Great Ape *Shigella* Resource Document

Priya Bapodra BVetMed MSc Dipl. ACZM FRCVS (Ape TAG)
Hayley Murphy DVM (Ape TAG)
Sam Rivera DVM Dipl. ACZM (Gorilla SSP)
Kathryn Gamble DVM MS Dipl. ACZM Dip. ECZM (Chimpanzee SSP)
Nancy Lung VMD MS (Orangutan SSP)

Goal

The goal is to provide stakeholders with information and potential resources given recent outbreaks of *Shigella* and related morbidity and mortality in great apes.

***Shigella* Background, Clinical Signs, Diagnosis, and Treatment Considerations**

- Family Enterobacteriaceae; Genus *Shigella*; four species: *Shigella dysenteriae* (serogroup A), *Shigella flexneri* (serogroup B), *Shigella boydii* (serogroup C), *Shigella sonnei* (serogroup D).
- Humans are the primary natural reservoir, but all primates can be infected and be asymptomatic carriers. *Shigella* is both zoonotic and anthropozoonotic (humans can infect animals).
- *Shigella* bacteria's ability to invade intestinal mucosa cells and produce cytotoxins varies by strain.
- Transmission
    - *Shigella* is shed in feces and highly contagious, with as few as ten organisms causing infection
    - Fecal oral – direct contact with infected animals' feces, or indirect contact with contaminated food, water sources and inanimate objects
    - Food borne – ingestion of contaminated food materials
    - Sexual contact
    - Mechanical insect vectors
    - Asymptomatic carriers (both humans and non-human primates) with no clinical signs can shed and contaminate environments
- Clinical signs
    - Incubation period (time from exposure to *Shigella* to development of clinical signs) is 1-6 days
    - Diarrhea, or dysentery (feces with mucus, blood, pus)
    - Abdominal cramping and pain
    - Tenesmus (straining to defecate)
    - Fever
    - Lethargy
    - Clinical signs may be self-limiting within 5-10 days, but more severe signs are often seen in non-human primates, especially with immunocompromise or bacteremia. Mortality is possible.
    - Post-*Shigella* infection sequalae include arthritis, neuritis, vulvovaginitis, chronic colitis, conjunctivitis, and hemolytic uremic syndrome.
- Diagnosis
    - Fecal PCR testing (stool or rectal swab, https://vrlsat.com/vrl-test-list/) is sensitive in detecting the bacteria's DNA in submitted sample, although the bacteria may not be viable.
    - Fecal culture is not recommended as the only first line screening test as the organism is difficult to isolate, and culture is not as sensitive as PCR. Culture isolation is improved with the collection of fresh samples and the use of enrichment media. Additionally, a positive culture is

needed for antimicrobial susceptibility testing and sequencing for public health and epidemiological investigations.
    - Co-infections with other enteric pathogens are often noted, therefore apes also should be tested concurrently for other common enteric (intestinal) pathogens such as *Salmonella*, *Campylobacter*, and *Balantidium*.
    - Routine lab work to evaluate for systemic organ effects and infection/ sepsis.
    - Imaging such as radiographs, CT, and ultrasound since gastrointestinal complications such as abdominal abscessation, intestinal rupture, and intussusception are possible consequences.
    - Serological testing has not been found to be useful in humans and is not available for apes to detect carrier status.
- Treatment options
    - Medical management of apes with diarrhea is variable based on institutional history and clinician preference. Given recent experiences in the North American ape population, earlier diagnostic testing and supportive care may be prudent especially in higher risk animals, such as geriatric apes, animals with pre-existing clinical conditions, immunocompromised individuals, juveniles, and during times of increased environmental or social stress i.e., during introductions, separated housing, recent transfers.
    - Treatment is dependent on the severity of clinical signs, but supportive care is helpful to hasten recovery in even mildly affected animals.
    - Fluid support and electrolyte replacement ranges from oral rehydration to aggressive IV fluid therapy and is critical to recovery.
    - Clinically affected animals that receive early, aggressive, and consistent management appear to recover faster than when treatment is delayed.
    - Antimotility agents or anti-diarrheal agents that reduce frequency and intensity of bowel movements are **contraindicated** with enteric pathogens.
    - Analgesics to control pain may assist with abdominal discomfort, and therefore encourage appetite and oral medication compliance. Medication selection should consider the presence of GI ulceration and drug influence on GI motility.
    - Since antimicrobial resistance develops rapidly with antibiotic use in *Shigella* infected animals, their use should be considered carefully and reserved for acute infections in immunocompromised/ higher risk animals, and for animals which are critically ill with life-threatening infections.
        - Unlike with other bacterial infections, antibiotic use in shigellosis does not result in rapid resolution of the infection.
        - Good patient compliance and appropriate antibiotic selection after antimicrobial susceptibility testing is required to limit resistance development.
        - Antibiotic use can reduce the severity and duration of clinical signs, and intensity and duration of bacterial shedding.
        - Antibiotics should **not** be used in attempt to eliminate carrier status.
    - Blood products
        - Plasma transfusions are indicated in animals with marked blood and fluid loss from diarrhea, or in cases of overwhelming systemic infection/sepsis. Donors and recipients should be cross matched prior to the transfusion. Oral use of plasma may potentially increase local immunity within the intestinal tract.
        - Many apes that may be potential donors or recipients may already have recorded blood types from a 2010 study on ape blood types. QR code to manuscript is noted at the end of this document, but please contact kgamble@lpzoo.org for a manuscript copy and for further specifics.
        - An Ape TAG document titled ‘Great Ape Plasma Banking Considerations’ was recently developed and shared on various listservs. Given the possible internal and external

need for plasma and immunoglobulin support, ape holding facilities are encouraged to develop proficiency in plasma banking and resolve any potential barriers to blood product collection, storage, and use prior to a clinical need.
        - Whole blood transfusions are indicated if the ape has substantial hemorrhagic diarrhea or has become anemic.
    - Prebiotics and probiotics to introduce or replenish competitive bacteria have been found to be helpful in humans in reducing the invasion of intestinal tissue by *Shigella*, and subsequent local inflammation. Although no studies have been done in apes, prebiotic/ probiotic use should be considered during times of perceived stress or as adjunct therapy in animals within the higher risk categories listed previously.

***Shigella* Infection: Husbandry Considerations**

- Isolation of clinically affected and recovering animal(s) in areas with impervious floors which can be disinfected thoroughly. The consideration for social stress of isolation needs to be made.
- To limit exposure of *Shigella* to unaffected or naïve apes and zoo wide, separate clinically affected animals. Only essential personnel should manage clinically affected and high shedding animals.
- Utilize personal protective equipment (PPE) to limit human exposure including masks and eye protection when cleaning *Shigella* contaminated habitats.
- Test potentially contaminated feed, water sources, surfaces, and healthy asymptomatic animals before giving access to a previously contaminated region (by PCR, with subsequent culture for any positive samples).
- Ensure adequate pest and insect management strategies exist to prevent the spread of *Shigella* by mechanical vectors, especially during an outbreak.
- Recovered animals should be tested to determine shedding patterns and when they can be released from any implemented isolation measures. The testing of recovered animals would be at a higher frequency and for longer intervals than for routine population surveillance, which would include potentially non-exposed or entirely naïve animals. Recommendations/ considerations would include:
    - Individual fecal samples (ideally) or thorough group samples (representative sampling from multiple bowl movements).
    - Submission of weekly or every other week fecal samples for PCR for 2 months, or every 4 weeks for 4 months. Fecal culture should be performed on any PCR positive samples.
    - If all fecal samples test PCR negative during this time period, sampling and testing should be performed monthly for an additional 8-10 months. Provided samples continue to test PCR negative, testing should be continued semi-annually as part of routine population surveillance.

***Shigella* Infection: Prevention Considerations**

- Asymptomatic carriers and infrequent/unpredictable shedding make control difficult, and eradication highly improbable. As noted previously, antibiotics are **not** indicated to eliminate carrier status.
- No vaccination exists and immunity from infection is short lived, making animals susceptible to reinfection and recurring clinical signs.
- In light of an increase in the incidence of *Shigella* outbreaks in SSP ape populations, strong consideration should be given to including *Shigella* surveillance in institution specific ape preventive medicine protocols to identify if animals within the collection are already asymptomatic carriers. Given that primates can be reservoir hosts, the likelihood of moderate to high population prevalence seems high although population wide surveillance has not been conducted.
- Appropriate PPE is imperative in *Shigella* prevention and outbreak management, especially for staff working with apes, preparing diets, and in contact with any aspect of ape housing since apes can be exposed and infected by asymptomatic shedding human caretakers. Any humans with gastrointestinal

disease or diarrhea should be precluded from primate care until clinical signs are fully resolved. Non-animal care staff access behind the scenes in primate areas is strongly discouraged.

- Preshipment testing and quarantine protocols need to reflect the perceived increasing prevalence of *Shigella* infections. Fecal PCR surveillance preshipment and post transfer should be conducted, and isolation of incoming apes in habitats with impervious floors should be considered while being mindful of well-being concerns and limiting stress which is a possible risk factor in the development of clinical signs from *Shigella* infection.
- SSP and TAG veterinary advisors are **not** recommending halting animal transfers for population needs. Instead involved facilities should consider increased pre-and post-shipping testing of animal(s), initial then ongoing *Shigella* surveillance of the receiving facility, and critical evaluation of quarantine practices. Consideration to use the recovered animal screening approach for at least two months before and after shipment is encouraged, especially if the receiving facility has a history of no *Shigella* shedding.
- Consider the use of prebiotics and probiotics both preshipment and during quarantine, and at other times of potential stress, in the hopes that administration may reduce *Shigella* shedding.
- Consider the use of neuroleptics and other pharmaceuticals at times of potential stress, such as at the time of animal moves or during facility construction projects.
- A consideration should be made with regards to maintaining animals which are known high asymptomatic shedders on impervious floors as part of routine management, versus on bio floors or deep bedded substrate floors. A risk analysis should be conducted to determine the benefits of this substrate on general health and social dynamics, and the potential risk of the substrate being a source of exposure to naïve apes.
- The overall well-being of a known high shedding primate should be strongly considered, especially if the animal must be isolated long-term from other naïve or non-shedding conspecifics, or if currently being singly housed due to conspecific death(s). Euthanasia may need to be considered.

Resources Available to Ape Holding Facilities

- Several outbreaks in primates have occurred within the last 10 years. Below is a shortlist of facilities, affected species, and contact details of recently affected institutions. Listed veterinarians are committed to being resources in the event of a facility-based outbreak, especially to help provide specific drugs doses used, and testing regimens followed.
    - Jacksonville Zoo and Gardens (bonobos, gorillas, asymptomatic non-ape primates), Dr. Kelsey McClure, mcclurek@jacksonvillezoo.org, 303 501 5787
    - Busch Gardens Tampa (gorillas), Dr. Allison Peterson, allison.peterson@buschgardens.com, 507 382 1073
    - Albuquerque BioPark (chimpanzees, gorillas, orangutans, siamangs), Dr. Carol Bradford, cbradford@cabq.gov, 505-259-5092
    - Taronga Wildlife Hospital (gorillas), Dr. Gabrielle Tobias, gtobias@zoo.nsw.gov.au
- Local human health departments will be able to share any increases in regional human infections and may provide assistance and expertise in investigations to attempt to identify source of outbreak, recommendations regarding biosecurity protocols, and staff education.
- Ape TAG and SSP Veterinary Advisors
    - Priya Bapodra (Ape TAG) – priya.bapodra@columbuszoo.org, 740 255 4504
    - Hayley Murphy (Ape TAG) – hmurphy@dzs.org
    - Sam Rivera (Gorilla SSP) – srivera@zooatlanta.org
    - Kathryn Gamble (Chimpanzee SSP) – kgamble@lpzoo.org
    - Nancy Lung (Orangutan SSP) – nancylung2@gmail.com

References

- Infectious Disease Manual 2023, AAZV Animal Health and Welfare Committee Publication (https://www.aazv.org/page/IDM)

- CDC *Shigella* Factsheet (https://www.cdc.gov/*Shigella*/about/index.html)

- CDC Traveler's Health Yellow Book 2024, Shigellosis (https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/shigellosis)

- Gamble KC, JA Moyse, JN Lovstad, CB Ober, EE Thompson. Blood groups in the SSP, EEP, and managed *in situ* populations of bonobo (*Pan paniscus*), common chimpanzee (*Pan troglodytes*), gorilla (*Gorilla* ssp.), and orangutan (*Pongo pygmaeus* ssp.). 2010. Zoo Biol 30(4): 427-444.