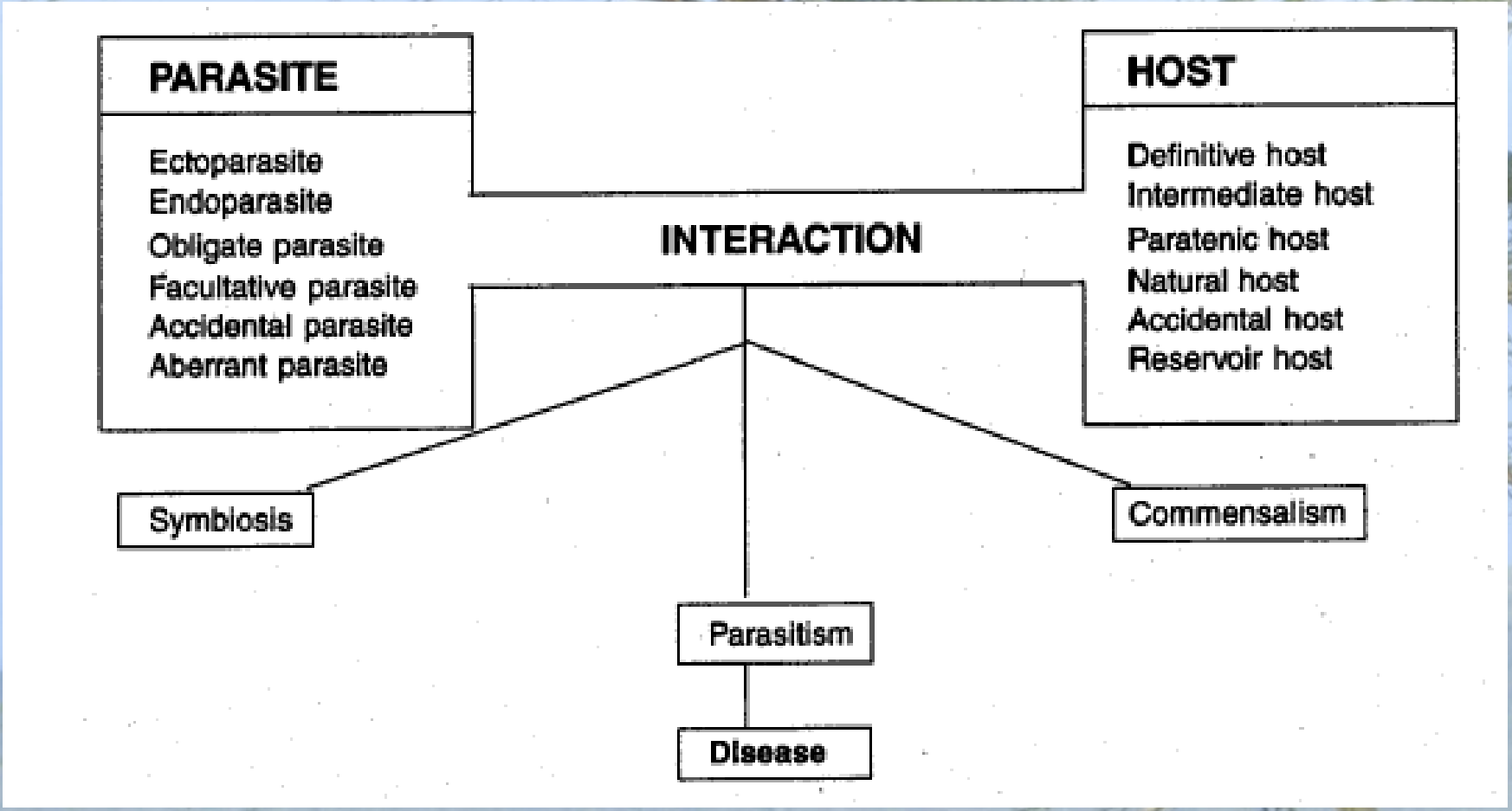
Parasites
(intestinal parasites)

General considerations

Definition

- A *parasite is defined as an animal or plant which harm, others cause moderate to severe diseases, lives in or upon another organism which is called Parasites that can cause disease are known as host.*
- This means all infectious agents including bacteria, viruses, fungi, protozoa and helminths are parasites.
- Now, the term ***parasite*** *is restricted to the protozoa and helminths of medical importance.*
- *The host is usually a larger organism which harbours the parasite and provides it the nourishment and shelter.*
- Parasites vary in the degree of damage they inflict upon their hosts.

Host-parasite interactions



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Classes of Parasites 1.

- Parasites can be divided into ***ectoparasites***, such as ticks and lice, which live on the surface of other organisms, and ***endoparasites***, such as some protozoa and worms which live within the bodies of other organisms
- Most parasites are obligate parasites: they must spend at least some of their life cycle in or on a host.

Classes of parasites 2.

- ***Facultative parasites***: they normally are free living but they can obtain their nutrients from the host also (acanthamoeba)
- When a parasite attacks an unusual host, it is called as ***accidental parasite*** whereas a parasite can be ***aberrant parasite*** if it reaches a site in a host, during its migration, where it can not develop further.

Classes of parasites 3.

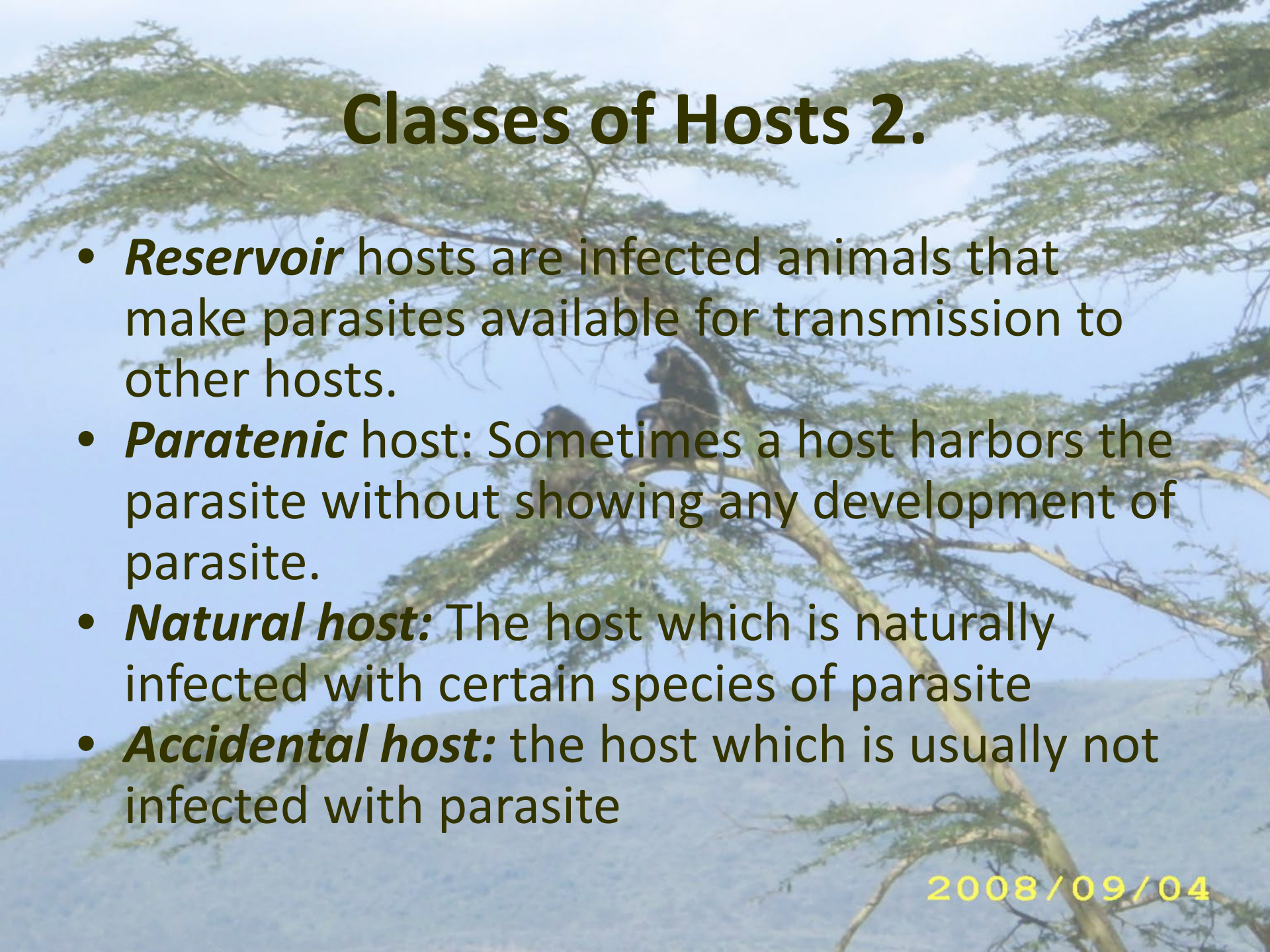
- Parasites can also be classified by the duration of their association with their hosts.
  - *Permanent parasites such as tapeworms remain in or on the host once they have invaded it*
  - *Temporary parasites such as many biting insects feed and leave their hosts*
  - *Hyperparasitism refers to a parasite itself having parasites. Some mosquitoes, which themselves are temporary parasites may also harbour malarial parasites. Such insects serve as vectors of transmission of various diseases*

Classes of Hosts 1.

- ***Definitive*** hosts if they harbor a parasite while it reproduces sexually or as
- ***Intermediate*** hosts if they harbor the parasite during some developmental stages
  - The mosquito is the definitive host for the malarial parasite because it reproduces sexually in the mosquito; the man is the intermediate host, even though man suffers greater damage from the parasite

Classes of Hosts 2.

- ***Reservoir*** hosts are infected animals that make parasites available for transmission to other hosts.
- ***Paratenic*** host: Sometimes a host harbors the parasite without showing any development of parasite.
- ***Natural host:*** The host which is naturally infected with certain species of parasite
- ***Accidental host:*** the host which is usually not infected with parasite



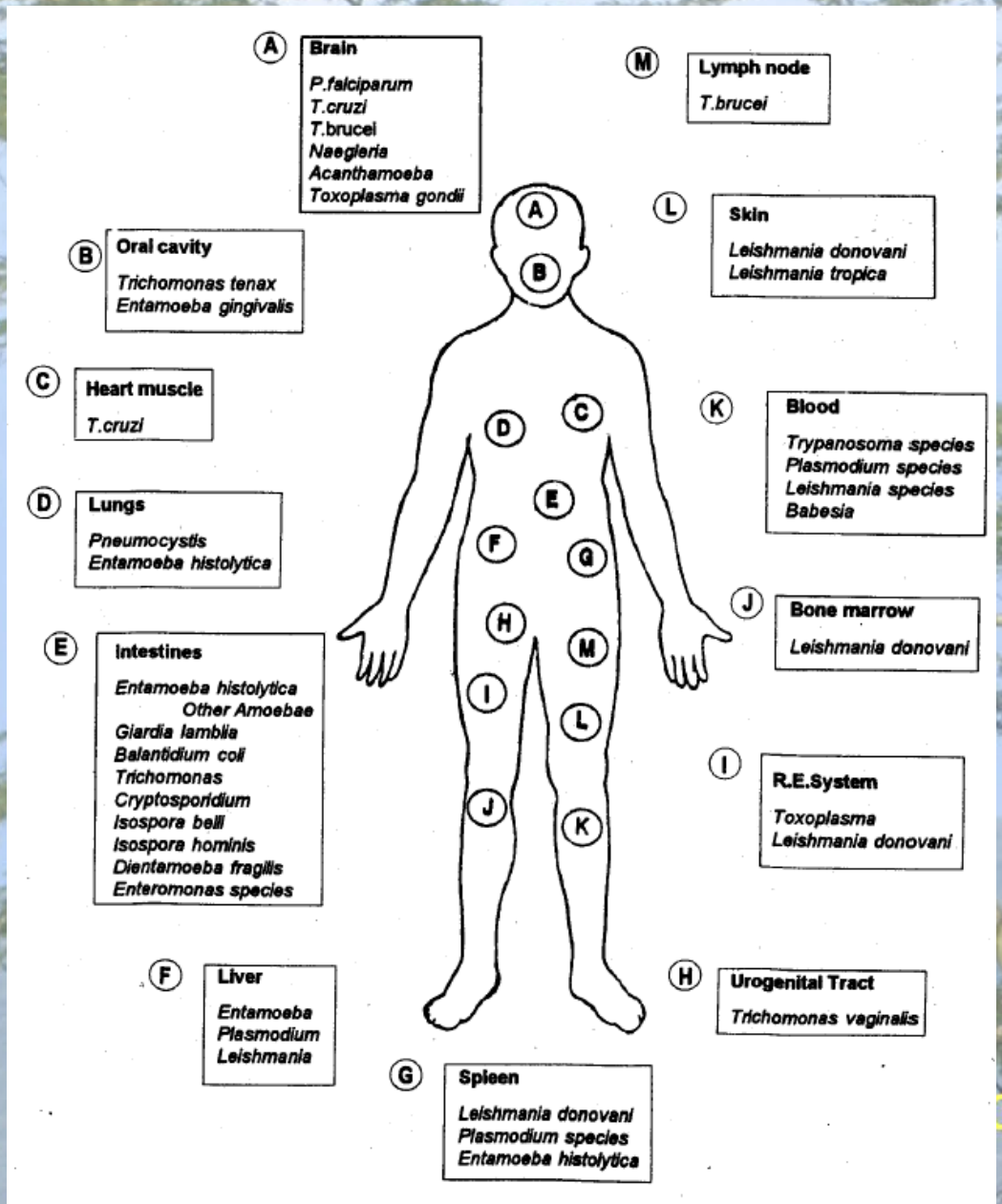
Host-Parasite Relationship

- The relationship between a parasite that does no harm to the host under normal circumstances is called ***symbiosis***
- The relationship may alter if the normal defense of the host are weakened and the parasite may cause a disease (***opportunism***)
- One type of symbiosis is known as ***commensalism*** in which one organism is benefitted and the other remains unaffected.
  - *Some of the parasites which constitute normal flora such as Entamoeba gingivalis, Trichomonas tenax are commensal parasites.*

Factors responsible for pathogenicity of parasites

- Trauma (hookworms, roundworms, taeniasis
- Lytic necrosis (amoebiasis)
- Inflammation (trichinellosis, leishmaniasis)
- Toxins (amoebiasis)
- Allergic manifestations (visceral larva migrans, roundworm infection)

Location of protozoa in various organs of body



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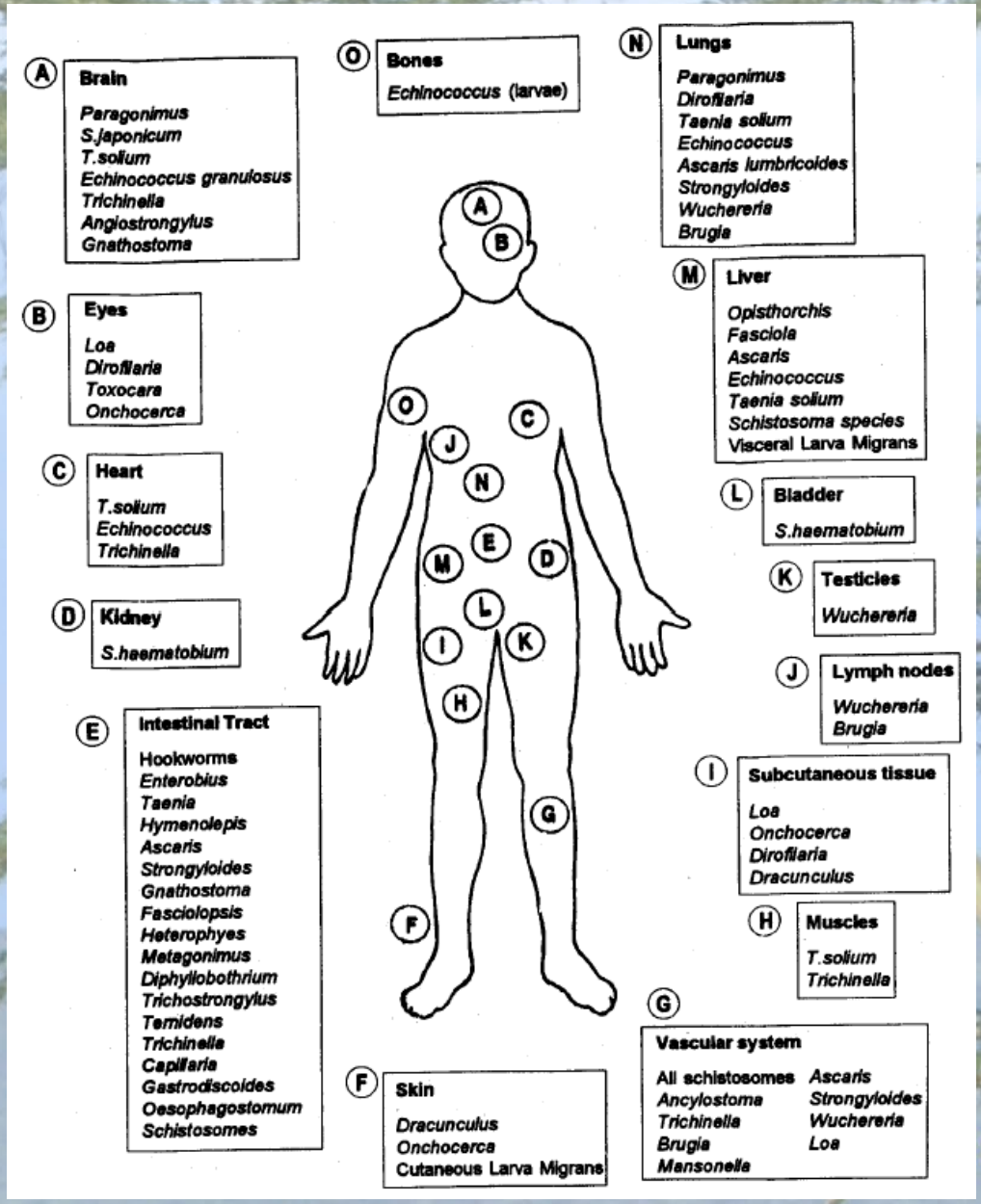
Location of helmints in various organs of body



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Skin manifestations of parasitic diseases

True parasites of dermal tissue	Leshmania tropica Onchocerca Loa loa
Lesions at site of entry	Trypanosoma Leishmania donovani Schistosoma Strongyloides
Lesions at site of exit	Dracunculus
Dissemination from viscera	Taenia solium Entamoeba histolytica Gnathostoma Leishmania donovani
Sensitivity reaction	Ascaris Echinococcus
Secondary changes due to lymphatic bloc	Wuchereria Brugia

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Gastrointestinal tract manifestations of parasitic diseases

Manifestation/ Syndrome	Examples
Dysentery	Entamoeba histolytica Balantidium coli Trichuris trichura Schistosoma Gastrodiscoides Oesophagostomium
Malabsorption syndrome	Giardia Strongyloides Capillaria Isospora
Localised pain	Ascaris Entamoeba histolytica Taenia Oesophagostomium Anisakis
Intestinal obstruction	Ascaris Entamoeba histolytica (amoeboma) Schistosoma (granuloma) Taeniasis Strongyloides
Intestinal perforation	Ascaris Strongyloides

Liver diseases

- Space occupying lesions in parenchyma which may be due to *Entamoeba histolytica* or *Echinococcus*
- *Schistosomes* may cause granulomas
- *Plasmodium* and *Trypanosoma* may cause damage to liver tissue by secondary mechanisms. In both these conditions, hepatomegaly occurs which is also seen in kala-azar and toxoplasmosis

Cardiac diseases (Myocarditis)

- Trypanosoma cruzi
- Trypanosoma brucei
- Toxoplasma gondii
- Trichinella spiralis
- Sarcocystis
- Rare conditions:
  - Hydatid cyst
  - Cysticercosis
  - Heterophysiasis
  - Amoebiasis

Pulmonary manifestations of parasitic diseases

Syndrome/ dysease	Examples
Interstitial pneumonitis	Pneumocystis cerinii Toxoplasma gondii
Pulmonary eosinophilia	Larval nematodes (ascaris larva, etc.)
Focal lesions in lung parenchyma	Echinococcus Entamoeba histolytica Dirofilaria immitis
Pulmonary oedema	Plasmodium falciparum

Splenomegalia and anaemia

Acute splenomegaly	Chronic splenomegaly	Anaemia
Acute malaria	Malaria	Malaria
Trypanosomiasis	Tropical splenomegaly syndrome	Babesiosis
Toxoplasmosis	Kala azar	Hookworm disease
Toxocariasis	Hydatid cyst	Trichuriasis
Katayama syndrome	Amoebic abscess	Diphyllobotriasis

Ocular manifestations of parasitic disease

Chorioretinitis	Space occupying lesion	Orbital oedema
Onchocerciasis	Cysticercosis	American trypanosomiasis
Toxoplasmosis	Schistosomiasis	Trichinosis
Toxocariasis	Brugiasis	Loiasis Sparganosis Larval cestodes

Lymphadenopathia

- American trypanosomiasis
- African trypanosomiasis
- Visceral leishmaniasis
- Toxoplasmosis

Disorders of muscle

- Trichinella
- Taenia solium
- Toxoplasma
- Sarcocystis
- Angiostrongylus

CNS manifestations of parasitic diseases

Encephalopathy	Space occupying lesion	Meningitis
Cerebral malaria	Larval cestodes (e.g. hydatid cyst)	Angiostrongylus Naegleria
Trypanosomiasis	Ectopic trematodes (e.g. paragonimiasis)	
Toxoplasmosis	Migrating nematodes (*Gnathostoma, Toxocara*)	
Trichinosis	Amoebic brain abscess (E. histolytica, Acanthamoeba, Cysticercus)	

Systemic manifestations

Fever

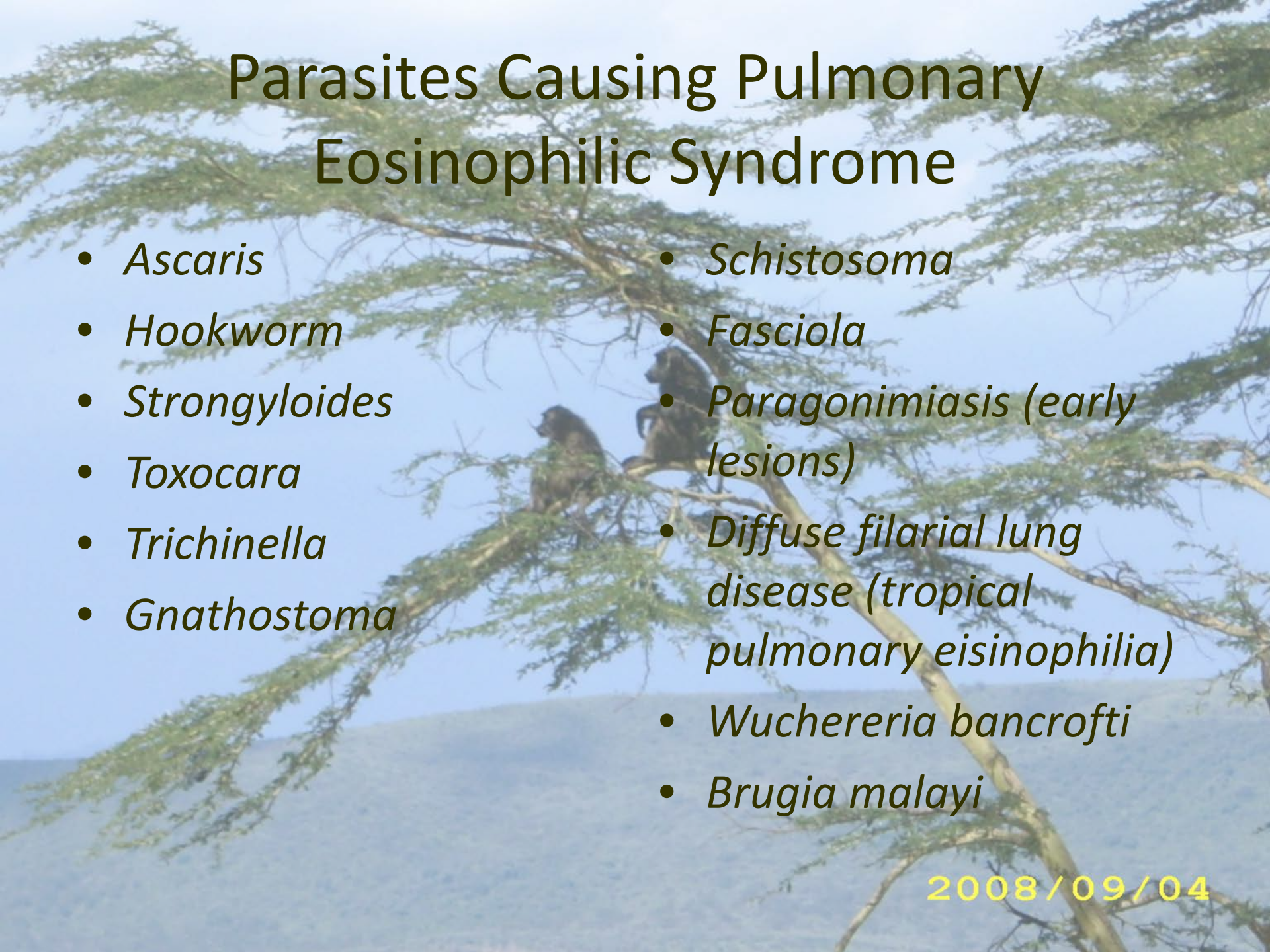
- Malaria
- Leishmaniasis
- Trypanosomiasis
- Toxoplasmosis
- Babesiosis
- Trichinosis
- Tropical pulmonary eosinophilia
- Toxocariasis
- Ascaris pneumonitis
- Lymphatic filariasis
- Pneumocystis carinii

Immunsuppression

- Malaria
- African trypanosomiasis
- Kala-azar
- Schistosomiasis
- Severe onchocerciasis
- Elephantiasis

Parasites Causing Pulmonary Eosinophilic Syndrome

- *Ascaris*
- *Hookworm*
- *Strongyloides*
- *Toxocara*
- *Trichinella*
- *Gnathostoma*
- *Schistosoma*
- *Fasciola*
- *Paragonimiasis (early lesions)*
- *Diffuse filarial lung disease (tropical pulmonary eisinophilia)*
- *Wuchereria bancrofti*
- *Brugia malayi*



Intestinal helmints

General Concepts

- The helminths are worm-like parasites. The clinically relevant groups are separated according to their general external shape and the host organ they inhabit. There are both hermaphroditic and bisexual species. The definitive classification is based on the external and internal morphology of egg, larval, and adult stages.
- **Flukes (Trematodes):**
- Adult flukes are leaf-shaped flatworms. Prominent oral and ventral suckers help maintain position in situ. Flukes are hermaphroditic except for blood flukes, which are bisexual. The life-cycle includes a snail intermediate host.
- **Tapeworms (Cestodes):**
- Adult tapeworms are elongated, segmented, hermaphroditic flatworms that inhabit the intestinal lumen. Larval forms, which are cystic or solid, inhabit extraintestinal tissues.
- **Roundworms (Nematodes):**
- Adult and larval roundworms are bisexual, cylindrical worms. They inhabit intestinal and extraintestinal sites.

Introduction

- Helminth is a general term meaning worm.
- The helminths are invertebrates characterized by elongated, flat or round bodies. In medically oriented schemes the flatworms or platyhelminths (platy from the Greek root meaning “flat”) include flukes and tapeworms. Roundworms are nematodes (nemato from the Greek root meaning “thread”).
- Helminths develop through egg, larval (juvenile), and adult stages. gives the names applied to various larval helminths.
- Knowledge of the different stages in relation to their growth and development is the basis for understanding the epidemiology and pathogenesis of helminth diseases, as well as for the diagnosis and treatment of patients harboring these parasites.
- The contributions of various stages to disease are listed in

Common larval forms of helmints found in humans

Flukes (Trematodes)	Tapeworms (Cestods)	Roundworms (Nematodes)
Miracidium[a]	Cysticercus[b,c,d]	Rabditiform[d]
Sporocyst[a]	Cysticercoid[b]	Filariform[b]
Redia[a]	Coenurus[b,d]	Microfilaria[a,d]
	Coracidium[a]	
Cercaria[a,b,c]	Procercoid[a,b]	
Metacercaria[b]	Plerocercoid[a,b,c,d] (sparganum)	
	Hydatid[a,c,d]	

[a] Infective to or develops within intermediate hosts or vectors
[b] Infective stage for humans
[c] Cause of pathogenic changes in humans
[d] Can be isolated from human host and, therefore, is important in definitive diagnosis

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Stages of helmints commonly responsible for pathologic changes in humans

Helminths	Egg	Larva	Adult
Flukes	+	+*	+
Tapeworms	–	+	+
Nematodes	–	+	+

* Migrating and developing larva forms may cause transient pathologic responses in the host.

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Helminths

- Platyhelminths and nematodes that infect humans have similar anatomic features that reflect common physiologic requirements and functions.
- The outer covering of helminths is the cuticle or tegument. Prominent external structures of flukes and cestodes are acetabula (suckers) or bothria (false suckers).
- Male nematodes of several species possess accessory sex organs that are external modifications of the cuticle. Internally, the alimentary, excretory, and reproductive systems can be identified by an experienced observer.
- Tapeworms are unique in lacking an alimentary canal.
- This lack means that nutrients must be absorbed through the tegument.
- The blood flukes and nematodes are bisexual.
- All other flukes and tapeworm species that infect humans are hermaphroditic.
- With few exceptions, adult flukes, cestodes, and nematodes produce eggs that are passed in excretions or secretions of the host. The various stages and their unique characteristics will be reviewed in more detail as each major group of helminths is considered.

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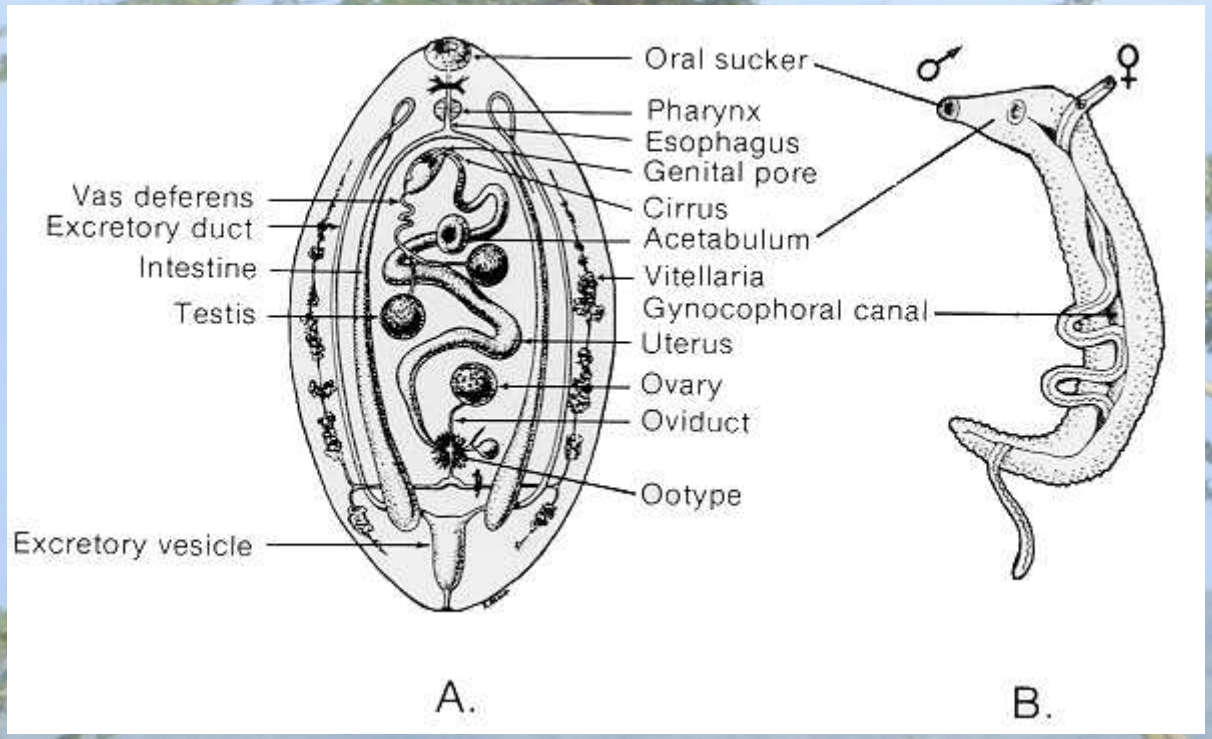
Flukes

- The structure of flukes is summarized in and.
- A dorsoventrally flattened body, bilateral symmetry, and a definite anterior end are features of platyhelminths in general and of trematodes specifically.
- Flukes are leaf-shaped, ranging in length from a few millimeters to 7 to 8 cm. The tegument is morphologically and physiologically complex.
- Flukes possess an oral sucker around the mouth and a ventral sucker or acetabulum that can be used to adhere to host tissues.
- A body cavity is lacking. Organs are embedded in specialized connective tissue or parenchyma. Layers of somatic muscle permeate the parenchyma and attach to the tegument.

Flukes



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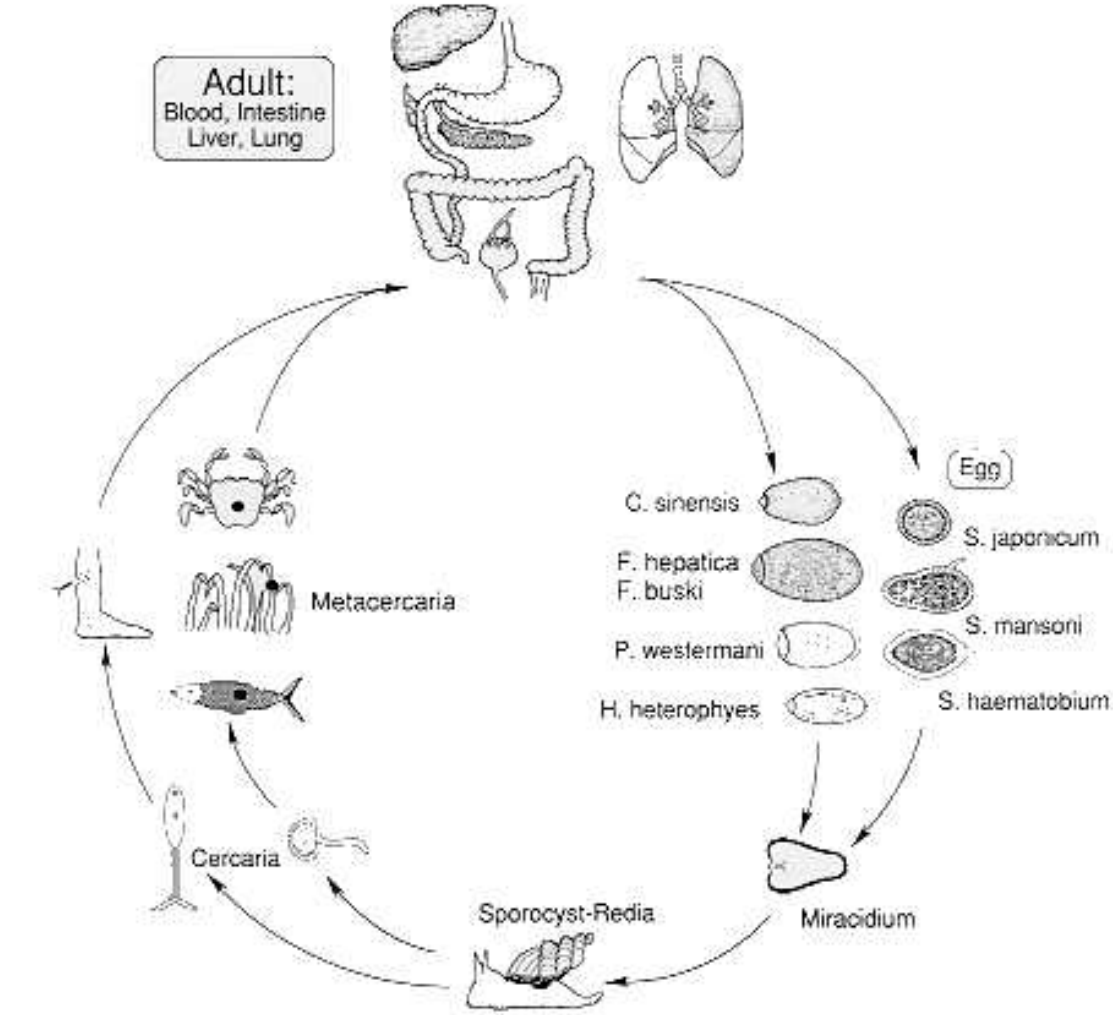
Flukes



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Flukes

- Flukes have a well-developed alimentary canal with a muscular pharynx and esophagus.
- The intestine is usually a branched tube (secondary and tertiary branches may be present) consisting of a single layer of epithelial cells.
- The main branches may end blindly or open into an excretory vesicle.
- The excretory vesicle also accepts the two main lateral collecting ducts of the excretory system, which is of a protonephridial type with flame cells.
- A flame cell is a hollow, terminal excretory cell that contains a beating (flamelike) group of cilia.
- These cells, anchored in the parenchyma, direct tissue filtrate through canals into the two main collecting ducts.

Flukes

- Except for the blood flukes, trematodes are hermaphroditic, having both male and female reproductive organs in the same individual.
- The male organ consists usually of two testes with accessory glands and ducts leading to a cirrus, or penis equivalent, that extends into the common genital atrium.
- The female gonad consists of a single ovary with a seminal receptacle and vitellaria, or yolk glands, that connect with the oviduct as it expands into an ootype.
- The tubular uterus extends from the ootype and opens into the genital atrium. Both self- and cross-fertilization occur.
- The components of the egg are assembled in the ootype.
- Eggs pass through the uterus into the genital atrium and exit ventrally through the genital pore.
- Fluke eggs, except for those of schistosomes, are operculated (have a lid).

Flukes

- The blood flukes or schistosomes are the only bisexual flukes that infect humans.
- Although the sexes are separate, the general body structure is the same as that of hermaphroditic flukes.
- Within the definitive host, the male and female worms inhabit the lumen of blood vessels and are found in close physical association.
- The female lies within a tegumental fold, the gynecophoral canal, on the ventral surface of the male.
- The medically important flukes belong to the taxonomic category Digenea.
- This group of flukes has a developmental cycle requiring at least two hosts, one being a snail intermediate host.
- Depending on the species, other intermediate hosts may be involved to perpetuate the larval form that infects the definitive human host.

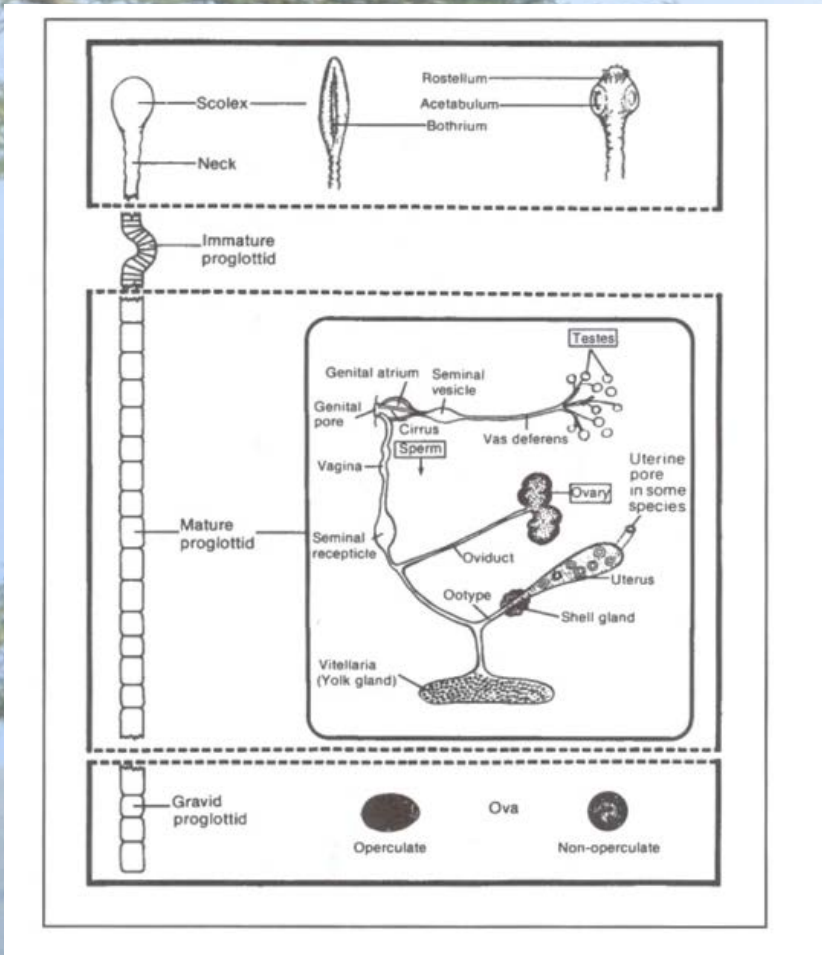
Flukes

- Flukes go through several larval stages, each with a specific name, before reaching adulthood.
- Taking into account variations among species, a generalized life cycle of digenetic flukes runs the following course.
- Eggs are passed in the feces, urine, or sputum of humans and reach an aquatic environment.
- The eggs hatch, releasing ciliated larvae, or miracidia, which either penetrate or are eaten by a snail intermediate host.
- In rare instances land snails may serve as intermediate hosts.
- A saclike sporocyst or redia stage develops from a miracidium within the tissues of the snail.
- The sporocyst gives rise either to rediae or to a daughter sporocyst stage. In turn, from the redia or daughter sporocyst, cercariae develop asexually and migrate out of the snail tissues to the external environment, which is usually aquatic.

Flukes

- The cercariae, which may possess a tail for swimming, develop further in one of three ways.
- They either penetrate the definitive host and transform directly into adults, or penetrate a second intermediate host and develop as encysted metacercariae, or they encyst on a substrate, such as vegetation, and develop there as metacercariae.
- When a metacercarial cyst is ingested, digestion of the cyst liberates an immature fluke that migrates to a specific organ site and develops into an adult worm.

Tapeworms (Cestodes)



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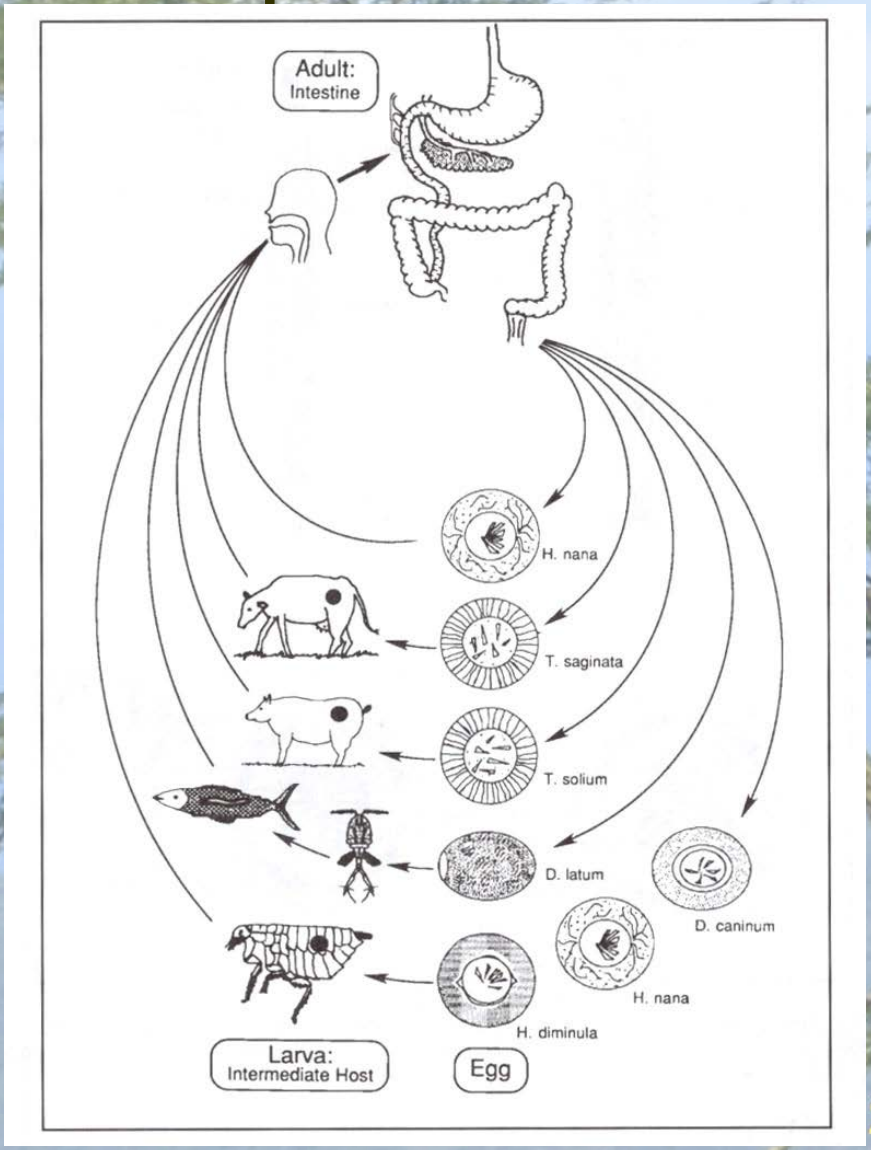
Tapeworms (Cestodes)

- Whereas flukes are flattened and generally leaf-shaped, adult tapeworms are flattened, elongated, and consist of segments called proglottids.
- Tapeworms vary in length from 2 to 3 mm to 10 m, and may have three to several thousand segments.
- Anatomically, cestodes are divided into a scolex, or head, which bears the organs of attachment, a neck that is the region of segment proliferation, and a chain of proglottids called the strobila.
- The strobila elongates as new proglottids form in the neck region.
- The segments nearest the neck are immature (sex organs not fully developed) and those more posterior are mature.
- The terminal segments are gravid, with the egg-filled uterus as the most prominent feature.

Tapeworms



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Tapeworms (Cestodes)

- The scolex contains the cephalic ganglion, or “brain,” of the tapeworm nervous system.
- Externally, the scolex is characterized by holdfast organs.
- Depending on the species, these organs consist of a rostellum, bothria, or acetabula.
- A rostellum is a retractable, conelike structure that is located on the anterior end of the scolex, and in some species is armed with hooks.
- Bothria are long, narrow, weakly muscular grooves that are characteristic of the pseudophyllidean tapeworms.
- Acetabula (suckers like those of digenetic trematodes) are characteristic of cyclophyllidean tapeworms.
- Differential features of pseudophyllidean and cyclophyllidean tapeworms are listed
- Most human tapeworms are cyclophyllideans.

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Differences between Pseudophylidean and Cyclophylidean Tapeworms

Differentiating Feature	Pseudophyllidea	Cyclophyllidea
Scolex	Two sucking grooves (bothrial)	Four muscular suckers (acetabula)
Genital pore	Center of each proglottid	Margin(s) of each proglottid [may be located On both sides in an irregular pattern (Taenia spp); all on the same side (Hymenolepis spp); or each proglottid may have a pore on each side (dipylidium caninum)]
Uterine pore	Center of proglottides on ventral surface	Absent; uterus ends blindly
Uterus (gravid)	Relatively long and coiled	Saclike, highly branched
Eggs	Operculate	Nonoperculate
Oncosphere	Ciliated (coracidium)	Nonciliated
Larvae	Procercoid and plerocercoid; both forms solid	Cysticercoid, cysticercus, hydatid; all forms cystic

Tapeworms

- A characteristic feature of adult tapeworm is the absence of an alimentary canal, which is intriguing since all of these adult worms inhabit the small intestine.
- The lack of an alimentary tract means that substances enter the tapeworm across the tegument.
- This structure is well adapted for transport functions, since it is covered with numerous microvilli resembling those lining the lumen of the mammalian intestine.
- The excretory system is of the flame cell type.

Tapeworms

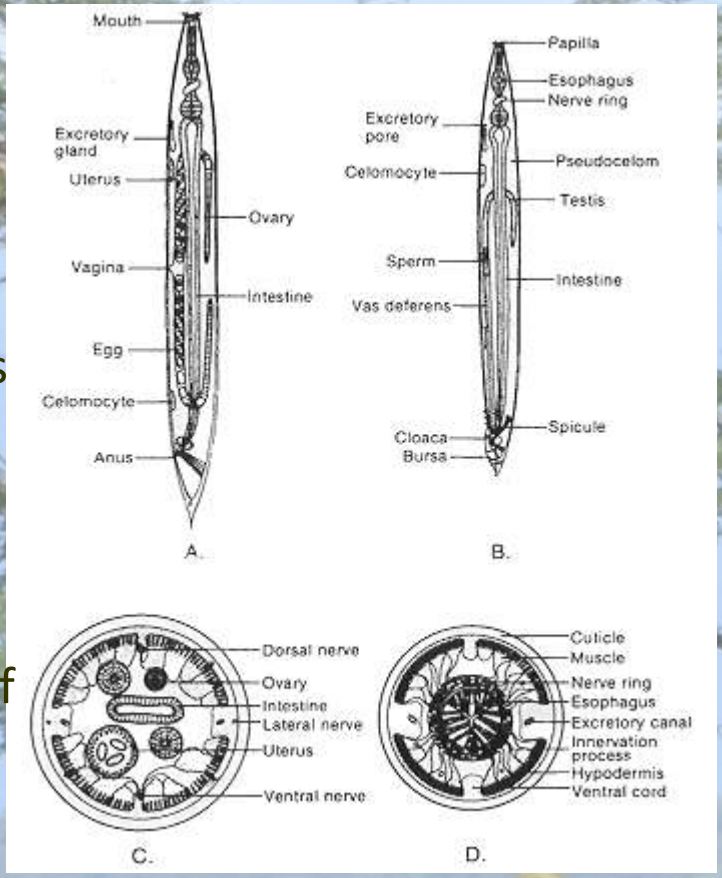
- Cestodes are hermaphroditic, each proglottid possessing male and female reproductive systems similar to those of digenetic flukes.
- However, tapeworms differ from flukes in the mechanism of egg deposition.
- Eggs of pseudophyllidean tapeworms exit through a uterine pore in the center of the ventral surface rather than through a genital atrium, as in flukes.
- In cyclophyllidean tapeworms, the female system includes a uterus without a uterine pore.
- Thus, the cyclophyllidean eggs are released only when the tapeworms shed gravid proglottids into the intestine. Some proglottids disintegrate, releasing eggs that are voided in the feces, whereas other proglottids are passed intact.

Tapeworms

- The eggs of pseudophyllidean tapeworms are operculated, but those of cyclophyllidean species are not.
- Eggs of all tapeworms, however, contain at some stage of development an embryo or oncosphere.
- The oncosphere of pseudophyllidean tapeworms is ciliated externally and is called a coracidium.
- The coracidium develops into a procercoid stage in its micro-crustacean first immediate host and then into a plerocercoid larva in its next intermediate host which is a vertebrate.
- The plerocercoid larva develops into an adult worm in the definitive (final) host.
- The oncosphere of cyclophyllidean tapeworms, depending on the species, develops into a cysticercus larva, cysticercoid larva, coenurus larva, or hydatid larva (cyst) in specific intermediate hosts.
- These larvae, in turn, become adults in the definitive host illustrates these larval forms and representative life cycles.

Roundworms

In contrast to platyhelminths, nematodes are cylindrical rather than flattened; hence the common name roundworm. The body wall is composed of an outer cuticle that has a noncellular, chemically complex structure, a thin hypodermis, and musculature. The cuticle in some species has longitudinal ridges called alae. The bursa, a flaplike extension of the cuticle on the posterior end of some species of male nematodes, is used to grasp the female during copulation.



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Roundworms

- The cellular hypodermis bulges into the body cavity or pseudocoelom to form four longitudinal cords—a dorsal, a ventral, and two lateral cords—which may be seen on the surface as lateral lines.
- Nuclei of the hypodermis are located in the region of the cords. The somatic musculature lying beneath the hypodermis is a single layer of smooth muscle cells.
- When viewed in cross-section, this layer can be seen to be separated into four zones by the hypodermal cords.
- The musculature is innervated by extensions of muscle cells to nerve trunks running anteriorly and posteriorly from ganglion cells that ring the midportion of the esophagus.
- The space between the muscle layer and viscera is the pseudocoelom, which lacks a mesothelium lining.
- This cavity contains fluid and two to six fixed cells (celomocytes) which are usually associated with the longitudinal cords.
- The function of these cells is unknown.

Roundworms

- The alimentary canal of roundworms is complete, with both mouth and anus.
- The mouth is surrounded by lips bearing sensory papillae (bristles).
- The esophagus, a conspicuous feature of nematodes, is a muscular structure that pumps food into the intestine; it differs in shape in different species.
- The intestine is a tubular structure composed of a single layer of columnar cells possessing prominent microvilli on their luminal surface.
- The excretory system of some nematodes consists of an excretory gland and a pore located ventrally in the mid-esophageal region.
- In other nematodes this structure is drawn into extensions that give rise to the more complex tubular excretory system, which is usually H-shaped, with two anterior limbs and two posterior limbs located in the lateral cords.
- The gland cells and tubes are thought to serve as absorptive bodies, collecting wastes from the pseudocoelom, and to function in osmoregulation.

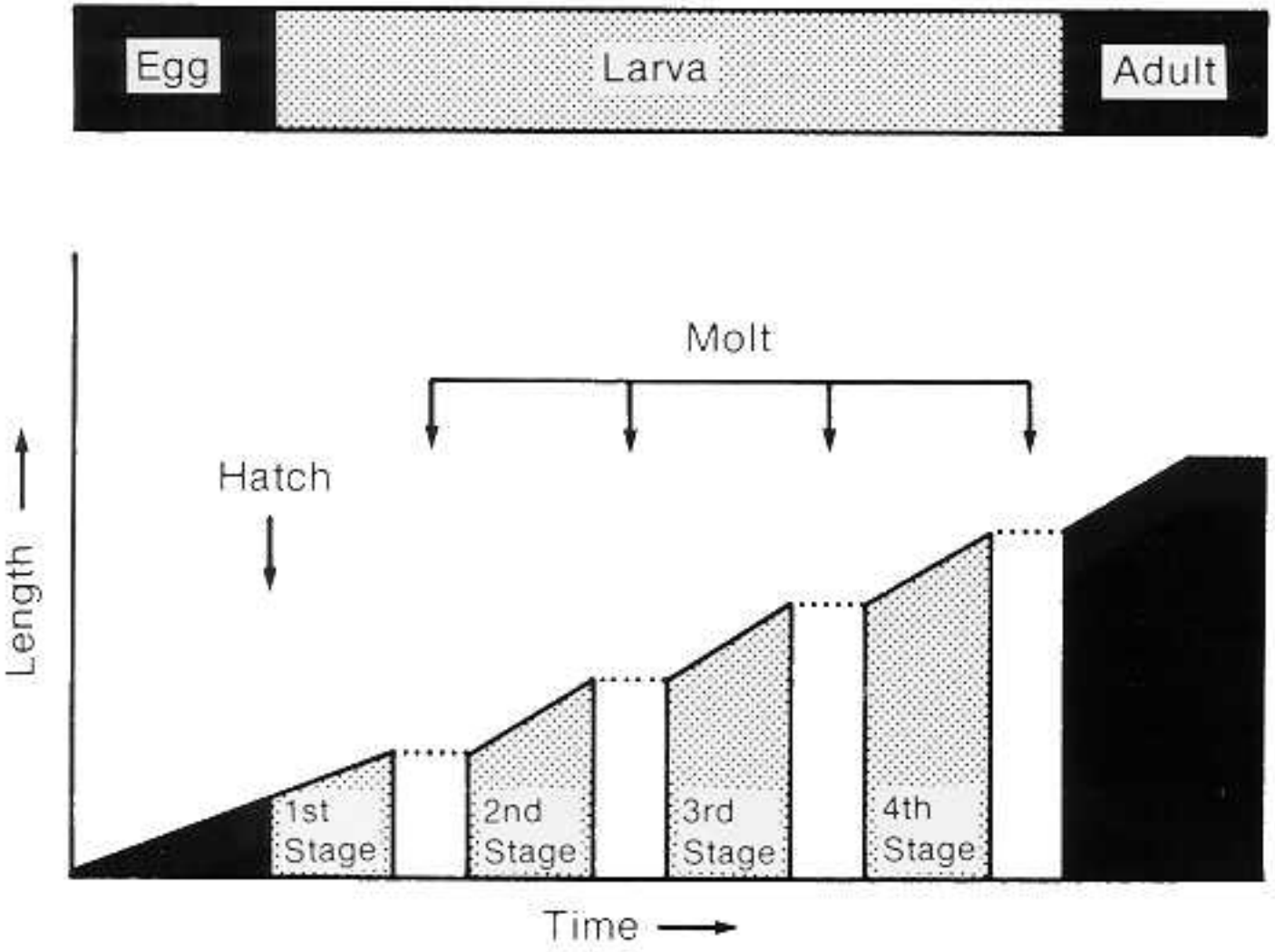
Roundworms

- Nematodes are usually bisexual.
- Males are usually smaller than females, have a curved posterior end, and possess (in some species) copulatory structures, such as spicules (usually two), a bursa, or both.
- The males have one or (in a few cases) two testes, which lie at the free end of a convoluted or recurved tube leading into a seminal vesicle and eventually into the cloaca.
- The female system is tubular also, and usually is made up of reflexed ovaries.
- Each ovary is continuous, with an oviduct and tubular uterus.
- The uteri join to form the vagina, which in turn opens to the exterior through the vulva.

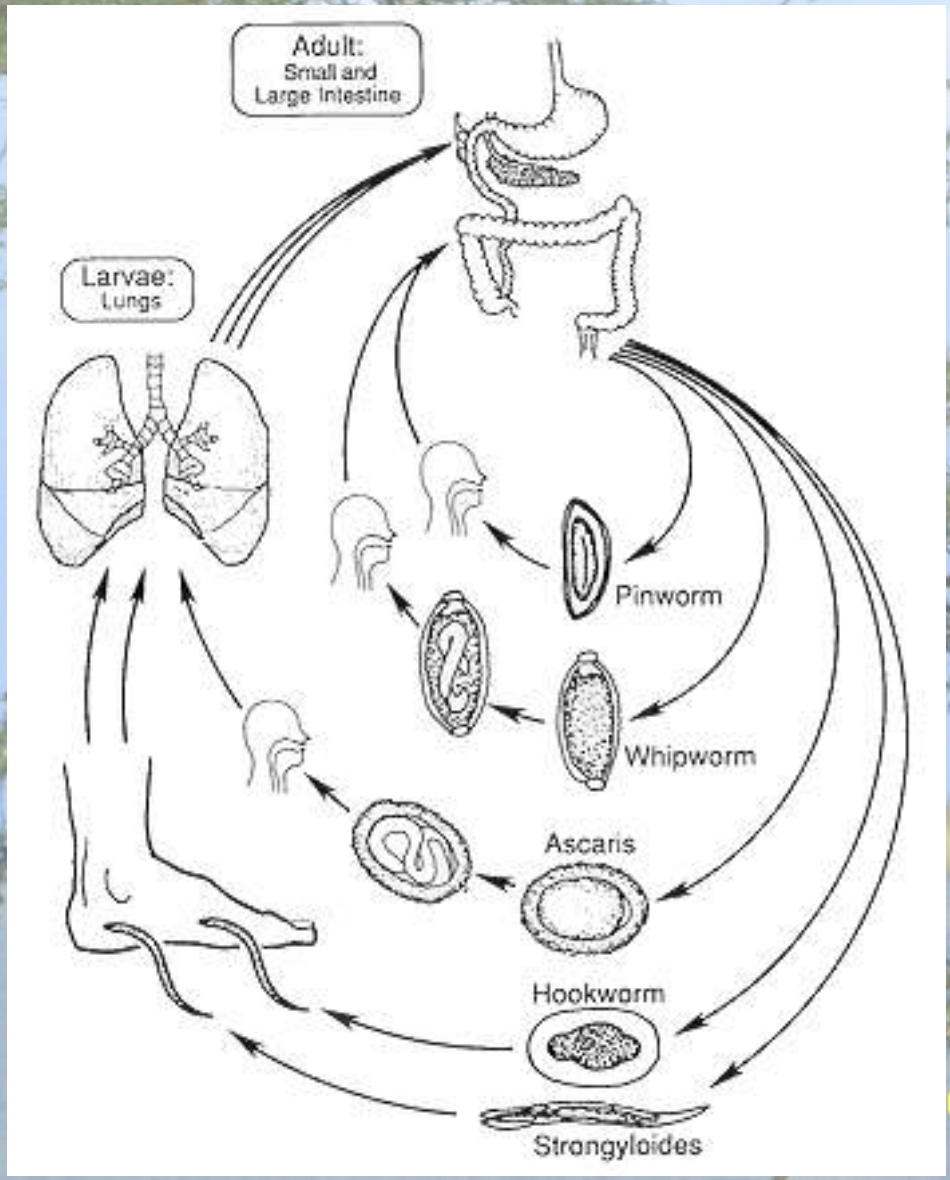
Roundworms

- Copulation between a female and a male nematode is necessary for fertilization except in the genus *Strongyloides,* in which parthenogenetic development occurs (i.e., the development of an unfertilized egg into a new individual).
- Some evidence indicates that sex attractants (pheromones) play a role in heterosexual mating.
- During copulation, sperm is transferred into the vulva of the female.
- The sperm enters the ovum and a fertilization membrane is secreted by the zygote.
- This membrane gradually thickens to form the chitinous shell.
- A second membrane, below the shell, makes the egg impervious to essentially all substances except carbon dioxide and oxygen.
- In some species, a third proteinaceous membrane is secreted as the egg passes down the uterus by the uterine wall and is deposited outside the shell.
- Most nematodes that are parasitic in humans lay eggs that, when voided, contain either an uncleaved zygote, a group of blastomeres, or a completely formed larva.
- Some nematodes, such as the filariae and *Trichinella spiralis*, produce larvae that are deposited in host tissues.

Roundworms


Egg
Larva
Adult
Molt
Hatch
Length
1st Stage
2nd Stage
3rd Stage
4th Stage
Time

Roundworms



008/09/04

Flatworms	Fluke/ trematode (Trematode infection)	Blood fluke	Schistosoma mansoni/japonicum/ haematobium, Trichobilharzia (Swimmer's itch			
		Liver fluke	Clonorchis sinensis (Clonorchiasis), Fasciola hepatica/ gigantica (Fascioliasis), Opistotorchiasis			
		Lung fluke	Paragonimus westermani (Paragonimiasis)			
		Intestinal fluke	Fasciolopsis buski			
	Cestoda (Tapeworm infection)	Cyclophyllidae	Echinococcus granulosus/ Echinococcus multilocularis (Echinococcosis), Taenia saginata (beef)/ Taenia asiatica/ Taenia solium (pork) (Taeniasis, Cysticercosis), Hymenolepis nana/ Hymenolepis diminuta (Hymenolepiasis),			
		Pseudophyllidae	Diphyllobothrium latum (Diphyllobothriasis), Spirometra erinaceieieropei (Sparganosis), Diphyllobothrium mansonoides (Sparganosis)			
Roundworms	Secernentea		Spirurida	Camallanina		Dracuncula mediensis (Dracunculiasis)
				Spirurina	Filaroideae (Filariasis)	Onchocerca volvulus (Onchocerciasis), Loa loa (Loa loa filariasis), Mansonella (Mansonelliasis), Dirofilaria repens (Dirofilariasis), Wuchereria bancrofti, Brugia malayi, Brugia timori
					Thelazioidea	Gnathostoma spinigerium/ Gnathostoma hispidum (Gnathostomiasis), Thelazia (Thelaziasis)
					Spiruroidae	Gongylonema
			Strongylida (hookworm)	Ancylostoma duodenale/ Ancylostoma brasiliense (Ancilostomiasis, cutaneous larva migrans), Necator americanus (Necatoriasis), Angiostrongylus cantonensis (Angostrongyliasis), Metastrongylus (Metastrongyliasis)		
			Ascaridida	Ascaris lumbricoides (Ascariasis), Anisakis (Anisakiasis), Toxocara canis/ Toxocara cati (Visceral larva migrans), Baylisascaris		
			Rhabditida	Strongiloides stercoralis		
			Oxyurida	Enterobius vermicularis (Enterobiasis), Pinworm)		
	Adenophorea	Trichinella spiralis (Trichinosis), Trichusris trichiura (Trichuriasis, Whipworm), Capillaria philippinensis (Intestinal capillariasis), Capillaria hepatica				