Introduction to Multicellular Parasites

Multicellular parasites are eukaryotic organisms in the Kingdom Animalia (like us). Although they are macroscopic (obviously visible to the naked eye), they are often included in microbiology textbooks for two reasons:

1) The eggs and larvae (immature forms) of multicellular parasites are microscopic and microbiologists are often involved in their identification within human/animal tissues and/or excrement. Diagnosis and treatment requires identification of the parasites present.
2) Many external parasites are vectors, involved in the transmission of disease-causing agents including bacteria, viruses, protozoa, and other multicellular parasites. Since epidemiology is an important aspect of microbiology, the identification of vectors and appreciation for the role they play in disease transmission is essential.

Multicellular parasites, like single-celled forms are chemoheterotrophs that rely on other organisms for their nutritional needs. They vary considerably in size and form, but can be divided into two categories on the basis of their relationships with their hosts.

a) **Endoparasites** – Endoparasites are those found living inside the bodies of host organisms. Some of these spend a portion of their life-cycle in water or soil, but their mature forms live within animal hosts and are often highly adapted to this specialized environment.

b) **Ectoparasites** – Ectoparasites are those found living outside the bodies of host organisms. Many ectoparasites live on or near the organisms they require for nutrients, while some spend considerable time away from their hosts. In some cases, only the females require a blood meal and males of the species feed on plants or other materials.

**Helminthes** – The term helminth means worm, and applies to multicellular endoparasites. These are classified as **flatworms** (phylum Platyhelminthes) or **roundworms** (phylum Aschelminthes, Nematoda depending on the reference used). Helminthes, especially flatworms, are highly adapted to life inside a host animal and typically have the following characteristics.

1. **Poorly developed gastrointestinal systems** – Because they live within the intestines, bloodstream, skeletal muscle or other tissues of their host, where nutrients are abundant, helminthes do not need a complex system for taking in and breaking down food. Some flatworms have no gastrointestinal system at all, but absorb nutrients and eliminate waste through their body wall.
2. **Poorly developed nervous and muscular systems** – Since multicellular parasites live inside their hosts, they don’t need eyes, ears or a keen sense of smell to detect potential predators nor a brain to facilitate escape. They have little need for a muscular system because they have no place to go.
3. **Well developed reproductive systems** – Because parasites live inside one host organism, and must pass future generations to other host organisms, they typically produce huge numbers of offspring and often have complex life cycles (especially flatworms).

Many flatworms are **monoeocious** (monoeocious = in one house), i.e., they have both male and female reproductive systems within each individual organism. This doubles the reproductive potential of the organisms, because each mating session results in the fertilization of two female systems instead of just one. Flukes in the genus *Schistosoma* are an exception, and have separate sexes, i.e., are **dioecious**. Many types of animals including the slugs and snails of garden and forest are monoeocious, while roundworms, some flatworms and vertebrate animals like us, are dioecious.
In addition to producing huge numbers of progeny, most parasites provide little or no care for their offspring. The large numbers increase the parasite population's chances for survival, because even if most young are lost before they reach adulthood, there are always more to take their place. Many types of helminthes have complex life cycles involving more than one type of host organism. The host supporting adult parasites (and where sexual reproduction occurs) is called the **definitive host** and is often human. The host supporting immature parasites (and where asexual reproduction often occurs) is called the **intermediate host** and is frequently some type of water snail. There are significant advantages gained by having adult and immature populations separated in time and space; some of these are described below.

a) When adults and offspring occupy different habitats, there is **less competition between them for available nutrients and living space**. Parasite young are not pestering their parents for money or car keys and are not taking all the food from the refrigerator.

b) When adults and offspring occupy different hosts, there is potentially **less damage to the supporting organism, and it is less likely to die**. If a host dies, the endoparasites present are likely to die with it (or if circumstances permit, gain access to a new host by being ingested).

c) When adults and offspring occupy different hosts, their population is likely to be **dispersed more widely in the environment and this will increase the population's chances for survival**. Even if some hosts die, the parasite population will survive, because not all members are eliminated.

Some examples of significant parasites and their life cycles will be presented here as augmentation to information provided in the laboratory. Identification of specific parasites and their taxonomy will be required for laboratory exam I, while life-cycle information will be included in the first lecture exam.

1. **Fasciola hepatica** (Sheep Liver fluke) – *Fasciola hepatica* is a type of parasite potentially encountered locally. Adult flukes typically inhabit the sheep liver (sheep = **definitive host**), where they mate and female systems release huge numbers of eggs (up to 0.5 million per day). Eggs exit the host in fecal material released into the environment, and hatch into ciliated larval forms called **miracidia** (singular = **miracidium**). Miracidia swim around until finding a water snail (**intermediate host**), and then they burrow in and form **sporocysts** (singular = **sporocyst**, a sac-like asexual reproductive body). Inside each sporocyst are formed many **rediae** (singular = **redia**), and inside each redia form multiple **cercariae** (singular = **cercaria**). Each cercaria is equipped with a tail, allowing it to exit the snail and swim a short distance before settling on grass and other water vegetation. Once settled, the cercariae lose their tails and form dormant structures called **cysts**. When eaten by sheep, the larvae pass to the duodenum where they excyst (become active), burrow through the gut wall and travel to the liver, completing the life cycle. Since each female reproductive system (each fluke) can produce up to \( \frac{1}{2} \) million eggs, and each egg can yield as many as 300 cercariae, the reproductive potential of *Fasciola hepatica* is enormous.

Though not usually involved as definitive hosts, humans can contract *Fasciola hepatica* by drinking contaminated water or by ingesting raw water plants (e.g., water cress or other greens) collected from areas where sheep have been pastured. *Fasciola hepatica* may also infect dogs, bears, deer and other wild animals.

2. **Schistosoma mansoni, japonicum** and **haematobium** (blood flukes) – Blood flukes live inside blood vessels associated with the gut (*S. mansoni* and *japonicum*) or urinary tract (*S. haematobium*), of humans (humans are the definitive hosts for these species). Their life cycle is similar to that of sheep liver flukes except that the cercariae released from infected water snails can burrow directly through the skin; they do not have to be eaten. Though blood fluke infection is often asymptomatic, a common manifestation of infection with *S. haematobium* is blood in the urine. In some regions near the Aswan dam (Egypt) infection is so common that individuals not producing
red-colored urine are considered to be abnormal. Chronic infection with blood flukes can result in a condition known as Schistosomiasis or Bilharzia. Symptoms (damage to liver, kidneys and blood vessels accompanied by anemia and fatigue) are due primarily to inflammatory responses the host organisms launch against parasite eggs that are continuously released by female flukes (around 100 each day). Adult flukes avoid attack by antibodies and immune cells by coating themselves in human antigen, i.e., they become "invisible" to the immune system, and are not attacked.

A condition known as "swimmers itch" may be caused by fluke larvae penetrating the skin. The flukes involved are not typically human parasites and are unable to mature within their human hosts.

3. *Taenia saginata, solium, asiatica* and *pisiformis* (tapeworms) – These four different species of *Taenia* infect cattle, pigs and dogs (respectively), but can also infect humans. Adult tapeworms live in the intestine where they mate and produce huge numbers of eggs within body segments called proglottids. When mature, the proglottids break away from adult worms and their load of eggs is released into the environment with fecal material. An adult tapeworm can hang in the intestine shedding proglottids (segments of the worm loaded with eggs) for years. Eggs are typically ingested by another animal, and then travel to the intestine where they hatch into larval worms. The larvae then burrow through the intestinal wall, enter the bloodstream and travel to muscle tissue where they form cysts (although it is possible for tapeworm larvae to reach any portion of the body served by the cardiovascular system). If another animal eats the infected meat, the larva excyst and attach to the intestinal wall where they mature, mate and produce more eggs.

Humans can acquire pork tapeworms (*Taenia solium* or *T. asiatica*) by ingesting raw or poorly cooked pork tissue (meat) or beef tapeworms (*T. saginata*) by ingesting raw or poorly cooked beef. Under these circumstances, humans will have adult tapeworms living within their intestines. Historical documents indicate that former physicians occasionally provided overweight patients with tapeworm larvae (in capsule form) as a means of inducing weight loss. Humans can also acquire pork tapeworms by accidentally ingesting tapeworm eggs. When this occurs, the eggs hatch in the gut, burrow through the intestinal wall and form cysts within various tissues (typically the brain or eyes). The encysted larvae can cause considerable damage.

There are several other genera of tapeworms, and nearly all types of meat (except fowl) have the potential of carrying tapeworm larvae. Tapeworm larvae are not killed by freezing, so meat intended for ingestion should be thoroughly cooked.

4. *Necator americanus* and *Ancylostoma duodenale* (hookworms) – Parasites within the genera *Necator* and *Ancylostoma* are recognized as New World and Old World hookworms respectively. Adult hookworms live within the small intestine where they attach to the gut wall and feed on blood. They are dioecious, so after mating, only the females release eggs (thousands per day). These exit the host in fecal material and hatch into larval forms in warm, damp soil. The larvae (rhabditiform) live in soil, feeding on bacteria for some period of time; then they become non-feeding (filariform) larvae that seek a new host and burrow through the skin (usually soft tissue between the toes or through the soft skin of small children sitting and playing in the dirt). The filariform larvae enter the bloodstream, travel to the lung, migrate into the alveoli and are then swept up the airways (bronchioles, bronchi and trachea) until they reach the pharynx. There they cause a "tickling" sensation; are coughed up and swallowed. Upon entering the gut, the worms attach, feed and mature into breeding adults; completing the life cycle.

Young humans with heavy hookworm infestations experience anemia due to blood loss (some due to feeding worms and some due to leakage accompanying the release of potent anticoagulants),
potentially resulting in mental and physical retardation. Ground itch can accompany larval penetration of the skin and pneumonia can occur in response to worms entering the lungs. Hookworms in the genus *Necator* are endemic to rural areas in the Southeastern part of the United States.

The larvae of hookworms associated with non-human animals will sometimes penetrate human skin and cause a condition called "creeping eruption". Rather than completing their life cycle, these larvae creep about just under the skin creating a severe itching sensation and emotional stress (because they are often misdiagnosed as poison oak/ivy and they do not go away with the application of topical treatments prescribed). Effective treatment typically involves the use of liquid nitrogen applied directly to the skin surface.

5. *Trichinella spiralis* – Roundworms in the genus *Trichinella* cause trichinosis, a condition resulting from damage caused by larval worms penetrating various tissues throughout the body. Adult worms live in the intestinal mucosa and females produce live larvae that are distributed in the bloodstream. The larvae burrow into various organs, but can only develop within striated muscle cells (skeletal or cardiac) where they form cysts. When muscle tissue (meat) is eaten raw or poorly cooked, the larvae excyst within the intestine and mature into adults. Symptoms of trichinosis include acute gastroenteritis after eating raw or poorly cooked meat, followed 1 to 2 weeks later by fever, muscle pain and edema. Cardiac and central nervous system damage is common. Avoiding trichinosis is a primary reason for making certain pork is thoroughly cooked prior to ingestion, but *Trichinella* can also be found in bear, dear and seal meat.

6. *Dirofilaria immitis* (canine heartworm) – Dogs are considered the definitive hosts for roundworms in the genus *Dirofilaria*; however, these parasites can infect over 30 different types of animals including humans. Though some adult worms inhabit the heart, most reside in the lower pulmonary arteries and lungs where they cause inflammation resulting in damage to vessel walls and surrounding tissues. Heavy infestations can cause congestive heart failure and death. Adult worms (and sometimes sub-adults), mate and the females release live larvae (*microfilariae*) into the bloodstream. These are picked up by a biting mosquito (vector) and transmitted to the next host when the mosquito bites again. Microfilariae circulate throughout the body and require about one year to reach full maturity. Adult parasites may persist within the host for 5 to 7 years.

Humans bitten by mosquitoes carrying microfilariae can become infected with canine heartworms. The parasites typically die within the lungs causing pulmonary symptoms (granuloma formations) that can be mistaken for lung cancer.

7. *Ascaris lumbricoides* – Large roundworms in the genus *Ascaris* can be acquired by humans through the accidental ingestion of eggs (usually in soil contaminated by human or animal feces). Adult *Ascaris* worms live in the intestine where the females release eggs (thousands per day) that exit the host in fecal material. When the eggs are ingested, the rhabditiform larvae burrow through the gut wall, enter the bloodstream, travel to the lungs, penetrate the alveoli and are then swept up the airways (bronchioles, bronchi and trachea) into the pharynx where they are swallowed. Upon returning to the intestine, they mature into adult individuals that may grow to nearly 1 foot in length.

Hundreds of millions of people throughout the world are infected with *Ascaris* worms, though most infestations are asymptomatic. Adult worms can cause abdominal pain, or obstruction and will occasionally become migratory, exiting the host through the mouth or nose. This is very disturbing to the individuals experiencing ascariasis as these large worms cannot go unnoticed.
8. *Enterobius vermicularis* (pinworms) – Pinworms are small roundworms that inhabit the human colon as adults. At night, females migrate to the anus and deposit eggs around the anal opening. These generate an itching sensation that commonly stimulates a scratching response in small children. Eggs on tiny fingers are then spread throughout the home exposing everyone present to pinworms. Eggs are readily ingested from fingers or can be taken in with contaminated air; in either case, they hatch within the small intestine in about 6 hours. The larvae mature into adults that migrate to the colon, completing the life cycle.

Pinworm infection is often asymptomatic, though scratching of the anus may cause tissue abrasion leading to secondary bacterial infection. The small, white adult worms are sometimes found in diapers or on the anal region of young children (typically causing stress in parents and/or caregivers). Pinworm infestations occur throughout the world, are the most common form of roundworm infection in the United States and are very difficult to control.

9. *Dracunculus medinensis* (Guinea worm) – Guinea worm infection can be acquired by drinking water contaminated with water fleas (*Cyclops* species) carrying the larval forms of *Dracunculus medinensis*. After being ingested, the water fleas die and release the worm larvae within the gut. The larvae then burrow through the stomach or intestinal wall and enter the abdominal cavity. After about three months, the larvae mature within the host body cavity, mate and then the males die and their bodies are absorbed. About a year after mating, the female worms migrate to the surface (just under the skin) to release their young. They form painful blisters on the skin which eventually rupture exposing one end of the female worm. These blisters cause a burning sensation and encourage infected hosts (often children) to submerge the afflicted limbs (usually feet) in water. There the female worms release huge numbers of larvae into the water where they can be ingested by *Cyclops* to complete the life cycle.

In addition to causing the formation of painful blisters, the symptoms of Guinea worm infection can include fever, nausea and vomiting. Allergic reactions can produce rashes, diarrhea, dizziness and localized edema. Symptoms typically persist until the adult worm is removed, a process that can take weeks. Secondary bacterial infection is common.

Providing people in endemic areas with clean drinking water, or a means to avoid the ingestion of *Cyclops* could result in the eradication of guinea worm infection. The World Health Organization in partnership with the Carter Center and UNICEF have been actively pursuing this goal.

Many additional endoparasites are known to infect humans, and considerable information is available on-line. For this class, students are encouraged to learn the examples provided, to know their life cycles and to be familiar with the different modes of transmission involved (ingestion, burrowing through the skin, or vector bite).

**Ectoparasites** – Ectoparasites are multicellular parasites that live outside their hosts and include a variety of insects (fleas, lice, mosquitoes, tse-tse flies, kissing bugs, etc.) and spider-like organisms (ticks and mites). These organisms are significant to microbiologists because they are vectors involved in the transmission of disease-causing agents (bacteria, protozoa, viruses and multicellular helminth parasites). Gaining a thorough understanding of vector life cycles, habits and habitats is essential to control efforts and prevention of vector-transmitted disease. The cost of vector control is prohibitive in many countries, and vector-transmitted diseases continue to plague human populations throughout the world. Global climate change is likely to increase the severity of this problem.

**Note** – This is the end of material being covered on Lecture Exam No. 1