









## Nematodes impact human life in many important ways



#### Nematodes cause numerous human diseases Nematodes are abundant

- pathogens in life-stock and pets Nematode are important
- pests of many crops Nematodes provide
- powerful genetic models to study the basis of development, aging and many diseases including cancer



Disease	Global Prevalence (millions)	Population at Risk	Regions of Highest Prevalence	Source
Ascariasis	807	4.2 bil lion	East Asia and Pacific Islands, sub-Saharan Africa, India, South Asia, China, Latin America and Caribbean	Bethony et al., <sup>e</sup> de Silva et al. <sup>7</sup>
Trichuriasis	60.4	3.2 billion	Seb-Saharan Africa, East Asia and Pacific Islands, Latin America and Caribbean, India, South Asia	Bethony et al " <sup>e</sup> de Silva et al ?
Hookworm infection	576	3.2 bil lion	Sub-Saharan Africa, East Asia and Pacific Islands, India, South Asia, Latin America and Caribbean	Bethony et al.," de Silva et al."
Schistosomiasis	207	779 million	Sub-Saharan Africa, Latin America and Caribbean	Steinmann et al.®
Lymphatic filariasis	120	1.3 billion	India, South Asia, East Asia and Pacific Islands, sub- Saharan Africa	Ottesen, <sup>9</sup> WHO <sup>10</sup>
Trachoma	84	590 million	Sub-Saharan Africa, Middle East and North Africa	International Trachoma Initiative, <sup>11</sup> Médecins sans Frontières <sup>12</sup>
Onchocerciasis	37	90 million	Sub-Saharan Africa, Latin America and Caribbean	Basáñez et al. <sup>13</sup>
Leishmania sis	12	350 million	India, South Asia, sub-Saharan Africa, Latin America and Caribbean	Desjeux <sup>14</sup>
Chagas' disease	8-9	25 million	Latin America and Caribbean	WHO <sup>13</sup>
Leprosy	0.4	ND	India, sub-Saharan Africa, Latin America and Caribbean	International Federation of Anti-Leprosy Associ- ations <sup>16</sup>
Human African trypanosomias is	0.3	60 million	Sub-Saharan Africa	Févre et al. <sup>37</sup>
Dracunculiasis	0.01	ND	Sub-Saharan Africa	Carter Center <sup>20</sup>
Buruli ulcer	ND	ND	Sub-Saharan Africa	Global Buruli Ulcer Initiative <sup>15</sup>

abclass	Order (Suborder)	Superfamily	Genus and species	Probable prevalence in humans
denophorea	Enoplida	Trichuroidea	Trichinella spiralis Trichinella papuae Trichinella zimbabwiensis Trichuris trichiura Capillaria hepatica Capillaria philippinensis	49 million Thousands ? 500 million Rare Thousands
cermentea Rhabdit Strongy	Phabditida Strongylida	Rhabditoidea Ancytostomatoidea Trichostrongyloidea Metastrongyloidea	Strongyloides stercorois Strongyloides Nileborni Palodern strongvlaides Rhabdits sp.n.denale Necotor americanus Ancylostoma brazilense Ancylostoma brazilense Ternieten keninutus Desphagostomum biurcum Desphagostomum biurcum Sympamus lennynes Tirkhostrongylus cantonensis	70 million Thousands Rare Rare 700-900 million Thousands Thousands Rare New Rare 10 million Rare Thousands
	Oxyurida Ascaridida	Oxyuroidea Ascaridoidea	Parastrongylus costaricensis Enterabius vermicularis Ascaris lumbricoides Toxocora canis Toxocora cati Lagochilascaris minor Baylisoscaris procyonis Anisakis spp.	Thousands 400 million 800-1000 million Thousands Thousands Rare Rare Rare Rare
	Spirurida (Spirurina)	Spiruroidea Gnathostomatoidea Thelazoidea Filarioidea	resentancerrand/dbc/pients Gongylonen pulchrum Gongylonen pulchrum Theitara calipaeda Wuchereria bancrothi Brugia tmari Brugia tmari Brugia tmari Dado on Onchocerta perstans Mansonella streptocerca Mansonella azerdi	Rare Thousands Rare 120 million <sup>2</sup> 6 million 33 million 33 million 47 million 2 million 15 million
	Spirurida (Camallanina)	Dracunculoidea	Dirafilaria spp. Dracunculus medinensis	Rare <3 million <sup>4</sup>

#### Soil-transmitted nematodes • 'Unholy trinity': Ascaris lumbricoides, Trichuris trichiura, and the hookworms The global burden of disease is an estimated 22.1 DALYs to hookworm, 10.5 million to A. lumbricoides, 6.4 million to T. trichiura=total of 39 million life years (Kirwan et al. 2009) • Major problem for children 5-14 years old Cause morbidity by affecting nutritional ٠ equilibrium inducing intestinal bleeding, competing for absorption of micronutrients, reducing growth and food intake Fecal-oral route 11 🍕

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#### Common characteristics of Ascaris spp.

- Cause the most common helminth infections
  - An estimated 1.5 billion persons are infected (1/4 world's population?)
- Two main populations
  - A. lumbricoides
  - A. suum
- Adult worms can lay up to 200,000 eggs per day





### Ascaris: Epidemiology

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- · Worldwide distribution
- High prevalence in tropical and subtropical regions, and areas with inadequate sanitation.

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- In the U.S., approximately 4 million people are infected.
  - High-risk groups: international travelers, recent immigrants (especially from Latin America and Asia), refugees, and international adoptees.
  - Indigenous to the rural southeast, where cross-infection by pigs with the nematode Ascaris suum is thought to occur.
- Transmission enhanced by asymptomatic carriers that continue to shed eggs for years

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- Abdominal complications- penetration of intestine or appendix, peritonitis leads to death
- Tx with albendazole, mebendazole, ivermectin

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### Baylisascaris procyonis

- Large intestinal nematode of raccoons
- Transmitted by fecal-oral contamination
- First infection reported in 1984
  Humans and other mammals are accidentally infected and disease can be fatal
- Young childrenOver 50 species of birds and
- mammals can act as intermediate or paratenic host







#### **Geographic Distribution**



- U.S.-infected raccoons are common in the Middle Atlantic, Midwest, Northeast regions, and are well documented in California and Georgia.
- Proven human cases have been reported in California, Oregon, New York, Pennsylvania, Illinois, Michigan, and Minnesota, with a suspected case in Missouri.
- B. procyonis has a widespread geographic distribution, with infection rates as high as 70% in adult raccoons and exceeding 90% in juvenile raccoons
- Predator animals may become infected by eating a smaller animal that has been infected with Baylisascaris.

(ear <sup>a</sup>	Location	Age	Sex	Clinical	Outcome	Reference
980	Pennsylvania	10 mo	Male	Eosinophilic meningoencephalitis	Fatal	17
1984	Illinois	18 mo	Male	Eosinophilic meningoencephalitis	Fatal	18
1990	New York	13 mo	Male	Eosinophilic meningoencephalitis	Severe neurologic sequelae	19
1992	California	29 yr	Male	Diffuse unilateral subacute neuroretinitis	Ocular sequelae	21
1991	Germany	48 yr	Female	Diffuse unilateral subacute neuroretinitis	Ocular sequelae	22
1995	Massachusetts	10 yr	Male	Esoinophilic cardiac pseudotumor	Fatal	20
1996	Michigan	6 ут	Male	Chorioretinitis, neurologic deficits	Severe neurologic sequelae	23
1996	Michigan	2 уг	Male	Eosinophilic meningoencephalitis, chorioretinitis	Severe neurologic sequelae	23
1997	California	13 mo	Male	Eosinophilic meningoencephalitis	Severe neurologic sequelae	2
1998	California	11 mo	Male	Eosinophilic encephalitis	Severe neurologic sequelae	1
1999	California	17 yr	Male	Eosinophilic meningoencephalitis	Fatal	ъ

#### Baylisascariasis

- The severity of the disease depends to a large extent on how many eggs are ingested.
- Human infections can be asymptomatic, yet infections often result in severe disease manifestations
  - Larvae that continue to grow and wander in body
  - Penetrate the gut wall and migrate to a wide variety of tissues (liver, heart, lungs, brain, eyes)
  - Infection can result in visceral larva migrans (VLM) or ocular larva migrans (OLM)
  - Larvae tend to invade the spinal cord, brain, and eye of humans, resulting in permanent neurologic damage, blindness, or death
     Symptoms appear 1-3 weeks after infection, can take as long as 2 months

Baylisacariasis: OLM, CNS involvement

### **Diagnostics/Treatment**



- No widely available definitive diagnostic tests
  - Many cases are not diagnosed
  - Examination of tissue biopsies can be extremely helpful if a section of larva is contained
  - Ocular examinations revealing a migrating larva, or lesions consistent with a nematode larva are often the most significant clue to infection with Baylisascaris
- Albendazole recommended
- Laser treatment of the eye for larvae



#### Hookworm spp.

- Necator americanus ("American killer")

   Was widespread in the Southeastern U.S. early in the 20th century.
  - Most common hookworm worldwide
- Ancylostoma duodenale
- WHO- 740 million affected globally
- Filariform juvenile worms penetrate skin
- Hookworm infection leads to anemia, protein deficiency, malnutrition
- Hookworm disease is a leading cause of morbidity in children and pregnant women, and can have adverse results for the mother, the fetus and the neonate.









## **Diagnosis and Treatment**

- Examination of the eggs cannot distinguish between N. americanus and A. duodenale
- Larvae can be used to differentiate between *N. americanus* and *A. duodenale*
- Need to distinguish between the rhabditiform larvae of hookworms and those of Strongyloides stercoralis
- Treatment- Albendazole, with mebendazole and pyrantel pamorate as alternatives

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- Human whipworm
- Second most common nematode parasite of man
- Worldwide distribution
- WHO-795 million affected globally
- 2.2 million infected in U.S. (mostly Southern)





#### Trichuris: Clinical features

- Most frequently asymptomatic
- No tissue migration
- Heavy infections, especially in small children, can cause gastrointestinal problems (abdominal pain, diarrhea, rectal prolapse)
  - Possible growth retardation
- Treatment
   Mebendazole
  - Albendazole

Trichuris egg- note two bulbs that allow exit of larval stage



## The WHO helminth control program for school aged children



- Children are continuously exposed to infection
- Children grow rapidly and are especially susceptible to infection and the associate morbidity
- Chronic helminth infection seems to have a negative impact on cognitive development
- 10 cents annually per child covers drug cost
- The program is heavily based on drug treatment

## Capillaria spp.

- Similar in morphology to Trichuris spp.
- Three species reported in humans, but Capillaria philippinensis most common
- Ingestion of raw or undercooked fish
- C. philippinensis is endemic in the Philippines and also occurs in Thailand, Taiwan.
  - Rare cases reported from other Asian countries, the Middle East, and Colombia.
- Rare human infections with *C. hepatica* (hepatic capillariasis) and *C. aerophila* (pulmonary capillariasis) have been reported worldwide.

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#### Disease, etc.

- Intestinal capillariasis (*C. philippinensis*) manifests as abdominal pain and diarrhea
- A protein-losing enteropathy can develop which may result in death from loss of electrolytes, heart failure, secondary bacterial infection
   Hepatic capillariasis (C. hepatica) manifests as an
- acute or subacute hepatitis with eosinophilia, with possible dissemination to other organs.
- Pulmonary capillariasis (*C. aerophila*) may present with fever, cough, asthma, and pneumonia, and also may be fatal.
- Dx: eggs, larvae and/or adult worms in the stool, also intestinal, liver, lung biopsies/necropsies.
- Tx: Mebendazole, albendazole is an alternative.

Capillaria egg- note similarity to Trichuris, but more round



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# Strongyloides stercoralis Threadworm Exists as a free-living animal and also as a parasite Filariform infective larvae and a free-living rhabditiform larvae Autoinfection is important 3-100 million people estimated to be infected

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## Outbreaks

- Several outbreaks of *A. cantonensis* disease in humans have been reported in the Pacific islands and more than 2800 cases have been documented worldwide.
  - >47% cases in Thailand
  - Custom of eating raw/undercooked snails (Pila spp) with alcohol
- In the past 10 years, several major outbreaks of the disease have been reported in endemic regions, especially in China (nine outbreaks in mainland China and three in Taiwan).
- Caribbean islands
  - First case of human angiostrongyliasis was reported in Cuba in 1973
  - Increasing numbers of A. cantonensis cases, most notably in Costa Rica and Jamaica.

### Hawaii Outbreak

#### 1-6-09: ANGIOSTRONGYLUS MENINGITIS - UNITED STATES: (HAWAII): ProMED-mail

- 3 residents of Hawaii (big island) contracted Angiostrongylus meningitis
  - 2 people in comas
  - Home-grown produce suspected as source of infection
- More cases suspected, but others have not gone to the hospital because they do not have medical insurance.
- Angiostrongylus cantonensis is spreading in countries of the Pacific rim including Hawaii probably spread by rats carried on ships.

#### Angiostrongyliasis: Clinical Features

#### Eosinophilic meningitis

- Ingested larvae eventually reach the CNS in ~2 weeks where they usually die shortly thereafter.
   Severe headaches, nausea, vomiting, neck stiffness, seizures, and neurologic
- abnormalities. - The incubation time is highly variable, ranging from 1 day to several months, depending on the number of parasites involved.
- depending on the number of parasites involved.
   Occasionally, ocular invasion occurs and surgery is required to remove worms
- Abdominal angiostrongyliasis mimics appendicitis, with eosinophilia
- Most cases of human angiostrongyliasis are mild and self-limiting, but death can occur in severe cases without prompt and proper treatment.



## Treatment/Prevention of Angiostrongyliasis

- Thiabendazole for early, invasive stages
- Relief of symptoms for A. cantonensis infections can be achieved by the use of analgesics, corticosteroids, and careful removal of the cerebral spinal fluid at frequent intervals.
- Avoid eating raw or undercooked intermediate and paratenic hosts (snails, other mollusks) or potentially contaminated vegetables.
- Eradicating molluscan hosts and rats near houses and vegetable gardens







#### Anisakiasis

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- Within 6 hours after ingestion of infected larvae, they penetrate stomach or intestine, causing violent abdominal pain, nausea, and vomiting may occur.
- If the larvae pass into the bowel, a severe eosinophilic granulomatous response may also occur 1-2 weeks following infection
- · Anisakis simplex allergy
  - Allergic reactions to A. simplex should be suspected when allergic-like reactions occur after eating seafood, yet the results of skin tests to seafood are negative.
  - Allergic reactions may be triggered by dead parasites.
  - Since the allergens are not always destroyed by heat, allergic reactions may even occur after food is cooked.



# Prevention

- Caution with raw, salted, pickled fish
- FDA guidelines for retailers who sell fish intended to be eaten raw.
  - Freezing fish to -31°F for 15 hours or -4°F for 7 days to kill parasites and physical examination
- Commercial blast-freezing can render juveniles harmless





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