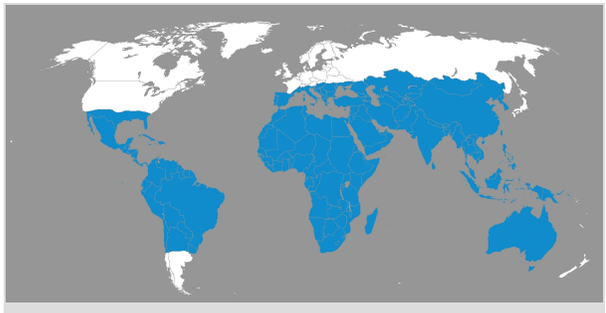
Background

Global Burden | Causative Agents & Transmission | Transmission | Current Control Strategy | Existing Products | Get Involved

What is Soil-Transmitted Helminths: Ascariasis and Trichuriasis?

Soil-transmitted helminths are a family of intestinal worms that include the organisms that cause ascariasis, hookworm (profiled separately), and trichuriasis. Ascariasis and trichuriasis are transmitted through ingestion of parasite eggs in contaminated soil. While ascariasis and trichuriasis are associated with a relatively small number of deaths, they can result in intestinal symptoms, weakness, and malnutrition which, over time, can impact childhood development and adult productivity.

Global Burden



Areas endemic for soil-tranmitted helminths.
(WHO, 1993)

Ascariasis, also known as common roundworm, and trichuriasis, also known as whipworm, are found throughout the tropics and subtropics. It is estimated that more than 1 billion people are infected worldwide including 300 million suffering from severe morbidity.[1]

WHO Region	DALY (in thousands)[1]	
	Ascariasis	Trichuriasis
Africa	915	236
Americas	60	73
Eastern Mediterranean	162	61
South-East Asia	404	372
Western Pacific	308	269
Total:	**1,849**	**1,011**

The economic impact of ascariasis and trichuriasis is difficult to estimate. The WHO estimates that deworming may increase adult income by 40%.[1]

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Causative Agent and Transmission

A. lumbricoides from a child in Kenya.
(Photo: J. Gathany, 2007)

Ascariasis is caused by the intestinal roundworm, *Ascaris lumbricoides*. Humans become infected by ingesting eggs from contaminated soil. The eggs release larvae in the small intestine which bore through the intestinal wall and circulate through the lymphatic system, ultimately reaching the lungs. Over a period of 2-3 months larvae mature through a process that involves coughing up and swallowing larvae from the lungs. Once swallowed, the worms return to the small intestine, were the adult female worm begins producing around 200,000 eggs per day. The eggs are shed into the feces allowing the infection to propagate. Most infections with ascariasis are asymptomatic, but moderate to heavy worm burdens can cause malabsorption of nutrients or obstruction of the intestine.

Trichuriasis, more commonly known as whipworm, is caused by the roundworm *Trichuris trichiura*. As with ascariasis, humans become infected by ingesting eggs from contaminated soil. The larvae of *T. trichiura* emerge in the small intestine and develop into adults in the large intestine where 3,000-7,000 eggs are shed into the feces per day. Although infection with a small number of worms is usually asymptomatic, heavier infections can cause diarrhea, cognitive impairment, and prolapsed rectum.

Transmission

Female worms shed eggs into the stool of the host. When latrines or toilets are not available, eggs from the feces of infected hosts contaminate the soil and water. New hosts become infected upon ingestion of contaminated soil or water, often on unwashed food or from unwashed hands.

Current Control Strategy

Current control strategies for ascariasis and trichuriasis include a combination of mass drug administration (MDA) with benzimidazoles (albendazole or mebendazole) and improvement of sanitation to reduce fecal contamination in the local environment.

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Existing Products

Drugs

Benzimidazoles (albendazole or mebendazole), pyrantel pamoate, and levamisole are all used to treat soil transmitted helminths, including ascariasis and trichuriasis. Mass drug administration programs primarily consist of once-per-year single dose treatment with albendazole. Although this regimen is sufficient for the treatment of ascariasis, the impact on trichuriasis is less clear.

Drug Efficacy Based on Meta Analysis[2,3]

Treatment	*A. lumbricoides*		*T. trichiura*	
	Cure Rate (%)	Egg Reduction (%)	Cure Rate (%)	Egg Reduction (%)
Albendazole (1 day)	88	87-100	28	0-90
Albendazole (3 days)	N/A	N/A	53	81-100
Mebendazole (1 day)	95	96-100	36	81-93
Mebendazole (3 days)	92	91-100	63-80	38-99
Pyrantel pamoate (1 day)	88	88	31	52
Pyrantel pamoate (3 days)	92	99	27	77
Levamisole (1 day)	92	92-100	10	42

Albendazole is also used for MDA to treat lymphatic filariasis and other soil transmitted helminths, such as hookworm, providing crossover treatment for ascariasis and trichuriasis.

Tribendimidine was approved for the treatment of soil transmitted helminths in China in 2004. Despite positive efficacy data in animals and humans from China, the use of tribendimidine will likely remain limited until the drug is approved by the U.S. FDA or European regulatory agencies.[3]

Vaccines

There is currently no vaccine approved for the prevention of ascariasis or trichuriasis.

Diagnostics

Diagnosis of ascariasis and trichuriasis relies on microscopic examination of feces for egg contamination. This has an overall low sensitivity. Furthermore, eggs of *A. lumbricoides* and *T. trichuris* are difficult to distinguish from the eggs of other worm infections.

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References

1. WHO (2010) First WHO report on neglected tropical diseases 2010: working to overcome the global impact of neglected tropical diseases.
2. Keiser J and Utzinger J (2008). "Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis". *JAMA* 299 (16): 1937–48.
3. Keiser J and Utzinger J (2010) “The drugs we have against major helminth infections.” *Advances in Parasitology* **73**: 197-229.

Get Involved

To learn how you can get involved in neglected disease drug, vaccine or diagnostic research and development, or to provide updates,

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Pipeline & Analysis

Drugs | Vaccines | Diagnostics | Get Involved

Drugs

PIPELINE

Product/Research Program	Developers	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Cry5B	University of California, San Diego					

ANALYSIS

The development of novel drugs for ascariasis is not considered an immediate priority. New drugs for trichuriasis, which is less well controlled by single dose therapy with current drugs, may represent a greater need. Although drug resistance is possible, it is not yet widespread. A proposed target product profile (TPP) for soil transmitted helminthes was recently published.[1] At this point in time however, resources are focusing more heavily on improving the coverage of mass drug administration among school children rather than new product development.

Future drug discovery programs will most likely focus on new or optimized combination therapy programs, discovery of single products that can target multiple parasitic or neglected diseases in a single dose, or the repurposing of veterinary medications for worm infections, such as emodepside, monepantel, or derquantel. Although repurposing of veterinary medications may represent the fastest path to new anti-helminth drugs, formal development of these drugs in humans is not currently active.[1]

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Vaccines

Vaccines are not currently being developed for ascariasis or trichuriasis. However, these worms may share some homologous antigens with other helminths. More research is needed to understand the potential for cross protection against these worms through vaccines currently in development for the prevention of other helminth infections such as hookworm or schistosomiasis.

Diagnostics

New point-of-care diagnostics are needed for use in parallel with mass drug administration (MDA) programs. A key challenge of MDA is determining when mass treatment should stop. Diagnostics that can be used in extremely rural areas by minimally trained community volunteers (potentially those already involved in the MDA program) are needed to determine when transmission of hookworm has been interrupted in a village. The same diagnostics should be used to monitor communities to ensure reintroduction does not occur.

References

1. Olliaro P et al. (2011) “Potential Drug Development Candidates for Human Soil-Transmitted Helminthiases.” *PLoS Neglected Tropical Diseases* **5**: e1138.

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Tools

Drugs | Vaccines | Diagnostics | Get Involved

The tools available for the development of drugs, vaccines, and diagnostics for ascariasis and trichuriasis are summarized below. Overall, the tools available to study these organisms are limited.

Drug Development Tools

Basic Research: Target Identification	Target Validation	Screening: Hit/Lead Identification Optimization	Pre-clinical Validation	Clinical Validation
Genome: *Ascaris lumbricoides* EST library available No sequencing or EST libraries available for *Trichuris trichuria* **Key databases:** http://www.nematode.net **In vitro culture:** Eggs from adult *Ascaris suum* (pig model) can be isolated, hatched, and the larvae maintained in culture for about a month. Many people develop severe allergic reactions to handling adult worms making them difficult to work with in the laboratory. *Haemonchus contortus* is also used as a model system.	**Gene knock-outs:** No **Conditional gene knock-outs:** No **Transposon mutagenesis:** No **RNAi:** Yes **Other antisense technology:** Yes **Viability assays:** Possible with adult worms but not common **Transcription microarrays:** Limited, primarily only for *Ascaris suum* (pig model) **Proteomics:** Limited, primarily only for *Ascaris suum* (pig model) **Crystal structures:** Limited	**Whole-cell screening assays:** No **Enzymatic screening assays:** Limited	**Animal models:** Yes *Ascaris suum* pig and mouse models *Trichuris muris* mouse model *Trichuris suis* pig model	**Monitoring treatment efficacy:** Yes **Availability of endpoints:** Yes, clearance of eggs from stool **Availability of surrogate endpoints:** No **Access to clinical trial patients/sites:** Formal clinical trial sites not established, but patient populations may be identified through ongoing MDA programs.

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Vaccine Development Tools

Basic Research: Antigen Identification	Immune Response Characterization	Clinical Validation
See drug development tools above	**Predictive animal models:** Pig model more relevant, but more reagents are available for mouse model. **Detection of endogenous antigen specific response in clinical samples:** Yes **Natural immunity well characterized:** No, studies ongoing but complex. Primary focus of basic research is on allergens associated with ascaris worms.	**Surrogate markers of protection:** No **Challenge studies possible:** No

Diagnostic Development Tools

Basic Research: Biomarker Identification	Biomarker Validation	Clinical Validation
See drug development tools above	**Biomarkers known:** Yes **Access to clinical samples:** Yes **Possible sample types:** Stool	**Access to clinical trial patients/sites:** Yes, if through MDA programs **Treatment available if diagnosed:** Yes

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Product Details

Cry5B

Synonyms:
Cry5B

Disease:
Soil-Transmitted Helminths: Ascariasis and Trichuriasis

Specific Indication:

Product Type:
Drug

PRV Elegible?
Yes

Target/Technology:
Natural products

Mechanism of Action:
Bacterial toxin

Molecule Class:
Recombinant protein

Administration Route:

Notes:

Cry5B is a natural bacterial toxin that is currently used in genetically engineered food crops to kill helminth pests. The protein is now being modified to kill soil transmitted helminths of humans. There is potential to express the protein in common bacteria already used in foods, such as lactobacillus used in yogurt, to treat human helminth infections.

Clinical Trials:

Publications:

2020915

Developer Details

GlaxoSmithKline (United Kingdom)

Type	Disease	Product/Research Program	Current Phase
Drug	Soil-Transmitted Helminths: Ascariasis and Trichuriasis	Albendazole	Approved

University of California, San Diego (United States)

Type	Disease	Product/Research Program	Current Phase
Drug	Soil-Transmitted Helminths: Ascariasis and Trichuriasis	Cry5B	Discovery