrillaris in a group of captive northwest bornean orangutans (pongo pygmaeus pygmaeus)**

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**Abstract**: Granulomatous amoebic encephalitis caused by the free-living amoeba Balamuthia mandrillaris is a highly fatal disease that was first isolated from a mandrill (Mandrillus sphinx), and has since been diagnosed in several nonhuman primates including orangutans. Indirect immunofluorescence antibody (IFA) techniques for Balamuthia have been used in the fields of human medicine and epidemiology both for exposure assessment and screening of clinical patients for antemortem diagnosis. Stored serum samples from five captive Northwest Bornean orangutans (Pongo pygmaeus pygmaeus), including one who had died from B. mandrillaris infection, housed at a single facility were screened with a human IFA assay for B. mandrillaris. Only the single, clinically affected individual was seropositive, and the results suggest that the use of the available human B. mandrillaris IFA assay is a novel diagnostic option for detection of Balamuthia antibodies in this species. A validated screening serological test could be used in individuals exhibiting signs consistent with granulomatous amoebic encephalitis to facilitate earlier antemortem diagnosis of Balamuthia infection, which is critical if treatment is to be pursued. This pilot study presents the use of serological detection methods for B. mandrillaris screening in a nonhuman primate. Subsequent use of the B. mandrillaris IFA assay in the larger captive population should be pursued for validation of the test and to provide further information on seroprevalence and evaluation of risk factors for exposure to Balamuthia and subsequent development of disease.

**Summary**:

Intro:

* Balamuthia mandrillaris
  + free-living amoeba
  + found in soil and likely water sources worldwide
    - most cases occur in hot, dry climates
  + it is the only species within genus Balamuthia
  + transmission - most commonly by inhalation or inoculation through broken skin
  + exposure common but infection is rare
  + highly fatal neurological syndrome - granulomatous amoebic encephalitis (GAE)
  + signs develop weeks or years after infection
  + both immunocompromised and immunocompetent individuals have been diagnosed
    - infection more common in immunocompromised individuals or in young and elderly
  + humans and Old World primates most commonly affected, documented cases reported in domestic species such as dog, horse, and sheep
  + reported in gorillas, an orangutan, a gibbon, a colobus monkey, and a mandrill from zoological collections
  + no cases have been documented in free-ranging wildlife
  + rapid disease course, poor response to medical therapies, and fatality rate of 90% in human patients
  + Diagnosis by three main diagnostic tests: indirect immunofluorescence assay, immunohistochemistry, and PCR
  + no serological testing has been evaluated for use in identifying clinical cases in primates or determining exposure risk
* objectives: demonstrate the successful use of human B. mandrillaris IFA assay to detect Balamuthia antibodies in a nonhuman primate, and investigate exposure to B. mandrillaris in a small group of captive Northwest Bornean orangutans at a single zoological institution

M+M:

* serum from 5 orangutans used for human IFA assay for B. mandrillaris
  + 1 orangutan died of B. mandrillaris

Results/Discussion:

* animal with fatal disease from B. mandrillaris was seropositive, no other orangutans had evidence of exposure leading to seroconversion
* study identified an orangutan with chronic Balamuthia seropositive status that developed acute neurological disease at least 2 years after seroconversion, exposed to B. mandrillaris >2 years prior to fatal infection
* Balamuthia infection
  + Often chronic course of vague clinical signs with or without significant neurological signs prior to death, or a subacute course of progressive neurological disease and death
  + unexplained weight loss - common finding in chronic cases
  + infection through inhalation or inoculation of contaminated soil through breaks in skin, followed by subsequent hematogenous spread and crossing of Balamuthia organisms across blood-brain barrier
  + skin lesion in conjunction with neurological signs - clinician suspicion for Balamuthia amoebic encephalitis in nonhuman primates
  + clinical signs in humans - fever, nausea, headache, abnormal mentation, hemiparesis, cranial nerve palsy, photophobia, and seizures

Conclusion:

* study demonstrated successful use of a human Balamuthia mandrillaris IFA assay to detect Balamuthia antibodies in a clinically affected orangutan 🡪utility for antemortem diagnosis
* demonstrated first use of this assay to evaluate exposure to B. mandrillaris in a captive population housed at a single facility with a history of fatal Balamuthia amoebic encephalitis
* demonstration of chronic infection of > 2 years in an individual who succumbed to an acute course of Balamuthia amoebic encephalitis