Republic of Iraq
Ministry of higher education &scientific research
Al-Frat Al-Awsat Technical University
Technical institute of Karbala
Department of Community Health Technologies

هورية العراق
ارة التعليم و البحث العلمي
عة الفرات الاوسط التقنية
معهد التقني / كربلاء
م تقنيات صحة المجتمع

Educational Bag
Of
Medical Microbiology 2

For Students of the First Stage – Seconed Course /
Department of Community Health Technologies

Praprared by

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lecturer

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General Objectives and Foundations of Medical Microbiology for The First Stage/ Seconed Course

Objectives of the subject :

General objectives :

Student will be able to know a simple general idea about :

Pathogenic parasitic organisms, parasitic insects and immunity of humman body against microbial pathogene.

Special objectives :

Student will be able to :

- Do diagnosis for some simple cases in his field work, instead of specialest, when specielest is absent.
- Do some tests in the accidental cases.
- Collect, preserve and transport the pathgenic samples.

Theoretical vocabulary

Week	Details
1	Introduction of parasites.
2	Protozoa , Entamoeba histolytica.
3	Flagellates, giardia . trichomonase .
4	Blood flagellates, leishmania.
5	Sporozoa, plasmodium , toxoplasma.
6	Helimenthes , taenia .
7	Echinococcus granulosis.
8	Hymenolipes nana
9	Trematoda helminthes .
10	Schistosomes
11	Immune system , organs of immune systems.
12	Antibody &antigen .
13	Antibody &antigen reactions .
14	Hypersensitivity .
15	Autoimmune diseases.

General view about Parasitology , Definition, Classification of Parasites

- **Medical Parasitology**: is the branch of medical sciences dealing with organisms (parasites) which live temporarily or permanently, on or within the human body (host).
- **Parasite:** is a living organism, which takes its nourishment and other needs from a host.
- **Host:** the **host** is an organism which supports and harbors the parasite.
- **Pathogen:** A microorganism capable of causing an infection.
- **Vector:** Animal that serve as a carrier of parasites.

❖ Types of Parasites:

1) **Ectoparasite** – a parasitic organism that lives on the outer surface of its host, e.g. lice, ticks, mites etc.
2) **Endoparasites** – parasites that live inside the body of their host, e.g. *Entamoeba histolytica*.
3) **Obligate Parasite** - This parasite is completely dependent on the host during a part or all of its life cycle, e.g. Plasmodium spp.
4) **Facultative parasite** – an organism that exhibits both parasitic and non-parasitic modes of living and hence does not absolutely depend on the parasitic way of life, but is capable of adapting to it if placed on a host. E.g. *Naegleria fowleri*
5) **Accidental parasite** – when a parasite attacks an unnatural host and survives. E.g. *Hymenolepis diminuta* (rat tapeworm).
6) **Opportunistic parasite**- that is capable of producing disease in an immune deficient host (like AIDS and cancer patients) e.g. *Toxoplasma gondii*.

❖ Types of Hosts:

Hosts are classified according to their role in the life cycle of the parasite into:

1) **Definitive (final) host**– a host that harbors a parasite in the adult stage or where the parasite undergoes a sexual method of reproduction.
2) **Intermediate host** - harbors the larval stages of the parasite or an asexual cycle of development takes place. In some cases, larval development is completed in two different intermediate hosts, referred to as first and second intermediate hosts.
3) **Reservoir host** – a host that makes the parasite available for the transmission to another host and is usually not affected by the infection.
4) **Accidental host** – a host that is under normal circumstances not infected with the parasite.

❖ Relationship between the hosts and parasite:

In biology, the relationship between two organisms is mainly in the form of **symbiosis,** defined as "life together", i.e., the two organisms live in an association with one another. Thus, there are at least three types of relationships based on whether the symbiont has beneficial, harmful, or no effects on the other

a. **mutualism -** both organisms are benefited
b. **commensalism -** in which one partner benefits from the association, but the host is no harmed.
c. **parasitism -** the relationship between two lives organisms one organism is benefited at the expense of another (host).

❖ Life cycle of parasites:

Two forms of life cycle of parasites as the following:

1- **Direct life cycle**: is one in which the organism is passed from one host to next through the air by fomite or in contaminated food or water.

2- **Indirect life cycle**: the organism develops or multiplies in vector or in an intermediate host.

❖ Modes of transmission of parasites:

1- Fecal-oral route

2- Food/ water/ soil

3- Direct skin penetration

4- Ingestion of larvae

5- Arthropod vector

6- Rarely: mother to offspring

7- Direct and indirect contact

❖ Classification of Medical Parasitology

Parasites of medical importance come under the kingdom called protista and animalia. Protista includes the microscopic single-celled eukaroytes known as protozoa (unicellular parasites). In contrast, helminthes or metazoan are macroscopic. Medical Parasitology is generally classified into:

A. **Medical Protozoology** - Deals with the study of medically important protozoa that affect man.

B. **Medical Helminthology (metazoology)** - Deals with the study of helminthes (worms) that affect man.

C. **Medical Entomology** - Deals with the study of arthropods which cause or transmit disease to man.

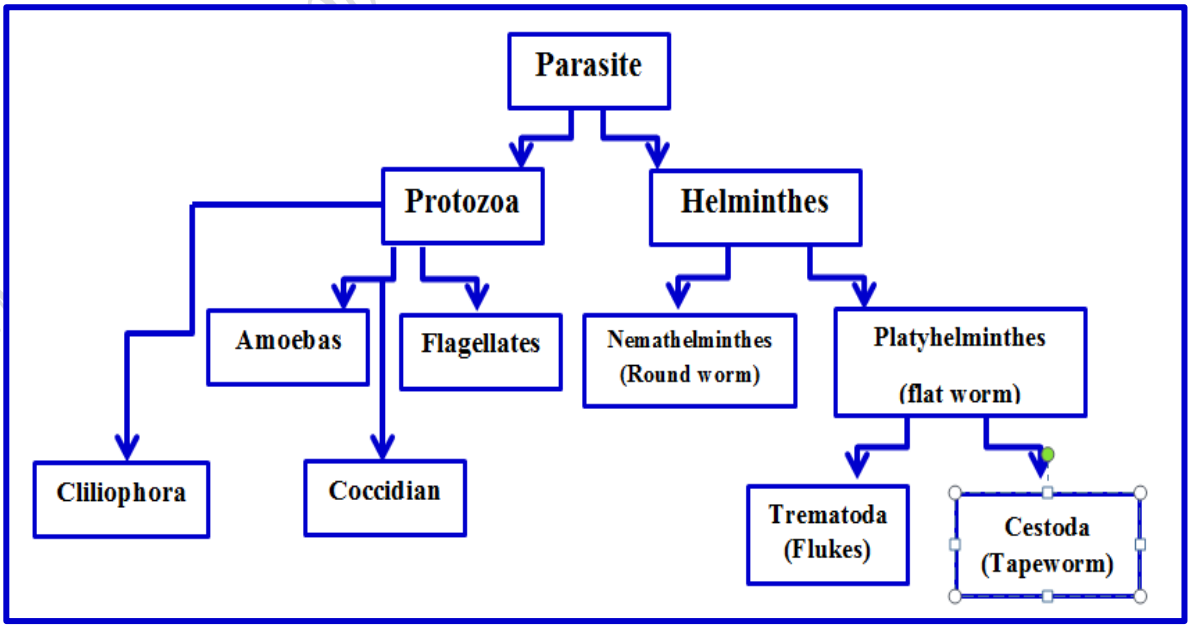


Figure: Classification of medical parasitology

General properties of protozoa and helminthes

Protozoa	Helminthes
Unicellular Single cell for all functions	Multicellular Specialized cells
• **Amoebas**- move by protoplasmic projections called pseudopodia (false feet). • **Flagellates**- move by whip-like, thin structures called flagella. • **Cliliophora**- move by means of short hair-like projections called cilia. • **Coccidian**- does not have locomotor organelles.	• **Nemathelminthes**- round worm, unsegmented worm • **Platyhelminthes** **-Trematoda**- Flukes worm, leaf like, unsegmented worm. **-Cestoda**- tape like worm, segmented worm.

Intestinal protozoa *Entamoebia histolytica* and *E.dispar*
(disease,life cycle, diagnosis,mode of transmission)

Amoeba or Rhizopoda Class

❖ General properties:

i. Amoeba primitive unicellular microorganisms with a relatively simple life cycle which can be divided into two stages:

• **Trophozoite** – actively motile feeding stage.

• **Cyst** – quiescent, resistant, infective stage.

ii. Their **reproduction** is through **binary fission**, e.g. splitting of the trophozoite.

iii. **Motility** is accomplished by extension of **pseudopodia ("false foot")**

☒ Entamoeba histolytica

Disease: amoebic dysentery.

Habitat: large intestine.

Geographical distribution: worldwide.

Infective stage: Quadranucleated cyst.

❖ **Mode of infection or transmission:** fecal-oral. Ingestion food and water contaminated with mature cyst (Quadranucleated cyst).

❖ Morphological features

(a) Trophozoite

- ✓ Viable trophozoite vary in size from about 10-60μm in diameter.
- ✓ Motility is rapid, progressive, and unidirectional, through pseudopods.
- ✓ The nucleus is characterized by arranged chromatin on the nuclear membrane and the presence of a small, compact, centrally located karyosome.
- ✓ The cytoplasm is usually described as finely granular with few ingested bacteria or debris in vacuoles. In the case of dysentery, however, **RBCs may be visible in the cytoplasm**, and **this feature is diagnostic for *E.histolytica*.**

(b) Cyst

- ✓ The cyst may be rounded or oval contain one or two nuclei (immature cyst) or four nuclei (mature nuclei). Cysts range in size from 10-15µm.
- ✓ The immature cyst has inclusions namely; glycogen mass and chromatoidal bars.
- ✓ As the cyst matures, the glycogen completely disappears; the chromotiodials may also be absent in the mature cyst.

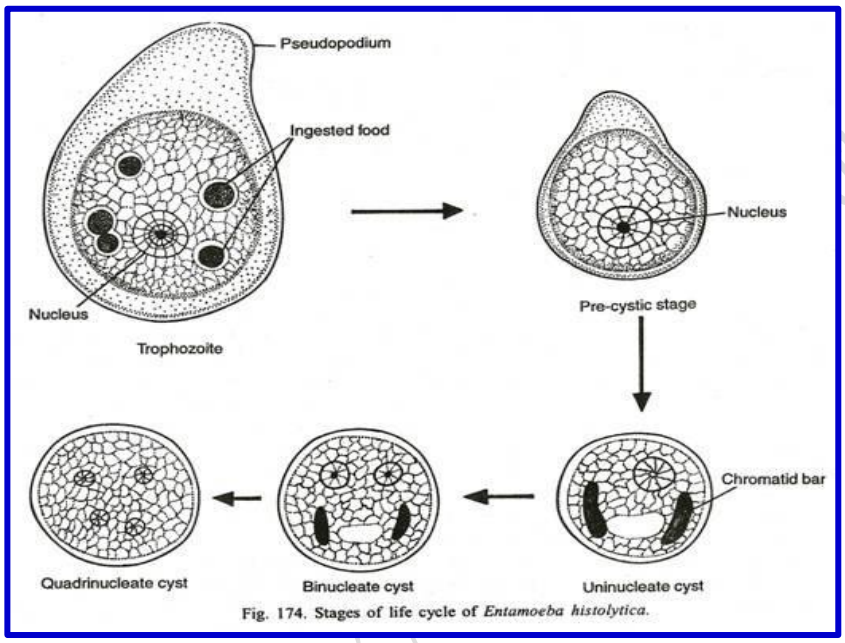


Fig. 174. Stages of life cycle of *Entamoeba histolytica*.

Trophozoite of *Entamoeba histolytica*

Maturation stages of *E.histolytica*: trophozoite →1 nucleus cyst→2 nucleus cyst → 4 nucleus cyst (Quadranucleated cyst**)**

❖ Pathogenesis

Trophozoites divide and produce extensive local necrosis in the large intestine. Invasion into the deeper mucosa with extension into the peritoneal cavity and caused **(bloody diarrhea)**. This can lead to secondary involvement of other organs, primarily the liver but also the lungs, brain, and heart. **Extraintestinal amebiasis** is associated with trophozoites.

❖ Life cycle of Entamoeba histolytica:

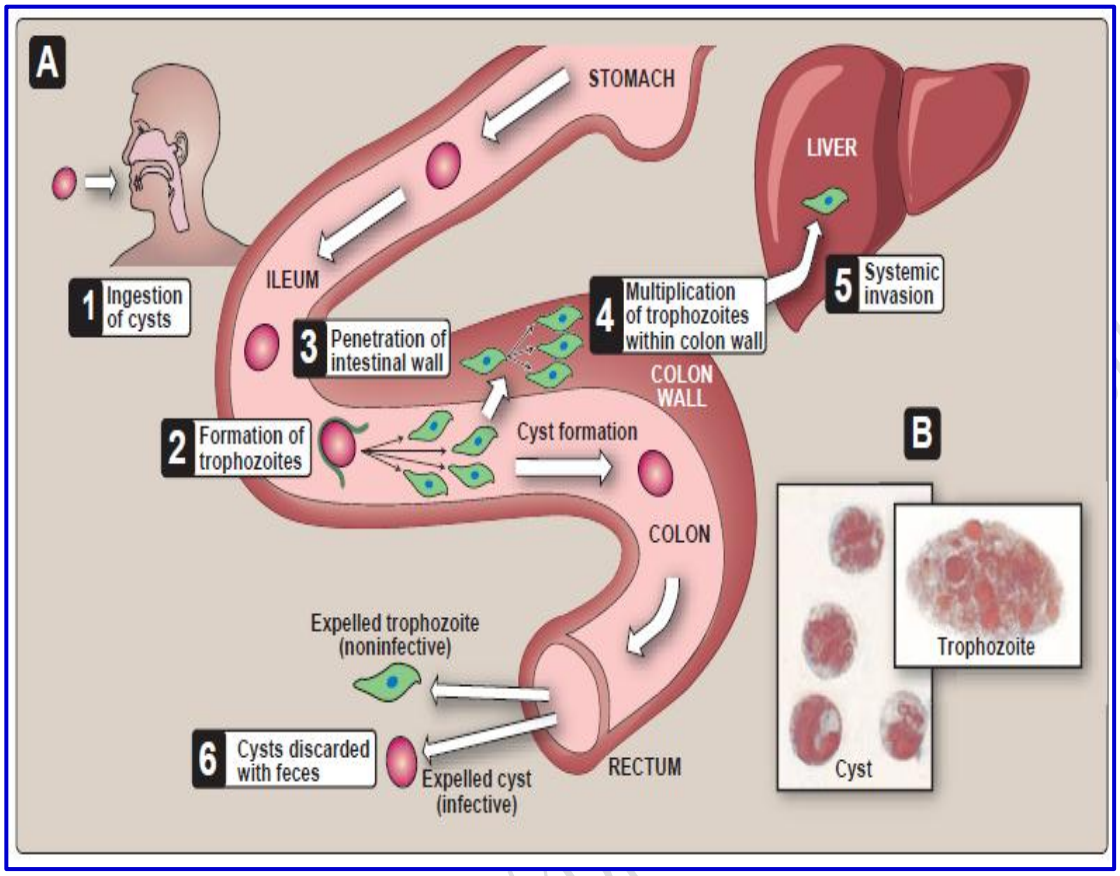


Figure: Life cycle of *Entamoeba histolytica*

☒ Entamoeba dispar:

Nonpathogenic, it is similar to **Entamoeba histolytica** in morphological characters but different in **biochemical**, **genetical,** and **immunological features**. **Entamoeba dispar** also infected human as **Entamoeba histolytica**.

❖ Laboratory diagnosis:

1) Direct (fecal smears) or (stained smears):

-**Trophozpite:** in liquid stool of patient with acute dysentery.

-**Cyst:** in formed or solid feces of chronic patient and carriers.

2) Concentration methods of stool.

3) Sigmoidoscope examination Biopsy.

4) serological tests: for antibodies to *E.histolytica*.

Giardia lamblia & *Trichomonas vaginalus*
(disease,life cycle, diagnosis,mode of transmission)

Pathogenic Flagellates

❖ **General properties:**

Flagellates are **unicellular** microorganisms. Their **locomotion** is by lashing a tail-like appendage called a **flagellum** or flagella and **reproduction** is by **simple binary** fission.

❖ **There are three groups of flagellates:**

1. Luminal or digestive or intestinal flagellates: *Giardia lamblia*
2. Genital flagellates: *Trichomonas vaginalis*
3. Hemoflagellates: Leishmania species.

I-Luminal flagellates (intestinal flagellates)

☒ **Giardia lamblia**

Disease: Giardiasis

Habitat: duodenum and jejunum (small intestine).

Geographical distribution: Giardia lamblia has a worldwide distribution.

Infective stage: cyst

❖ **Mode of infection or transmission:** fecal-oral. Ingestion food and water contaminated with cyst (Quadranucleated cyst).

❖ **Morphological features:** the life cycle consists of **two stages**, the **trophozoite** and **cyst**.

✓ **The trophozoite** is 10-12 µm long and 5-7µm wide anteriorly. It is bilaterally symmetrical, **pear-shaped** with **two nuclei** (large central karyosome), **four pairs of flagella**, **two axonemes**, and a **suction disc** with which it attaches to the intestinal wall.

✓ **<u>The oval cyst</u>** is 8-14µm long and 7-10µm wide, thick-walled with **four nucleus** and several **internal fibera**. Each cyst gives rise to **two trophozoites** during excystation in the intestinal tract.

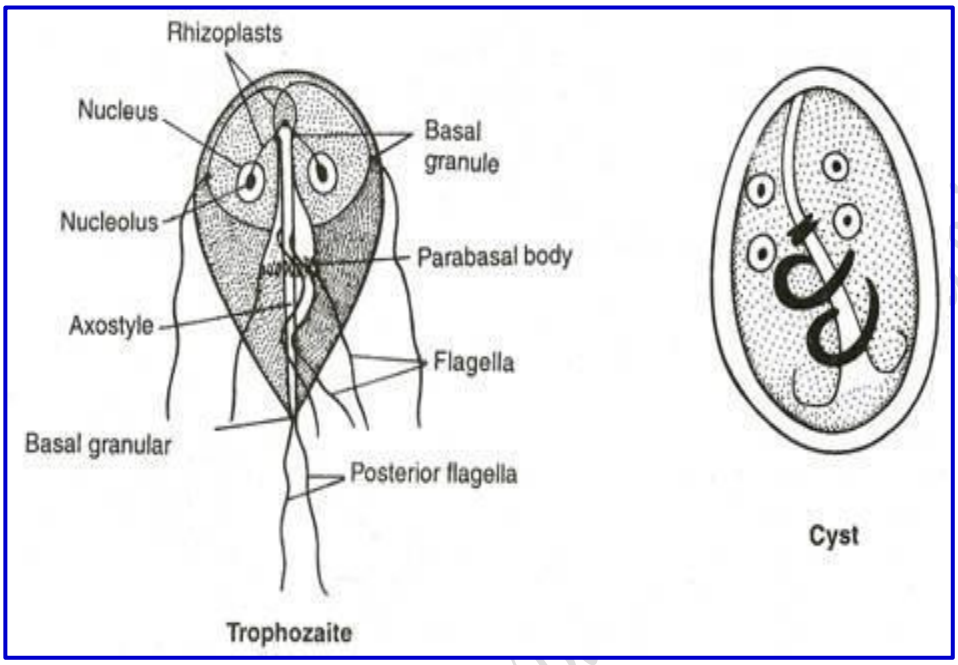


Figure: Trophozoite and cyst of *Giardia lambilia*

❖ **<u>Life cycle of *Giardia lambilia*:</u>**

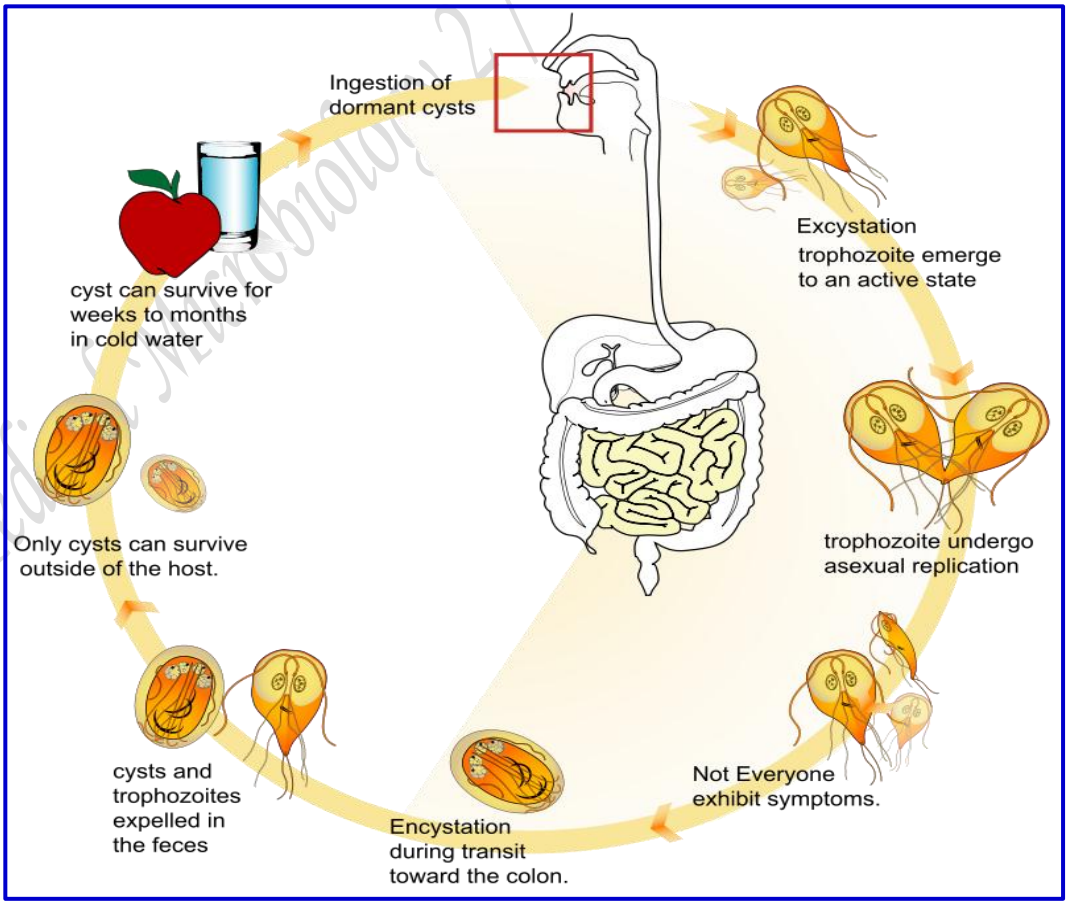


Figure: Life cycle of *Giardia lambilia*

❖ **Pathogenesis:** Infection with *G.lamblia* is initiated by ingestion of cysts. Gastric acid stimulates excystation, with the release of trophozoites in duodenum and jejunum. The trophozoites can attach to the intestinal villi by the ventral sucking discs without penetration of the mucosa lining, but they only feed on the mucous secretions. In symptomatic patients, however, mucosa-lining irritation may cause increased mucous secretion and dehydration. Symptomatic giardiasis ranges from mild diarrhea to severe malabsorption of lipid and vitamins.

❖ **Laboratory diagnosis:**

1-Examination of diarrhoeal stool- trophozoite or cyst, or both may be recovered in wet preparation.

In examinations of stool: Formed stool found cyst
Diarrhea stool found trophozoite

2- Serological test: To detect Giardia antigen in stool.

II- Genital flagellates

☒ **Trichomonas vaginalis**

Disease: Trichomoniasis

Habitat: The trophozoite is found in the urethra & vagina of women and the urethra & prostate gland of men.

Geographical distribution: This parasite has worldwide distribution**.**

Infective stage: trophozoite**.**

❖ **Mode of infection or transmission:** sexual intercourse is the primary mode of transmission. Occasionally, infections can be transmitted by fomites**.**

❖ **Morphological features:** It exists only as a trophozoite form, and measured 7-23µm long & 5-15µm wide. It is pear-shaped organism with a central nucleus and four anterior flagella; and undulating membrane extends about two-thirds of its length.

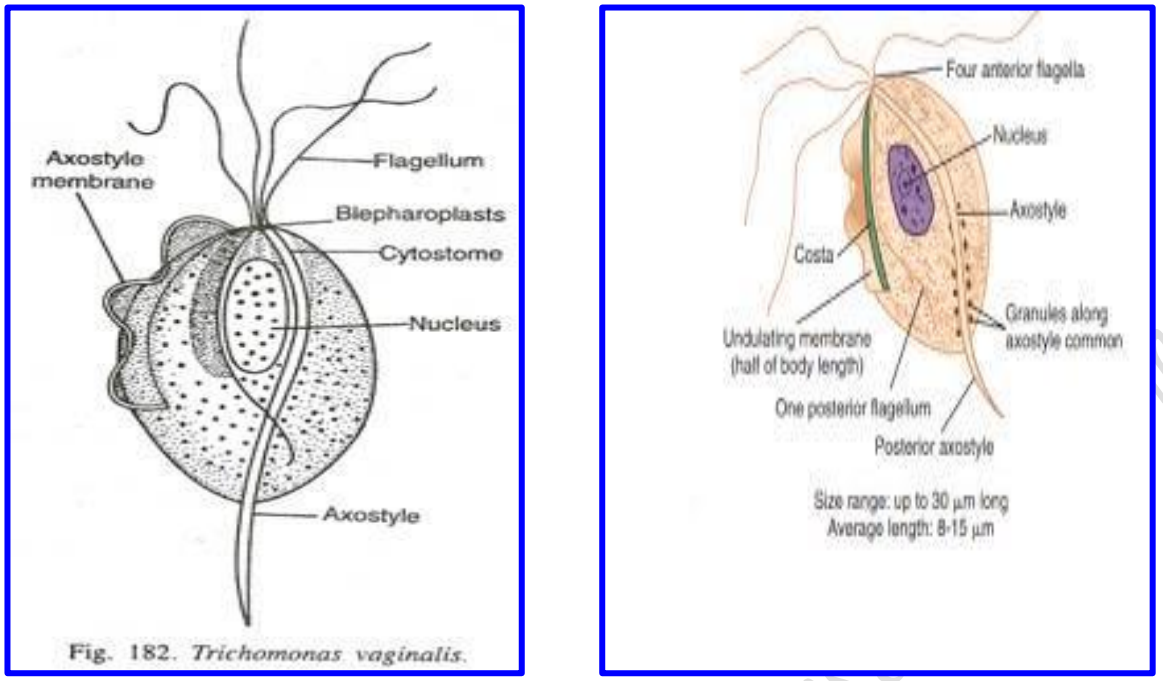


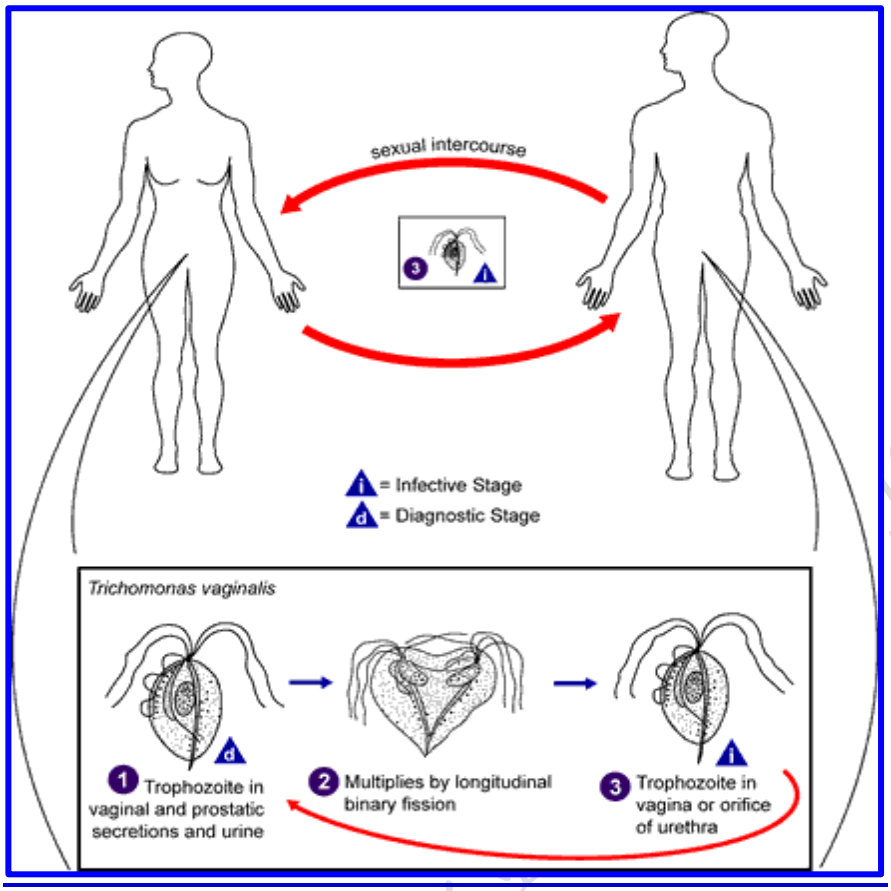
Figure: Trophozoite of *Trichomonas vaginalis*

❖ Life cycle of Trichomonas vaginalis

1)*Trichomonas vaginalis* resides in the female lower genital tract and the male urethra and prostate.

2) where it replicates by binary fission .

3) The parasite does not appear to have a cyst form, and does not survive well in the external environment. *Trichomonas vaginalis* is transmitted among humans, its only known host, primarily by sexual intercourse



Life cycle of *Trichomonas vaginalis*

❖ **Pathogenesis:** The trophozoite is found in the urethra & vagina of women and the urethra & prostate gland of men. After introduction by sexual intercourse, proliferation begins which results in inflammation & large numbers of trophozoite in the tissues and the secretions. The onset of symptoms such as vaginal or vulvar pruritus and discharge is often sudden and occurs during or after menstruation as a result of the increased vaginal acidity. The vaginal secretions are liquors, greenish or yellowish, sometimes frothy, and foul smelling. Infection in the male may be latent, with no symptoms, or may be present as self-limited, persistent, or recurring urethritis.

Laboratory diagnosis

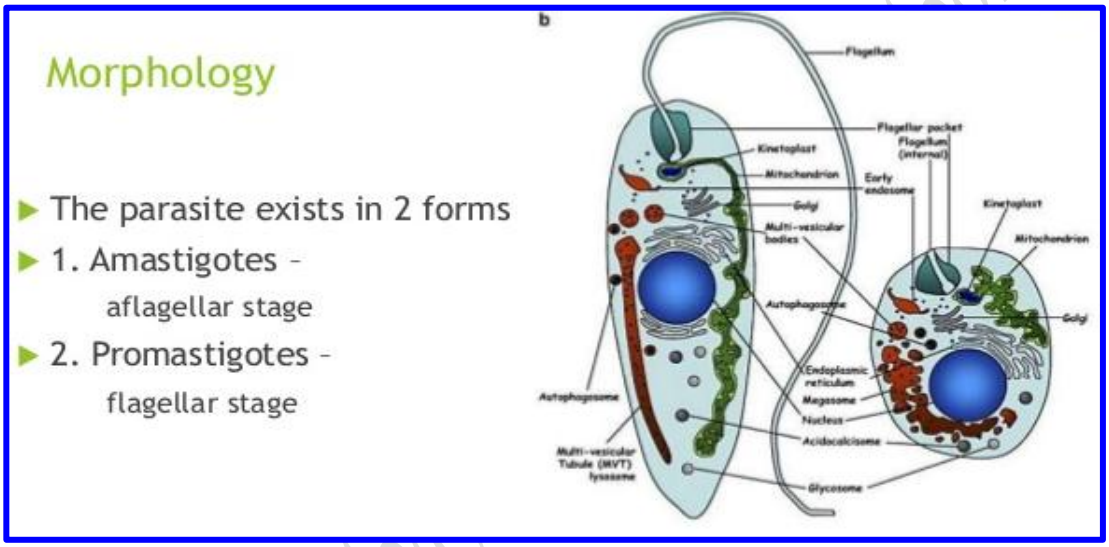
- ✓ **In females**, T. vaginalis may be found in urine sediment, wet preparations of vaginal secretions.
- ✓ **In males** it may be found in urine, wet preparations of prostatic or urethral secretions.

Leishmania spp **(disease, life cycle, diagnosis, mode of transmission)**

III- Hemoflagellates:

☒ Leishmania Species

The species of leishmania exist in two forms, **amastigote (aflagellar)** and **promastigote (flagellated)** in their life cycle. In the digestive tract of appropriate insects, the developmental cycle is also simple by **longitudinal fission** of promastigote forms.



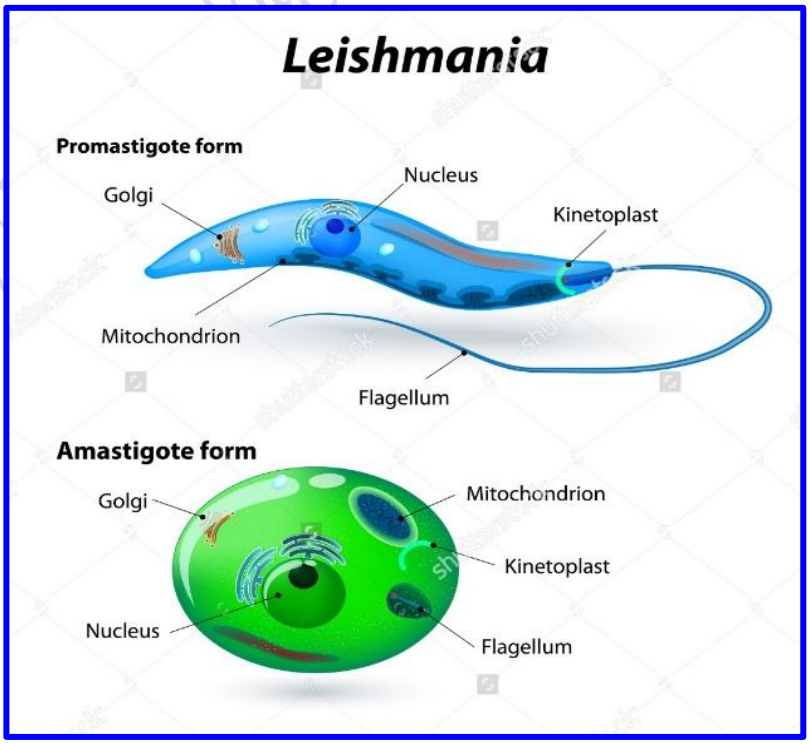


Figure: Promasitgote & amasigote forms of Leishmania

❖ **Morphological feature:**

The amastigote stage appears as an oval or rounded body, measuring about 2-3µm in length; and the promastigotes are 15-25µm lengths by 1.5-3.5µm breadths.

Infective stage for human (final host): Promastigote

Infective stage for insect (intermediate host): Amastigote

Comparison between Leishmania Species

Leishmania	***Leishmania donovani***	**Old World Cutaneous Leishmaniasis** *1-L.tropica minor* (dry cutaneous Leishmaniasis) *2-L.tropica major* (wet cutaneous leishmaniasis) *3-L.aethiopica* (cutaneous Leishmaniasis)	**New World Cutaneo Leishmaniasis** *1-Leishmania mexica* *(*Cutaneous leishmaniasis.) *2-Leishmania brazilien* (mucocutaneous or cutaneo Leishmaniasis)
Species Clinical disease	Veseral Leishmaniasis kala-azar (black sickness) or dumdum fever	Cutaneous leishmaniasis ***(Oriental sore)***	Mucocutaneous leishmaniasis
Habitat	Reticuloendothelial system (liver, spleen and bone marrow)	skin found in endothelial cells of the capillaries of the infected site (inside macrophages)	mucous membranes of t mouth & nose (insi macrophages)
Geographical distribution	In many parts of Asia, Africa and Southeast Asia, European, Near Eastern, and Africa	In many parts of Asia, Africa, Mediterranean Europe and the southern region of the former Soviet Union.	In south & Central America
Mode of infection	-Insect by sand fly or - by blood transfusion	-Insect by sand fly or - by blood transfusion	-Insect by sand fly or - by blood transfusion

❖ **Life cycle of Leishmania Species:** The life cycle of *Leishmania* involves two different hosts: a **female sand fly** and **mammals (including humans and dogs).** They are transmitted to human and animals **via bite by infected sand flies.**

✓ Amasigote that are ingested by sand flies (intermediate host) from a blood an infected mammal assume the Promasitgote form.

✓ Promasitgote multiply in the gut and eventually invade buccal cavity of the sand fly.

✓ blood meal on a human or animal inject the parasite into the skin.

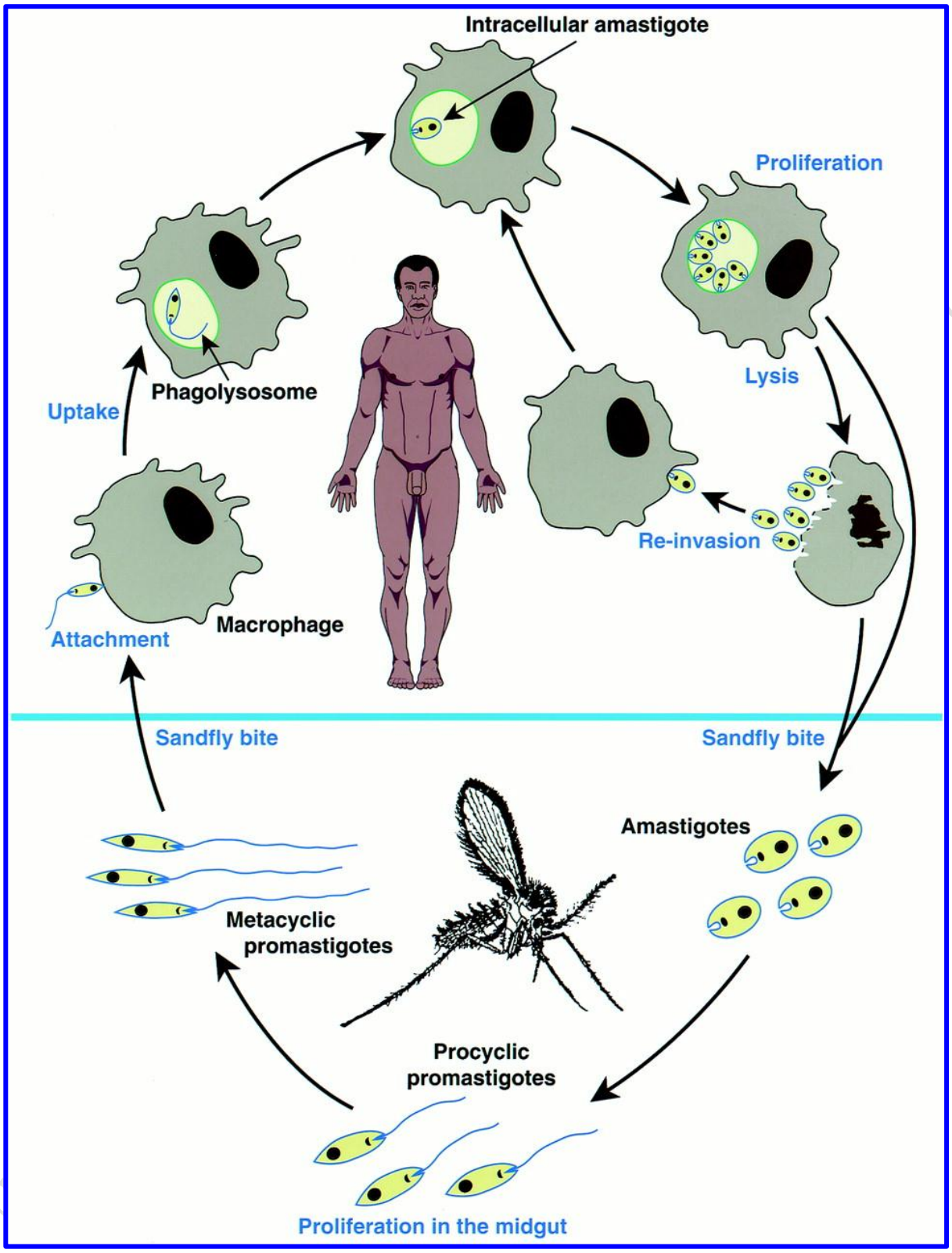


Figure: Life cycle of *Leishmania Species*

❖ Laboratory diagnosis:

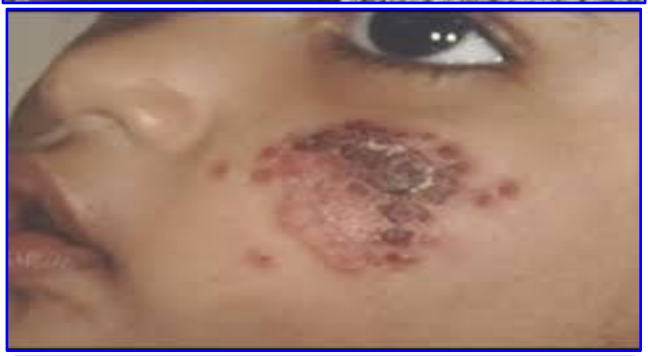
Veseral leishmaniasis	• Examination of tissue biopsy, spleen aspiration, bone marrow aspiration or lymph node aspiration in properly stained smear (e.g. Giemsa stain). • The amastigotes appear as intracellular & extra cellular L. donovan (LD) bodies. • Culture of blood, bone marrow, and other tissue often demonstrates the promastigote stage of the organisms. • Serologic testing is also available.
Cutaneous and Mucocutaneous leishmaniasis	• Demonstration of the amastigotes in properly stained smears from touch preparations of ulcer biopsy specimen. • Serological tests based on fluorescent antibody tests. • Leishman skin test in cutaneous species.

Some pictures on Leishmaniasis

Veseral Leishmaniasis
kala-azar

Veseral Leishmaniasis
kala-azar

Cutaneous leishmaniasis
(Oriental sore)



Cutaneous leishmaniasis
(Oriental sore)

Mucocutaneous leishmaniasis

Mucocutaneous leishmaniasis

Sand fly

Sporozoa Malaria & *Toxoplasma gondii* (disease, life cycle, lab diagnosis, mode of transmission)

☒ COCCIDIA (SPOROZOA)

Sporozoa is a class of coccidian. The life cycle of sporozoa is characterized by an alternation of generations, i.e. sexual **(gametogony)** and asexual **(schizogony)** reproduction. The locomotion of a mature organism is by **body flexion, gliding, or undulation of longitudinal ridges**. **Sporozoa** includes two classes:

1- ***Malaria*** *Spp.*

2- ***Toxoplasma gondii***

****

- **Malaria** is a class of coccidian. The genus Plasmodium that are the causes of malaria.

There are four species of malaria infecting humans, namely:

1-***Plasmodium falciparum:*** **malignant tertian malaria**

2-Plasmodium vivax: **benign tertian malaria**

3-Plasmodium ovale: **ovale malaria**

4-Plasmodium malariae: **quartain malaria**

Geographical distribution: region with warm climates.

Vector or final host: **female anopheles mosquitoes.**

Intermediate host: human

Infective stage for human: sporozoites.

Habitat: red blood cells & liver.

Mode of infection: 1-by female Anopheles mosquitoes bite

2- by blood transfusion

3- congenital transmission.

❖ Life cycle:

The life cycle of malaria is passed in two hosts (**alternation of hosts**) and has sexual (**gametogony**) and asexual (**schizogony**) (**alternation of generations**).

-Vertebrate host - man (intermediate host), where the **asexual cycle** takes place. The parasite multiplies by **schizogony** and there is formation of **male and female gametocytes** (**gametogony**).

-Invertebrate host - mosquito (definitive host), where the **sexual cycle** takes place. Union of male and female gametes ends in the formation of **sporozoites (sporogony).**

The life cycle of Malaria passes in four stages:

Three in man :-

1- **Pre-erythrocytic schizogony** **2- Erythrocytic schizogony** **3-Exo-Erythrocytic schizogony**

One in mosquito – 4- Sporogony

Introduction into humans - when an infective female Anopheles mosquito bites man, it inoculates saliva containing **sporozoites (infective stage).**

- **Life cycle in man** - sporozoites reach the blood stream and within **30 minutes** enter the **parenchymal cells of the liver**, initiating a cycle of **schizogony**. Multiplication occurs in tissue **schizonts**, to form thousands of tiny **merozoites**. Merozoites are then liberated on rupture of schizonts about **7th – 9th day** of the bites and enter into the blood stream. These merozoites either invade the RBC's or other parenchymal liver cells. In case of *P. falciparum* and possibly *P. malariae*, all merozoites invade RBC's without re-invading liver cells. However, for *P. vivax* and *P. ovale*, some merozoites invade RBC's and some re-invade liver cells initiating further ***Exo-erythrocytic*** schizogony, which is responsible for **relapses.** Some of the merozoites remain dormant (**hypnozoites**) becoming active later on.

  Erythrocytic schizogony (blood phase) is completed in 48 hrs in *P. vivax*, *P. ovale*, and *P. falciparum*, and 72 hrs in *P. malariae*. The merozoites reinvade fresh RBC's repeating the schizogonic cycles Erythrocytic merozoites do not reinvade the liver cells. These undergo no further development until taken by the mosquito.

- **Sporogony (life cycle in mosquito):**

  When a female anopheles mosquito bites an infected person, it takes up these gametocytes with the blood meal . The gametocytes, then, mature and

become **microgametes** (male) and **macrogametes** (female) during a process known as **gametogenesis.** The time needed for the gametocytes to mature differs for each plasmodium species: **3- 4 days for *P. vivax* and *P. ovale*, 6- 8 days for *P. malariae* and 8- 10 days for *P. falciparum*.**

In the mosquito gut, the microgamete nucleus divides three times producing eight nuclei; each nucleus fertilizes a macrogamete forming a **zygote**. The zygote, after the fusion of nuclei and the fertilization, becomes the so-called **ookinete**. The ookinete, then, penetrates the midgut wall of the mosquito, where it encysts into a formation called **oocyst**. Inside the oocyst, the ookinete nucleus divides to produce thousands of **sporozoites** (**sporogony**). Sporogony lasts **8- 15 days.**

Thousands of sporozoites develop inside the oocysts. Oocysts rupture and sporozoites are liberated in the body cavity and migrate everywhere particularly to the salivary glands.

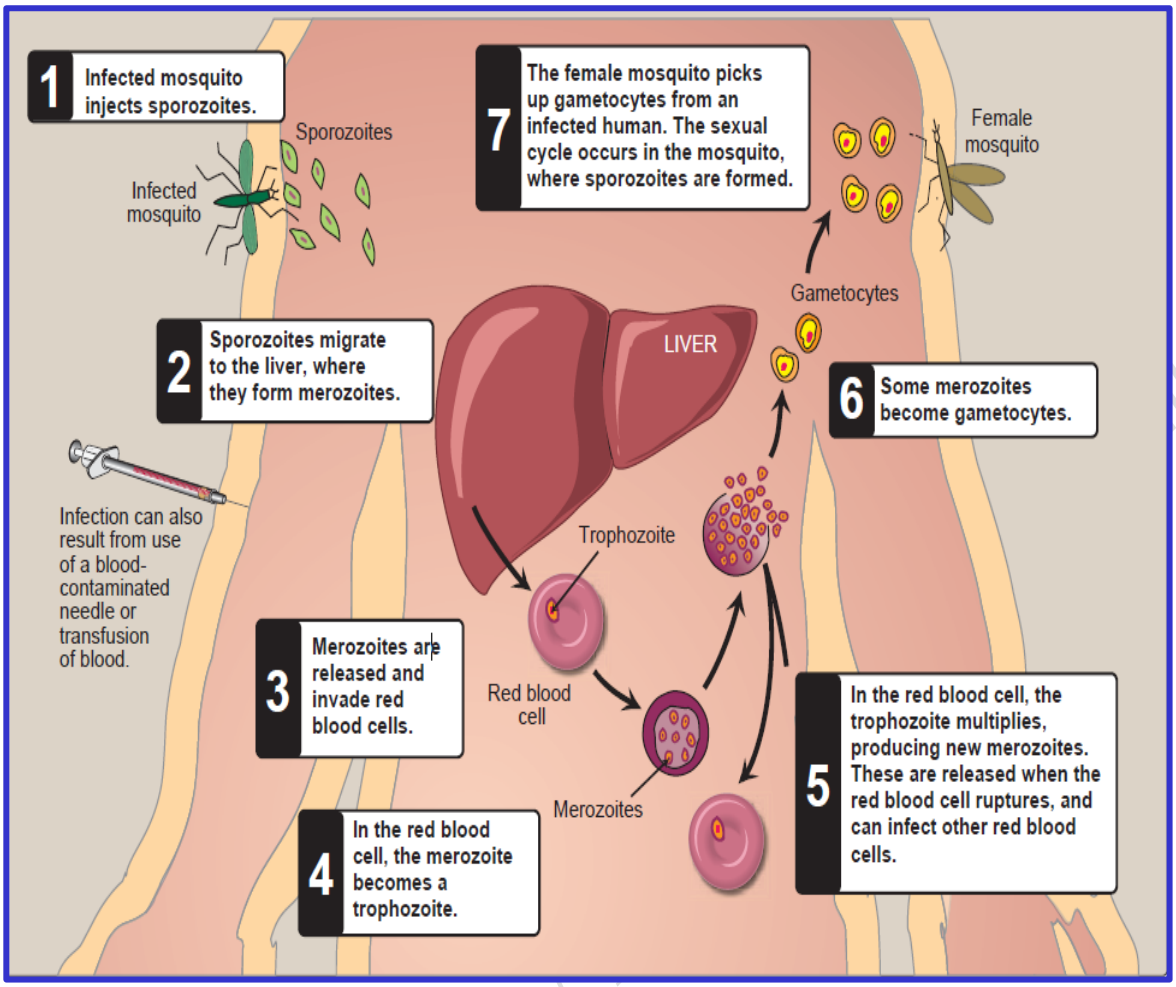


Figure: life cycle of Malaria

- **Pathogenesis:** disease of malaria is caused by the asexual Erythrocytic cycle. The rupture of infected of RBCs to completion of **schizogony occurs every 48hr with *P.vivax* and *P.ovale*, 36 to 48 hours with *P. falciparum* and every 72hr with *P.malariae*.** The patient experiences vague flu-like symptoms, such as headache, muscle pains, photophobia, anorexia, nausea and vomiting. As the infection progresses, increased numbers of rupturing erythrocytes liberate merozoites as well as toxic cellular debris and hemoglobin in to circulation. In combination, these substances produce the typical pattern chills, fever and malarial rigors. These paroxysms usually reappear periodically (**generally every 48 hours**) as the cycle of infection, replication, and cell lyses progresses. The paroxysms may remain relatively mild or may progress to severe attacks, with hours of **sweating, chills, shaking persistently, and high temperatures.**

❖ Frequency of malaria relapses:

- ☒ *P. falciparum*: occur with few weeks or months and die out usually within a year.
- ☒ *P.vivax*:occur mostly in the first year and die within 3 years of the original infection.
- ☒ *P.malariae*: persist for several years.
- ☒ *P.ovale:* rarely occur.

❖ Laboratory diagnosis

1- Microscopic examination of thick and thin films of blood is the method of choice for confirming the clinical diagnosis of malaria and identifying the specific species responsible for disease.

- ☒ Malaria parasites in thick and thin blood films are best stained at pH 7.1 – 7.2 using a Romanowsky stain (contains azure dyes and eosin).
- ☒ The thick film is a concentration method that may be used to detect the presence of organisms. The thin film is most useful for establishing species identification.

2- Serologic procedures are available but they are used primarily for epidemiological surveys or for screening blood donors.

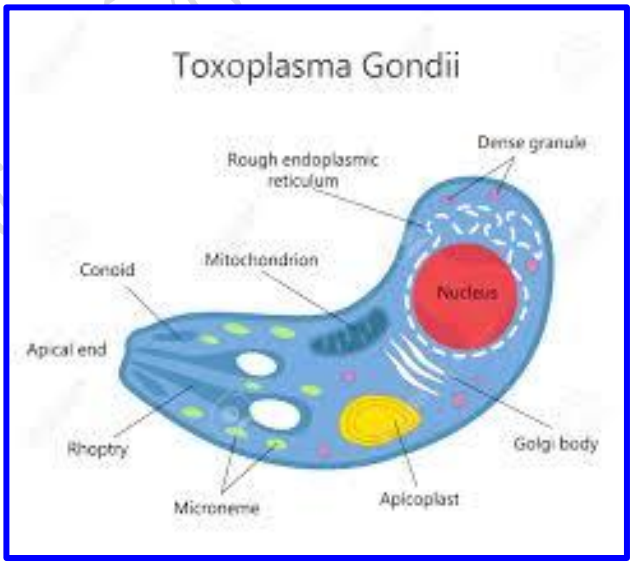
II- *Toxoplasma gondii:* another Coccidian parasites
(disease, life cycle, lab diagnosis, mode of transmission)

- **Disease:** toxoplasmosis
- **Definitive hosts:** domestic cat and other felines.
- **Intermediate hosts:** Humans and other mammals (ex: sheep, pig)
- **Habitat:** small intestine, brain, lungs, liver, Bone marrow, and eyes.
- **Geographical distribution:** This parasite has worldwide distribution.
- **Infective stage:** mature Oocyste.

Mode of infection or transmission:

1- Acquired by ingestion of contaminated food and water with oocyste.
2- Transplacental transmission from an infected mother to the fetus.
3- Blood transfusion or tissue transplantation.
4- Ingestion of oocyste in under cooked infected meat.
5- Earthworm and arthropods may serve as a mechanical vector of the oocyste.

Morphology of toxoplasma: toxoplasma are small, **crescent in shape** measuring 2-3x4-7µ with Central nucleus, usually with one end rounded and the other end pointed.



Toxoplasma gondii

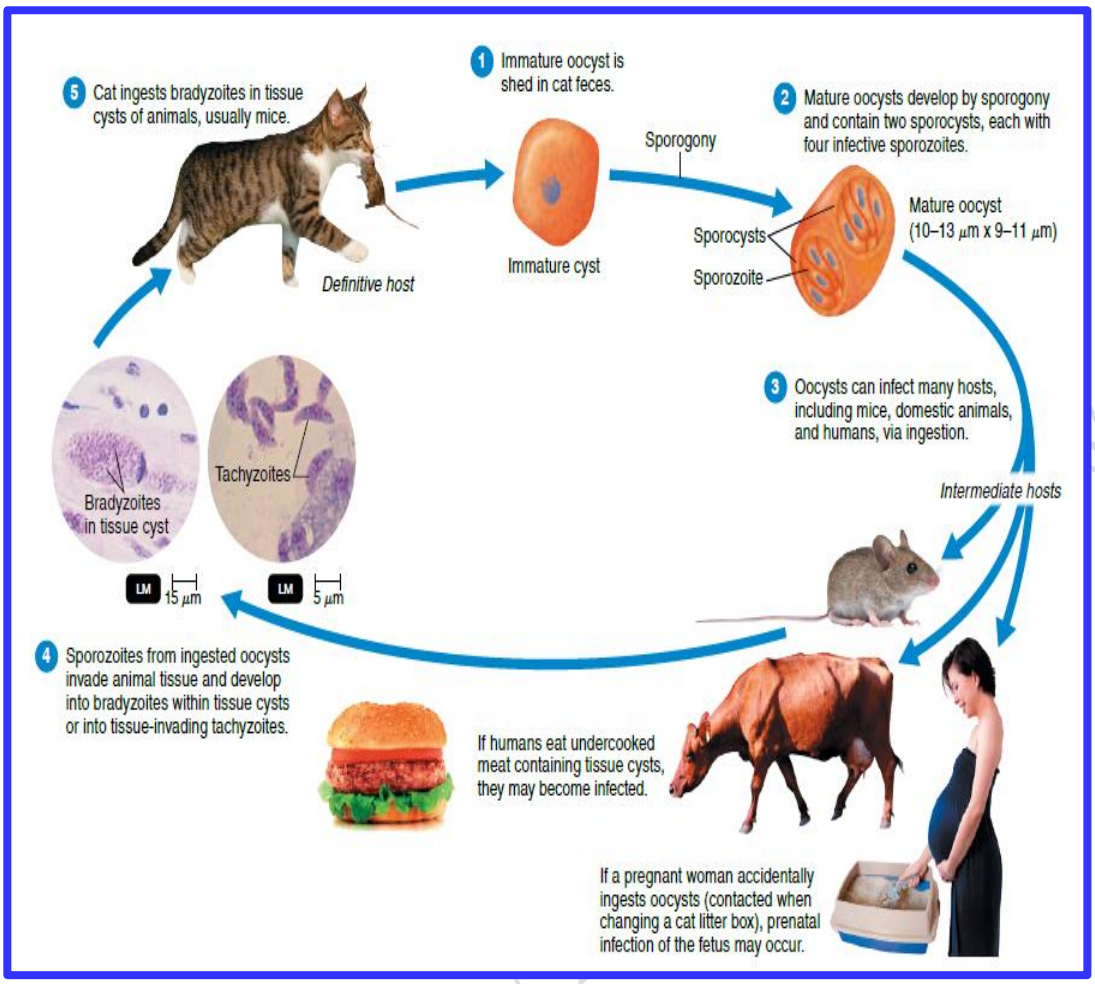
Important features: ***Toxoplasma gondii*** occurs in three forms- **trophozoite**, **tissue cyst** and **oocyst**. **The trophozoite and tissue cyst represent stages** in **asexual multiplication (schizogony)**, while **the oocyst** is formed by **sexual reproduction**

(gametogony or sporogony). All three forms occur in **final host** while the trophozoite and cyst tissue found in **intermediate host.**

- **Clinical feature:** Toxoplasmosis can be asymptomatic (no clinical symptoms) or can have more severe consequences. After infection of the intestinal epithelium, the organisms spread to other organs, especially the brain, lungs, liver, and eyes. Most primary infections in immunocompetent adults are asymptomatic. Congenital infection can result in abortion, stillbirth, or neonatal disease with encephalitis, chorioretinitis and hepatosplenomegaly. Fever, jaundice, and intracranial calcifications are also seen.

- **Life cycle:**

  Life cycle of *T. gondii*. Sexual and asexual reproduction of Toxoplasma take place in felids and warm-blooded intermediate hosts, respectively. Oocysts are formed by the fusion of micro-and macrogametes in the gut epithelium of cats, followed by shedding to the environment. Oocyst sporulation occurs under convenient climate conditions. The uptake of sporulated oocyst by intermediate host via food-or waterborne transmission initiates asexual reproduction. Following ingestion, sporozoites are released from oocyst, penetrate to the epithelial cells of small intestine and differentiate into tachyzoites causing acute infection. Short after, tachyzoites are disseminated to the whole body and turn into bradyzoite-containing cysts leading chronic infection mostly in neural and muscular tissues. If a cat (or a human) eats the intermediate host, the tissue cysts get ingested and the parasite activates in the small intestine.



Life cycle of *T. gondii*

Laboratory diagnosis:

1-Serological test:

- Sabin Feldman dye test - Immunofluroesecent Antibody test
- Idirect haemagglutination

2-Microscopic examination:

-identification of toxoplasma by using Giemsa stained preparation from Bone marrow, liver or spleen aspiration or from body fluids.

3-Blood and cerebrospinal fluids findings in toxoplasmosis.

Introduction of Helminthes

Tape worms :Taenia saginata & Taenia solium

Medical Helminthology

- **Medical helminthology:** is concerned with the study of helminthes or worms.
- **Helminthes** are trophoblastic metazoa (multi-cellular organisms).

The helminthes are classified into three major groups. These are:

1- Cestodes (Tape worms)

2- Trematodes (Flukes)

3- Nematodes (Round worms)

The Trematodes and Cestodes are groups of flat worms.

Differences between Cestodes, Trematodes, and Nematodes

Characters	Cestodes	Trematodes	Nematodes
Shape	Tape-like; segmented	Leaf-like; unsegmented	Enlongated, cylindrical; unsegmented
Sexes	Not separated, I.e., hermaphrodite (monoecious)	Not separate (monoecious) except schistosomes which are diecious	Separated (diecious)
Head	Suckers, often with hooks	Suckers, without hooks	No Suckers, no hooks, well developed buccal capsule in some species
Alimentary Canal	absent	Present but incomplete; no anus	Present and complete; anus present
Body Cavity	absent	absent	present

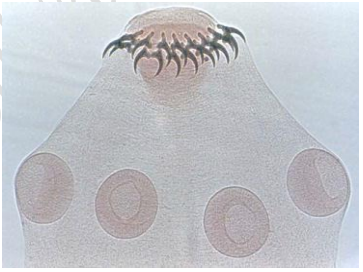
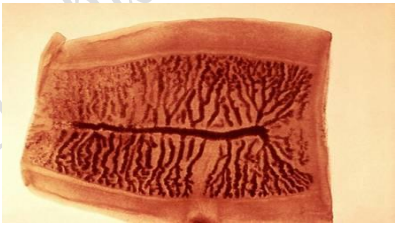
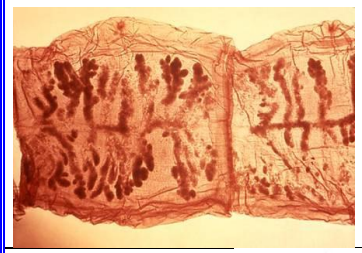
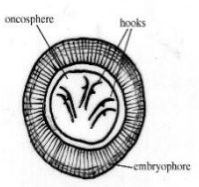
CESTODES (TAPEWORMS)

- **Features of Tapeworm:**

1- Tapeworms are hermaphroditic.
2- They consist of an anterior attachment organ or scolex and a chain
3- Segments (proglottids) also called strobilla.
4- It has suckers
5- It has rosetellum

6- Have no body cavity
7- Have no alimentary canal

Taenia Tapeworm: comparison between taenia species

Characters	*Taenia saginata*	*Taenia solium*
Geographical Distribution	worldwide	Europe, central America, Ethiopia
Common Name	Beef tapeworm	Pork tapeworm
Disease	Taeniasis	Taeniasis
Habitat	Intestinal tract	Intestinal tract
Intermediate Host	beef	pigs
Final Host	man	Man
Infective Stage	cysticercus bovis larvae	cysticercus cellulosae larvae
Length Of Worm	3- 10 meters	2-5 meters
Number Of Segments	1000-2000	1000
Head	Rounded 2mm in diameter, 4 suckers, without Hooklets 	Globular, 1mm in diameter, 4 suckers , with Hooklets 
Gravid Segment	2 wide, 20 mm long	8 mm wide, 13 mm long
Uterus Branch	15-30 	5-10 
Egg	Rounded, 30-35 µm in diameter hexacanth embryo surrounded with thick striated wall	 The same

Mode of transmission:

- Humans become infected with taenia tapeworm by:

- ✓ ingesting inadequately **cooked beef with cysticercus bovis larvae**, containing an invaginated protoscolex (***Taenia saginata*** *)*.
- ✓ ingesting inadequately **cooked pork with cysticercus cellulosae larvae**, containing an invaginated protoscolex (***Taenia solium***).

Life cycle of taeniasis:

Life cycle of *T.saginata* and *T. solium*-The worm passes its life cycle in **two hosts**:

1. **The definitive host**: man which harbours the adult worm.
2. **The intermediate host:** Cattle or pigs which harbours the larval stage.

• The adult worm lives in the small intestine of man.

• The eggs or gravid segments are passed out with the faeces of human.

• The animals swallow these eggs during grazing in the field.

• On reaching the alimentary canal of the intermediate host, the radially striated walls of the eggs rupture and oncosheres are liberated.

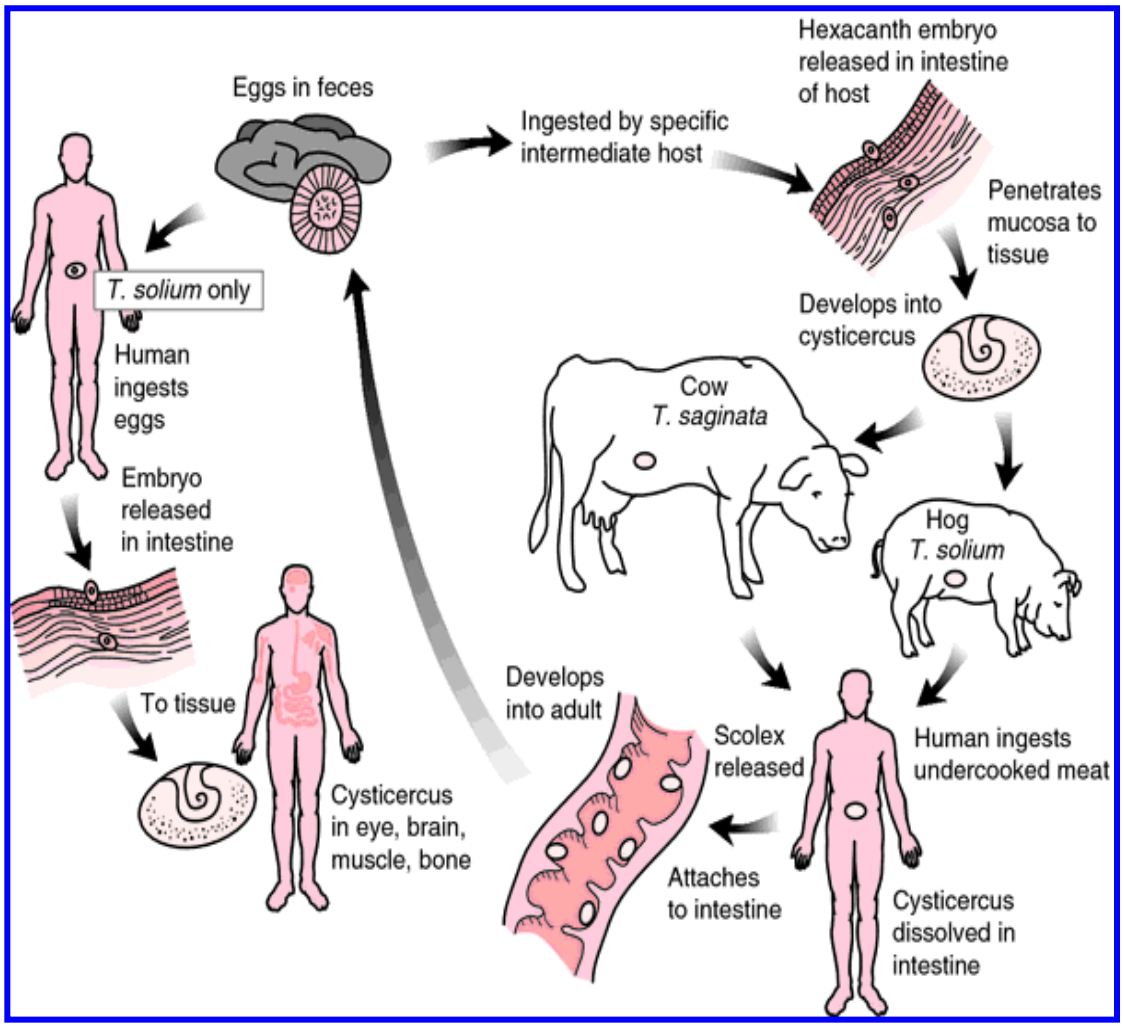
•These penetrate the gut wall with the aid of their hooks and gain entrance into the portal vessels or mesenteric lymphatics then to the systemic circulation.

• The naked oncospheres are filtered out from the circulating blood into the muscular tissues.

• Ultimately they settle down in the muscular tissue and undergoes further development.

Clinical Presentation:

Taenia saginata taeniasis produces only mild abdominal symptoms. The most striking feature consists of the passage of proglottids. Occasionally, appendicitis or cholangitis can result from migrating proglottids. *Taenia solium* taeniasis is less frequently symptomatic than*Taenia saginata* taeniasis. The main symptom is often the passage of proglottids. Infected persons may complain of epigastric pain, abdominal discomfort, diarrhea, weight loss, hunger sensation, vomiting.



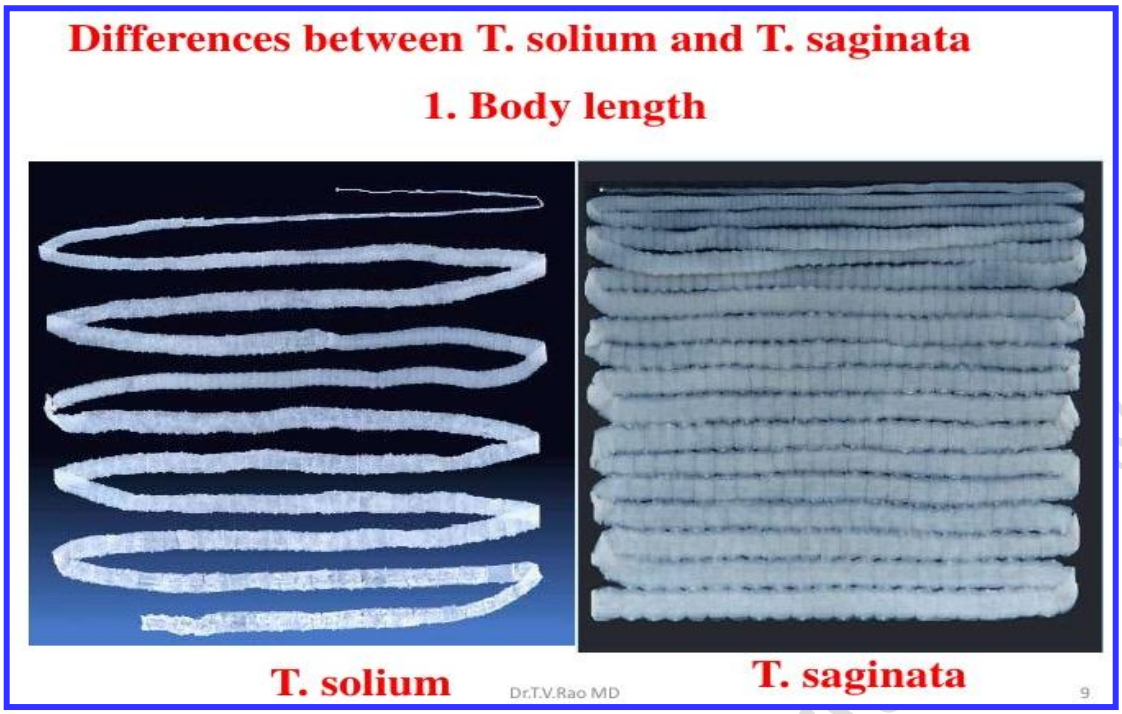
Life cycle of *T.saginata* and *T. solium*

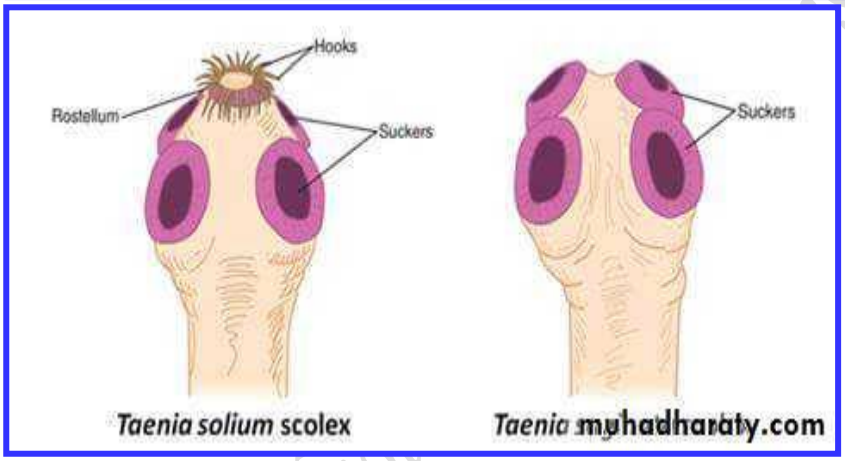
Laboratory Diagnosis:

Diagnosis of intestinal taeniasis can be made by recovery of the characteristic ova in the stool. However, the ova of *T. solium* and *T. saginata* are identical and diagnosis is made by the recovery of the segments or scolex.

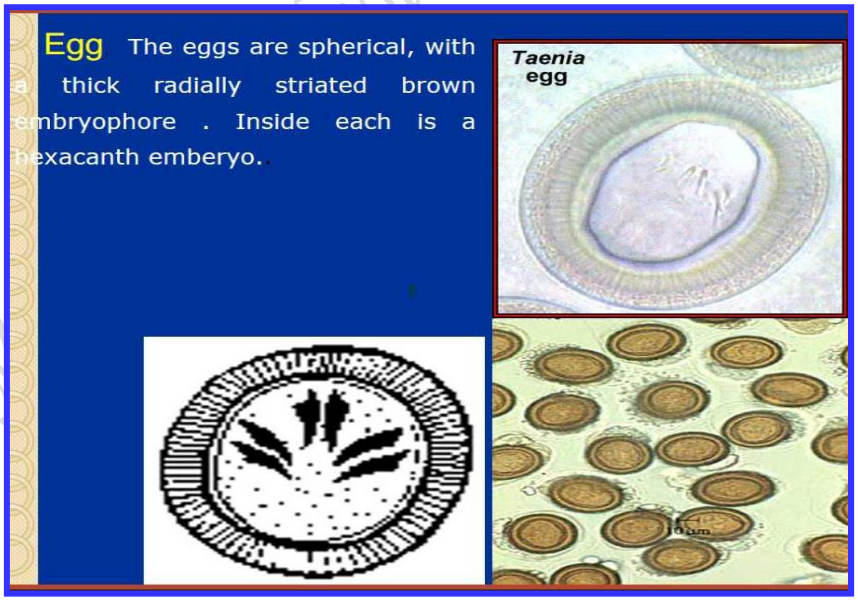
T. saginata

T. solium





Head of Taenia Spp



Taenia eggs

Another tape worm

Echinococcus granulosis & Hymenolipes nana

- **Echinococcus granulosis**
  - **Common name:** dog tape worm
  - **Disease:** Echinococcosis or hydatid cyst
  - **Geographical distribution:** warm climate countries
  - **Habitat:** small intestine
  - **Infective stage:** Eggs
  - **Final host:** dog and other carnivore
  - **Intermediate host:** man, cattle, sheep
- **Mode of infection:** Ingestion of eggs by the following ways:

  i) Ingestion of water or vegetables polluted by infected dog feces.

  ii) Handling or caressing infected dogs where the hairs are usually contaminated with eggs.
- **Morphology:** The adult worm measures 3-6 mm in length (up to 1 cm). It has **scolex, neck** and **strobilla**. **Adult worms** live in small intestine of definitive host (dog). human is an intermediate host carrying the **hydatid cyst (larva).**

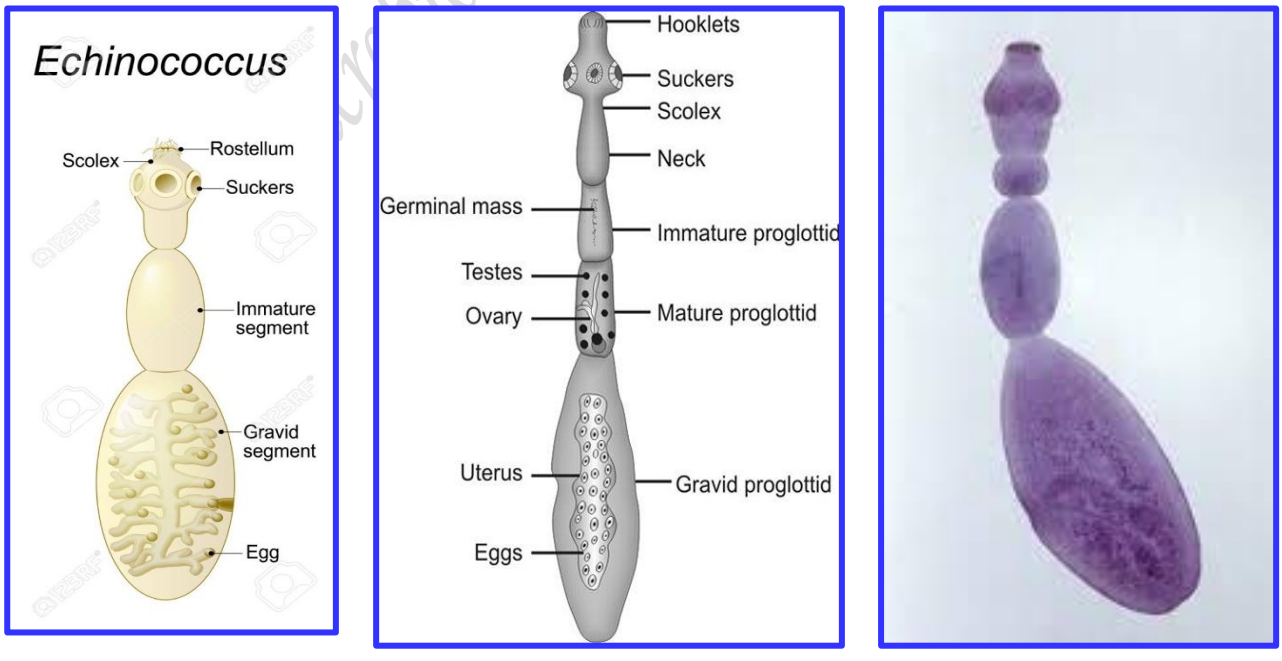


Figure: Adult worm of Echinococcus granulosis

Life cycle:

Oncosphere hatch in duodenum or small intestine into embryos (oncosphere) which:

1) Penetrate wall and then Enter to the portal veins
2) Migrate via portal blood supply to organs: eg: lungs, liver, brain etc., thus, causing extra intestinal infections. In these organs, larvae develop into hydatid cysts. The cysts may be large, filled with clear fluid and contain characteristic protoscolices (immature forms of the head of the parasite).
3) These mature into developed scolices, which are infective for dogs.

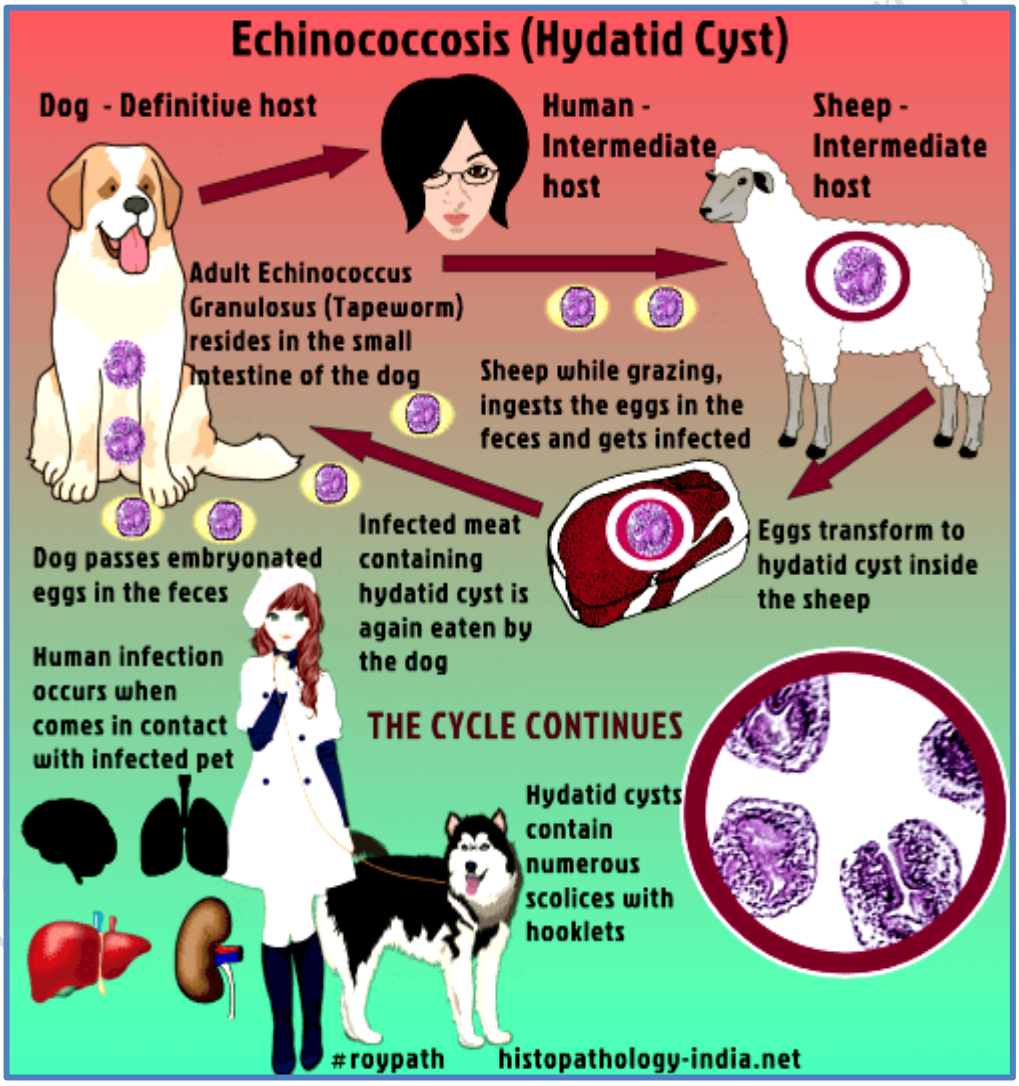


Figure: Life cycle of *Echinococcus granulosus*

Clinical features:

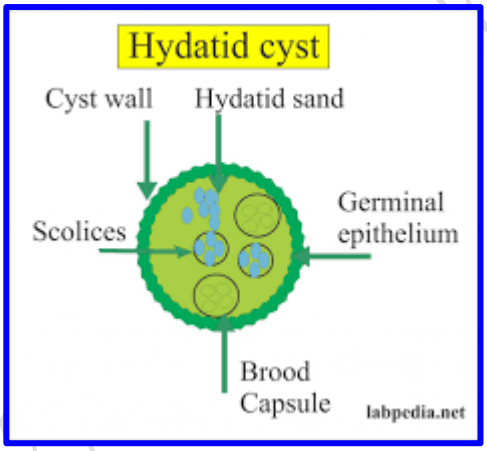
Asymptomatic infection is common, but in symptomatic patients It may cause:

- ✓ Cough - with hemoptysis in lung hydatid disease.
- ✓ Hepatomegaly - with abdominal pain and discomfort

- ✓ Pressure -from expanding cyst
- ✓ Rupture of cyst - severe allergic reaction - anaphylaxis.

Laboratory Diagnosis:

1) Serology test: indirect heamagglutination test, complement fixation test, latex agglutination.
2) Casoni´s test: it is skin test made up by injection 0.2ml of filtered, sterile, diluted fluid of hydatid cyst intradermal. Positive results appears by characteristic reading of skin within 10-20 minutes of injection.



Hydatid cyst

Eggs of *Echinococcus granulosus*

Another tape worm *Hymenolipes nana*

Hymenolepis nana

- **Common name:** Dwarf Tapeworm
- **Disease:** Hymenolepiasis
- **Geographical distribution:** warm climate countries
- **Habitat:** small intestine
- **Infective stage:** eggs
- **Final host:** man

Mode of infection: Infection takes place by:

1. Ingestion of egg with contaminated raw vegetables.
2. Direct infection from a patient
3. Auto infection: the eggs of H. nana are infective as soon as they are passed with feces by the patient.

Morphology: **Adult worm** measures 1-3 cm in length. It is made up of head (scolex), neck and segmented body. The head carries four suckers and a rostellum armed with one row of hooks. The segments of the body are divided into **mature** and **gravid segments**. In the mature segment, there are three testes in the middle. **The egg,** is rounded, about 40 microns in diameter. It contains a six- hooked oncosphere within a rigid membrane (the embryosphere). This embryosphere has two polar thickening or knobs from which project 4-8 long, thin filaments called polar filaments.

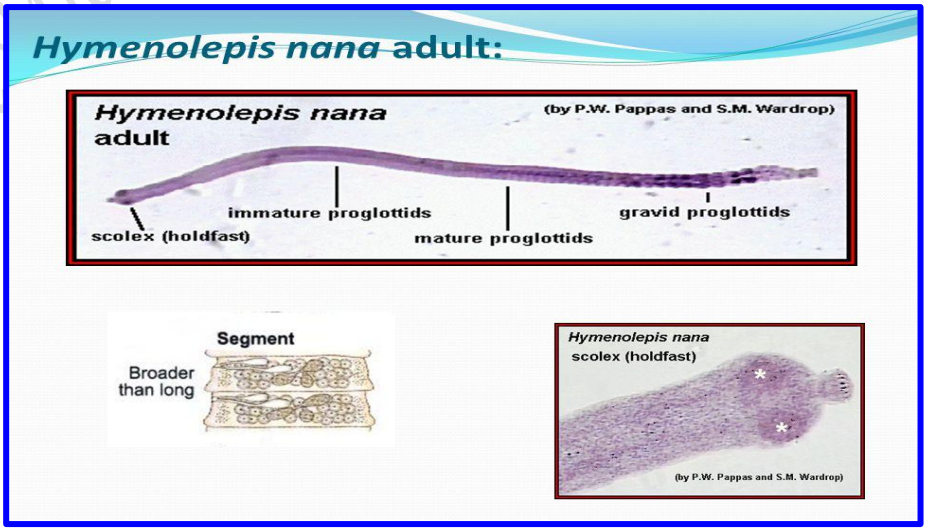


Figure: ***Hymenolepis nana***

Pathogenicity: Light infections produce no symptoms. In fairly heavy infections, children may show lack of appetite, abdominal pain and diarrhea.

Life Cycle:

The lifecycle of *H. nana* does not require an intermediate host, complete development occurring within the villi of a single host, resulting in a 'direct' life cycle.

The eggs that are released from mature proglottids in the upper ileum are usually passed out in the feces. If swallowed by another human they develop into hexacanth oncospheres and burrow into the villi of the small intestine. This is where they develop into tailless cysticercoids and then migrate towards the ileum and attach to commence the formation of proglottids.

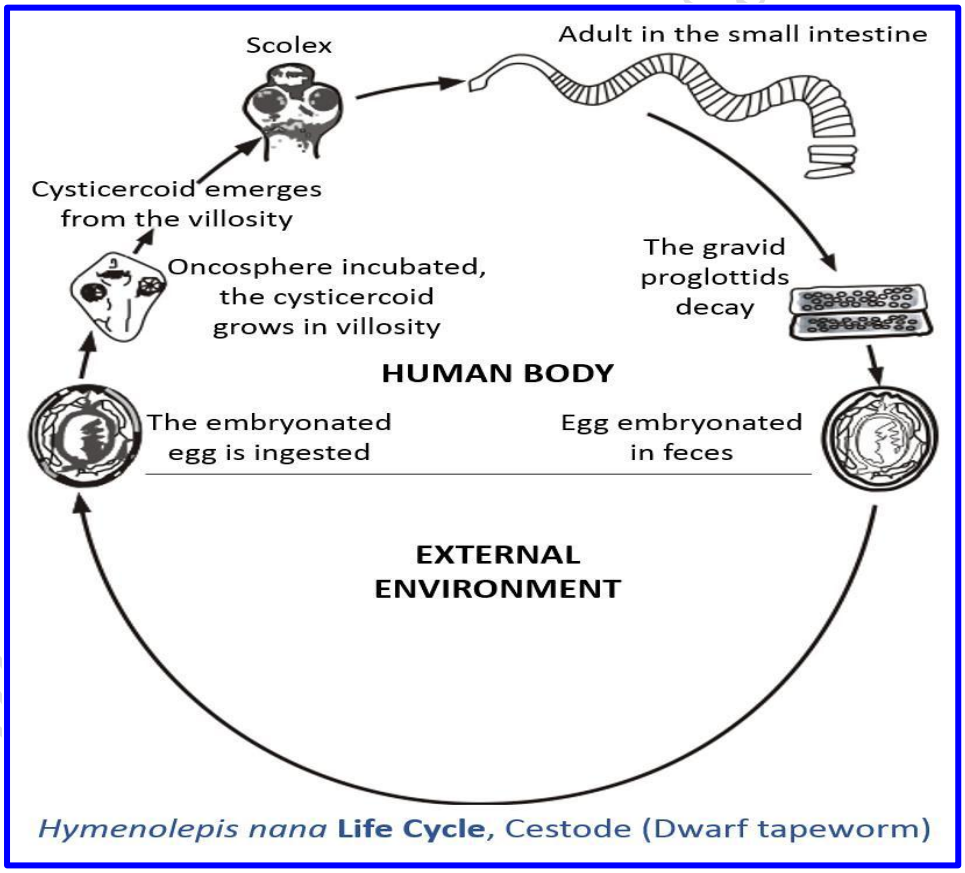


Figure: Life cycle of *Hymenolepis nana*

Laboratory diagnosis:

Diagnosis is based on recovery and identification of the characteristic ova in feces. Adult worms and proglottids are rarely seen in stool samples.

Schistosomiasis (Trematodes fluke worm) & Ascariasis (Intestinal Nematodes, round worms)

Trematodes (Blood Flukes)

These are flukes that reside mainly in the blood vessels of various organs and the **schistosomes** are the **commonest flukes in many countries.**

Schistosomiasis (Bilharziasis):

The schistosomes cause intestinal, hepatosplenic, pulmonary, urogenital, cerebral and other forms of schistosomiasis. Schistosome is the **only fluke with separate sexes.** The **female worm lies in the gynecophoral canal of the male**.

There are three medically important species:

1. ***Schistosoma mansoni*:** causes intestinal schistosomiasis.
2. ***Schistosoma haematobium*:** causes vesical (urinary) schistosomiasis.
3. ***Schistosoma japonicum*:** causes intestinal schistosomiasis.

- **Infective Stage:** Cercariae
- **Disease:** Bilharziasis
- **Final Host:** Man
- **Intermediate Host:** Snail.
- **Common Name:** Blood Flukes worm

Mode of Transmission:

Schistosome infection in humans occurs by contact with **fresh water** contaminated by **cercariae**, the free-swimming, infectious stage of schistosomes that are released by the **intermediate host snail** and that **penetrate the intact human skin.**

Morphology of Schistosomes:

The Schistosomes are long and cylindrical in shape. It is well adapted to life in blood vessels of their hosts, the male fluke is folded to form groove called (gynecophoral canal) in which the female fluke lies inside it. The female is long, thin and dark appearance in color compared with male. The numbers of eggs varies according to the species.

Comparison between *Schistosoma* species

Characters	*Schistosoma haematobium*	*Schistosoma mansoni*	*Schistosoma japonicum*
Disease	urinary schistosomiasis bilharziasis	intestinal schistosomiasis bilharziasis	intestinal schistosomiasis bilharziasis
Habitat	Bladder and pelvic plexuses veins	Veins of small and large intestine and hepatic veins	Both superior and anterior mesenteric veins
Infective Stage	Cercariae (daily production 400)	Cercariae (daily production 1000-3000)	Cercariae (daily production 15-150)
Morphology of Eggs	Egg has terminal spine	Egg has lateral spine	Egg has lateral knop
Size of Adult Worm	10-14 x 0.8 mm	6-12 x 2 mm	12-20 x 0.8 mm
Final Host	human	human	human
Intermediate Host	Snail (Bulinus)	Snail (Biomphalaria)	Snail (Oncomilania)

Life Cycle of Schistosomes:

Adult worms reside in pairs: the female lying in the gynecophoral canal of the male. After fertilization, eggs are passed into the venules. A larval form – the miracidium - develops within the egg. Its lytic enzymes and the contraction of the venule rupture the wall of the venule liberating the egg into the perivascular tissues of the intestine (*S. mansoni*) , or superior and anterior mesenteric veins (*S. japonicum*) , or urinary bladder (*S. haematobium*). The eggs pass into the lumens and organs and are evacuated in the feces (*S. mansoni*) and (*S. japonicum*) or the urine (*S. haematobium*). On contact with fresh water the miracidia hatch from the eggs and swim about until they find the appropriate snail, which they penetrate. After two generations of sporocyst development and multiplication within the snail, the fork-tailed cercariae emerge. Infection to man takes place during bathing or swimming. The cercariae penetrate the skin, are carried into the systemic circulation and pass through to the portal vessels.

Symptoms and complications: Patients infected with *S. haematobium* suffer from terminal haematuria and painful micturition. There is inflammation of the urinary bladder (cystitis), and enlargement of spleen and liver, *S. haematobium* causes

squamous cell carcinoma in the bladder.Patients infected with *S. mansoni* suffer from cercarial dermatitis (swimmers itch) and dysentery (mucus and blood in stool) as well as enlargements of the spleen and liver.

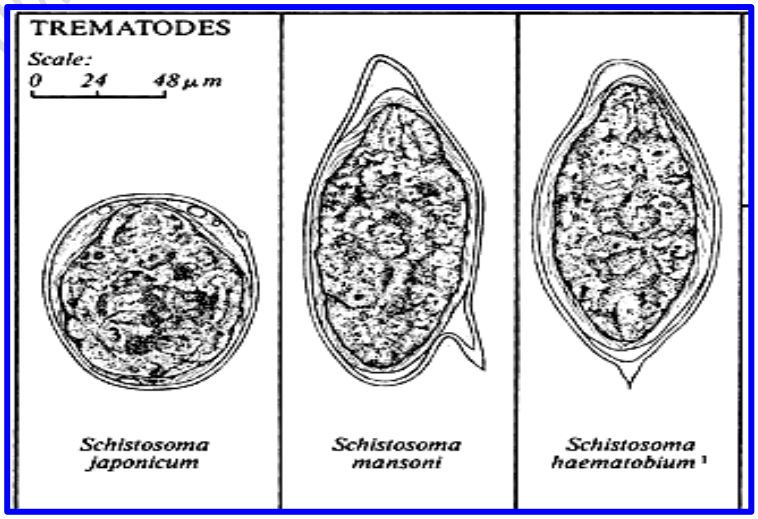
- **Anemia in Schistosomes:** the mature flukes ingest red blood cells from their host. The digested blood is excreted by the flukes and found as Schistosomal pigment in the reticuloendothelial cells of the host. Loss of RBCs also occurs as the eggs penetrate through the blood vessels into the bladder and wall of intestine.

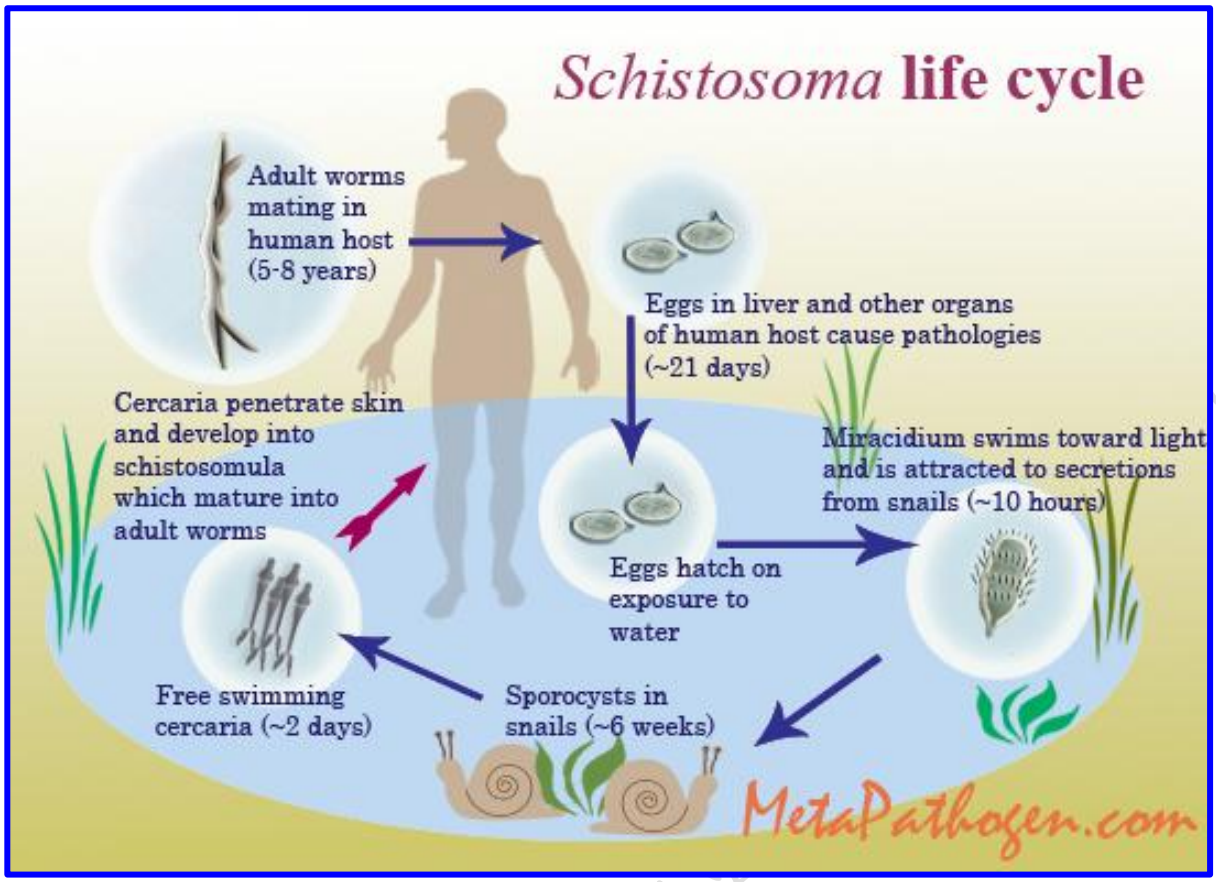
Laboratory Diagnosis:

- ***S. mansoni*:** ♦ Microscopic examination of the **stool** for eggs after concentration by sedimentation method. The egg has characteristic lateral spine**.** ♦ Rectal snip
- ***S. haematobium*:** ♦ Examination of the **urine** after allowing it to sediment in a conical urinalysis glass. A drop from the sediment is taken and examined for eggs. Egg has terminal spine.

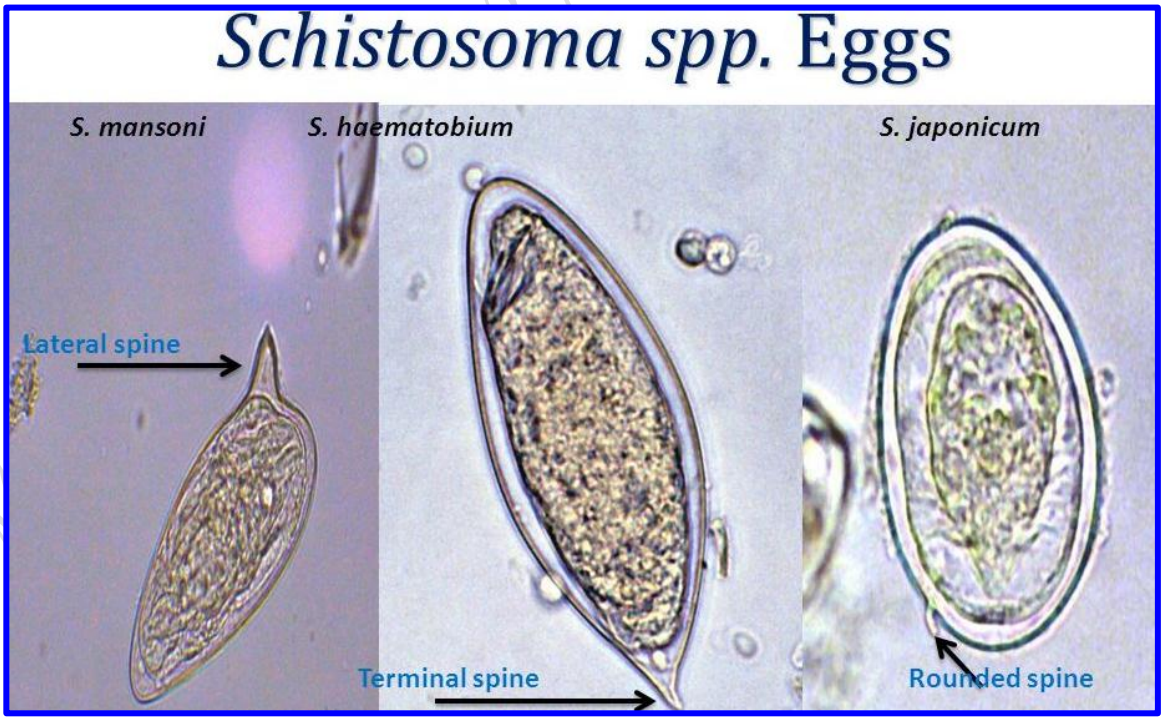
  ♦ Biopsy from bladder
- ***S. japonicum*:** ♦ Microscopic examination of the **stool** for eggs after concentration by sedimentation method. The egg has characteristic lateral knop**.**

The Eggs of Schistosomes spp





The life cycle of *Schistosomes spp*



Nematodes (Round Worms)

Properties of Nematodes:

1. Enlongated, cylindrical; unsegmented bodies are known as nematodes or **roundworms**
2. Separated sexes (diecious)

Ascaris lumbricoides

- **Disease:** ascariasis
- **Habitat:** small intestine
- **Infective stage:** fertilize egg which contain larvae
- **Common name:** roundworms
- **Final host:** have one host , **human** only .
- **Geographical distribution:** worldwide.

Morphology: Male adult worm measures 15-20 cm in length. The posterior end is curved ventrally. The female worm measures 20-40 cm in length. Its posterior end is straight.

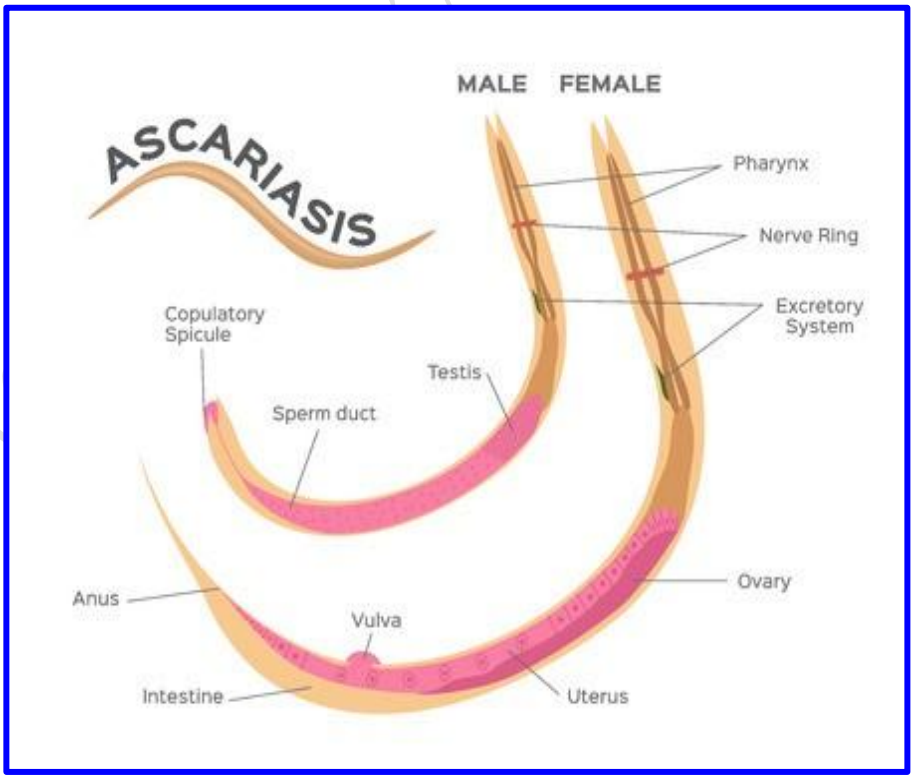


Figure: Adults of *Ascaris lumbricoides*

- **Infective stage and modes of infection:** The egg containing larva when ingested with contaminated raw vegetables causes ascariasis.
  - **Life cycle:** Ingested eggs hatch in the duodenum. The larvae penetrate the intestinal wall and circulate in the blood. From the heart they migrate to the lungs, ascend to the trachea, descend to the esophagus and finally reach the small intestine to become adult. The female pass immature eggs which pass to the soil and mature in 2 weeks.

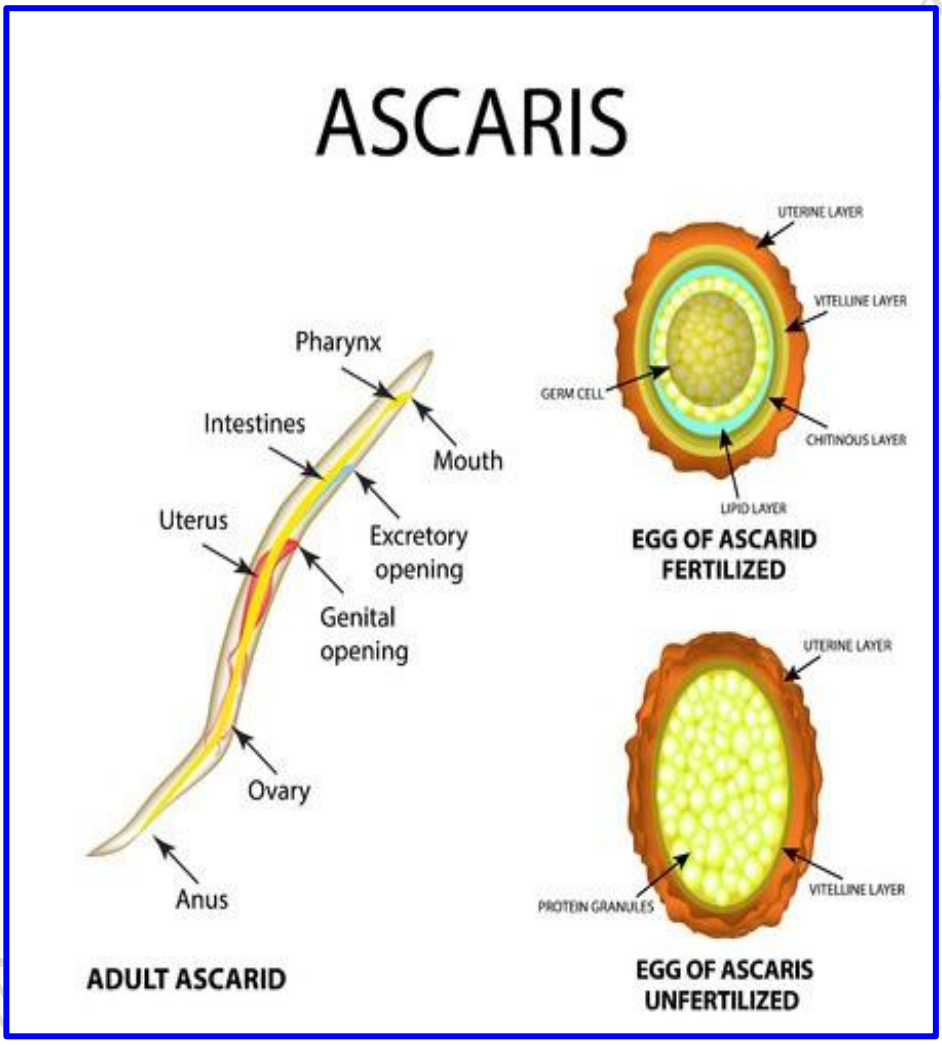


Figure: Adults and egg of *Ascaris lumbricoides*

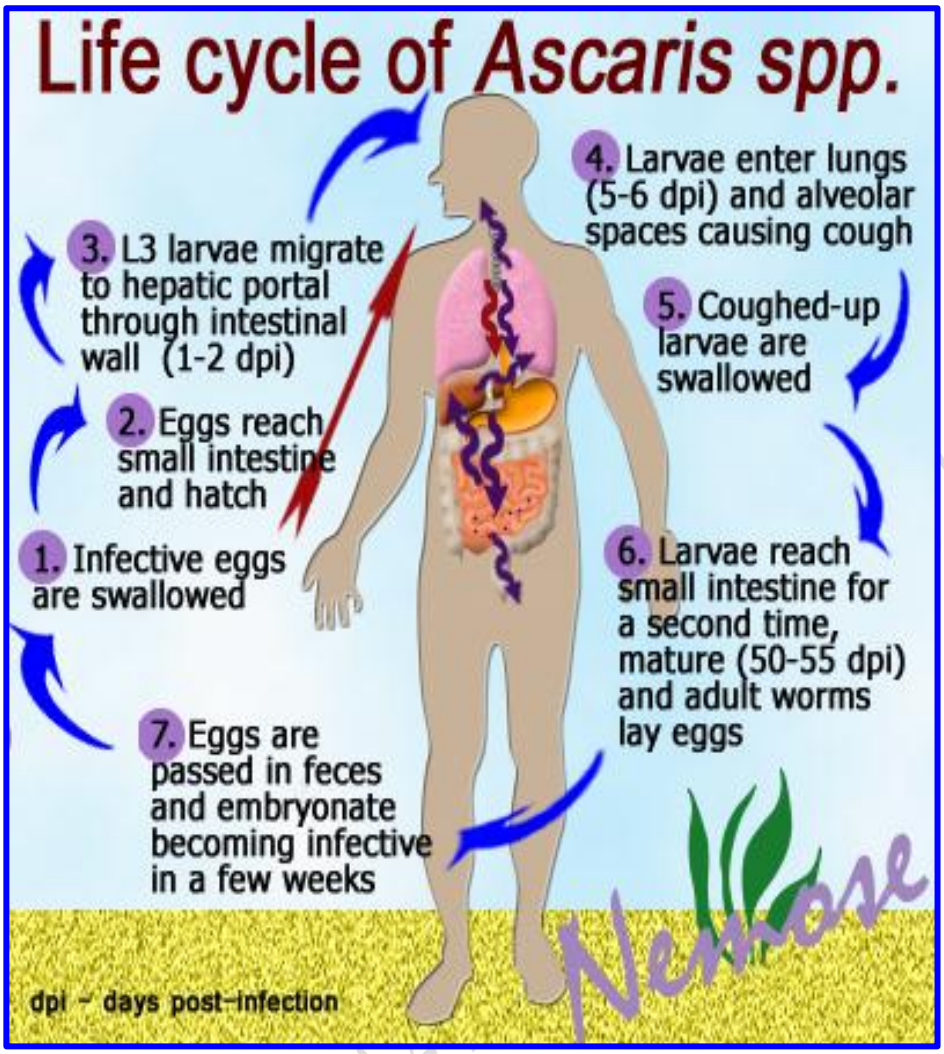


Figure: Life cycle of *Ascaris lumbricoides*

- **Pathogenecity and clinical features:** Adult worms in the intestine cause abdominal pain and may cause intestinal obstruction especially in children. Larvae in the lungs may cause inflammation of the lungs (Loeffler's syndrome) – pneumonia-like symptoms.
- **Laboratory Diagnosis:**

1. Examination of stool for fertilized eggs by direct saline smear method.
2. Demonstration of adult worms in the stool.
3. Occasionally the larvae in sputum.

Immune System

The Immune System: The immune system is designed to recognize and respond to non-self-antigen in a coordinated manner.

- Additionally, cells that are diseased, damaged, distressed or dying are recognized and eliminated by the immune system.

The immune system is divided into 2 complementary arms: the **innate** and the **adaptive** immune systems.

I- Innate Immunity(nonspecific):
Resistance to infection that an individual possess from birth by the genetic or constitutional makeup.

- It involves several defensive barriers:
  - ✓ Anatomic and physical (skin, mucous membranes and normal flora)
  - ✓ Physiologic (temperature, pH, anti-microbial and cytokines)
  - ✓ Complement
  - ✓ Cellular: phagocytes and granulocytes

II- Adaptive Immunity (specific): Resistance to infection that an individual acquires during his life.

- The components of the adaptive immune response are B and T lymphocytes and their effector cells.

Innate and adaptive immune response:

The innate and adaptive arms of the immune response work in collaboration to stop an infection. Once a pathogen has broken through the anatomic and physiologic barriers, the innate immune response is immediately activated, oftentimes it is able to contain and eliminate the infection.

Primary and Secondary Immune Response:

- **The primary immune response:** occurs when an antigen comes in contact to the immune system for the first time. During this time the immune system has to learn to recognize antigen and how to make antibody against it and eventually produce memory lymphocytes.
- **The secondary immune response**: occurs when the second time or (3rd, 4th, etc.) the person is exposed to the same antigen. At this point immunological memory has been established and the immune system can start making antibodies immediately.

Comparison between innate and adaptive immunity

Characteristics	Innate	Adaptive
Specificity	For pathogen-associated molecular patterns (PAMPs)	For specific antigens of microbial and non microbial agents
Diversity	Limited	High
Memory	No	Yes
Self-reactivity	No	No
Components		
Anatomic and physiologic barriers	Skin, mucosa, normal flora, temperature, pH, antimicrobials, and cytokines	Lymph nodes, spleen, mucosal-associated lymphoid tissues
Blood proteins	Complement	Antibodies
Cells	Phagocytes, granulocytes and natural killer (NK) cells	B lymphocytes and T lymphocytes

Differences between Primary and Secondary Immune Response

No.	Primary Immune Response	Secondary Immune Response
1	This occurs as a result of primary contact with an antigen.	This occurs as a result of second and subsequent exposure of the same antigen
2	Responding cell is naïve B-cell and T-cell.	Responding cell is memory cell.
3	Lag phase is often longer (4-7 days), sometimes as long as weeks or months.	Lag phase is shorter (1-4 days) due to the presence of memory cell.
4	First antibody produced is mainly IgM.	Mainly IgG antibody is produced.
5	Antibody level declines rapidly.	Antibody level remain high for longer period.

- **Immune Organs:**

A. Primary

1. **Thymus** is the site for maturation of **T cells**
2. **Bone marrow** and fetal liver are the sites for maturation of **B cells.**

B. Secondary

1. **Lymph node :** Site where immune response is initiated, stimulation of immunity and cell growth.

2. **Spleen:** Site of immune responses to antigens in blood, Filter for dead erythrocytes and microbial particulates, especially encapsulated bacteria

3. **Mucosa-associated lymphoid tissue (MALT):** like in Intestine.

4. **Tonsils and adenoids:** Highly populated by B cells

- **Immune System Cells:**
- **Properties of Immune system cells:**

1. Immune cells can be distinguished by morphology, cell surface markers, and function

2. Development of the various cell lineages from stem cells in the bone marrow requires specific hematopoietic growth factors, cytokines, and/or cell-cell interactions.

Major Cells of the Immune System

	Cell Type	Functions
I-Granulocytes		
1	**Neutrophils**	Phagocytose and kill bacteria
2	**Eosinophils**	Involved in allergic reactions
3	**Basophils, and mast cells**	Release histamine and other mediators of allergic and anaphylactic responses
II-Myeloid cells		
1	**Macrophages**	-Phagocytose and digest bacteria, dead host cells, and cellular debris -Secrete cytokines that promote acute phase and T cell responses
2	**Dendritic cells**	-Process and present Ag to T cells -Secrete cytokines that promote and direct T cell response -Required to initiate T cell response
II-lymphocytes		
1	**B cells**	-Process and present Ag to class II MHC restricted T cells -On activation, generate memory B cells and plasma cells
2	**Plasma cells**	Synthesize and **secrete Ab**
3	**T cells**	**-Helper T cells :** Recognize Ag associated with class II MHC molecules
		-Cytotoxic T : Recognize Ag associated with class I MHC molecules
4	**Memory B or T cells**	-Generated during primary response to an Ag and mediate **more rapid secondary response** on subsequent exposure to same Ag
5	**Natural killer cells**	Kill virus-infected and tumor cells by perforin or Fas-mediated, MHCindependent mechanism Kill Ab-coated cells by ADCC

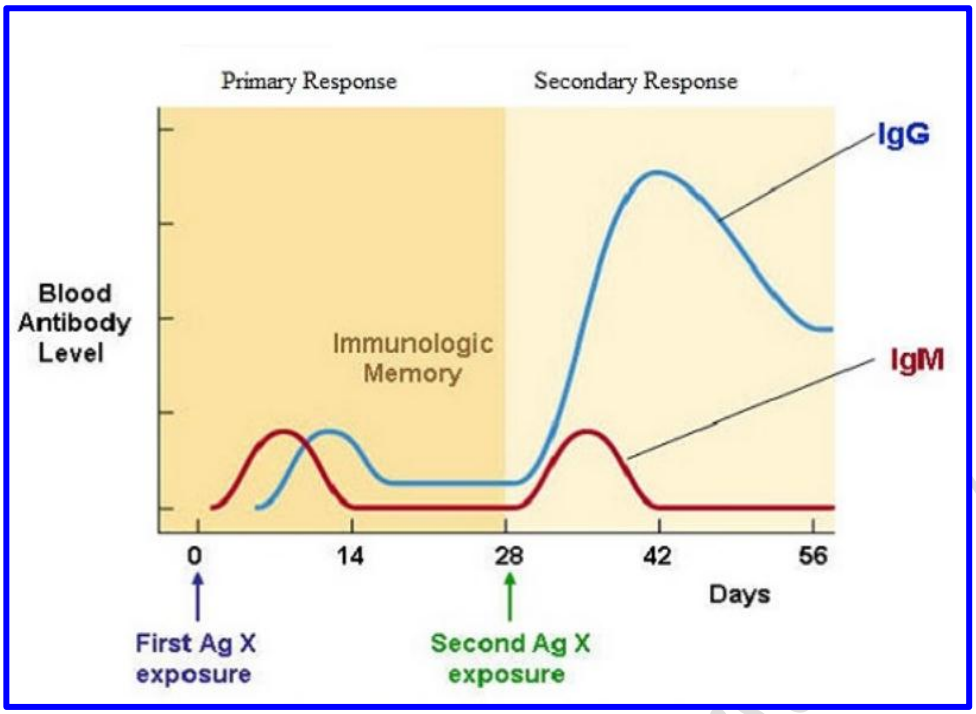


Figure: Primary and Secondary Immune Response

Antibodies and Antigen:

Antibodies: also called **immunoglobulins**, **Y-shaped** molecules are proteins produced by the body that help fight against foreign substances called **antigens (**viruses, bacteria, or other chemicals).

Structure of Antibodies:

Antibodies are heavy (~150 kDa) globular plasma proteins. The basic structure of all antibodies are same.

There are **four polypeptide chains**: **two** identical **heavy chains** and **two** identical **light chains** connected by disulfide bonds. There are five types of **immunoglobulins** (Ig) **heavy chain** denoted by the Greek letters: α, δ, ε, γ, and μ. There are two types of Ig **light chain**, which are called lambda (λ) and kappa (κ).

An antibody is made up of a **variable region** and a **constant region**, and the region that changes to various structures depending on differences in antigens is called the **variable region**, and the region that has a constant structure is called the **constant region.**

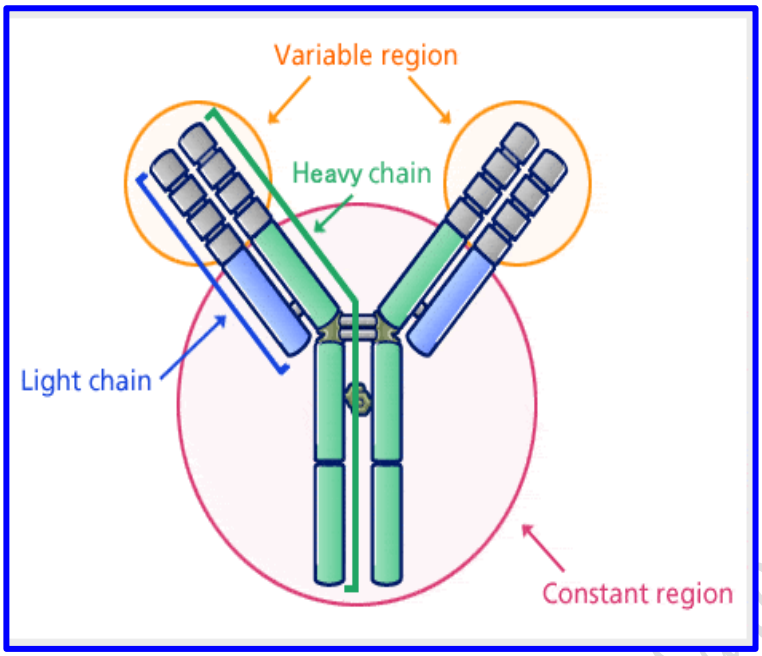


Figure: Antibody structure

Types of Antibody:

Serum containing antigen-specific antibodies is called antiserum. **The 5 types – IgG, IgM, IgA, IgD, IgE – (isotypes)** are classified according to the type of heavy chain constant region, and are distributed and function differently in the body.

Functions of Antibody:

1. **IgG** provides long term protection because it persists for months and years after the presence of the antigen .
2. **IgG** protect against bacteria, viruses, neutralize bacterial toxins, trigger compliment protein systems and bind antigens to enhance the effectiveness of phagocytosis.
3. Main function of **IgA** is to bind antigens on microbes before they invade tissues.
4. **IgA** are also first defense for mucosal surfaces such as the intestines, nose, and lungs.
5. **IgM** is Primary response, fixes complement.
6. IgM is involved in the ABO blood group antigens on the surface of RBCs.
7. **IgM** enhance ingestions of cells by phagocytosis.
8. **IgE** bind to mast cells and basophils which participate in the immune response.

9. Some scientists think that **IgE** purpose is to stop parasites.
10. **IgD** is present on the surface of B cells and plays a role in the induction of antibody production.

- **Antigen:** is any foreign substance that stimulates the immune system to produce antibodies.

Antigen properties:

1. Immunogenicity: Ability of an antigen to induce immune response in the body (both humoral and/or cell mediated).

2. Antigenicity (immunological reactivity): Ability of an antigen to combine specifically with the antibodies and/or T-cell-surface receptors.

Some terms:

- **Immunogens:** any Molecules that stimulate immune responses.
- **Hapten or Incomplete Antigen:** These are the foreign substance, usually non-protein substances. Unable to induce an immune response by itself, they require carrier molecule to act as a complete antigen.
- **Adjuvants:** Substances that can enhance the immune response to an immunogen are called adjuvants. They are usually added to vaccines to increase the immunogenicity of the vaccine antigen.

- **Chemical Nature of Antigens (Immunogens)**

A. Proteins

The vast majority of immunogens are proteins.

B. Polysaccharides

Pure polysaccharides and lipopolysaccharides are good immunogens.

C. Nucleic Acids

Nucleic acids are usually poorly immunogenic.

D. Lipids

In general lipids are non-immunogenic, although they may be haptens.

Types of Antigens:

Antigens are categorized into broad classes of antigens based on their origin.

1. **Endogenous Antigens:** Endogenous antigens are that have been generated within previously-normal cells as a result of normal cell metabolism or because of viral or intracellular bacterial infection (which both change cells from the inside in order to reproduce).
2. **Exogenous Antigens:** Exogenous antigens are antigens that have entered the body from the outside, for example by inhalation, ingestion, or injection.
3. **Autoantigens:** Autoantigens are normal "self" protein or complex of proteins or nucleic acid that is attacked by the host's immune system, causing an autoimmune disease.
4. **Tumor Antigens (Neoantigens):** These antigens are presented by MHC I or MHC II molecules on the surface of tumor cells.

Factors Influencing Immunogenicity:

There are various factors that influence immunogenicity of an antigen:

1. **Size of the antigen:** Larger is the size (e.g. hemoglobin), more is the immunogenicity.

2. **Chemical nature:** Proteins are stronger immunogens than carbohydrates followed by lipid and nucleic acids.

3. **Susceptibility of antigen to tissue enzymes**—It increases immunogenicity by exposing more epitopes of the Ag.

4. **Structural complexity** of the antigen increases immunogenicity.

5. **Foreignness to the host:** More is the foreignness of Ag, more is the immunogenicity.

6. **Adjuvant.**

Antigen-Antibody Reactions

The interactions between antigens and antibodies are known as ***antigen–antibody reactions***. The reactions are highly specific, and an antigen reacts only with antibodies produced by itself or with closely related antigens. Antibodies recognize molecular shapes (epitopes) on antigens.

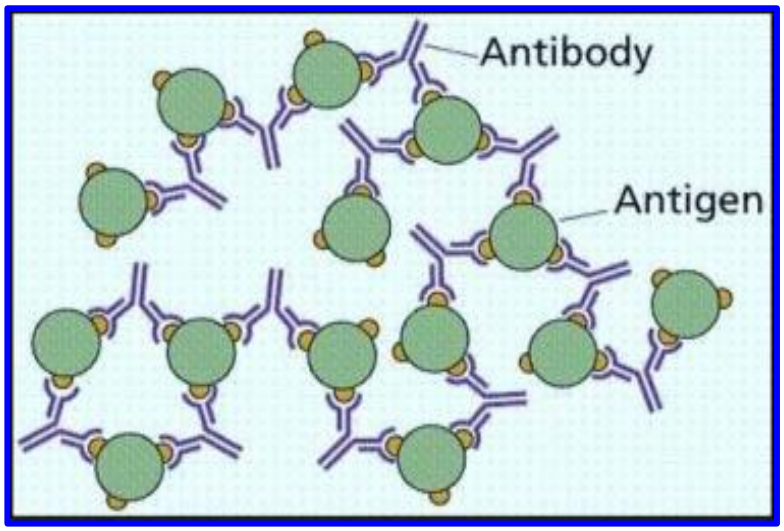


Figure: Ab-Ag Reaction

General Features of Ab-Ag reaction:

- ✓ Antigen and antibody bind through non-covalent bonds
- ✓ There is no irreversible chemical alteration in either of the participants, i.e., antigen or the antibody.
- ✓ The antigen and antibody binding is reversible.
- ✓ Binding can be prevented or dissociated by high ionic strength or extreme pH.

Physicochemical Properties of Ab-Ag reaction:

- ✓ **Electrostatic bonds, hydrogen bonding, van der Waals bonds, and hydrophobic interactions** are the intermolecular forces involved in antigen-antibody reactions.
- ✓ All these types of intermolecular forces depend on the close proximity of the antigen and antibody molecules.

Types of Ag-Ab reactions:

1. Agglutination
2. Precipitation
3. Complement Fixation
4. Enzyme Linked Immunosorbent Assay

5. RadioImmuno Assay
6. Western Blotting

Hypersensitivity:

Hypersensitivity: is an undesirable reaction produced by normal immune system. It includes **allergy** and **autoimmunity**.

Allergy: is a pathological reaction of the immune system to external antigens - allergens , which exist normally in the environment (pollens, molds, animals, foods, insect stings, etc.).

Allergens: are substances usually protein in nature. Simple low molecular weight substances are only partial antigens (hapten), become a complete antigen in the body after binding with internal protein.

Autoimmunity is a pathological reaction in which the immune system directly or indirectly targets and damages own cells. The effect may range from discomfort, organ damaging to fatality.