Soil-transmitted helminths

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List of modules

1. Soil Transmitted Helminths
2. Hookworm and Toxocariasis and Guinea Worm
3. Filariasis and Onchocerciasis
4. Schistosomiasis and Cestodes

Photo credit: http://www.pathobio.sdu.edu.cn/sdjsc/engparabook/ch087.htm
Introduction to Soil-Transmitted Helminths

- Nematode infections are the most common worldwide
- Most common in areas of poverty and with poor sanitation facilities/practice
- Part of the development takes place outside of the human body in soil
- Infection occurs in contact with parasite eggs or larvae in contaminated soil - direct or ingestion

Photo credit: A. Tayea, 2007
Introduction to Soil-Transmitted helminths

• Many of those infected are symptomatic (depends on the intensity of infection), although may be insidious and result in significant long term morbidity:
  ✓ Malnutrition, malabsorption, and anemia
  ✓ Impaired physical and cognitive development

• In more severe cases, overt disease:
  ✓ Intestinal obstruction, rectal prolapse, and abscesses
  ✓ Involvement of other organs/systems (e.g. ocular)

Global distribution of soil-transmitted helminth infections

Areas where STH are a public health problem
Areas where STH are transmitted

Three types of transmission

TYPE 1: Direct

- Eggs are passed in stool, they hatch and re-infect within 2-3 hours by being carried from the anal margin to the mouth without reaching soil
- If they do reach soil, they do not require a period of development there
- Example: *Enterobius vermicularis* (threadworm)
TYPE 2: Modified Direct

- Eggs are passed in stool into soil and **undergo stages of development in soil**
- Eventually ingested, hatch and release larvae which penetrate stomach wall and enter circulation
- Upon reaching the lungs, they are passed up the respiratory tract and re-swallowed → reaches intestine, becomes adult worm
- Example: *Ascaris lumbricoides* (roundworm), *Toxocara spp.*, *Trichuris trichiura*

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Ascaris Lumbricoides (roundworm)
Three types of transmission

TYPE 3: Penetration of the skin

- Eggs are passed in stool into soil, hatch into larvae and undergo further development
- **Penetrate the skin**, reach circulation and lungs ➔ passed up the respiratory tract and re-swallowed
- Reaches intestine where it becomes an adult worm
- Example: *Ancylostoma duodenale and Necator americanus* (hookworms), *Strongyloides stercoralis*

[Image of Necator Americanus (Hookworm)]

List of module sections

1. Epidemiology
2. Risk Factors
3. Life cycle/biology
4. Symptoms
5. Diagnosis
6. Treatment
7. Control

http://www.wsp.org/Hygiene-Sanitation-Water-Toolkit/graphics/cartoon-09.gif
Ascaris lumbricoides

ROUNDWORM
Intestinal Nematode
1.1 Epidemiology: *Ascaris lumbricoides*

- Most common helminth infection globally, infecting up to one third of the world’s population
- Responsible for 10,000-20,000 deaths annually (CDC)
- Most common in tropical, sub-tropical areas, but also in rural areas in developed countries
  - Mainly found where there are poor sanitation and hygiene practices
- Children particularly vulnerable because of behavior conducive to transmission of the organism
  - More hand-to-mouth contact, hygiene habits
1.2 Risk factors: *Ascaris lumbricoides*

- Faecal-oral transmission route
- Poor sanitation and/or personal hygiene
- Poor household and/or environmental hygiene
- Use of night soil (human excrement) as fertilizer for crops or gardens
- Geophagia (deliberate consumption of earth, soil, or clay)
  ✓ Most often seen in tribal and rural societies among children and pregnant women

Photo: http://farm5.static.flickr.com/4038/4173815367_a5044893a8_o.jpg
1.3 Biology: *Ascaris lumbricoides*

- Largest parasitic worm in humans
  - Female: 20-25 cm x 3-6 mm (can grow up to 40 cm)
  - Male: 15-31 cm x 2-4 mm
  - Female can produce up to 200,000 eggs each day
- Inhabit small intestine
- Ingested eggs hatch in small intestine
  - Larvae pass through intestine wall, migrate through the liver and heart up to lungs, and are coughed up and swallowed back into intestine
- Signs/symptoms can manifest along any stage of life cycle

Photo: [http://www.visualphotos.com/photo/1x6027393/nematode_worms_ascaris_lumbricoides_z180045.jpg](http://www.visualphotos.com/photo/1x6027393/nematode_worms_ascaris_lumbricoides_z180045.jpg)
1.3 Biology: *Ascaris lumbricoides*

1) Immature ova is passed in stool into soil
2) Fertilization/development of embryo within 2-4 months
3) Fertilization/development of embryo within 2-4 months
4) Ingestion of ova with second stage
5) Rhabditiform larvae hatch
6) Penetrate mucous membranes of stomach, enter circulation traveling to lungs. Burrows through alveoli, passing up respiratory tract.
7) Swallowed a second time and enters esophagus reaching intestine where become adult worms

*Period from infection to first passage of ova in the stool is 60-70 days*
Larvae migration:

- Symptoms caused by actual physical presence and eosinophilic inflammatory response
- Loeffler’s Syndrome:
  - Damage to the lungs during migration (potentially fatal)
  - May have fever, cough, sputum, asthma, skin rash, eosinophilia, radiologic pulmonary infiltration
  - Charcot-Leyden crystals associated with lysed eosinophils
  - When larvae reach circulation they can cause localized symptoms (may wander to brain, eye or retina causing granulomas)

Photo: http://download.imaging.consult.com/ic/images/S1933033207701568/mmc5-midi.jpg
1.4 Symptoms: *Ascaris lumbricoides*

**Adult worms:**
- Light-moderate infections are often asymptomatic
- Heavy infection can cause intestinal colic
- Aggregate masses can cause volvulus, intestinal obstruction, or intussusception
- Wandering Ascarids
  - Ileus from mechanical obstruction, bowel perforation in the iliocecal region, acute appendicitis, diverticulitis, gastric/duodenal trauma
  - Blocking to the ampulla of Vater with pancreatic necrosis

Photo: [http://drugline.org/ail/pathography/277/](http://drugline.org/ail/pathography/277/)
1.4 Symptoms: *Ascaris lumbricoides*

**Adult worms:**

- Wandering Ascarids continued
  - ✔ Blocking of common bile duct with obstructive jaundice
  - ✔ Entry of liver parenchyma with abscess
  - ✔ Invasion of genital tract
- An Ascaris mass removed from a child in Kenya (see right)
1.4 Symptoms: *Ascaris lumbricoides*

**Nutritional:**

- Ascaris can cause physiological abnormalities in the small intestine resulting in:
  - Malabsorption of nutrients
  - Nutritional deficiency
  - Vitamin A deficiency (results in night blindness)
  - Growth failure
  - Cognitive impairment

Photo: http://ars.els-cdn.com/content/image/1-s2.0-S1526054207001285-gr2.jpg
1.5 Immunity: *Ascaris lumbricoides*

- Humans acquire only partial immunity to re-infection
  - Demonstrated in some children where *Ascaris* infection is hyperendemic
  - Serology shows evidence of ongoing inflammatory processes (especially in individuals who developed immunity as compared with susceptible ones)
- Humoral immune reaction with Th2 response directed against the migrating larval stage
- Geographical variance in immune spectrum, suggesting some genetic contribution to immune system response to infection
1.6 Diagnosis: *Ascaris lumbricoides*

- Passage of worms in stool, at times through nose or mouth
- Eggs in faeces
  - Fertile eggs measure 45 x 60 μm – contains unsegmented embryo
  - Non-fertile eggs measure 40 x 90 μm
  - WHO definition of heavy infection is > 50,000 eggs/g of faeces
- High eosinophilia in larval ascaris, but not in adult infection (then suspect *Toxocara* or *Strongyloides* spp. infection)
- Radiography: cylindrical filling defects or string-like shadows ➔ better visualized by CT scans

Photo: http://3.bp.blogspot.com/_lWVA0quuxNE/TRQ7cdxnTXI/AAAAAAAAABY/udlSrGQEysUt1600/AscarisInMouthandNose.jpg
1.6 Diagnosis: *Ascaris lumbricoides*

- Serology: little role, due to cross-reactivity with other helminthic infections
- In many settings in developing countries, diagnosis of intestinal worms/parasites is largely clinical
  - Suggested by cough, abdominal distension, or non-specific systemic symptoms such as failure to thrive
  - For example, in field settings, small children presenting with “cough” and/or “headache” are often given the general diagnosis of “IP” (intestinal parasites) and given antihelminthic therapy
1.6 Diagnosis: *Ascaris lumbricoides*

- A fertilized Ascaris egg (see right)
1.7 Treatment: *Ascaris lumbricoides*

- **Drugs of choice:**
  - Albendazole, Mebendazole, Pyrantel pamoate
  - Levamisol, Ivermectin (less effective)

- **Treatment of complications:**
  - Prednisolone therapy (hypereosinophilia)
  - Supportive treatment with antispasmodics, nasogastric tube, IV fluids
  - Rarely enterotomcy is required

- **Correction of nutritional status if evidence of impairment, supplementation**
1.8 Control: *Ascaris lumbricoides*

- Efforts to disrupt the faecal-oral transmission cycle
  - Improve sanitation facilities and their use
  - Regular de-worming in risk areas and children
- Avoid using night soil (human excrement) or animal (particularly swine) faeces as fertilizer
  - Where this is not possible, care to thoroughly wash, cook or peel fruits/vegetables produced
- Public education on importance of sanitation, hygiene and relationship with parasitic infections

Trichuris trichiura

WHIPWORM
Intestinal Nematode
2.1 Epidemiology: *Trichuris trichiura*

- Worldwide distribution – more prevalent in warm, humid tropical regions
- Estimated 0.8 billion people are infected globally, greatest in Southeast Asia and to a less extent equatorial Africa and Central and South America (CDC)
- Mean intensity of infection is greatest in children aged 4-10 years, maximum prevalence usually attained before 5 years of age
- Further basic information can be found at: http://emedicine.medscape.com/article/788570-overview
2.2 Risk factors: *Trichuris trichiura*

- Factors conducive to faecal-oral transmission route
- Poor general hygiene and sanitation practices
- More common among children
- Using night soil to fertilize crops
- Poor food hygiene

Photo: http://3.bp.blogspot.com/_rJRxVYdf8ZQ/R5jQs0kJC_I/AAAAAAAAAQg/1oCAuYBIR0k/s400/e-histol-life.gif
2.3 Biology: *Trichuris trichiura*

- Greyish-white worm, often slightly pink
- Lives in cecum and appendix
- **Male:** 30-45 mm long, thinner anterior portion (containing a cellular esophagus), thicker posterior portion, caudal curved extremity with a single spicule in the sheath which is studded with spines
- Female: 30-35 mm long, posterior half occupied by a stout uterus packed with eggs.
- Egg: 50x22 µm – contains a single embryo
  - Female worm produces 2,000-10,000 eggs/day for ≥5 yrs

Photo: http://www.microbeworld.org/images/stories/twip/t_trichuris_adult_male.jpg
2.3 Life cycle

- Worms live in cecum or appendix
- Eggs are laid unsegmented, embryonation takes 21d
- Can withstand cold temperatures but not desiccation
- Infection directly from contaminated feces
- Eggs hatch after being swallowed in the intestine, where the shell is digested by intestinal juices and the larva emerges in the small intestine
- Penetrates the villi and develops for a week until it re-emerges and passes to the cecum and colorectum → attaches itself to the mucosa → becomes adult
- Incubation period (period from ingestion of egg to appearance of egg in stool): 60-90d
2.4 Pathology: *Trichuris trichiura*

- Strongly related to worm burden/intensity
- Many cases asymptomatic or mild
  - Non-specific symptoms such as abdominal discomfort, irritability in children
- Severe infections
  - Spread throughout the colon to rectum → hemorrhages, mucopurulent stools, dysentery, rectal prolapse
  - Related mucosal damage may facilitate other infections, like *Shigella*, *Entamoeba histolytica*, *Campylobacter jejuni*
2.5 Symptoms

- Majority of infections are mild or asymptomatic
  - Epigastric pain
  - Nausea, vomiting
  - Distension, flatulence
  - Weight loss

- In asymptomatic cases, the worms live harmlessly in caecum/appendix

- Moderate infections
  - Growth deficit
  - Anemia
2.5 Symptoms

• Severe infections, *Trichuris* dysentery syndrome
  ✓ Severe chronic diarrhea or dysentery with blood and mucous in stool
  ✓ Dehydration, Rectal prolapse
  ✓ Colonic intussusception/obstruction
  ✓ Hypoproteinemia
  ✓ Chronic iron deficiency anemia
  ✓ Clubbing (condition affecting the fingers/toes in which the extremities are broadened and the nails are shiny and abnormally curved)
  ✓ Cognitive deficits → often irreversible by anti-helminthic treatment

• Also associated with appendicitis in tropical areas
  ✓ Possibly due to super-infection with bacteria

Clubbing definition - The American Heritage® Medical Dictionary Copyright © 2007, 2004 by Houghton Mifflin Company. Published by Houghton Mifflin Company. All rights reserved.
2.6 Diagnosis

- Often an incidental diagnosis during evaluation for other parasites (*A. lumbricoides, E. histolytica*)
  - Characteristic eggs in stool

- Kato Katz Method (WHO): characteristic barrel shape of eggs with two terminated polar plugs, brown outermost layer
  - Egg count enables quantification of intensity of infection
  - WHO defines severe infection > 10,000 eggs/g of feces

- Proctoscopy (if dysentery): numerous worms attached to the mucosa (reddened, ulcerated)

- Honeycomb appearance of the small intestine
Adult worms

Eggs

Photo credit of eggs: CDC. http://phil.cdc.gov/phil/details.asp
2.7 Treatment

- Albendazole or mebendazole
  - As single doses, several days may be required for severe infections
  - Note: regional differences in albendazole susceptibilities

- Combination albendazole with ivermectin

- Iron supplementation as necessary
2.8 Control

- As with other STHs, control involves breaking the faecal-oral transmission cycle
  - Improved sanitation
  - Improved hygiene, especially handwashing
  - Avoiding crops fertilized with human manure and thorough washing/disinfection of such foods before preparation

- Health education in communities,

- Regular de-worming
  - Also helps address other STHs
Strongyloides stercoralis

Intestinal Nematode
3.1 Epidemiology: *Strongyloides stercoralis*

- Caused by parasitic roundworm *Strongyloides stercoralis*, or rarely *S. fülleborni* (parts of Africa and Asia, Papua New Guinea)
- Worldwide distribution, especially prevalent in tropical Central and South America, China, South-east Asia
- Estimated 200 million infected worldwide
  - Unreliable estimates of global prevalence due to difficulties in diagnosis
- Infection ranges from subclinical to life-threatening hyper-infection and disseminated disease

3.2 Risk factors: *Strongyloides stercoralis*

**Risk factors for infection:**
- Partly transmitted via percutaneous route
- Poor sanitation or hygiene

**Risk factors for hyper-infection:**
- Immunocompromised state
- Pre-existing condition (e.g. underlying malignancy)
- Corticosteroid therapy or immune suppressive therapy
- Malnutrition, alcoholism, or HTLV-1 infection
3.3 Biology: *Strongyloides stercoralis*

- **2 forms:** parasitic (internal) and free-living (external)
- **3 developmental forms:** adult, rhabditiform and filariform (infective) larva
- **Adult worm:** 2.5 x 0.034 mm, tapers anteriorly and ends in a conical tail. Vulva in posterior third of body, prominent uterus containing 50 eggs (55 x 30 µm)
- **Internal sexual cycle**
  - Male worm disappears quickly from bowel after oviposition in intestine
  - Eggs hatch immediately in the bowel into male and female rhabditiform larvae, which pass out in the feaces to continue external sexual cycle
3.3 Biology: *Strongyloides stercoralis*

- **External sexual cycle**
  - Free-living rhabditiform larvae develop into living adults which copulate in the soil and produce eggs.
  - Free-living female is smaller (1 x 0.05mm) than parasitic female. The vulva lies posteriorly and the uterus contains eggs (70 x 40 µm).
  - Parasitic and free-living rhabditiform larvae develop indistinguishably into filariform larvae, which can remain alive in the soil for many weeks.
3.3 Life cycle

1. Rhabditiform larvae in the intestine are excreted in stool.
2. Development into free-living adult worms.
3. Eggs are produced by fertilized female worms.
4. Rhabditiform larvae hatch from embryonated eggs.
5. The rhabditiform larvae develop into infective filariform.
6. Infective filariform larvae penetrate the intact skin initiating the infection.
7. The filariform larvae enter the circulatory system, are transported to the lungs, and penetrate the alveolar spaces. They are carried to the trachea and pharynx, swallowed, and reach the small intestine where they become adults.
8. Adult female worm in the intestine.
9. Eggs deposited in intestinal mucosa, hatch, and migrate to lumen.
10. Autoinfection: Rhabditiform larvae in large intestine, become filariform larvae, penetrate intestinal mucosa or perianal skin, and follow the normal infective cycle.

https://www.cdc.gov/dpdx/
• In some circumstances the external cycle can be omitted

  o Filariform larvae develop internally and reinvade bowel or skin → enter circulation → migrate to lungs → penetrate alveoli and travel up trachea → swallowed and reach intestine

  o Usually a small population of adult worms maintains itself in the small intestine for many yrs (> 30) in the absence of further infection from the outside
3.4 Pathology

- Filariform larvae cause petechial hemorrhages at the site of skin invasion (usually perianal skin/buttocks or wrists) accompanied by intense pruritus and edema.

- Upon migration through lungs, young worms may cause symptoms resembling bronchopneumonia with some lobular consolidation.

- Female worms deposit eggs beneath the villi of intestinal mucosa.

3.4 Pathology

• Severe infections
  o First stage larva develop in intestine → bore into wall of duodenum and jejunum → develop to adult stage → produce ova while encysted in the bowel → spread to lymphatic system → enter circulation and reach liver, kidneys, gallbladder, brain, lungs and rarely myocardium

• Larva may carry microorganisms (e.g. *E. coli*) which can cause overwhelming septicemia

• Incubation period: infection to appearance of rhabditiform (larvae in stool) ~1 month
3.4 Pathology

Free-living adult female *S. stercoralis*, alongside rhabditoid larva

Photo credit: both images from CDC-DPDx from http://www.dpd.cdc.gov/dpdx/HTML/ImageLibrary/Strongyloidiasis_il.htm
3.5 Immunity

- Achieved in many individuals after 3 primary infections

- Humoral antibody-mediated immunity
  - Initiated by infective stage larva with Type I reaction – eosinophilic tissue response → peripheral eosinophilia often with urticarial rashes
  - Produced antibodies often cross react with other helminths

- Cell-mediated immunity: elicited by adult and larval worms in the tissues → cell mediated granulomatous reaction

- If cell-mediated immunity is suppressed (e.g. by drugs) → generalized hyperinfection syndrome results, causing massive (often fatal) strongyloidiasis

- In persons co-infected with HTLV-1, production of IFNγ may decrease production of antibodies that take part in the immune response
3.6 Symptoms (uncomplicated disease)

- Cutaneous (uncomplicated disease)
  - Recurrent urticaria at sites of penetration of filariform larvae
  - Larva currens
    - Pruritic, raised lesions
    - Visibly migrating
    - Pathognomonic for strongyloidiasis

- Abdominal (chronic, uncomplicated disease)
  - Epigastric pain (middle or LUQ)
  - Bleeding
  - Nausea, vomiting, diarrhea (may alternate with constipation)
  - Small bowel obstruction with severe infection
  - Weight loss

*Can also have a dry cough or sore throat at the 6th – 9th day of infection, although relatively rare in uncomplicated strongyloidiasis.*
3.6 Symptoms (complicated disease)

- Severe complicated strongyloidiasis caused by massive tissue invasion in setting of debilitating disease, malnutrition, serious illness, immunocompromise (e.g. steroids or HTLV-1 co-infection)
- Hyperinfection with large larvae burden
  - Enteritis, colitis, malabsorption
- Disseminated disease
  - Fever
  - Pulmonary: resembles closely tropical pulmonary eosinophilia, hypereosinophilia
    - Pneumonitis
    - Pleural effusion
    - Abscess

*In pulmonary involvement in disseminated disease, there can also be haemoptysis and shortness of breath.
3.6 Symptoms (complicated disease)

- Disseminated disease
  - Intestinal
    - Severe abdominal pain, diarrhea
    - Protein-losing enteropathy
    - Generalized edema, abdominal distention
    - Ileus, necrotizing jejunitis
  - Neurologic
    - Headache
    - Convulsions
    - Stupor
    - Meningitis (*E. coli* in 30% of immunocompromised patients)
  - Septicemia with enteric organisms
    - Shock
    - Multiple petechiae, periumbilical purpura
3.7 Diagnosis

- Raised IgE levels

- In later stages chronic moderate eosinophilia – may persist for years
  - Leukocytosis up to 25K/mL
  - Eosinophilia 10-12K/mL

- Rhabditiform larva in stool, duodenal aspirate
  - Fecal examination methods or culture on charcoal at 26°C
  - Baermann technique: more sensitive than direct microscopy
  - Serial stool samples, as diagnostic yield for single sample is relatively low (30%)

- Kato-Katz method does NOT detect S. stercoralis
  - Explains why global prevalence might be underestimated
3.7 Diagnosis

• ELISA Serum IgG
  ✓ More sensitive than coprology (the study and analysis of feces, as for diagnostic purposes) but also labor intensive
  ✓ Prone to cross-reaction with other helminths and filariae

• Gelatin particle indirect agglutinin test is considered to be more practical than ELISA for mass screening

Coprology definition - Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition. © 2003 by Saunders, an imprint of Elsevier, Inc. All rights reserved.
3.8 Treatment

- Treatment recommended regardless if the infection is symptomatic given potential severity of hyperinfection

- Immunocompromised individuals (on steroids, chemotherapy, HIV, pre-transplantation etc.) should be screened and treated

- Drug of choice: ivermectin single dose repeated after 1 week, or daily for 3 days

- Less efficacious: albendazole, mebendazole, thiabendazole

- Decrease of efficacy in co-infection with HTLV-1
3.9 Control

• Improve awareness of disease and risk factors
  o Especially in areas where infection related to occupational risks (e.g. rice fields)

• Improved sanitation and hygiene practices
  o Especially where disease is endemic

• Improve case detection and treatment to reduce reservoir, autoinfection

• Many control measures for *Strongyloides* also target other STHs!
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