Parasites

part 7, Trematode Diseases

a human “blood fluke”

Schistosoma mansoni

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Origins of this article

Since childhood I am fascinated by creepy organisms. I gave talks to medical trainees about spotted fevers and the ticks that spread them. I volunteered in West Africa in 2004, sometimes treating malaria and other tropical diseases. For the past decade I use old microscopes as a hobby, and recently I contribute to *Micscape* magazine.

My curiosity makes for long articles. Today I discuss trematode caused human diseases, and eventually I'll relate my own and other true stories about patients with parasites. I have some vintage slides of parasites, allowing me to illustrate a few kinds. I focus on human parasites, but many of my images show parasites of animals.

Disclaimers

I am a doctor of general internal medicine but **nothing in this article should be used to diagnose or treat medical conditions**. Medical Parasitology is a subspecialty needing both knowledge and judgement calls. The few times I encountered parasites locally, I consulted the US CDC website and state health department.

Be skeptical and investigate for yourself if something seems unlikely. You can learn a lot from the internet, or be fooled by it. Science is never finished; it advances by adapting models when new evidence accumulates.

Think you have parasites? Consult your doctor. If you live in the USA or Western Europe having serious parasites is very unlikely, so the doctor may dismiss your self diagnosis without testing and offer you $100 of anxiety pills. An alternative healer might happily order $200 of questionable parasite tests and sell you a worthless $200 parasite cleanse. Serious human parasites are now rare in wealthy nations. Soap, shoes, flush toilets, clean water and cooked food are generally your best bets against parasites.

Disclaimer to the disclaimer
Immigrants or travelers returning from the tropics and patients on certain medications really could have life threatening parasites, which most US doctors now know little about. Remind the doctor about travel or immunocompromise to lessen the chance of becoming a medical error in these special cases.

Cover page photomicrograph

Schistosoma mansoni, can be acquired through the skin in sub-Saharan Africa, the middle East and parts of Latin America. Acute or chronic schistosomiasis (aka snail fever or bilharzia) may result. Paired male and female worms ("blood flukes") live clasped together for years in veins near the colon. Vintage Carolina slide, stained. 2.5X objective, dark field. Male worm, about 1 cm long, 05mm wide.

Other illustrations

If not noted otherwise, photomicrographs are mine, taken with AO/Reichert microscopes with USB camera. With a 0.5X reducer (added late 2017) my 2.5X objective images are about 5 mm across, the 4X about 3 mm, 10X about 1.1 mm, 40X about 0.3 mm (300 microns), and 100X about 125 microns. Some images adjusted for brightness and contrast. Some patient photos of mine from West Africa are also included.

Contents

This month part 7, Trematode Diseases

Future installments:

Chapter 3 continues with B) nematode worms, and C) some other helminths

Chapter 4 Ectoparasites

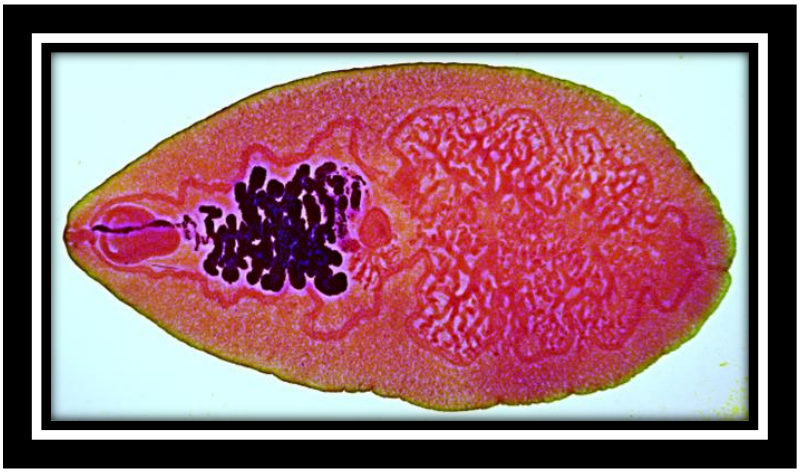
Chapter 5 Clinical observations, bad stories, good parasites

including Morgellons disease, West African cases, possible parasite benefits

Parasites **(an overall introduction)**

Life spreads into every nook and cranny where it can survive, including inside and outside the bodies of animals. Those bodies turned out to be very comfy and tasty. Evolution thus produced and adapted many endoparasites (like intestinal worms) and ectoparasites (like lice). Most wild animals have parasites, as did most humans in the past. Most individuals are not harmed, but hosts are sometimes injured by heavy infestation or complications. In poor and tropical areas many people are still harmed and even killed, including about 600,000 annual deaths from malaria. Some ectoparasites also act as vectors to spread bacteria and viruses that cause Lyme disease, encephalitis, plague and other illness. Nearly half of humans still have parasites, most commonly helminths (worms) and hidden toxoplasmosis, but they don't make most of us sick. Parasites come from many different branches of life, but especially from protozoans, flatworms, roundworms, and arthropods (including ticks, crustaceans, insects). I discuss especially three main kinds of parasites of humans: protozoan parasites, worms (helminths), and ectoparasites.

Parasites are most harmful today in poor areas of the world. We need to continue life saving efforts to control malaria, worms, and other neglected tropical diseases. Still, most of you reading this need not fear parasites. Anxiety about parasites is far more common than parasitic disease in the developed world. Parasites may be the majority of animal species in the wild, and the balance of nature might be hurt if we continue to extinct parasite species faster than we can discover them.



Fasciolopsis buski, giant human intestinal fluke. Slide photographed on fluorescent light. Fluke 3.3 x 1.9 cm

Dermacentor variabilis male wood tick, my yard May 2024, 2.5X obj., stitch, body about 5 mm long

Part 7 Trematode Diseases of Humans

Worms that are parasites are called **helminths**, the big two kinds being flatworms and roundworms. Platyhelminthes (flatworm) biology and trematode tricks were discussed last time. Today I discuss human diseases caused by trematodes, including schistosomes (odd trematodes) causing much human suffering and death in poor tropical Africa, and typical digenean trematode flukes that cause a lot of suffering in poor tropical Asia.

Taxonomy

Kingdom Animalia, Phylum Platyhelminthes

traditional taxonomy scheme:

	Class Turbellaria (free living flatworms)	about 6000 species, < 20% of all flatworm species
parasitic	Class Monogenea (fish ectoparasites) ~5k species Class Cestoda (tapeworms) ~5k species Class Trematoda (flukes & schistosomes) ~20k species	about 30,000 species, > 80% of all flatworms

Newer phylogenetic classification (based on relatedness; genomic)

Class Catenulida (only about 100 species, small free living)

Subphylum Rhabditophora

Classes Turbellaria, Monogenea, Cestoda, Trematoda, others

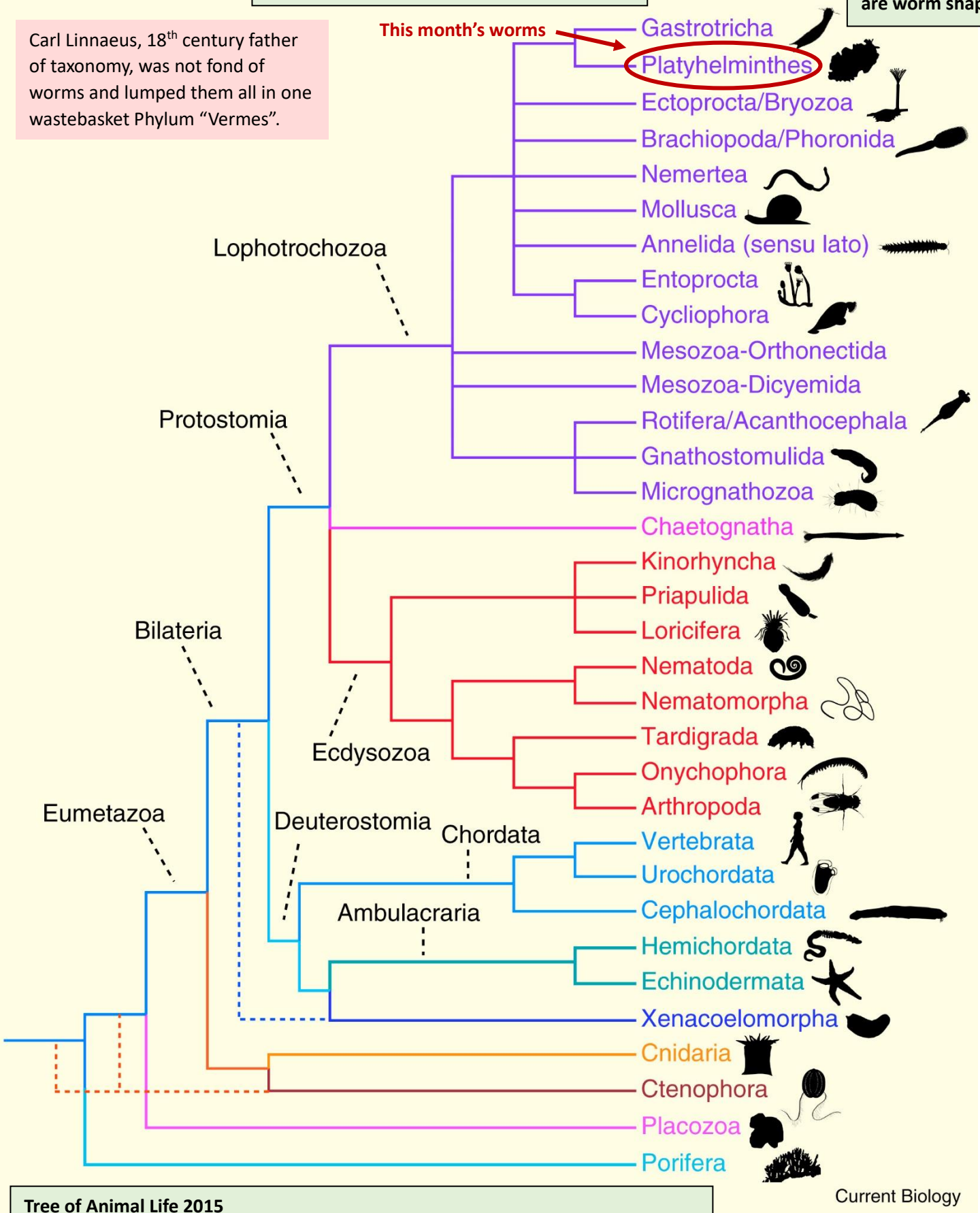
"dangling" orders include Rhabdocoela, Polycladida, Tricladida (planaria), many others

Not discussed yet are other worm parasites: Nematoda, Acanthocephala, etc.

Worms on a tree of animal life

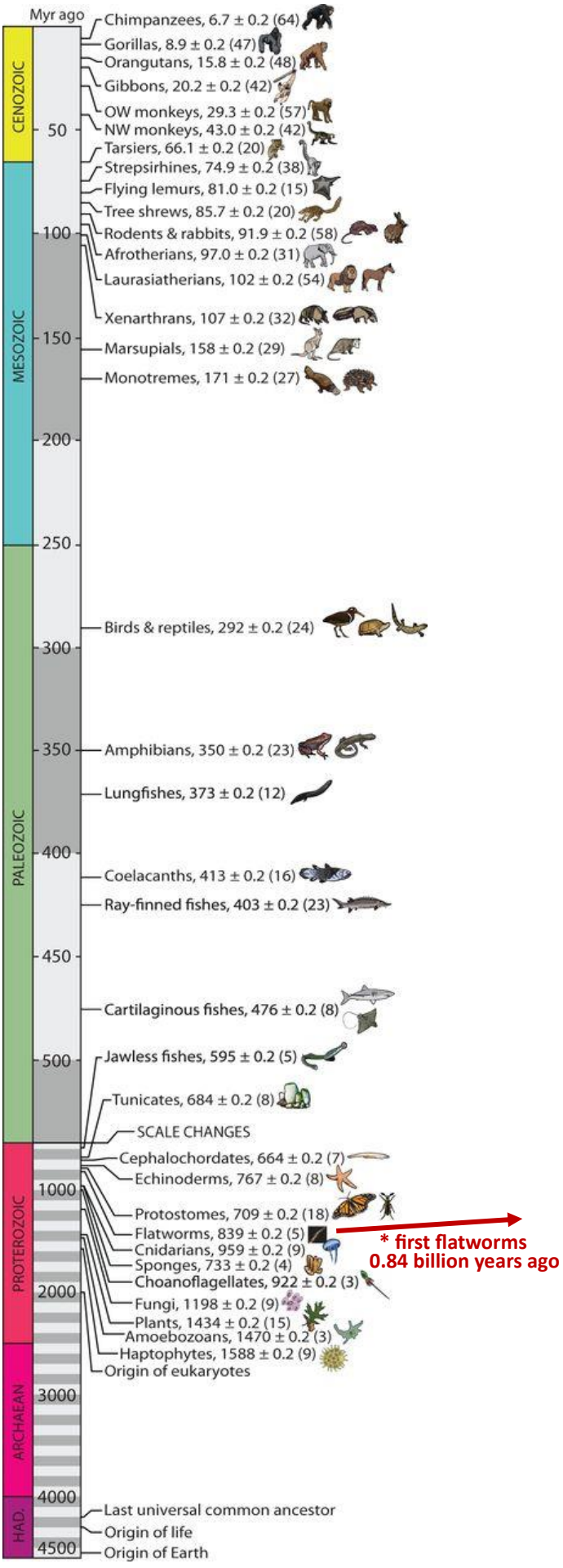
Note how many animal outlines are worm shaped

Carl Linnaeus, 18th century father of taxonomy, was not fond of worms and lumped them all in one wastebasket Phylum "Vermes".



Tree of Animal Life 2015
Best estimate of the phylogenetic relationships of major animal phyla. Major clades named. Some alternative possible positions are indicated by dashed lines. Telford, Budd, Philippe, Phylogenomic Insights into Animal Evolution **Current Biology** 2015

Flatworms on a timeline of life*



Times of diversification of select groups, by genomic clocks

Hedges et al Tree of Life Reveals Clock-Like Speciation and Diversification 2015 **Molecular Biology Evolution**

The 3 major kinds of flatworm are tapeworms, flukes and free living. Tapeworm and fluke vintage slides: *Dipylidium caninum*, 2 pored dog tapeworm slide by JD Mizelle, helminthologist U of Illinois 1930s. Ward's slide of *Fasciolopsis buski*, the "giant human intestinal fluke", this one is about 3.5 cm long.

Tapeworms and flukes have free living cousins, such as this friendly little *Dugesia sp* (or related) planaria, Order Tricladida. from stream, Red Wing, Minnesota USA, 4X objective, dark field, head ~1.5 mm wide

Worms

You know what a worm is; it's a wriggly tube shaped animal. Being slender and legless is useful for moving through granular substrates like dirt. Father of taxonomy Carl Linnaeus lumped all worms together as "Vermes" as they have a similar shape, but we now divide worms among 30 different animal phyla based on body plan and heredity. The biggest 3 phyla of worms are Platyhelminthes, Nematoda and Annelida: flatworms, roundworms and segmented worms.

The most classic of all parasites are intestinal worms. Unlike protozoan parasites, these are multicellular animals and the adults are often large enough to be seen without a microscope.

Parasitic worms are also called **helminths**. The most common parasitic worms of humans are soil transmitted helminths, and the big three worldwide are **nematodes**: roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworm (*Necator americanus* and *Ancylostoma duodenale*). As many as 2 billion humans may still be infected with soil borne helminths, although most infected individuals don't feel ill.

Flatworms get their own phylum, **Platyhelminthes**. In the evolution of animals, flatworms were the first "regular animals". They "invented" bilateral symmetry (a right and left) are mobile, and some have a pair of eyes. You may know of planaria, 1-2 cm long freshwater flatworms that grow back into 2 worms when cut in half. Flatworms have a simple body plan without a true body cavity. Being flat has the advantage of every cell being not too far from the animal's surface, allowing oxygen and carbon dioxide exchange without circulatory or respiratory organs. Flatworms have a simple digestive system with a mouth only (it doubles as anus) often coupled with a very muscular pharynx, and a branched gut to deliver nutrients. Flatworms were the first animals to be predators and also the first to become parasites.

Flatworms: most species of the first regular animals became parasites

Platyhelminthes is the oldest phyla of worms. Flatworms may have split from simpler animals (sponges, corals) about 839 million years ago (per genomic clocks), so they have had more time to evolve than most other animals. What did they do with all that time? Some are free living and some developed poisons, but the majority of flatworms got expert at being parasites. Platyhelminthes is the "most parasitic" of major phyla of animals. Some are hunters or scavengers, but more than 80% of 30,000+ described species are parasites. Tapeworms are still widespread where meat supplies are unsafe. In some parts of Africa and southeast Asia the biggest parasite health burden is caused by parasitic blood, liver and bladder flukes. Some trematodes developed host behavior modification, flashing signals to predators, clonal larva factories and other amazing life cycle "tricks" during long coevolution with their hosts.

Examples of major Platyhelminth (flatworm) groups

Class Catenulida, tiny free living

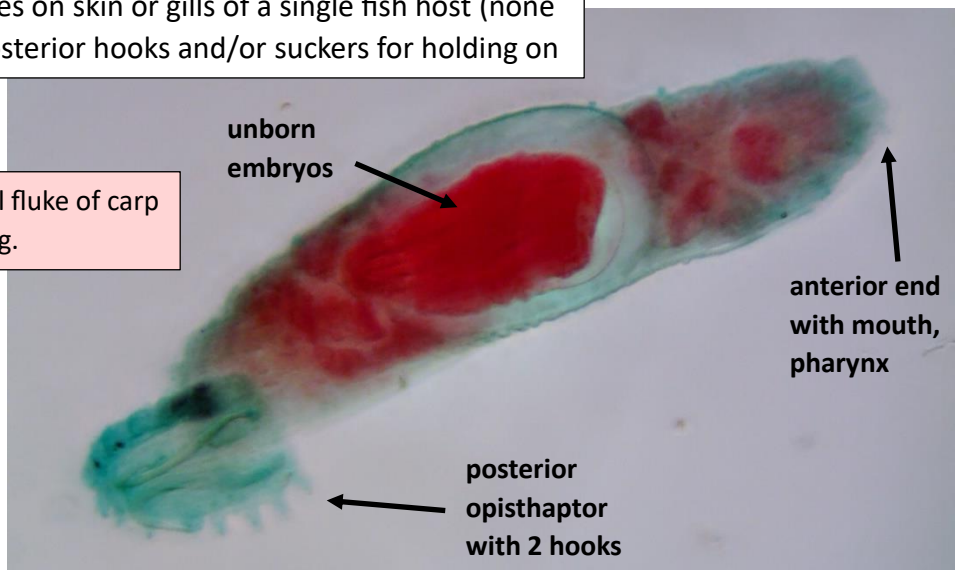
Stenstomum sp catenulid free living flatworm
20X objective, oblique. worm ~ 0.5 mm long

Order Tricladida free living

Dugesia sp ? free living planarian
2.5X obj., worm about 1 cm long

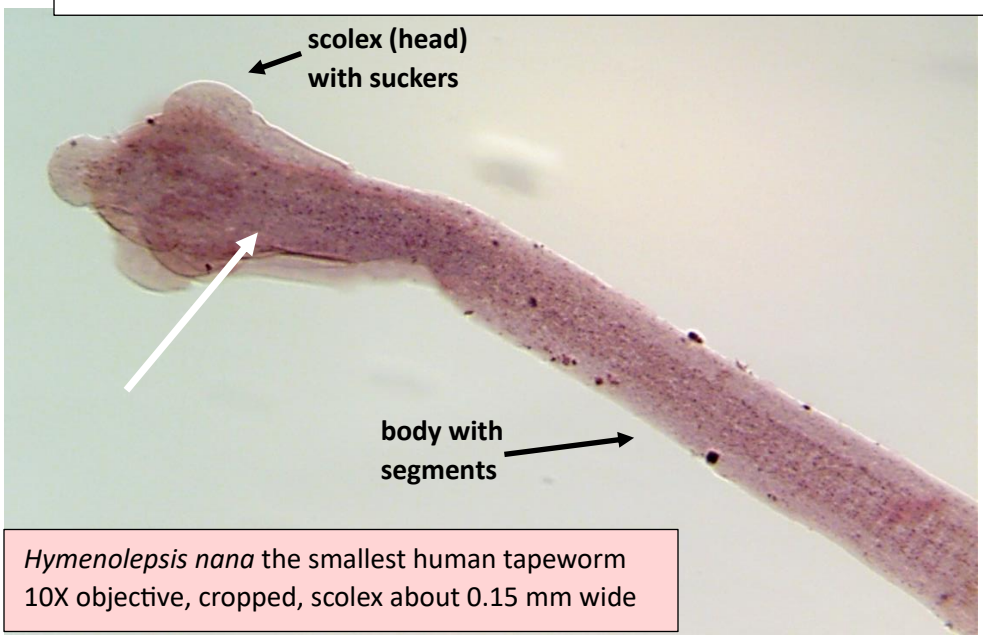
Class Monogenea, tiny ectoparasites on skin or gills of a single fish host (none infest humans), most have large posterior hooks and/or suckers for holding on

Gyrodactylus elegans monogenean gill fluke of carp
20X objective, fluke about 0.5 mm long.



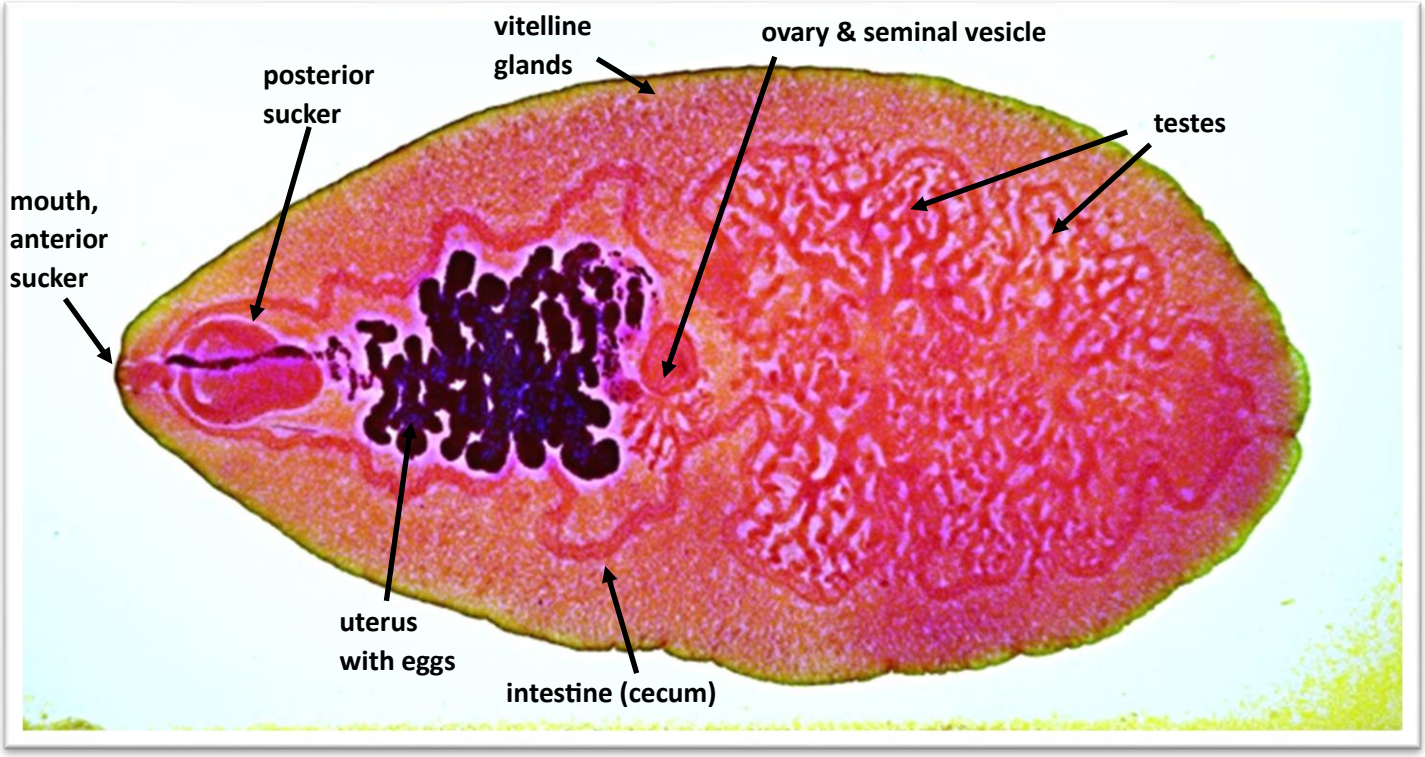
Two classes in Phylum Platyhelminthes have human helminths:

Class Cestoda, intestinal parasites, head modified for attachment, body segmented, i.e**. tapeworms**



Hymenolepsis nana the smallest human tapeworm
10X objective, cropped, scolex about 0.15 mm wide

Class Trematoda, flukes with complex life cycles that may involve blood, gut or lungs



Fasciolopsis buski the giant human intestinal fluke *ex Homo*
This one is 3.4 x 1.9 cm, about half of maximum size.
Ward's slide, digital photograph on a closet light, color adjusted

Flukes

Trematodes (named for their 2 suckers which can look like perforations) are also called flukes, as most adults have a flat elliptical shape, like a flounder fish or a leaf. Over 20 thousand trematode species are known. They are all parasitic with complex digenean life cycles, requiring 2 to 4 different hosts. The first intermediate host is a mollusk and the definitive host is often a vertebrate. 8 typical life stages are eggs, then miracidia, sporocysts, rediae, cercariae, metacercaria and adults. Species infesting humans may live in the gut, the lungs or deep in the blood and internal organs. The migrating worms sometimes cause fevers with acute infection, and with re-infections and time immune reactions to worms or eggs may cause chronic and sometimes fatal organ damage. Blood trematodes, the schistosomes, are second only to malaria in the number of parasitic deaths they cause, mostly in the tropics. Trematodes are highly adapted to complex parasitic lives, with their various life stages becoming adept in host anatomy, travelling through our bodies guided by smells.

The biggest human fluke is *Fasciolopsis buski* the “giant intestinal fluke” which can reach 8 cm (3 inches) long. The smallest fluke to infect humans is *Metagonimus yokogawai*, just 0.5 mm long. Most flukes are hermaphrodites; individuals have both male (testes) and female (ovaries) gonads. (Schistosomes are outliers, differing from other trematodes in having a round cross section and separate male and female sexes). Trematodes are prodigious egg makers; *Fasciola hepatica* can produce up to 25,000 eggs per day (luckily, the eggs quickly pass out of the body and cannot reinfect the host directly). Although hermaphroditic, flukes mate with another when possible; cross fertilization creates more variation than self-fertilization.

Having co-evolved with their hosts for hundreds of millions of years, trematodes have learned amazing tricks. Schistosomes swim through your blood from organ to organ to meet a mate. Host behavior modification has been seen in many trematode intermediate hosts, promoting their being eaten by a definitive host. Some humble trematode parasites have also evolved social behavior, producing a caste system of queens and soldiers reminiscent of ant colonies.

Puma concolor
I previously lived in Colorado and occasionally saw the shy great cats. They can carry tapeworms and nematodes including *Trichinella*.
Image from Animals Around the Globe

A rose by any other name… gets confusing

Scientific names are more specific than common names. The mountain lion is also called a cougar, puma or Florida panther depending on where you live, but is *Puma concolor* to biologists all over the world.

But biologists have their own confusing common language versions of proper biological names.
Class Trematoda are digenean* (aka digenetic) parasitic flukes (not including monogenean flukes). But trematodes (not capitalized)** is sometimes used informally for all fluke shaped flatworms. Monogeneans are fluke shaped but are closer to Cestoda and more distantly related to Trematoda by recent genomic research.

*Digenean or digenetic refers to having a life cycle requiring at least two host species, also called heteroxenous or indirect parasitism. Monogeneans complete their life cycle in one host, aka monoxenous or direct parasitism.

** *Senso lato* means in the broad sense, a made up Latin phrase to describe other made up terms. Biologists make up more Latin and Greek than a medieval priest or even Harry Potter at Hogwarts. Hence my need for glossaries.

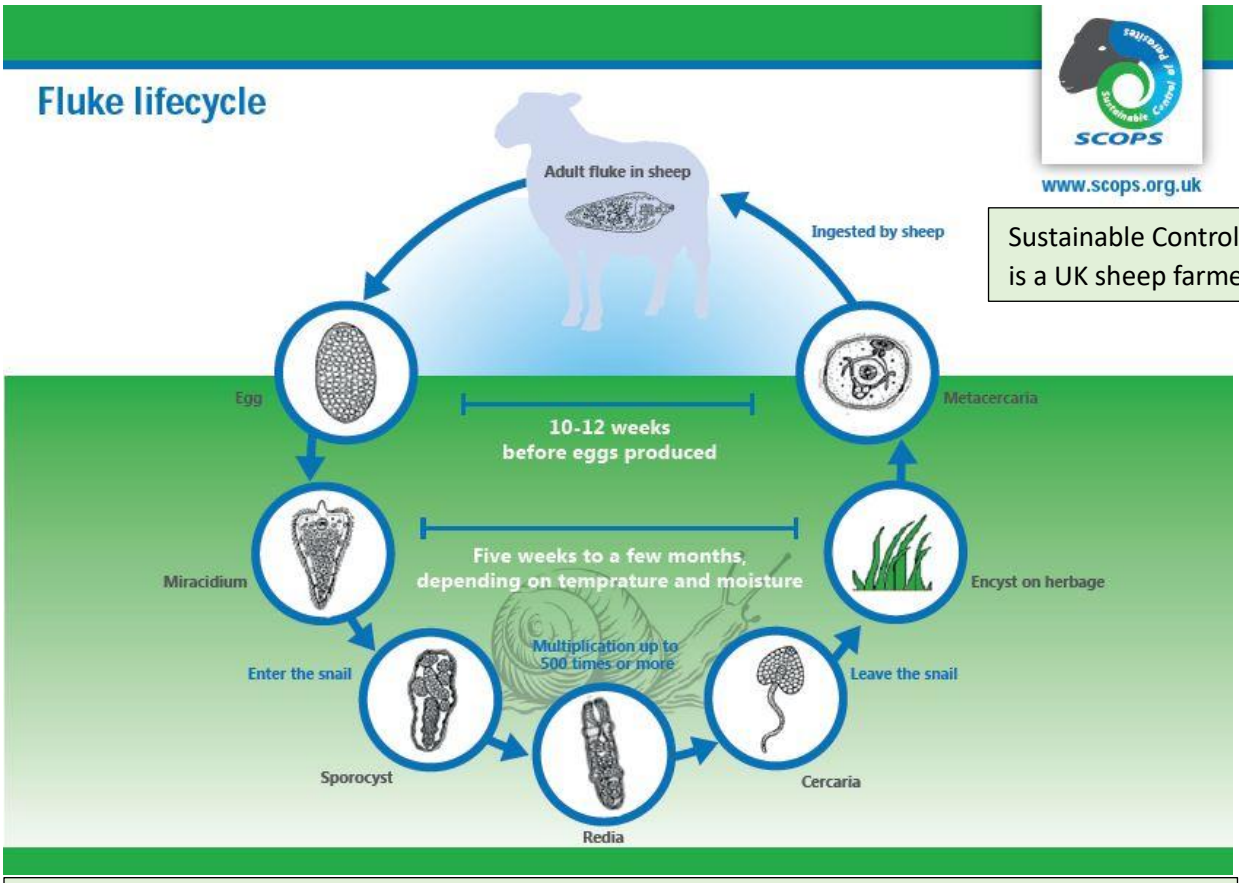
Class Trematoda

The largest group of all flatworms is **digenean trematode flukes**, a class of about 20,000 known species, all parasitic. They typically have a flat elongated leaf like shape, with 2 suckers and an outer layer of tegument (once thought to be acellular and now known to be a syncytium of fused cells). They are hermaphrodites with multiple (often 8) life stages in multiple hosts presenting many variations of complex heteroxenous life cycles with vertebrate definitive hosts and 1 to 3 invertebrate (or invertebrate plus vertebrate) intermediate hosts. Flatworms were around for over 300 million tears before gastropods appeared in the early Cambrian 530 million years ago and Devonian lobe-finned fish crawled onto land 375 million years ago. Ever since, trematodes, mollusks and land vertebrates have been co-evolving, with flatworms adapting to us. About 80 million years ago the schistosomes split off from other trematodes. They are oddballs with a different anatomy than other trematodes, and cause the most fatal of trematode diseases.

Figuring out parasite life cycles has been accomplished by smart and brave field scientists since the 1800's, when microscopes got really good. *Schistosoma haematobium* was found by German surgeon Theodor Bilharz in an Egyptian autopsy in 1851, and linked to hematuria. A snail intermediate host was suspected but not proved experimentally until 1915 by Leiper. *Paragonimus westermani*, the human lung fluke, was seen in humans by Ringer in 1879. The next year Manson found eggs in sputum and suspected a snail intermediate host, which was proved by multiple Japanese scientists around 1920. The human liver fluke, *Clonorchis sinensis*, was described by McConnell in 1875 and the snail and fish intermediate hosts host were found by Muto and Kobayashi in 1918 and 1915 respectively. Each of the CDC life cycle charts in this article were heroic scientific accomplishments that can better human health.

Schistosomes are weird but deadly trematodes. Other digeneans are hermaphrodites and flat but schistosomes have separate males and females, and are round in cross section. The genus *Schistosoma* probably arose in Asia about 80 million years ago as their ancestors moved from bird to rodent hosts, then they spread to Africa and eventually to our human ancestors.

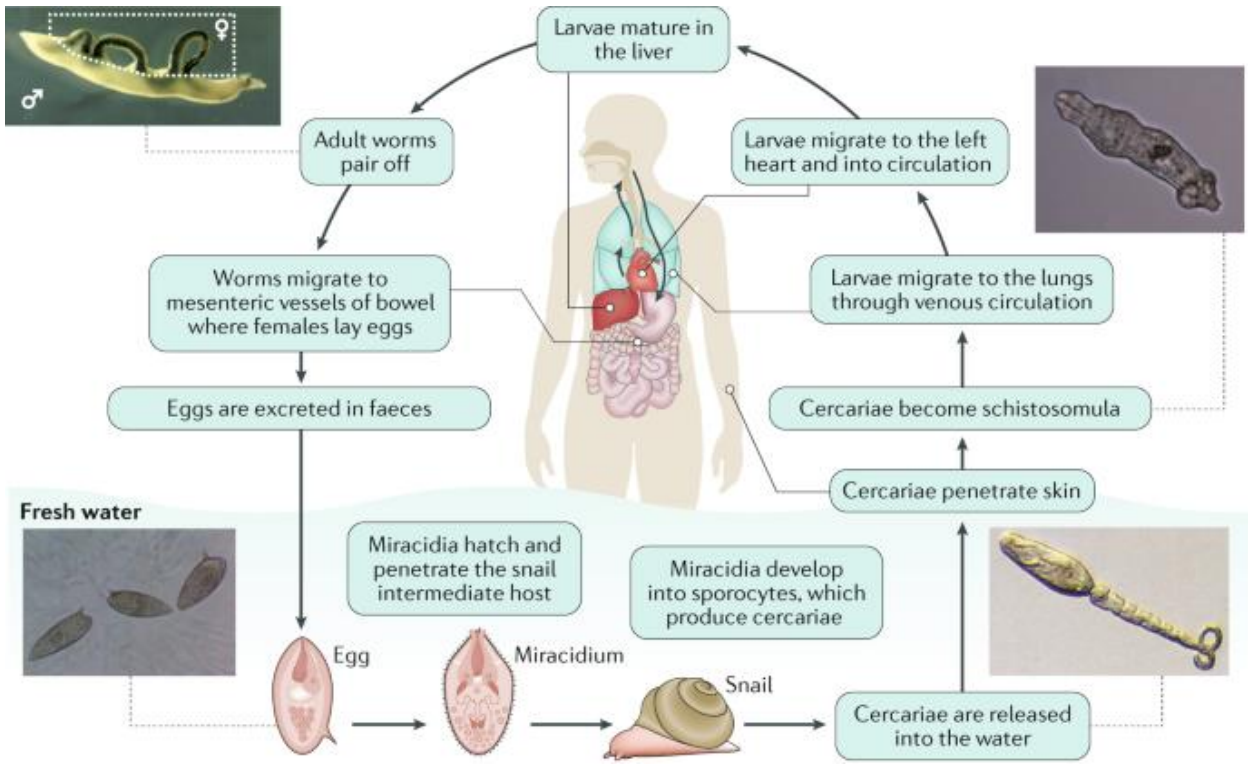
Schistosomes are monogamous: female and male worms pair off for life. A female worm lives permanently in a deep groove that runs the length of the male, a position called *in copula*. They embrace inside human veins, mating and producing eggs for up to 40 years. Charming, but schistosomiasis kills more humans than any other parasitic disease except malaria.



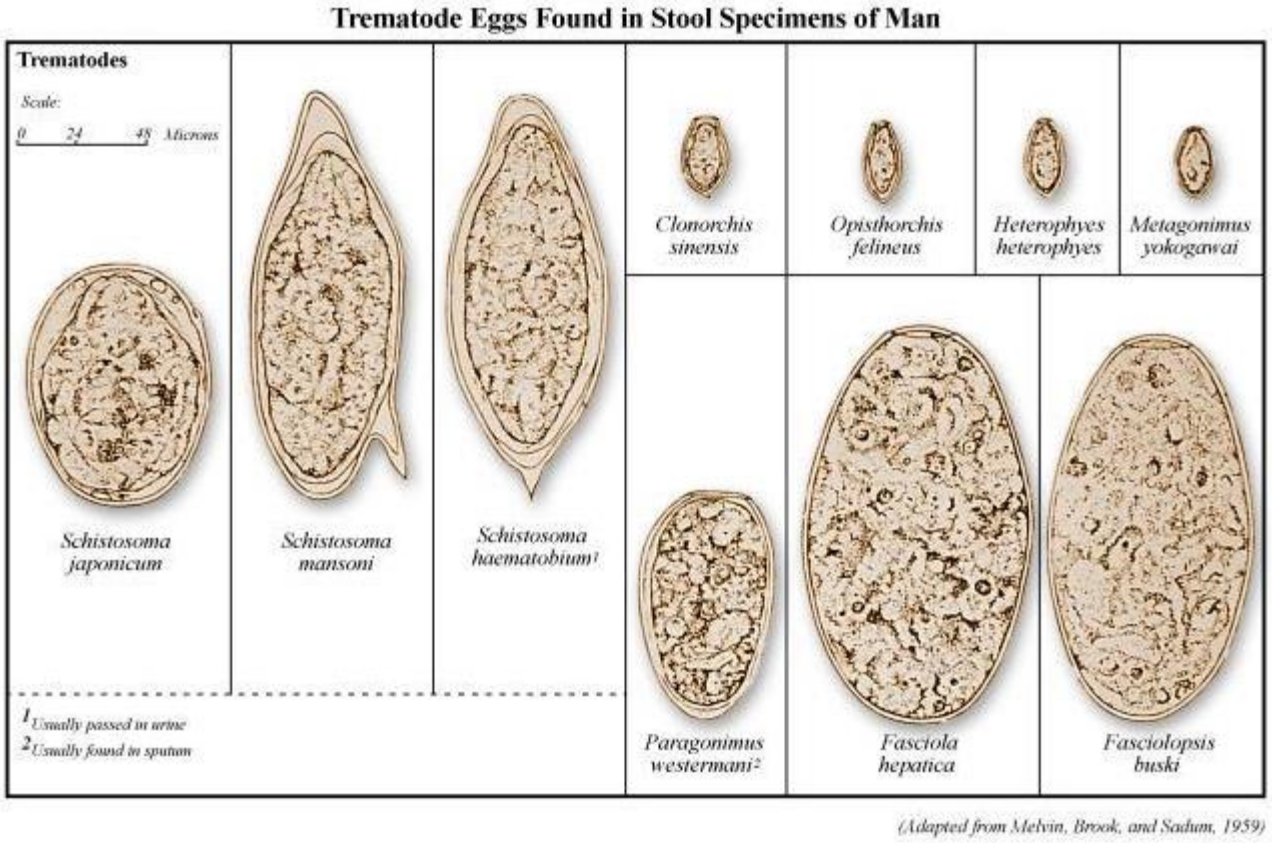
www.scops.org.uk

Sustainable Control of Parasites is a UK sheep farmer group

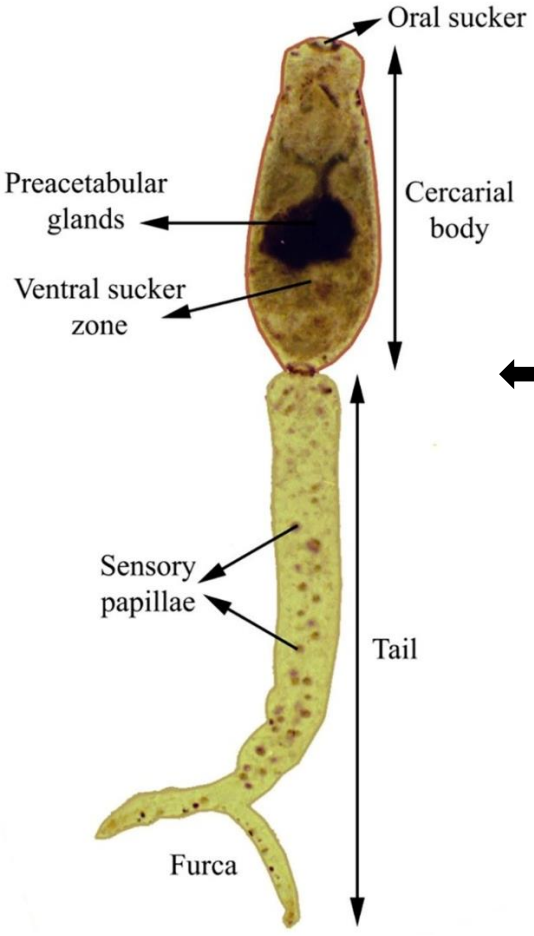
A digenean trematode life cycle in the 2 hosts of *Fasciola hepatica*, the sheep liver fluke.
Stages: 1. egg 2. miracidium 3. sporocyst 5. redia 6. cercaria 7. metacercaria 8. adult fluke.



Life cycle of *Schistosoma mansoni* in snail intermediate and human definitive hosts
Stages: 1. egg 2. miracidium 3. sporocyst 5. cercaria 6. schistosomulum 8. adult worms
image from McManus et al **Nat Rev Dis Pr** 2018



Eggs of trematode species parasitizing man
Eggs are a dispersal and a diagnostic stage (by fecal smears under a microscope)
image from Johns Hopkins Antibiotic Guide



This is what burrows into your skin and blood vessels

Cercaria of *Schistosoma mansoni* is a dispersal and infective stage adapted for swimming and skin penetration. It then drops the tail to become a schistosomulum.
Whole ~ 0.2 mm long (body 100 µ, tail 125 µ)
image Boissier et al **Waterpathogens** 2019

Human trematode diseases

There are so many trematode diseases that a comprehensive review is beyond the limitations of this work, but I will highlight some of the most important. I will start with diseases caused by schistosomes, as they kill more people on earth than any other helminth parasite (only malaria, caused by the protist parasite *Plasmodium*, has a higher death toll). Schistosomes are acquired when their cercaria larva penetrate your skin. The other fluke diseases are foodborne.

Further explanation of my Disclaimer

I review basic aspects of some diseases caused by parasites, but **this incomplete survey cannot be used to diagnose or treat illness**. It can serve as a reminder that parasites do cause human illness, particularly in poor, tropical, undeveloped places. But parasites are rarely the leading cause of common symptoms like fever, diarrhea or cough. Pathogenic viruses and bacteria more commonly cause acute disease than parasites. Confirming a parasitic disease with lab testing is seldom straightforward. In resource poor settings no diagnostic tests or only "simple" stool microscopy looking for eggs in feces may be available. Egg identification requires expert experience and often flotation processing of multiple stool specimens, and does not work unless the patient is at a stage of disease with adult intestinal worms laying eggs. In resource rich nations not used to seeing parasites, antigen or serologic tests might be available, but specific for just one parasite at a time. Serology looks for specific antibodies, which the patient might not make in the first 2 weeks of infection, and eggs might not be produced for months, until larvae mature into adults. Tests done too soon or too late may be worthless. Ordering serology tests for ten different parasites might cost well over $1000 US. If the patient having a parasite is a 1 in 1000 long shot and the test is 99% specific (very good) then 10 out of 11 (91%) of positive tests will still be false positives, meaning the test wrongly says the patient has a disease they don't really have. If we still go ahead and decide to treat with an antiparasitic drug, it might be so rarely used that the local pharmacy won't have it and neither the doctor or the pharmacist will be familiar with the drug's side effects and risks. Some anti-parasitic drugs are arsenic, mercury or antimony compounds that are quite toxic and may need expert advice and special monitoring.

Luckily, in the US and Western Europe most people who think they have parasites are wrong, but in a few rare cases they really do have parasites. If you think you have a parasite start with a local doctor you trust. See also "Parasites that US doctors should know about" information box on the last page of this article for some general advice on how to approach a US or European healthcare provider if you think you might have parasites.

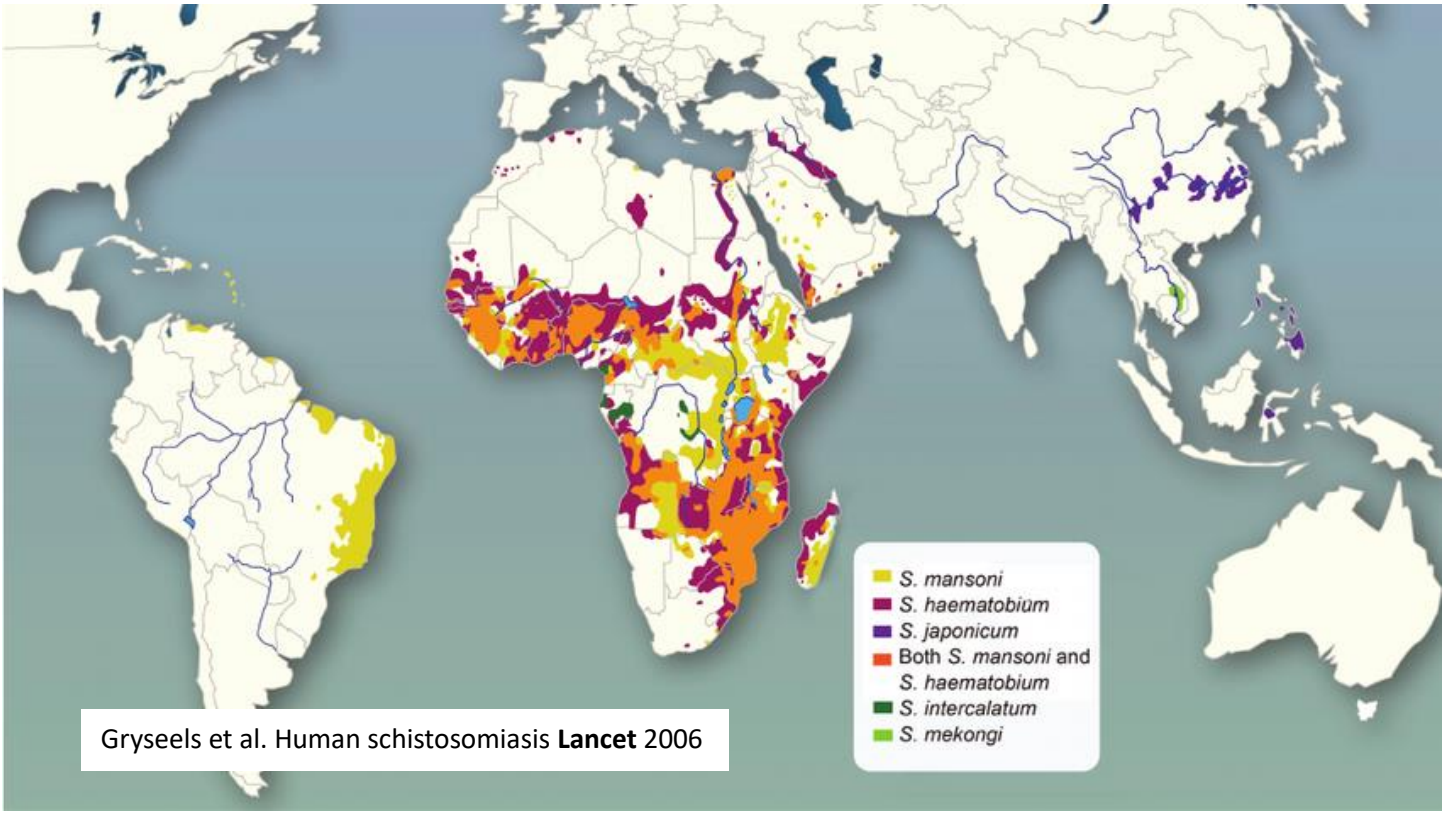
Schistosomiasis: blood fluke diseases

Organism, impact

Schistosomiasis (aka bilharzia after German doctor Bilharz, who described a case in 1851) is a set of acute and chronic diseases (including cercerial dermatitis, snail fever, chronic schisomiasis) caused by trematodes in the genus *Schistosoma*, mostly *S. mansoni, S. japonicum* or *S. heamatobium*, and less commonly *S. mekongi* or *S. intercalatum.* Schistomes are called blood flukes because the sexually reproducing adults live inside human veins. Per the WHO, schistosomasis affects almost 240 million globally and continues to kill about 200,000 people annually, mostly in Africa, more than any other worm parasite of humans.

Geography, acquisition

Schistosoma mansoni is widespread in Africa, parts of the Middle East, and in parts of South America and the Caribbean (brought to the New World by the transatlantic slave trade).
S. haematobium occurs in Africa and in parts of the Middle East, Turkey, and India.
S. japonicum is in parts of China, Philippines, Thailand and Indonesia (eliminated from Japan).
S. mekongi and *S. intercalatum* occur in parts of southeast Asia and central Africa respectively.



Gryseels et al. Human schistosomiasis **Lancet** 2006

Schistosoiasis is acquired wading or swimming in lakes or rivers containing certain snail intermediate hosts which release microscopic cercaria that burrow into human skin.

Life Cycle, pathophysiology of *Schistosoma spp.*

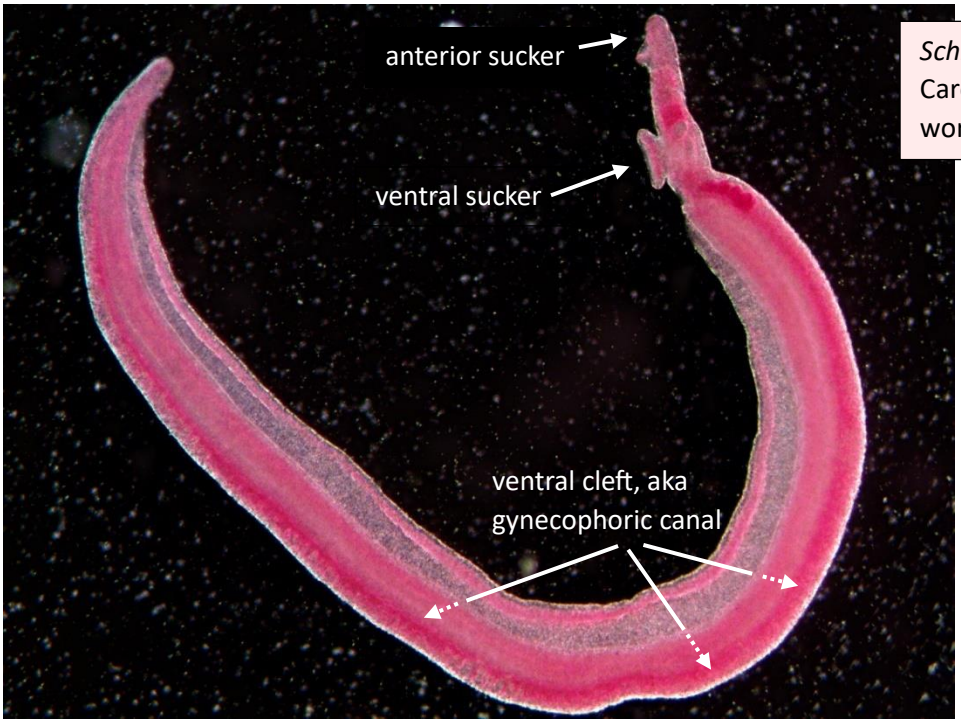
Cercaria penetrate human skin at hair follicles, drop their forked swimming tails, then circulate, mature and live in human blood in several organs, eventually getting eggs into feces or urine.

When moving through the skin, cercaria may illicit localized inflammation.

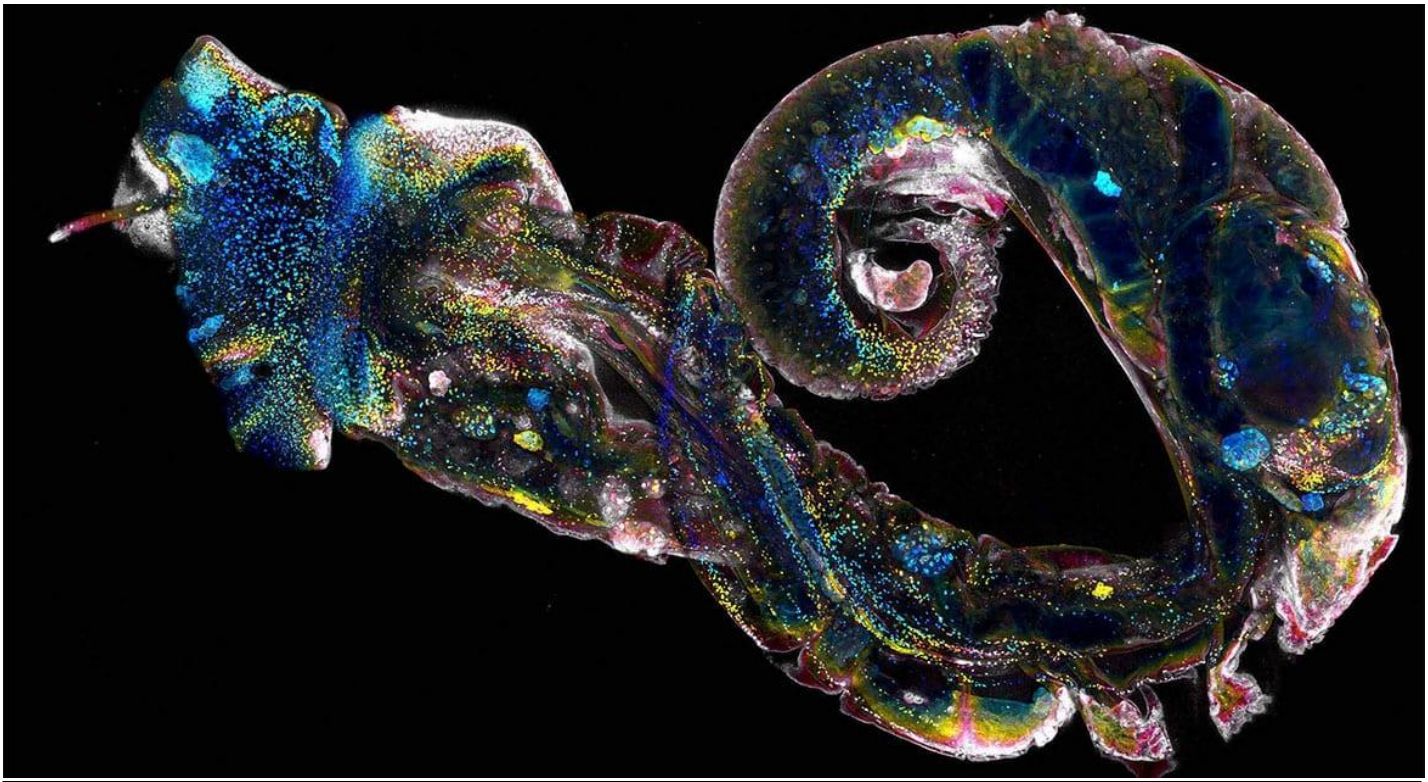
After about 2 to 4 weeks of developing in liver portal veins, mated adult worms start to produce eggs. Some people then develop a febrile systemic hypersensitivity reaction to the eggs, especially the first time (in kids and travellers) or if heavy infestation.

Mated adults can live copulated in mesenteric venules (small veins) for 3 up to 40 years while producing about 300 to 2000 eggs daily, depending on species. A few of these spiked eggs end up migrating through the wall of the intestine or bladder into feces or urine to continue the parasite's life cycle, but most circulate and get lodged in the host, over half in the liver (just downstream of where the parents live in the human ciculatory system). Host reactions to those eggs can cause chronic schistosomiasis with many manifestations in multiple organ systems. Patients may or may not become ill. The schistomes appear to modualte the host response, overall turning it down somewhat and promoting granuloma formation (the egg is protected and can still migrate). The human immune system walls off attackers it can't kill in granulomas, and the liver portal triads and abdominal mesentery become full of egg granulomas (egg surrounded by macrophages and fibrous tissue). Fibrosis in the liver can cause cirrhosis and portal hypertension (but seldom liver failure), splenomegally, caput medusa (ropey veins visible on the abdomen), anemia, throbocytopenia and then bleeding or other infections (some schistosomiasis patients are more suceptible to *Salmonella*). Migrating eggs cause intestinal ulcerative lesions that can progress to focal fibrosis, strictures, fistulas, and papillomatous growths, causing bloody diarrhea and resultant anemia. Eggs can also end up in the lungs, genitals, eye, skin and central nervous system, with granuloma formation and dysfunction in those organs.

Schistosomes are odd trematodes, being gonochoric with separate male and female sexes, and having round instead of flat bodies (more typically worm like, although males have a V-like cross section). Schistosomes ("split body") are named for the male's deep ventral cleft that holds a female worm for a lifetime together in a human vein. Schistosomes have been called the most romantic parasites, but are also the deadliest trematodes for humans.



Schistosoma mansoni adult male, Carolina slide. 4X obj., dark field, worm about 1 cm long long

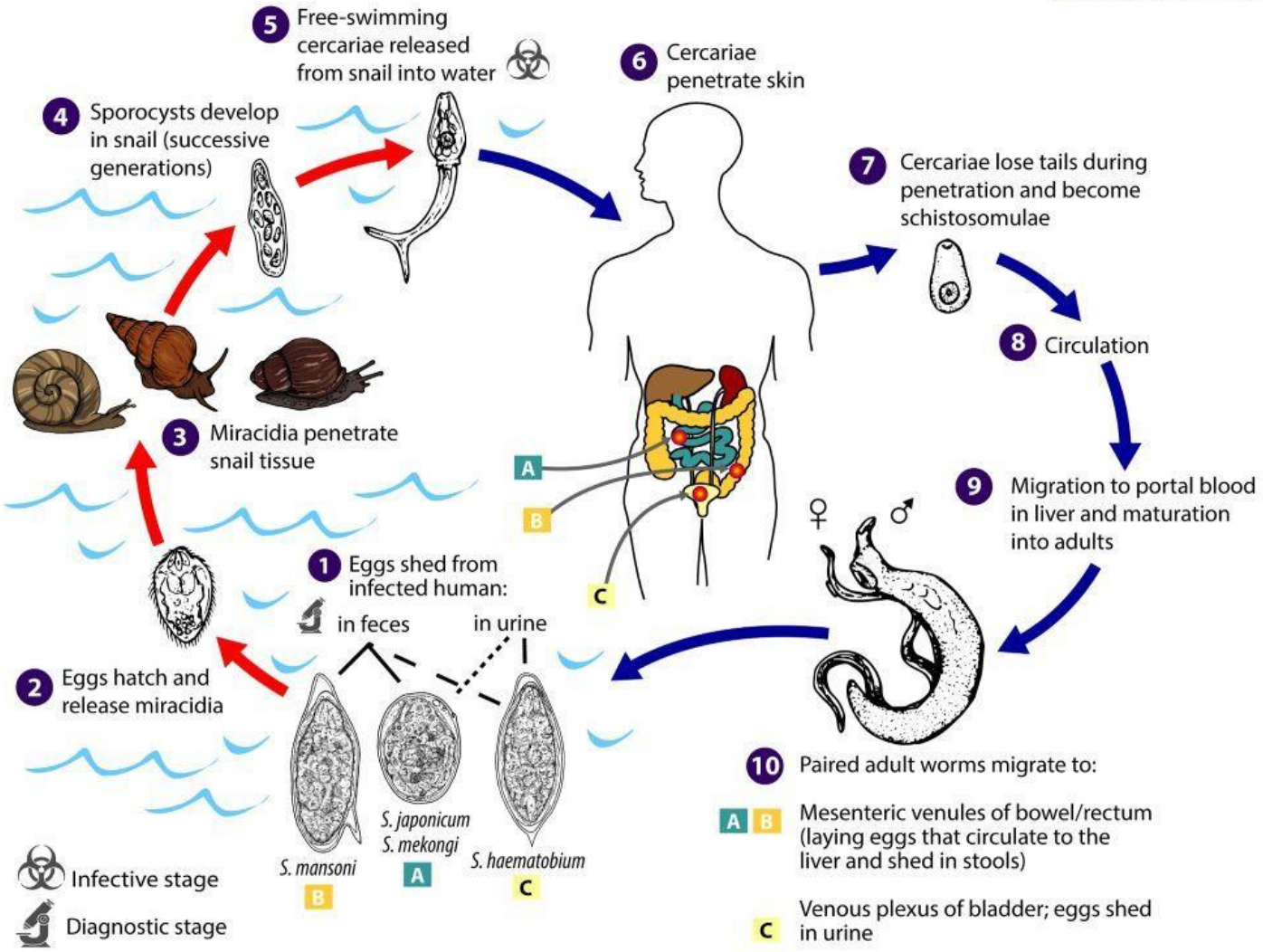


Small snail with shell removed, showing thousands of schistosome parasites. All digenean trematodes have complex multi-host life cycles including asexual reproduction in an intermediate host that is usually a mollusk.
confocal microscopy by Wang and Newmark, Morgridge Institute, University of Wisconsin, USA

DPDx

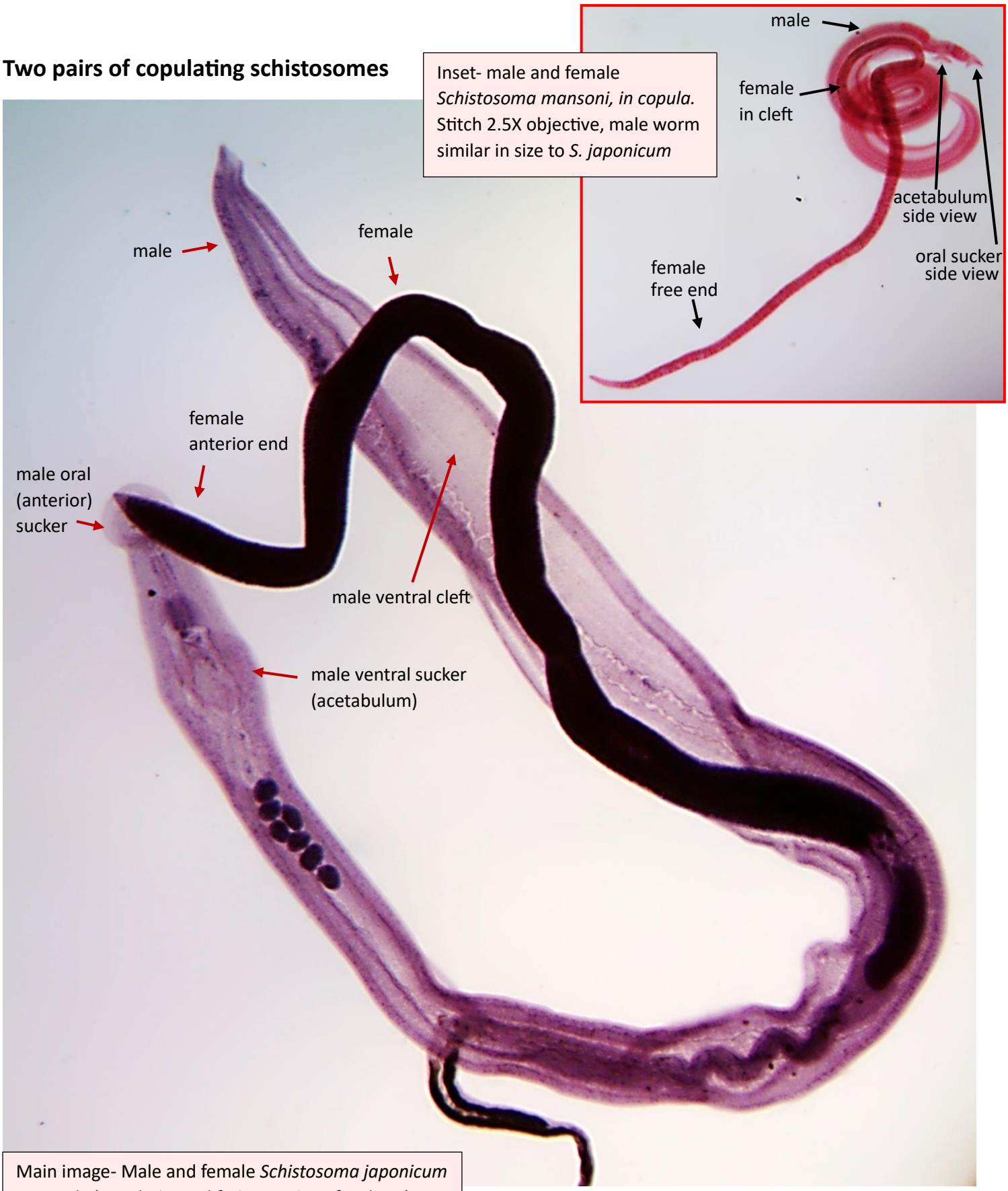
Schistosoma spp.

CDC



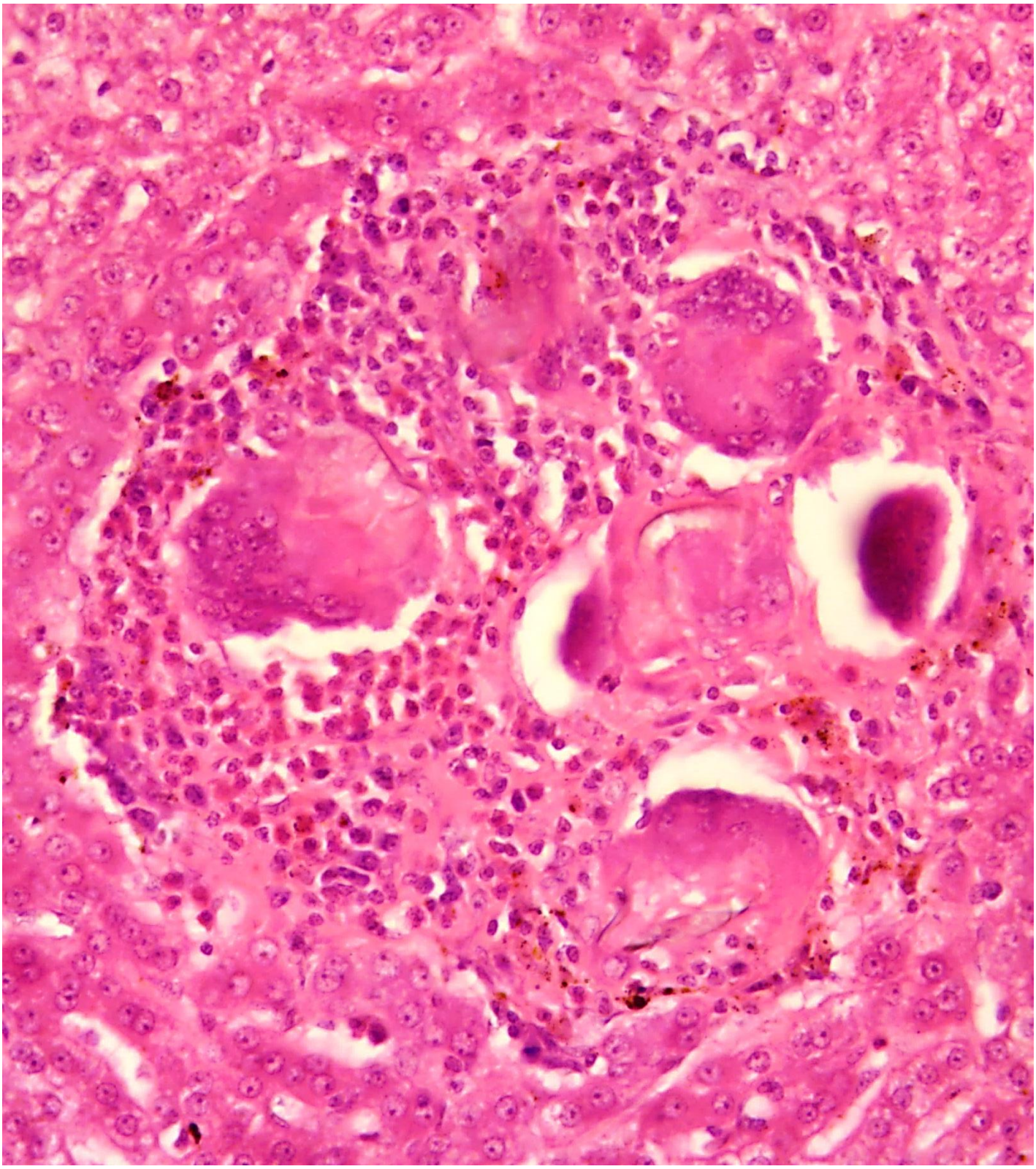
1. human releases eggs containing miracidia in feces or urine into water 2. eggs hatch releasing miracidia which 3. swim and penetrate a snail (intermediate host). 4 and 5. Within snail, the miracidia progress through 2 generations of sporocysts to become many cercariae. 6. Free-swimming cercariae released from snail **penetrate the skin** of human host. 7. Cercariae lose their forked tail, becoming schistosomula. 8 and 9. The schistosomulae **migrate via venous circulation** to lungs, then to the heart, and then **develop in the liver**, exiting the liver via the portal vein system when mature. 10. Paired (male and female) adult worms migrate (depending on their species) to **intestinal veins in the bowel or rectum or to the venous plexus of the genitourinary tract, where they reside and lay eggs**.
S. japonicum is more frequently found in the superior mesenteric veins draining the small intestine (see A).
S. mansoni occurs more often in the inferior mesenteric veins draining the large intestine (see B).
S. intercalatum and S. guineensis go to the inferior mesenteric plexus, lower in the bowel than S. mansoni.
S. haematobium inhabits the venous plexus of the bladder (see C), but it can also go to the rectal venules.
The females (size 7 to 28 mm, depending on species) deposit eggs in the small venules of the portal and perivesical systems. The eggs are moved progressively toward the lumen of the intestine (S. mansoni, S. japonicum, S. mekongi, S. intercalatum/guineensis) and of the bladder and ureters (S. haematobium), and are eliminated with feces or urine.

Two pairs of copulating schistosomes



Inset- male and female *Schistosoma mansoni, in copula.* Stitch 2.5X objective, male worm similar in size to *S. japonicum*

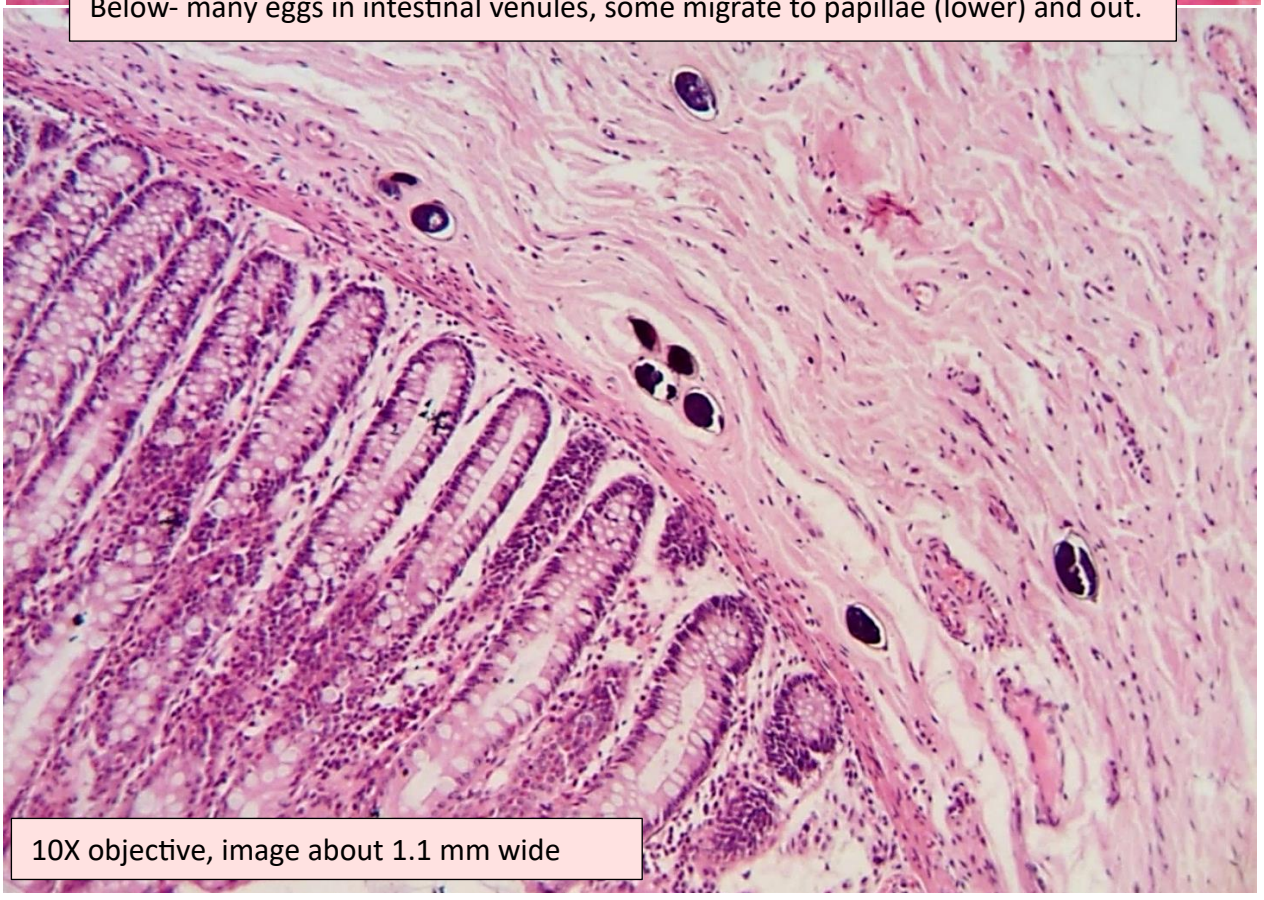
Main image- Male and female *Schistosoma japonicum in copula* (copulation, a lifetime activity for them) Ward's slide, stitched using 2,5X objective, image is about 5 mm across and the male is about 1 cm long



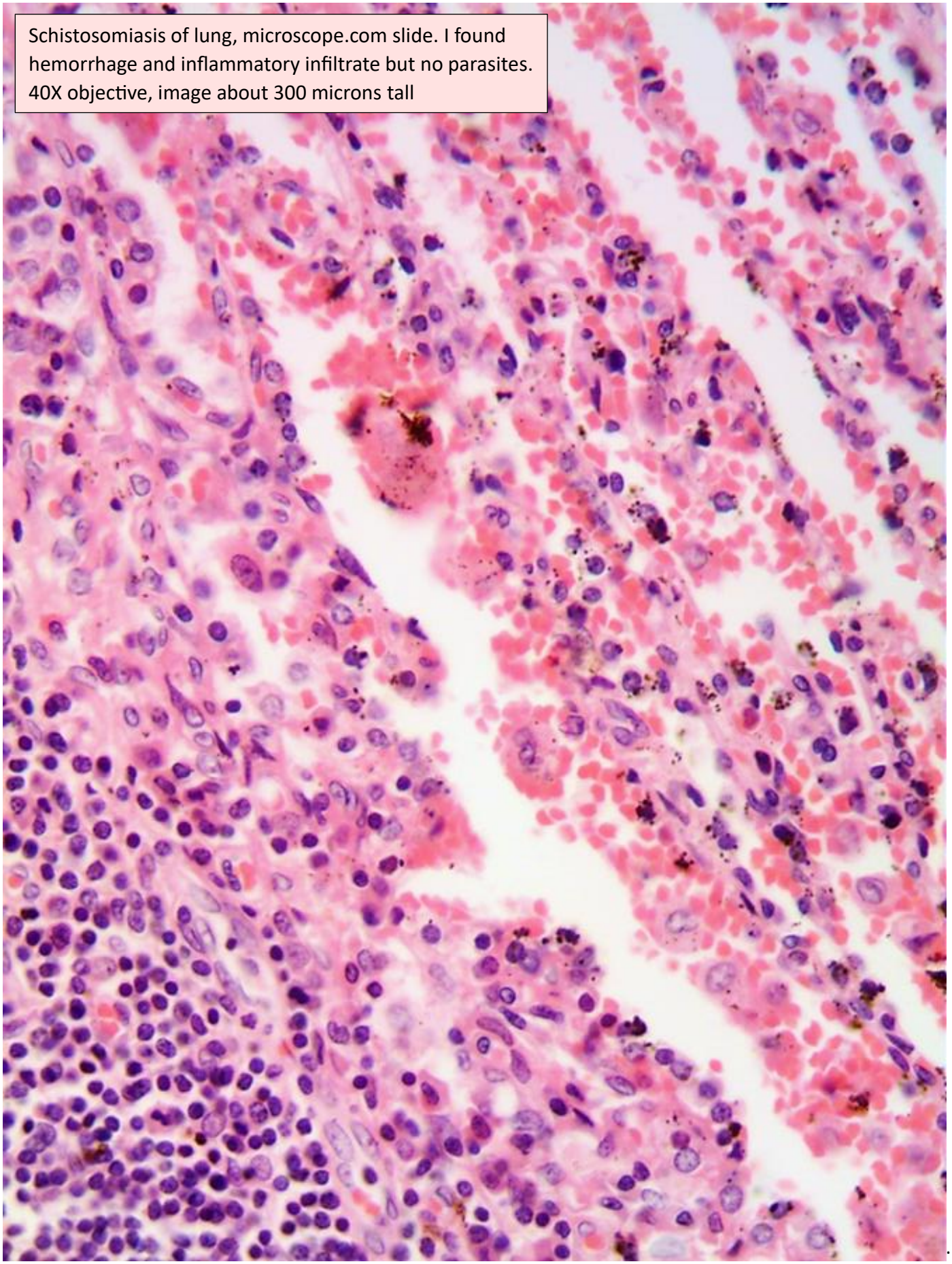
Schistosoma japonicum hepatic granuloma with eggs and multinucleated giant cells in human liver. Army Medical School slide, circa 1950s. Stitched with 40X objective, image ~ 350 microns (0.35 mm) tall

40X objective, image about 300 microns wide

Two human schistosomiasis pathology slides from microscope.com pathology set.
Above- 2 eggs in liver, minimal granuloma formation so far.
Below- many eggs in intestinal venules, some migrate to papillae (lower) and out.



10X objective, image about 1.1 mm wide


Schistosomiasis of lung, microscope.com slide. I found hemorrhage and inflammatory infiltrate but no parasites. 40X objective, image about 300 microns tall

Symptoms, signs of schistosomiasis

Cercaria of human or nonhuman schistosomes can cause cercarial dermatitis with itching and a papular/follicular rash. The rash and itching will resolve spontaneosly.

Acute Katayama fever (aka snail fever) is a serum sickness like reaction to new egg production. Symptoms may include fever, chills, cough, nausea, abdominal pain, malaise, myalgia and hives. Signs may include marked eosinophilia.

Chronic schistosomiasis can have a myriad of symptoms and signs that vary by species and by parasite egg load. Some *Schistosoma* infected individuals are asymptomatic, yet some others will die from the infection. Life is a crap shoot we all lose some day.

Schistosoma mansoni, *S. japonicum*, *S. mekongi* or *S. intercalatum* can cause bloody diarrhea leading to anemia that can cause weakness, and less often pain. In all species, schistosome eggs go to the liver and intestinal mesenteries, sometimes causing hepatic cirrhosis, splenomegaly and other abominal findings, and placing patients at risk for bleeding and infectious complications.

Schistosoma haematobium heads for the urinary bladder and bladder ulcerations can cause hematuria and dysuria. Over time, chronic cystitis develops and sometimes strictures that may cause urinary obstruction. Papillomatous masses in the bladder are common, and in a few cases transform to squamous cell carcinoma of the bladder (parasitic carcinogenesis). *S. haematobium* can also cause genitourinary schistosomiasis. Girls and women can suffer painful bleeding vulvar, vaginal, cervical lesions and infertilty from tubal lesions. Men can suffer pain and swelling from testicular or prostate involvement.

In *Schistosoma mansoni* and sometimes *S. japonicum* egg deposition in pulmonary capillaries can lead to oblitertive arteritis with development of pulmanry hypertension, causing chronic shortness of breath. Over time the heart is stressed and severe heart failure (cor pulmonale type) with leg edema and worsening dyspnea can develop.

In a few cases (including very rarely even in the lightly infected, with any species) reactions to schistosome eggs or worms in the central nervous system cause neurologic complications. Most common is acute tranverse myelitis, with spinal cord eggs causing back pain with distal paralysis. Rarely, brain lesions can cause seizures or stroke like focal weakness. Having parasite eggs circulating all around the body magnifies life's random component.

Diagnostic tests

Eggs may be seen in the stool specimens (urine for *S. haematobium*) if paired adults are still alive. Rectal snip biopsies can sometimes find old schistosome eggs. Serologic tests are available but don't confirm active infection or parasite load. DNA antigen tests might give additional information, and have been used during readication campaigns.

Treatment of schistosomiasis

Supportive care might include iron for anemia, analgesics for pelvic pain, and other measures.

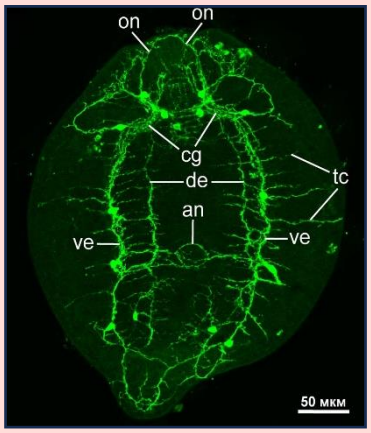
Praziquantal 2 or 3 doses in a single day can kill adult schistosome worms. Treament is often delayed 6 to 8 weeks in returning travellers, as the drug does not kill schistosomulae. Reccomended treatment of acute Katayama fever may be a brief course of prednisone, followed weeks later by praziquantal (evidence for treatment is limited). In chronic schistosomiasis the damage is already done and antiparasitic drugs may not help.

Prevention

Control efforts in endemic areas include mass drug administration of praziquantal (to everyone in a village periodically without individual diagnostic testing, eradication of host snails, and using safe or treated sources of water for drinking and bathing. One clinical parasitoligist reccomends travellers "towel off vigorously" after swimming in the great lakes of the African rift zone.

What a worm knows about your internal anatomy

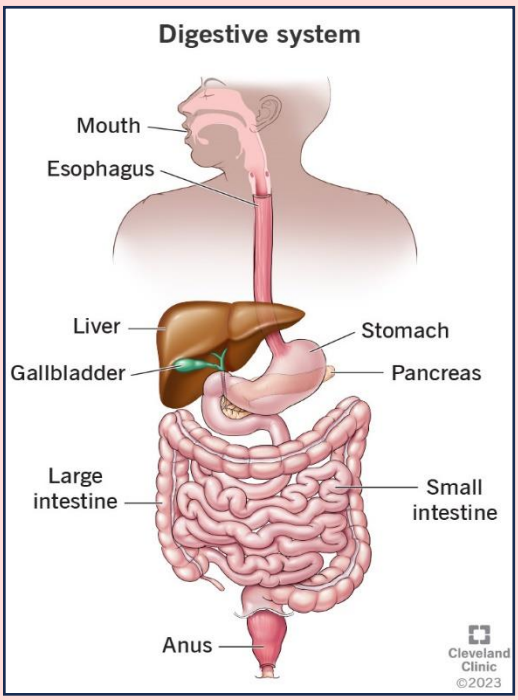
Helminth parasites take epic journeys through animal bodies during their complex life cycles. How can they do that? Flatworms have a simple nervous system including a pair of nerve cords and 2 cerebral ganglia (little brains). The two ganglia and connections between have about 80 cells in *Triaenophorus nodulosus*, the pike tapeworm, compared to about 80 billion in your brain. Worms also have peripheral nerves including sensory neurons for chemicals (taste), pressure and temperature (plus free-living flatworms have eyes, although most parasitic flukes do not). Trematodes have muscles to move and suckers to hold on with. With limited information and a billion times less neurons than you have, flukes wriggle from one organ to another in your body, eventually laying eggs and continuing the life cycle.



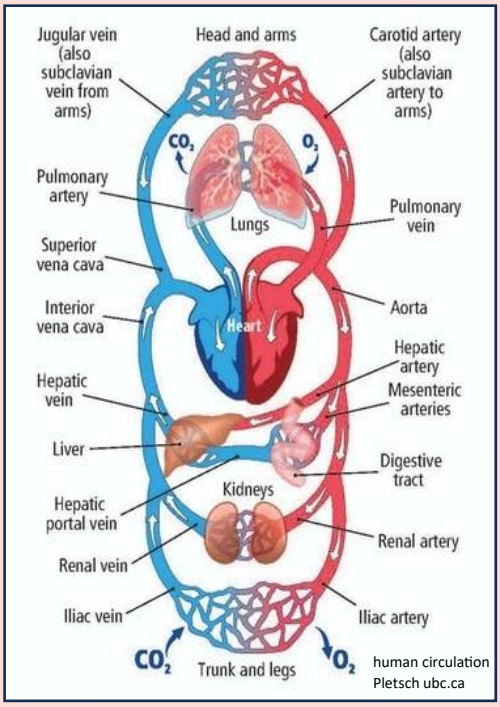
Serotonin neurons of metacercaria of *Diplostomum pseudospathaceum* (an eye fluke in fish 2nd intermediate hosts, we humans also have the feel good neurotransmitter) an – nerves of ventral sucker; cg – cerebral ganglion; de – dorsal nerve cord; on – nerves of ventral sucker; tc – transverse commissures; ve – ventral nerve cord. Image A Petrov in Zaitseva et al. zin.ru/ neuromorphology

Despite having very few neurons, tiny trematodes navigate the human body with ease. Schistosomes live in specific blood vessels as adults while other flukes get into the intestines, liver or lungs. After a hard journey, sometimes several times around a whole human body, each is adapted by eons of evolution to settle into hanging on in a blood vessel or being bathed in digested food or caustic bile or being exposed to air. What life can do is amazing.

Oversimplified, the human gut is simple, a long coiled up tube about 9 meters (30 feet) long. A small side branch goes to the liver and pancreas. The bigger main bile ducts and gallbladder are under the liver, which is full of smaller bile ducts. Worms can use chemical clues to crawl through the GI system. By contrast the adult circulatory system contains about 60,000 miles (!) of vessels, going every which way. The heart and arteries distribute oxygen and nutrients, and veins help move wastes. Arteries branch smaller and smaller until ending in capillaries about 5 microns wide, where blood exchanges molecules with cells. Downstream of this veins merge becoming bigger as they return to the heart. Then all the blood is pumped through the lungs and their pulmonary capillaries. The gut has an extra venous system; the portal vein branches and ends in about 10 micron wide liver sinusoids, then venules merge into a hepatic vein.



Somehow, juvenile schistosomes and nematodes are programmed to use pressure and chemical signals to know which capillaries to exit. After entering skin capillaries schistosomulae go through lungs and heart and exit into the liver. *Ascaris* larvae enter gut capillaries and exit in the lungs, mature, and later exit into the alveoli (air sacs). Even single celled plasmodia (malaria parasites) migrate from skin vessels to liver and back into the blood. Evolution invented some amazing parasites as life pushed into every chance opportunity.



human circulation Pletsch ubc.ca

Clonorchiasis, Opisthorchiasis and Fascioliasis: liver fluke diseases

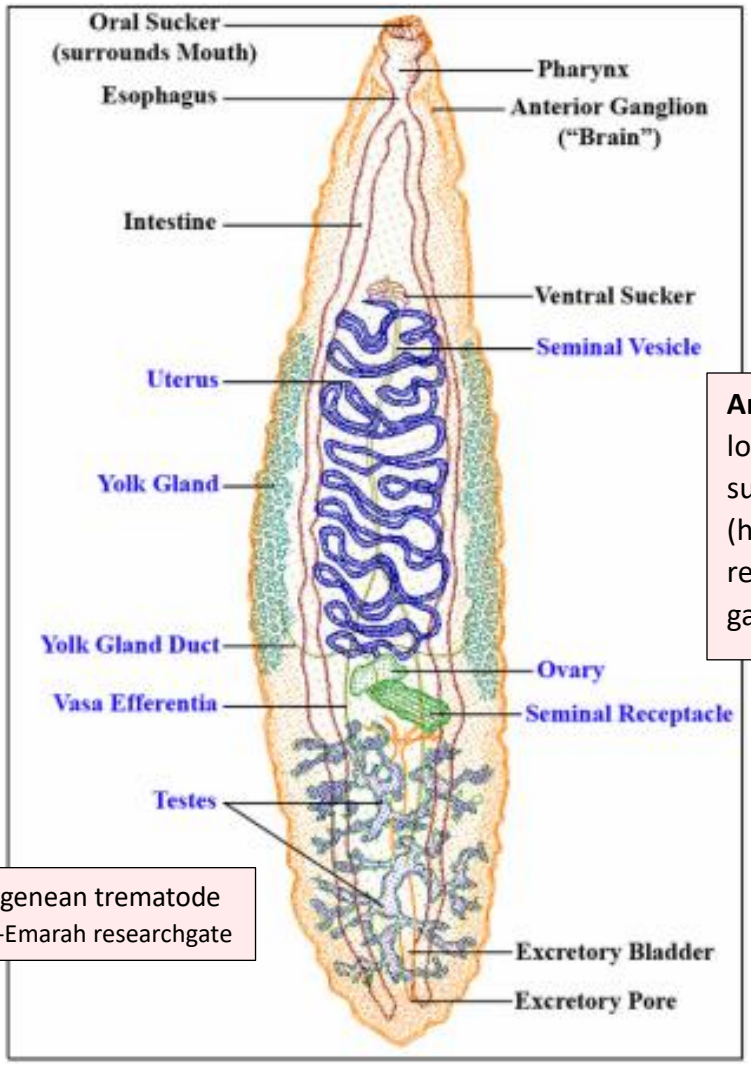
Organisms, impact

Clonorchis sinensis (the Chinese liver fluke), ***Opisthorchis viverrini*** (the Southeast Asian liver fluke), ***O. felineus*** (the cat liver fluke) and ***Fasciola hepatica*** (the common liver fluke or sheep liver fluke) are digenean trematodes whose fairly large, leaf shaped adult worms (often 2 to 7 cm long and half as wide) can live in the human liver and bile ducts, causing three diseases: clonorchiasis, fascioliasis and opisthorchiasis. *Clonorchis* alone is thought to infect about 35 million people in east Asia (up from about about 7 million in the 1990s), and causes about 5000 cases a year of bile duct cancer, which is most commonly fatal. Estimates regarding *Fasciola* range from about 2 to 17 million infected, but many patients are asymptomatic.

Geography, acquisition

Species of *Clonorchis* and *Opisthorchis* (both in family Opisthorchiidae) are widespread in east Asia spread by seafood, and species of *Fasciola* are found worldwide (associated with ruminant livestock as a zoonotic reservoir although transmision is not from animals).
Clonorchiasis is aquired by eating raw or undercooked fish (including sushi) containing metacecariae in some parts of China, South Korera and other places in east Asia (or occasionally from imported fish or shrimp). Opisthorchiasis is also acquired from raw or undercooked fish. These two diseases cannot be spread by direct human contact or contaminated drinking water.
Fascioliasis is aquired by eating raw watercress or water chestnuts (aka caltrop nuts or the devil pod) or other edible aquatic plants containing encysted metcecariae or from water contaminated by livestock or raw vegetables washed in contaminated water. Fascioliasis from *F. hepatica* occurs in over 70 countries worldwide having sheep, cattle or goat farming, and is low level endemic in temperate Eurasia. It is found in US livestock but most US human cases are in immigrants or travelers. Less commonly, fascioliasis is caused by *Fasciola gigantica*, the giant liver fluke, endemic to tropical countries in south and southeast Asia and Africa, also acquired by eating contaminated watercress or other aquatic vegetation.
The lancet fluke *Dicrocoelium dendriticum,* famous for manipulating the behavior of its ant intermediate host, is widespread in sheep and causes rare human biliary infections.

In the hospital I recently took care of an elderly ethnic Chinese man who immigrated to the US from Indonesia. He would only well cooked foods. Nothing raw, pickled or steamed, not even fresh fruits. His US relatives thought his diet was odd, but it sort of made sense, having lived in a global food borne parasite hotspot for most of his life.

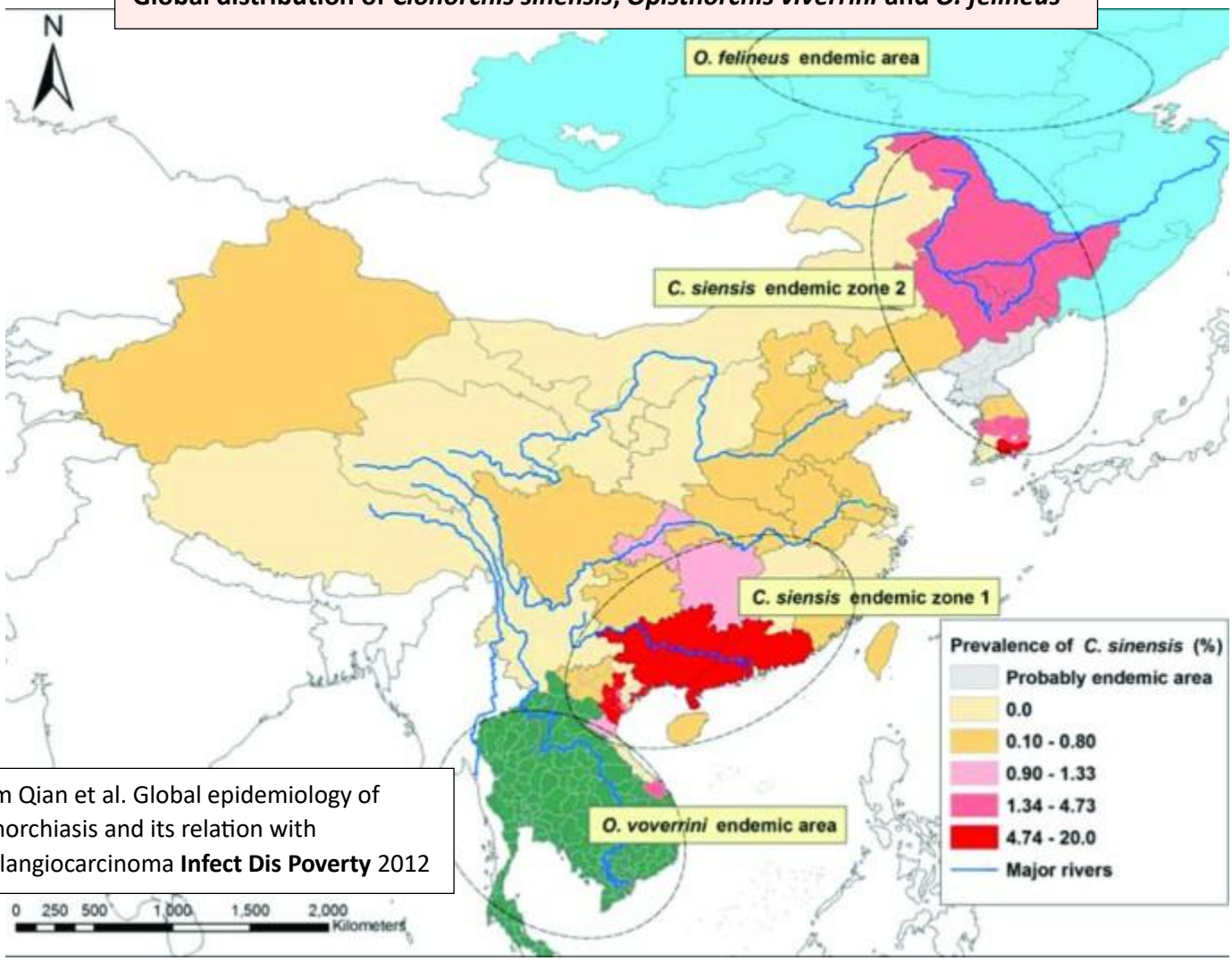


Digenean trematode
Al-Emarah researchgate

Anatomy: digenean trematodes typically have flat, long, leaf shaped bodies with anterior and ventral suckers. Like other helminths, much of their (hermaphroditic) bodies are comprised of various reproductive organs. Thin small bodies allow good gas exchange without respiratory or cardiac systems.

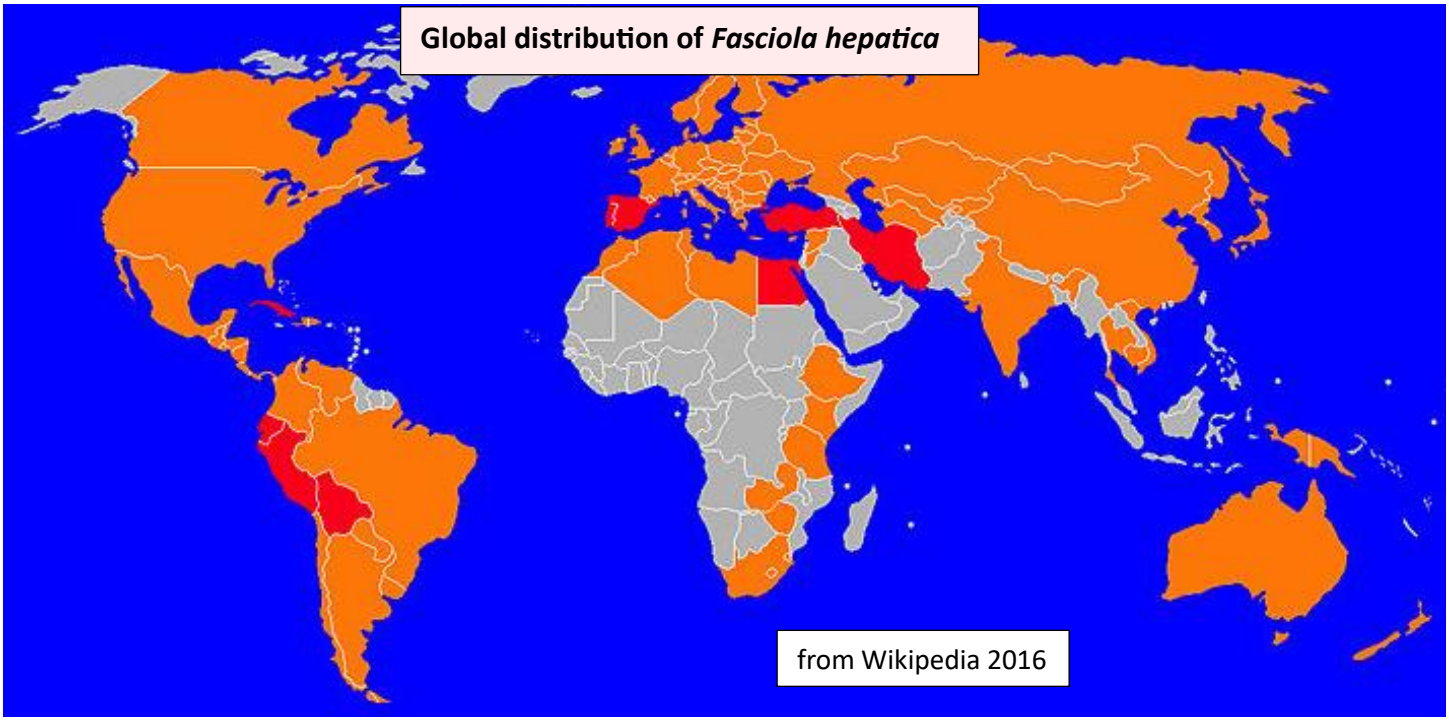
Clonorchis sinensis Chinese liver fluke *ex Homo* liver, slide Oregon State U., USA 4X obj, dark field, stitched, fluke ~ 1.2 cm long

Global distribution of *Clonorchis sinensis*, *Opisthorchis viverrini* and *O. felineus*



from Qian et al. Global epidemiology of clonorchiasis and its relation with cholangiocarcinoma **Infect Dis Poverty** 2012

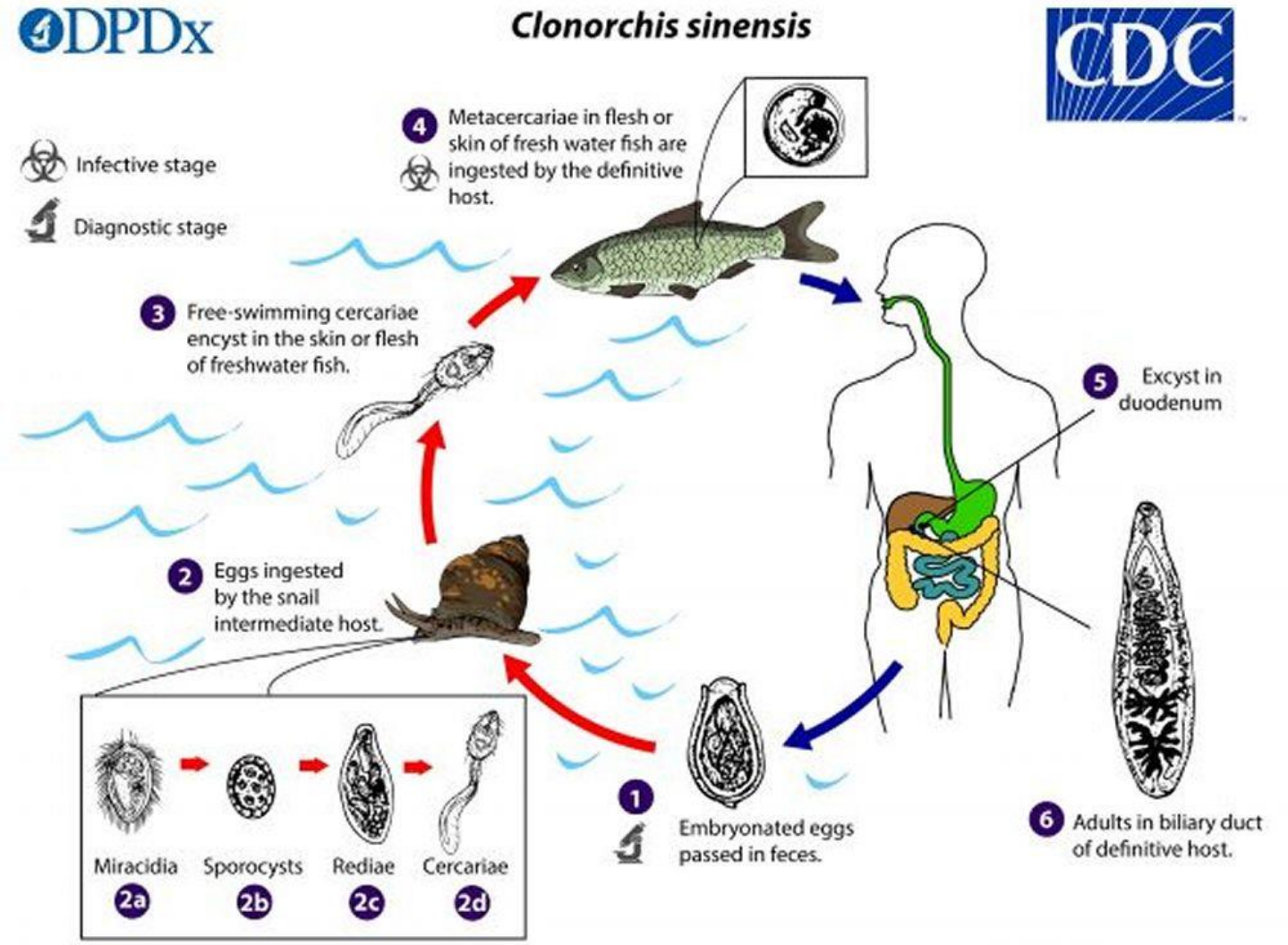
Global distribution of *Fasciola hepatica*



from Wikipedia 2016

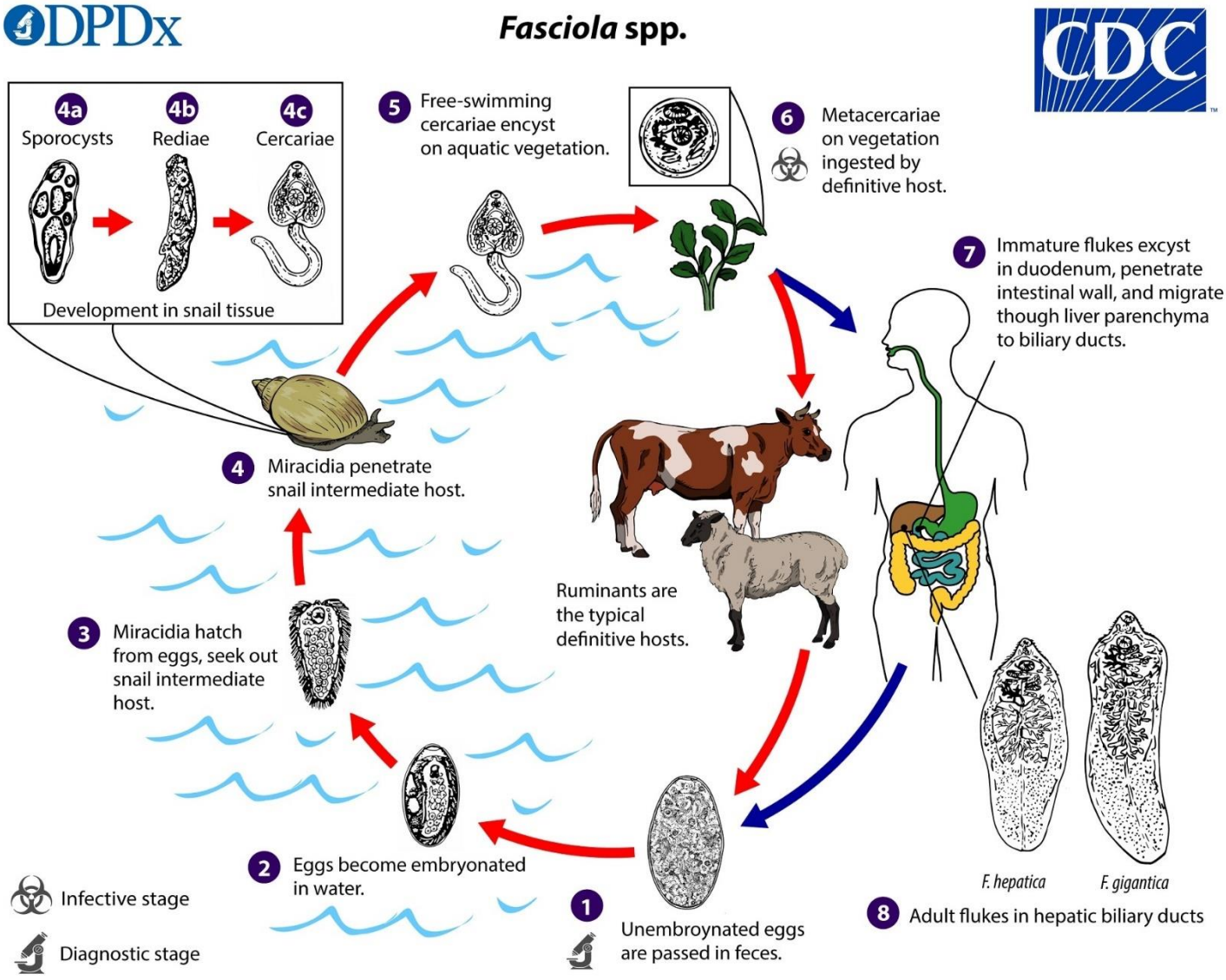
Life cycles of liver flukes

Tiny about 0.15 mm long ***Clonorchis* or *Opisthorchis*** metacercariae are encysted in the skin or flesh of fish or shrimp second intermediate hosts. Upon human ingestion of raw fish, the metacerciae are freed in the duodenum and swim up the bile ducts into the liver. They mature into adult hermaphrodite worms in about a month, which can live for up to 25 years in the bile ducts, eating liver tissue and laying about 4000 eggs a day. The eggs are ingested by snails and eventually produce many cercariae, which encyst on fish, completing the circle of life.



1. Clonorchis sinensis eggs are discharged in the biliary ducts and passed in feces. 2. Eggs are ingested by a snail intermediate host. Eggs release miracidia, which undergo asexual reproduction via sporocysts, rediae, and cercariae (2a-d). Free-swimming cercariae are released from the snail and, soon come in contact and penetrate the flesh of freshwater fish, where they encyst as metacercariae (4). Infection of humans occurs by ingestion of undercooked, salted, pickled, or smoked freshwater fish. After ingestion, the metacercariae excyst in the duodenum (5) and ascend the biliary tract through the ampulla of Vater. Maturation takes approximately one month. The adult flukes (measuring 10 to 25 mm by 3 to 5 mm) reside in small and medium sized biliary ducts in the liver (6).

Metacercariae of ***Fasciola*** on watercress or caltrops nuts are ingested with the plant and after excysting take an indirect route to the liver, across the intestinal wall and through the peritoneum. Adult *Fasciola* worms in the liver can live up to 13 years and produce up to 25,000 eggs a day. The eggs are eaten by snails allowing asexual cloning of the next life stages.



1. Fasciola eggs are discharged into the biliary ducts and excreted in feces. 2. Eggs become embryonated in water, 3. releasing miracidia, which invade a snail intermediate host. 4 in snail, the parasites undergo asexual reproduction via sporocysts, rediae, and cercariae. 5. swimming cercariae are released from the snail and encyst as metacercariae on aquatic vegetation or other surfaces. 6. Fascioliasis is acquired by eating plants, especially watercress, containing metacercariae. 7. After ingestion, the metacercariae excyst in the duodenum. 8. They migrate through the intestinal wall, peritoneal cavity, and liver parenchyma into the biliary ducts, where they develop into adults. Maturation into adult flukes usually takes about 3–4 months; development of *F. gigantica* may take somewhat longer than *F. hepatica*.

Do not open this nut with your teeth if you wish to avoid liver flukes. Caltrops nuts are also known as water chestnuts, bat nuts, buffalo nuts and the devil pod. The nuts are the edible fruit of *Trapa bicornis* and 2 other *Trapa spp*. found in southeast Asia and Africa. The plant lives in shallow freshwater, and if infected intermediate host sails in the family Lymnaeidae (some *Galba, Fossaria,* and *Pseudosuccinea* spp) are present, the skin of the nut could contain encysted *Fasciola hepatica* or *H. gigantica* metacercariae.

Bat nut image from eBay ($19.19 for 2 with shipping, sold for their “metaphysical properties”)
Galba truncatula (Eurasia)*, Fossaria bulamoides* (western US)*, Pseudosuccinea columella* (South America) snail images CDC

Pathophysiology, symptoms and signs

A few liver flukes are usually asymptomatic but in acute cases with many parasites in bile ducts **clonorchiasis, opisthorchiasis or fascioliasis** can cause abdominal pain, vomiting, fever, facial edema, juandice and eosinophilia. Chronic liver fluke infection can cause bile duct inflamation that may lead to intermittent acute pain from cholngitis (bile duct infection), cholelithiasis (gallstones), cholecystitis (gallbladder infection) and pancreatitis (pancreatic inflammation).

Heavy chronic infections can cause inflammation, intermitent obstruction and infections of large and small bile ducts. This can lead to biliary sclerosis, portal fibosis and sometimes hepatic cirrhosis with ascites and portal hypertension, resulting in hepatomegally, bleeding and infections, including liver abscesses. The Chinese liver fluke *Clonorchis sinensis* is a carcinogenic parasite and in rare cases (about 5000 peaple a year worldwide) causes cholangiocarcinoma, an often fatal bile duct cancer.

Diagnostic tests

Finding specific trematosde eggs in stool can confirm infection, but also occurs in asymptomatic cases. Serology (antibody) tests can be useful in early (it takes about 3 or 4 months from exposure to adults making eggs) or late cases (adults die after a decade or so). Eosinophilia is common in most helminth infections. Lab abnormalities of liver disease (such as high bilirubin, transaminases and high alkaline phosphatase, low blood cell counts i.e. anemia and throbocytopenia) occur but nonparasite causes (chronic viral hepatiris, alcoholism, steatohepatitis) may be more common cauises of these findings. Imaging may show hepatosplenomegally or cirrhosis, sometimes multiple round hypodense lesions in the liver, and in a few cases of fascioliasis adult worms are seen in the extrahepatic bile ducts. Severe acute complicaions like obstructive cholecytitis might lead to surgery yielding an adult worm to confirm the diagnosis.

Treatment of liver flukes

For clonorchiasis or opisthorchiasis antiparasitic drug treatment is praziquantel 3 times a day for 2 days or albendazole once a day for 7 days

For fascioliasis treatment is 2 triclabendazole 2 doses on 1 day. Nitazoxanide is a possible alternative. Supportive care should be provided as needed, and a few patients may need surgery. Expert help from the CDC or state health department should also be sought in the US.

Fasciolopsiasis, heterophyiasis, echinostomiasis and related intestinal flukes

Organisms, impact

The giant intestinal fluke *Fasciolopsis buski* causes the disease fasciolopsiasis, whreas intestinal flukes *Heterophyes heterophyes* and several *Echinostoma* species cause heterophyiasis and echinostomiasis. *Metagonimus yokogawai, Nanophyetus salmincola, Gymnophalloides seoi* and other intestinal flukes also cause human disease in some locales. Over 80 species of trematodes (including "liver flukes" like Fasciola and animal flukes that occasionally get off track) have been associated with some cases of foodborne trematodiasis; this article is not comprehrensive. *Haplorchis* and *Himasthla spp.* trematodes cause human disease rarely, and are notable for having rediae soldier and queen castes in the snail intermendiate hosts. Prevalence estimates range greatly from 6 million to 40-50 to 74.7 million people infected with intestinal flukes (some authors and artificial intelligence include liver flukes with intestinal flukes). Luckily many cases are asymtomatic, and deaths are uncommon. As with liver flukes, poor areas in southeast Asia are particularly hard hit by intestinal flukes.

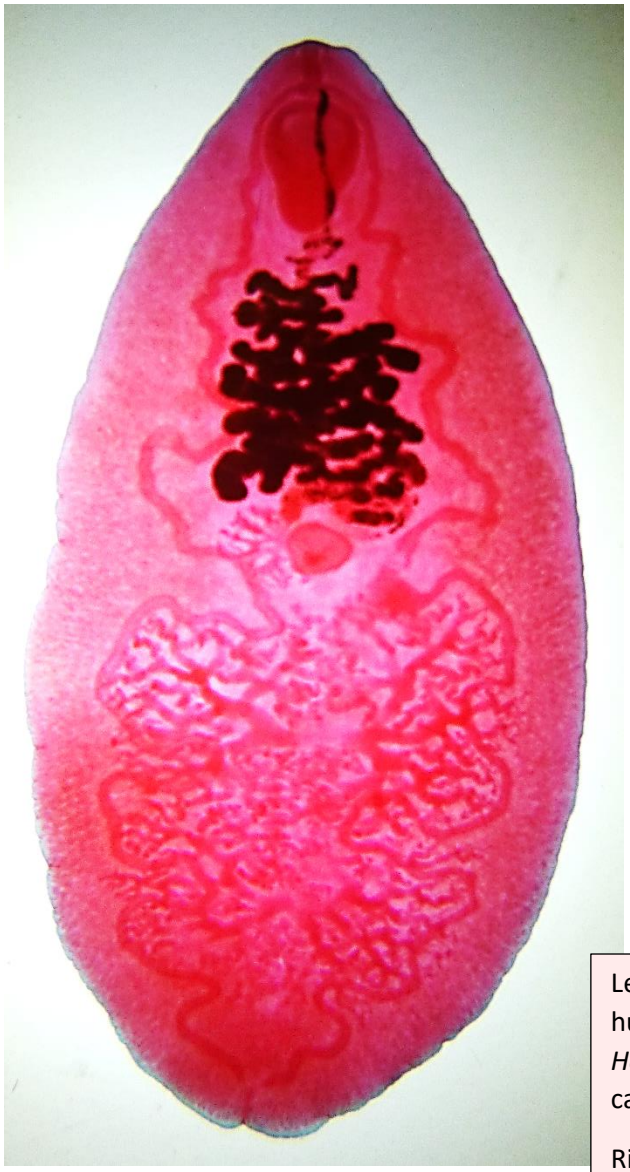
Acquisition, geography

Fasciolopsiasis is usually acquired drinking contaminated water or eating metcercariae on contaminated water plants inclubing bamboo shoots or watercress. *F. buski* is found in pig raising areas of Asia and India.
Heterophyiasis and *Metagonimus* infection are acquired by eating raw or undercooked freshwater or brackish fish in east Asia, the Middle East (including Sudan, Egypt, Israel) and southeast Europe and Spain. Echinostomiasis is acquired by eating raw or undercooked clams, snails, tadpoles, frogs, snakes, snails, and fish (first or second intermeiade hosts) in southeast and east Asia. *Nanophyetus salmincola* is (rarely) acquired from undercooked salmon.

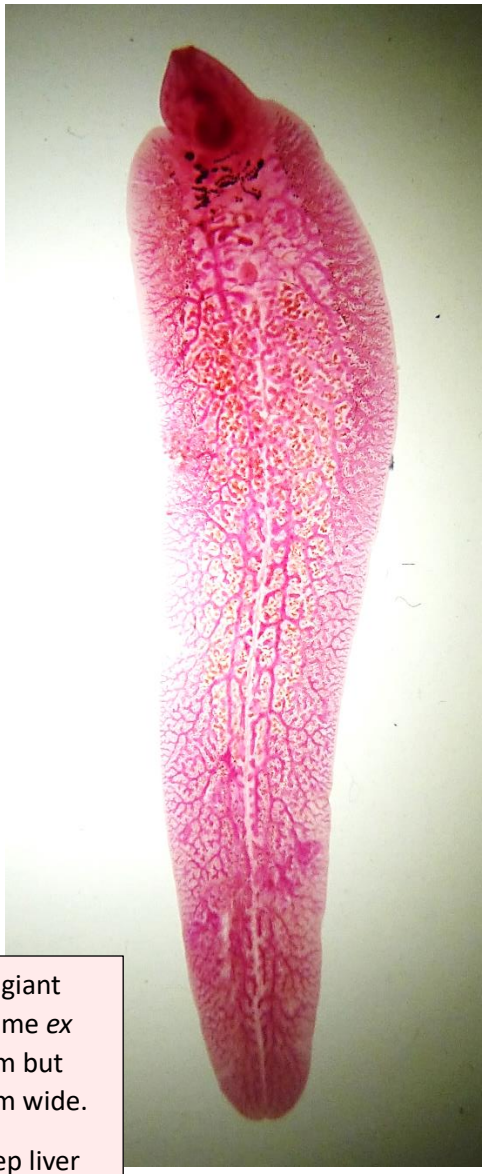
Life cycle, pathophysiology of intestinal flukes

Intestinal flukes are commonly asypmtomatic unless the parasite load is high. These trematodes live in your intestine and eat some of your food, which may not be noticeable. Already malnourished children are more likely to develop symptoms and be harmed by the stealing of protein and calories. Many flukes hold on with their suckers but the spiny collar of *Echinostoma* penetrates the intestinal mucosa, which can cause a small ulcer, sometimes anemia and very rarely intestinal perforation.

Nanophyetus salmincola can cause salmon poisoning disease (SPD), first noted in dogs in 1814 and later shown to infect humans with milder disease. Dogs can be killed by SPD via coinfection with *Neorickettsia helminthoeca,* a rickettsial bacteria inside the metacercaria.



2 Big Flukes that infest humans

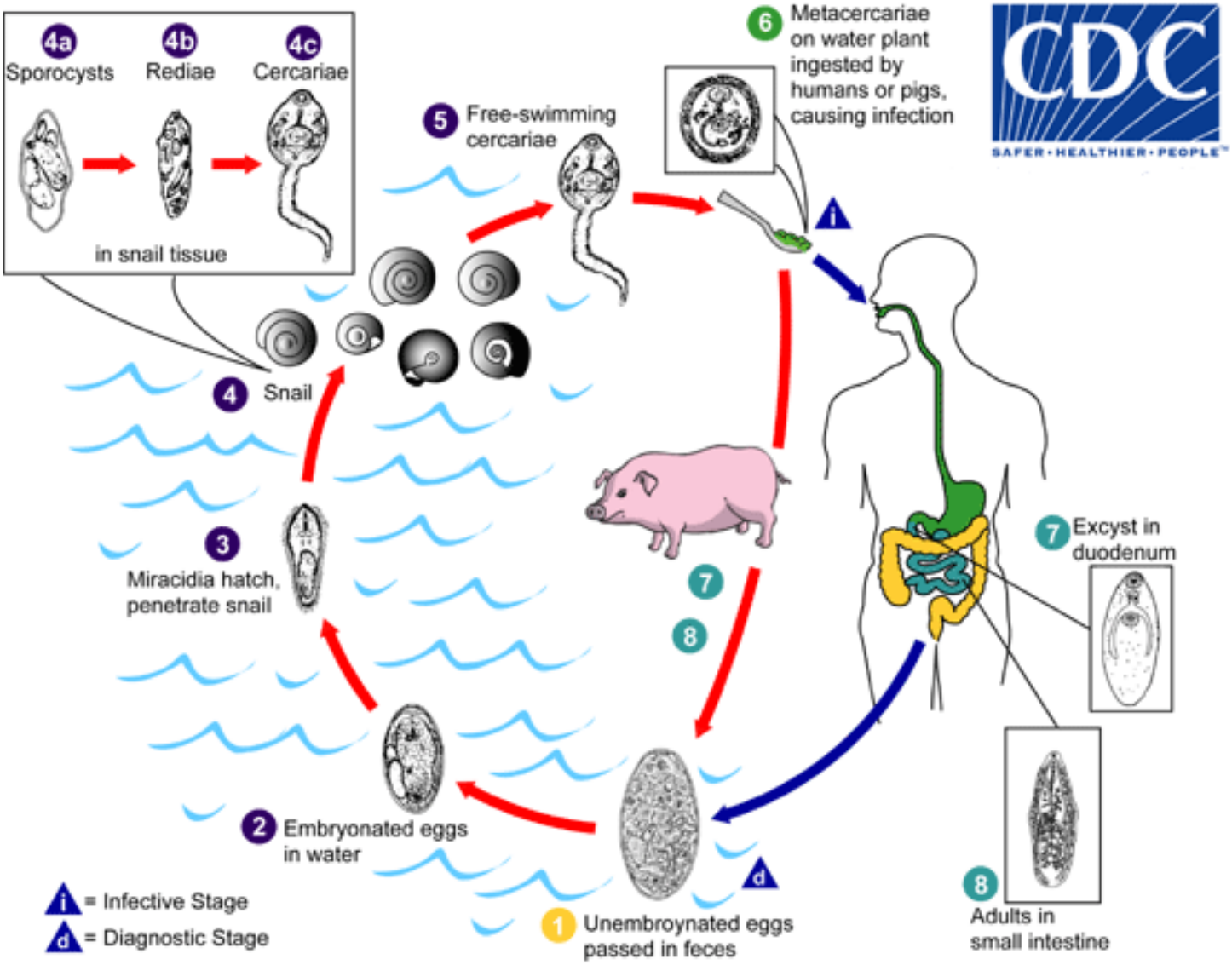


Left- *Fasciolopsis buski* is the giant human intestinal fluke, presume *ex Homo*. This one is 3.3 x 1.9 cm but can be 7.5 cm long and 2.5 cm wide.

Right- *Fasciola hepatica*, sheep liver fluke, presume *ex Ovis*, about 4 cm x 1 cm; perhaps stretched out as usually about 3 x 1.5 cm; 'shoulders' distinguish it from *F. gigantica.*

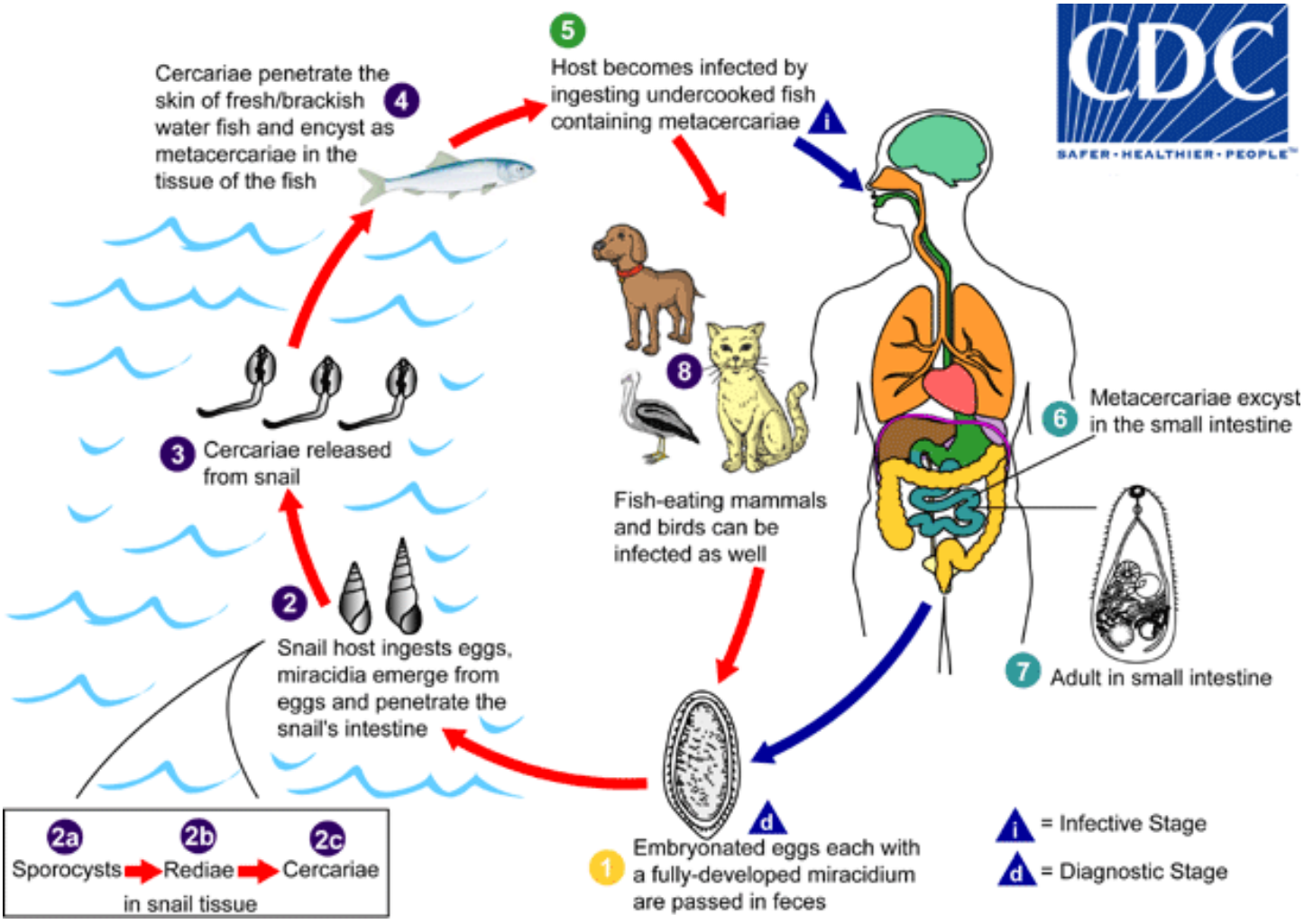
Flukes photographed on dollar store LED closet light with plastic diffuser. Vintage slides below about actual size, 3 inch long, monitor dependent.

Life cycle of the giant intestinal fluke *Fasciolopsis buski*



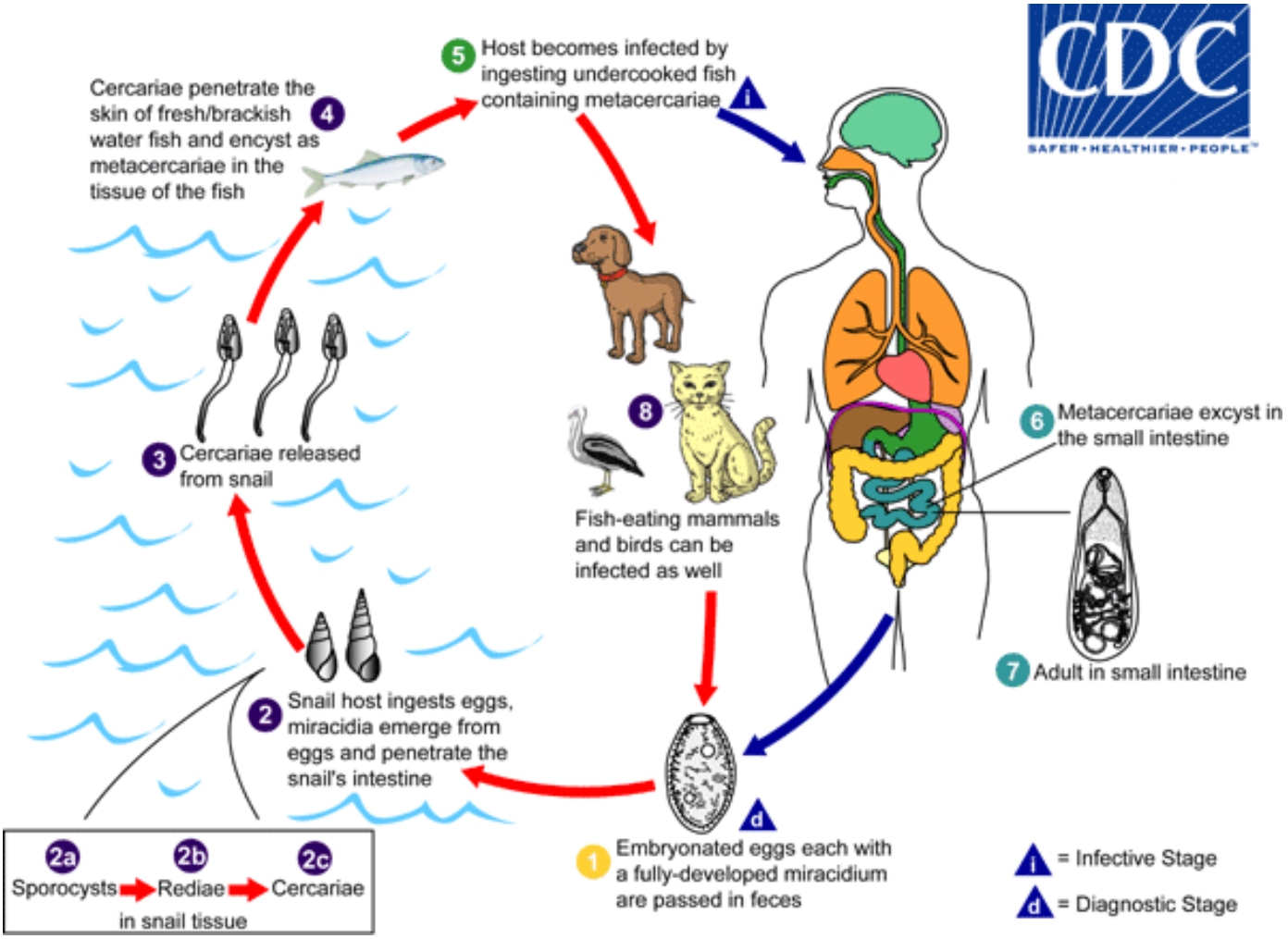
Immature eggs are discharged into the intestine and stool 1. Eggs become embryonated in water 2, eggs release miracidia 3, which invade a suitable snail intermediate host 4. In the snail the parasites undergo asexual reproductive stages (sporocysts 4a, rediae 4b, and cercariae 4c). The cercariae are released from the snail 5 and encyst as metacercariae on aquatic plants 6. The mammalian hosts become infected by ingesting the plants. The metacercariae excyst in the duodenum 7 and attach to the intestinal wall (of pigs or humans). There they develop into adult flukes (20 to 75 mm by 8 to 20 mm) in about 3 months, 8. Adult worms have a life span of about one year.

Life cycle of the minute instinal fluke *Heterophyes heterophyes*

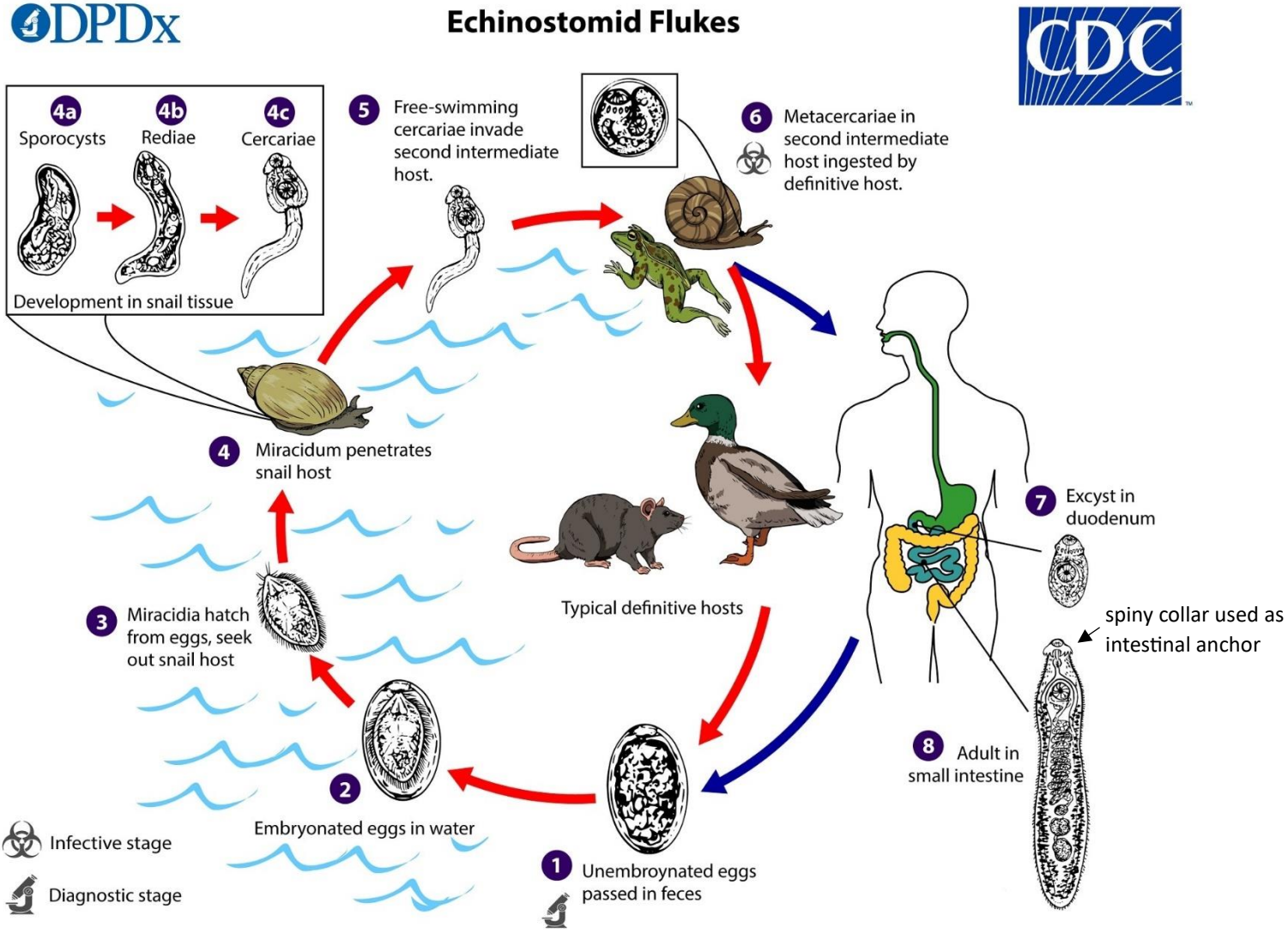


Adults release embryonated eggs with a fully-developed miracidium, and eggs are passed in the host's feces[1]. After ingestion by a snail (first intermediate host), the eggs hatch and release miracidia which penetrate the snail's intestine[2]. Genera *Cerithidia* and *Pironella* are important snail hosts in Asia and the Middle East respectively. The miracidia undergo asexual reproductive stages in the snail, sporocysts[2a], rediae[2b], and cercariae[2c]. Many cercariae are produced from each redia. Cercariae are released from the snail[3] and encyst as metacercariae in the tissues of a suitable fresh/brackish water fish (second intermediate host)[4]. The definitive host becomes infected by ingesting undercooked or salted fish containing metacercariae[5]. After ingestion, the metacercariae excyst, attach to the mucosa of the small intestine[6] and mature into adults (measuring 1.0 to 1.7 mm by 0.3 to 0.4 mm)[7]. In addition to humans, various fish-eating mammals (e.g., cats and dogs) and birds can be infected by *Heterophyes heterophyes*[8].

Life cycle of *Metagonimus yokogawai* another tiny intestinal fluke

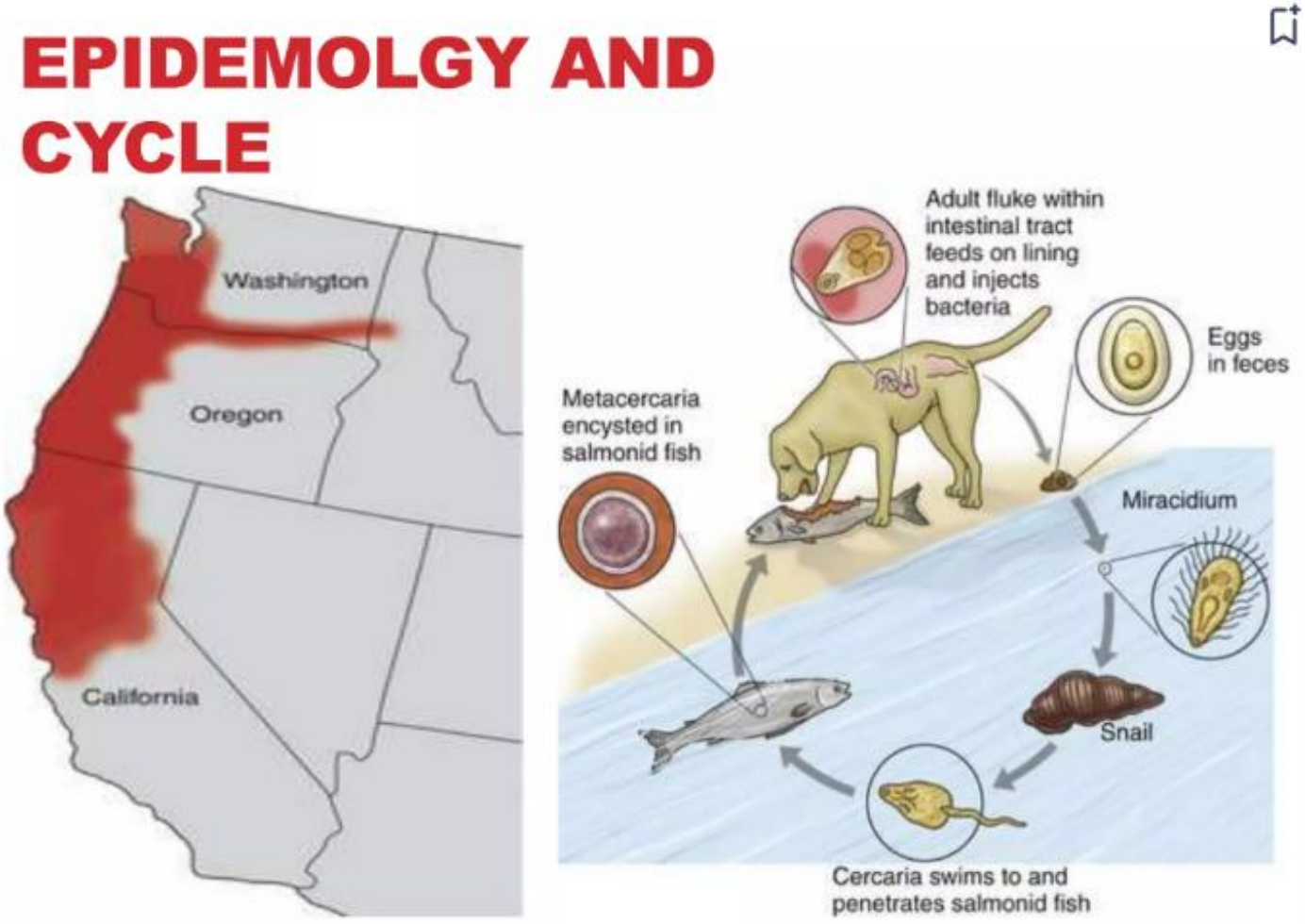


Fully embryonated eggs each with fully-developed miracidia are passed in the host's feces 1. After ingestion by a snail first intermediate host, the eggs hatch releasing miracidia which penetrate the snail's intestine 2. Snails of the genus *Semisulcospira* are the most frequent intermediate host for *Metagonimus yokogawai*. The miracidia undergo several rounds of asexual reproduction in the snail, sporocysts 2a, rediae 2b, and cercariae 2c. Many cercariae are produced from each redia. The cercariae are released from the snail 3 and encyst as metacercariae in the tissues of a suitable fresh/brackish water fish second intermediate hosts 4. The definitive host becomes infected by ingesting undercooked or salted fish containing metacercariae 5. After ingestion, the metacercariae excyst, attach to the mucosa of the small intestine 6 and mature into adults (measuring 1.0 mm to 2.5 mm by 0.4 mm to 0.75 mm) 7. In addition to humans, fish-eating mammals (e.g., cats and dogs) and birds can also be infected by *M. yokogawai* 8.



Echinostomid flukes undergo a multi-host (indirect) trematode life cycle. Unembryonated eggs are passed in feces of definitive hosts 1 and develop in water 2. Miracidia hatch in about about 3 weeks 3, after which they swim and penetrate the first intermediate host, a snail 4. Intramolluscan stages include a sporocyst stage, one or two generations of rediae, and cercariae, which are released from the snail. The cercariae may encyst as metacercariae within the same first intermediate host or leave the host and penetrate a new second intermediate host 5. The definitive host becomes infected after eating metacercariae in infected second intermediate hosts 6. Metacercariae excyst in the duodenum 7 and adults reside in the small intestine (for some species, occasionally in the bile ducts or large intestine) 8. Adults are 2-10 mm long depending on species, and can live a few months.

Occurence and life cycle of *Nanophyetus salmincola,* cause of salmon poisoning disease



Nanophyetus salmincola is endemic to the Pacific northwestern United States. Canids are the definitive host and pass eggs in feces. Miracidia penetrate a snail first intermediate host and after asexual amplification yield multiple cercariae which find and penetrate salmonoid fish second intermediate hosts. Moazzam's study found an average of 200 to 2500 metacercariae per steelhead salmon from different locations, inflicting reduced swimming ability and increased mortality on some fish. When those fish are eaten by dogs the metacercariae mature into 1 to 2.5 mm long adult flukes in the dog's intestine. The metacercariae carry *Neorickettsia helminthoeca* giving the dog a sometimes fatal rickettsial bacterial infection. In contrast, humans are not susceptible to the bacteria and usually have a milder gastrointestinal infection from the small flukes that resolves in a few months, even if not treated.

-image from talk by Dr. M Moazzam at slideshare.net

Symptoms and signs of foodborne intestinal trematodes

Most intestinal fluke infections are asymptomatic. Light infections usually resolve within a year even without treatment. The nonspecific GI symptoms that may occur with increased parasite load can be similar to the acute symptons of fascioliasis and other liver flukes. Heavy infestation with *Fasciolopsis buski* may cause anorexia, vomiting, diarrhea or abdominal pain starting a month or 2 after acqusition of metcecariae. Peripheral eosinophilia occurs in some cases. In severe fasciolopsiasis cases, malabsorptive diarrhea can cause edema and ascites due to protein loss. Vitamin B12 deficiency and anemia may also occur.

Echinostomiasis is often asymptomatic even with intestinal ulcers (painless), but anemia and rare deaths from intestinal perforation have occurred with *Artyfechinostomum malayanum.* Intestinal infection with 1 ½ mm long *Heterophyes* adults is usually asymptomatic. However, heavy *Heterophyes* or *Metagonimus* infections can cause symptoms similar to fasciolopsiasis, starting about 9 days after eating contaminated fish.

Nanophyetus salmincola can cause salmon poisoning disease, causing abdominal discomfort, diarrhea and vomitting in people about a week after eating undercooked infected salmon.

Diagnostic tests

Diagnosis is usually based on microscopic examination of eggs in the stool. Careful measurements must be taken to avoid confusion between the eggs of *Fasciolopsis, Echinostoma, Fasciola* and other trematodes. Definitive identification is based on examination of adults passed in stool.

Treatment of intestinal flukes

If drug treatment is required, Fasciolopsiasis, heterophyiasis, *Metagonimus yokogawai* and *Nanophyetus salmincola* infections are treated with praziquantal, 3 doses in 1 day

(Additionally dogs infected with *Nanophyetus salmincola* are also given a course of doxycycline for the associated *Neorickettsia helminthoeca* rickettsial infection.)

The parasites are foodborne. Improved food and water hygenic practices (proper washing of vegetables and thorough cooking of fish, mollusks and vegetables) can prevent many foodborne trematode infections.

Paragonimiasis: oriental lung fluke infection

Organisms, impact

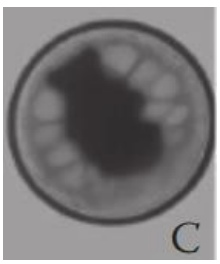
Infection with the lung fluke *Paragonimus westermani* or another of more than 10 related species causes the disease paragonimiasis. About 20 million people have paragonimiasis, and about 290 million people live in parts of 48 countries that put them at risk. Most cases are in southeast Asia, but *Paragonimus spp.* are worldwide. *P. kellicotti* is endemic to North America. Pargonimiasis is reported to have a 5% case fatality rate but global death rates are unknown.

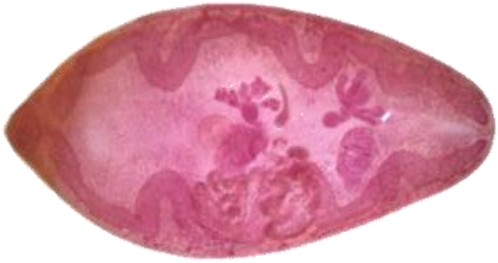
Geography, acquisition

Paragonimus westermani is a foodborne trematode acquired by eating eating raw, pickled, or undercooked freshwater crustaceans such as crabs, especially in Korea, China or Japan. *Paragonimus spp.* are distributed throughout southeast Asia, Africa and the Americas. *Paragonimus westermani* is found in southeast Asia and Japan. *Paragonimus kellicotti* is low level endemic in the northwest USA. From 1965 to 2007, only 6 cases of nonimported paragonimiasis were reported in the United States (other cases were in immigrants or travellers). In 2010 the CDC reported 9 cases of paragoniamiasis caused by eating crayfish while canoeing or camping along multiple rivers in Missouri, USA.

Life cycle, pathophysiology

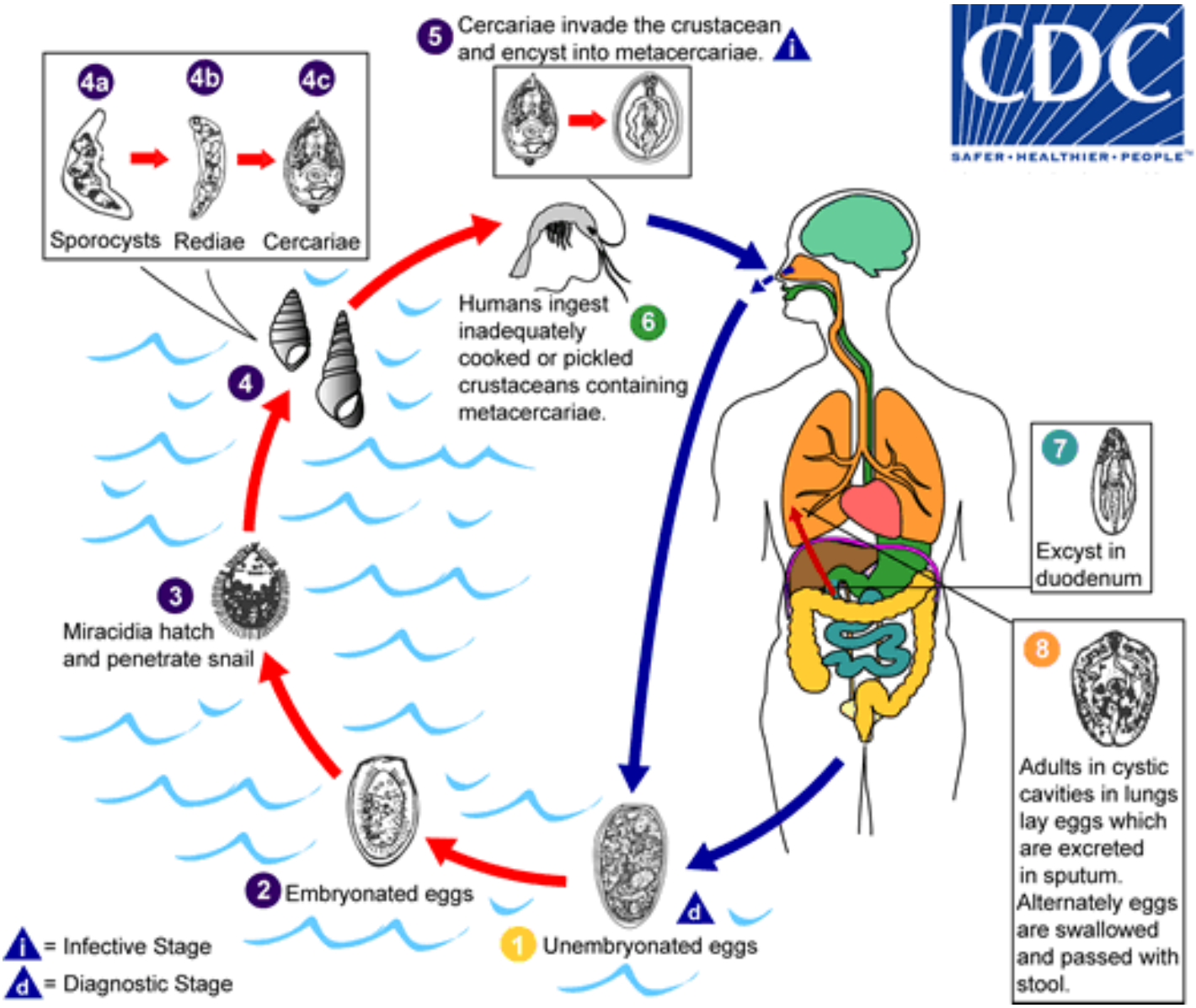
People are the usual definitive host of *P. westermani*, which passes through two intermediate aquatic hosts, a snail then a crustacean. Metacercaria (about 0.4 mm diameter) acquired by eating uncooked crabs or crayfish pentetrate the duodenal intestinal wall into the peritoneal cavity, then the diaphrahm and pleura to reach the thoracic cavity, then pentrate the lungs. The metacercaria encyst again and develop into 8-12 mm long adult flukes in the lungs. 65 to 90 days after eating the wrong crab, the lung flukes start depositing eggs into the sputum which can be coughed up, or swallowed to pass in feces, completeing the parasite's small circle of life. Adult worms may lay eggs for 20 years and live up to 25 years. But some metacercaria get lost on their journey through your body and might end up in the brain, lymph nodes, liver, spleen, muscles, skin or spinal cord. It is a dead end for the fluke and possible trouble for you if the errant worm cyst is in your brain.





Far left- encysted metacercaria Near left- adult *Paragonimus westermani* metacercaria about 450 microns, adult worm about 8 to 12 mm long, hermaphroditic. Magnified about 50X far left and 5X near left, depending on your monitor.
Images Kong et al and Wikipedia respectively

Life cycle of *Paragonimus westermani,* the oriental lung fluke



Eggs are excreted unembryonated in the sputum, or swallowed and passed with stool 1. In freshwater the eggs become embryonated in 2-3 weeks 2, and miracidia hatch and seek the first intermediate host, a snail, and penetrate its soft tissues 3. Miracidia undergo asexual reproductive stages inside the snail 4: sporocysts 4a, rediae 4b, with the latter giving rise to many cercariae 4c, which emerge from the snail. The cercariae invade the second intermediate host, a crustacean such as a crab or crayfish, where they encyst and become metacercariae. This is the infective stage for the mammalian host 5. Human infection with *P. westermani* occurs by eating inadequately cooked or pickled crab or crayfish that harbor metacercariae of the parasite 6. The metacercariae excyst in the duodenum 7, penetrate through the intestinal wall into the peritoneal cavity, then through the abdominal wall and diaphragm into the lungs, where they become encapsulated and develop into adults 8. (7.5 to 12 mm by 4 to 6 mm). The worms can also reach other organs and tissues, such as the brain and striated muscles, respectively. However, when this takes place completion of the life cycles is not achieved, because the eggs laid cannot exit these sites. Time from infection to oviposition is 65 to 90 days. Infections may persist for 20 years in humans. Animals such as pigs, dogs, and a variety of feline species can also harbor *P. westermani*.

Symptoms and signs of paragonimiasis

As with other foodborne flukes, most patients are asymptomatic. Patients with heavy parasite loads may develop acute paragonimiasis starting 2 days to 2 weeks after ingestion as the metcercaria penetrate and migrate. Diarrhea, abdominal pain, fever, cough, urticaria, hepatosplenomegaly, pulmonary abnormalities, and eosinophilia have been reported.

Most symptoms of chronic paragonimiasis stem from lung involvement and may include gradual onset of chronic cough, hemoptysis (bloody sputum), chest pain and dyspnea. Eosinophilia is variable and chest imaging is nonspecific. The clinical picture closely resembles tuberculosis. One Ecudoran immigrant to Spain had *Paragonimus uterobilateralis* eggs and adults found in a lung lobectomy surgery specimen (done for persistant hemotysis and local bronciectasis on CT) done 4 years after treament of proven pulmonary TB.

Variable or no symptoms can result from flukes encysted in places other than lungs. Brain lesions may be asymtomatic or may cause seizures, local weakness or difficulty speaking (stroke like symptoms, but lesions should be seen on CT scan).

Diagnostic tests

Paragonimiasis is usually diagnosed by finding eggs in microscopic examination of sputum or feces. Enzyme immunoassay antibody tests for *Paragonimus* have been developed and may help distinguish chronic paragonimiasis fro tuberculosis in some immigrants. As noted above, adult flukes have rarely been found in tissue specimens.

Treatment of paragonimiasis

If drug treatment is needed, praziquantel 3 times a day for 2 days is the medication of choice. If praziquantal is unavailable, triclabendazole can be an alternative.

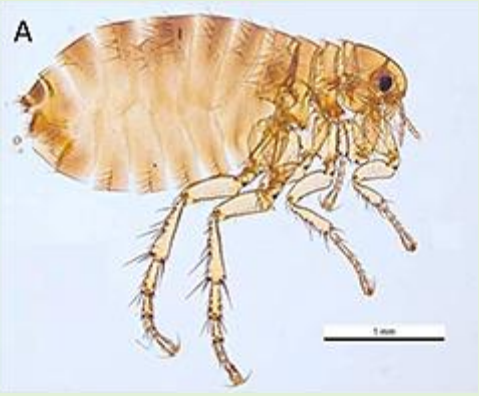
Surgery to remove cysts is sometimes performed (purposely or not.) Steroids are sometimes used temporarily to prevent brain swelling in the case of CNS involvement.

Prevention is by not eating undercooked crabs or crayfish from affected waters.

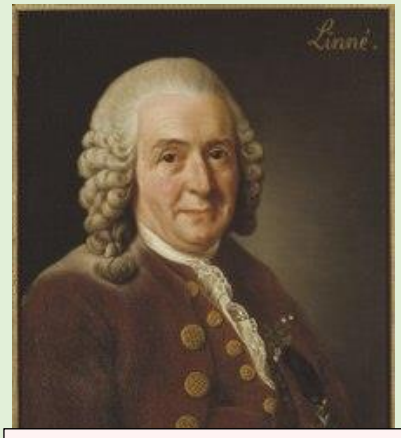
Linnean Taxonomy

Taxonomy is the science of classifying organisms. Swedish genius Carl Linnaeus (b1707-d1778) set up the system scientists still use today (with modifications) in his *Systema Naturae* in 1735. His system is a hierarchy of different sized groups from Kingdom down to species, and an individual species is referred to by a binomial name that includes genus and species, i.e. *Homo sapiens*. Linnaeus classified organisms according to obvious physical characters. Naming and classifying organisms gave Darwin a head start when he did his work one century later. Modern taxonomy usually classifies organisms into ranked groups based on their evolutionary ancestry (a literal family tree). Many but not all taxonomic groups are clades, all the descendants of a common ancestor. We break that rule sometimes because some subgroups seem distinct (birds are in a clade with dinosaurs, and insects are in a crustacean clade). We have also added more levels to taxonomy, particularly at the top levels after late 20th century biochemical and DNA methods allowed us to better see distinctions between microbes. There are just 2 domains: Prokarya (bacteria and archaea) and Eukarya (everything else). Taxonomy continues to change as science gets more data. There are 4 or 5 eukaryotic kingdoms in most schemes now days: Protozoa, (Chromista), Plantae, Fungi, Animalia.
An example of modern classification, that of the human flea, an animal first named by Linnaeus:

bar 1 mm, K Walker Museum Victoria



Domain	Eukarya
Kingdom	Animalia
Phylum	Arthropoda
Class	Insecta
Order	Siphonaptera
Family	Pulicidae
Genus	Pulex
Species	irritans
Binomial	*Pulex irritans* Linnaeus 1758



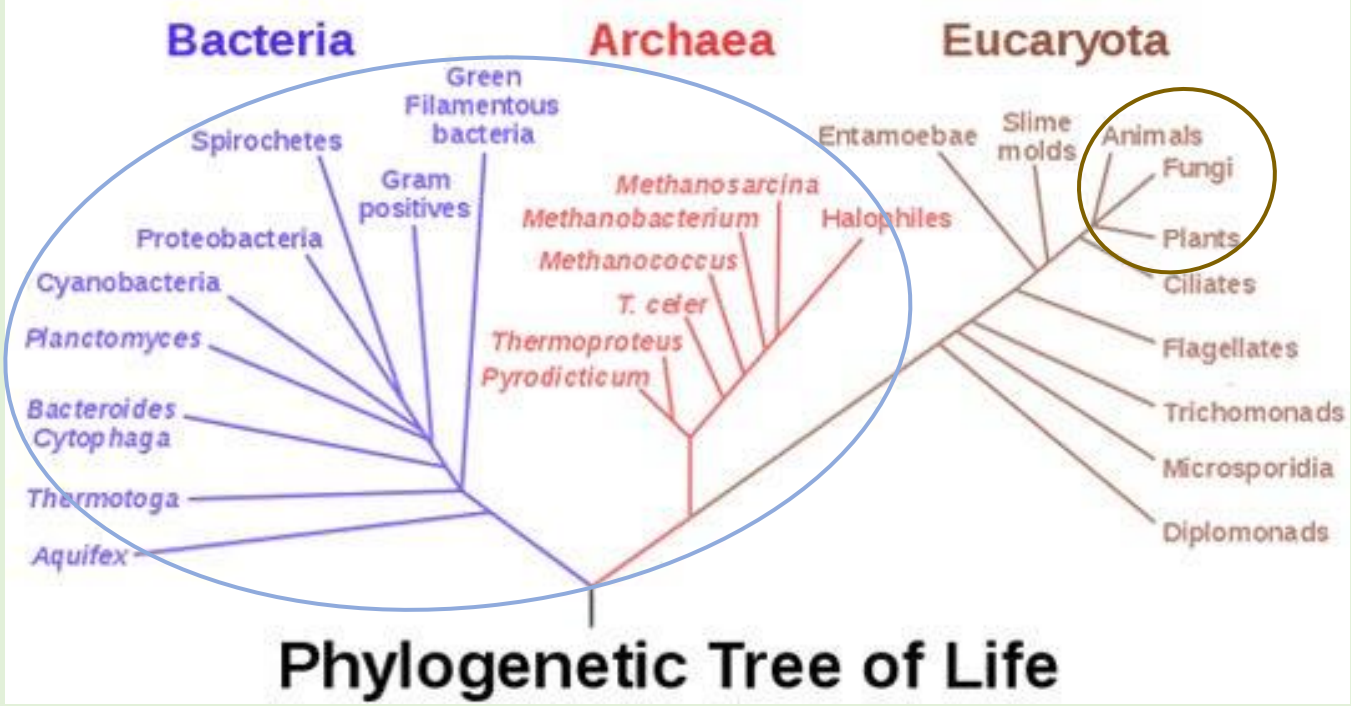
Linnaeus 1775 by Roslin, wikipedia

Evolution explains a lot

In 1859 evolution was a new theory, laid out in clear, logical and humble detail by Charles Darwin in his book *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. Darwin had gathered thousands of his own and others' observations about the varieties of life, but at that time known fossils were fewer and the mechanisms of inheritance were unknown (Czech monk Gregor Mendel discovered the laws of genetics in pea plants in the 1860's but no one knew it for decades). Evolution is now a proven fact: millions of new bits of evidence show life slowly evolved into a myriad of different forms on planet earth. Evolution remains a powerful and changing (all science is subject to modification by additional data) central theory in biology that makes sense of puzzling new evidence from research, like 5 legged frogs and the COVID virus changing to be less deadly. I see evolution in action in the hospital as bacteria continually evolve to be resistant to the most used antibiotics.

Upon careful reflection Darwin's theory seems inevitable. People create different kinds of pigeons and other animals through selective breeding. Nature does much the same thing. Darwin saw there is a struggle in nature for organisms to survive and produce offspring. It is observed that all organisms come from the reproduction of parent organisms, that there are differences between individuals in a group (i.e. some are faster or slower) and that parents make imperfect copies of themselves (we now know genes are shuffled and may mutate). In real circumstances (gazelles being chased by cheetahs for example) survival is not just random but favors certain bodily abilities (i.e. running faster) so the next generation comes from selected (faster) surviving parents and so each new generation becomes slightly adapted in particular ways. Over deep time (the earth is now known to be about 4.55 billion years old) a single cell became all the amazing life on the planet today, from bacteria to *Paramecium* to grass to mushrooms to worms to you. Every living thing becomes fined tuned for its way of life, making life look like it was designed. Yet there is no designer, just the results of how natural life processes work out based on chemistry, physics and maths.

Most life is prokaryotic: Bacteria and Archaea, very tiny, no nucleus, on left. All multicellular organisms are in the small brown circle on the right. Between are Protists, bigger than bacteria, but mostly microscopic, nucleated single celled life. Carl Woese used ribosome RNA data for his 1990s tree.



Phylogenetic Tree of Life

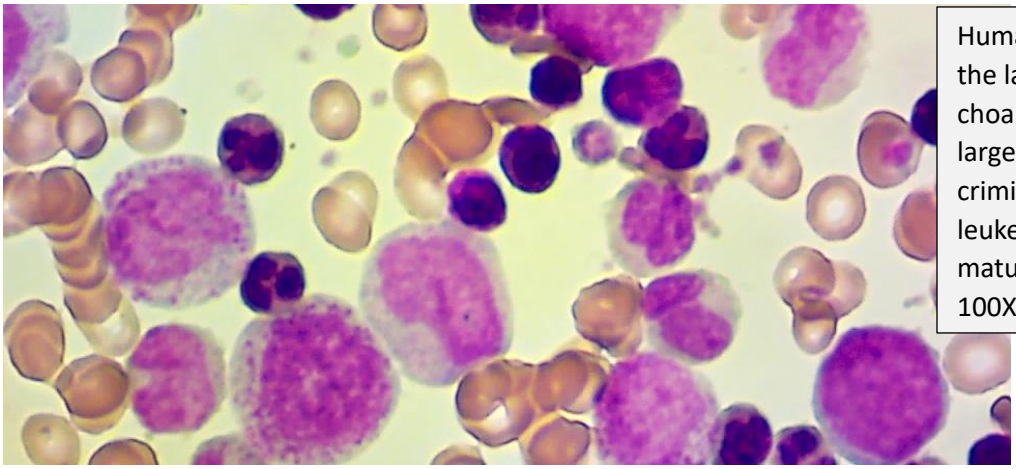
Cell Theory and the Theory of Evolution

These 2 great ideas are the foundation of modern biology and underlie scientific agriculture and healthcare. Both theories arose in mid19th century Europe and are reproven a million times daily in applications around the world. (Soviet biologist Lysenko rejected Darwinism 1930s-60s as capitalist, worsening famines in Russia and Mao's China.)

As atoms make up matter, cells are the basic unit of all life. Robert Hooke saw tiny boxes in cork with his microscope in 1665, calling them "cells". German scientists Theodor Schwann and Matthias Jakob Schleiden had better microscopes and in 1838 proposed all plants and animals are made up of cells. The multi-talented Rudolph Virchow completed the basic cell theory in 1855 by proclaiming all cells come from preexisting cells, in Latin *"omnis cellula e cellula."*

Around the same time, a humble genius In England solved the mystery of why we have so many different kinds of animals and plants. In 1859 Charles Darwin published *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. Evolution is so logical it is inevitable. Living beings copy themselves, but often slightly imperfectly. In the struggle to live and breed some individuals can run faster or are otherwise favored. So the next generation comes from survivors that are a little different. Some populations get split up by barriers. Over deep time (life on earth is about 3.8 billion years old) a single cell divided zillions of times and became all the amazing life on the planet today, from bacteria to *Paramecium* to mushrooms to trees to you. Every living thing becomes fined tuned for its way of life, making life look like it was designed. Yet there was no designer, just the logical results of how natural life processes worked out, explainable by chemistry and physics.

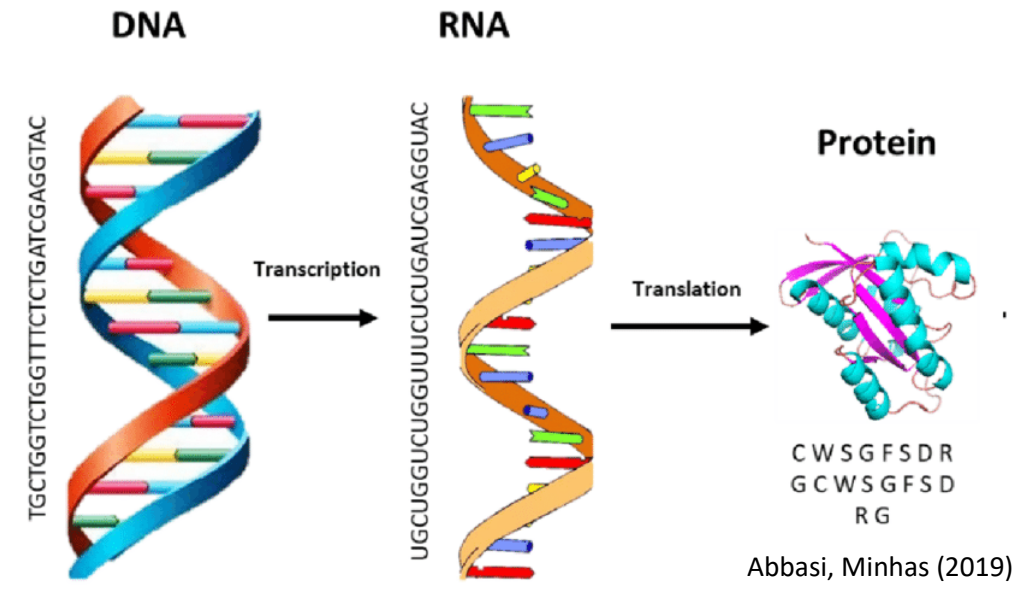
Run the evolutionary clock backwards and eventually you get to the first living cell. Every cell in every being is a direct descendant of that single cell (if life arose more than once, the others got wiped out long ago). Everything alive today uses variations of the same DNA and protein biochemistry of our common ancestor cell. That first very tiny cell grew and split into 2 daughters. They also split into 2 and so on. Thanks to exponential math they filled the oceans. Some learned to make food from sunlight, producing oxygen as a toxic waste. After billions of generations there were many different kinds of cells and one day one gobbled up another as lunch, but the lunch didn't die. The "lunch" became mitochondria, finding a nice new place to live and paying rent with high energy molecules. Naked DNA got organized into chromosomes inside a nucleus and life was off to do bigger things. With extra stored information, daughter cells could be different than each other yet still programmed to cooperate with each other. Multicellular life was born: bodies made of thousands or millions or eventually trillions of cells. Inside your body is a wonderland. It's like a bustling city with skyscrapers and highways and factories populated by 35 trillion resident cells. All those cells came from 1 cell formed when your mom and dad had sex. And those sex cells came in turn from earlier and earlier cells. We have a massive convoluted family tree, all the way back to the first bacterial cell at a steaming hot, sulfurous deep sea vent 3.8 billion years ago. During all those years there were only a few great leaps; most of the changes were tiny and incremental (but added up over time). You, *Homo sapiens*, might be one of the great leaps, or not. You have the abstract reasoning required for complex language and math, leading to civilization and eventually to modern technologies powerful enough to destroy the planet or to create a paradise on earth. Please choose the latter.



Human blood cells, distant descendants of the last universal common ancestor and of choanoflagellate protozoa. In this case the large purple cells belong to a dangerous criminal gang (suspect chronic myelogenous leukemia with many large blasts and smaller maturing neutrophils, 1950's hospital slide) 100X oil obj, cropped, RBCs about 7 µ wide

The central dogma of molecular biology: DNA ➡ RNA ➡ protein

Czech monk Gregor Mendel worked out laws of inheritance in pea plants in the 1860s. In the early 20th century chromosomes and their gene subunits were studied extensively in *Drosophila* (fruit flies). Chemists found the most important chemicals in cells seemed to be a myriad of different proteins (polymers of amino acid building blocks) that make up cell structures and carry out complex chemical reactions. In 1953 Watson and Crick (after seeing Rosalind Franklin's data) solved the puzzle of the helical shape of the DNA molecule (deoxyribonucleic acid). Armies of scientists figured out the central dogma of biology: how life works on a molecular level. Information in DNA is *translated* into mRNA, which leaves the nucleus and is *transcribed* into a unique protein by ribosomes (complex nanomachines consisting of protein and special RNA). Based on the physics of water solutions, each protein self folds into a unique 3D shape that lets it do its job. The human genome was first sequenced in 2003. It is mind boggling. Each of your 200 very different types of cells (skin, blood, etc.) contains the same complete blueprint for a human. A complex system of **epigenetic** chemical tags turns genes off and on as needed so the single cell fertilized egg inside your mom could develop into the unique 35 trillion cell mass that is you. Epigenetics also means genes are not destiny. Much more ill health is caused by poverty and social discrimination than by genes. Parasitic diseases show this, becoming mostly relegated to poor people deprived of their share of wealth created by modern technology.



Abbasi, Minhas (2019)

Genomics has been a boon to biology research in the past 50 years. We can now explore evolutionary relationships through DNA trees, clone and genetically manipulate cells and animals, and can sequence the whole transcriptome (all the mRNA) of human cells to see what genes they are using (and which are silent).

Mirroring society, scientists have long been racist and thought discovering genes proved their case. Linnaeus did not include dark skinned peoples in *Homo sapiens*. A century ago most anthropologists were "**scientific racists**" (a pseudoscientific oxymoron) and eugenicists who believed nonwhites corrupt human bloodlines (a belief repeated by Hitler and a recent US president). Racism is pervasive, but **scientifically, race does not exist**. **Race is a social construct.** Some 19th and 20th century US state laws said people with 1/8 or even "one drop of black blood" were black. You can often guess the ancestry of a person from skin color, but DNA tests show you are sometimes wrong. Virchow tried to divide 19th century German school kids into racial groups using scientific body measurements but he couldn't: variation within each group was bigger than the difference between purported racial groupings.

Parasite glossary part 1

Parasite an organism that lives in or on another, taking nutrients that would have benefited the host (many viruses, bacteria and fungi fit the definition but we call them acute pathogens instead)

Host a larger organism that harbors a parasite (a potentially harmful organism) (smaller organisms helpful to, or neutral for a host are beneficial or commensal, not parasitic)

Endoparasite lives inside of host **Ectoparasite** lives on outside of host

Definitive host organism that harbors adult (sexually reproductive stage) parasites

Intermediate host organism that harbors immature stages (which often reproduce asexually)

Free living not a parasite; photosynthesizes or is a predator/scavenger, does not live inside creatures

Infestation harboring an animal (worm, arthropod) in or on body (**infection** is microbe/pathogen in body)

Parasite load number of parasites per host (affects potential harm of parasites)

Vector an organism (usually an intermediate host) that passes a parasite between hosts

Reservoir a population or community of organisms that can permanently harbor a parasite population

Zoonosis a disease transmitted from animals to people; many parasitic diseases are zoonotic

Parasite life cycle stages through which the parasite grows, reproduces and transmits itself in 1 or more hosts

Monoxenous also known as **monogenean** or **direct** parasitism; life cycle requires only a single host species

Heteroxenous aka **digenean, digenetic** or **indirect**; life cycle requires one or more extra intermediate hosts

Direct transmission hosts touch each other (sex counts), passing on a free-living life stage (including skin to skin passing lice) or by ingestion of free-living parasite or eggs (i.e. fecal-oral, by food with contaminated dirt)

Indirect transmission from one host to another through an intermediate host (i.e. a vector such as a tick)

Trophic transmission by eating an organism that contains a parasite (i.e. predation, or via uncooked meat)

Vertical transmission from mother to offspring (i.e. toxoplasmosis can by passed to fetus with severe results)

Iatrogenic transmission by medical care (i.e. from blood transfusion or organ transplant)

Parasitoid tiny wasps (some are “fairy flies”) whose larva eat a host from inside, eventually killing it

Hyperparasite a parasite of a parasite, i.e. some parasitoid wasps prey on other parasitoid wasps

Parasite glossary part 2

Brood parasitism raised by parents of another species, i.e. cuckoo birds lay eggs in other species' nests

Sexual parasitism i.e. male anglerfish attach to a female and shrink to just tiny sperm-making parasites

Micropredator steals body fluids without consuming the whole victim (i.e. mosquitoes, aphids)

Kleptoparasite steals food from other species, i.e. frigatebirds and hyenas grab food from other animals

Social parasitism i.e. some butterfly larvae mimic ants in shape and smell, and are cared for by ant workers

Parasitic castration some trematode and arthropod parasites gain added resources by neutering the host

Carcinogenic parasite increases cancer risk; some blood flukes can cause bladder, bile duct or liver cancer

Aberrant Host one that cannot support parasite development aka a dead end host

Accidental Host not the usual host, but can support parasite development (with or without dispersal)

Paratenic Host an accidental intermediate host that may be able to pass on the parasite

Autoinfection transfer of new parasite stage within one host, as occurs with some nematodes and flatworms

Hyperinfection repeated autoinfection leading to high parasite load and dissemination beyond usual infected organs (i.e. in the nematode *Strongyloides* runaway hyperinfection can be fatal)

Cloaca single opening of reproductive, GI and urinary tracts (in most vertebrates except mammals)

Coprozoic or Coprophagous living in or eating feces; typically harmless and pass through if ingested

Cyst fluid pocket bounded by membrane or wall; **encysted** organism can be parasite dispersal stage

Dispersive stage form of organism that travels by swimming or drifting in water, or inside a motile host

Egg cell aka ovum is a female reproductive cell (gamete) **Egg** is organic structure containing an embryo

Endemic means a disease is native to a particular place, typically cases occur much of the time

"ex" came from indicated host (i.e. *ex Homo sapiens* denotes specimen removed from a human)

Exotic a non-native species; if a nuisance or harmful then called an **invasive** species

Facultative or **Opportunistic Parasite** lives either free living or parasitic life cycle, depending on opportunity

Parasite and Biology glossary part 3

Microorganisms all life too small to see with the naked eye, including bacteria, protists and tiny animals

Prokaryote tiny cells without nuclei (bacteria, archaea) **Eukaryote** has nucleated cells (all other life)

Protozoa aka protists, single celled eukaryotes; free living (*Paramecium*) or parasitic (*Plasmodium*)

Helminth any parasitic worm (and occasionally used more broadly for any worm)

Platyhelminthes flatworms, the first worm phylum to evolve, and majority of species are parasitic

Cestodes tapeworms; parasitic flatworms with bodies like a segmented ribbon, no mouth

Hydatid Cyst cysts within cysts of larval *Echinococcus* sp. tapeworms, causes hydatid disease in organs

Trematodes flukes; parasitic flatworms with bodies mostly shaped like a narrow leaf

Nematodes aka roundworms, mostly tiny very abundant worms, most free living but many parasitic

Filaria a superfamily of insect transmitted nematodes that live in host lymph and blood

Microfilaria infectious often blood borne pre-larval or stage 1 filariform larva of filarial nematodes

Hologonic having a single sex (female) colony; **or** gonads with germ cells throughout, i.e. *Strongyloides*

Arthropods animals with exoskeleton and jointed legs, includes mites, ticks, crustaceans, insects

Instar life stages in arthropods and nematodes, defined by molting

Genotype the genetic (DNA) code of an organism **Phenotype** is the observed appearance

Phylogeny hereditary and evolutionary relationships of different groups (**Taxonomy** mostly follows it)

Gravid filled with eggs, as in a mature (female or hermaphrodite) nematode, or a tapeworm proglottid

Oviparous produces eggs **Viviparous** live birth of formed, often motile young

Senso lato (describes a taxonomic group) in a broad sense **Senso stricto** in a strict sense

Ecology science of complex relationships between living organisms and with their physical environment

Botany, Zoology, Mycology, Microbiology, Developmental Biology, Evolutionary Biology, Cell Biology, Physiology, Anatomy, Taxonomy, Biochemistry, Genetics, Paleobiology a few other branches of Biology

Symbiosis a close relationship between two species which benefits at least one species.
Mutualism benefits both species. **Commensalism** benefits one species; the other is unharmed.

Syncytium many cells fused into 1 multinucleate cell, i.e. helminth tegument, muscle fibers, in some infections

Sex Glossary (because sex is more complicated than I remembered)

Reproduction and sex can be accomplished in many confusing ways. With variations, the birds and the bees inherited sex from protists: eggs and sperm fuse to become the next generation. Sex has big advantages over splitting in half: by reducing what is passed on to a single cell most parasites are given the slip, and by combining genetic information from two parents, variation is boosted so evolution has more to select from.

Asexual Reproduction- genetic material is passed from only 1 parent to the next generation.

Binary fission- most cells pinch in 2 during mitosis, a few multicellular organisms also divide evenly
Budding- creating a growing blob that cleaves off, as in yeast and hydra
Fragmentation- metazoan (multicellular animal) dividing into many parts, as in some free living flatworms
Vegetative propagation- many plants and some animals (sea squirts) grow new individuals from runners
Sporogenesis- creation of small resistant forms as in ferns, moss, many fungi (by mitosis or meiosis)
Sporulation- in apicomplexan protists the oocyst nucleus divides by meiosis to form 8 haploid sporozoites
Merogeny- protist merozoites undergo additional rounds of asexual reproduction (i.e. erythrocytic cycle)
Sporocyst- trematode miracidia nucleus divides stepwise to form multiple germ balls which each become a redia, that may undergo another round of asexual reproduction before making multiple cercariae
Polyembryony- a single zygote becomes multiple identical clone embryos. Trematode sporocysts and redia are polyembryonic, as are social insect workers and armadillos (always identical quadruplets). Via differences in gene expression genetically identical clones may become different phenotype castes.
Parthenogenesis- development from an unfertilized egg, common in bdelloid rotifers, nematodes, social insects, rare vertebrates ("virgin births" are known in zebra sharks, boa constrictors Komodo dragons, turkeys). Parthenogenesis in flowering plants is called apomixis (clonal seed production).
Clones- multiple genetically identical copies, created asexually (phenotypes vary in some cases)

Sexual Reproduction- gametes derived from 2 parents join to become a single celled zygote which develops into an organism or organisms. Because of its advantages sex is common among bacteria (by conjugation and environmental gene acquisition) and eukaryotes (through gamete based sex).

Mitosis- standard eukaryotic cell division with 2 copies of each chromosome to both diploid daughter cells
Meiosis- Two sets of cell divisions create gametes with segregation of chromosomes into haploid sets
Diploid- full set of chromosomes from mom and dad (46 in most people, 23 pairs inc. 2 sex chromosomes)
Haploid- half set of chromosomes; found in gametes (4 in fruit flies, 23 in man, 39 in dog, 52 in carp)
Somatic cell- almost all cells in body, diploid, divide by mitosis
Germ cell/germ line- haploid gametes and those diploid cells that will produce gametes by meiosis
Gametes- sex cells: female egg/ovum and usually smaller motile (in higher animals) male sperm
Zygote- the single cell formed by fusion of gametes, i.e. the fertilized egg
Types fertilization- 1.conjugation 2. external fertilization (in water) 3. internal fertilization (by insertive sex)
Alternation of generations- diploid then haploid every other generation; obvious in corals and "lower" plants; in "higher" plants and animals only tiny gametes are haploid
Hermaphroditic- aka monoecious; both sex gonads in one individual (same time or sequential), common in plants and invertebrates; many mate with another hermaphrodite, some can self-fertilize (asexual)
Unisexual- aka dioecious or gonochoric ; separate sexes, individuals are male or female
Gender- a human social construct, not always congruent with biologic sex

(I am now an honorary biology professor, having succeeded in making sex boring.)

Privileged to be parasite-free

Most people reading this article don't need to worry very much about parasites personally, as they are probably living in a privileged place during a privileged time.

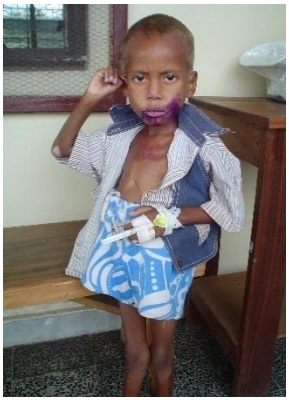
Since the origin of *Homo sapiens* in Africa about 300,000 years ago, most people harbored potentially harmful parasites in and on their bodies. Lice and intestinal worms were nearly universal. Then a combination of industrial and social revolutions starting almost 300 years ago greatly improved health and comfort for most people today. If you are reading this then it is likely you have clean water and food supplies, shoes, indoor plumbing, window screens, floor boards and a solid roof, all diminishing the chances of worms burrowing into your feet or swallowed in contaminated water, and of bites by infected mosquitoes or reduviid bugs. In the past century **better living standards, scientific knowledge and public health measures eliminated the most significant human parasites from most developed nations.**

Great strides continue to made fighting parasites and poverty in the world. The WHO estimates intestinal worm infestations dropped from 60% to 25% of all humans so far in this century. Global median annual income more than doubled between 2000 and 2019 from $1325 to $2759 (with the mean about $12000 in 2019, and yours is likely higher). Global life expectancy increased 6.6 years between 2000 and 2019 from 66.8 to 73.4 years average (even as life expectancy in the US began to decline during the same timeframe).

But the global gains in well being are far from being evenly distributed. Severe inequalities make averages (means) deceptive when **almost half of the world's total wealth is held by the top 1%, and the bottom half divvies up just 0.74%**. Most people are poor and live in the "majority world" (a newer term for what we also call the third or developing world) and they are still lacking in money, health and fair governance. Without all the luxuries we take for granted, the parasites they suffer from are just a small part of the unfair miseries (wars, famines, imprisonment without trial if they criticize the dictator) borne by the powerless majority. **Most people today (4.3 billion) live in 95 countries with authoritarian regimes**.

Some people may feel sad about this sorry state of affairs. For some readers the best way to worry about parasites is by helping out people with parasites who have little way to help themselves. You might consider a charitable donation to Oxfam, Against Malaria Foundation or Deworm the World.

It's also perfectly fine to feel grateful for the cosmic lottery you've won. You weren't born in medieval times, living 30 miserable years with lice and worms. Many *Micscape* readers are males in rich European or North American countries. You likely know a European language and have computers and microscopes. You may be privileged by your race, gender, citizenship (in a former imperial power), and by your political and economic systems. **You likely enjoy the full modern wealthy liberal package: democracy, free speech, free press, good schools, private property, strong currency** and **universal health care** (last not available in US).



Left- a malnourished, parasite infested West African boy in *Medicines sans Frontiers* clinic, Liberia, 2004

Right- a *Micscape* contributor from Russia

(names withheld for privacy)

US and European doctors should know about some vector borne diseases

Some diseases spread by the bites of insects and other arthropods are caused by parasites (i.e. malaria, leishmaniasis) and were covered in these articles. But many other vector borne diseases are caused by viruses or bacteria, not parasites. The definition of "parasite" is arbitrary, focusing on animals (protozoa used to be thought tiny animals) that exploit other animals. On the other hand, viruses and rickettsial bacteria are obligate intracellular parasites, but are instead considered acute pathogens (many can kill a host quickly). Some are rare and odd infections, spread by mosquitoes or creepy ticks that suck blood (ectoparasite vectors). Because these infections can be quickly fatal and may not respond to the most common antibiotics, these diseases are vital to know. Although not parasites in the strict sense, vector borne diseases often end up in a seldom accessed old memory space next to parasites in doctor's heads.

Where I live in the northern US, the black legged tick *Ixodes scapularis* (locally called deer ticks) can carry bacteria causing Lyme disease, anaplasmosis, borreliosis and ehrlichiosis, and the Powassan virus (in addition to the protist parasite *Babesia*). Some of our common *Culex* mosquitoes (*C. tarsalis, C. pipiens, C. restuans*) carry West Nile virus and Western Equine Encephalitis and St. Louis Encephalitis viruses.

Parasites that US doctors should know about (but may not)

Because most harmful parasites have been eliminated from rich countries, doctors in the United States learn very little about parasites during their training. Most doctors know about just two nonfatal protist parasites, vaginal ***Trichomonas*** infections and diarrhea caused by ***Giardia***. They both are treated with a common antibiotic, and many US doctors have never prescribed an anti-parasitic drug, unless maybe for a **scabies** mite skin rash. Perhaps 60 million people in the United States have asymptomatic latent toxoplasmosis, but that asymptomatic condition is not treated. **Cutaneous larva migrans** and **swimmer's itch** are harmless rashes after swimming or wading in contaminated water. They are caused when certain animal related roundworm larvae or schistosome cercariae penetrate your skin, but aren't very serious conditions as you are a dead end host for dog, cat, or duck micro-parasites that die under your skin.

Just one intestinal helminth is still endemic in the United States, nematode ***Enterobius vermicularis***, also called **pinworm**. It is most common in daycare age kids and although not harmful it can cause severe rectal itching and can recur after treatment. 20 to 40 million Americans may have pinworms, although many have no itching. There are shameful cases of doctors laughing at patients who thought they had intestinal worms when they really did have pinworms. Enterobiasis can be diagnosed by an old fashioned "scotch tape" microscopic exam (which most providers cannot order from a lab) and is treatable.

It is true that in developed nations symptomatic helminth infections are rarer than patients with a mistaken belief that worms are crawling in their body (about 2 to 27 per 100 thousand people per year in studies of **delusional parasitosis**). Because sometimes the patient is right, it might be prudent to do a CBC with differential (looking for eosinophilia, which is more commonly from allergies). Stool specimen microscopic exams for parasite eggs and select serologies might be indicated <u>if</u> a patient has risk factors. No test is perfect, and if lab tests are done indiscriminately, most "positive" results will really be false positives.

Immigrants to the U.S. from developing countries, **travelers** returning from the tropics, and patients who are **immunosuppressed** by disease or medication are prone to parasitic infections. Very rarely Americans get parasites from food prepared by immigrant cooks, produce that came from Latin America, or by exposure to farm, pet or wild animals. Travelers can bring home various parasitic hitch hikers. Many parasitic infections (Chagas disease, schistosomiasis) require years of reinfections before severe illness, so a brief vacation is lower risk. A very serious acute infection in returned travelers is falciparum malaria. On average about 2000 people a year have malaria in the United States, and 7 of them died in 2018. Most of these victims came back from vacation in the tropics, or were immigrants returning from visiting family back home, and a very few cases were acquired in the southern U.S. or from blood transfusions. If you run a fever after returning from a trip to the tropics see a doctor and emphasize that you were in the tropics and could have malaria. Special blood smears and serology tests can diagnose malaria. People with weak immune systems caused by cancer treatments, HIV infection or some arthritis drugs are more susceptible to all infections, viral, bacterial and parasitic. Even with infection they may not run a fever or feel very sick. The nematode worm *Strongyloides* causes about 15 deaths a year in the US, mostly in patients immunocompromised by HIV virus or by steroids given for COPD. Unfortunately, many US doctors lack training about parasites. If you do not think the doctor has diagnosed you correctly, seek another opinion. If you slowly get ill with intestinal or other symptoms after foreign travel or immune compromise and have reason to think it is parasitic, see your primary doctor if you trust them. Or consider going to a travel or infectious disease doctor/provider, as they often know more about parasitic and rare infections.

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Micscape is a high quality website hosted in the UK and made great by amateur contributors from around the globe. *Micscape* Magazine always has lots of good information for hobby microscopists wanting to learn more about how to do it yourself.

For 2024 I offer *Micscape's* readers a series of articles about parasites, illustrated in part from my slide collection.

I am incurably curious about parasites and keep thinking I should know more. I had fun learning about amazing adaptations by trematodes, and I look forward to discussing trematode human diseases next time. The internet makes it easy to learn more, so my articles are always longer than I intended at first.

Just look at the interesting pictures if you want. Don't be freaked out by parasites. They are everywhere in nature, but seldom cause harm to humans in the developed world, with a few exceptions.

Some people are real experts and know much more than I do on these subjects. I would be pleased to have any mistakes or misunderstandings corrected.

I am Ed Ward in the state of Minnesota, USA.
Your comments are always welcomed, my email is eward1897 AT gmail DOT com

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