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

جمهورية العراق
وزارة التعليم و البحث العلمي
جامعة الفرات الاوسط التقنية
المعهد التقني / كربلاء
قسم تقنيات صحة المجتمع

Educational Bag Of Medical Microbiology

For Students of the First Stage / Department of Community Health Technologies

Praprared by

Dr. Balqees Sadoon Jasim

lecturer

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General Objectives and Foundations of Medical Microbiology for The First Stage

Objectives of the subject :

General objectives :

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

Pathogenic micro organisms, parasitic organisms, parasitic insects and immunity

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	History of microbiology, site of microorganism in the world of the living & the branches of microbiology.
2	Bacterial morphology,bacterial cell structure.
3	Bacterial requirement, growth curve
4	Controle of microorganisms.
5	Septic respiratory system .
6	Septic digestive system.
7	Food poisoning.
8	Contamination of hospitals .
9	General characters of fungi .
10	Fungal diseases.
11	The viruses , shapes , sizes & some viral diseases.
12	Introduction of parasites.
13	Protozoa , Entamoeba histolytica.
14	Flagellates, giardia . trichomonase .
15	Blood flagellates, leishmania.
16	Sporozoa, plasmodium , toxoplasma.
17	Helimenthes , taenia .
18	Echinococcus granulosis.
19	Hymenolipes nana
20	Trematoda helminthes .
21	Trepanoma ,schistosomes
22	Immune system , organs of immune systems.
23	Antibody &antigen .
24	Antibody &antigen reactions .
25	Hypersensitivity .
26	Autoimmune diseases.
27	Discuss the report of bacteria .
28	Discuss the report of parasite .
29	Discuss the report of fungi & viruses.
30	Discuss the report of immunity.

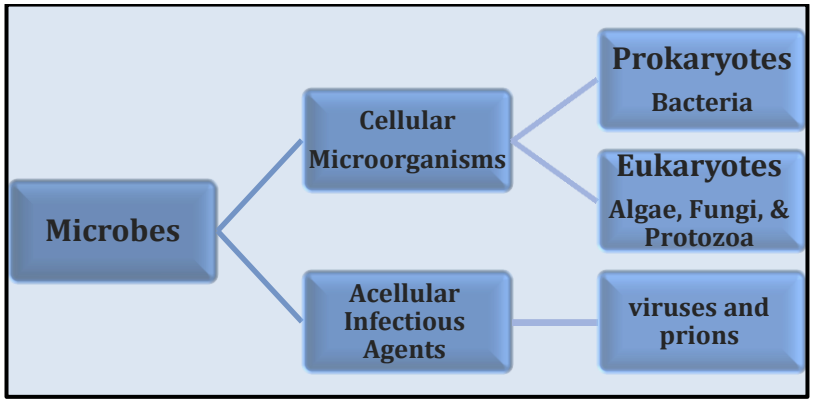
Introduction of Medical Microbiology Unite

General view about Microbiology, History and Branches of Microbiology

The Science of Microbiology:

Microbiology is the study of living organisms (microbes) of microscopic size, a large and divers e group. **Microbes** consist of two major groups:

(1) cellular microbes (2) acellular microbes



Eukaryotic cells possess a true nucleus, whereas Prokaryotic cells do not.

Figure 1. Acellular and cellular microbes.

History:

The science of medical microbiology dates back to the pioneering studies of Pasteur and Koch, who isolated specific agents and proved that they could cause disease by introducing the experimental method. The methods they developed lead to the first golden age of microbiology (1875-1910), when many bacterial diseases and the organisms responsible for them were defined.

Louis Pasteur

Louis Pasteur is also known as ***father of microbiology***. He has many contributions to microbiology:

1. He has proposed the ***principles of fermentation*** for preservation of food.
2. He introduced ***sterilization techniques*** and developed steam sterilizer, hot air oven and autoclave.
3. He described the method of ***pasteurization of milk***.
4. He had also contributed for ***designing the vaccines*** against several diseases such as ***anthrax***, ***cholera*** and ***rabies.***
5. He disproved the theory of spontaneous generation of disease and postulated the ***'germ theory of disease'***. He stated that disease cannot be caused by bad air or vapor, but it is produced by the microorganisms present in air.
6. ***Liquid media*** concept- He used ***nutrient broth*** to grow microorganisms.
7. He was the founder of the ***Pasteur Institute, Paris.***

Robert Koch

Robert Koch provided remarkable contributions to the field of microbiology:

1. He used of ***solid media*** *for culture* of bacteria-Eilshemius Hesse, the wife of Walther Hesse, one of Koch's assistants had suggested the use of **agar** as solidifying agent.

2. He also introduced methods for ***isolation of bacteria in pure culture.***

3. Described ***hanging drop method for testing motility.***

4. Discovered bacteria such as the ***anthrax bacilli***, ***tubercle bacilli*** and ***cholera bacilli***.

5. Introduced ***staining techniques*** by using ***aniline dye***.

6. **Koch's phenomenon**: Robert Koch observed that ***guinea pigs*** already infected with ***tubercle bacillus*** developed a ***hypersensitivity reaction*** when injected with ***tubercle bacilli*** or its ***protein***. This reaction is called ***Koch's phenomenon***.

Paul Ehrlich

1. He was the first to report the ***acid-fast nature of tubercle bacillus.***

2. He developed techniques to ***stain tissues and blood cells.***

3. He proposed a ***toxin - antitoxin interaction*** called as ***Ehrlich phenomenon*** and also introduced methods of ***standardizing toxin and antitoxin***.

4. He proposed the 'side chain theory for antibody production'.

5. He discovered 'salvarsan', an arsenical compound (magic bullet) for treatment of syphilis, hence known as ***father of chemotherapy***.

6. The bacteria 'Ehrlichia'was named after him.

Other Important Contributors in Microbiology

1. **Antonie Philips van Leeuwenhoek:** Discovered ***single-lens microscope*** and named organisms as '***Little animalcules'.***

2. **Edward Jenner:** Developed the ***first vaccine of the world***, the ***smallpox vaccine*** by using ***cowpox virus***.

3. **Joseph Lister:** He is considered to be the ***father of antiseptic surgery***. He used carbolic acid during surgery.

4. **Hans Christian Gram:** He developed '***Gram stain'***.

6. **Ernst Ruska**: He was the founder of ***electron microscope.***

7. **Alexander Fleming:** He discovered the ***antibiotic penicillin.***

8. **Elie Metchnikoff:** He described ***phagocytosis and termed phagocytes.***

9. **Kleinberger:** He described the existence of ***L forms of bacteria.***

10. **Barbara McClintock:** She described ***transposons.***

11. **Walter Gilbert and Frederick Sanger:** were the first to develop (1977) the method of ***DNA sequencing.***

12. **Karry Mullis:** Discovered ***Polymerase Chain Reaction (PCR).***

Branches of Microbiology:

On basis of Taxonomic characters Microbiology is further divided into the following branches

1. Bacteriology
2. Mycology
3. Phycology
4. Parasitology
5. Immunology
6. Virology

1. Bacteriology:

Bacteriology is a branch of Microbiology that deals with study of **Bacteria.**

2.Mycology:

Mycology is a branch of microbiology that deals with study of **Fungus.**

3. Phycology:

Phycology is a branch of microbiology that deals with the study of **Algae**. They are photosynthetic, eukaryotic, and multi cellular organism.

4. Parasitology:

It is a branch of biology that deals with the study of parasites. This branch mainly include the study of three major groups: **Protozoa, Parasitic Worms** (**Helminths**), and **Arthropods.**

5.Immunology:

Immunology is a branch of microbiology that deals with the study of **Immune system** of all organism specially human being and animals. In this branch of microbiology the relationships between **host body, pathogen** and **immunity** is studied.

6. Virology:

This branch of microbiology deals with the study of **Viruses**.

Types of Microorganisms:

The agents of human infectious diseases belong to five major groups of organisms:

Bacteria, Fungi, Protozoa, Helminths, and Viruses.

1.Bacteria:

Bacteria (singular: **bacterium**) are unicellular organisms that lack a nuclear membrane and true nucleus. They are classified as **prokaryotes.** Their mode of multiplication is by Binary fission.

2. Fungi:

Fungi (singular: **fungus**) are **eukaryotes** organisms whose cells have a distinct nucleus containing the cell's genetic material (DNA), is surrounded by Chitin or cellulose or both. Organisms in the Kingdom Fungi may be unicellular or multicellular.

3.Protozoa:

Protozoa (singular: **protozoan**) are unicellular eukaryotic Microbes. Protozoa move by pseudopods, flagella, or cilia.

4.Multicellular Parasites:

Multicellular animal parasites are eukaryotes. The two major groups of parasitic worms are the flatworms and the roundworms, collectively called **helminths**.

5.Viruses:

Viruses are the smallest infectious particles (virions); they can be seen under an ***Electron Microscope***. Structurally very simple, a virus particle contains a core made of only one type of nucleic acid, either DNA or RNA.


Medical Bacteriology Unite

Structure and Morphology of Bacterial Cell

Bacteria: are unicellular having both **DNA and RNA**. They are capable of performing all essential processes of life, e.g. growth, metabolism and reproduction. Bacteria are **prokaryotes**, their cells lack nuclei and organelles, which distinguish them from the "true" cells of eukaryotes .

Bacterial Cell Structure:

Anatomy of a bacterial cell can be divided into:

I. Cell envelope and its appendages. **II. Cell interior.**

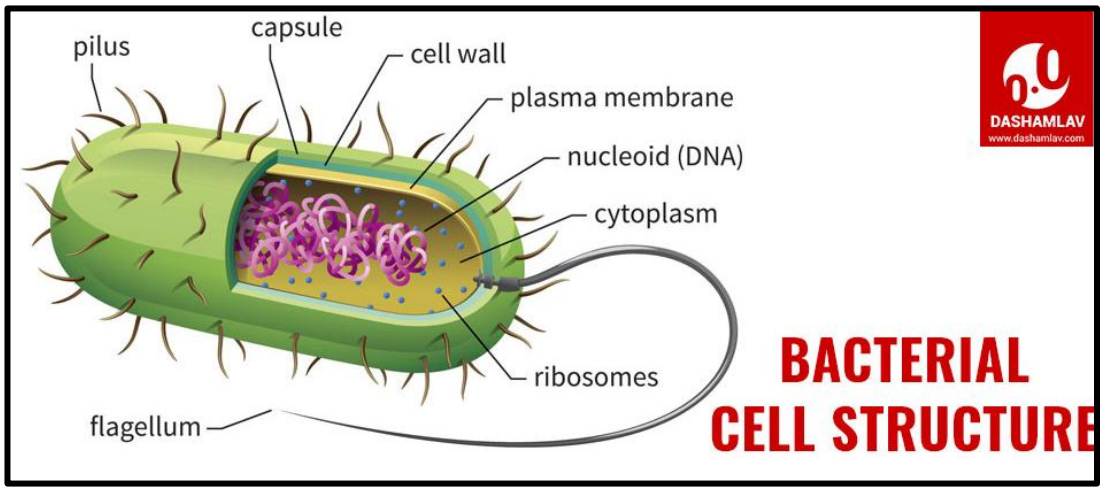


Figure: structure of a bacterial cell

I-Cell envelope and its Appendages:

1.Cell wall: The cell wall is the layer that lies just outside the plasma membrane. It is strong and relatively rigid, and openly porous. The cell wall is composed of peptidoglycan.

❖ **Functions of the cell wall:**

1. It maintains the characteristic shape of bacteria.

2. It protection of cytoplasmic membrane against osmotic pressure .

3. It also functions in adhesion of one bacteria with other bacteria and with mammalian cells.

2. **Cytoplasmic or plasma membrane**: It is present beneath the cell wall and surrounds the living matter of the bacterial cell. It is thin (5–10 nm thick), elastic and can only be seen with electron Microscope. Chemically composed of a phospholipid bilayer **and proteins.**

❖ **Functions of cytoplasmic membrane:**

Semipermeable membrane: Controlling the inflow and outflow of metabolites to and from the otoplasm.

2. Involved in outer membrane and cell wall synthesis, and in the assembly and secretion of extra cytoplasmic and extracellular substances.

3. Generation of ATP energy **.**

3.Capsule: Many bacteria form a thick outer capsule outside of their cell walls called glycocalyx**.** These polymers are usually composed of polysaccharides and sometimes protein.

❖ **Functions of capsule:**

1.Capsules act as a virulence factor by protecting the bacterium from ingestion by phagocytosis.

2. Protection of the cell wall from various types of antibacterial agents and antibiotics.

4.Pili (Fimbriae): are slender, hair like, proteinaceous appendages on the surface of many bacteria**.** They are shorter and thinner than flagella and emerge from the cell wall. They originate in the cytoplasmic membrane and are composed of structural protein subunits termed **pilins**.

❖ **Functions of Pili**:

1.Fimbriae function as organs of adhesions. These outgrowths assist the bacteria in attaching to other cells and surfaces, such as teeth, intestines. Without pili, many disease-causing bacteria lose their ability to infect because they're unable to attach to host tissue.

2. Specialized pili (**Sex pili**)are used for conjugation, during which two bacteria exchange fragments of plasmid DNA.

5.Flagella: (singular, flagellum) are hair like structures that provide a means of locomotion of bacteria . These are hair-like, helical cytoplasmic appendages. The flagella may be present at one or both ends of the bacterial cell and in some cases they are present along the sides or all around the bacterium.

❖ **Functions of Flagella:** Flagella are responsible for the motility of the bacteria.

Help the bacterium move toward nutrients; away from toxic chemicals.

II-Cell interior:

1.Cytoplasm: The cytoplasm of the bacterial cell is a viscous watery solution or soft gel, containing a variety of organic or inorganic solutes, and numerous **ribosomes** and **polysomes.** The cytoplasm of bacteria differs from that of the higher eukaryotic organisms in not containing an **endoplasmic reticulum** , **mitochondria, lysosomes** but contain specialized parts rather than distinct organs surrounded by membranes. These specialized parts are called **organelles**.

❖ **Functions of Cytoplasm:** The components of the cytoplasm are responsible for cell growth, netabolism, elimination of waste and replication (reproduction) of the cell.

2.Ribosomes: Ribosomes are microscopic "factories" , it is responsible on bacterial protein synthesis. Bacterial ribosomes are slightly smaller (10–20 nm) than eukaryotic ribosomes and they have a sedimentation rate of 70S (S or Svedberg unit).

❖ **Functions of** Ribosomes : They translate the genetic code from the molecular language of nucleic acid to that of amino acids—the building blocks of proteins.

3.Nucleoid : The nucleoid is a region of cytoplasm where the chromosomal DNA is located. It is not a membrane bound nucleus, but simply an area of the cytoplasm where the strands of DNA are found. Most bacteria have a **single, circular chromosome.**

❖ **Functions of Nucleoid** : bacterial chromosome that is responsible for replication by simple fission.

4. Plasmids: Bacteria may possess extra cellular genetic elements in the cytoplasm consisting of DNA termed **plasmids.**

Functions of plasmids: it is give certain properties to bacterial cell such as drug

resistance, and toxigencity which may constitute a survival advantage.

Difference between Gram-Positive and Gram-Negative Bacteria:

Bacteria can be gram-positive or gram-negative depending upon the staining methods.

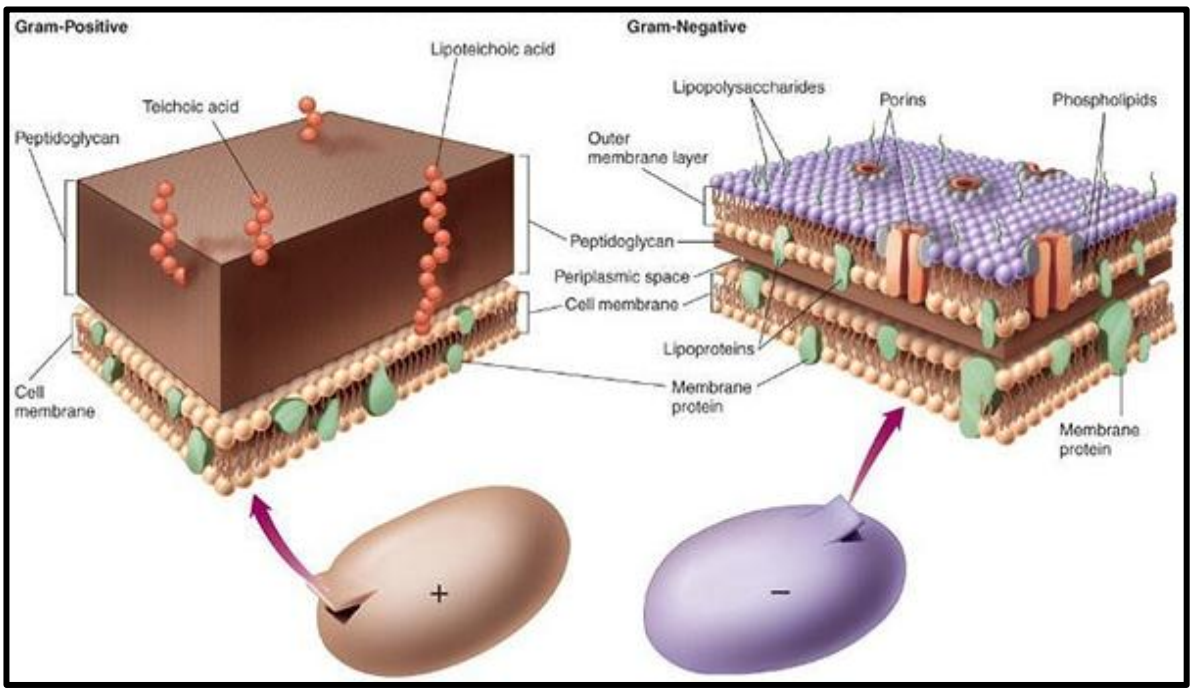


Figure: Cell Wall of Gram-Positive and Gram-Negative Bacteria

Following are the important differences between gram-positive and gram-negative bacteria:

	Gram-Positive bacteria	Gram-Negative bacteria
Cell Wall	A single-layered, smooth cell wall	A double-layered, wavy cell-wall
Cell Wall thickness	he thickness of the cell wall is 20 to 80 nanometres	The thickness of the cell wall is 8 to 10 nanometers
Peptidoglycan Layer	It is a thick layer/ also can be multilayered	It is a thin layer/ often single-layered.
Teichoic acids	Presence of teichoic acids	Absence of teichoic acids
Outer membrane	The outer membrane is absent	The outer membrane is present (mostly
Flagella Structure	Two rings in basal body	Four rings in basal body
Lipopolysaccharide	Absent	Present
Toxin Produced	Exotoxins	Endotoxins or Exotoxins
Resistance to Antibiotic	More susceptible	More resistant
Gram Staining	These bacteria retain the **crystal violet colour** and appear as **purple-coloured** .	These bacteria do not retain the stain colour and **appear as pink-coloured** .

Size of Bacteria:

The average diameter of **spherical** bacteria is **0.5-2.0µ** . For **rod-shaped** or **filamentous bacteria**, length is **1-10µ** and diameter is **0.25-1 µ.**

The smallest bacteria are members of genus *Mycoplasma* which are only 0.3 µm, as small as the largest viruses.

Morphology of Bacteria:

Bacteria morphology or shape are classified into three basic groups: **Cocci, Bacilli,** and **Spirochetes (Spiral).**

The **cocci** are round, the **bacilli** are rods, and the **spirochetes** are spiral-shaped. Some bacteria are variable in shape and are said to be **pleomorphic** (many-shaped). The shape of a bacterium is determined by its **cell wall**.

Arrangement of Bacteria:

The microscopic appearance of a bacterium is one of the most important criteria used in its identification.

(I) Spherical Bacteria: Bacteria, which are spherical in shape, are called '**coccus' (plural: cocci)**

On the basis of arrangement of individual organisms, they are described:

1. **Coccus:** The spherical bacteria cells, called cocci, are present as single individuals.

2. **Diplococcus:** The cocci are arranged in pairs. Ex: ***Streptococcus pneumonia, Moraxella catarrhalis, Enterococcus spp, Neisseria gonorrhea.***
3. **Streptococcus:** The cocci are arranged in chains. Ex: ***Streptococcus pyogenes, Streptococcus pneumonia, Streptococcus mutans.***
4. **Tetrads:** The cocci are arranged in packets of four cells. Ex: **A*erococcus, Pediococcus, and Tetragenococcus***.
5. **Staphylococcus:** The cocci are arranged in grape-like clusters. Ex: ***Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus aureus, Staphylococcus capitis.***
6. **Sarcinae :** The cocci are arranged in a cuboidal manner. Ex: ***Sarcina aurantiaca, Sarcina lutea, Sarcina ventriculi.***

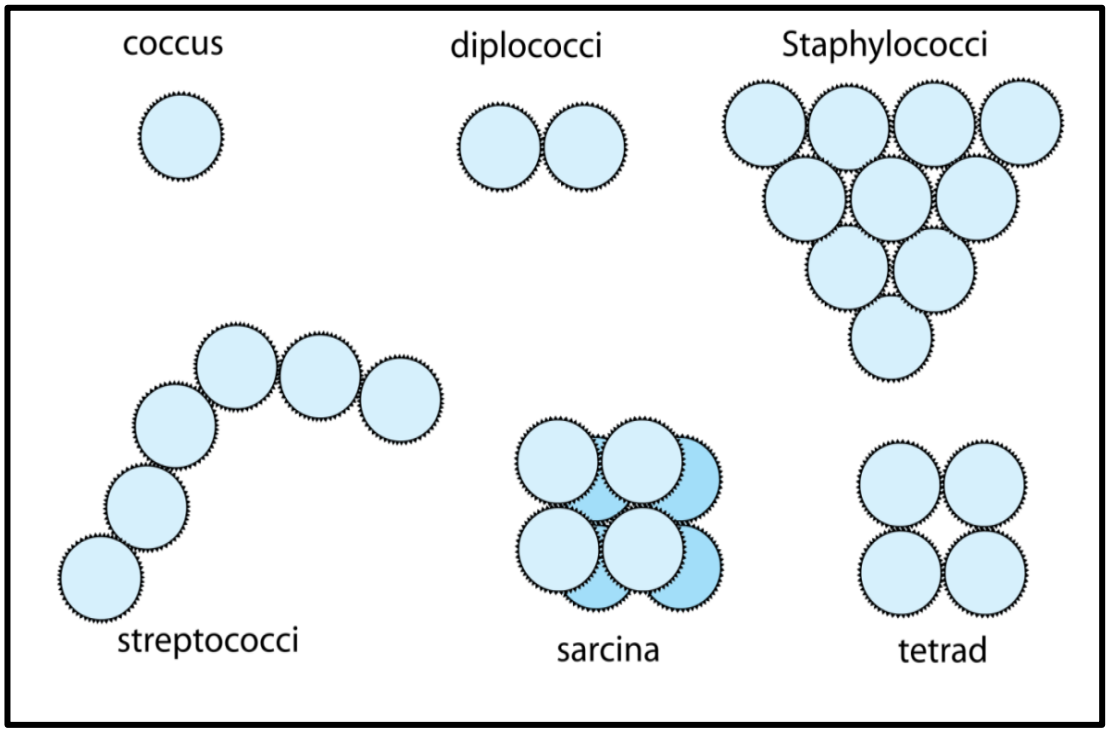


Figure: Arrangement of cocci

(II) Rod-shaped Bacteria: The cylindrical or rod-shaped bacteria are called **'bacillus' (plural: bacilli).**

1. **Bacillus:** Bacilli are the bacteria which are rod-shaped and are present as single cells. Ex: ***Bacillus cereus***.
2. **Diplobacillus:** The bacilli are arranged in pairs. Ex: ***Moraxella bovis, Klebsiella.***
3. **Streptobacillus:** The bacilli are arranged in chains. Ex: ***Streptobacillus moniliformi***.
4. **Coccobacilli:** As the name suggests, coccobacilli resemble both cocci as well as bacilli. Ex: ***Chlamydia trachomatis, Haemophilus influenza, Gardnerella vaginalis.***
5. **Pallisades**: Pallisades are the type of bacilli bacteria that resemble a picket fence structure ,they appear similar to Chinese letters. Ex: ***Corynebacterium diphtheria*** .

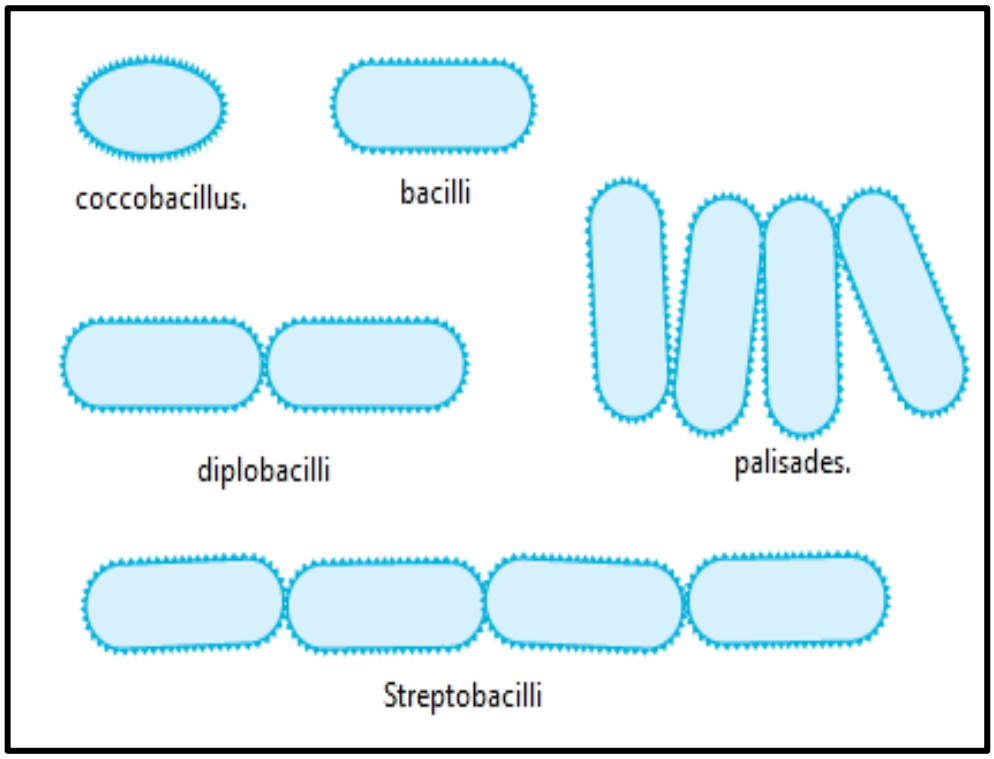


Figure: Arrangement of bacilli

III. Shape of Spiral: These bacteria are spiral or helical in shape. Based on the thickness, flexibility and motility**.**

1.Spirilla (Spirillum): These are gram-negative, spiral or helical in shape, **rigid bacteria** having external flagella. Ex: ***Campylobacter jejuni, Helicobacter pylori.***

2.Spirochetes: Spirochetes are spiral bacteria having a helical shape, **thin and flexible** and have an **axial filament** which helps in motility.. They have internal periplasmic flagella. Ex: ***Leptospira, Treponema pallidum.***

3. Vibrio: These are the slightly curved bacteria resembling a comma shape. Ex: ***Vibrio parahaemolyticus, Vibrio cholera.***

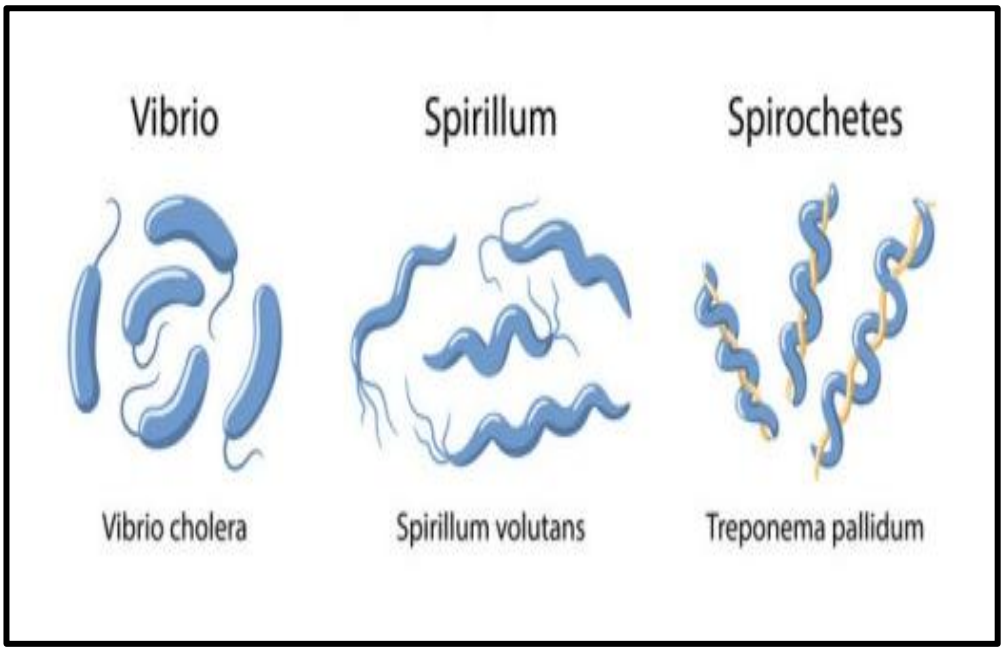


Figure: Shape of Spiral bacteria

Other Shapes of Bacteria:

1.Filamentous Bacteria: These are bacteria that are long, thin, and filament-shaped. They, sometimes, divide to form branches resembling strands of hair called mycelium. Example: ***Actinomycetes,*** *Streptomyces* species**.**

2.Pleomorphic Bacteria : A few bacteria lack rigid cell walls, and their flexible plasma membrane allows them to change shape. These are called pleomorphic bacteria. Example: ***Mycoplasma pneumoniae***.

3.**Appendaged Bacteria**: The bacteria that produce a unique structure like **pillus or fimbriae** are called **appendaged bacteria**.These bacteria are more virulent than other bacteria that do not form these appendages. Ex: ***Neisseria gonorrheae***.

Bacterial Requirement, Growth Curve

Requirements for Microbial Growth

As all living organisms, microorganisms also require a combination of various physical and chemical factors for their growth and multiplication.

The requirements for microbial growth can be divided into two main categories: **physical** and **chemical.**

- **Physical requirements** include temperature, pH, and osmotic pressure.
- **Chemical requirements** are **macromolecules** (carbon, nitrogen, hydrogen, sulfur, phosphorus, oxygen) and **micro molecules** (trace elements and organic growth factors as magnesium, potassium, sodium, calcium and iron in their ionised forms)

I-Physical Requirements:

1) **Temperature: Optimum temperature:** Each bacterial species has an optimal temperature for growth and a temperature range above and below which growth is blocked.

   Bacteria are divided into three groups on the basis of temperature ranges through which they grow:

   i. **Mesophilic:** Bacteria which grow between 20°C - 45°C.
   ii. **Psychrophlic:** Psychrophilic bacteria (cold-loving) are organisms that grow between 0-20°C. They are soil and water saprophytes.
   iii. **Thermophilic:** Thermophiles (heat-loving) have growth range of 50–80°C.

Note: **Most microorganisms grow well at the temperatures favored by humans. The optimum temperature for many pathogenic bacteria is about 37^{o}C, and incubators for clinical cultures are usually set at about this temperature.**

2) **pH: Optimum pH:** at which the organism grows best.

   Microorganisms are classified into three primary groups on the basis of their preferred range of pH:

   i. **Acidophiles:** Microorganisms which grow at pH (3-5).
   ii. **Neutrophiles:** Microorganisms which grow best at neutral pH (6-8).

iii. **Alkaliphiles:** Microorganisms which grow best under alkaline conditions pH as high 10.5.

Note: **Most pathogenic bacteria grow best at a neutral or slightly alkaline pH (7.2–7.6).**

3) **Osmotic Pressure:** Microorganisms require **water** for growth as they obtain almost all their nutrients in solution from the surrounding water.

Osmotic pressure: is the force water exerts on the semi-permeable membrane (plasma membrane) surrounding the cell.

A bacterial cell may be subjected to any of three kind of osmotic solutions: isotonic, hypotonic, and hypertonic.

i. **Isotonic (isoosmotic)** solution is a medium in which the overall concentration of solute equals that found inside a cell . Water leaves and enters the cell at the same rate.
ii. **Hypotonic (hypoosmotic**) environment/medium in which the concentration of solute is lower outside than inside the cell, water flows into the cell. If this influx of water is uncontrolled, the cell may eventually burst.
iii. **Hypertonic (hyperosmotic)** environment where the concentration of solute is higher outside the cell, water is lost from the cell resulting in dehydration, shrinkage of the plasma membrane and eventual death.

II-Chemical Requirements:

1-Major Elements (Macroelements or Macronutrients): These include carbon, oxygen, hydrogen, nitrogen, sulfur, phosphorus, potassium, magnesium, calcium, and iron.

- **Carbon** is the structural back bone of living matter; it is needed for all the organic compounds that make up a living cell. According to source of carbon the bacteria can be classified into:

i. Autotrophs: Organisms that can use **inorganic carbon** in the form of carbon dioxide as their carbon source are called autotrophs .

ii. Heterotrophs: Organisms that use **organic carbon** are called heterotrophs. They are unable to utilize carbon dioxide as the sole source of carbon and use reduced, preformed organic molecules as carbon sources.

- **Hydrogen** is also an important molecule that participates in energy generation processes in most microorganisms.

- **Nitrogen** is needed for the synthesis of proteins and nucleic acids, as well as for important molecules such as ATP.
- **Oxygen** is of central importance to the respiration of many microorganisms. Based on their O2 requirements, Bacteria can be classified into:

i. Obligate aerobes: These have an obligate requirement for oxygen (O2), Ex: ***Cholera vibrio***.

ii. Facultative anaerobes: These are ordinarily aerobic but can also grow in the absence of oxygen. Most bacteria of medical importance are facultative anaerobes.

iii. Microaerophilic organisms: These grow best at low oxygen Ex: ***Campylobacter* spp**.

iv. Obligate anaerobes: These don't use O2 may even die on exposure to oxygen, Ex: ***Clostridium tetani.***

2. Trace Elements: Some elements, termed as **trace elements** or **micronutrients**, are required in very minute quantities by all cells. They include **potassium, sodium, magnesium, calcium, iron cobalt, zinc**, and **copper**.

2. **Growth Factors:** Some bacteria require certain organic compounds in minute quantities known as **growth factors** or **bacterial vitamins.**

The Microbial Growth Curve

Bacterial growth: is proliferation of bacterium into two daughter cells, in a process called binary fission.

Generation Time: the generation time is also called the doubling time and is defined as the time it takes for the population to double through one round of binary fission.

Bacterial doubling times vary enormously. ***Escherichia coli*** can double in as little as **20 minutes** under optimal growth conditions in the laboratory, bacteria of the same species may need **several days** to double . Most **pathogens grow rapidly**, like *E. coli*, but there are exceptions. For example, ***Mycobacterium tuberculosis***, the causative agent of tuberculosis, has a generation time of between **15 - 20 hours.**

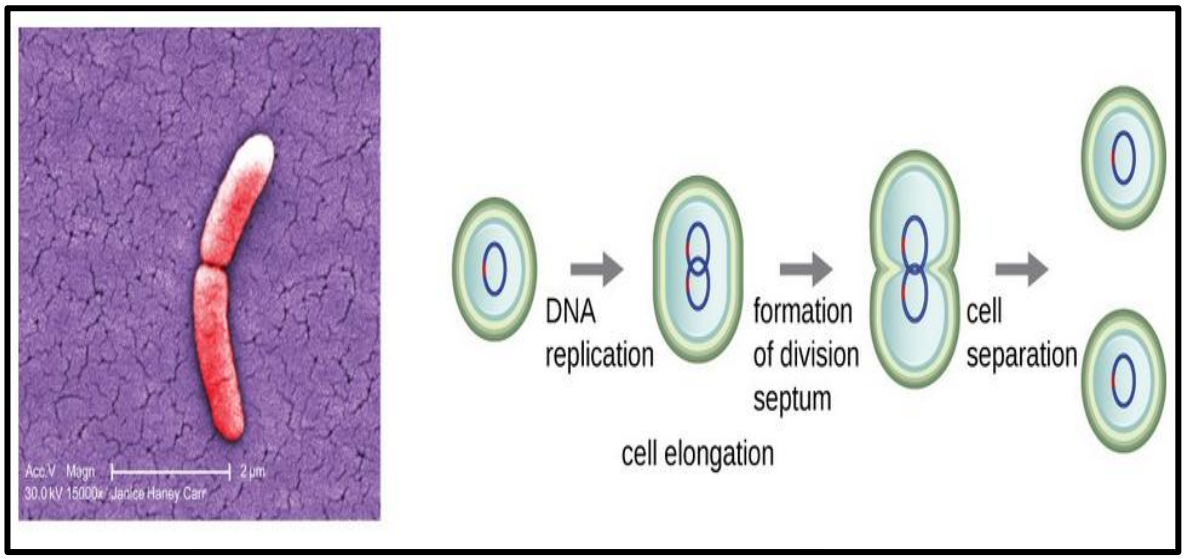


Figure : Binary Fission in Bacteria

Bacterial Growth Curve:

If a suitable liquid medium is inoculated with bacterium and incubated, its growth follows a definitive course. Small samples are taken at regular intervals after inoculation and plotted in relation to time. A plotting of the data will yield a characteristic growth curve.

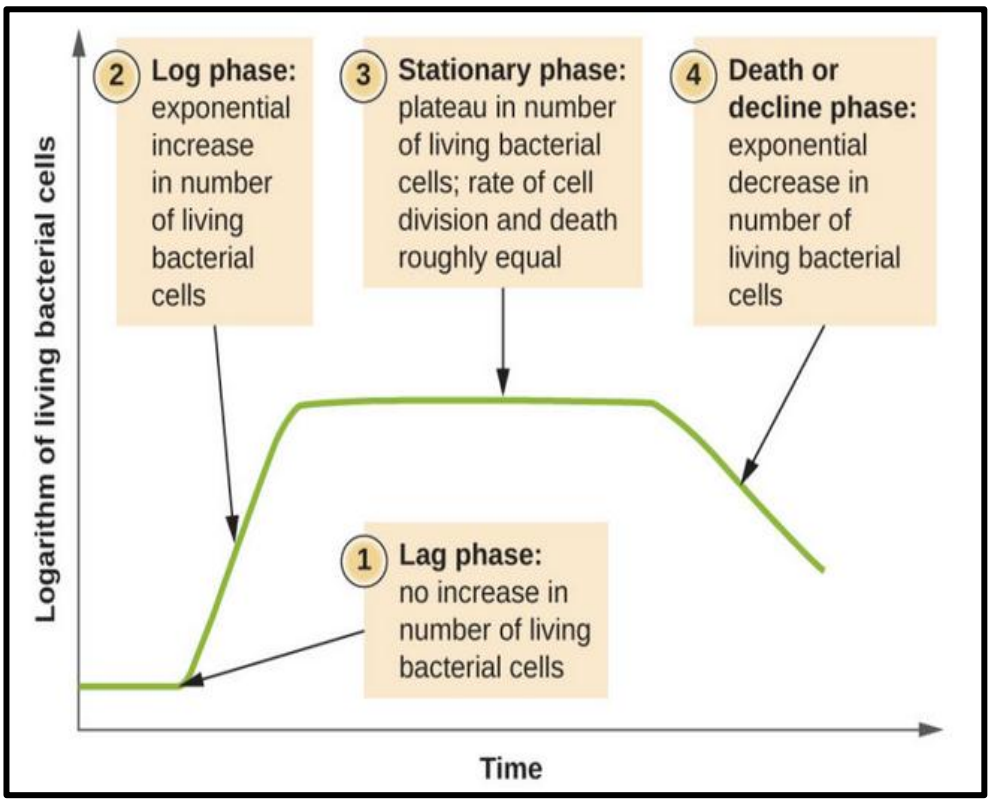


Figure : Bacterial Growth Curve

Phases of Bacterial Growth Curve:

The bacterial growth curve can be divided into four major phases: lag phase, exponential or log (logarithmic) phase, stationary phase and decline phase.

These phases reflect the physiologic state of the organisms in the culture at that particular time.

1. Lag phase: When microorganisms are introduced into fresh culture medium, usually no immediate increase in cell number occurs, and therefore this period is called the **lag phase**. After inoculation, there is an increase in cell size at a time when little are no cell division is occurring. During this time, however, the cells are not dormant. This initial period is the time required for adaptation to the new environment, during which the necessary enzymes and metabolic intermediates are built up in adequate quantities for multiplication to proceed.

2. Log (logarithmic) or exponential phase: Following the lag phase, the cells start dividing and their numbers increase exponentially with time.

3.Stationary phase: After a varying period of exponential growth, cell division stops due to depletion of nutrients and accumulation of toxic products. Eventually growth slows down, and the total bacterial cell number reaches a maximum and stabilizes. The number of progeny cells formed is equal to the number of cells that die.

4. Decline or death phase: The death phase is the period when the population decreases due to cell death. Cell death may also be caused by autolysis besides nutrient deprivation and build-up of toxic wastes.

Control of Microorganisms

Control of microorganisms is essential in order to:

1. Prevent the transmission of diseases and infection,
2. Stop decomposition and spoilage,
3. Prevent unwanted microbial contamination.

Microorganisms are controlled by means of **physical agents** and **chemical agents.**

Physical agents: include such methods of control as **high or low temperature**, **desiccation, osmotic pressure, radiation,** and **filtration.**

chemical agents: refers to the use of **disinfectants, antiseptics, antibiotics,** and **chemotherapeutic antimicrobial chemicals.**

Basic terms used in discussing the control of microorganisms include:

- **Sterilization:** is the process of destroying all living microorganisms.
- **Disinfection:** is the elimination of microorganisms, but not necessarily endospores, from inanimate objects or surfaces.
- **Disinfectant:** is an agents used to disinfect inanimate objects but generally to toxic to use on human tissues.
- **Antiseptic:** is an chemical agent that kills or inhibits growth of microbes but is safe to use on human tissue.
- **Sanitizer**: is an agent that reduces microbial numbers to a safe level.
- **Cidal:** An agent that is cidal in action will kill microorganisms.
- **Static:** An agent that is static in action will inhibit the growth of microorganisms.
- **Cleaning:** Cleaning is removal of visible soil (e.g., organic and inorganic material) from objects and surfaces. It is normally accomplished manually or mechanically using water with detergents or enzymatic products.
- **Decontamination:** Decontamination removes pathogenic microorganisms from objects so they are safe to handle, use, or discard.

I- Physical Methods:

Physical Methods include the application of high temperatures, low temperatures, radiation, filtration, and desiccation (drying). Many of these methods nonspecifically kill cells by **disrupting membranes**,

changing membrane permeability, or damaging proteins and nucleic acids by denaturation, degradation, or chemical modification.

A. High Temperatures:

High Temperatures usually lead to **cidal action**, since they **denature microbial enzymes** and other **proteins.** High temperature may be applied as either **moist heat** or **dry heat.**

1- **Moist heat** : is generally more effective than dry heat for killing microorganisms because of its ability to **penetrate microbial cells** and causes **coagulation and denaturation of proteins**.

i. **Temperature below 100°C:** The process of heating a liquid food or beverage either at 63°C for 30 minutes or 72°C for 15 seconds to enhance their shelf life and destroy harmful microorganisms.

- **Pasteurization of milk,** pasteurization process kills only vegetative cells but not the spores, at **63**°C for **30** minutes.
- **Vaccine bath:** (vaccine sterilization)
- **Serum bath:** (serum contaminants, does not kill spores survive)
- **Inspissation:** (egg and serum containing media, can kill spores)

ii. At a temperature of 100°C: Boiling at 100°C is a moist heat for the removal of pathogenic vegetative microbes and some spores.

- **Tyndallization:** is a method that is used for sterilization of media with sugar and gelatin at 100°C for 30 minutes on three successive days so as to preserve sugar which might be decomposed at a higher temperature.
- Moist heat at 100°C is applicable for contaminated dishes, beddings, pipettes, and other instruments that are not soiled or contaminated as well as for objects that are temperature sensitive.

iii. At temperatures above 100°C: Moist heat sterilization above 100°C involves sterilization by **steam under pressure** by using **autoclave** for destroy bacterial endospores.

- The temperature used in is 121°C at 15 lbs (pounds) pressure for 15 minutes.
- Autoclaves are used for the sterilization of contaminated instruments, culture media, dressings, solutions, syringes, etc.

2- **Dry heat:** kills microorganisms through a process of protein oxidation rather than protein coagulation. Include:

i. **Red Heat:** By using Bunsen burner flame, commonly used for sterilization of instruments like incubation loops, wires, and points of forceps till they become red hot.

ii. **Flaming:** Materials are passed through the flame of a bunsen burner without allowing them to become red hot. Glass slides, scalpels, Mouths of culture tubes.

iii. **Incineration:** This is an excellent method for destroying materials such as contaminated clothes, cotton wool stoppers, animal carcasses and pathological materials. It involves burning of materials in incinerators.

iv. **Hot air oven:** Hot air oven is a method of dry heat sterilization which allows the sterilization of objects that cannot be sterilized by moist heat. The commonly-used temperatures and time that hot air ovens need to sterilize materials are **170°C for 40** minutes, **160°C for 60 minutes**, and **20 minutes at 180°C**

Uses of Hot Air Oven for Sterilization of:

1. Glassware like glass syringes, petri dishes, pipettes and test tubes.
2. Surgical instruments like scalpels, scissors, forceps etc.
3. Chemicals like liquid paraffin, fats etc.

B. Low Temperature:

Low temperature inhibits microbial growth by slowing down microbial metabolism. Examples include refrigeration and freezing. Refrigeration at 5°C slows the growth of microorganisms and keeps food fresh for a few days. Freezing at -10°C stops microbial growth, but generally does not kill microorganisms, and keeps food fresh for several months.

C. Desiccation:

Desiccation, or drying, generally has a static effect on microorganisms. Lack of water inhibits the action of microbial enzymes. Dehydrated foods, for example, do not require refrigeration because the absence of water inhibits microbial growth.

D. Osmotic Pressure:

Adding high concentration of salt or sugar to a solution creates a hyperosmotic solution that can draws out the water from the microorganism cells which kills the microbes through plasmolysis. This technique is used for preserving jellies, jams, syrups, pickles, etc.

E. Radiation:

Radiations are very effective methods for sterilization. It can **penetrate the objects deeply and can sterilize it**. Disadvantages of radiations includes its complexity and need of specialized people for using these techniques. It can be fatal if not used properly. Radiation depending on its **wavelength, intensity** and **duration of exposure**.

Radiation Types:

Non-ionizing: uses longer wavelength and lower energy.

Non Ionizing radiations such as Infrared radiation and UV radiation.

- **UV Radiation** is used to sterilize hospitals, operating theatre and laboratories.
- **Infrared Radiation** is used for rapid mass sterilization of syringes and catheters.

Ionizing radiation: is the use of short wavelength, high-intensity radiation to destroy microorganisms. Ionizing radiations such as Gamma rays, and X rays.

- **Gamma rays** are used in sterilization of disposable petri dishes, plastic syringes, antibiotics, vitamins, hormones and fabrics.
- **X rays** are used in sterilization of instruments such as syringes, gloves, dressing packs, foods and pharmaceuticals.

F. Filtration:

Microbiological membrane filters provide a useful way of sterilizing materials such as vaccines, antibiotic solutions, animal sera, enzyme solutions, vitamin solutions, and other solutions that may be damaged or denatured by high temperatures or chemical agents. The filters contain pores small enough to prevent the passage of microbes and allow the organism-free fluid to pass through. The liquid is then collected in a sterile flask.

II- Chemical Methods:

Chemical Sterilization is the process of removal of microorganisms by the use of chemical bactericidal agents. **Chemicals** - many of these are called **antiseptics** or **disinfectants** or both.

The chemical method of sterilization can be categorized as **liquid** , **gaseous** sterilization, **antibiotics,** and **chemotherapeutic.**

1.Gaseous sterilization involves the process of exposing equipment or devices to different gases in a closed heated or pressurized chamber.

2.Liquid sterilization is the process of sterilization which involves the submerging of equipment in the liquid sterility to kill all viable microorganisms and their spores.

Chemical Compounds Commonly Used as Antiseptics and Disinfectants

Compound	Type of Action	Applications
Hydrogen peroxide (3%)	Disinfectant/antiseptic	External surfaces, live tissue
Hypochlorites (0.5%) (Chlorox)	Disinfectant	External surfaces, non-living
Iodine (1% in 70% alcohol)	Disinfectant/antiseptic	External surfaces, live tissue
Iodophors	Disinfectant/antiseptic	External surfaces, live tissue, surgical scrub
Lysol (5%)	Disinfectant	External surfaces, non-living
Phenol (5%)	Disinfectant	External surfaces, non-living
Hexachlorophene (pHisohex)	Disinfectant/antiseptic	External surfaces, live tissue surgical scrub
Formaldehyde (4%)	Disinfectant	External surfaces, non-living
Zephrin and other quaternary ammonium compounds	Disinfectant	Exernal surfaces, non-living
Alcohol (ethyl or isopropyl at 70%)	Disinfectant/antiseptic	External surfaces, unbroken skin
Organic mercury (merthiolate, mercurochrome)	Disinfectant/antiseptic	External surfaces
Potassium permanganate	Antiseptic	superficial skin fungus infections
Silver nitrate (1%)	Antiseptic	prevent newborn eye infections
Ethylene oxide gas (12%)	Sterilizing disinfectant	Linens, heat labile plastics
Glutaraldehyde	Sterilizing disinfectant	metal instrument sterilization
Formaldehyde (20% in alcohol)	Sterilizing disinfectant	metal instrument sterilization
Hydrogen peroxide (3%)	Disinfectant/antiseptic	External surfaces, live tissue
Hypochlorites (0.5%) (Chlorox)	Disinfectant	External surfaces, non-living

3.Chemotherapeutic (Antimicrobial Chemicals):

Antimicrobial chemotherapy is the use of chemicals to inhibit or kill microorganisms in or on the host. Chemotherapy is based on **Selective Toxicity**. This means that the agent used must **inhibit or kill the microorganism** in question **without seriously harming the host**.

Based on their origin, there are 2 general classes of antimicrobial chemotherapeutic agents:

I. Antibiotics: substances produced as metabolic products of one microorganism which inhibit or kill other microorganisms.

Ex: a. **Penicillins** (produced by the mold *Penicillium*)

b. **Cephalosporins** (produced by the mold *Cephalosporium*)

c. Nystatin (produced by the bacterium *Streptomyces*), and others.

II. Antimicrobial chemotherapeutic chemicals: chemicals synthesized in the laboratory which can be used therapeutically on microorganisms.

Ex: **Fluoroquinolones**, **Metronidazole**, **Sulfonamides and Trimethoprim**, etc.

There are a number of factors which influence the antimicrobial action of disinfectants and antiseptics, including:

1. The **concentration** of the chemical agent.

2. The **temperature** at which the agent is being used. Generally, the lower the temperature, the longer it takes to disinfect or decontaminate.

3. The **kinds of microorganisms** present. Endospore producers such as *Bacillus* species, *Clostridium* species, and acid-fast bacteria like *Mycobacterium tuberculosis* are harder to eliminate.

4. The **number of microorganisms** present. The more microorganisms present, the harder it is to disinfect or decontaminate.

5. The **nature of the material bearing the microorganisms**. Organic material such as dirt and excreta interferes with some agents.

There are 2 common antimicrobial modes of action for disinfectants, antiseptics, and sanitizers:

1. They may **damage the lipids and/or proteins of the semipermeable cytoplasmic membrane** of microorganisms resulting in **leakage of cellular materials** needed to sustain life.

2. They may **denature microbial enzymes and other proteins,** usually by disrupting the hydrogen and disulfide bonds that give the protein its three-dimensional functional shape. This **blocks metabolism**.

Some Microbial Diseases Unite

Respiratory System infections

The principal function of the respiratory tract is gas exchange. It is therefore constantly exposed to the gaseous environment, including particulate microbes, such as **bacteria, viruses and fungal spores.**

The respiratory system is divided into two main components:

Upper respiratory tract: Composed of **Nose and nasal cavity, Sinuses ,epiglottis, pharynx, and larynx,** the organs of the upper respiratory tract are located **outside the chest cavity**.

Lower respiratory tract: Composed of **trachea**, **lungs**, and all segments of the **bronchial tubes (including Bronchioles and alveoli)**, the organs of the lower respiratory tract are located **inside the chest cavity.**

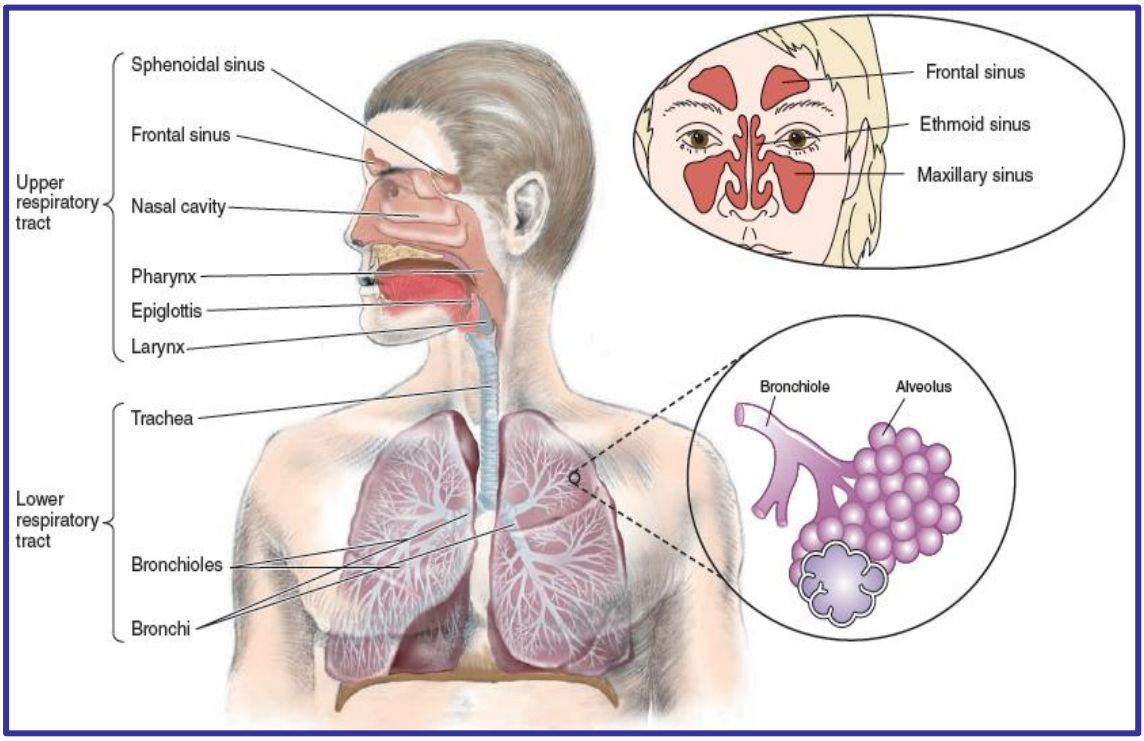


Figure: Respiratory System Parts

Upper Respiratory Infections:

Common Cold, Sinusitis, Pharyngitis and Tonsillitis**, Epiglottitis and Laryngotracheitis.**

Etiology*:** Most upper respiratory infections are of **viral etiology.** Epiglottitis and laryngotracheitis are exceptions with severe cases likely caused by ***Haemophilus influenzae type b. Bacterial pharyngitis is often caused by ***Streptococcus pyogenes.***

***Pathogenesis*:** Organisms gain entry to the respiratory tract by inhalation of droplets and invade the mucosa. Epithelial destruction may ensue, along with redness, edema, hemorrhage and sometimes an exudate.

***Clinical Manifestations*:** Initial symptoms of a cold are runny, stuffy nose and sneezing, usually without fever. Other upper respiratory infections may have fever. Children with epiglottitis may have difficulty in breathing, muffled speech, drooling and stridor. Children with serious laryngotracheitis (croup) may also have tachypnea, stridor and cyanosis.

Table of Summarized of Upper Respiratory Infections

Disease	Define	Causative agent	
		Viruses	**Bacteria**
Common Cold	Or called (**Rhinitis**) Inflammation of the mucous membranes that line the nose.	*Rhinoviruses* *Adenoviruse* *Coronaviruses* *Parainfluenza viruses* *Influenza Viruses* *Respiratory syncytial virus* *Coxsackie A viruses*	Rare
Sinusitis	Inflammation of the membranes lining the sinuses.	Rare	*Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.
Pharyngitis and tonsillitis	is an inflammation of the pharynx and tonsils involving lymphoid tissues , are associated with pharyngeal pain (sore throat) and the clinical appearance of erythema and swelling of the affected tissues.	*Adenoviruses, Parainfluenza viruses, Influenza viruses, Rhinoviruses, Coxsackie A Or B Virus, Herpes simplex virus, Epstein-Barr virus*	*Streptococcus pyogenes* *Corynebacterium diphtheria* *Staphylococcus aureus,* *Haemophilus influenzae* (usually in infants)
Epiglottitis	Inflammation of the upper airway in epiglottis and other soft tissues above the vocal cords.	Rare	*Haemophilus influenzae,* *Streptococcus pneumoniae,* *Corynebacterium diphtheriae,* *Neisseria meningitidis*
Laryngotracheitis	Inflammation of the upper airway is localized to the laryngeal structures, including the vocal cords. It sometimes extends to the trachea (laryngotracheitis)	*Parainfluenza virus* (most common) *Influenza virus* *Respiratory syncytial virus* *Adenoviruses*	*Haemophilus influenzae* *Staphylococcus aureus*

Lower Respiratory Infections:

Bronchitis, Bronchiolitis and Pneumonia

Etiology*:** Causative agents of lower respiratory infections are **viral or bacterial.** Viruses cause most cases of bronchitis and bronchiolitis. In community-acquired pneumonias, the most common bacterial agent is ***Streptococcus pneumoniae. Atypical pneumonias are cause by such agents as ***Mycoplasma pneumoniae***, ***Chlamydia spp, Legionella, Coxiella burnetti*** and viruses.

***Pathogenesis*:** Organisms enter the distal airway by inhalation, aspiration or by hematogenous seeding. The pathogen multiplies in or on the epithelium, causing inflammation, increased mucus secretion, and impaired mucociliary function; other lung functions may also be affected. In severe bronchiolitis, inflammation and necrosis of the epithelium may block small airways leading to airway obstruction.

***Clinical Manifestations*:** Symptoms include cough, fever, chest pain, tachypnea and sputum production. Patients with pneumonia may also exhibit non-respiratory symptoms such as confusion, headache, myalgia, abdominal pain, nausea, vomiting and diarrhea.

Table of Summarized of Lower Respiratory Infections

Disease	Define	Causative agent	
		Viruses	**Bacteria and Fungi**
Bronchitis and Bronchiolitis	**Bronchitis and bronchiolitis** involve inflammation of the bronchial tree. **Bronchitis** is usually preceded by an upper respiratory tract infection or forms part of a clinical syndrome in diseases such as influenza, rubella, pertussis, scarlet fever and typhoid fever. **Bronchiolitis** is a viral respiratory disease of infants and is caused primarily by *Respiratory syncytial virus.*	*Parainfluenza viruses, Influenza viruses, Respiratory syncytial virus, Adenoviruses, Measles*	*Bordetella pertussis, Haemophilus influenzae Mycoplasma pneumoniae Chlamydia pneumonia*e
Pneumonia	An infection and resulting inflammation deep in the lungs, affecting the small air sacs (alveoli) and nearby tissue.	*Influenza viruses, Respiratory syncytial virus, Rhinoviruses*	*The most common cause of* ***bacterial pneumonia*** *is* ***Streptococcus pneumoniae.*** *Other bacteria are:* *Mycoplasma pneumoniae* *Haemophilus influenzae* *Legionella pneumophila* *Mycobacterium tuberculosis* can cause pneumonia. ***Fungal pneumonia*** *Pneumocystis jirovecii, Cryptococcus species, Histoplasmosis species*

Types of pneumonia:

Pneumonia can also be classified according to where or how it was acquired.

1) **Hospital-acquired pneumonia (HAP)**

This type of bacterial pneumonia is acquired during a hospital stay. It can be more serious than other types, as the bacteria involved may be more resistant to antibiotics.

2) **2Community-acquired pneumonia (CAP)**

Community-acquired pneumonia (CAP) refers to pneumonia that's acquired outside of a medical or institutional setting.

3) **Ventilator-associated pneumonia (VAP)**

When people who are using a ventilator get pneumonia, it's called VAP.

4) **Aspiration pneumonia**

Aspiration pneumonia happens when inhale bacteria into lungs from food, drink, or saliva. This type is more likely to occur if found swallowing problem or resultant to use of certain medications, alcohol, or other drugs.

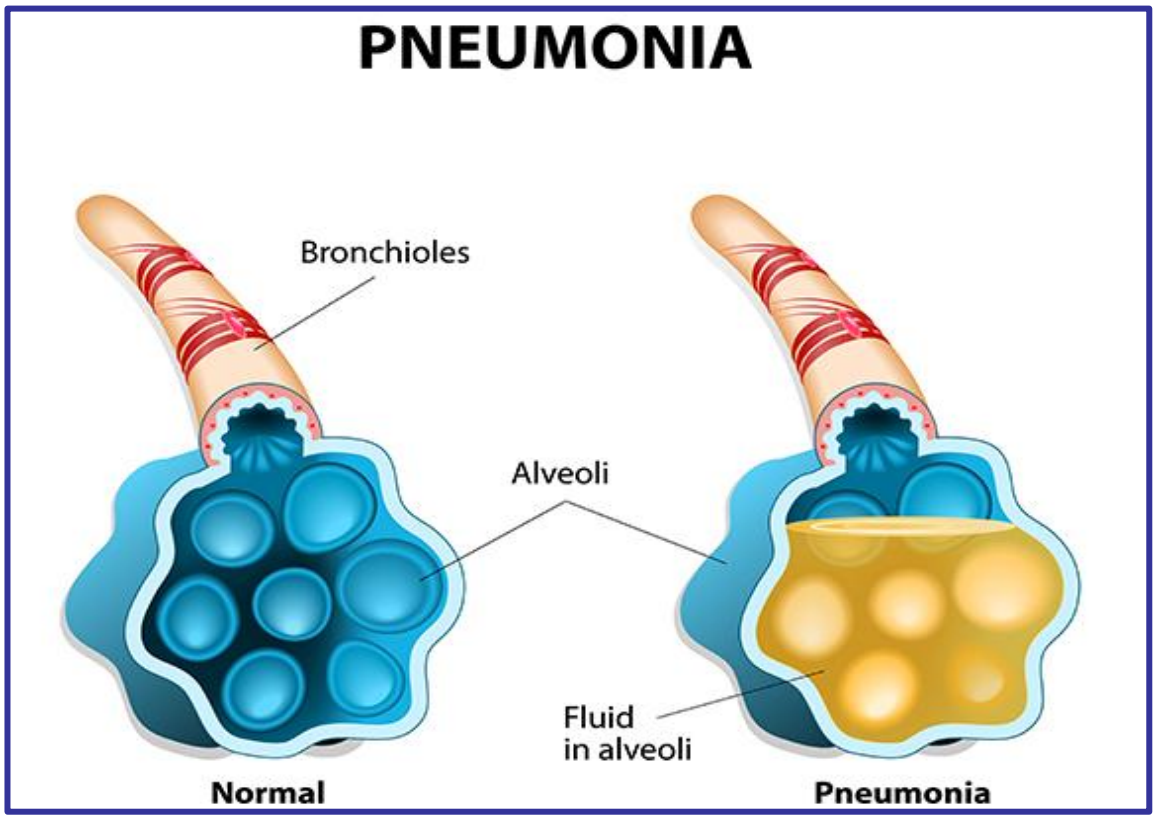


Figure: Pneumonia

Gastrointestinal Tract Infections and Food Poisoning

Gastrointestinal tract infections (Gastroenteritis):

Gastroenteritis is the inflammation of the gastrointestinal tract (GI) which is composed of stomach and intestines(small and large intestines). GI disease may be caused by many different types of **bacteria, viruses, and parasites.**

Mode of Transmission and Infection:

Acquisition may be **foodborne, waterborne, or via person-to-person spread**. Infections of the gastrointestinal tract can be grouped into those that remain localized in the gut and those that invade beyond the gut to cause infection in other sites in the body. In order to spread to a new host, pathogens are excreted in large numbers in the faeces and must survive in the environment for long enough to infect another person directly or indirectly through contaminated food or fluids.

Clinical Manifestations:

The clinical symptoms are nearly identical. Symptoms include **anorexia, nausea, vomiting, diarrhea, and abdominal discomfort.**

Clinical Basic Terms:

Diarrhea: Abnormal faecal discharge characterized by frequent and/or fluid stool; usually resulting from disease of the small intestine and involving increased fluid and electrolyte loss.

Bloody diarrhea: diarrhea in which there is macroscopically visible blood in afresh specimen.

Dysentery: An inflammatory disorder of the gastrointestinal tract often associated with blood and pus in the faeces and accompanied by symptoms of pain, fever, abdominal cramps; usually resulting from disease of the large intestine

Enterocolitis: Inflammation involving the mucosa of both the small and large intestine.

Food borne illness: any disease of microbial origin caused by, or thought to be caused by, the consumption of food or water.

Dehydration: define as an imbalance of fluids resulting from excessive fluid loss (as in vomiting and diarrhea) or inadequate fluid intake (due to nausea or loss of appetite).

- ***Note:** Diarrhea without blood and pus is usually the result of enterotoxin production, whereas the presence of blood and/or pus cells in the faeces indicates an invasive infection with mucosal destruction.*

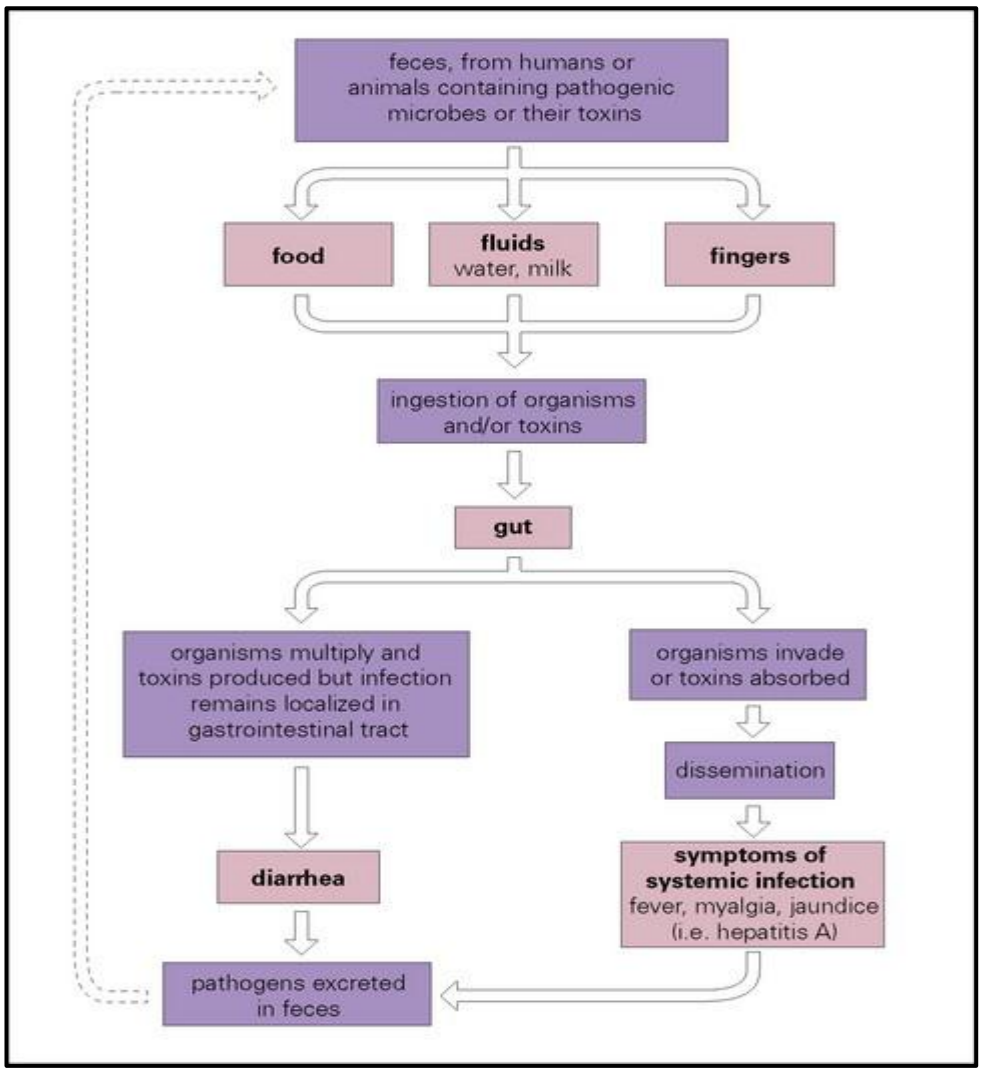


Figure: Mode of Transmission and Infection

Etiology of Gastrointestinal tract infections:

Viruses including ***Rotavirus,Adenovirus, Astrovirus, Enterovirus, Norovirus, Hepatitis A, Caliciviruses.***

Bacteria including ***Campylobacter jejuni, Clostridium difficile, E. coli, Helicobacter pylori, Salmonella, Staphylococcus aureus, Yersinia enterocolitica.***

Parasites including ***Cryptosporidium parvum, Entamoeba histolytica, Giardia lamblia.***

Bacteria cause gastroenteritis by several mechanisms:

1-Enterotoxins: are produced by certain species (eg, ***Vibrio cholerae***, enterotoxigenic strains of ***E. coli***, ***Clostridium*** *difficile*) that adhere to intestinal mucosa without invading. These toxins impair intestinal absorption and cause secretion of electrolytes and water by, resulting in watery diarrhea.

2-Exotoxins: that are ingested in contaminated food are produced by some bacteria (eg, *Staphylococcus aureus*, ***Bacillus cereus,*** *Clostridium perfringens*). The exotoxin can cause gastroenteritis without bacterial infection. These toxins generally cause acute nausea, vomiting, and diarrhea within 12 hours of ingestion of contaminated food.

3-Mucosal invasion: occurs with other bacteria (eg, *Shigella*, *Salmonella*, *Campylobacter*, ***Clostridium difficile*****, some** *Escherichia coli* subtypes) that invade the mucosa of the small bowel or colon and cause microscopic ulceration, bleeding, exudation of protein-rich fluid, and secretion of electrolytes and water.

Bacterial Gastroenteritis:

1-Escherichia coli infection:

The gram-negative rod *Escherichia coli* is a common member of the normal gut flora of the colon. Although the vast majority of *E. coli* strains are helpful commensal bacteria, some can be pathogenic and may cause dangerous diarrheal disease.

Source of infection: Undercooked meat,Lettuce, sprouts and other vegetables, Unpasteurized milk, Fruit juices.

Pathogenic group *E. coli*	
Enteropathogenic *E. coli* (EPEC)	causes watery diarrhea. Cause sporadic cases and outbreaks of infection in babies and young children .
Enterotoxigenic *E. coli* (ETEC)	produces two toxins (one similar to cholera toxin) that cause watery diarrhea and heat-labile toxins. This subtype is lso known as traveler's diarrhea in people visiting the developing world.
Enterohaemorrhagic*E. coli* (EHEC)	is the most clinically significant subtype in the US. It produces Shiga toxin, which causes bloody diarrhea (hemorrhagic colitis). Thus, these subtypes are sometimes termed Shiga toxin–producing *E. coli* (STEC).
Enteroinvasive *E. coli* (EIEC)	causes bloody or non bloody diarrhea, primarily in the developing world.
Enteroaggregative *E. coli* (EAEC)	causes diarrhea of lesser severity but longer duration than the other subtypes.

2-Salmonellosis:

Salmonella gastroenteritis, also called **salmonellosis**, is caused by the rod-shaped, gram-negative bacterium *Salmonella*. Two species, ***S. enterica*** **and** ***S. bongori***, cause disease in humans, but *S. enterica* is the most common. The most common serotypes of *S. enterica* are Enteritidis and Typhi.

However, salmonellosis is caused by exogenous agents, and infection can occur depending on the serotype, size of the inoculum, and overall health of the host.

- **Source of infection:** Infection is caused by ingestion of contaminated food, handling of eggshells, or exposure to certain animals. *Salmonella* is part of poultry's microbiota, so exposure to raw eggs and raw poultry can increase the risk of infection.

Typhoid Fever

Certain serotypes of *S. enterica*, primarily serotype Typhi (***S. typhi***) and (***S.paratyphi***), cause a more severe type of salmonellosis called **typhoid fever**. This serious illness, causes high fever, body aches, headache, nausea, lethargy, and a possible rash.

Some individuals carry ***S. typhi*** without presenting signs or symptoms (known as asymptomatic carriers) and continually shed them through their feces. These carriers often have the bacteria in the gallbladder or intestinal epithelium.

- **Source of infection:** Individuals consuming food or water contaminated with these feces can become infected.

3-Shigellosis (Bacillary Dysentery): When gastrointestinal illness is associated with the rod-shaped, gram-negative bacterium *Shigella*, it is called **bacillary dysentery**, or **shigellosis**. Infections can be caused by ***S. dysenteriae, S. flexneri, S. boydii,*** **and** ***S. sonnei*** that colonize the GI tract.

- **Source of infection:** Shigellosis can be spread from hand to mouth or through contaminated food and water. Most commonly, it is transmitted through the fecal-oral route.

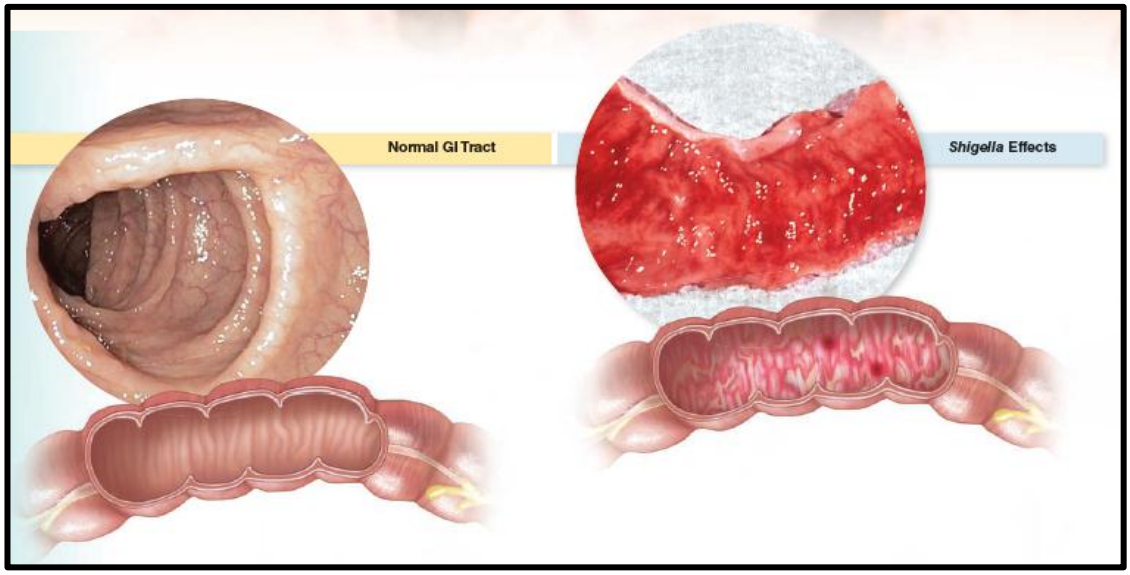


Figure: The appearance of the large intestinal mucosa in *Shigella* dysentery.

4- Cholera and Other Vibrios:

The gastrointestinal disease **cholera** is a serious infection It is caused by ***Vibrio cholerae*** serotype O1, a gram-negative, flagellated bacterium in the shape of a curved rod (vibrio). Because *V. cholerae* is killed

by stomach acid, relatively large doses are needed for a few microbial cells to survive to reach the intestines and cause infection. Diarrhea is so profuse that it is often called "rice water stool,". The motile cells travel through the mucous layer of the intestines, where they attach to epithelial cells and release **cholera enterotoxin.**

- **Source of infection:** often associated with poor sanitation, especially following natural disasters, because it is spread through contaminated water and food that has not been heated to temperatures high enough to kill the bacteria.

V. parahemolyticus is causes gastrointestinal illness with signs and symptoms such as watery diarrhea, nausea, fever, chills, and abdominal cramps. The bacteria produce a heat-stable hemolysin, leading to **dysentery** and possible disseminated disease.

- **Source of infection:** is associated with consumption of contaminated seafood.

5-*Campylobacter jejuni* Gastroenteritis:

Campylobacter is a genus of gram-negative, spiral or curved bacteria. They may have one or two flagella.

***Campylobacter jejuni* gastroenteritis**, a form of campylobacteriosis, is a widespread illness that is caused by ***Campylobacter jejuni*.**

- **Source of infection:** The primary route of transmission is through poultry that becomes contaminated during slaughter. Handling of the raw chicken in turn contaminates cooking surfaces, utensils, and other foods. Unpasteurized milk or contaminated water are also potential vehicles of transmission. In most cases, the illness is self-limiting and includes fever, diarrhea, cramps, vomiting, and sometimes dysentery. More serious signs and symptoms, such as bacteremia, meningitis, pancreatitis, cholecystitis, and hepatitis, sometimes occur.

6-Peptic Ulcers:

The gram-negative bacterium ***Helicobacter pylori*** is able to tolerate the acidic environment of the human stomach and has been shown to be a major cause of **peptic ulcers**, which are ulcers of the stomach or duodenum. The bacterium is also associated with increased risk of stomach cancer . According to the CDC, approximately two thirds of the population is infected with *H. pylori*, but less than 20% have a risk of developing ulcers or stomach cancer.

H. pylori colonizes epithelial cells in the stomach using pili for adhesion. These bacteria produce urease, which stimulates an immune response and creates ammonia that neutralizes stomach acids to provide a more suitable microenvironment.

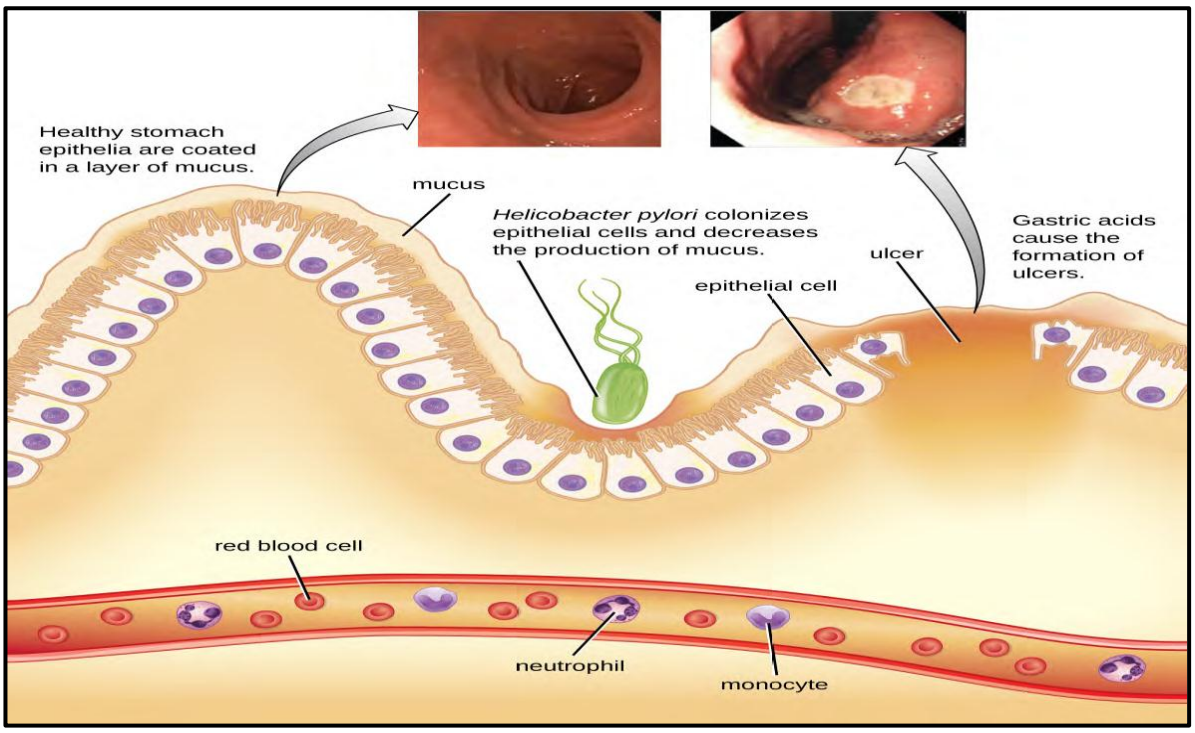


Figure: *Helicobacter* infection decreases mucus production and causes peptic ulcers

***7-Clostridium perfringens* Gastroenteritis:**

Clostridium perfringens is a gram-positive, rod-shaped, endospore-forming anaerobic bacterium that is tolerant of high and low temperatures. At high temperatures, the bacteria can form endospores that will germinate rapidly in foods or within the intestine.

- **Source of infection:** is associated with undercooked meats and other foods.

8-Clostridium difficile:

Clostridium difficile is a gram-positive rod that can be a commensal bacterium as part of the normal microbiota of healthy individuals. When the normal microbiota is disrupted by long-term antibiotic use, it can allow the overgrowth of this bacterium, resulting in **antibiotic-associated diarrhea** caused by *C. difficile*.

Infections begin with focal necrosis, then ulceration with exudate, and can progress to **pseudomembranous colitis**, which involves inflammation of the colon and the development of a pseudomembrane of fibrin containing dead epithelial cells and leukocytes**.**

***9-Yersinia* Gastroenteritis:**

The genus *Yersinia* a gram-negative rod that causes the gastroenteritis. However, ***Y. enterocolitica* and *Y. pseudotuberculosis*** can cause gastroenteritis. Intoxication can also result because of the activity of its endotoxin and exotoxins (enterotoxin and cytotoxin).

- **Source of infection:** The infection is generally transmitted through the fecal-oral route, with ingestion of food or water that has been contaminated by feces.

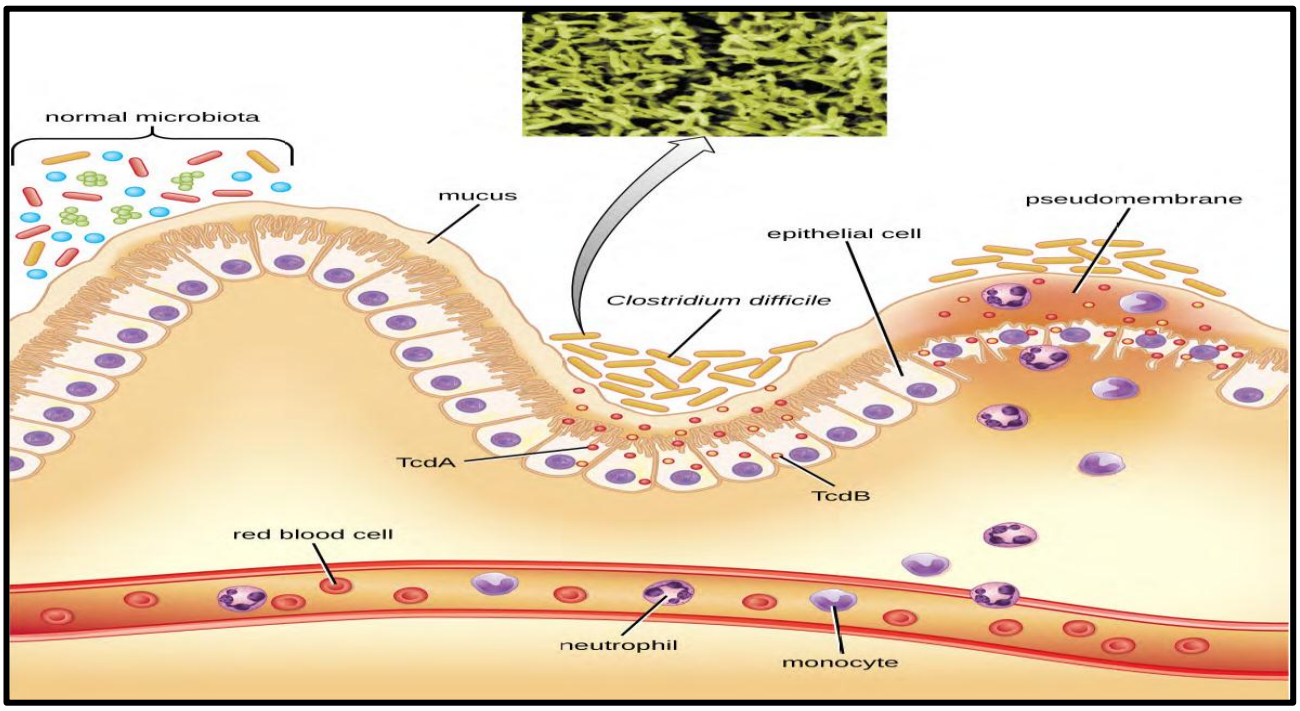


Figure: *Clostridium difficile* is able to colonize the mucous membrane of the colon when the normal microbiota is disrupted.

Bacterial Gastroenteritis		
Organism	**Clinical Syndrome**	**Pathogenic Mechanism or Virulence Factors**
Salmonella serotypes	Dysentery	Mucosal invasion
Salmonella Typhi	Enteric fever	Penetration, spread
Shigella spp.	Dysentery	Endotoxin, enterotoxin, shiga toxins in some strains
Shigella dysenteriae (Shiga)	Dysentery	Mucosal invasion, Endotoxin
Campylobacter jejuni	Dysentery	Adhesions, exotoxin, induction of autoimmunity
Escherichia coli (EIEC)	Dysentery	Mucosal invasion
E coli (ETEC)	Dysentery	Enterotoxins
E coli (EHEC)	Watery diarrhea	Enterotoxins
E coli (EPEC)	Watery diarrhea	Adherence
E coli (EAEC)	Chronic diarrhea	Shiga toxins, Adherence
Vibrio cholerae	Watery diarrhea	Cholera toxin (CT)
Vibrio parahaemolyticus	Watery diarrhea	heat-stable hemolysin
Yersinia enterocolitica ***Y. pseudotuberculosis***	Enteric fever	Penetration, spread, enterotoxin and cytotoxin
Clostridium difficile	Dysentery	Enterotoxins , Cytotoxins
Clostridium perfringens	Watery diarrhea	Enterotoxins
Helicobacter pylori	Peptic ulcers	Endotoxin

Food Poisoning:

Food poisoning occurs after consumption of food containing toxins, which may be chemical (e.g. heavy metals) or bacterial in origin. The bacteria multiply and produce toxins within contaminated food. The organisms may be destroyed during food preparation, but the toxin is unaffected, consumed and acts within hours.

Symptoms of Food Poisoning:

- ☒ Nausea
- ☒ Vomiting
- ☒ Diarrhea or bloody diarrhea
- ☒ Abdomen pain (Crampy pains)
- ☒ Feeling weak
- ☒ Fever or chills/sweating
- ☒ Headache

Causes Food Poisoning:

1- Infections with microbes—**viruses**, **bacteria**, and **parasites**—cause most food poisoning.

2- Harmful chemicals also cause some cases of food poisoning (lead or cadmium).

Bacterial Caused food poisoning:

It is of two types summarized in below table:

Toxic type. **2- Infection type.**

Table summarized Bacterial Caused food poisoning

Etiology	Incubation Period	Clinical Findings	Characteristic Foods or Source of Bacteria	Virulence Factors
Toxic type: In this type, the disease follows ingestion of food with preformed toxin.				
Bacillus cereus (gram^{+}, aerobic, rod)	1-6 h	Vomiting, diarrhea	Rice, meat, vegetables	1- diarrheal toxin (enterotoxin) 2-vomiting toxin (neurotoxins) Heat-stable toxin, heat-labile toxin
Clostridium botulinum (gram+, anaerobic, rod)	12-72 h	Neuromuscular paralysis	Improperly preserved vegetables, meat, fish	botulinum toxin Heat-stable toxin
Staphylococcus aureus (gram+, aerobic, coccus)	2-4 h	Vomiting	Meats, custards, salads	Heat-stable exotoxin
Infection type: In this type, multiplication of bacteria occurs *in vivo* when infective doses of microorganisms are ingested with food and release the toxin in the bowel.				
Clostridium perfringens (gram^{+}, anaerobic, rod)	9-15 h	Watery diarrhea	Meat, poultry	Enterotoxin- heat-labile
***Salmonella* Spp** (Gram –ve, rods, Facultative aerobic)	6-48 h	Dysentery	Poultry, eggs, meat	Adhesins, endotoxin
***Shigella* Spp** (Gram –ve, rods, Facultative aerobic)	12-48 h	Dysentery	Contaminated Food and water	Endotoxin,enterotoxin, shiga toxins in some strains.
Vibrio parahaemolyticus (Gram –ve, vibrio, Facultative aerobic)	10-24 h	Watery diarrhea	Shellfish	Powerful enterotoxin

Hospital-Acquired Infection

Hospital Acquired Infections (HAIs) or Nosocomial Infections:

The terms *hospital infection, hospital-acquired infection* or *nosocomial infection* (from *nosocomeion,* meaning hospital) defined as**: the infections acquired in hospital by a patient.**

Microorganisms Implicated in HAIs:

I- ESKAPE pathogens—They are the multidrug resistant isolates present in a hospital, such as ***E****nterococcus faecium,* ***S****taphylococcus aureus,* ***K****lebsiella pneumoniae,* ***A****cinetobacter baumannii,* ***P****seudomonas aeruginosa,* ***E****nterobacter* species.

II- Other common infections that can spread in hospitals include:

- *Escherichia coli,* Nosocomially acquired *M. tuberculosis, Legionella pneumophila, Candida albicans*
- *Clostridium difficile* diarrhea.
- Blood borne infections (BBIs) transmitted through contaminated needle prick injury or mucocutaneous exposure of blood include- HIV, hepatitis B and C viruses.

Sources of infections:

Hospital infection may be exogenous or endogenous in origin.

A. Exogenous:

Exogenous source may :

1. **Contact with other patients and staff. (cross-infection)**

2. **Environmental sources:** These include inanimate objects, air, water and food in the hospital. **(environmental infection)**

B. Endogenous:

A high proportion of clinically apparent hospital infections are endogenous **(self-infection),** the infecting organism being derived from the patient's own skin, gastrointestinal or upper respiratory flora.

Factors Influencing Hospital Associated Infections:

1. **Age:** Natural resistance to infection is lower in infants and the elderly.

2. **Susceptibility to infection:** Preexisting disease, such as diabetes, or other conditions, and the medical or surgical treatment, including immunosuppressive drugs, radiotherapy or splenectomy, may also reduce the patient's natural resistance to disease.

3. **Hospital environment:** Patients shed pathogen from their bodies; hospital personnel spread them through their hands and clothes. Equipment may be contaminated. Pathogens are present in the hospital

dust and air, and sometimes even in antiseptic. Contamination of hospital food or water may cause outbreaks of infections.

4. **Diagnostic or therapeutic procedures.**

5. **Drug-resistance:** The hospital microbial flora is usually multidrug resistant due to injudicious use of antibiotics, thus limiting the choice of therapy.

6. **Transfusion:** Blood, blood products and intravenous fluids used for transfusion, if not properly screened, can transmit many infections.

7. **Advances in medical progress:** Advances in treatment of cancer, organ transplantation, implanted prostheses and other sophisticated medical technologies enhance the risk of infection to patients.

Routes of Transmission:

1. **Contact:**

Direct contact: Spread from person to person (***Staphylococcal*** and ***Streptococcal*** sepsis).

Indirect contact: Spread via contaminated hands or equipment (enterobacterial diarrhoea, ***Pseudomonas aeruginosa*** sepsis).

2. **Airborne spread**

i. **Droplets**

ii. **Dust:** Dust from bedding, floors; exudate dispersed from a wound during dressing and from the skin by natural shedding of skin scales, spread to the susceptible site, e.g. *Ps aeruginosa*, ***S****taphylococcus aureus*.

iii. **Aerosols:** Aerosols produced by nebulizers, humidifiers and air conditioning apparatus transmit certain pathogens to the respiratory tract. Occurrence of legionellae in hospital water supply and a number of persons with an impaired immune system has led to outbreaks of infection mainly with *Legionella pneumophila.*

3. **Oral route:** Hospital food contains gram-negative bacilli which are most often antibiotic resistant *(P. aeruginosa, E. coli, Klebsiella* spp. and others), which may colonize the gut and later cause infection in susceptible patients.

4. **Parenteral route (inoculation):** Certain infections may be transmitted by blood transfusion or tissue donation, contaminated blood-products (factor VIII), contaminated infusion fluids and from accidental injury with contaminated sharp instruments (HIV, hepatitis B and C*).*

5. **Self-infection and cross-infection:** ***Self infection*** may occur due to transfer into the wound of *Staphylococci* (or occasionally *Streptococci*) carried in the patient's nose and distributed over the skin,

or of coliform bacilli during surgery. Alternatively, ***cross-infection*** may result from *Staphylococci* or coliform bacilli derived from other patients or healthy staff carriers.

Common Hospital-Acquired Infection:

1. Urinary Tract Infection: Most hospital-acquired infections of the urinary tract are associated with urethral catheterization. Ex: *Escherichia coli, Klebsiella, Proteus, Serratia, Pseudomonas, Providencia* and *Candida albicans.*

2. Respiratory Infections: Aspiration in unconscious patients and pulmonary ventilation or instrumentation may lead to nosocomial pneumonia, cardiopulmonary disease. Ex: *Staphylococcus aureus, Klebsiella spp., Enterobacter, Serratia, Proteus, Escherichia coli, Pseudomonas aeruginosa, Acinetobacter, Legionella pneumophila* and respiratory viruses.

3. Wound and Skin Sepsis: The incidence of postoperative infection is higher in elderly patients. Most wound infections manifest within a week of surgery. ***S****taphylococcus aureus* is the predominant pathogen, followed by *Pseudomonas aeruginosa* and then *Escherichia coli, Proteus, enterococci***.**

4. Gastrointestinal Infections: Food poisoning and neonatal septicemia in hospital have been reported. These infections are mainly associated with *salmonella* and *Shigella sonnei*.

5. Burns: *Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter* and *Streptococcus pyogenes* are responsible for hospital-acquired infections in cases of burns.

6. Bacteremia and Septicemia: These may be consequences of infections at any site but are commonly caused by infected intravenous cannulae. Gram-negative bacilli are the common pathogens. *Staphylococcus epidermidis* **bacteremia** is seen commonly in patients with artificial heart valves.

Diagnosis and Control of Hospital Infection:

The most important steps in' preventing nosocomial infections are to first recognize their occurrence and then establish policies to prevent their development. Hospital infection may occur sporadically or as outbreaks.

Etiological diagnosis is by the routine bacteriological methods of smear, culture, identification and sensitivity testing.

The provision of sterile instruments, dressings and fluids is of fundamental importance in hospital practice. The cause of infection may be a defective autoclave or improper techniques, such as boiling infusion sets in ward sterilizers.

Prevention:

The hospital-acquired infections can be prevented by following means:

1. **Sterilization:** The provision of sterile equipment, instruments, dressings, surgical gloves, facemasks, theater clothing and fluids.

2. **Cleaning and disinfection:** The general hospital environment can be kept in good order by attention to basic cleaning, waste disposal and laundry.

3. **Skin disinfection and antiseptics:** Procedures for preoperative disinfection of the patient's skin and for surgical scrubs are mandatory within the operating theater.

4. **Rational antibiotic prophylaxis**

5. **Protective clothing**

6.**Personnel:** Hepatitis B vaccine should be given to all health care workers.


Medical Mycology Unite

General Properties, Classification and Laboratory Diagnosis of Fungi

Mycology: is the study of fungi.

Fungi: Fungi are large group of eukaryotes; include molds, yeasts, and mushrooms.

Mycoses (Fungus Infections): Infection caused by fungus is known as mycosis.

General Characters of Fungi:

1) Fungi are eukaryotes with a higher level of biologic complexity than bacteria.
2) They are spore-bearing, reproducing both **sexually** and **asexually**.
3) They possess rigid cell walls containing **chitin, mannan** and other **polysaccharides**.
4) They possess true nuclei with nuclear membrane and paired chromosomes.
5) The cytoplasmic membrane contains sterols. Cytoplasmic contents include mitochondria and endoplasmic reticulum.
6) Fungi may be **unicellular** or may differentiate and become **multicellular** by the development of long, branching filaments.
7) Most fungi are obligate or facultative aerobes.
8) They lack the chlorophyll of plants, therefore needing to acquire nutrients from the external environment.
9) The diseases caused by fungi are called mycoses.
10) These infections vary greatly in their manifestations but tend to present with **subacute** or **chronic features**, often relapsing over time. Acute disease, such as that produced by many viruses and bacteria, is uncommon with fungal infections.

Fungal requirement and Nutritional Adaptations:

Conditions for best fungal growth:-

1. **Temperature:** 25- 30 degree celsius.
2. **Humidity:** high moist humid environment.
3. **pH:** Molds differ in their pH requirements. Most will grow well over the pH range 3-7. Grow best at pH 5.0.
4. **Nutrients:** Nutrient requirements for molds may vary from mold to mold. Some molds may thrive well on substrates with high sugar or salt content.
5. **Light:** Many molds species grow well in the dark, but some prefer daylight or alternate light and darkness for them to produce spores.
6. **Aeration:** Nearly all moulds require air to grow. Aerobic (filamentous, bread mold) or facultative anaerobes (yeast).
7. Fungi need lots of water to grow.

8. Require organic compounds for energy and carbon.
9. Most fungi are more resistant to osmotic pressure (can grow in high sugar or salt concentration).

Classification of Fungi:

I-Morphological Classification:

On the basis of morphology, there are four groups of fungi:

1. **Yeasts:** Yeasts are round or oval unicellular fungi. Most reproduce by an asexual process called budding.

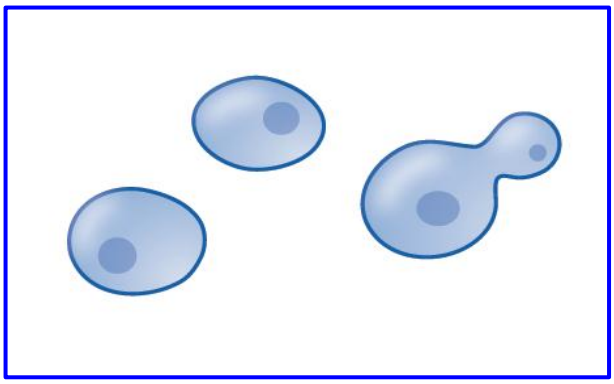


Figure : Yeast

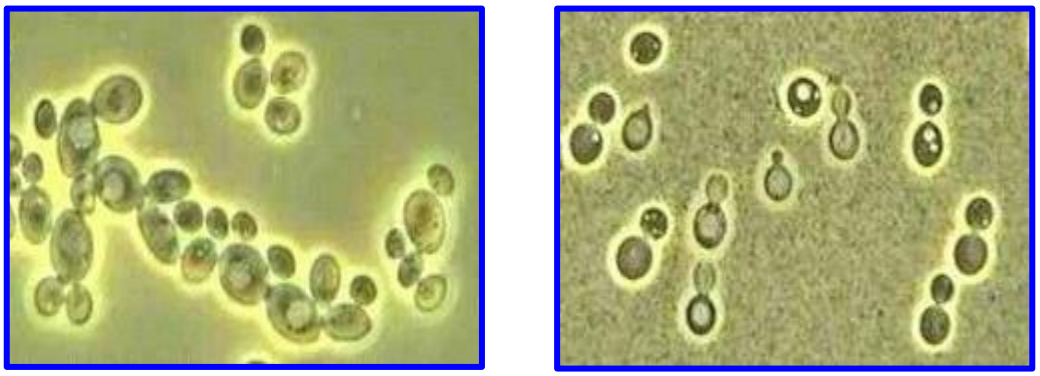


Figure : Yeast and Yeast budding

2. **Yeast-like fungi:** *Yeast-like fungi* grow partly as yeast and partly as elongated cells resembling hyphae. The latter form a *pseudomycelium.*

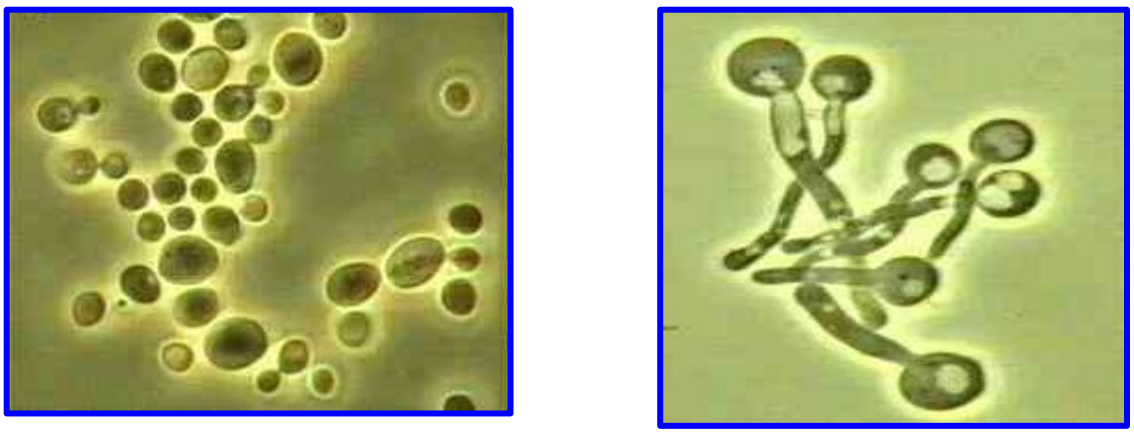


Figure :Yeast-like fungi

3. **Molds (filamentous fungi):** grow as **long filaments (hyphae)** and form a mat (**mycelium**), and reproduce by the formation of different types of spores.

Hyphae: are filamentous cellular units of molds and mushrooms. Found two types of hyphae:

Types of hyphae

1) **Non-septate hyphae:** have no cross walls, broad hyphae with **irregular width**, and **broad angle of branching**.
2) **Septate hyphae:** have **cross walls** and fairly regular width (tube-like).

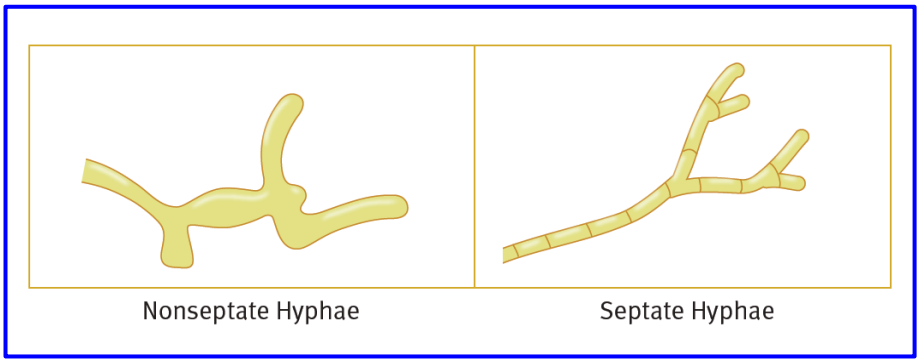


Figure: types of hyphae

The **Mycelium**: is the mat of hyphae.

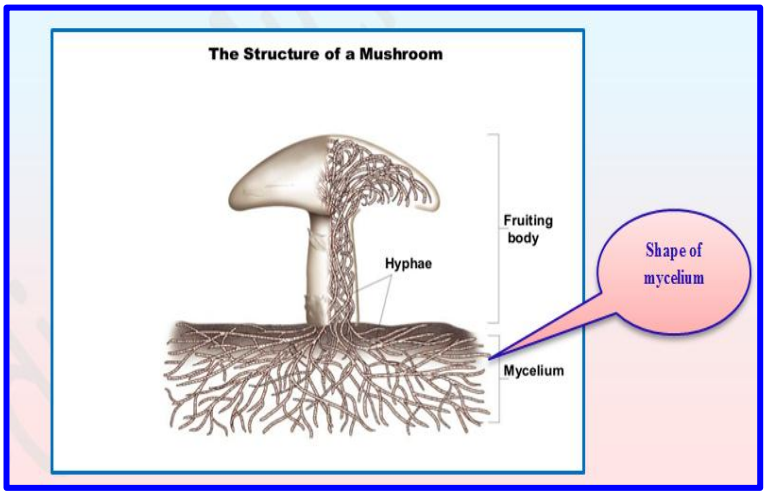


Figure:Fungi Body and Mycelium

4. **Dimorphic fungi:** Many fungi pathogenic to man have a yeast form in the **host tissue and in vitro at 37°C on enriched media and mold form *in vitro* at 25°C.**

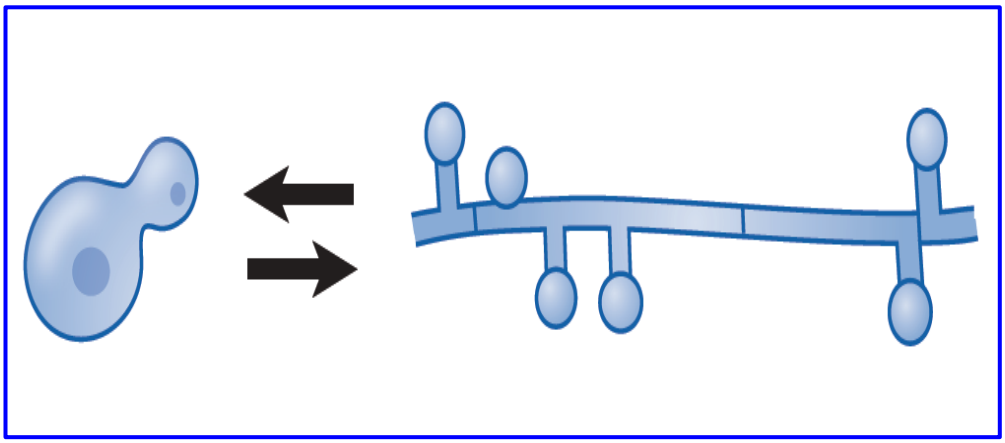


Figure :Dimorphic fungi

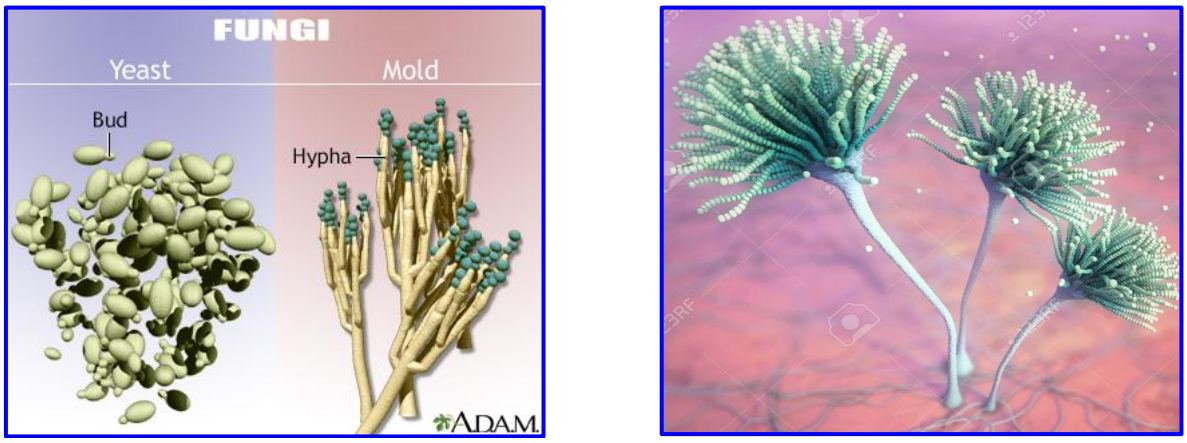


Figure :Mold and Fungi

Pseudohyphae: are hyphae with constrictions at each septum. (*Ex: Candida albicans*)

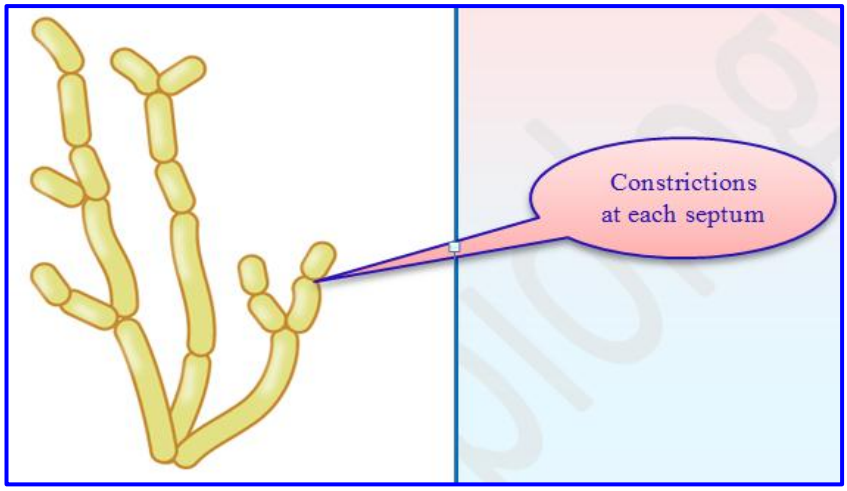


Figure :Dimorphic fungi

II-Classification of Fungi according to mycoses (fungal infection):

Classification of fungal disease according to primary sites of infections is as follows **:**

1. **Superficial mycoses:** These infections are limited to the outermost layers of the skin and hair.

2. **Cutaneous mycoses:** Infections that extend deeper into the epidermis as well as invasive hair and nail diseases.

3. **Subcutaneous mycoses:** These infections involve the dermis, subcutaneous tissues, muscle, and fascia.

4. **Systemic mycoses:** Systemic mycoses-infections that originate primarily in the lung but that may spread to many organ systems. Systemicmycoses are caused by inhalation of airborne spores.

5. Opportunistic mycoses: Opportunistic infection occurrs in patients with debilitating diseases. Opportunistic infections are caused mainly by fungi that are normally avirulent.

III-Taxonomical Classification:

Based on the production of sexual spores, the Kingdom Fungi has been divided into four medically important phyla.

1. Zygomycota: produce sexual spores known as zygospores and possess aseptate hyphae.

2. Ascomycota: They produce sexual spores known as ascospores and possess septate hyphae.

3. Basidiomycota: They produce sexual spores known as basidiospore.

4. Deuteromycota (Fungi Imperfecti): Sexual state is either absent or unidentified yet, e.g. most medically important fungi.

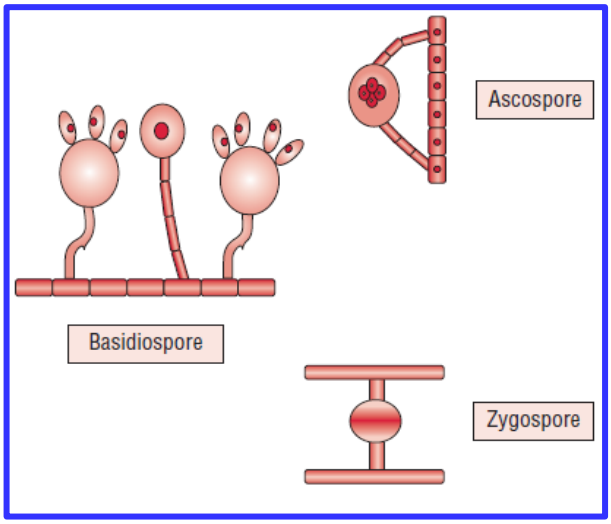
Reproduction and sporulation:

Types of fungal spores: Fungal spores are of two types- sexual and asexual spores.

A. Sexual spores: Sexual spore is formed by fusion of cells and meiosis as in all forms of higher life. Sexual spores are of four types:

1. Oospore الابواغ البيضية او الملقحه
2. Ascospore الابواغ الزقية
3. Zygospore الابواغ الزيجية
4. Basidiospore الابواغ الدعاميه

- ***Note:*** ***Fungi that do not form sexual spores are termed "imperfect" and are classified as fungi imperfecti.***



Oospore

Figure: Sexual spores

Steps of fungal sexual reproduction, include the following three stages:

1) First, during **plasmogamy** (union of cytoplasm'), two haploid cells fuse, leading to a dikaryotic stage where two haploid nuclei coexist in a single cell.
2) During **karyogamy** ('nuclear marriage'), the haploid nuclei fuse to form a diploid zygote nucleus.

3) Finally, **meiosis** takes place in the gametangia (singular, gametangium) organs, in which gametes of different mating types are generated. **At this stage, spores are disseminated into the environment, and the cycle can start again.**

B. Asexual spores: These spores are produced by mitosis. These may be **vegetative spores** or **aerial spores**.

Fungi can reproduce asexually by **fragmentation, budding**, or **producing spores**.

- **Fragments** of hyphae can grow new colonies,
- whereas, during **budding**, a bulge forms on the side of the cell, the nucleus divides mitotically, and the bud ultimately detaches itself from the mother cell.

Asexual reproduction: Most fungi of medical interest propagate asexually by forming **conidia** (asexual spores).

a. Vegetative spores

i. *Blastospores:* These are formed by budding from parent cell, as in yeasts.

ii. *Arthrospores:* These are formed by the production of cross-septa into hyphae resulting in rectangular thick-walled spores.

iii. *Chlamydospores:* These are thick-walled resting spores developed by rounding up and thickening of hyphal segments.

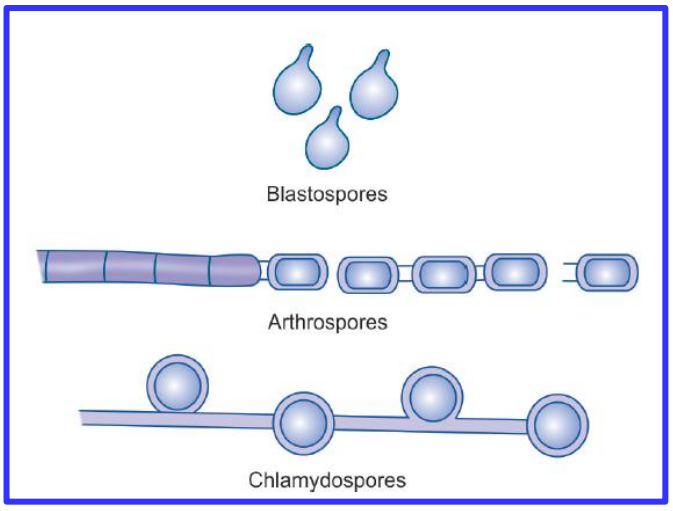


Figure: Vegetative spores

b. Aerial spores

i. **Conidiospores:** Spores borne externally on sides or tips of hyphae are called ***conidiospores.***

ii. **Microconidia:** When conidia are small and single, these are called ***microconidia.***

iii. **Macroconidia:** These are large and septate conidia and are often multicellular.

iv. **Sporangiospores:** These are spores formed within the sporangium. They develop on the ends of hyphae called ***sporangiophores.***

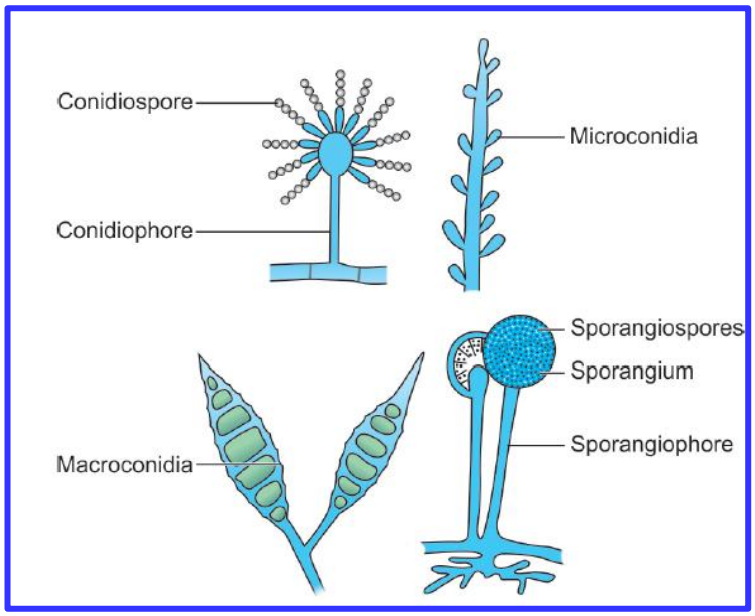


Figure: Aerial spores

Laboratory Diagnosis:

A.Collection and Processing of Specimens: The sampling procedures vary according to the area and type of tissue involved. Causative agents of mycoses can be identified by the following methods.

B. Direct Microscopy:

I. Potassium Hydroxide (KOH) Preparation

II. Potassium Hydroxide (KOH) with Calcofluor White: Addition of Calcofluor white and subsequent examination by fluorescence microscopy enhances the detection of most fungi.

III. Gram-staining: It is used for the diagnosis of yeast infections of mucous membranes.

IV. India Ink Preparations: It may be used for detecting encapsulated yeast *Cryptococcus neoformans* in cerebrospinal fluid (CSF).

C. Culture: special fungal media include— **Sabouraud agar.** Another media include potato dextrose or the slightly modified potato flakes agar (PFA), and brain heart infusion (BHI) agar with blood and antibiotics.

Cultures are routinely incubated in parallel at room temperature 25°C (room temperature for weeks) and at 37°C for days.

D. Serologic Tests:

a. **Detection of Fungal antibodies.**

b. **Detection of Antigen detection.**

E. Polymerase Chain Reaction (PCR): Polymerase chain reaction (PCR) for detection of fungal DNA in clinical material.

Fungal Disease

Fungal infections are most often acquired from the external environment. One common mechanism of infection is by the inhalation of infectious conidia generated from environmental molds.

Clinical Manifestations of Fungal Diseases:

Fungal diseases are grouped into the following three categories of clinical manifestations:

• ***Fungal infections,*** which are the most common mycoses, are caused by the presence in the body of either true pathogens or opportunists.

• ***Toxicoses*** (poisonings) are acquired through ingestion, as occurs when poisonous mushrooms are eaten.

• ***Allergies*** (hypersensitivity reactions) most commonly result from the inhalation of fungal spores.

Symptoms of fungal diseases (subcutaneous, cutaneous, superficial):

The symptoms produced by fungal infection with subcutaneous, cutaneous, superficial mycosis generally causes:

- ✓ Itching
- ✓ Reddened skin
- ✓ Inflammation

Superficial Mycoses *: (Spherical yeasts, Molds*)

Involves dead layers of skin and its appendages without any inflammatory response. Includes- Tinea versicolor, Tinea nigra, Piedra (black and white).

1- **Tinea versicolor:** chronic superficial skin infection with hypo or hyperpigmented areas. **Asymptomatic** lesions identified by **pigment**, caused by ***Malassezia furfur***.

2- **Tinea nigra:** chronic superficial infection, black lesions on **palms and Soles**, caused by ***Exophiala werneckii.***

3- **Piedra (black and white):** ***White Piedra*** –White nodule on hair shaft , caused by ***Trichosporoon***.

Black Piedra –Black nodule on hair shaft, causative Agent is ***Piedraia hortae***

Cutaneous Mycoses: *Only molds.*

Dermatophytoses: also known as **tinea** or **ringworm** Infect superficial keratinized structures, **skin, hair, nails. Spread by direct contact.** It's called "ringworm" because it can cause a circular rash (shaped like a ring) that is usually red and itchy.

Causative agents: ***Microsporum spp., Trichophyton spp., Epidermophyton floccosum***

Ringworms caused by several different fungi and classified by the location on the body:

1. Tinea capitis = ringworm of the scalp
2. Tinea corporis = ringworm of the nonhairy skin of the body (trunk and limbs).
3. Tinea cruris = jock itch
4. Tinea unguium = ringworm of the nails
5. Tinea barbae = ringworm of the bearded region
6. Tinea pedis = ringworm of the feet, caused athlete's foot
7. Tinea manuum= ringworm of the hand
8. Tinea faciei=Infection of the nonbearded area of face
9. Tinea imbricate=Concentric lesions of the skin

Subcutaneous Mycoses: *Round budding yeast/ Molds.*

These are caused by fungi that grow in soil and on vegetation and are introduced into subcutaneous tissue through **trauma.**

1- **Mycetoma:** is a chronic, slowly progressive granulomatous infection of the skin and subcutaneous tissues.caused by Soil fungi (***Petriellidium, Madurella***)

2- **Sporotrichosis *or Gardener's Disease:*** *caused by* ***Sporothrix schenckii*** is a **dimorphic** fungus. The mold form lives on plants and the yeast form occurs in human tissue. **Causes local pustule and ulcer with nodules along draining lymphatics**

Sytemic Mycoses:

All the four fungi causing systemic mycoses are **dimorphic.** Transmission is by **inhalation of spores**, which then transform into the **yeast phase in lungs**, and become **molds in dirt**. so NO Person-Person transmission

1- **Histoplasmosis:** Histoplasmosis or Darling's disease is caused by dimorphic fungus- ***Histoplasma capsulatum***.

- Asymptomatic infrection or mild pneumonia starts as mild flu like illness, disseminated in immunocompromised.

- **Inhaled** microconidia **develop into yeasts** within macrophages**.** (**His**toplasma **Hi**des in macrophages)

2- **Coccidioidomycosis:** (also called desert rheumatism or Valley fever or California fever), is a systemic fungal disease caused by a dimorphic soil dwelling fungus- ***Coccidioides immitis.*** Asymptomatic or mild pneumonia. Dissemination leads to bone granulomas or **meningitis**.

3- **Blastomycosis :**(also known as North American blastomycosis or Chicago disease) is a fungal infection of humans and other animals, notably dogs and cats, caused by the dimorphic fungus ***Blastomyces dermatitidis***. Acute pulmonary , disseminates with fever, night sweats, weight loss, and lung granulomas. Others include: Skin lesions, osteomyelitis and CNS involvement in AIDS patients (brain abscess)

4- **Paracoccidioidomycosis:** is a systemic disease caused by the dimorphic fungus- ***Paracoccidioides brasiliensis***. *Acute form (or juvenile type):* It affects young adults under 30 years age.*Chronic form (or adult form):*Common (90%) variety affecting older men, but less severe, manifested as progressive pulmonary disease, skin lesions.

Opportunistic Mycoses: *All Monomorphic*

Opportunistic mycoses are caused by a group of fungi, which are normally a part of human anatomical flora (e.g. ***Candida***) or found in nature and frequently isolated as laboratory contaminants (e.g. ***Aspergillus, Rhizopus* and *Penicillium***).

1- ***Candidiasis: caused by Candida albicans (yeast only)***: the most important species of *Candida*, causes **oral thrush, vaginitis, esophagitis, diaper rash, and chronic mucocutaneous candidiasis.** It also causes disseminated infections such as right-sided endocarditis (especially in intravenous drug users), bloodstream infections (**candidemia**), and endophthalmitis. Infections related to indwelling intravenous and urinary catheters are also important.

- *Candida* species are a part of normal flora of the skin and mucosa including gut flora.

Predisposing factors that are associated with increased risk of infection with *Candida* include-

- Physiological state: Extremes of age (infancy, old age), pregnancy
- Low immunity: Patients on steroid or immunosuppressive drugs, post transplantation, malignancy, HIV
- Patients on broad spectrum antibiotics suppresses the normal flora
- Diabetes mellitus, febrile neutropenia and zinc or iron deficiency.

2- Cryptococcosis: ***Cryptococcus neoformans*** ***(yeast only)*** causes cryptococcosis, especially cryptococcal meningitis. Cryptococcosis is the most common life-threatening fungal disease in AIDS patients. **Usually asymptomatic,** can cause pneumonia, Bone and skin granulomas. Dissemination causes **cryptococcal meningitis, subacute.** Transmission- Inhalation of spores.

- **Virulence factors:**

— Polysaccharide capsule – Anti-capsular antibodies are not protective

— Phenyloxidase enzyme responsible for production of melanin when grown on Niger seed agar

3- Aspergillosis : caused by ***Aspergillus fumigatus*** ***(mold only)***, Molds grow in pulmonary cavities and produce **aspergilloma** (fungus ball), requiring **surgery.**

Clinical Manifestations

Clinical manifestations of aspergillosis depend on the site of involvement. The incubation period varies from 2 to 90 days.

1.Pulmonary aspergillosis : Various forms include Allergic bronchopulmonary aspergillosis (ABPA), Asthma, Extrinsic allergic alveolitis, Aspergilloma (fungal ball) and Chronic cavitary pulmonary aspergillosis

2. Invasive sinusitis: Invasive sinusitis, chronic granulomatous sinusitis**,** maxillary fungal ball and allergic fungal sinusitis

3. Ocular aspergillosis: Keratitis and endophthalmitis

4. Ear infection: Otitis externa

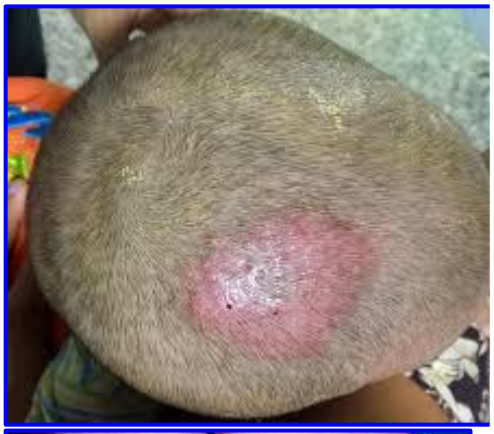
5. Others: Endocarditis, brain abscess, skin lesions and onychomycosis.

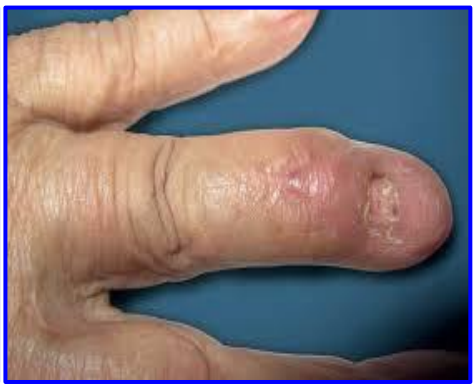
- **A*flavus*-** *grows on* ***cereal or nuts*** *produces* ***aflatoxins (toxic, carcinogenic to liver)***
- *Aspergillus* species are widely distributed on decaying plants, producing chains of conidia.
- **Transmission by airborne conidia** colonize and invade **abraded skin,** wounds, burns, ear, cornia

4- Zygomycosis: Zygomycosis or mucormycosis represents group of life-threatening infections caused by aseptate fungi belonging to the phylum zygomycota, saprophytic Molds everywhere. Examples include: ***Rhizopus***, *and* ***Mucor(mold only)***.

These organisms are transmitted by **airborne asexual spores and invade tissues** of patients with reduced host defenses. They proliferate in the walls of blood vessels, particularly of the **paranasal sinuses, lungs, or gut, and cause infarction and necrosis of tissue distal to the blocked vessel**.

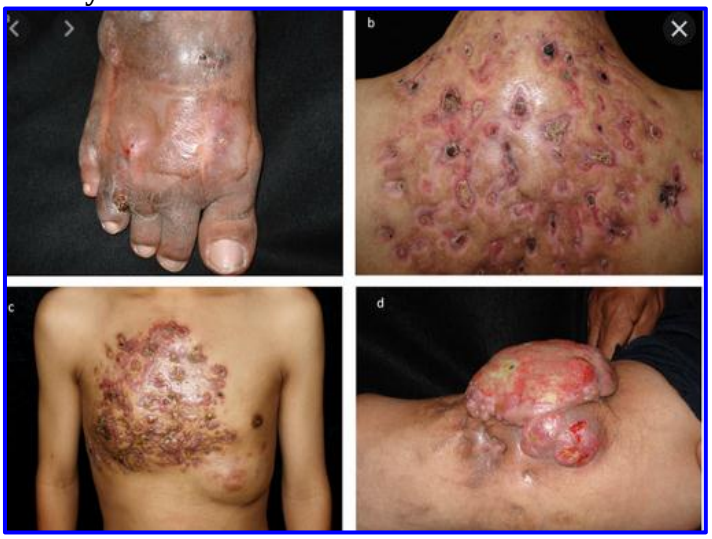
Some Fungal Diseases Pictures



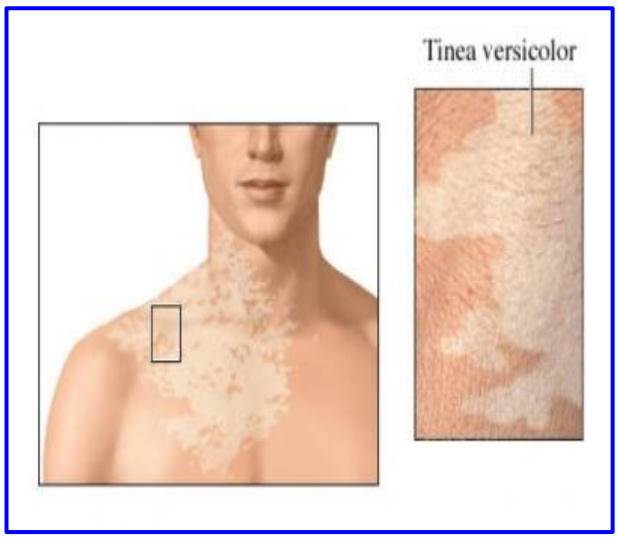


Cutaneous Mycoses

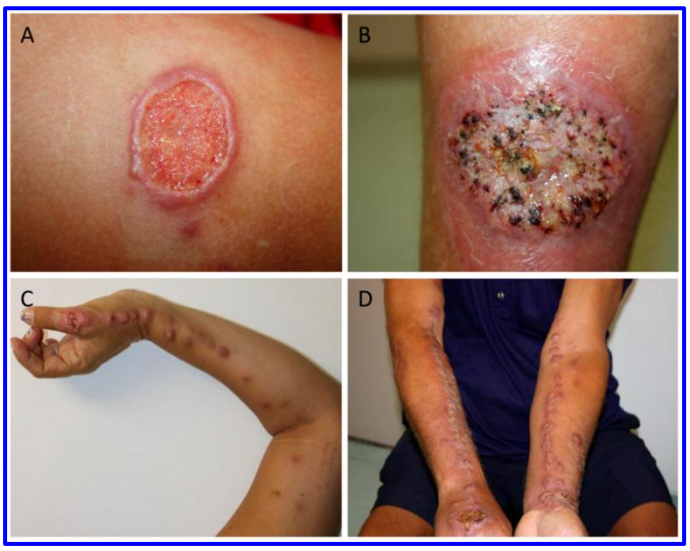
Zygomycosis



Mycetoma infection

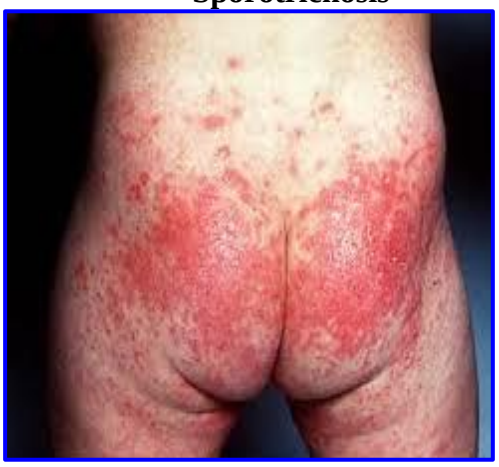


Tinea versicolor

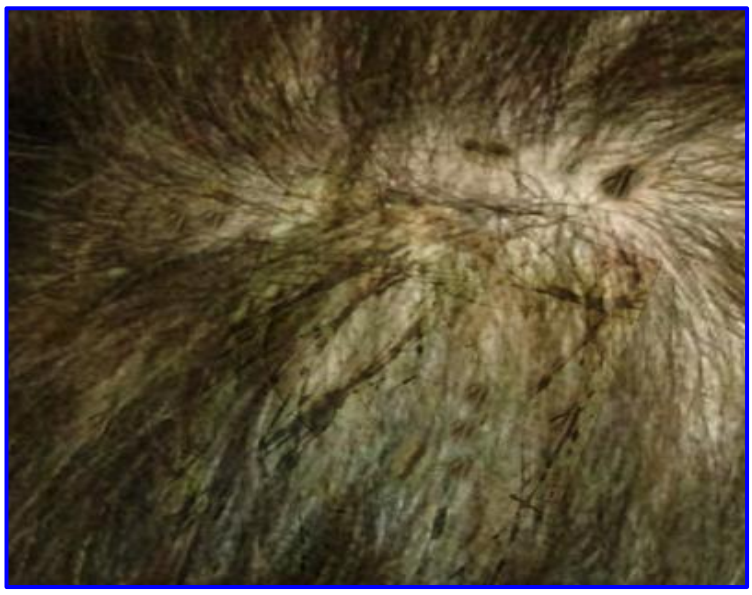


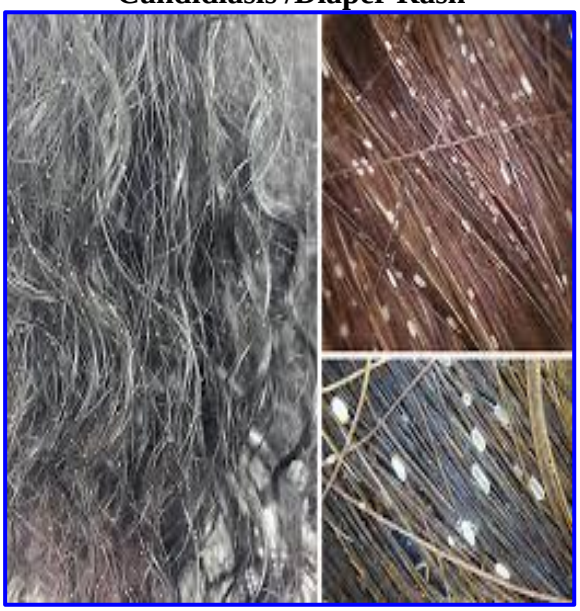
Sporotrichosis

Candidiasis /Oral Thrush

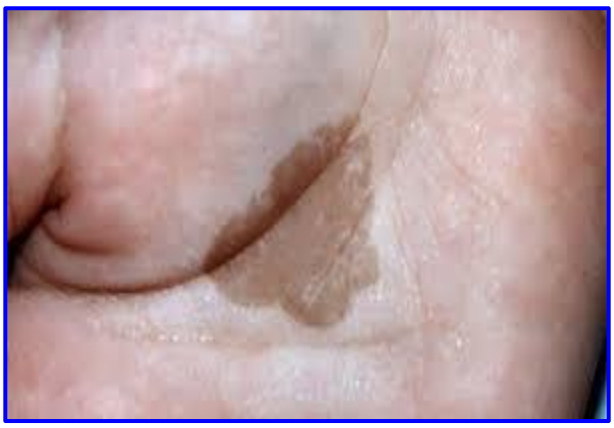


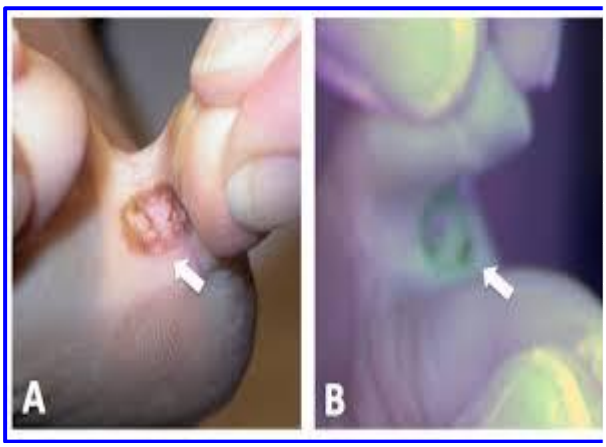
Candidiasis /Diaper Rash





Piedra (black and white)





Tinea nigra


Medical Virology Unite

Introduction to Medical Virology
General properties of virus, Structure, Classification and Diseases of viruses.

- **Medical virology:** The science that deal with the study of the medically important viruses, which infect humans.
- **Viruses**: **'virus' (from the Latin 'poison'):** infectious agent of small size and simple composition that can multiply only in living cells of animals, plants, or bacteria.
- **Virion**: A complete infectious virus particle.

General characters of viruses:

1. Virus particles are very small in size; they are between 20-500 nm (nanometer) in diameter. 1 nm= 1/1000 μm, 1 μm=1/1000 mm.
2. Viruses are not cells, do not have nuclei or mitochondria or ribosomes or other cellular components.
3. Viruses are obligatory intracellular microorganisms, Multiply inside the cells.
4. Viruses genomes which either DNA or RNA, but not both.
5. Virus does not affect with antibiotics.
6. Most viruses sensitive to interferon.
7. Viruses cannot grow on artificial media, but only in living cells (specific host, Lab. Animals, chicken embryonated eggs & tissue culture).
8. Some viruses cause latent infection.
9. Viruses cannot be seen by ordinary microscope, but only by Electron microscope (EM)

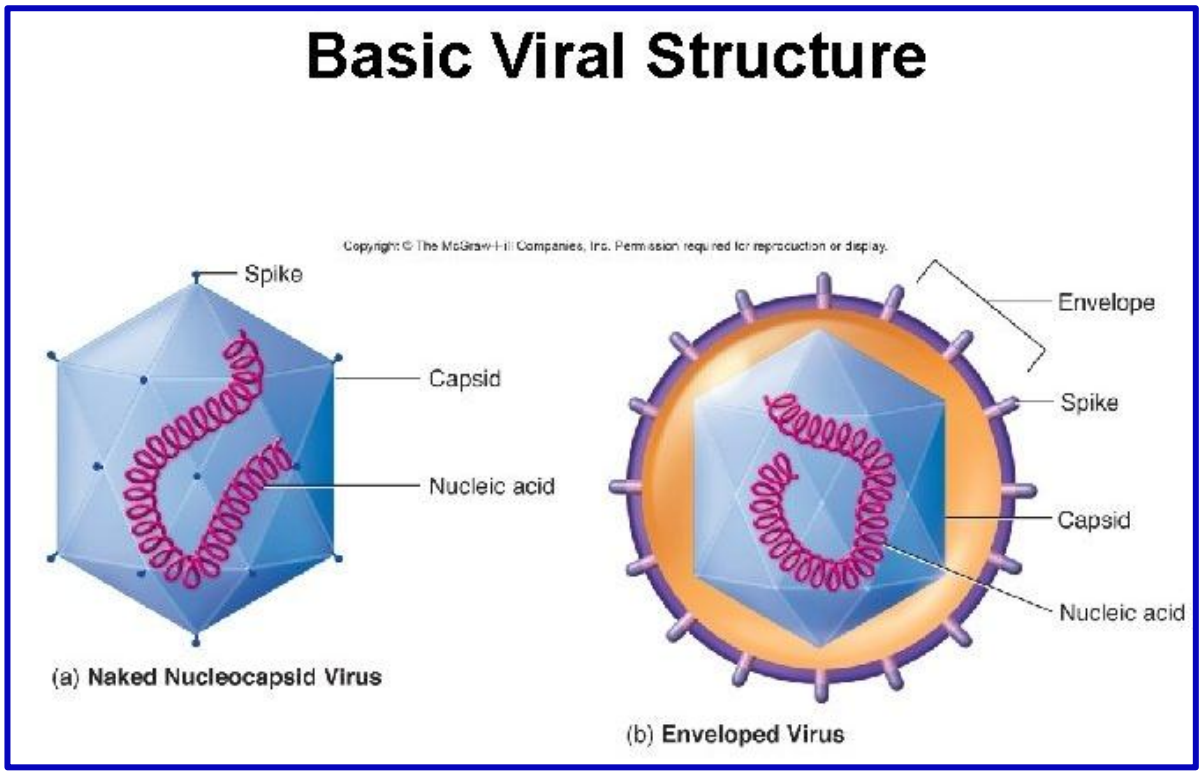
Structure of Viruses:

1. A **nucleic acid** genome either DNA or RNA.

2. A **protein coat (capsid):** The capsid is responsible for protecting the contents of the core and Establishing what kind of cell the virion can attach to Infecting that cell. The **nucleic acid genome** plus the protective **protein coat** = **nucleocapsid.** The nucleocapsid may have **icosahedral** or **helical** symmetry.

3. **Envelope (lipid membrane):** found in some viruses, made of lipid derived from the host cell. Enveloped viruses obtain their envelope by budding through a host **cell membrane**. In some cases, the virus buds through the **plasma membrane.**

4. Spikes: These are glycoprotein projections which have enzymatic and/or adsorption and/or hemagglutinating activity. They arise from the envelope and are highly antigenic.



Virion Nucleocapsid Symmetry:

A) Icosahedral: Icosahedron: 20 faces, 12 corners or vertices, 5-fold symmetry around vertices. The capsid shell is made of repeating subunits of viral . All faces of the icosahedron are identical. The nucleic acid is packaged inside the capsid shell and protected from the environment by the capsid. Examples:(Adenovirus, Coxsackie virus, CMV, EBV, Hepatitis virus, Polio virus, Rubella virus)

The structural units are known as **capsomers** - capsomers may contain one or several kinds of polypeptide chain.

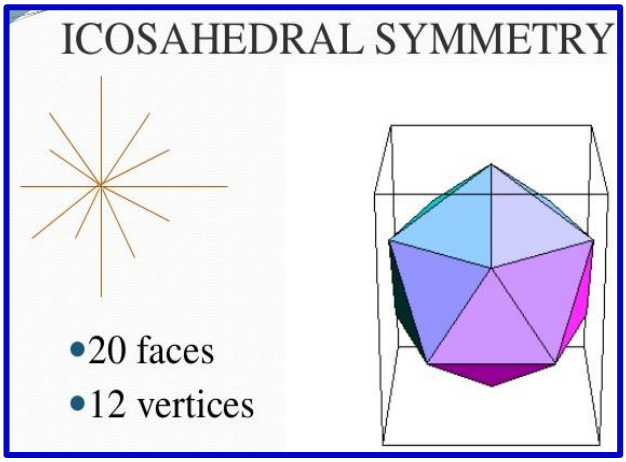


Figure: Icosahedral virus

B) Helical: Protein subunits interact with each other and with the nucleic acid to form a coiled, ribbon like structure: e. g. tobacco mosaic virus, influenza virus, rabies virus.

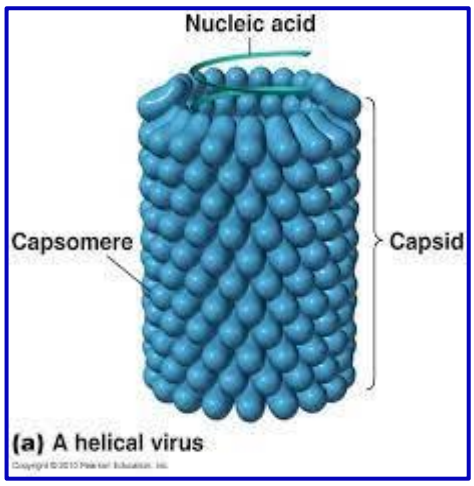


Figure: Helical virus

C) Complex: Regular structures, but nature of symmetry not fully understood. Example: poxviruses, Bacteriophage.

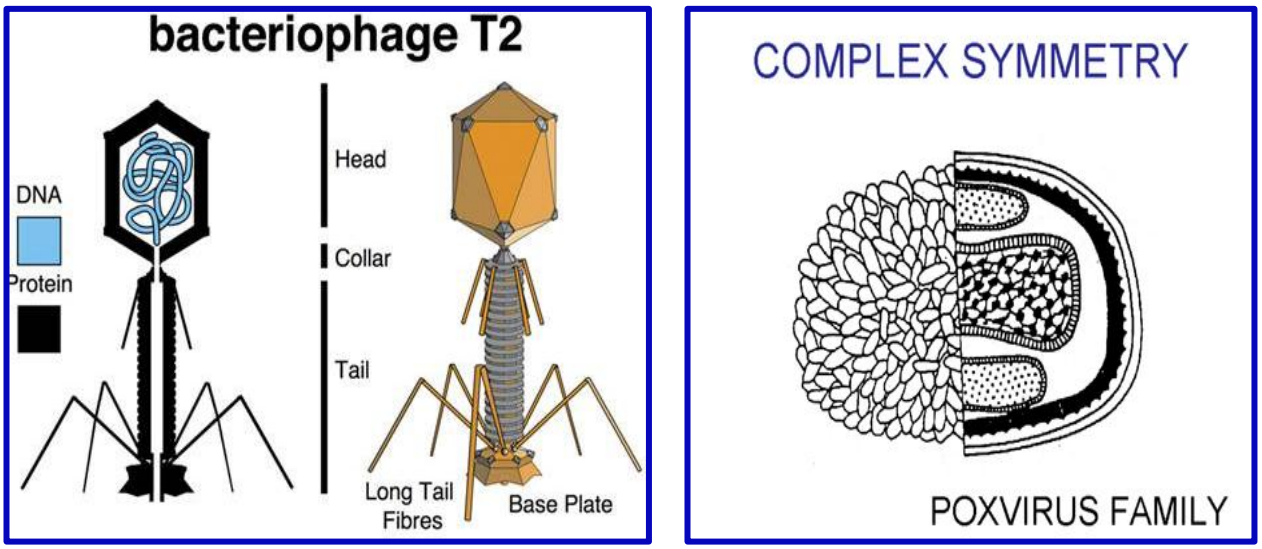


Figure: Complex virus

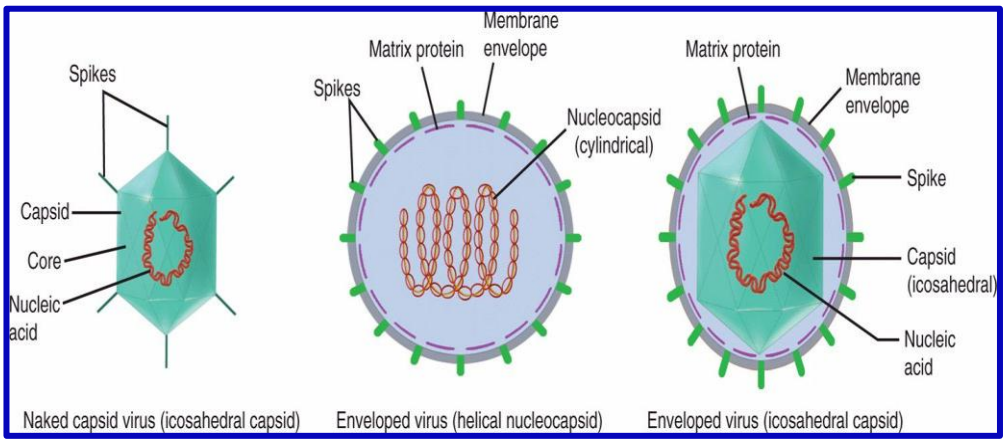


Figure: Naked and Enveloped viruses

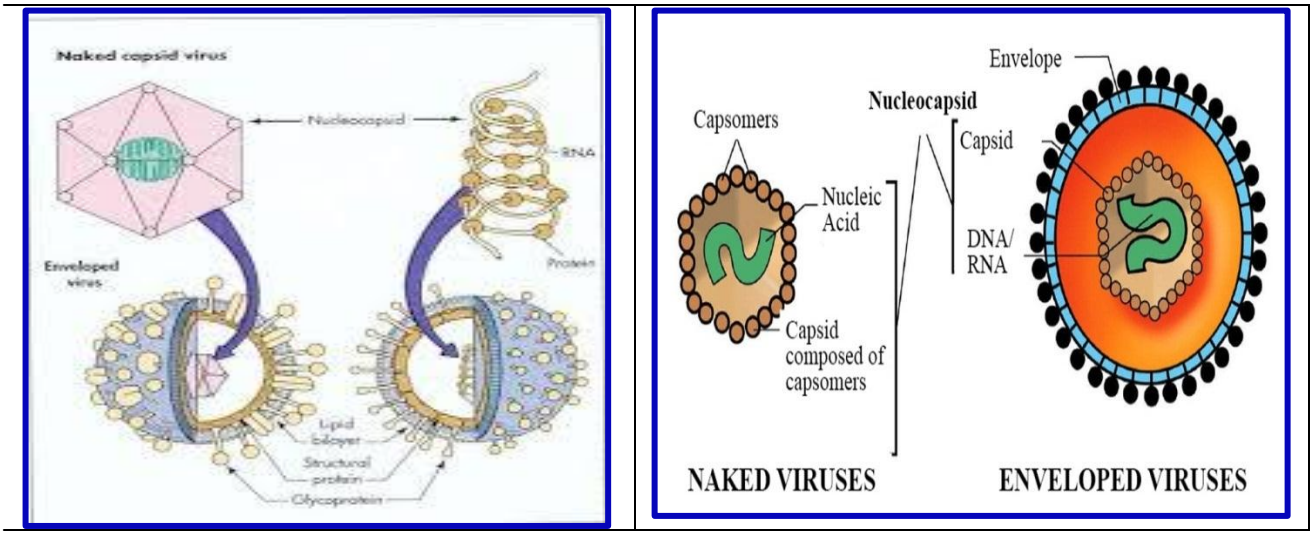


Figure: Naked and Enveloped viruses

Classification of Viruses:

Viruses are mainly classified by phenotypic characteristics, such as morphology, nucleic acid type, mode of replication, host organisms, and the type of disease they cause.

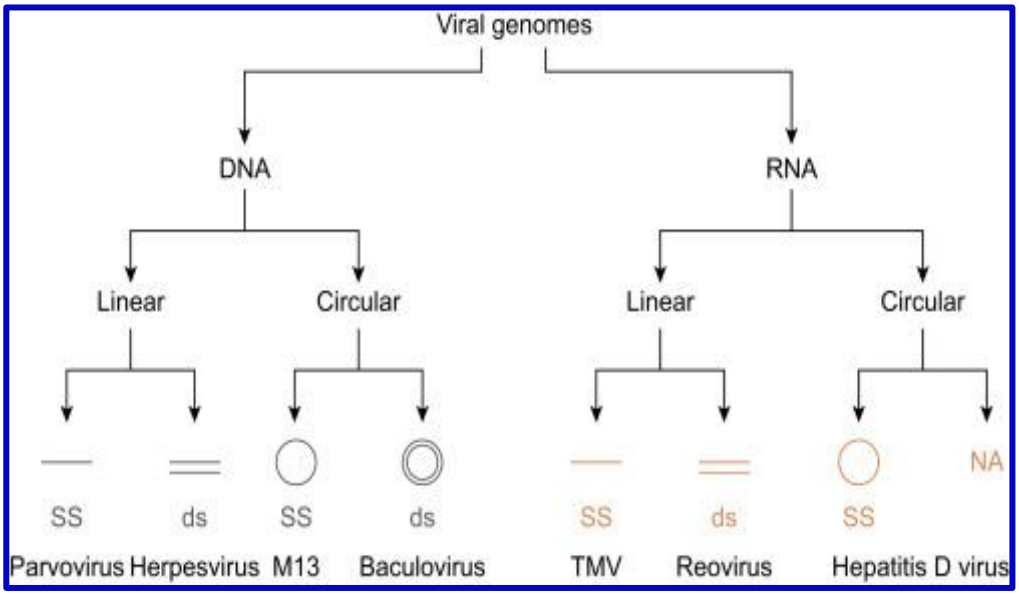
1- Morphology:

- Helical
- Icosahedral
- Complex

2- Nucleic acid type and mode of replication: The Baltimore classification system based on:

A. Genetic contents, **(DNA or RNA)** which may be:

- **Single stranded (ss) or**
- **Double stranded (ds).**
- **Linear or circular.**
- **Non-segmented or segmented.**



B. Replication strategies of viruses, Sense (positive or negative), and method of replication.

Viral Replication:

Viruses are totally dependent on a **host cell to replicate**. The general strategy of replication is similar:

1-Adsorption (attachment): Highly specific, the surface of the virion contains structures that interact receptors on the surface of the host cell. It defines and limits the host species and type of cell that can be infected by a particular virus.

2-Uptake (Penetration): The process whereby the virion enters the cell; as a result of fusion of the viral envelope with the plasma membrane of the cell or endocytosis.

3-Uncoating: The protein coat of the virion dissociates and the viral genome is released into the cytoplasm.

4-Early phase: Transcription of viral mRNA and translation of a number of non-structural ("early") proteins takes place.

5-Genome replication: Multiple copies of the viral genome are synthesized by a viral polymerase.

6-Late phase: Transcription and translation of viral mRNA and synthesis of the structural "late" proteins which are needed to make new virions.

7-Assembly (of new virions): The proteins self-assemble and a genome enters each new capsid. This takes place either in the nucleus or in the cytoplasm of the cell, or sometimes, just beneath the cell surface.

8-Release of progeny virions: Release of new infectious virions is the final stage of replication. This may occur either by **budding from plasma membrane** (for enveloped viruses), or else by **disintegration (lysis)** of the infected cell (for naked viruses).

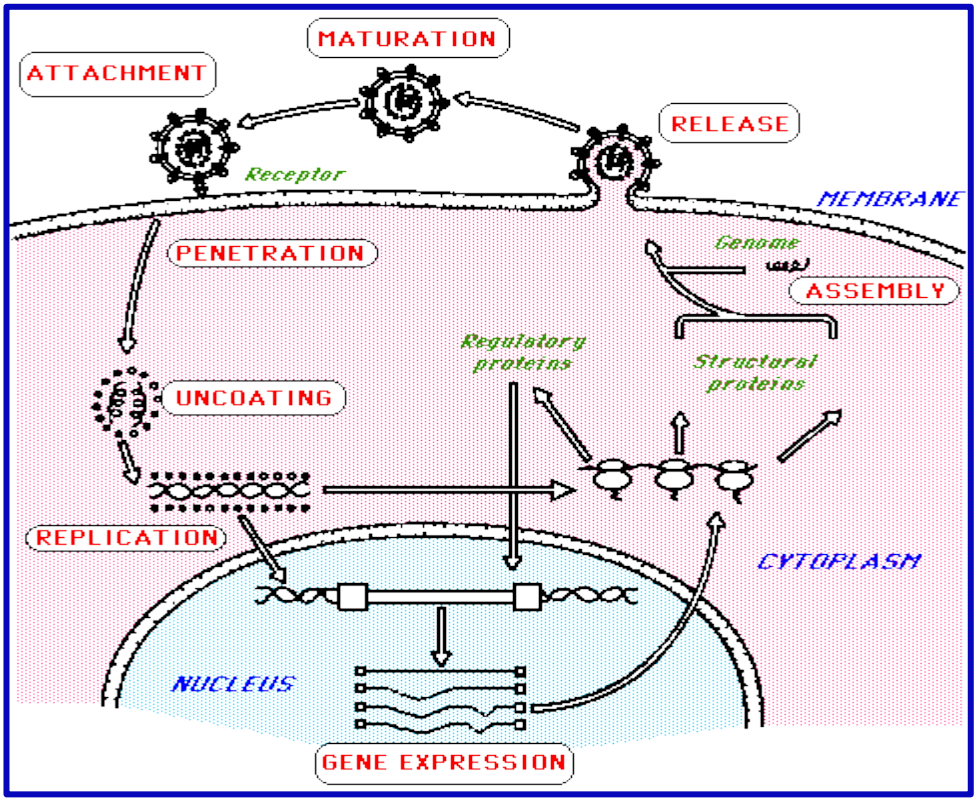


Figure: Viral Replication

Viral Replication Human diseases caused by viruses: the Common Route of Transmission are:

1. Airborne 2. Direct-Contact 3. Food-Borne & Waterborne

1-Airborne Viral Diseases: when humans are source, airborne viruses are propelled from respiratory tract by coughing, sneezing, or vocalizing.

Examples: 1. Chicken Pox and Shingles (Varicella-Zoster Virus) 2. Influenza (Influenza virus), 3-Coronavirus.

2- (A) Direct-Contact Viral Diseases:

Direct personal contact = touching, kissing, sexual contact, contact with body fluids, contact with open wounds

Examples: 1-Viral Hepatitides (HBV, HCV, HDV) 2- HIV (AIDS).

2- (B) Direct-Contact Viral Diseases (Zoonotic Diseases):

Human viral infections in animal reservoirs before transmission to and between humans Examples: 1. Ebola Hemorrhagic Fever (Ebola virus) 2. Rabies (Rabies virus)

3- Food & Waterborne Viral Diseases:

Virions transmitted via ingestion of contaminated food or water. Often a fecal-oral route. May not necessarily produce gastrointestinal disease. Examples:

1. Poliomyelitis (Poliovirus)
2. Hepatitis A virus (HAV).

Atypical Virus like Particles:

There are four exceptions to the typical virus as described previously:

Defective viruses: Composed of viral nucleic acid and proteins, but cannot replicate without a helper virus.

Pseudoviruses: Contain host DNA instead of viral DNA.

Viriods: Consist of a single molecule of circular RNA with no protein coat or envelope.

Prions: Smallest known infectious particles.

Laboratory Diagnosis:

There are four approaches to confirming a viral infection in the laboratory:

- Serology demonstrating an antibody response in a patient's serum.
- Direct detection of viral antigens in a clinical sample.
- Virus culture.
- Viral nucleic acid detection.

Some Viral Diseases:

Diseases	Viruses
Respiratory Viral Infections	**-Rhinovirus** - common cold **-Influenza virus- Seasonal influenza**. **-Respiratory Syncytial Virus (RSV-** both upper respiratory infections (like colds) and lower respiratory infections (like pneumonia **and bronchiolitis).** **-SARS-COV-2** is a respiratory coronavirus that causes COVID-19 infection.
Viral Skin Infections	**-Herpes simplex virus-1 (HSV-1)**- causes cold sores. **-Varicella-zoster virus (VZV)** causes itchy, oozing blisters
Viral Food Poisoning	**Hepatitis A**, **Norovirus, Rotavirus**
Viral Infections & Sexually transmitted viral infections (STIs)	**-Human papillomavirus (HPV)**- genital warts while others increase the risk of cervical cancer. **-Herpes simplex virus-2 (HSV-2)- Genital herpes.** **-Human immunodeficiency virus (HIV)-** acquired immune deficiency syndrome (AIDS).


Medical Parasitology Unite

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.

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.

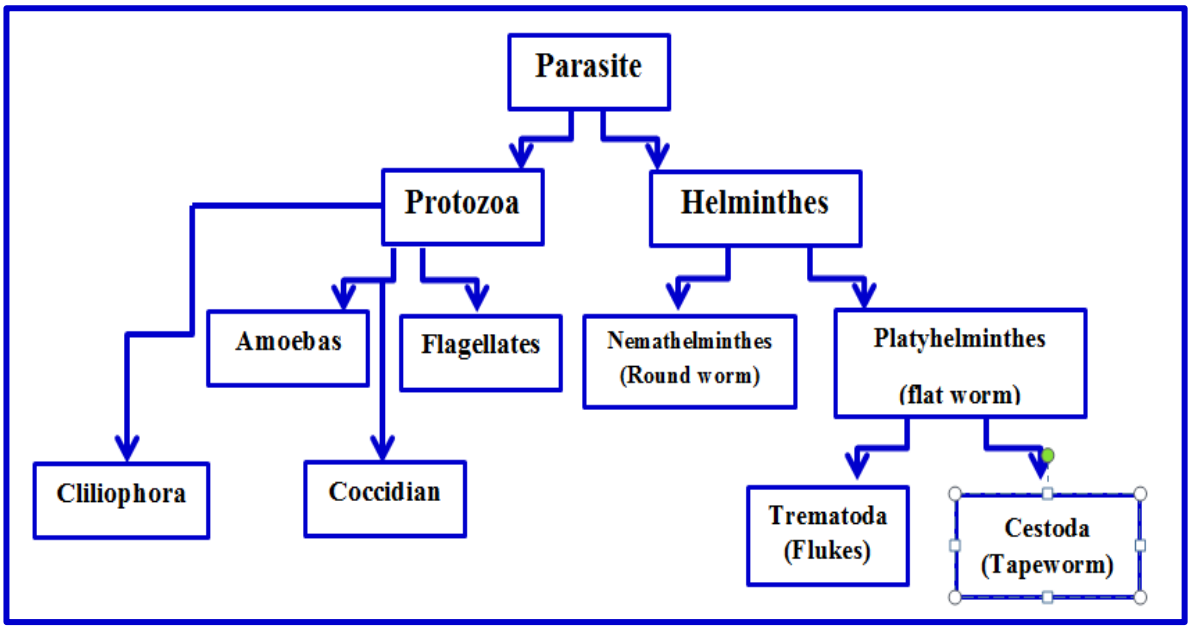


Figure: Classification of medical parasitology

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.

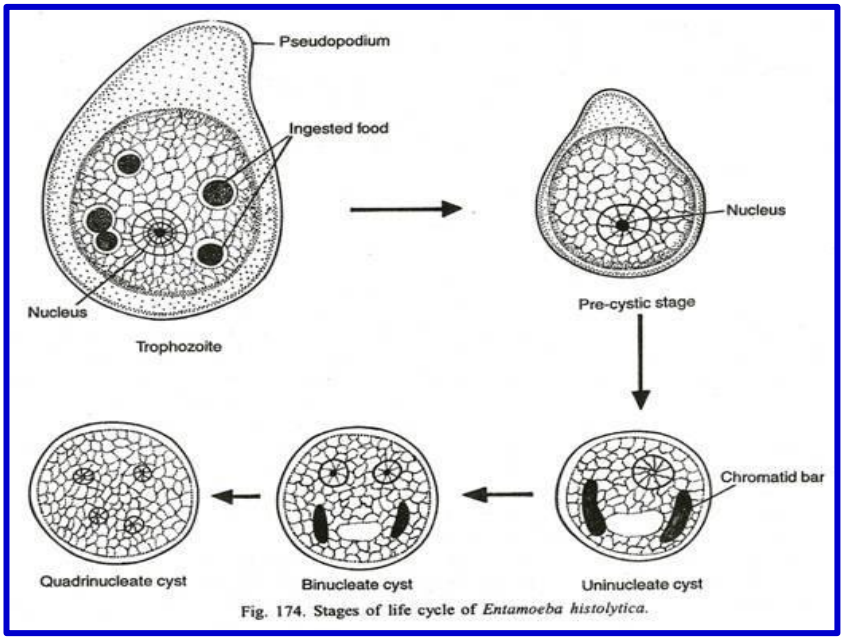


Fig. 174. Stages of life cycle of *Entamoeba histolytica*.

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

Trophozoite of <u>Entamoeba</u> <u>histolytica</u>

Life cycle of Entamoeba histolytica:

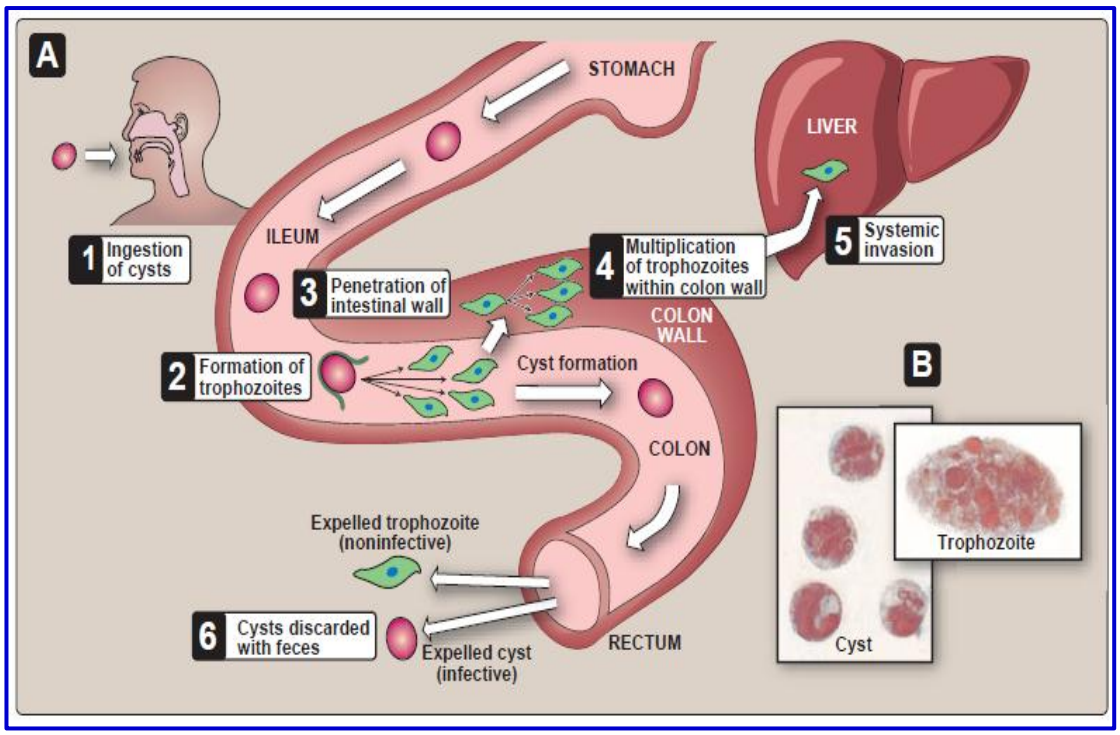


Figure: Life cycle of *Entamoeba histolytica*

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.

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
t (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.
- ✓ **The oval cyst** 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.

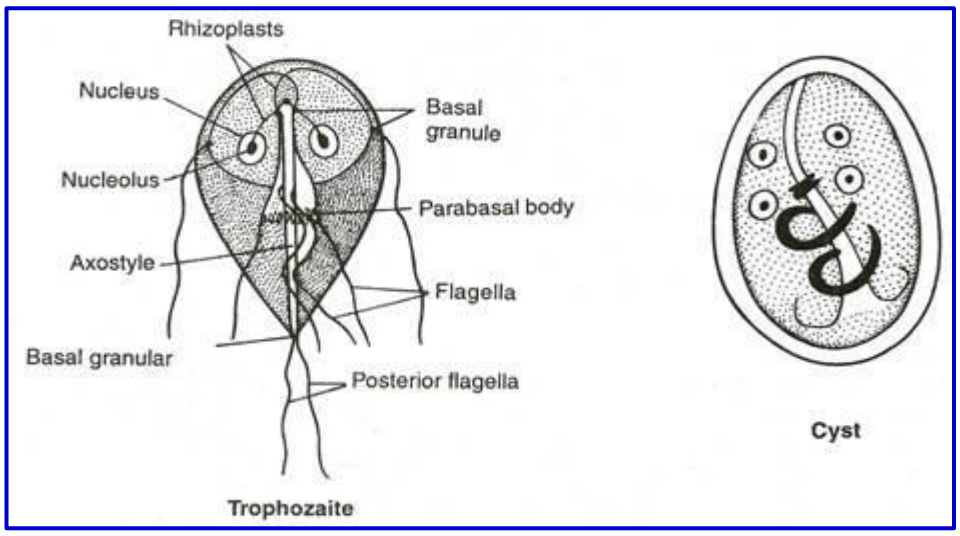


Figure: Trophozoite and cyst of *Giardia lambilia*

Life cycle of *Giardia lambilia*:

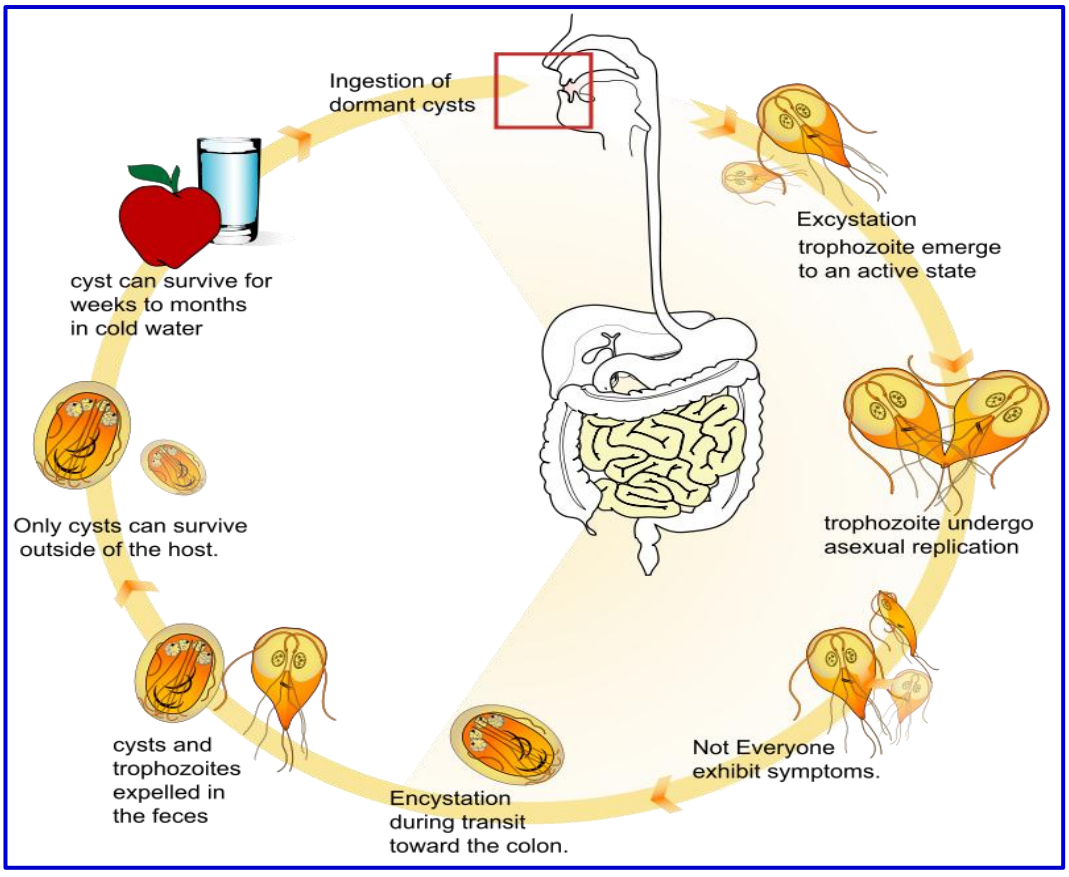


Figure: Life cycle of *Giardia lambilia*

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

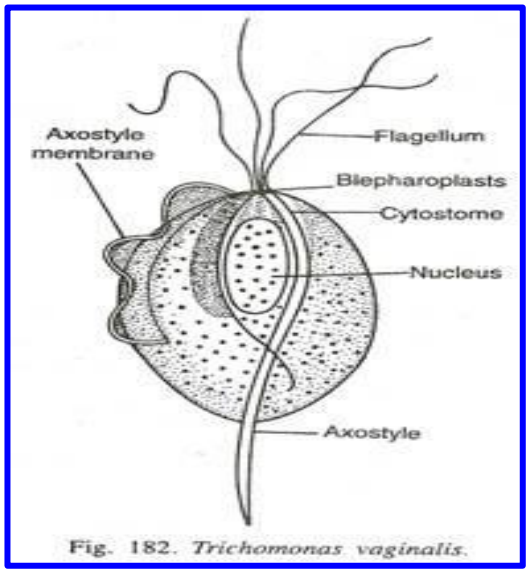
Habitat: The trophozoite is found in the urethra & vagina of women and the urethra & prostate gland of men.

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.



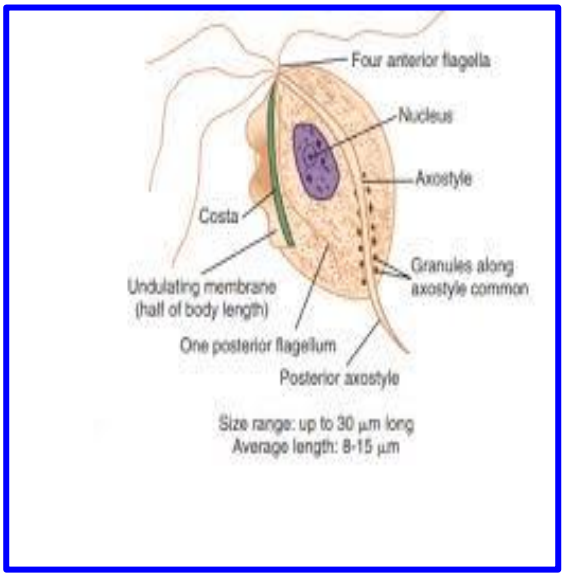


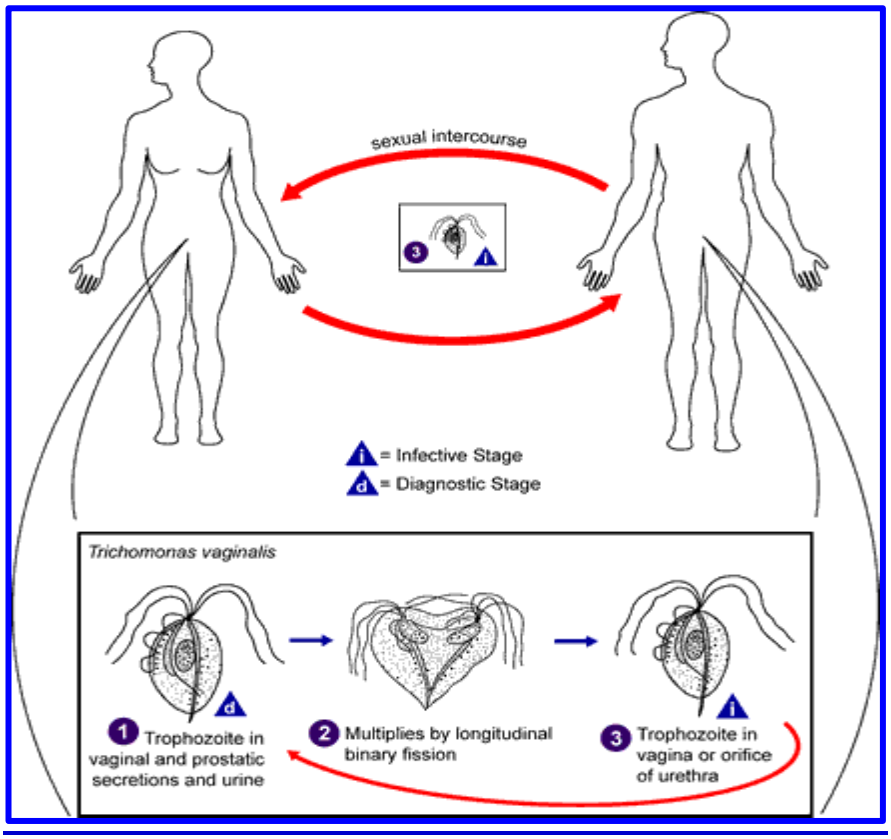
Figure: Trophozoite of *Trichomonas vaginalis*

❖ 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



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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

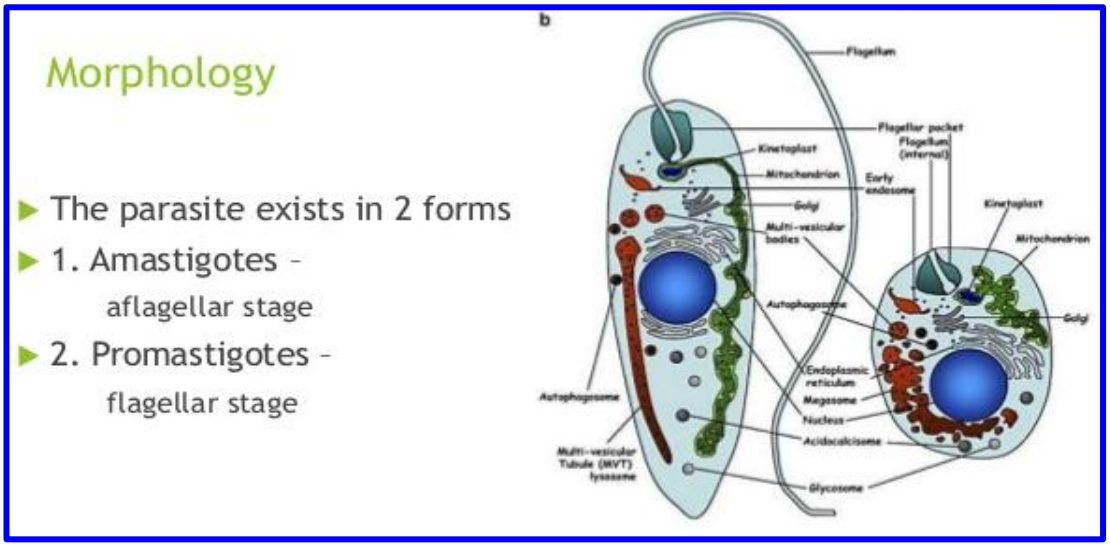
- ✓ **In females**, T. vaginalis may be found in urine sediment, wet preparations of vaginal secretions.
- ✓ **In males** it may be found in urine, wet preparations of prostatic or urethral secretions.

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.



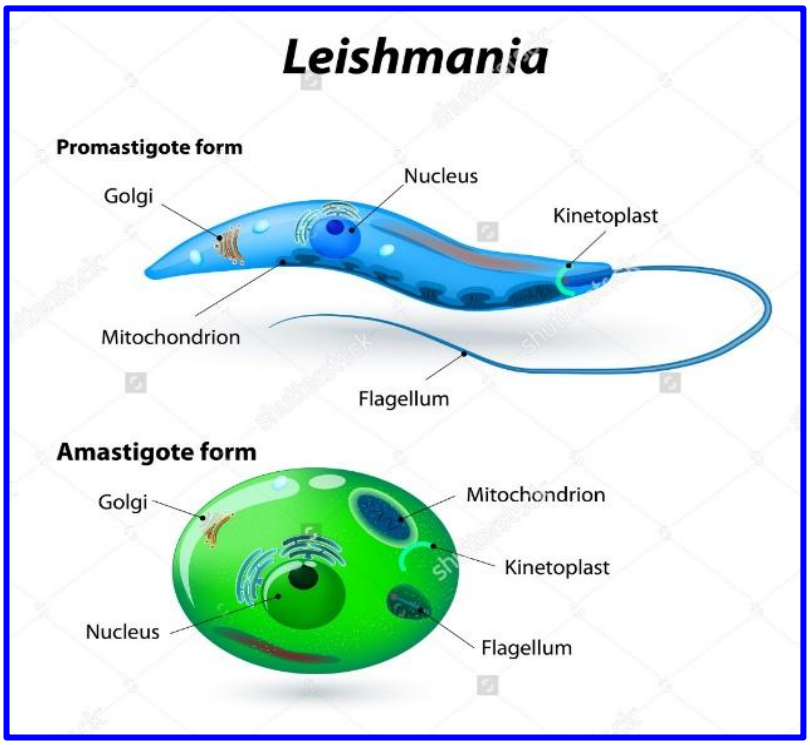


Figure: Promasitgote & amasigote forms of Leishmania

❖ 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 Cutaneous Leishmaniasis** *1-Leishmania mexicana (*Cutaneous leishmaniasis.) *2-Leishmania braziliensis* (mucocutaneous or cutaneous 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 the mouth & nose (inside 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.

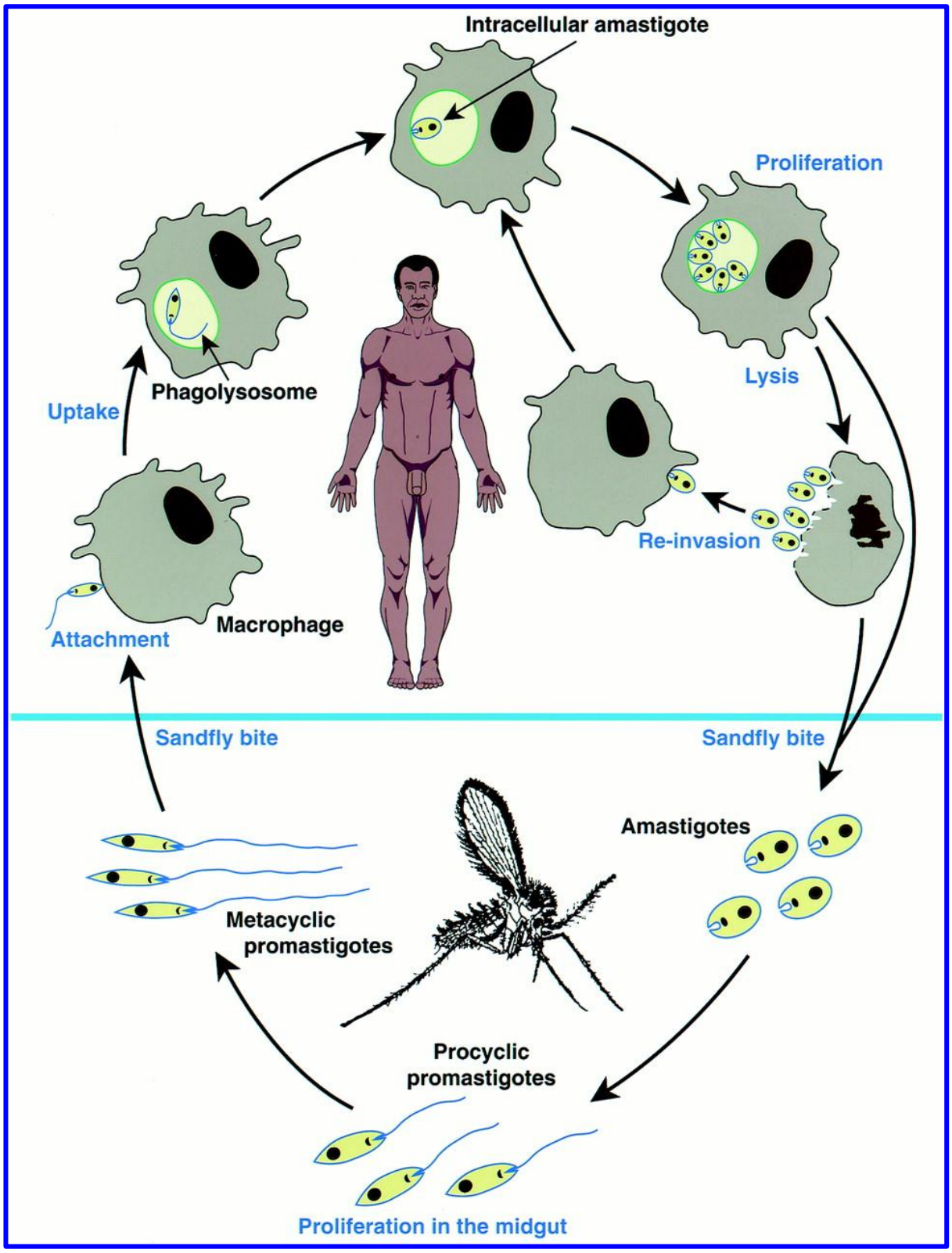


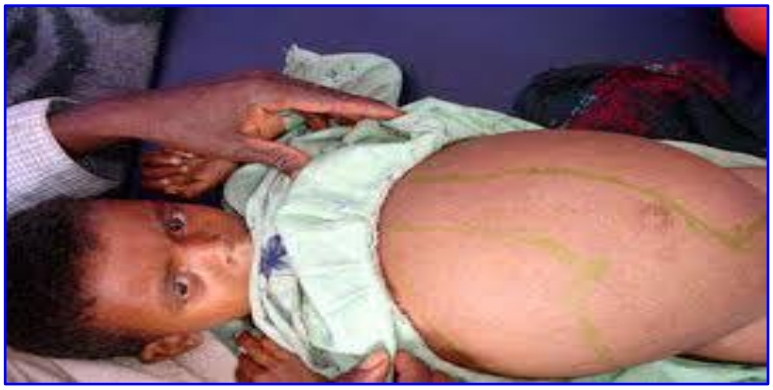
Figure: Life cycle of Leishmania Species

❖ 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.

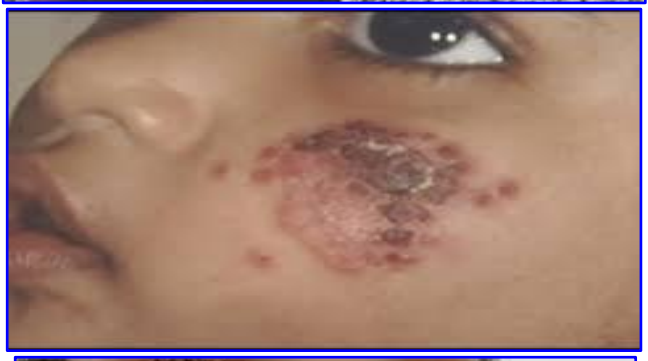
Some pictures on Leishmaniasis

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.

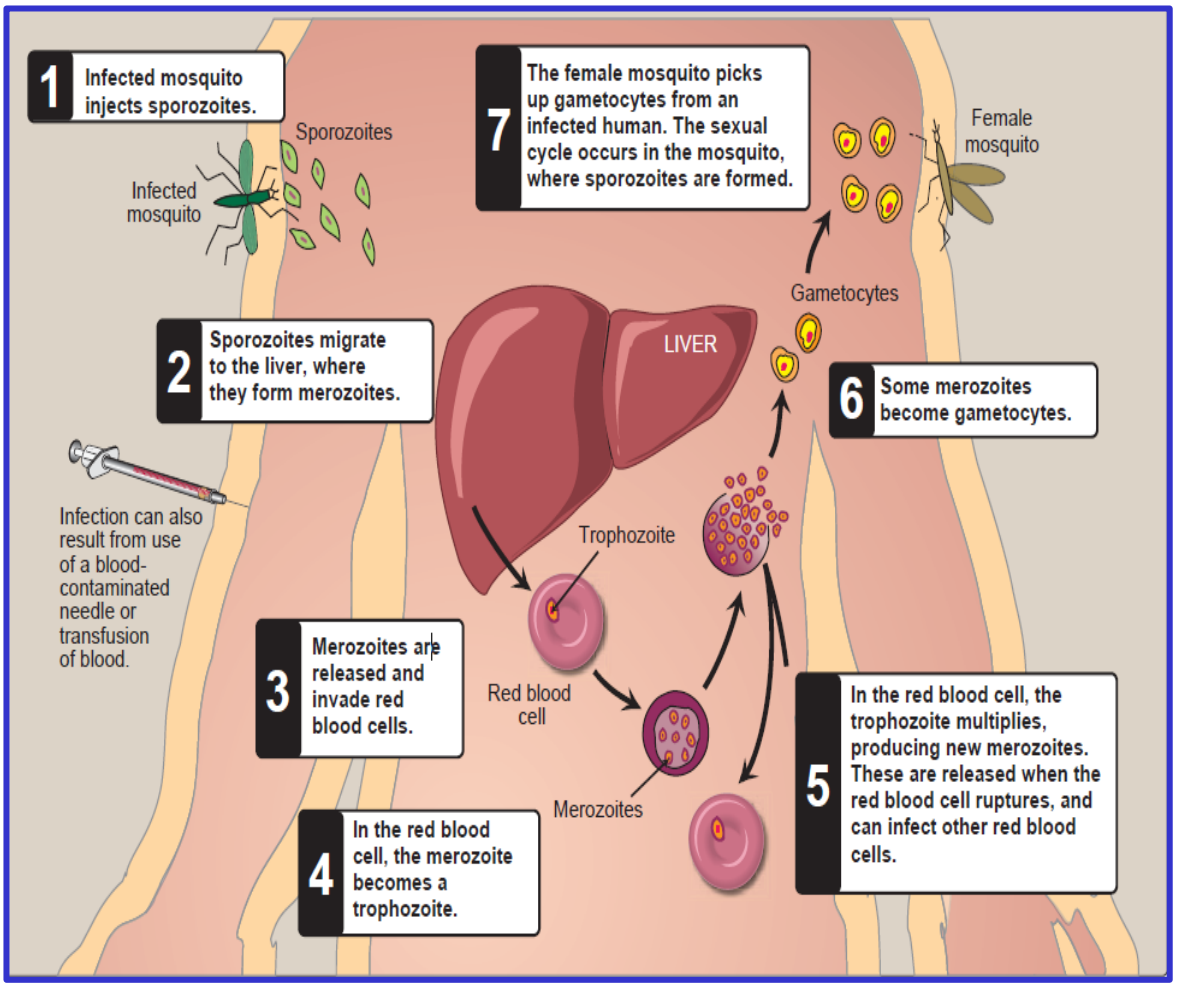


Figure: life cycle of Malaria

❖ **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.

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II- *Toxoplasma gondii:* another Coccidian parasites

- ❖ **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.

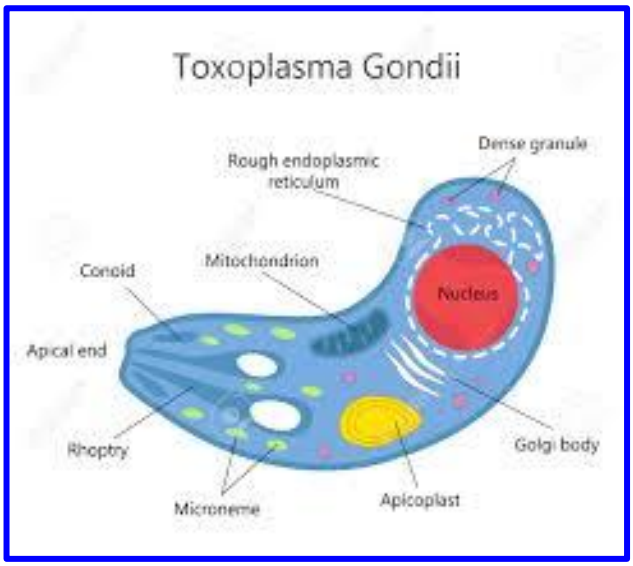
2- Transplacental transmission from an infected mother to the fetus.

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

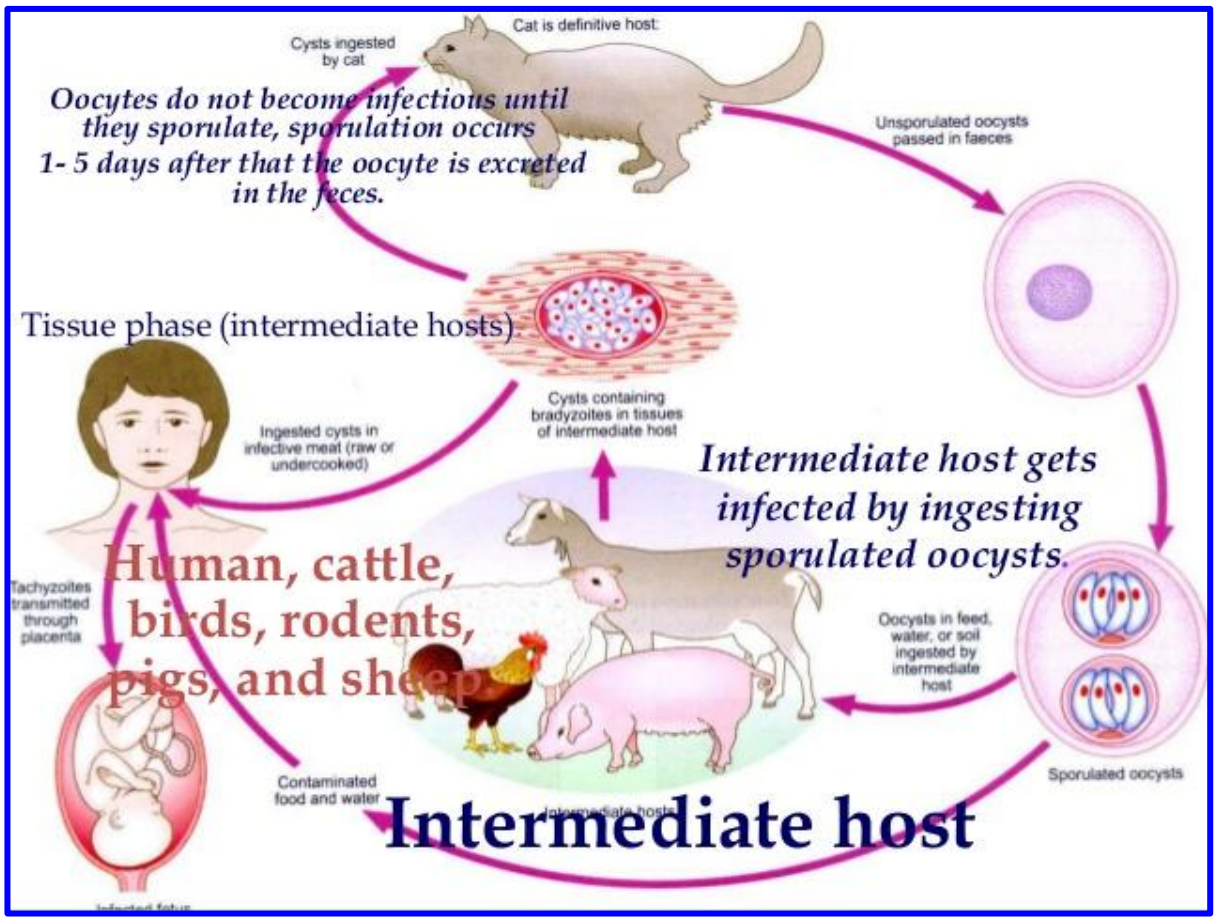
Important features: ***Toxoplasma gondii*** occurs in three forms- **trophozoite**, **tissue cyst** and **oocyst**. **The trophozoite and tissue cyst represent stages** in **asexual multiplication (schizogony)**, while **the oocyst** is formed by **sexual reproduction (gametogony or sporogony).** All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

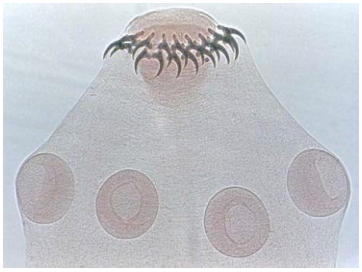
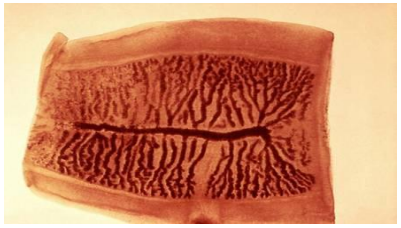
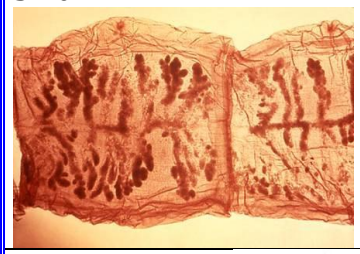
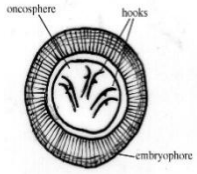
CESTODES (TAPEWORMS)

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.

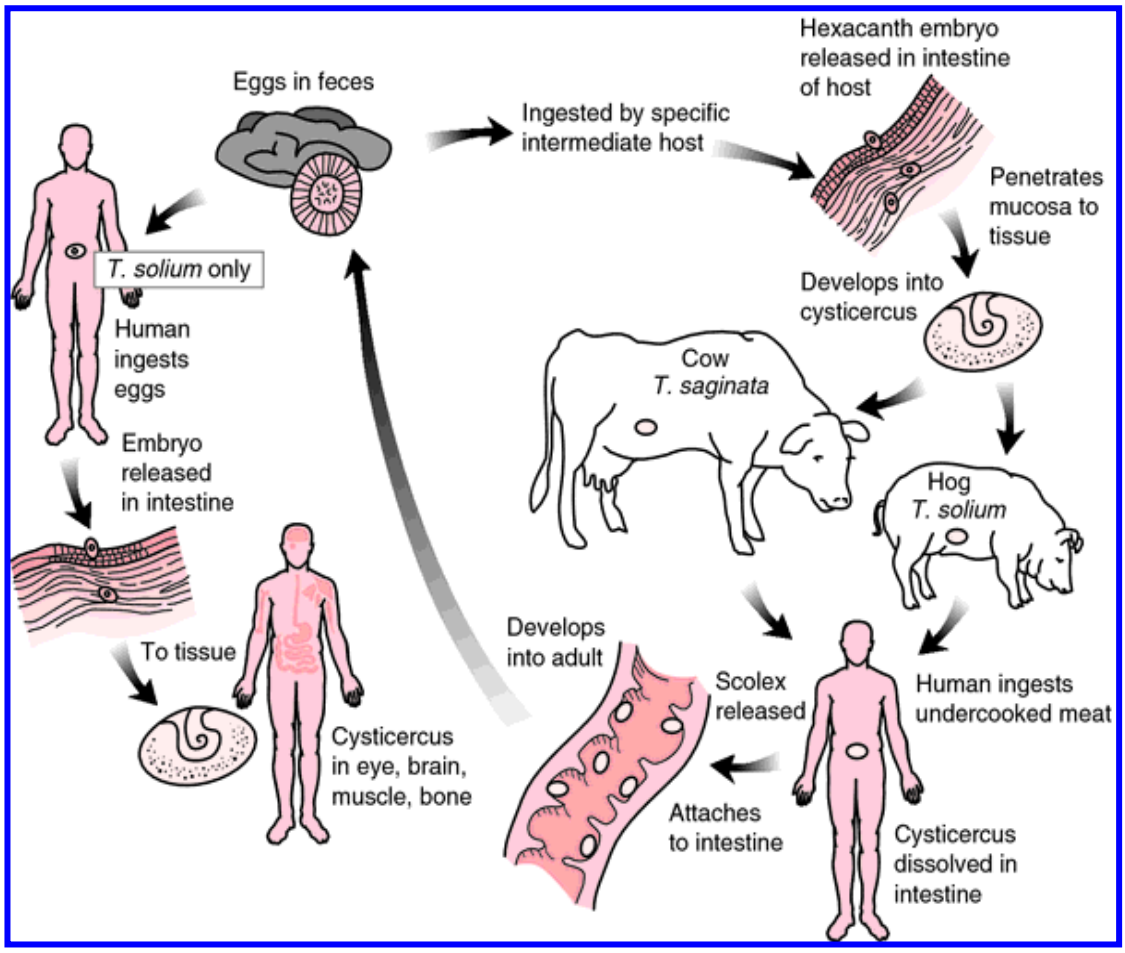
•These penetrate the gut wall with the aid of their hooks and gain entrance into the portal vessels or mesenteric lymphatics then to the systemic circulation.

• 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.



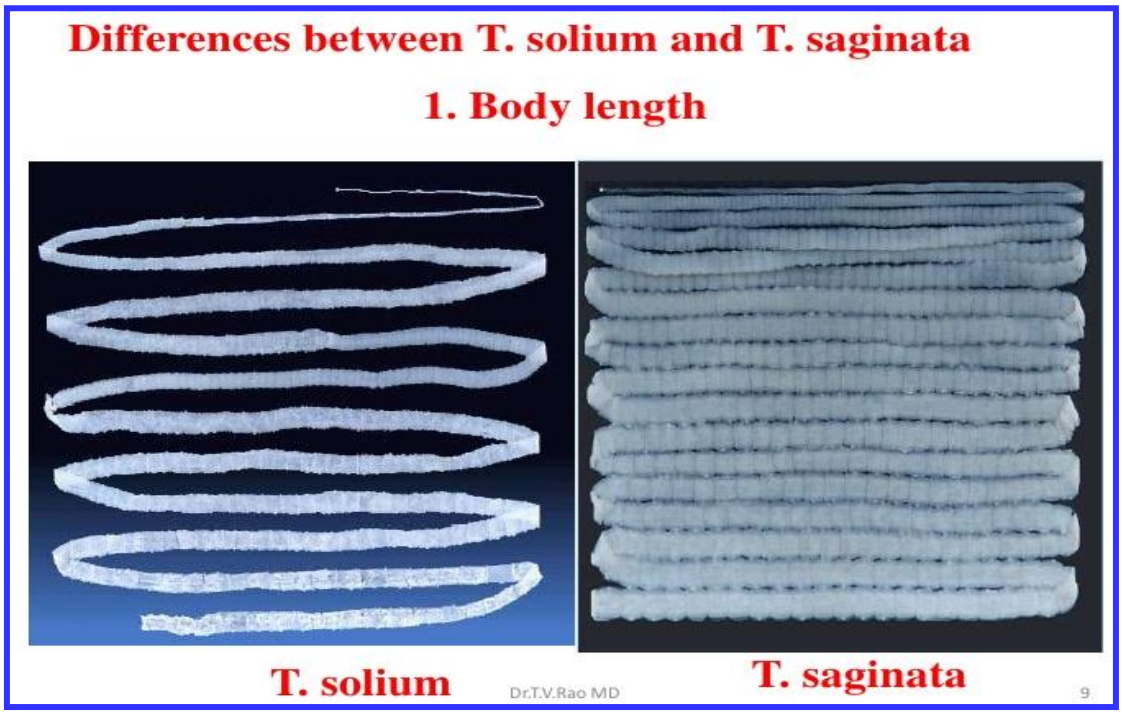
Life cycle of *T.saginata* and *T. solium*

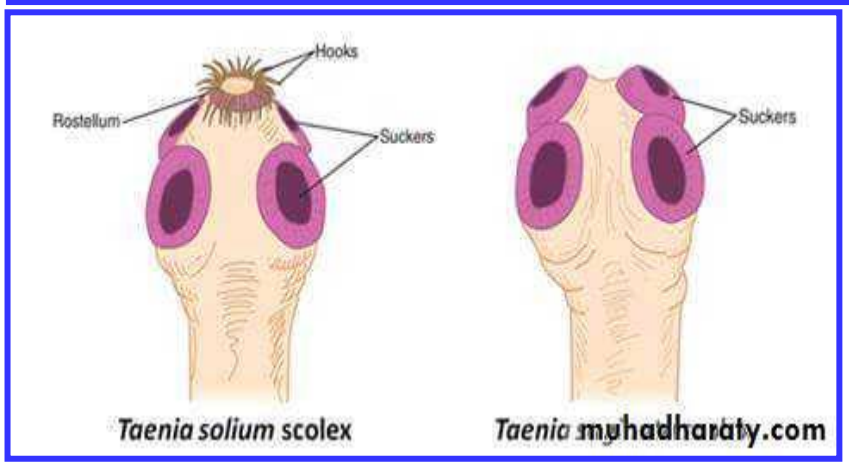
Laboratory Diagnosis:

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.

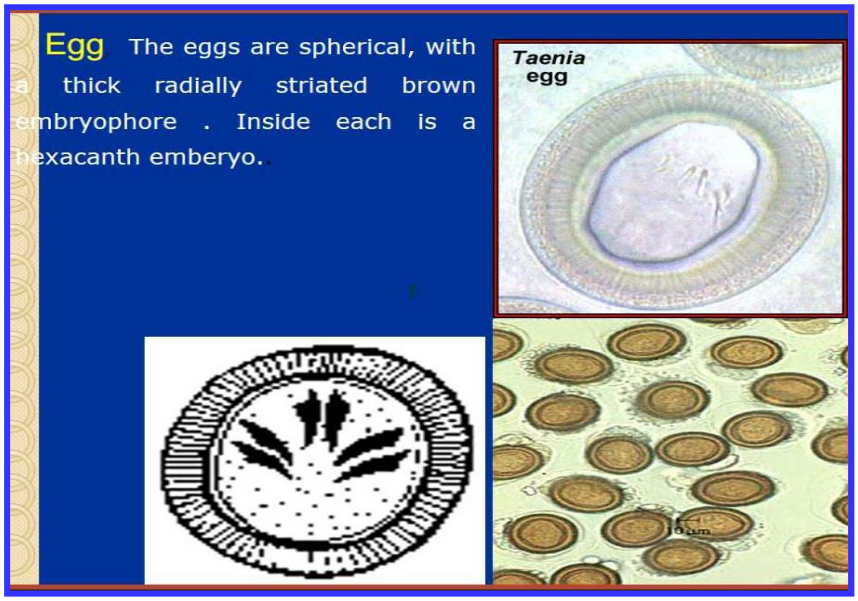
T. saginata

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).**

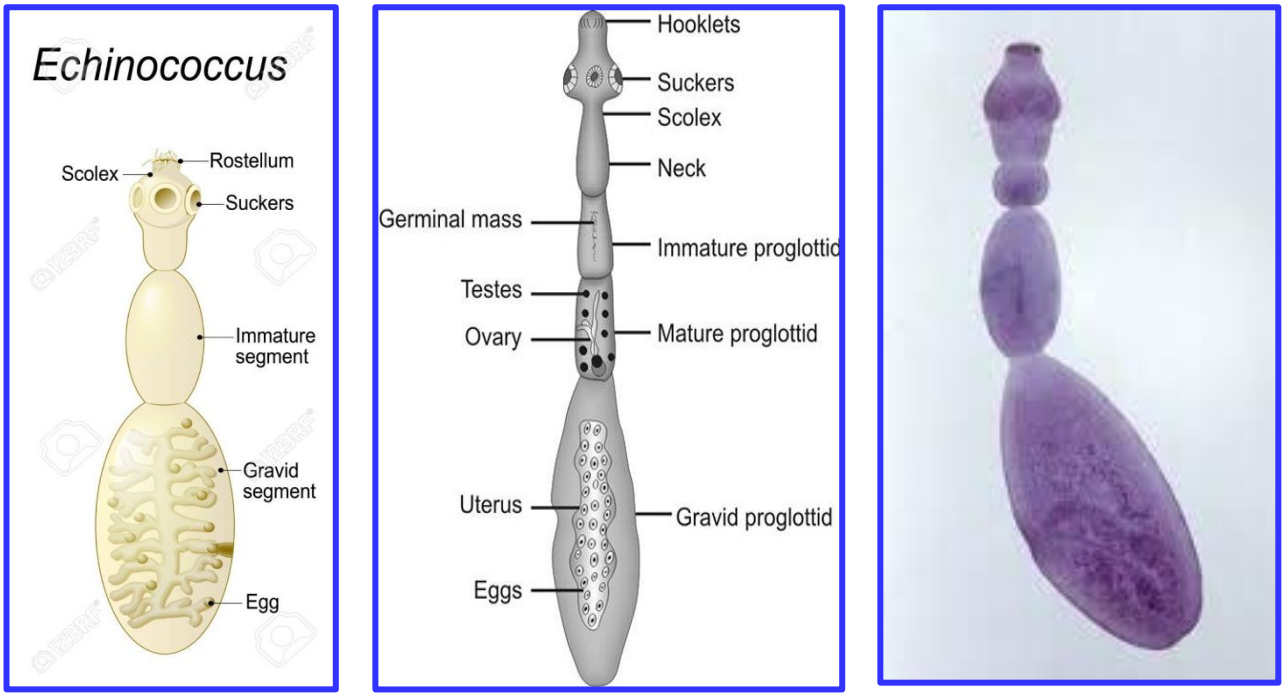


Figure: Adult worm of Echinococcus granulosis

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.

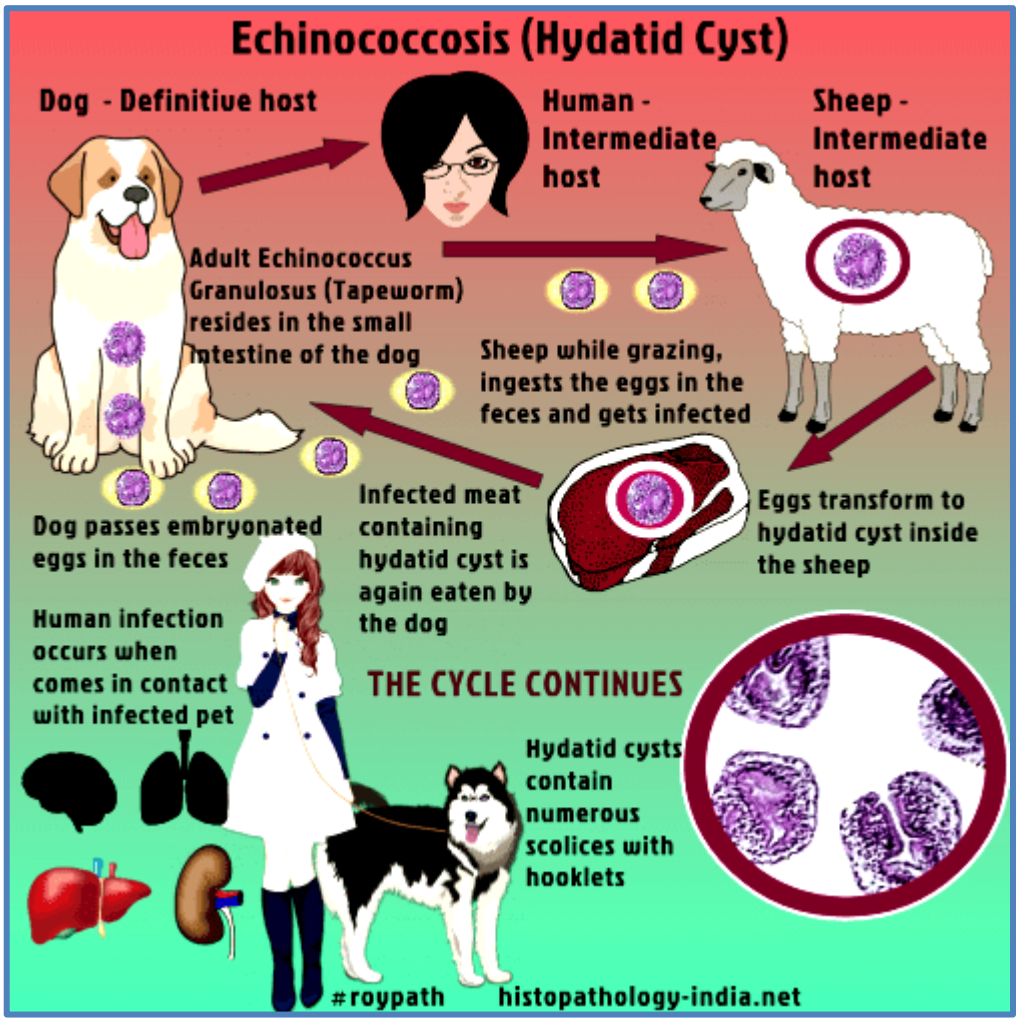


Figure: Life cycle of *Echinococcus granulosus*

Clinical features:

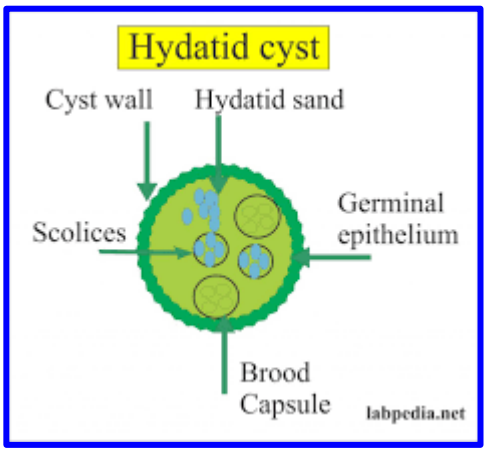
Asymptomatic infection is common, but in symptomatic patients It may cause:

- ✓ 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*

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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.

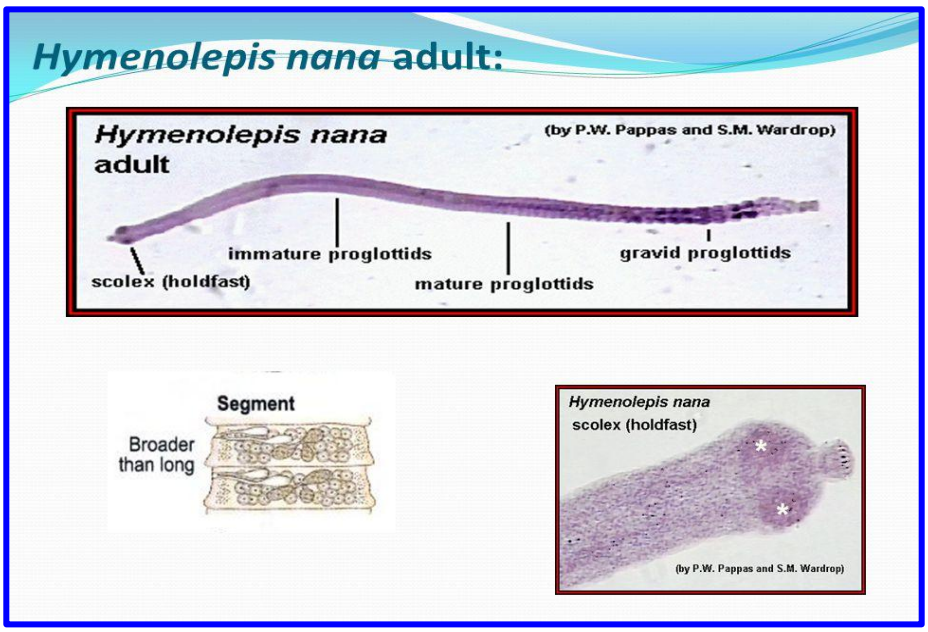


Figure: ***Hymenolepis nana***

- **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.

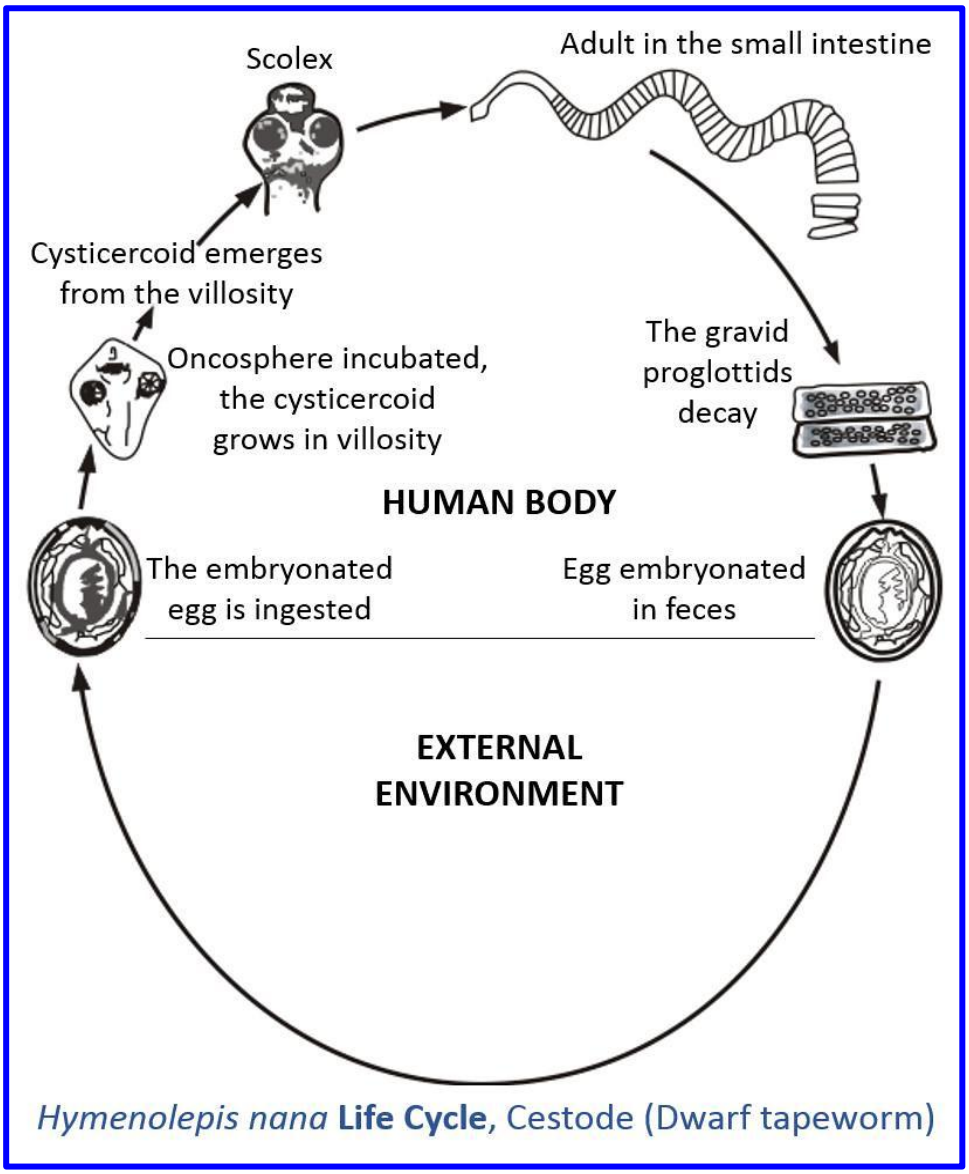


Figure: Life cycle of *Hymenolepis nana*

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:

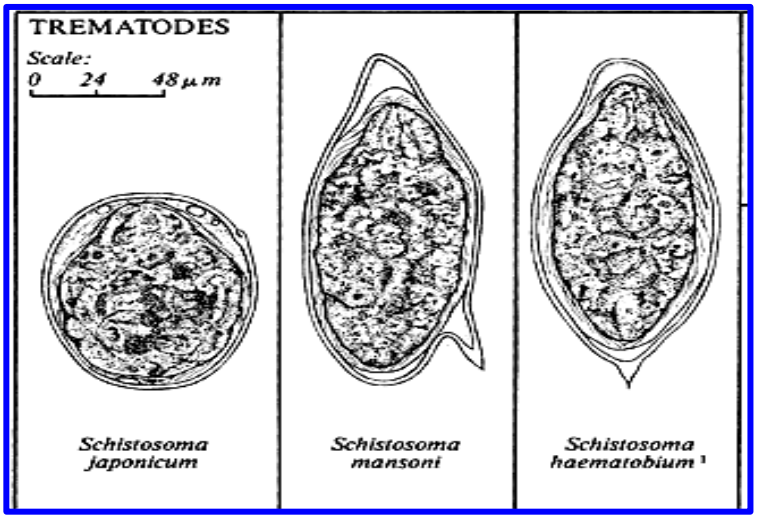
☒ ***S. mansoni*:** ♦ Microscopic examination of the **stool** for eggs after concentration by sedimentation method. The egg has characteristic lateral spine**.** ♦ Rectal snip

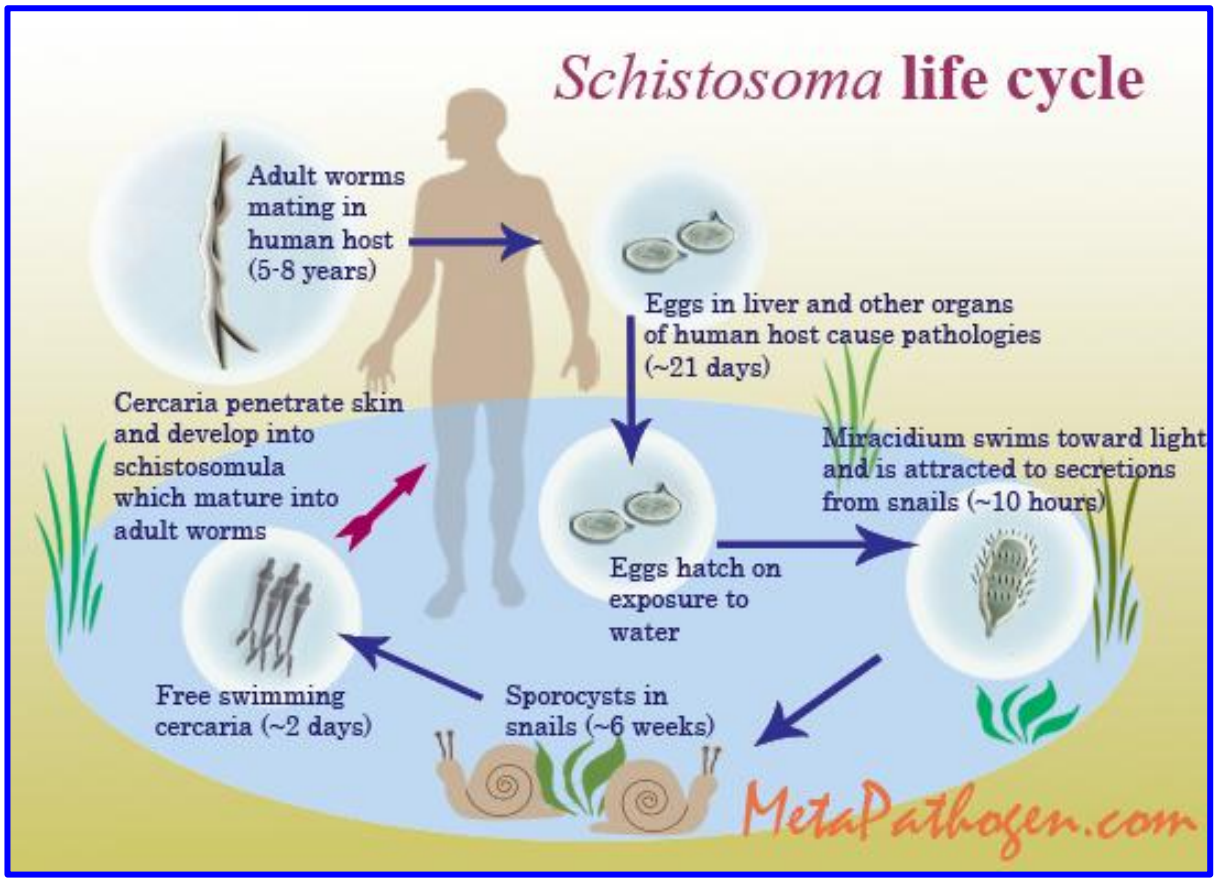
☒ ***S. haematobium*:** ♦ Examination of the **urine** after allowing it to sediment in a conical urinalysis glass. A drop from the sediment is taken and examined for eggs. Egg has terminal spine.

♦ Biopsy from bladder

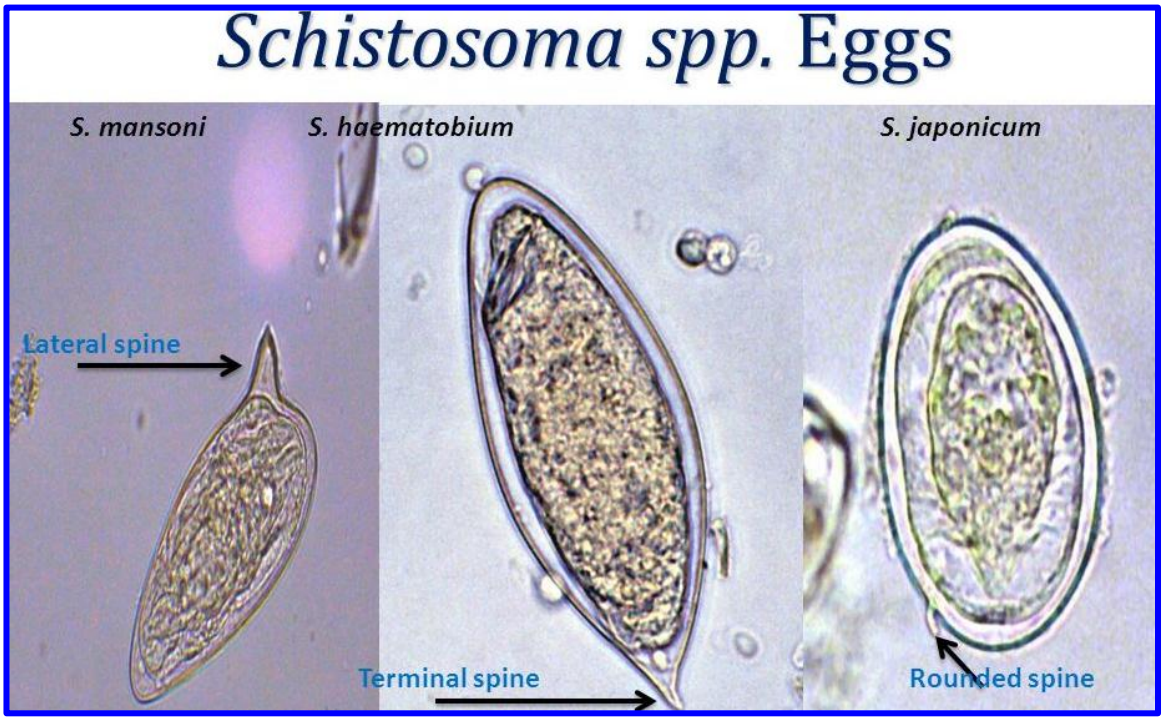
☒ ***S. japonicum*:** ♦ Microscopic examination of the **stool** for eggs after concentration by sedimentation method. The egg has characteristic lateral knop**.**

The Eggs of Schistosomes spp





The life cycle of Schistosomes spp



Nematodes (Round Worms)

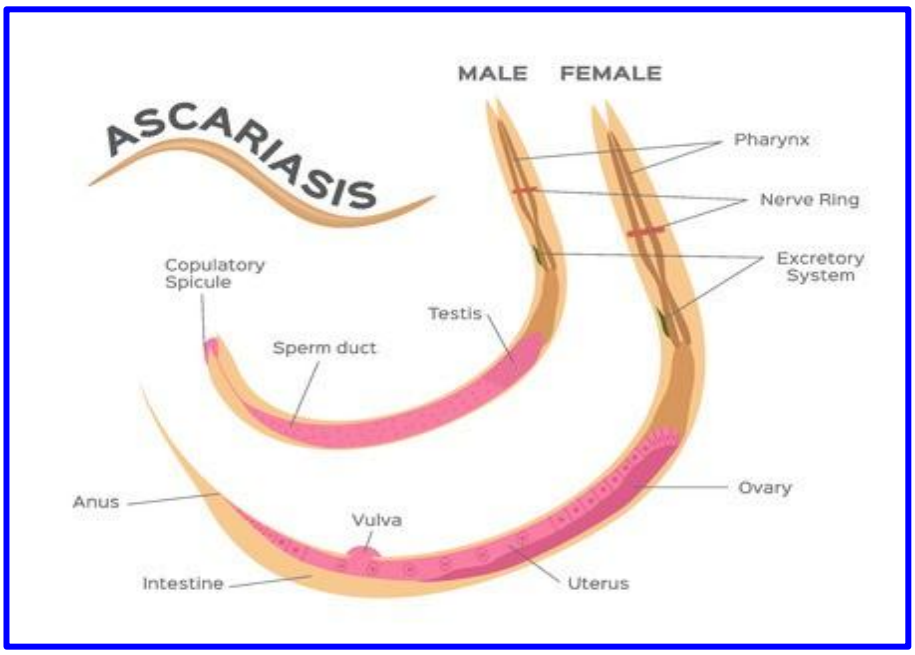
Properties of Nematodes:

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

Ascaris lumbricoides

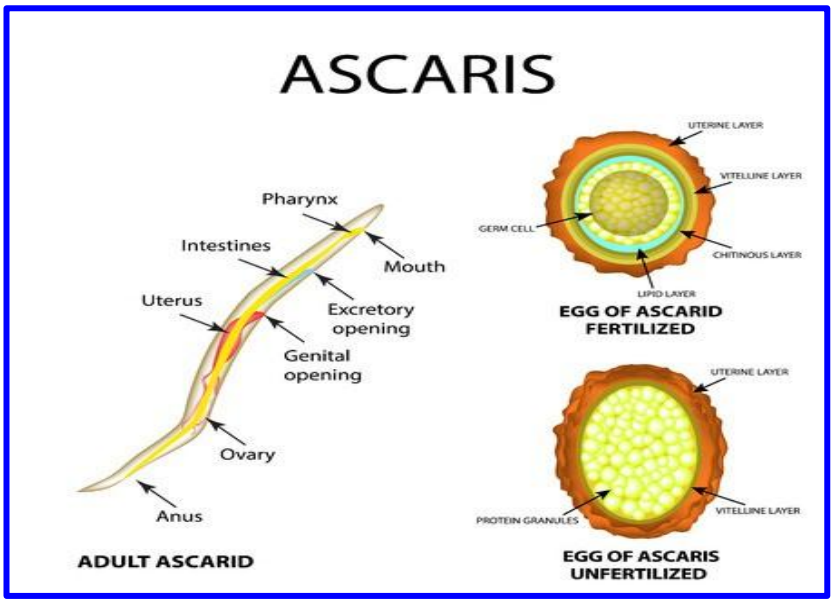
- **Disease:** ascariasis
- **Habitat:** small intestine
- **Infective stage:** fertilize egg which contain larvae
- **Common name:** roundworms
- **Final host:** have one host , **human** only .
- **Geographical distribution:** worldwide.

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.



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.



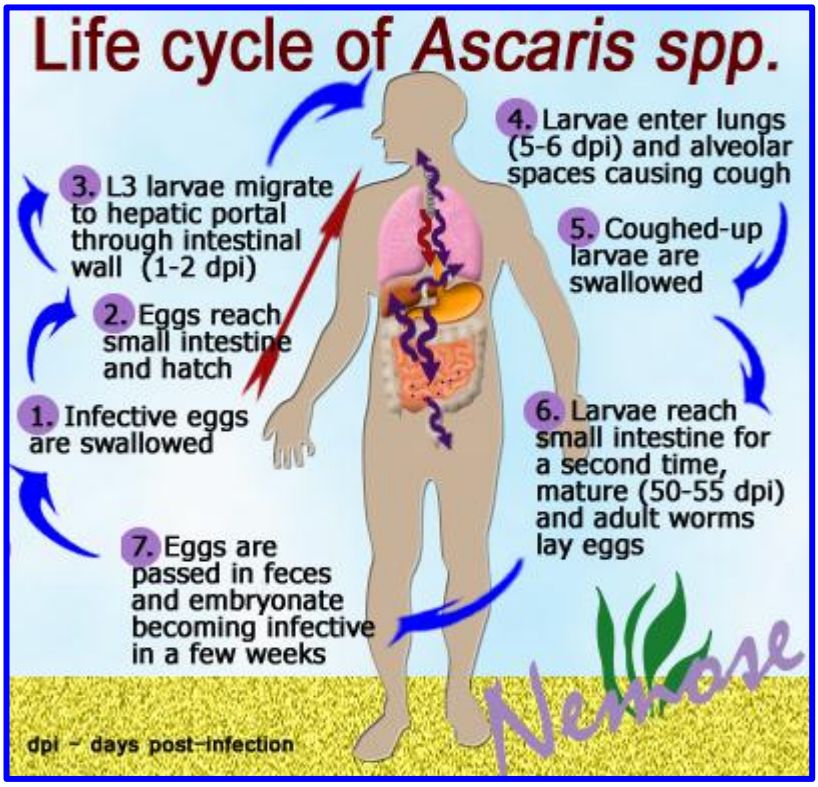


Figure: Life cycle of *Ascaris lumbricoides*

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.


Immunology Unite

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

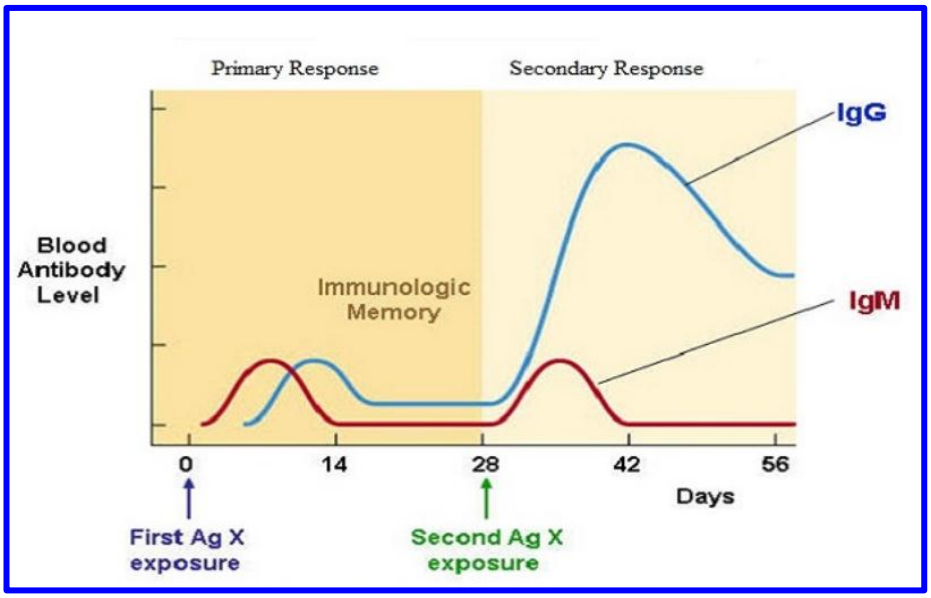


Figure: Primary and Secondary Immune Response

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.**

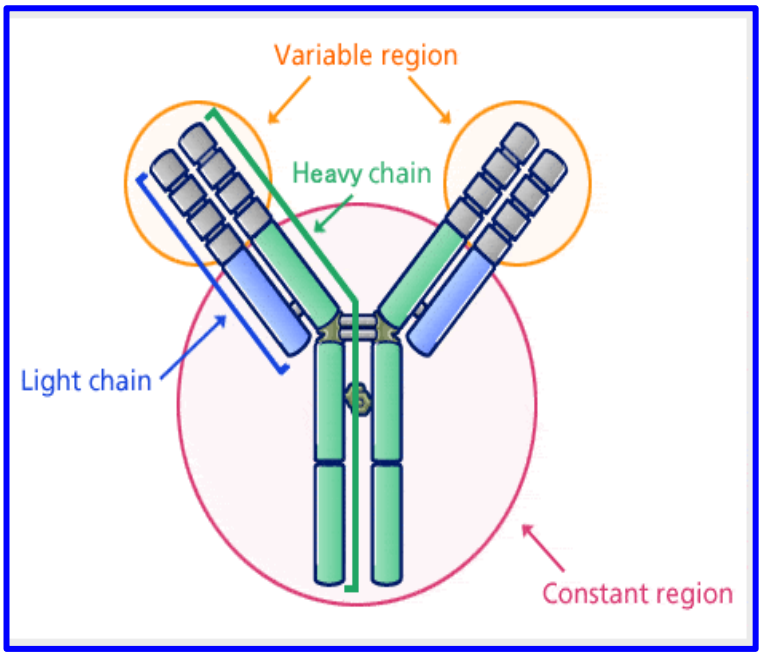


Figure: Antibody structure

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**'s 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.

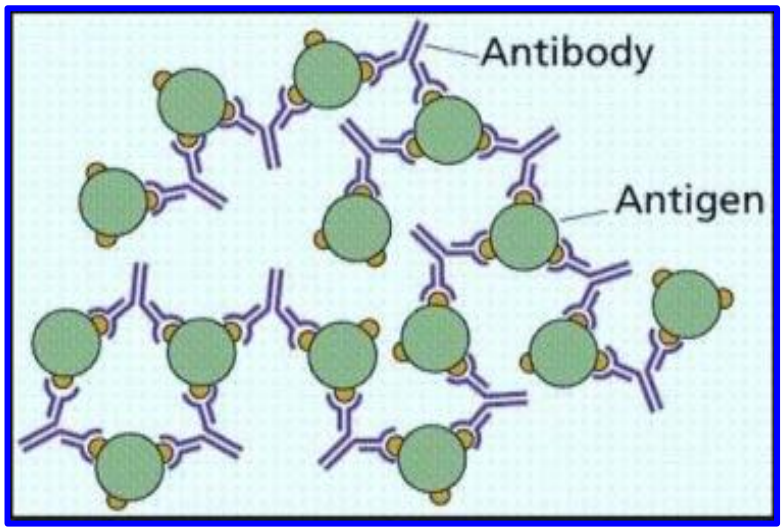


Figure: Ab-Ag Reaction

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.