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Letter to the Editor

Can resistant *Ancylostoma ceylanicum* arise, persist, and be transmitted between humans and animals?

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To the Editor

Ancylostoma ceylanicum is a zoonotic hookworm that is prevalent in Asia-Pacific region where it is predominant among humans and companion animals [1–3]. This hookworm is reported to affect nearly 30% to 50% of people in countries within Southeast Asia [2, 4, 5]. Among animals, particularly dogs and cats, prevalence rates are 35% but can be as high as more than 95% within the same region [5, 6]. Hence, it is now believed that this zoonotic hookworm is the number one cause of infections among animals and is second only to *Necator americanus* among humans [2, 7]. Transmission dynamics, as revealed by phylogenetic and population genetics analysis, show that there are three pathways that *A. ceylanicum* takes to proliferate between humans and animals (Figure 1). A larger group of the population circulates between humans and animals, while two smaller populations persist within both hosts [2, 6, 8]. The true zoonotic nature of this hookworm presents a serious One Health threat to human and animal populations cohabitating in endemic areas.

Control and elimination has primarily been through pharmaceutical interventions: Mass Drug Administration (MDA) with benzimidazoles in humans and routine veterinary deworming for pet animals [9–11] . Resistance to benzimidazoles, such as albendazole and fenbendazole, is caused by specific genetic variations known as Single Nucleotide Polymorphisms (SNPs) in the *β-tubulin isotype 1* gene [14]. These SNPs result in amino acid substitutions in the protein, altering its structure and hindering the drug's ability to bind to its target site [12]. The F167Y and Q134H mutations have been reported in the dog hookworm, *A. caninum*, in the United States [13, 14]. Moreover, the mutations have also been reported in the human hookworm, *Necator americanus* [15]. Among, *A. ceylanicum*, mutations have been found in laboratory specimens that have been induced to gain resistance against albendazole [16]. The documented emergence of drug resistance in other hookworm species, the aforementioned study of laboratory-induced resistance, and its potential for widespread distribution highlight the danger of resistance development in *A. ceylanicum*. Such resistance could significantly compromise our ability to control and eliminate this parasite, posing a serious risk to public health.

Can *A. ceylanicum* develop resistance to benzimidazole drugs, outcompete other parasite species after treatment, and be spread between animals and humans (Figure 2)? Given the potential transmission routes of zoonotic *A. ceylanicum* and the risk of drug resistance development from both

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animals and humans, repeated drug treatments could lead to the emergence of resistant hookworm populations that can spread between human and animal populations. If resistant *A. ceylanicum* populations become widespread in both humans and animals, it could have severe consequences for public health and veterinary medicine. One way to determine if drug-resistant *A. ceylanicum* populations have emerged is to analyze the genetic makeup of isolates from both humans and animals using the *β-tubulin isotype 1* gene as a marker. By analyzing the genetic makeup of these isolates, researchers can potentially trace the lineage and transmission routes of drug-resistant zoonotic hookworms. This analysis may reveal information about how genetic variations associated with benzimidazole resistance are transmitted between humans and animals. The occurrence of these mutations has been reported. While whole-genome sequencing could provide more comprehensive genetic information, it requires substantial resources and collaboration. In addition to genetic analysis, it will be crucial to monitor the emergence of drug resistance in both humans and animals following established guidelines from organizations like the World Health Organization and the World Association for the Advancement of Veterinary Parasitology [17–19].

In conclusion, the zoonotic nature of *A. ceylanicum* presents a significant One Health challenge due to its potential for transmission between humans and animals. The emergence of benzimidazole resistance poses a significant threat to public health and animal welfare. Population genetic analysis using the β-*tubulin isotype 1* gene can be employed to track the transmission dynamics of resistant hookworms and assess their potential for zoonotic circulation. By understanding the genetic structure and transmission pathways of these resistant populations, we can develop more effective control strategies and mitigate the risks associated with benzimidazole resistance. Effective control and preventative efforts against drug-resistant *A. ceylanicum* may include combination treatment, targeted treatment to the most at-risk populations, and monitoring resistance occurrence.

In the Asia-Pacific region, most *A. ceylanicum* infections are transmitted between humans and animals (Red), with fewer isolates occurring and persisting solely in humans (Green) or animals (Orange) [2, 4, 6, 8].

Figure 1. The transmission dynamics of *Ancylostoma ceylanicum* in the Asia-Pacific region.

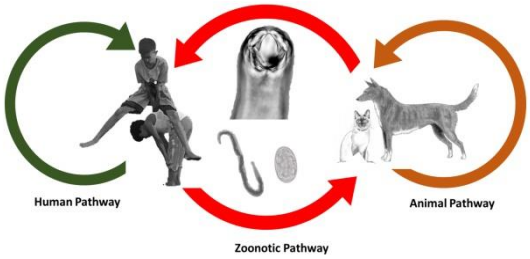
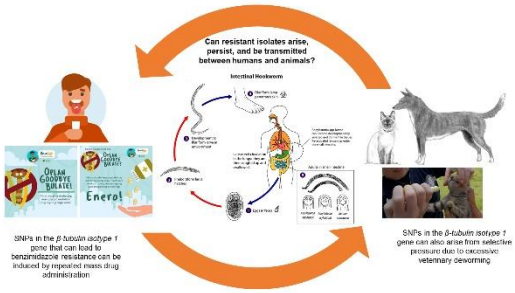


Figure 2. Can resistant *Ancylostoma ceylanicum* isolates arise, persist, and be transmitted between humans and animals?



Drug resistance in *A. ceylanicum* can arise from both human and animal interventions, such as mass drug administration and veterinary deworming. Due to the parasite's zoonotic nature, resistant hookworms could potentially become dominant in either humans or animals and spread between species.

Conflict of Interest

The author has no conflict of interest to declare.

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