# Strongyloidiasis Review and Recommendations:
## A Significant Disease of Orangutans

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**Key Messages from the FAQ's Below:**

- **Strongyloidiasis continues to be the #1 cause of mortality in orangutans aged 1 month to 8 years.**
- **Routine fecal screening methods will miss *Strongyloides* spp infections. Perform a Baermann technique for 5-7 days in a row to screen for *Strongyloides* spp in orangutans.**
- **If there is a clinical suspicion of strongyloidiasis, treatment should be initiated regardless of diagnostic results.**
- **All institutions with pregnant or infant/juvenile orangutans should prophylactically treat ALL orangutans in the group monthly with ivermectin at 200 µg/kg to reduce fecal shedding and environmental parasite load.**

**Why is strongyloidiasis so important for orangutans? Why do we care?**

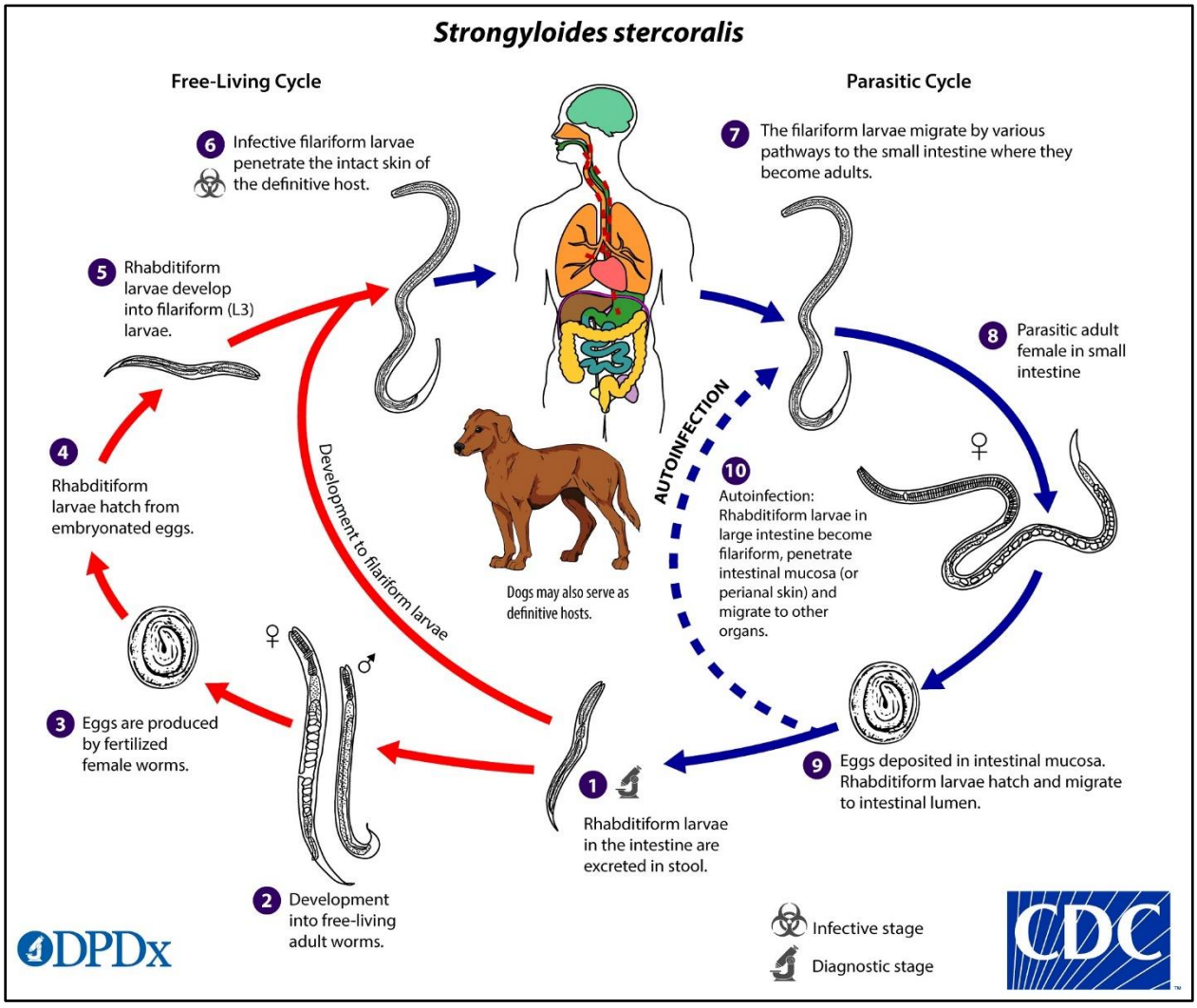
- Strongyloidiasis continues to be the **#1 cause of mortality** in orangutans aged 1 month to 8 years.
- In a 2012 survey, 27% of responding institutions reported diagnosing this parasite in a 10 year period. This likely under-represents the true prevalence of the parasite, since standard fecal screening methods are insensitive at identifying *Strongyloides* spp larvae.
- The SSP recommends that institutions **assume that ALL orangutan groups are chronic carriers of this parasite.**

**What is strongyloidiasis?**

- The term "strongyloidiasis" means an infection with *Strongyloides* spp nematodes.
- Two species are known to parasitize orangutans:
    - *Strongyloides stercoralis* (human = natural host)
    - *Stongyloides fuelleborni* (Old World apes and monkeys = natural host)
- The term "strongyles" refers to a general class of nematodes that affects a wide variety of species. This term is often used when talking about parasites in ungulates. The terms "strongyles" should NOT be confused with the terms "strongyloidiasis" or "*Strongyloides*" as they are NOT related.

**What is the life cycle for *Strongyloides* spp?**

- Adult worms live in the gastrointestinal tract of the host.
- Larvated eggs (rare) or larvae (more common) are shed in the feces. Shedding is often at low numbers and intermittent.
- Larvae from feces can take one of three routes:
    1. Autoinfection—The larvae reinfect the same host by penetrating the skin or large intestine.
    2. Infection of another host—The larvae penetrate the skin of a different host.
    3. Free-living—The larvae become free-living adult worms that reproduce and generate more infective larvae in the environment.
- Once inside the definitive host, larvae migrate through tissues and can be found throughout the body. Most often, they migrate to the lungs where they are coughed up and swallowed. Once in the gastrointestinal tract, they become adults and continue the life cycle.



**What clinical signs are produced in orangutans?**

- Adult orangutans
    - Most often this parasite goes undetected and does NOT produce any appreciable clinical signs.
    - Rarely, gastrointestinal signs such as intermittent diarrhea, constipation, abdominal pain, or bloating can occur.
    - Skin lesions such as itchiness (especially in the perianal area) or red rashes can be caused by migrating larvae penetrating the skin.
    - Individuals that are immunosuppressed from concurrent disease or other factors may be more predisposed to showing clinical signs.
- Infants and juveniles
    - Unfortunately, many orangutan infants or juveniles present with acute death. This occurs when a sudden, heavy worm burden creates massive inflammation as larvae migrate through the tissues.
    - The most common clinical sign is lethargy or generalized weakness.
    - Respiratory signs such as coughing can be present and may mimic viral respiratory infections.

**Why is strongyloidiasis such a problem for young orangutans when it seems so innocuous in adults?**

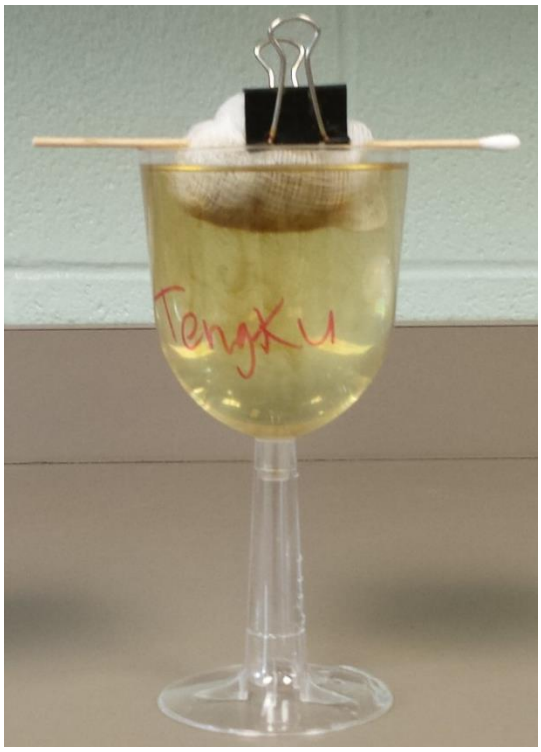
- The immune system of a young orangutan is naïve and does not have any immunity against migrating larval parasites.
- Infants and juveniles that begin to explore their environment can find themselves with sudden, high levels of exposure to the parasite.
- The relative size of the migrating parasite compared to a young orangutan is much larger than when compared to an adult orangutan.
- Routine parasite screening methods will often miss *Strongyloides* spp, resulting in the parasite going undetected for many years. This can result in increased environmental parasite loads, particularly when orangutans live in managed care.

**How can strongyloidiasis be diagnosed in an orangutan exhibiting clinical signs?**

- Fecal parasite testing in infants and juveniles exhibiting clinical signs are typically negative because the clinical signs are caused by migrating larvae. Adult worms are not yet present in the gastrointestinal tract, thus cannot be detected in feces.
- Fecal parasite testing could be performed in adult individuals housed in the same environment, but intermittent shedding results in many false-negative results.
- Serologic tests have been developed for humans, but they are not very specific when used in people, and they have not been thoroughly evaluated in orangutans.
- The Orangutan SSP recommends that if there is a clinical suspicion of strongyloidiasis, **treatment** should be initiated regardless of diagnostic results.

**How should one screen for *Strongyloides* spp in an orangutan group?**

- Due to intermittent shedding of the parasite, a single fecal sample will miss approximately 70% of cases. It is recommended that samples taken 5-7 days in a row be analyzed by multiple methods (direct, centrifugation, and Baermann's) to improve sensitivity.
- Direct microscopic exam, flotation techniques, and centrifugation techniques are often **not** effective at identifying *Strongyloides* spp. The Baermann technique has been shown to better concentrate the parasite and improve detection.
- Other techniques have also been described, including the charcoal culture method.
- The Orangutan SSP recommends performing a Baermann technique for 5-7 days in a row to screen for *Strongyloides* spp in orangutans. This helps to assess the efficacy of the preventive program.


The Baermann technique consists of suspending a fecal sample in a strainer in water for at least 8 hours. The larvae will swim out of the sample and will settle toward the bottom of a funnel-shaped apparatus. A modified funnel can be prepared using an inexpensive plastic wine glass. The sample is then removed from the bottom of the funnel and evaluated under a microscope.

**How can strongyloidiasis be prevented?**

- Prevention strategies have focused on two basic principles: 1) reducing environmental contamination, and 2) prophylactic treatment.
- Reducing environmental contamination includes regular cleaning and sanitation practices, reducing orangutan contact with feces, and changing out substrates and enclosure furnishings that become contaminated with feces.
- Prophylactic treatment includes the repeated use of antiparasitic drugs at regular intervals.

**What prophylaxis regimens are being utilized?**

- The most commonly utilized prophylactic regimen for orangutans in AZA-accredited institutions is monthly ivermectin administered orally.
- Ivermectin is the drug of choice in the treatment of strongyloidiasis in humans.
- Some AZA-accredited institutions also report utilizing other antiparasitic drugs including albendazole, fenbendazole, and pyrantel as well as rotating between different drugs each month. Efficacy of some of these drugs is not supported by the literature or by their use in human treatment regimens.
- To date, no adverse reactions or safety concerns have been reported to the SSP with the use of ivermectin as a prophylaxis for strongyloidiasis. Recent cases of morbidity and mortality from strongyloidiasis in orangutans have ONLY been reported from institutions NOT utilizing prophylactic treatment measures.
- For acute and chronic strongyloidiasis, the CDC recommends ivermectin 200 µg/kg orally for 1-2 days as first-line therapy. Relative contraindications include concomitant *Loa loa* infection, weight less than 15 kg, pregnancy, and breastfeeding. Alternatively, albendazole 400 mg orally twice a day for one week can be given. Relative contraindications include hypersensitivity to benzimidazole compounds and first trimester of pregnancy. A 2016 review of 7 trials found that ivermectin was more efficacious than albendazole and better tolerated than thiabendazole. Cure rates for ivermectin, albendazole, and thiabendazole were 74%-84%, 48%, and 69%, respectively. The main issue with thiabendazole was GI side effects.
- The Orangutan SSP recommends that all institutions with pregnant or infant/juvenile orangutans should prophylactically treat ALL orangutans in the group monthly with ivermectin at 200 µg/kg to reduce fecal shedding and environmental parasite load, thereby reducing the risk of *Strongyloides* spp infection to the infant. This includes infants as soon as they are able to start taking oral medications as well as pregnant and lactating females.
- The Orangutan SSP recommends ivermectin at 200 µg/kg orally once a month as the most commonly utilized prophylactic regimen due to its apparent safety and efficacy in orangutans.

**Wouldn't prophylactic treatment result in drug-resistant parasites?**

- The development of drug-resistance in parasites is a common concern for many parasites in many species. Drug-resistance can develop with the repeated use of a drug.
- Due to the intermittency and low-level of fecal shedding, it is difficult to measure the efficacy of drugs against *Strongyloides* spp. As such, it is difficult to identify when drug-resistance might be occurring.
- **To date, drug-resistance has not been identified as a significant problem when managing *Strongyloides* spp in orangutans or humans.**
- At this time, the high risk of mortality of infants not receiving prophylaxis outweighs the concern of drug resistance.
- If drug resistance is an institutional concern, or if signs of drug resistance become apparent, rotating different antiparasitic drugs could be utilized, as long as the drugs chosen for the rotation show efficacy against *Strongyloides* spp. The best choices are albendazole and ivermectin.
- The Orangutan SSP appreciates hearing about any evidence of drug resistance in *Strongyloides* spp. Should drug resistance become a greater concern across the orangutan population, the SSP recommendations will be adjusted accordingly.

**Is ivermectin safe to use in pregnant or lactating females?**

- In humans, ivermectin is classified as a "Category C" drug for use in pregnant women. This means that "either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal, or other) and there are no controlled studies in women or studies in women and animals are not available."
- Further investigation reveals that there are no controlled human studies and that this "Category C" classification was given due to ivermectin studies in mice, rats, and rabbits that utilized exceptionally high dosages (20 to 600 times the standard dosage) given daily over several days which resulted in clinical signs of toxicity in the adult animals, in addition to the fetal effects. When the standard dosage of 200 µg/kg was administered daily for multiple days, no adverse pregnancy outcomes were reported in these same studies.
- In humans, ivermectin is excreted in low concentrations in milk. In humans it is recommended that "ivermectin should be used in breast-feeding women only when the risk to the infant is outweighed by the risk of disease progress in the mother in the absence of treatment."
- Ivermectin is routinely utilized at standard 200 µg/kg dosage rates in a wide range of veterinary species during pregnancy and lactation without resulting in adverse outcomes.
- To date, no adverse events have been reported when administering ivermectin to pregnant or lactating orangutans.

**What are the key take-aways?**

- *Strongyloides* spp are common in orangutans.
- *Strongyloides* spp are difficult to detect by laboratory fecal examination in orangutan groups.
- Prophylactic treatment is easy.
- Prophylactic treatment is safe.
- Prophylactic treatment is effective in reducing mortality of infant/juvenile orangutans.