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المرحلة الأولى

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Lecture One; General view about microbiology, History of microbiology, Plants and animals

What is microbiology?

Microbiology:- Is the science which study of living organisms of microscopic size. The term was introduced by the French chemist Louis Pasteur.

Microorganisms are microscopic form of life-organisms that are too small to see with the unaided eye. They usually consist of a single cell and include bacteria, archaea, fungi, protozoa, and algae. We will include viruses in our lecture as well. While viruses are not microorganisms, we refer to them as microbes, a more general term that includes microorganisms and viruses. **Microbiology** then is the study of microbes.

Medical microbiology:- Is concerned with aetiology, pathogenesis, laboratory diagnosis and treatment of infections in an individual and with the epidemiology and control of infection in the community.

A microorganism is one of a very diverse group of organisms that typically are microscopic and occur as independent, rapidly producing units that are comparatively less complex than plants and animals and exists almost everywhere.

The easy way to remember these features is

M = Microscopic

I = Independent units

C = Complex (less)

R = Rapid growth rates

O = Omnipresent (present everywhere)

History of microorganisms

The science of microbiology dates back only a few hundred years, yet the recent discovery of *Mycobacterium tuberculoses* DNA in 3000 years old Egyptian mummies remind us that microorganisms have been around for much longer. In fact bacterial ancestors were the first living cells to appear on earth. While we now relatively little about what earlier people thought about the causes, transmission, and treatment of disease, the history of the past few hundred years is better known. ***Let's look now at some key developments in microbiology that has helped the field progress to its current high technology state.***

Although microbes are most ancient and they had the planet all for themselves initially, even after the advent of man they have been influencing his life both for good and bad since time immemorial. In a lighter vein one can say that ever since the first toast was proposed and the first loaf of bread was baked man has known the influence of microbes.

Microbes were observed for the first time by Leeuwenhoek (1632-1723) a little more than 300 years ago, (was one of the first people to observe microorganisms, using a microscope of his own design, and made one of the most important contributions to biology). And even then their role in human life was never contemplated (أعتبر او قدر). They were just thought to be cute tiny animalcules and their study was a mere curiosity. One of the most discoveries the history of biology occurred in 1665 with the help of relatively crude microscope. An English man, Robert Hooke, after observing a thin slice of cork, reported to the world that life's smallest structure unites were "little boxes," or "cells," as he called them. Using his improved version of a compound microscope (one uses two sets of lenses); Hooke was able to see individual cells. Hook's discovery marked the beginning of the cell theory, the theory that all living things are composed of cell. Subsequent investigation into the structure and functional of cells were based on this theory.

Through the Hook's microscope was capable of showing cells, he lacked the staining techniques that would have allowed him to see microbes clearly. The Dutch merchant and amateur scientist Antoni van Leeuwenhoek was probably the first to actually observe live microorganisms through magnifying lenses. Between 1673 and 1723, he wrote a series of letters to the Royal society of London describing the "animalcules" he saw through his simple, single-lens microscope. Van Leeuwenhoek made detailed drawings of "animalcules" in rainwater, in liquid in which peppercorns had soaked, and in material scraped from his teeth. These drawings have since been identified as representations of bacterial and protozoa. After Van Leeuwenhoek discovered the previously "invisible" world of microorganisms the scientific community of the become interested in the origin of these tiny living things. Until the second half of the nineteen century, many scientists and philosopher believed that some forms of life could arise spontaneously from nonliving matter, they called hypothetical process spontaneous generation. Not much more than 100 years ago, people community believed that toads, snakes, and mice could be born of moist soil; that flies could emerge from manure; and that maggots, the larvae of flies, could arise from decaying corpses.

This theory was disputed by Francesco Redi, who showed that fly maggots do not arise from decaying meat (as others believed) if the meat is covered to prevent the entry of flies. An English cleric named John Needham advanced spontaneous generation, but Lazzaro Spallanzani disputed the theory by showing that boiled broth would not give rise to microscopic forms of life.

Louis Pasteur and the germ theory; Louis Pasteur worked in the middle and late 1800s. He performed numerous experiments to discover why wine and dairy products became sour, and he found that bacteria were to blame. Pasteur called attention to the importance of microorganisms in everyday life and stirred

scientists to think that if bacteria could make the wine “sick,” then perhaps they could cause human illness.

Pasteur had to disprove spontaneous generation to sustain his theory, and he therefore devised a series of swan-necked flasks filled with broth. He left the flasks of broth open to the air, but the flasks had a curve in the neck so that microorganisms would fall into the neck, not the broth. The flasks did not become contaminated (as he predicted they would not), and Pasteur's experiments put to rest the notion of spontaneous generation. His work also encouraged the belief that microorganisms were in the air and could cause disease. Pasteur postulated the germ theory of disease, which states that microorganisms are the causes of infectious disease.

Pasteur's attempts to prove the germ theory were unsuccessful. However, the German scientist Robert Koch provided the proof by cultivating anthrax bacteria apart from any other type of organism. He then injected pure cultures of the bacilli into mice and showed that the bacilli invariably caused anthrax. The procedures used by Koch came to be known as Koch's postulates**.** They provided a set of principles whereby other microorganisms could be related to other diseases.

The development of microbiology, in the late 1800s and for the first decade of the 1900s, scientists seized the opportunity to further develop the germ theory of disease as enunciated by Pasteur and proved by Koch. There emerged a Golden Age of Microbiology during which many agents of different infectious diseases were identified. Many of the etiologic agents of microbial disease were discovered during that period, leading to the ability to halt epidemics by interrupting the spread of microorganisms.

Then, after World War II, the antibiotics were introduced to medicine. The incidence of pneumonia, tuberculosis, meningitis, syphilis, and many other diseases declined with the use of antibiotics.

Work with viruses could not be effectively performed until instruments were developed to help scientists see these disease agents. In the 1940s, the electron microscope was developed and perfected. In that decade, cultivation methods for viruses were also introduced, and the knowledge of viruses developed rapidly. With the development of vaccines in the 1950s and 1960s, such viral diseases as polio, measles, mumps, and rubella came under control.

Modern microbiology; Modern microbiology reaches into many fields of human endeavor, including the development of pharmaceutical products, the use of quality-control methods in food and dairy product production, the control of disease-causing microorganisms in consumable waters, and the industrial applications of microorganisms. Microorganisms are used to produce vitamins, amino acids, enzymes, and growth supplements. They manufacture many foods, including fermented dairy products (sour cream, yogurt, and buttermilk), as well as other fermented foods such as pickles, breads, and alcoholic beverages.

One of the major areas of applied microbiology is biotechnology. In this discipline, microorganisms are used as living factories to produce pharmaceuticals that otherwise could not be manufactured. These substances include the human hormone insulin, the antiviral substance interferon, numerous blood-clotting factors and clot dissolving enzymes, and a number of vaccines. Bacteria can be reengineered to increase plant resistance to insects and frost, and biotechnology will represent a major application of microorganisms in the next century.

Branches of microbiology

1- Bacteriology: Is the science which study of bacteria, the smallest, simple, single celled unicellular organisms. Because their genetic material is not enclosed in a special nuclear membrane, bacterial cells are called prokaryotes (prokaryotic organism), from the Greek word meaning prenucleus. Prokaryotes include both bacteria and the archaea.

2- Mycology: Is the science which study of fungi whose cells have a distinct nucleus containing the cells' genetic material (DNA), surrounding by a special envelope called the nuclear membrane. **Fungi** are group of eukaryotes that include both unicellular, microscopic forms (mold and yeast) and larger multicellular form mushrooms.

3- Phycology: Is the science which study of simple, photosynthetic eukaryotes with a variety of shapes and both sexual and asexual reproductive form called algae. The algae of interest to microbiologist are usually unicellular. The cell wall of many algae like those of plants, are composed of cellulose.

4- Protozoology: Is the science which study of protozoa. **Protozoa** are unicellular, eukaryotic microbes. Protozoa have a Varity of shapes and live either as free entities or as parasites (organisms that derive nutrients from living host).

5- Virology: Is the science which The study of viruses. **Viruses**-minute, unicellular particles that parasitize living things. Viruses are very different form the other microbial groups. They are so small that can be seen only with an electronic microscope, and they are acellular (not cellular).

Parasitology: Is the science which study of multicellular animal parasites. Including pathogenic protozoa, helminthes and certain insects.

Immunology. Is the science which study of systems of body defenses that protect against infection. This science includes serology, a discipline that tests the products of immune reactions in blood serum and helps in the diagnosis of infectious diseases.

Microbial taxonomy Is the science which study of classification, naming and identification of microorganisms.

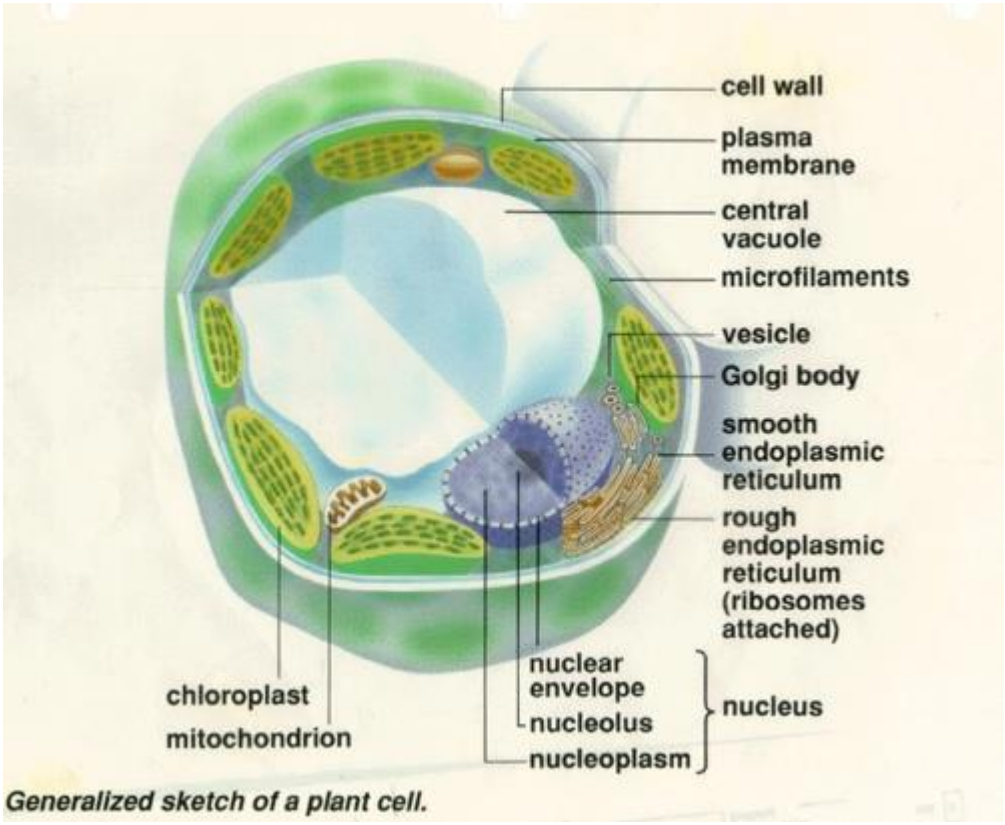
Plants

Plants can be divided into two groups**: plants1** and **plants2**. Plants1 contain all **photosynthetic organisms** which use light, H2O, and CO2 to make organic compounds and O2. **Plants1** are defined ecologically (based on their role in nature). Some plants1 can be bacteria or even animals! One example of this a green slug, *Elysia chlorotica*. Green slugs collect chloroplasts from algae and use them for their entire life as food producers. Therefore, green slugs are both animals and plants1.

Plants2 are all organisms from Vegetabilia kingdom. Normally, **plants2 are green organisms with a stem and leaves.** We can define them also as multi-tissued, terrestrial, and primarily photosynthetic eukaryotes. Those who fall into that category, are fully parasitic plants (mycoparasites like Pterospora, root parasites like Hydnora, stem parasites like Cuscuta, and internal parasites like Pilostyles) which do not practice photosynthesis but have tissues, terrestrial lifestyle and originated from photosynthetic ancestors.

Plants, like any multicellular organisms, are a mass of cells that show a complex division of labor. Plants have different types of cells. They have tissues and even organs. But the basic unit of plant life, the cell, has properties and structures that make it different from those of other life forms.

The plant cell is surrounded by the **Cell wall**, just external to the **Plasma membrane** forming the boundary of the **Protoplast.** The protoplast consists of the **Cytoplasm,** Endoplasmic reticulum, Golgi, Flagella and cilia, Cytoskeletal components and Mitochondria



Generalized sketch of a plant cell.

Cross section of plant cell

Animal Cell

Animals, plants, fungi, and protists all have eukaryotic cells, while bacteria and archaea have simpler prokaryotic cells. Eukaryotic cells are distinguished by the presence of a nucleus and other membrane-bound organelles. Animal cells, unlike plants and fungi cells, do not have a cell wall. Instead, multicellular animals have a skeleton which provides support for their tissues and organs.

Animal cells are the basic unit of life in organisms of the kingdom Animalia. They are eukaryotic cells, meaning that they have a true nucleus and specialized structures called organelles that carry out different functions of the body including producing and storing energy, making proteins, replicating the DNA, and transportation of molecules through the body. Animal cells do **not have** cell walls or chloroplasts, the organelle that carries out photosynthesis.

Animal Cell Structure

The cell has a variety of different parts. It contains many different types of specialized organelles that carry out all of its functions.

1- Nucleus

The nucleus contains a cell's deoxyribonucleic acid (DNA), its genetic material. DNA contains instructions for making proteins, which controls all of the body's activities. In the nucleus, **DNA is tightly winded around histones, which are proteins, to form structures called chromosomes**. DNA is located in the nucleolus region of the nucleus,. The nucleus is surrounded by a nuclear envelope (also called nuclear membrane), which separates it from the rest of the cell. **The nucleus also regulates the growth and division of the cell.** When the cell is

preparing to divide during mitosis, the chromosomes in the nucleus duplicate and separate, and two daughter cells are formed.

2- Ribosomes

Ribosomes are where proteins are synthesized. They are found within all cells, including animal cells. In the nucleus, a sequence of DNA that codes for a specific protein is copied onto a complementary messenger RNA (mRNA) chain. The mRNA chain travels to the ribosome via transfer RNA (tRNA), and its sequence is used to determine the correct placement of amino acids in a chain that makes up the protein. In animal cells, **ribosomes can be found freely in a cell's cytoplasm, or attached to membranes of the endoplasmic reticulum**.

3- Endoplasmic Reticulum

The endoplasmic reticulum (ER) is a network of membranous sacs called cisternae that branches off from the outer nuclear membrane. It modifies and transports proteins that are made by ribosomes. There are two kinds of endoplasmic reticulum, smooth and rough. Rough ER has ribosomes attached. Smooth ER does not have ribosomes attached and has functions in making lipids and steroid hormones and removing toxic substances

4- Vesicles

Vesicles are small spheres of a lipid bilayer, which also makes up the cell's outer membrane. They are used for transporting molecules throughout the cell from one organelle to another and are also involved in metabolism.

5- Golgi Apparatus

The Golgi apparatus, also called the Golgi complex or Golgi body, is also made up of cisternae, but the cisternae are not interconnected like those of the ER. The Golgi apparatus receives proteins from the ER and folds, sorts, and packages these proteins into vesicles.

6- Mitochondria

The process of cellular respiration occurs in the mitochondria. During this process, sugars and fats are broken down and energy is released in the form of adenosine triphosphate (ATP). So mitochondria are commonly known as "the powerhouse of the cell".

7- Cytosol

The cytosol is the liquid contained within cells. Cytosol and all the organelles within it, except for the nucleus, are collectively referred to as a cell's cytoplasm. This solution is mostly made of water, but also contains ions like potassium, proteins, and small molecules. The pH is generally neutral, around 7.

8- Cytoskeleton

The cytoskeleton is a network of filaments and tubules found throughout the cytoplasm of the cell. It has many **functions**: it gives the cell **shape, provides strength, stabilizes tissues, anchors organelles** within the cell, and has a role in cell **signaling**. There are three types of cytoskeletal filaments: microfilaments, microtubules, and intermediate filaments. Microfilaments are the smallest, while microtubules are the biggest.

9- Cell Membrane

The cell membrane surrounds the entire cell. Animal cells only have a cell membrane. The cell membrane is a double layer made up of phospholipids. Phospholipids are molecules with a phosphate group head attached to glycerol and two fatty acid tails. They spontaneously form double membranes in water due to the hydrophilic properties of the head and hydrophobic properties of the tails. The cell membrane is **selectively permeable**, meaning it only allows certain molecules through. Oxygen and carbon dioxide pass through easily, while larger or charged molecules must go through a special channel in the membrane.

Lecture Two; Shape of Bacteria, it's size it's arrangement

Bacterial morphology

What bacteria look like?

Bacterial exhibit several distinct shape, or morphologies. **Bacteria** are single-celles and are classified under the domain Prokaryota. They lack membrane-bound organelles like those found in eukaryotes. They are vary in shape which allows different types of bacteria to be classified based on their general shape.

There are the three primary major categories of bacteria based on their shapes: **Cocci, bacilli and spiral**

1- Cocci call Arrangements

Coccus is one of the three primary shapes of bacteria. Coccus (cocci plural) bacteria are round, oval, or spherical in shape. These cells can exist in several different arrangements that include:

a- **Diplococci:** cells remain in pairs after dividing.
b- **Streptococci:** cells remain in chains after dividing.
c- **Tetrad:** cells remain in groups of four and divide in two planes.
d- **Sarcinae:** cells remain in groups of eight and divide in three planes.
e- **Staphylococci:** cells remain in clusters and divide in multiple planes.

Bacillus Cell Arrangements

a- Bacillus is one of the three primary shapes of bacteria. Bacillus (bacilli plural) bacteria have rod-shaped cells. These cells can exist in several different arrangements that include:
b- Monobacillus: remains single rod-shaped cell after dividing.
c- Diplobacilli: cells remain in pairs after dividing.
d- Streptobacilli: cells remain in chains after dividing.
e- Palisades: cells in a chain are arranged side-by-side instead of end-to-end and are partially attached.
f- Coccobacillus: cells are short with a slight oval shape, resembling both coccus and bacillus bacteria.

Spirilla Cell Arrangements

Spiral shape is one of the three primary shapes of bacteria. Spiral bacteria are twisted and commonly occur in two forms: spirillum (spirilla plural) and spirochetes. These cells resemble long, twisted coils.

Spirilla

Spirilla bacteria are elongated, spiral-shaped, rigid cells. These cells may also have flagella, which are long protrusion used for movement, at each end of the cell. An example of a spirillum bacterium is *Spirillum minus*, which causes rat-bite fever.

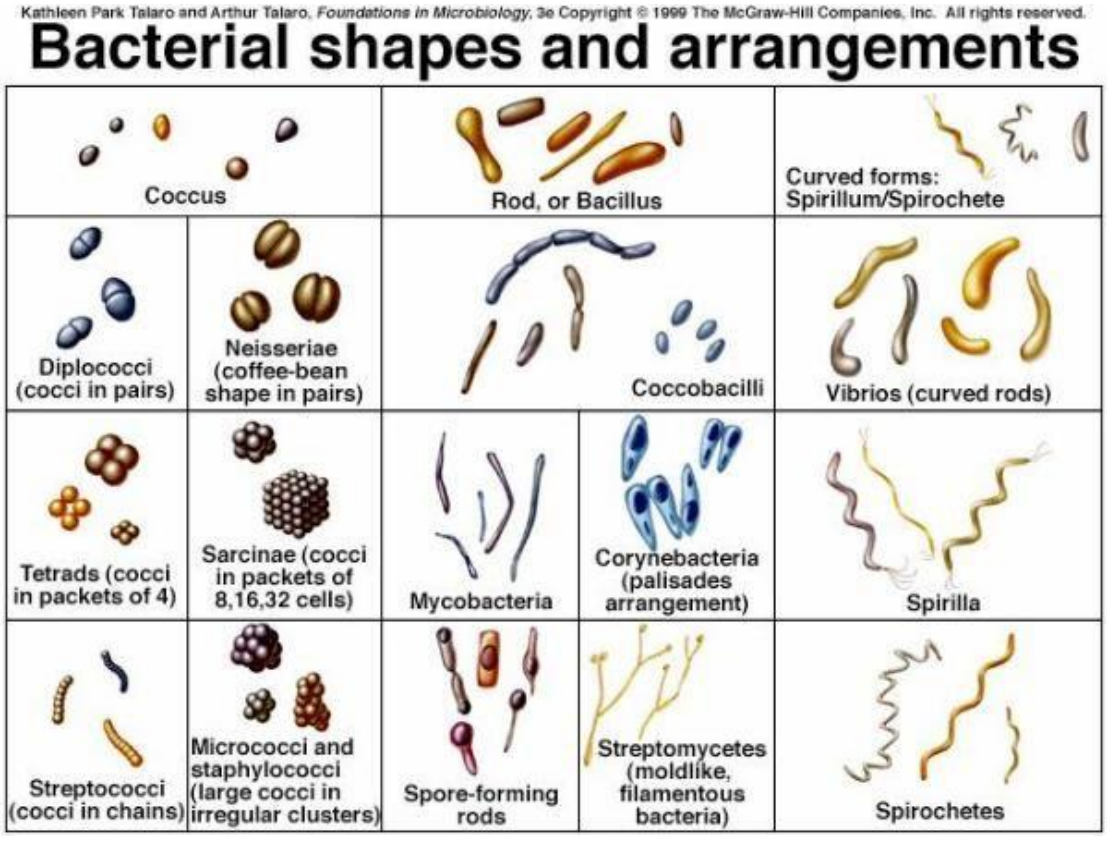
Spirochetes

Spirochetes (also spelled spirochaete) bacteria are long, tightly coiled, spiral-shaped cells. They are more flexible than spirilla bacteria. Examples of spirochetes bacteria include *Borrelia burgdorferi*, which causes Lyme disease and *Treponema pallidum*, which causes syphilis.

Vibrio Cell Arrangements

Vibrio bacteria have a slight twist or curve and resemble the shape of a comma. They also have a flagellum, which is used for movement. *Vibrio cholerae* which is responsible for cholera.

The shape of bacterial cells is determined by the organization of **the cell wall**, the semi-rigid structure surrounding the cell. However, because many bacterial species have similar morphologies and because environmental conditions and stress can sometimes cause changes in bacterial morphology, physical appearance is seldom conclusive for identifying bacterial species.



Some bacteria do not exhibit regular shapes, but may exhibit highly variable shapes. These bacteria are preferred to as **pleiomorphic**. Examples of these

pleiomorphic bacteria include member of the genus **Mycobacterium**, which do not make a cell wall, as a result, do not have a regular shape. Some bacteria grow in most **complex multicellular** arrangement. Soil bacteria for the **Actinomycete** group grow as irregularly branching filamentous called hyphae that are composite of chains of cells. **Hyphae** can form three dimensional network called mycelia that can rise above the substrate, penetrate down to the soil, or both. Many fungi eukaryotical organisms, form hyphae and mycelia superficially similar to the hyphae and mycelia formed by the bacterial species.

Size of bacteria

Just as bacteria come with range of shapes, bacteria also come in range of sizes, with cells of most bacterial species being somewhere between 0.5 µm and 5µm in length. Bacteria are usually smaller than eukaryal cells; even small eukaryal microbes such as yeast are typically at **least 5µm in diameter**.

Most bacteria cannot be seen by the unaided human eye. Microscopy, therefore, is an integral tool of microbiologist. Different types of microscopes, like electron microscopes and light microscop.es, aloe as to see objects of different sizes.

Bacterial cell structure

Capsule - Some species of bacteria have a third protective covering, a capsule made up of polysaccharides (complex carbohydrates). Capsules play a number of roles, but the most important are to keep the bacterium from drying out and to protect it from phagocytosis (engulfing) by larger microorganisms. The capsule is a major virulence factor in the major disease-causing bacteria, such as *Streptococcus pneumonia*

Cell wall: Each bacterium is enclosed by a semi-rigid cell wall. The bacterial cell wall consist of a highly crosslinked polysaccharide-peptide (protein-sugar) matrix called peptedoclycan. The cell wall necessary for bacterial shape and protection. The wall gives the cell its shape and surrounds the cytoplasmic membrane, protecting it from the environment, resist damage from osmotic pressure, mechanical force and shearing. The organization of peptedoglycan also give the bacterial cells their characteristic shapes.

According to the cell wall structure bacteria in general divided in to tow groups when stained with gram stain:- gram positive and gram negative

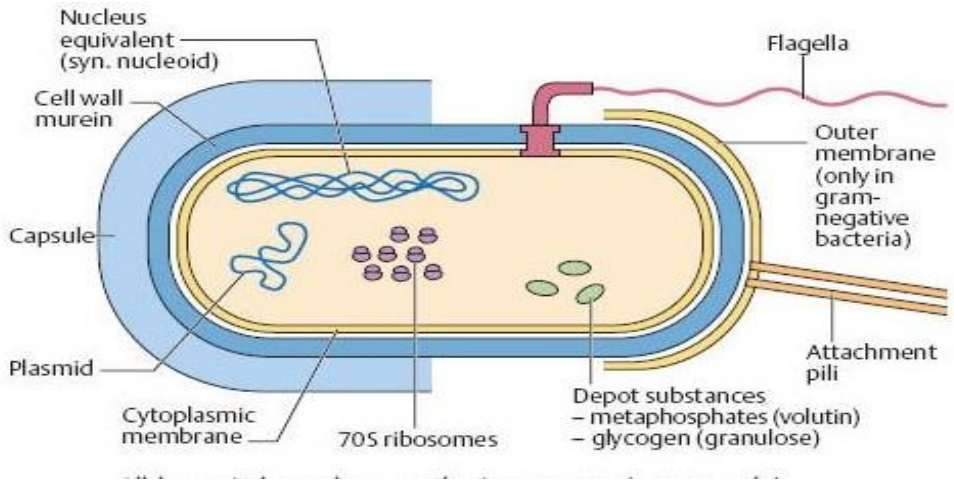
Characteristic	**Gram-negative Bacteria**	**Gram-positive Bacteria**
Wall Structure	They have a thin lipopolysaccharide exterior cell wall.	**The peptidoglycan layer** is thick
Effect of Dye	do not retain the crystal violet dye, and react only with a counter-stain, generally stain pink.	retain the crystal violet dye, and change into purple during staining identification.

Effect of Antibiotics	resistant to penicillin contain an endotoxin called LPS	susceptible to the enzyme lysozyme and to penicillin
Flagellum	If present, the flagellum has four supporting rings, namely 'L' ring, 'P' ring, 'M' ring, and 'S' ring.	The flagellum has two supporting rings, in the peptidoglycan layer, and in the plasma membrane.
Teichoic Acids	absent.	present.
Liproproteins	They are attached to the polysaccharide backbone.	absent.
Periplasmic Space	present.	absent.

The cell envelope: All cells are spatially defined at least one membrane, the plasma membrane. Most bacterial cells also contain the cell wall, and some bacterial cell contains a second membrane, the outer membrane. These layers in total are referred to as the cell envelope. **Plasma membrane:** Also refer to as cytoplasm Membrane: A layer of phospholipids and proteins, the structure of these phospholipids is amphipathic, meaning have a polar portion and a nonpolar potion. Encloses the interior of the bacterium, regulating the flow of materials in and out of the cell. This is a structural characteristic bacteria share with all other living cells; a barrier that allows them to selectively interact with their environment. Membranes are highly organized and asymmetric having two sides, each side with a different surface and different functions. Membranes are also dynamic, constantly adapting to different conditions.

Cytoplasm: The cytoplasm or protoplasm; is the aqueous environment within the plasma membrane. Contain a diverse array of component. The cytoplasm of bacterial cells is where the functions for cell growth, metabolism, and replication are carried out. It is a gel-like matrix composed of water, enzymes, nutrients,

wastes, and gases and contains cell structures such as ribosomes, a chromosome, and plasmids. Unlike the eukaryotic (true) cells, bacteria do not have a membrane enclosed nucleus. The chromosome, a single, continuous strand of DNA, is localized, but not contained, in a region of the cell called the nucleoid. All the other cellular components are scattered throughout the cytoplasm.



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 that is responsible for replication, although a few species do have two or more. Smaller circular auxiliary DNA strands, called plasmids, are also found in the cytoplasm.

Ribosomes: Ribosomes are microscopic "factories" found in all cells, including bacteria. They translate the genetic code from the molecular language of nucleic acid to that of amino acids—the building blocks of proteins. Proteins are the molecules that perform all the functions of cells and living organisms. Bacterial ribosomes are similar to those of eukaryotes, but are smaller and have a slightly different composition and molecular structure. Bacterial ribosomes are never bound to other organelles as they sometimes are (bound to the endoplasmic

reticulum) in eukaryotes, but are free-standing structures distributed throughout the cytoplasm. There are sufficient differences between bacterial ribosomes and eukaryotic ribosomes that some antibiotics will inhibit the functioning of bacterial ribosomes, but not a eukaryote's, thus killing bacteria but not the eukaryotic organisms they are infecting

Flagella: Flagella (singular, flagellum) are hairlike structures that provide a means of locomotion for those bacteria that have them. They can be found at either or both ends of a bacterium or all over its surface. The flagella beat in a propeller-like motion to help the bacterium move toward nutrients; away from toxic chemicals; or, in the case of the photosynthetic cyanobacteria; toward the light.

Pili: Many species of bacteria have pili (singular, pilus), small hairlike projections emerging from the outside cell surface. These outgrowths assist the bacteria in attaching to other cells and surfaces, such as teeth, intestines, and rocks. Without pili, many disease-causing bacteria lose their ability to infect because they're unable to attach to host tissue. Specialized pili are used for conjugation, during which two bacteria exchange fragments of plasmid DNA.

Lecture Five; Bacterial requirements growth curve.

Bacterial requirement

The growth of microorganisms is greatly affected by the chemical and physical nature of their surroundings.

Bacterial growth is a complex process involving numerous anabolic (synthesis of cell constituents and metabolites) and catabolic (breakdown of cell constituents and metabolites) reactions. In a homogeneous rich culture medium, under ideal conditions, a cell can divide in as little as 10 minutes.

The requirement for microbial growth can be divided into two main categories: physical and chemical. Physical aspects include temperature, pH, and osmotic pressure. Chemical requirement include sources of oxygen and sources of energy growth factors, include organic carbon (e.g. sugars and fatty acids) and metal ions (e.g. iron). Optimal temperature, pH and the need (or lack of need for oxygen) are important.

Culture media:-

The growth of bacteria required culture media that provide:-

1- All the essential nutrient
2- The proper concentration of salts and ions
3- The proper pH (relative acidity or alkalinity)
4- Moisture 5- Gas requirement 6- Temperature

Physical requirement

pH refers to the acidity or alkalinity of solution. Most bacteria grow best in a narrow pH range near neutrality, between pH 6.5 and 7.5. Very few bacteria grow at an acidic pH below 4.0. This is why a number of foods, such as pickles and many cheeses are preserved from spoilage by acids produced by bacterial fermentation. Nonetheless, some bacteria called acidophiles, are remarkably tolerant of acidity. Molds and yeasts will grow over a greater pH rang than bacteria, but the optimum pH of molds and yeasts is generally below that of bacteria usually pH 5-6.

pH:- The range of pH over which an organism grows is defined by three important points:

1- The minimum pH, below which the organism cannot grow.

2- The maximum pH, above which the organism cannot grow

3- The optimum pH, at which the organism grows best.

A- Acidophiles:- Microorganisms which grow at pH (3-5) are called.

B- Neutrophiles:- Microorganisms which grow best at neutral pH (6-8)

C- Alkaliphiles:- Microorganisms which grow best under alkaline conditions pH as high 10.5 are called.

Temperature:-

Each bacterial species grows at particular temperature, optimum, and maximum and minimum temperatures.

1- The minimum growth temperature is the lowest temperature at which the species will grow.

2- Optimum growth temperature is the temperature at which the species grows best.
3- The maximum growth temperature is the highest temperature at which is possible.

1- Psychrophilic:- The bacteria is growing between 0° C and 25° C. they are mostly soil and water bacteria
2- Mesophilic:- Some bacteria grow between 20° C and 44° C this group include bacteria producing disease.
3- Thermophilic:- The bacteria can grow between 50 and 80° C this bacteria will survive after pasteurization processes of milk.

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.

Osmotic Pressure

Osmotic pressure is the pressure required to prevent the movement of pure water (water with no solutes) into a solution containing some solutes. In other words, osmotic pressure is the pressure needed to stop the flow of water across the selectively permeable membrane.

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

An isotonic (isosmotic) solution is a medium in which the overall concentration of solute equals that found inside a cell (*iso* mean equal). Water leaves and enters the cell at the same rate the cell's contents are in equilibrium with the solution outside the cell wall.

A hypotonic (hypoosmotic) solution outside the cell is a medium whose concentration of solute is lower than the inside the cell (*hypo* means under or less). Most bacteria live in hypotonic solutions, and swelling is contained by the cell wall. Cells with weak cell walls, such as gram-negative bacteria, may burst or undergo osmotic lysis as a result of excessive water intake.

Microorganisms obtain almost all their nutrient in solution from the surrounding water. Thus, they require water for growth and are made up of 80-90% water. High osmotic pressures have the effect of removing necessary water from a cell. When a microbial cell is in a solution that has a higher concentration of solutes than in the cell (hypertonic), the cellular water passes out through the plasma membrane to the high solute concentration.

A hypertonic (hyperosmotic) solution is a medium having a higher concentration of solutes than the inside cell has (*hyper* means above or more). Most bacterial cells placed in hypertonic solution shrink and collapse or plasmolyze because water leaves the cells by osmosis.

Keep in mind the terms *isotonic*, *hypotonic*, and *hypertonic* described the concentration of solution outside the cell *relative* to the concentration inside the cell.

Chemical requirement

Microorganisms must have a supply of water to grow successfully as well as numerous other substances including mineral elements, growth factors, and gas, such as oxygen. All living organisms contain **certain macromolecules**, **include proteins, nucleic acid, lipid, and carbohydrates**. These macromolecules, are composed primarily of carbon (C), nitrogen (N), phosphorus (P), sulfur (S), oxygen (O), and hydrogen (H).

Bacterial cells also require several elements that are **micromolecules include Potassium, sodium, magnesium, calcium, and iron** (K^+, Na^+, Mg^+, Ca^+, and Fe^{2+}, Fe^{3+}) are the most abundant cations in the microbial cells. Chloride (Cl^-) is the major anion. K^+, Na^+, and Cl^-, have important function in controlling osmotic balance. Mg^+ associates with ATP, and it's a key component of many enzymes and protein-nucleic acid complexes such ads ribosome. DNA polymerase requires Mg^+ or Mn^+ as a cofactor for their activity. Virtually all chemical substances in microorganisms contain carbon in some form, whether they are proteins, fats, carbohydrates, or lipids. Perhaps 50 percent of a bacterium's dry weight is carbon. Carbon can be obtained from organic materials in the environment, or it may be derived from carbon dioxide. Both chemoautotrophic and photoautotrophic microorganisms obtain their energy and produce their nutrients from simple inorganic compounds such as carbon dioxide. **Chemoautotrophs** do so through chemical reactions, while **photoautotrophs** use photosynthesis. Among the other elements required by microorganisms are nitrogen and phosphorous. Nitrogen is used for the synthesis of proteins, amino acids, DNA, and RNA.

Gas requirement:- Microorganisms fall into several groups with respect to the effect of oxygen on their growth and metabolism:

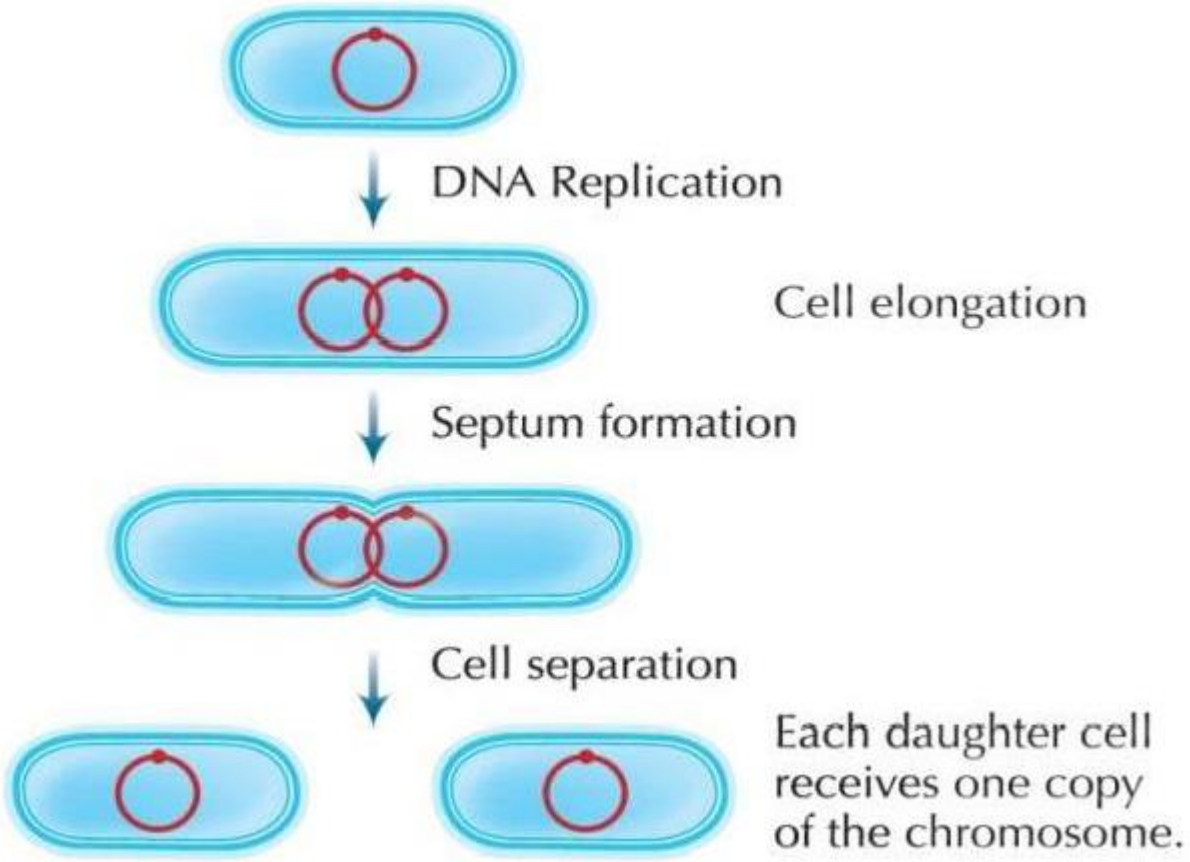
1- **Obligate aerobes** - use and require oxygen as electron acceptor - have respiratory enzymes and lack the capacity for fermentations - examples: Pseudomonas, some Bacillus
2- **Obligate anaerobes** - do not need or use O2 as a nutrient. In fact, O2 is a toxic substance, which either kills or inhibits their growth. Obligate anaerobic procaryotes may live by fermentation, anaerobic respiration - examples: Clostridium, Bacteroides

3- **Facultative organisms** - are organisms that can switch between aerobic and anaerobic types of metabolism. Under anaerobic conditions (no O2) they grow by fermentation or anaerobic respiration, but in the presence of O2 they switch to aerobic respiration. - examples: all Enterobacteriaceae (*E. coli*), some Bacillus
4- **Aerotolerant anaerobes** - grow either with or without oxygen, but metabolism remains fermentative and do not use oxygen - examples: *Enterococcus faecalis*, some Lactobacillus

Growth curve

The microbial Growth curve

Bacterial growth is a complex process involving numerous anabolic and catabolic reactions.



Bacterial Binary fusion

In Addition to determining the amount of bacteria in a sample at one point in time, we may, instead, want to determine how the amount of bacteria in a sample changes over time. We may, in other words, want to measure the growth of population. To track population density over time, we can analyze turbidity data obtained with a spectrophotometer. Inoculating cells into a vessel containing liquid medium initiate's growth. Nutrients are consumed and the microbial population expands, resulting in an increase in turbidity over time.

The lag phase: Microbial cultures often **grow very slowly** immediately after inoculation, particularly if the starting cells had previously slowed or stopped

growing, or were in a different medium. For a while, the number of cells changes very little because the cells do not immediately reproduce (adjusting) to their new environments. **The period of little or no cell division is called the lag phase**, and **it is variable depend on the**

1- Organism 2- The medium 3- Environmental conditions.

This lag phase may be virtually absent, or it could last for minutes, hour or several days. During this time, however, the cells are not dormant. The microbial population is undergoing a period of intense metabolic activity involving, in particular synthesis of enzymes and various molecules (altering gene expression, protein content, and membrane).

The log phase: As cells adjust to their new surrounding, intervals between cell divisions become progressively shorter until the population reaches its maximal growth rate. At this point, the average time interval from one division to the next, known as the generation time, is constant. **The rate at which cells divide is determined by**

1- the physiological capability of the organism
2- the nature of the medium
3- environmental condition.

When microbes are dividing by binary fission-one cell producing two cells by each division-the rate of the population is exponential. This stage of the culture is referred to as the exponential phase, or log phase.

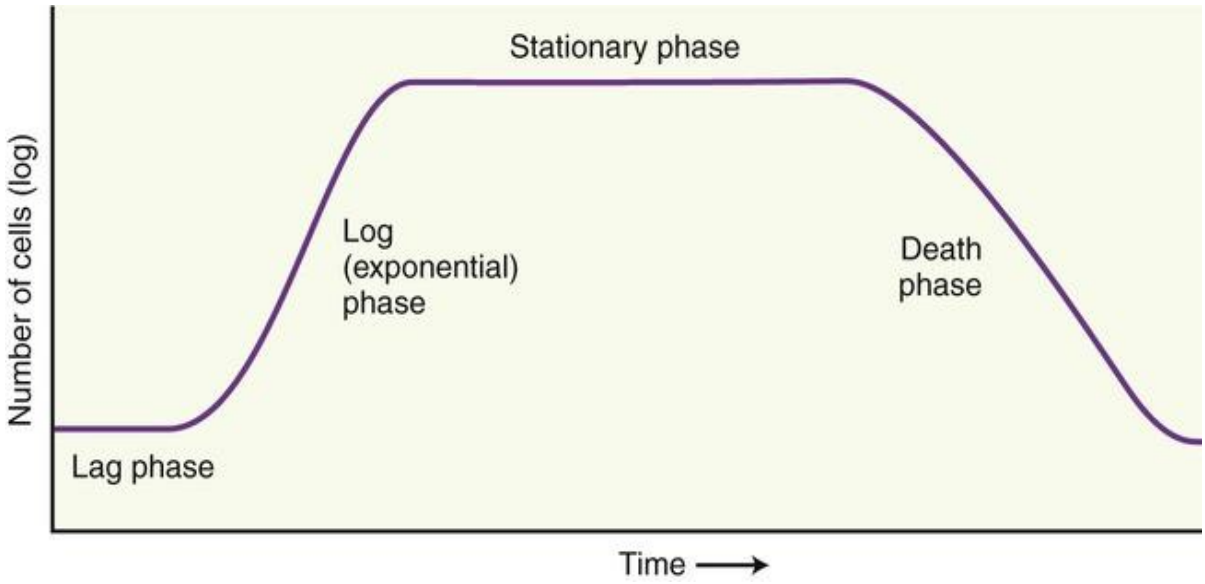
Stationary phase: Following the log phase, the growth is slows, until population growth stops completely, and the culture has reached stationary phase. In a batch culture, the concentration of the available nutrients in the medium is continually

declining as the number and total mass of cells increases. Basically, there will not be enough of some critical nutrient for the cells to keep operating macromolecular synthesis fast enough to sustain rapid growth. As the level of critical nutrient drops, the culture enters transitional period in which growth rate declines due to progressively longer intervals between cell division. Besides exhaustion of nutrients, other factors also can contribute to entry into stationary phase.

Death phase: The number of death eventually exceeds the number of new cells formed, and the population enters the death phase, or logarithmic decline phase. This phase continues until the population diminished to a tiny fraction of number of cells in the previous phase, or the population dies out entirely.

If a culture stays in stationary phase long enough, then cells may lose viability. When the concentrations of viable cells starts to decline, the culture inter the death phase the rate of decline in a cell population during death phase, like the rate of increase during log phase, is an exponential function. The rate of death depending on the organisms, the medium and environmental condition. To measure cell death, a method such as plate counting must be used that actually tests for viability. Direct count by microscopy, or culture turbidity measurements, may be misleading if non-viable cells remain intact, at least initially.

Growth Curve



Lecture Four; Control of microorganisms

Control of microorganisms is essential in order to prevent the transmission of diseases and infection, stop decomposfourition and spoilage, and 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.

Words are frequently used, and misused, in discussing the control of microbial growth is sterilization and disinfection.

Sterilization is the removal or destruction of all form of microbial life. Heating is the most common method used for killing microbes, including the most resistance form such as endospores. Sterilization by removal of microbes from liquid or gases can be done by filtration as well.

Disinfection is the elimination of microorganisms from inanimate objects or surfaces, using disinfectants agents, but generally to toxic to use on human tissues.

Physical methods of microbial control

As early the Stone Age it is likely that human were already using some physical methods of microbial control to preserve food. Drying (desiccation) and salting (osmotic pressure) were probably among the earliest techniques. When selecting methods of microbial control, consideration must be given to effects on things besides the microbes. For example, certain vitamin or antibiotics in a solution

might be inactivated by heat. Many laboratory or hospital materials, such as rubber and latex tubing, are damage by repeating heating. There are also economic considerations; for example, it may be less expensive to use presterilized, disposable plasticware than to repeat wash and restirelize glassware.

1- Heat

As we know microorganisms have a minimum, an optimum, and a maximum temperature for growth. Temperature outside these temperatures can be used to kill the certain microorganisms.

I- Dry heat sterilization

Dry heat kills microorganisms by oxidation effects rather than protein coagulation. One of the simplest methods of dry heat sterilization is

1- **direct flaming,** which use for example at microbiology laboratory to sterilize loops.
2- Another form of dry heat sterilization is **hot-air sterilization**. Items to be sterilized by placed in an oven. Microbiological ovens employ very high dry temperatures: 171°C for 1 hour; 160°C for 2 hours or longer; or 121°C for 16 hours or longer depending on the volume. They are generally used only for sterilizing glassware, metal instruments, and other inert materials like oils and powders that are not damaged by excessive temperature.
3- **Incineration:-** Incinerators are used to destroy disposable or expendable materials by burning. We also sterilize our inoculating loops by incineration.

II- Moist heat

Moist heat kills microorganisms primarily by coagulation of proteins (denaturation), which is caused by the breakage of the hydrogen bounds that hold

the proteins in their three-dimensional structure (this coagulation process is familiar to anyone who has watched an egg white frying).

One type of moist heat sterilization is

1- **boiling** which kills vegetative forms of bacterial pathogen, almost all viruses, and fungi and their spores within about 10 minutes, usually much faster. Free-following (unpressurized)
2- **steam** is equivalent in temperature to boiling water. Endospores, some viruses, however, are not destroyed this quickly. Some hepatitis viruses for example can survive up to 30 minutes of boiling, and some bacterial endospores can resist boiling more than 20 hours. Boiling is therefore not always a reliable sterilization procedure. However, brief boiling even at high altitude will kill most pathogens. The use of boiling to sanitize baby bottles is a familiar example.
3- **Pasteurization:-** used for milk sterilization. The intent of pasteurization of milk was to eliminate pathogenic microbs. It is also lowers microbial numbers, which prolongs milk's good quality under refrigeration.

Reliable sterilization with moister heat requires temperatures above that of boiling water. These high temperatures are most communally achieved by steaming under pressure in an autoclave. **Autoclaving** is the preferred method of sterilization, unless the material to be sterilized can be damage by heat or moister.

Autoclaving employs steam under pressure. Water normally boils at 100°C; however, when put under pressure, water boils at a higher temperature. During autoclaving, the materials to be sterilized are placed under 15 pounds per square inch (psi) of pressure in autoclave. When placed under 15 pounds of pressure, the boiling point of water is `raised to 121°C, a temperature sufficient to kill bacterial

endospores. The time the material is left in the autoclave varies with the nature and amount of material being sterilized; the higher pressure in the autoclave the higher temperature as clear in the table below.

The relationship between the pressure and the temperature of steam at sea level		
Pressure (psi) in excess of atmospheric pressure	**Temperature (C°)**	**Time/ mintue**
0 psi	100	
5 psi	110	
10 psi	116	
15 psi	**121**	**15**
20 psi	126	10
30 psi	135	3

Filtration

Filtration is the passage of liquid or gas through a screen like material with pores small enough to retain microorganisms. Filtration is used to sterilize heat sensitive material such as some culture media, enzymes, vaccines, and antibiotic solution.

Osmotic pressure

The use of hi concentration of salts or sugars to preserve food is based on the effects of osmotic pressure. High concentrations of these substances create a hypotonic environment that causes water to leave the microbial cell. The principle of osmotic pressure is used in the preservation of food. For example, concentrated salt solutions are used to cure meat, and thick sugar solutions are used to preserve fruits.

Radiation

Radiation has various effects on the cell, depending on its wavelength, intensity, and duration. Radiation that kills microorganisms (sterilizing radiation) is the of two types: ionizing and nonionizing.

1- **Ionizing radiation**: include gamma rays, X rays, or high energy electron beams-has a wavelength shorter than that of nonionizing radiation, less than 1 nm. Therefore, it carries much more energy.
2- **Nonionizing** radiation has wavelength longer than that of ionizing radiation, usually greater than about 1 nm. The best example of non ionizing radiation is the ultraviolet (UV) light (used to sterilize the objective surfaces). UV light damages the DNA of exposed cells.

Chemical methods of microbial control

Chemical agents are used to control the growth of microbes on both living tissue and inanimate objects. Unfortunately, few chemical agents achieve sterility; most of them simply reduce microbial population to safe level or remove vegetative forms of pathogens from objective. A common problem in disinfection is the selection of an agent. No single disinfection is appropriate for all circumstance.

Disinfectants antiseptics and sanitizers to control microorganisms

Disinfection is the elimination of microorganisms from inanimate objects or surfaces, whereas decontamination is the treatment of an object or inanimate surface to make it safe to handle.

The term disinfectant: - is used for an agent used to disinfect inanimate objects or surfaces but is generally too toxic to use on human tissues.

The term antiseptic: - refers to an agent that kills or inhibits growth of microbes but is safe to use on human tissue.

The term sanitizer describes: - an agent that reduces, but may not eliminate, microbial numbers to a safe level. Because disinfectants and antiseptics often work slowly on some viruses -such as the hepatitis viruses, bacteria with an acid-fast cell wall such as Mycobacterium tuberculosis, and especially bacterial endospores, produced by the genus Bacillus and the genus Clostridium, they are usually unreliable for sterilization by this methods.

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 interferes with some agents.

The best results are generally obtained when the initial microbial numbers are low and when the surface to be disinfected is clean and free of possible interfering substances.

There are two 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.

A large number of such chemical agents are in common use

1- **Phenol and derivatives Phenol (phenolics)** :- (5-10%) was the first disinfectant commonly used. However, because of its toxicity and odor, phenol derivatives are now generally used. These include orthophenylphenol, hexachlorophene, triclosan, hexylresorcinol, and chlorhexidine.

2- **Soaps and detergents Soaps** are only mildly microbicidal. Their use aids in the mechanical removal of microorganisms by breaking up the oily film on the skin (emulsification) and reducing the surface tension of water so it spreads and penetrates more readily. Some cosmetic soap contains added antiseptics to increase antimicrobial activity.

3- **Anionic (negatively charged) detergents**, such as laundry powders, mechanically remove microorganisms and other materials but are not very microbicidal.

4- **Cationic (positively charged) detergents** alter membrane permeability and denature proteins. They are effective against many vegetative bacteria, some fungi, and some viruses. However, bacterial endospores and certain bacteria such as Mycobacterium tuberculosisand Pseudomonasspecies are usually resistant. Cationic detergents include the quaternary ammonium compounds such as benzalkonium chloride, zephiran, diaprene, roccal, ceepryn, and phemerol.

5- **Alcohols:-** 70% solutions of ethyl or isopropyl alcohol are effectively kill bacteria and fungi but not endspores and non-enveloped viruses.

6- **Acids and alkalies: -** Acids and alkalies alter membrane permeability and denature proteins and other molecules. Salts of organic acids, such as calcium propionate, potassium sorbate, and methylparaben, are commonly used as food preservatives.. Heavy metals

7- **Heavy metals**: - Several heavy metals can be biocdal or antiseptic, such as mercury, silver, and copper, they acting by denature proteins.

8- **Halogens: -** Particularly Chlorine and iodine, are effective antimicrobial agents, both alone and as constituents of organic or inorganic compounds.

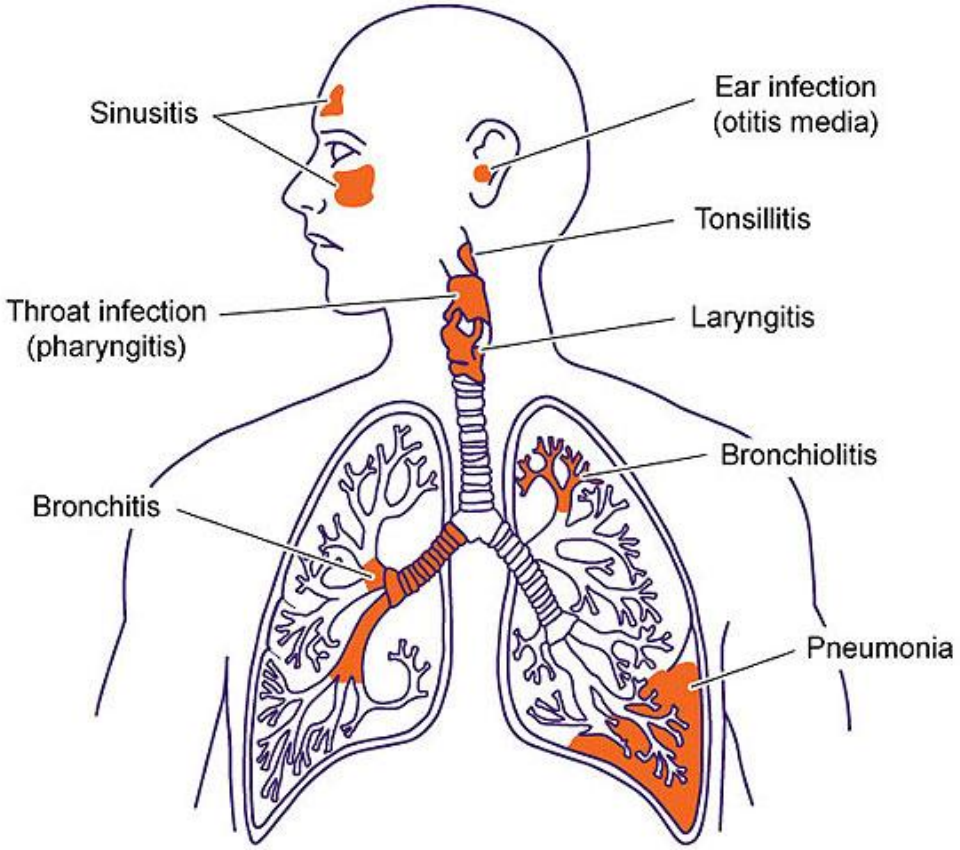
a- **Chlorine**:- Chlorine gas reacts with water to form hypochlorite ions, which in turn denature microbial enzymes. Chlorine is used in the chlorination of drinking water, swimming pools, and sewage. Sodium hypochlorite is the active agent in household bleach. Calcium hypochlorite, sodium hypochlorite, and chloramines (chlorine plus ammonia) are used to sanitize glassware, eating utensils, dairy and food processing equipment, hemodialysis systems, and treating water supplies.

b- **Iodine and iodophores**: - Iodine is one of the oldest and most effective antiseptics. It is effective against all kind of bacteria, many endospores, and various fungi, and some viruses.

9- **Aldehydes**: - Aldehydes, such as formaldehyde and glutaraldehyde, denature microbial proteins. Formalin (37% aqueous solution of formaldehyde gas) is extremely active and kills most forms of microbial life.

10- Ethylene oxide gas: - Ethylene oxide is one of the very few chemicals that can be relied upon for sterilization (after 4-12 hours exposure). Since it is explosive, it is usually mixed with inert gases such as freon or carbon dioxide. Ethylene oxide has very high penetrating power and denatures microbial proteins. Vapors are toxic to the skin, eyes, and mucous membranes and are also carcinogenic.

Lecture Five; Respiratory tract infection, Upper and Lower infection



The respiratory system is often separated into the **upper respiratory tract (URT)** consisting of nose, throat, and pharynx, and **the lower respiratory tract (LRT)** consisting of larynx, trachea, bronchial tube and alveoli.

1- Upper Respiratory Infections:

The most common diseases are those of the UTR are cold, sore throat (التهاب الحلق), Sinusitis, Pharyngitis, otitis media, bronchitis pneumonia, Epiglottitis and Laryngotracheitis

Causative agents, most upper respiratory infections are **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.

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 exudates.

Clinical symptoms: Initial symptoms of a cold are runny, stuffy nose (انسداد الأنف) and sneezing(العطاس) , usually without fever. Other upper respiratory infections may have fever. Children with epiglottitis may have difficulty in breathing, muffled speech (صوت خافت), drooling (سيلان اللعاب) Children with serious laryngotracheitis (التهاب الحنجرة) may also have tachypnea (تسارع التنفس), stridor and cyanosis (أزرقاق).

***Microbiologic Diagnosis*:** Common colds can usually be recognized clinically. Bacterial cultures of throat الحلق swab specimens are used for pharyngitis التهاب البلعوم, epiglottitis and laryngotracheitis (التهاب الحنجرة). Blood cultures are also obtained in cases of epiglottitis.

***Prevention and Treatment*:** Viral infections are treated symptomatically. Streptococcal pharyngitis and epiglottitis caused by *H influenzae* are treated with antibacterial. *Haemophilus influenzae* type b vaccine is commercially available and is now a basic component of childhood immunization program.

2- Lower Respiratory Infections: Bronchitis, Bronchiolitis and Pneumonia

Causative agents of lower respiratory infections are viral or bacterial. Viruses cause most cases of bronchitis and bronchiolitis (التهاب القصيبات). In community-acquired pneumonias (ذات الرئة) , 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. Nosocomial pneumonias and pneumonias in immunosuppressed patients have protean etiology with gram-negative organisms and staphylococci as predominant organisms.

Pathogenesis: Organisms enter the distal airway by inhalation, aspiration or by hematogenous seeding (دموي المنشأ). The pathogen multiplies in or on the epithelium, causing inflammation, increased mucus secretion, and impair mucociliary function (يضعف وظيفة الأهداب المخاطية) ; other lung functions may also be affected. In severe bronchiolitis, inflammation and necrosis of the epithelium may block small airways leading to airway obstruction (انسداد مجرى التنفس).

Clinical symptoms: Symptoms include cough (السعال) , fever, chest pain (الم في منطقة الصدر), tachypnea (تسارع التنفس) and sputum production (افراز القشع). Patients with pneumonia may also exhibit non-respiratory symptoms such as confusion, headache, myalgia (الم عضلي), abdominal pain, nausea, vomiting and diarrhea.

Microbiologic Diagnosis: Sputum specimens are **cultured for bacteria, fungi** and viruses**. Culture of nasal washings** is usually sufficient in infants with bronchiolitis. **Fluorescent staining technique** can be used for legionellosis. **Blood cultures** and/or **serologic methods** are used for viruses, rickettsia, fungi and many bacteria. **Enzyme-linked immunoassay methods** can be used for detections of microbial antigens as well as antibodies. Detection of nucleotide fragments specific

for the microbial antigen in question by DNA probe or polymerase chain reaction can offer a rapid diagnosis.

Prevention and Treatment: Symptomatic treatment is used for most viral infections. Bacterial pneumonias are treated with antibacterial. A polysaccharide **vaccine against 23 serotypes of *Streptococcus pneumoniae*** is recommended for individuals at high risk.

Example of some bacterial pathogens

There are many microorganisms causing respiratory tract infection. Some of pathogens and the other opportunistic [some of nonpathogenic bacteria (normal flora) may be change into pathogens in certain cases].

Streptococcus pyogenes

General characteristic

Gram positive cocci, occur as single, pairs, or chains, depending on the environment. Is a facultative anaerobic, heterogenous group, attached to epithelial surfaces via the lipotechoic acid portion of fambriae (pilli). Catalase negative, oxidase negatives.

Its three types of hemolytic enzymatic causes hemolysis of red blood cells on blood agar.

1- Beta (β) hemolytic group is characterized by complete lysis of red blood cells with clear zone surrounding the colony on blood agar media.
2- Alpha (α) hemolysis group is characterized partial lysis with green pigment surrounding the colony.
3- Gamma (γ) hemolytic group is characterized by absence of lysis.

Attributed of pathogenecity of *Streptococcus pyogenes*

- Posse M protein, a potent virulence bacteria found on fimbriae (الأهداب) that interferes with phagocytosis (عملية البلعمة).
- Has a nonantigenic hyaluronic acid capsule that promote invasiveness.
- Secret three serological type of erythrogenic toxins (سموم كريات الدم الحمراء) that require lysogenic for production and causes the rash Scarlet fever.
- Possess multiple other enzyme system (hyaluronodase, streptokinase and Streptodornase).
- Produce two hemolycin.
  a- Streptolysin **S** (a leukocidal protein responsaple for β hemolysis on blood agar plates)
  b- Streptolysin **O** (an oxygen sensitive leukocidal protein).

Clinical disease

1- **Streptococcal pharyngitits:-** Is characterized by sore throat, fever, headach, nosea, cervical lymphoadenopathy and leukocytosis.
2- **Scarlet fever:-** exihibits symptoms resembling those of streptococcal pharyngitis. Is accompanied (مصاحب ب) by rash caused by erthrogenic toxins.
3- **Rheumatic fever:-** Follows group A streptococcus throat infection in genetically predisposed individuals, however 20% of patients may show no early signs or symptoms. May damage heart muscle and valves.

Staphylococcus Spp.

The staphylococci are gram positive spherical cells usually arranged in irregular clusters. They grow on media. The important specices is *S. aureus* (pathogenic bacteria) and epedermidis (non pathogenic, but opportunistic.

Staphylococcus aureus

Is gram positive cocci arranged in cluster, is catalase positive only coagulase positive and β hemolytic.

Causes bacterial endocarditis usually acute food poisoning by toxin production, skin infection, cytolytic toxin (Alfa, Beta, Delta, Gama, leukocidin) are all hemolytic (leukocidin) and destroy cellular membranes. Produce enterotoxins by some strain are fast acting producing gastrointestinal symptoms in 2 to 6 hours causing vomiting. Have protein A (a surface protein) is antiphagocytic.

***Staphylococcus* epidermidis**

Is a coagulase negative staphylococcus, has are markable ability to adhere to artificals materials in the body (e.g prosthetic heart valves).

Corynebacterium diphtheria

Is gram positive club-shaped rod (called coryneform) often occurring in V-and L shaped arrangement or clumps sometimes called Chinese letter (Chinese characters). Produced exotoxin that cause heart and nerve damage. Causes diphtheria.

Haemophilis infeluenzae

Is gram negative pleumorphic rod and contain endotoxin-requires the X (heam) V (NAD) factors which although found in blood must be released by lysis.

Therefore, its cultured on chocolate agar or seen as satellite growth near *S. aureus* on blood agar.

Is an organisms that colonize the URT and in unvaccinated young children. May cause otitits media, meningitis, epiglotitis, cellulitis, bronchitis, bactermia, arthritis and conguctivitis. Most normal flora are not encapsulated and cause most otitits media, sinusitits and bronchitits infection. Where as serious disease is usually caused by encapsulated forms.

Streptococcus pneumoniae

Is part of the normal pharyngeal flora in 40-70% of human being. Its Gram positive, α hemolytic, lancet shaped, diplococcus. Has specific polysaccharide capsule with more than 80% different antigenic types. Is differented from other streptococci by

1- Sensitive to optichin
2- Sensitive to bile salt
3- Fermentation on inulin.

Pathogenecity

- Disease probably occur through multiplication virulence is attributed to the **phagocytosis capacity of the capsule.**
- Little evidence exists for **production of toxins**.
- Pathogenecity is associated with disturbance of normal defense barrier of the respiratory tract.

Lecture Six; Septic of Digestive System (Infection or Diseases)

Every cell of the body needs nourishment, yet most cells cannot leave their position in the body and travel to a food source, so the food must be converted to a usable form and delivered. The digestive system, with the help of the circulatory system, acts like a gigantic "meals on wheels," providing nourishment to over a hundred trillion "customer" cells in the body. It also has its own quality control and waste disposal system. The digestive system provides the body with water, electrolytes, and other nutrients.

Gastrointestinal tract (GI tract) digests food, absorbs nutrients and water into blood, and eliminates waste.

Gastrointestinal tract (GI tract) consists of the

a tube extending from the mouth, esophagus, stomach, small intestine, large intestine (colon), rectum and to the anus. And its associated accessory organs, primarily glands, which secrete fluids into the digestive tract. The digestive tract is also called the alimentary tract, or alimentary canal. The term gastrointestinal (gastro-intestinal; GI) tract technically only refers to the stomach and intestines but is often used as a synonym for the digestive tract.

The regions of the digestive tract include

Gastrointestinal tract diseases:-

Diseases of the digestive system usually result from the ingestion of microorganisms or their toxins in food and water throw Fecal–oral transmission can be interrupted by

1- proper disposal of sewage

2- disinfection of drinking water

3- proper food preparation and storage

4- 700 bacterial species in mouth

5- Stomach and small intestine have few resident microbes

6- Up to 40% of fecal mass is microbial cells

7- Bacteria in large intestine assist in degrading food and synthesizing vitamins. They also competitively inhibit pathogens, chemically alter medications, and produce carcinogens.

Bacterial Diseases of the Lower Digestive System

1- Infections caused by the growth of a pathogen in the intestines. Incubation times range from 12 hours to 2 weeks. Symptoms of infection generally include a fever.

2- Intoxication due to ingestion of preformed bacterial toxins. Symptoms appear 1–48 hours after ingestion of the toxin. Fever is not usually a symptom of intoxication.

3- Infections and intoxications cause diarrhea and dysentery (some gastroenteritis). Usually treated with fluid and electrolyte replacement.

Bacterial Infections

1- Shigellosis(Bacillary Dysentery). Symptoms:- Toxin, that cause inflammation and bleeding of the colon, including hemorrhagic colitis and hemolytic uremic syndrome (HUS). Severe diarrhea or dysentery.

2- Salmonellosis (Salmonella enterica) –Gastroenteritis, food poisoning, Typhoid Fever(Salmonella typhi) Only in humans (carriers); enteroinvasive.

3- Cholera (Vibrio cholerae). Primarily third world problem. Toxin. Severe diarrhea (rice water stool), extreme dehydration Cummings

4- Escherichia coli:- Gastroenteritis

5- Traveler's diarrheamay be caused by Enterotoxigenic strains (ETEC), present like mild form of cholera

6- Clostridium difficile–associated diarrhea. C. difficile growth following antibiotic therapy. Exotoxin production. From mild diarrhea to life threatening colitis

7- Nosocomial disease, associated with hospitalized patients and nursing home residents

8- Helicobacter pyloriGastritis. Inflammatory response to bacteria Peptic ulcer disease (gastric and duodenal ulcers), 30 -50 % of people in US infected –only ~ 15% develop ulcers. (Blood type O more susceptible). Bacteria produces urease (urea ammonia) –neutralizes stomach acid. Antibiotic treatment is effective

Viral Gastroenteritis

1- Rotavirus: 1-2 day incubation; 1 week illness. Main diarrheal illness of infants and children

2- Norovirus: 1-2 day incubation; 1-3 day illness, Treated withrehydration

What are bacterial digestive infections?

Gastrointestinal infections can be caused by a large number of microorganisms, including: bacterial, viral or parasitic

Bacterial digestive infections are diseases that affect the digestive organs as a result of ingesting of infectious bacterial organisms. Once a person is infected, the bacteria live in the intestines and are passed in the stool of the infected person. infections that cause gastroenteritis, an inflammation of the gastrointestinal tract involving both the stomach and the small intestine. The signs and symptoms of bacterial digestive infections can last five to seven days or longer. Bacterial infections causes nausea with or without vomiting, diarrhea, and abdominal pain, and other gastrointestinal symptoms. They may also cause bloody diarrhea, known as dysentery. Dehydration is the main danger of gastrointestinal infections, so rehydration is important, but most gastrointestinal infections are self-limited and resolve within a few days. However, in a healthcare setting and in specific populations (newborns/infants, immunocompromized patients or elderly populations), they are potentially serious. Rapid diagnosis, appropriate treatment and infection control measures are therefore particularly important in these contexts.

Campylobacter bacteria

Campylobacter is one of the most common bacterial cause of gastroenteritis worldwide and is frequent in children under two. It can cause diarrhea (sometimes bloody), abdominal cramps, vomiting and fever. It is usually food-borne through raw or undercooked meat (especially poultry) or through contaminated milk.

Clostridium difficile

Clostridium difficile infection is responsible for up to 25% of cases of antibiotic-associated diarrhea most often contracted in hospitals or healthcare institutions3. Elderly and immunocompromized patients are most at risk. The recent emergence of highly toxigenic and resistant C. difficile strains has led to more frequent and severe outbreaks, increased morbidity and mortality.

Escherichia coli

Escherichia coli, often called E. coli, is the leading cause of travelers' diarrhea and a major cause of diarrheal disease in the developing world, especially among children. People usually contract E. coli through ingestion of water contaminated with human or animal feces.

Escherichia coli O157:H7

Escherichia coli O157:H7 is a Shiga toxin-producing form of E. coli bacteria, which causes gastrointestinal infections with symptoms including bloody diarrhea and vomiting. Though it usually resolves after a few days, it can sometimes (5-10%4 of infections) lead to hemolytic uremic syndrome (HUS), which can result in kidney failure if untreated.

Helicobacter pylori

Helicobacter pylori, called H. pylori, is a cause of gastritis and is associated with the development of gastric and duodenal ulcers. It can cause stomach pain or nausea, but in many cases there are no symptoms. Infected people have a 10-20% lifetime risk of developing peptic ulcers and a 1 to 2% risk of stomach cancer5.

Salmonella and Shigella

Salmonella and Shigella are food-borne GI illnesses. Salmonella is common and is found in raw meats, poultry, seafood and eggs, as well as milk and dairy products. Acute symptoms include nausea, vomiting, abdominal cramps, diarrhea, fever, and headache. Shigella is frequently found in water polluted with human feces. Symptoms of shigellosis (bacillary dysentery) include abdominal pain, cramps, diarrhea, fever, vomiting, and blood, pus, or mucus in stool.

Staphylococcus aureus

Staphylococcus aureus is the most common cause of food intoxication, characterized by abrupt/violent onset, severe nausea, cramps, vomiting, and diarrhea using lasting 1-2 days. This opportunistic pathogen can be found on humans (skin, infected cuts, noses and throats) and has been associated with a wide range of foods including meat and meat products, poultry and egg products, salads, bakery products, and dairy products.

Yersinia enterocolitica

Yersinia enterocolitica, called Y. enterocolitica, is a relatively infrequent cause of diarrhea and abdominal pain. Infection is most often acquired by eating contaminated food, especially raw or undercooked pork products, as well as ice-cream and milk. Common symptoms are fever, abdominal pain, and diarrhea, which is often bloody.

Diagnosis TOP

When symptoms point to a possible gastrointestinal infection, diagnosis can be confirmed through laboratory tests used for culture or antigen detection from stool specimens. In certain cases (e.g. for E. coli, Salmonella, C.

difficile), antibiotic susceptibility testing is used to determine microbial resistance to antibiotic therapy, if appropriate. Particularly in hospital settings, rapid diagnosis provides important information for implementing infection control measures.

viral digestive infections include

Adenovirus

Adenovirus can cause diarrhea, fever, conjunctivitis, bladder infections and rashes, but the most common symptom is respiratory illness. After rotavirus, it is the most common cause of pediatric diarrhea.

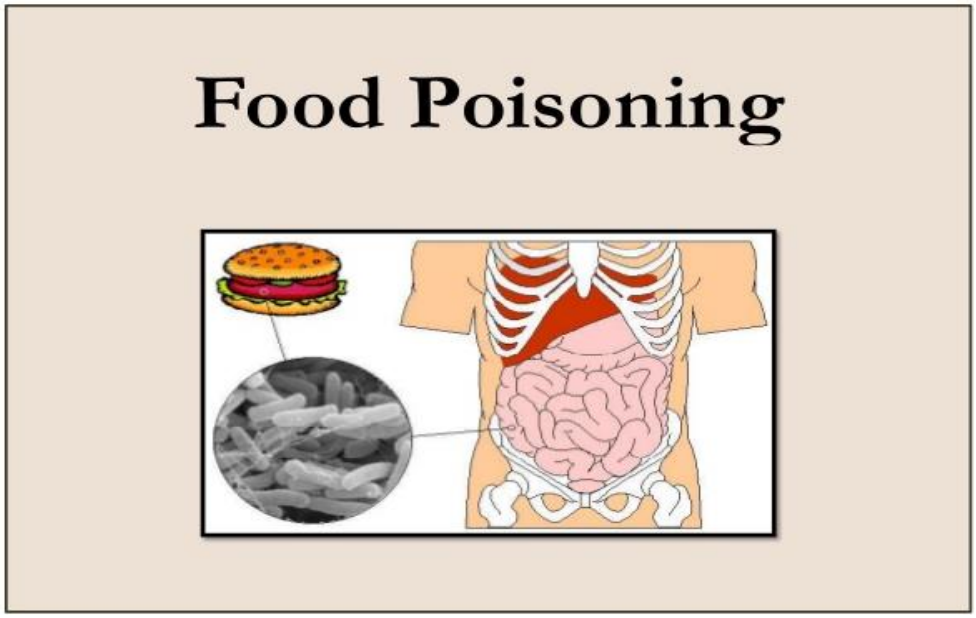
Rotavirus

Rotavirus is the most frequent cause of diarrhea in young children and infants and it is responsible for the most severe cases. There is a vaccine for rotavirus, but globally it causes more than ½ million deaths per year in children less than five years old.6 Most of these are in emerging countries.

There are no vaccines for most gastrointestinal infections. Exceptions:
Rotavirus. Adenovirus (limited availability)

Antibiotics may be recommended in particularly severe cases of gastroenteritis, or if a specific bacteria has been identified as the cause Antibiotics are not usually recommended as they have no effect on viral infections, may cause side effects and overuse increases the risk of resistant bacteria developing..

Lecture Seven; Food Poisoning, type of food poisoning according to bacterial infection



Food borne illness, or food poisoning:- Is acute gastroenteritis developing up to several hours after drink or consumption (eating) of contaminated, spoiled, or toxic food. The most common symptoms of food poisoning includes a number of disorders such as nausea, vomiting, and diarrhea ,feeling weak, fever or chills/sweating and headache. Food poisoning can be caused by eating food contaminated with bacteria, viruses, chemicals or poisonous metals such as lead or cadmium. Most food poisoning, however, is caused by bacteria therefore I will focus on bacterial food poisoning. *(Food which has become contaminated with harmful bacteria does not always taste bad. Most of the time it looks smells and tastes like it normally does).* Some food poisoning diseases are more common than others. For example, diseases caused by *Staphylococcus aureus* occurs a lots more often than disease caused by Clostridium botulinum.

Some foods cause food poisoning more than others and need to be cooked properly and/or kept in the refrigerator. These include chicken, meat, seafood, eggs, cooked rice, salami, milk and all dairy foods. ***It is important chicken is cooked properly to the bone and then kept in the fridge for no more than 2 days. If reheating chicken, or left-overs, make sure it is steaming hot and only reheat it once.***

The most common types of food poisoning bacteria are

Staphylococcus aureus

Staphylococcus aureus are gram positive bacteria, facultative anaerobic, are found on the skin, in sores, infected eyes and in the nose, throat, saliva and bowel of humans. There may be many of these bacteria in the yellow mucus (slimy substance) which comes from the nose or is coughed up when a person has a cold or a lung infection. *S. aureus* produce entero-toxin (poison) while growing (multiply) on food; the toxin causes the illness (food poisoning). The toxin is not destroyed by cooking the food.

Symptoms of staphylococcus food poisoning

Usually appear between 1 to 8 hours after eating the contaminated food. *S. aureus* toxin - 5 distinct antigenic types labeled A, B, C, D, E. They are water-soluble, low molecular weight proteins that are heat stable (resist boiling for 30 minutes). Their mode of action is unknown but they each cause an enteric effect (diarrhea) and a neurologic effect (vomiting).

***Bacillus* cereus**

B. cereus is a spore-producing bacterium (gram positive, aerobic, rod bacteria) produce two different toxins – one that causes vomiting and another that causes

diarrhea. The spore germination process of *B. cereus* produces several exotoxins which have either an enteric or a neurologic effect but not both. The type of toxin produced is dependent on the type of food that the spore germinates in. In a high protein food (meat) the enterotoxin is formed. In a high carbohydrate food (rice, pasta) the neurotoxin is formed. The enterotoxins stimulate the adenyl cyclase - cyclic AMP system in intestinal epithelial cells and cause fluid accumulation in the intestine. The neurotoxins cause vomiting through an unknown mechanism.

Symptoms of *B. cereus* food poisoning

Incubation period is 30 minutes to 5 hours for the vomiting toxin and 8 to 16 hours for the diarrheal toxin. Symptoms are generally mild and resolve within 24 hours.

Salmonella

There are hundreds of different types of salmonella bacteria but not all are harmful to humans. They are found mainly in the intestines, bowels and faeces of humans and other animals. It is the salmonella bacteria themselves which can cause salmonella food poisoning

The sources of salmonella food poisoning:

1- Poor food handling practices in the home or in food outlets
2- Seafood caught in polluted water or eggs with dirty shells
3- Meat or poultry which has been contaminated by poor food handling before it gets to the food outlet, such as at the abattoir

Symptoms of salmonella food poisoning

Salmonella food poisoning takes up to 48 hours to develop after the food is eaten. Symptoms include nausea, stomach cramps, diarrhea, fever and headache; it does

take 3 to 21 days. It can cause death in very young, weak or very old people. People who have cancer or are taking medication for serious health conditions such as heart, kidney or liver problems.

Clostridium (*Clostridium botulinum* or *Clostridium perfringens*

Clostridium bacteria are gram positive obligate anaerobic rod bacteria, found in the soil and in the intestines of animals, including cattle, poultry, fish and humans. Food poisoning caused by clostridium bacteria is important to know about because these bacteria are common in the environment.

Sources of clostridium food poisoning

From food handling practices in the home, in the factory or in a food outlet, especially relating to cooking and storage/refrigeration temperatures.

Symptom of clostridium food poisoning

Clostridium food poisoning symptoms occur about 12 hours after eating the contaminated food and are similar but usually less severe than the other types. The symptoms include stomach pains, diarrhea and sometimes nausea and vomiting. One type of clostridium bacteria produces a very serious food poisoning disease called **botulism**. This disease is caused by eating food which is contaminated with an extremely poisonous toxin produced by the bacteria ***Clostridium botulinum*.** Unless properly treated about one-third of people who get this disease die within 3-7 days. *C. botulinum* toxin include 8 distinct antigenic types labelled A, B, C_1, C_2, D, E, F, G. Types A, B, E, F and G are coded by chromosomal genes. C_1 and D are coded by phage genes that are lysogenic in *C. botulinum*. Types A, B and E cause almost all human botulism. All toxins are proteins of 150,000 molecular weight

that prevent release of acetylcholine at the neuro-muscular junction causing a flaccid paralysis.

The other type of clostridium causative agent is ***C. perfringens*** toxin - A single heat-labile protein of 34000 molecular weight inhibits glucose transport in intestinal epithelial cells, damages the intestinal epithelium and causes protein loss into the intestinal lumen. This activity is maximal in the ileum and minimal in the duodenum.

Campylobacter

Campylobacter species are typically spiral-shaped and able to move via unipolar or bipolar flagella. These bacteria are found in many animals including dogs, cats, cattle and poultry. The sources of infection from these bacteria are usually contaminated food and water.

Sources of campylobacter from:

1- Ingestion of contaminated food or water (especially undercooked chicken & creek or river water)
2- Contact with infected animals (especially puppies or kittens with diarrhea)
3- Poor food handling (especially by using the same chopping boards, knives and plates for raw and cooked chicken).

Campylobacter food poisoning symptoms

The symptoms occur usually after 2 to 5 days, include diarrhea which may sometimes be bloody, severe abdominal pain, stomach cramps, and fever. It is a serious disease in indigenous communities because of the possibility. Vomiting is not common. The most severe infections occur in the very young, the elderly and skinny people.

Escherichia coli

E. coli; is gram negative, facultative anaerobic, coccobacilli. The bacteria live in the gut of humans and animals and are mostly harmless. Some strains produce toxins that cause illness. Children under five and elderly people can get kidney failure with a distinctive rash (haemolytic uraemic syndrome) that can be fatal.

Sources of *E. coli* are:

1- Undercooked meat and small goods,
2- Lettuce, sprouts and other vegetables,
3- Unpasteurized milk,
4- Fruit juices.

E. coli food poisoning symptoms

Food poisoning symptoms appear after 2 to 8 days incubation period. Symptoms usually last 5 to 10 days.

Listeria

Listeria species are gram positive rod-shaped, facultative anaerobic and non spore-forming bacteria. The major human pathogen in the *Listeria* genus is *L. monocytogenes*. It is usually the causative agent of the relatively rare bacterial diseases listeriosis, a serious infection caused by eating food contaminated with the bacteria. The disease affects pregnant women, newborns, adults' weaker immune systems, and the elderly.

Symptoms of *Listeria* food poisoning

Symptoms occur after 3 to 70 days incubation period, it can include fever, headaches, cramps, aches and pains, nausea and diarrhea; although in healthy people there may not be any symptoms. Listeria can be serious, and sometimes fatal, in newborns, elderly people and people with a weakened immune system. If a pregnant women gets listeria she may only experience mild symptoms, but in it may lead to the premature birth or stillbirth of her unborn baby.

Sources of Listeria food poisoning

1- Raw seafood egg smoked fish, oysters, sashimi or sushi
2- Pre-prepared salads
3- Pre-cooked meats, eggs and small goods
4- Unpasteurized milk, soft serve ice creams and soft cheeses
5- Leftover meat which has been refrigerated longer than a day

Hepatitis A

Infection with Hepatitis A virus occur after incubation period is 15-50 days causes an inflammation of the liver. Symptoms can include fever, tiredness, and loss of appetite, nausea, stomach pains, dark urine and jaundice. Symptoms usually last several weeks. Children often have mild or no symptoms.

Sources of Hepatitis A food poisoning

1- Uncooked foods such as salads that have been handled by infectious people
2- Oysters raised in contaminated waters
3- Drinking contaminated water

Norovirus

Norovirus is a common illness in children and highly infectious. The symptoms are usually mild, but it can cause dehydration in children and elderly people. Oysters and other shellfish is the main Norovirus food poisoning

Rotavirus

Norovirus infection is a type of viral gastroenteritis (also known as ‘gastro’: inflammation of the stomach and intestines (bowels)). Noroviruses (previously known as Norwalk-like viruses) are small round structured viruses that are members of a group of viruses called caliciviruses.

Rotavirus

Rotavirus is a common cause of food poisoning in children under 2 years. Foods that have been handled by someone with rotavirus (it's not unusual for adults to show no symptoms when they have the virus). Symptoms occur after 24 to 72 hours incubation period.

Anyone can come down with food poisoning. Statistically speaking, nearly everyone will come down with food poisoning at least once in their lives.

There are some populations that are more at risk than others. Anyone with a suppressed immune system or an auto-immune disease may have a greater risk of infection and a greater risk of complications resulting from food poisoning.

How is food poisoning diagnosed?

The type of food poisoning based on the symptoms. In severe cases, blood tests, stool tests, and tests on food that the patient have eaten may be conducted to

determine what is responsible for the food poisoning also urine may be test to evaluate whether or not an individual is dehydrated as a result of food poisoning.

How is food poisoning treated?

Food poisoning can usually be treated at home, and most cases will resolve within three to five days. If you have food poisoning, it's crucial to remain properly hydrated. Sports drinks high in electrolytes can be helpful with this. Fruit juice and coconut water can restore carbohydrates and help with fatigue. Avoid caffeine, which may irritate the digestive tract. Decaffeinated teas with soothing herbs like chamomile, peppermint, and dandelion may calm an upset stomach. Over-the-counter medications like Imodium and Pepto-Bismol can help control diarrhea and suppress nausea. It's also important for those with food poisoning to get plenty of rest. In severe cases of food poisoning, individuals may require hydration with intravenous (IV) fluids at a hospital. In the very worst cases of food poisoning, a longer hospitalization may be required while the individual recovers.

Lecture Eight; Hospitals infection and control microorganisms

Contamination التلوث, as referred to in the healthcare states that it is "**the act of contaminating, especially the introduction of disease-producing organisms or infectious material on or into normally-sterile portions of the body."**

Contamination may include:

1- Toxic, corrosive (سامة، أكالة)
2- Infectious المعديات
3- Radioactive الأشعة
4- Flammable المواد القابلة للأشتعال
5- Chemically reactive/explosive(المتفجرات)
6- Extremely volatile المواد المتطايرة بشدة (thereby producing rapid cooling of the skin).
7- Odiferous/smelly or otherwise hazardous materials (المواد ذات الرائحة الكريهة أو الخطرة)

Hospital surfaces and frequently used medical equipments (medical devices, equipment and items used in hospitals) become contaminated by a variety of pathogenic and nonpathogenic organisms. The hands and gloves of healthcare workers readily acquire (يكتسب بسهولة) pathogens after contact with contaminated hospital surfaces and can transfer these organisms to subsequently touched patients and inanimate surfaces.

Types of microbiological pathogens

Contamination with infectious organisms (**microbiological contamination refers to the non-intended or accidental introduction of infectious material**).There is **a broad range of microbiological pathogens, which can cause contamination and thus infections, including**

1- Bacteria and their spors

a- *Gram-negative bacilli*

b- *Gram-positive cocci*

c- *Clostridium difficile*

2- Fungi: Although the majority of *Candida* infections are likely due to endogenous sources (i.e., arising from patient colonization)

a- *Candida albicans*

b- *Candida glabrata*

c- *Candida parapsilosis*

3- Viruses: Viruses can contaminate and survive in the inanimate environment

a- *Influenza virus*

b- *Parainfluenza virus*

c- *Enteric viruses*

d- *Hepatitis B virus*

e- Severe acute respiratory syndrome (SARS)–associated corona virus.

4- Contamination exists in possible exposures to various parasites including

a- various worms (مختلف الديدان)

b- ticks (القراد)

c- Lice (القمل)

d- Fleas (البراغيث)

5- Some botanicals such as plant spores(ابواغ النباتات) and pollens (حبوب اللقاح) .

Contamination sources مصادر العدوى

The two **major contamination sources** in hospitals are المصدرين الرئيسين لعدوى المستشفيات

1- Hospitals staff العاملون في المستشفيات : - Hospital patients مرضى المستشفيات can acquire يكتسبون organisms from many sources العديد من المصادر, including the environment البيئة . Furthermore, organisms still have to be transmitted تنتقل to patient, as this is thought to occur via staff hands أيدي العالمين. Hospital and clinical staff (for example, **nurses and doctors**) making the possibility for cross-contamination الانتقال المتبادل very high whenever they deliver patient care. Therefore, **they should wash their hands thoroughly before and after**

1- Eating or drinking
2- Smoking
3- Applying cosmetics وضع مواد التجميل
4- Preparing food
5- Performing clean or sterile procedures القيام بالإجرآت التعقيمية و التنظيف
6- Working with a patients

2- The Patient's Environment

Studies have shown that one of the most problematic areas for cross-contamination is the patient's entire bedside area including the:

1- Bed
2- Bedside table
3- Bedframe and rails (هيكل السرير والقضبان)
4- Bed clothes
5- Bedside chair

Control of hospitals' contamination strategies

Recognizing التعرف او تشخيص the types of contamination possible in a hospital/laboratory and other healthcare facilities وحدات او ردهات العناية is the first step toward controlling and eliminating it ازالة او القضاء من التلوث .

Two major categories for the intensity of cleaning are sterilization التعقيم and disinfection التطهير.

1- **Sterilization destroys يحطم** all microbial life كل الميكروبات on an object على المواد or surface and occurs through the use of heat, pressure الأسطح, or chemical methods.
2- Disinfection eliminates ازالة most microbes, excluding bacterial spores يستثنى منه سبورات البكتيريا, and typically involves the use of chemical agents.

Cleaning" is the process of removal of foreign material المواد الغريبة from a surface or object and may involve both mechanical processes عمليات ميكانيكية and the use of detergents المنظفات with water. Cleaning, alone, can reduce the organism load on a surface and, if used in conjunction بالأقتران او المزج with disinfection, may lead to significant مميز reductions ازالة in organism in shorter time بوقت اقصر.

Three types of available solutions can be used during cleaning:

1- **Detergents (المنظفات (الصابون و مساحيق الغسيل:-** which remove organic material and suspend oily materials
2- **Disinfectants المطهرات**:- which rapidly kill or inactivate infectious particles
3- **Detergent-disinfectants**:- which achieve both aims.

The spread of such biological material and organisms can produce illness, infection, or death, especially in susceptible individuals (such as the healthcare facility in-patient population), some ambulatory patients (المرضى المتنقلين), and/or in the care-provider/giver population.

Control of contamination significantly assists in reducing the transmission of pathogenic (disease-causing) organisms–such as those responsible for hepatitis-B, HIV/AIDS, and the organism which causes TB–to patients, among the patients, and between the patients and the caregiver/practitioner/staff / ممارس / الرعاية) (الموظفين.

Blood and other body fluids (i.e., blood borne pathogens) can enter the body of other patients, caregivers, and others by way of percutaneous injuries [such as cuts, punctures, injections (including unintended "needles ticks"), and implantations], as well as by other routes (such as receiving a transfusion of contaminated blood, practicing some forms of unprotected sex, etc.) Concern also exists about the possibility of contact of blood borne pathogens with other mucous membranes, e.g., mucocutaneous eye splashes, and contact of such materials with non-intact skin. The so-called "Universal Precautions" protection strategy for those working with such materials requires adoption of the attitude that the handling of all blood and body fluids from all patients be conducted as though the fluids were infectious. These, and other issues necessitate the imposition of rigorous biosafety techniques, procedures, and controls within the healthcare workplace.

The Hazards of Physical Agents

Healthcare facilities and associated laboratories often utilize physical agents استخدام العوامل الفيزيائية(which may pose a health and/or safety hazard مخاطر السلامة and a contamination consideration), including:

1- Ionizing radiation الأشعة المؤينة (particulate–including alpha, beta, neutron, etc.), and/or waves موجات الأشعة [including gamma, X-ray, and short wavelength ultraviolet (UV) energy]

2- Lasers (including their chemical and/or biological plumes from target materials);

3- Infrared (IR) energy, and visible “light” energy

4- Ultraviolet (UV) energy at a longer wavelength

5- Radiofrequency (RF) energy including electric and/or magnetic field components.

Lecture Nine; introduction fungi, structure types

Fungi

Fungi are large group of eukaryotes, includes yeast, filamentous fungi, and mushroom. Scientists once considered fungi plants before discovering that they are a distinctly different type of organism. Fungus not only provide us important foods, drugs as antibiotics, but also are important for degenerating dead plants and animals in the world. *The study of fungi is called mycology.*

General characters of fungi

1- Fungi are eukaryotic organisms in which they have well-defined nucleus.
2- Fungi are more complex microorganisms from bacteria except for yeast.
3- Most fungi are composed of networks of long hollow tubes called **hyphae**.
4- Each hyphae is bordered by a **rigid** wall usually made of **chitin**, the same material that forms the exoskeletons of insects (هياكل الحشرات).
5- Hyphae grow by elongation at the **tips** (قمم) and by branching to form a dense network called **mycelium**.
6- As the mycelium grows, it produces **huge fruiting bodies** and other structures which contain reproductive spores.

Fungal requirement

1- All Fungi are **chemoheterotrophs**.
2- Require **organic compounds** for energy and carbon.
3- Can be aerobic (filamentous, bread mold) or facultative anaerobes (yeast).
4- Most of the 200,000 or more fungal species are **decomposers** of dead plant material. Only about 200 species are implicated in human disease.

Fungal reproductive (fungi life cycle)

Fungi are capable of reproducing both sexually (جنسي) and asexually (لاجنسي).

1- Sexual reproduction

Sexual reproduction happens when specialized cells, gametes, unite to form a unique spore. **Fungal sexual spores' results from Sexual reproduction, consisting of three phases:-**

1- **Plasmogamy:-** A haploid nucleus of a **donor** (الواهب) cell penetrates the cytoplasm of a **recipient** (المستلم) cell
2- **Karyogamy: -** The donor and recipient nuclei **fuse** to form a **diploid zygote** nucleus.
3- **Meiosis: -** The diploid zygote nucleus gives rise to haploid nuclei (sexual spores) some of which may be genetic recombinants.

2- Asexual reproduction

They develop by branching and fragmentation of hyphae, while yeasts replicate through budding (التبرعم).

1- Fragmentation takes place when cells of the hyphae split (انقسام) off to form a different fungus.
2- A single fungus cell may divide in two to form a new fungus in a process termed as **budding** (التبرعم).
3- Sporformation: Spores commonly to identify fungus microscopically in laboratories.

a- **Conidiospore** – A unicellular or multicellular spore that is not enclosed in a sac. Are usually produced in a chain at the end of a **conidiophore**. (Example: Aspergillis).
b- Another type of conidiospore is an **arthrospore** – formed by fragmentation of a septate hyphae into single, slightly thickened cells. (Example: *Coccidioides immitis*).

c- Another type of conidiospore is a **blastospore** – bud comes off parent cell (Example: *Cryptococcus*).

d- **Chlamydospore** – a thick-walled spore formed by rounding and enlarging within a hyphal segment. Example: ~~*Candida albicans*~~.

e- **Sporangiospore** – A spore formed within a sporangium or sac at the end of aerial hyphae. (Example: Rhizopus).

Fungi: Vegetative Structures

1- Molds and Flesh Fungi

a- **Thallus – long filaments** of cells joined together (called hyphae). Color, consistency (ثبات) of growth.

b- **Septa (الحواجز) cross-wall**s dividing the hyphae into distinct (متنوعة) uninucleate cell like units (called septate hyphae).

c- **Vegetative hyphae (الهايفات الخضرية)** portion that is used to obtain nutrients (growth below surface of media).

d- **Aerial hyphae (الهايفات الهوائية)** projects above media on which fungus is growing and often contains spores.

e- **Mycelium** (الحصيرة) filamentous mass

2- Yeasts

a- Non-filamentous unicellular fungi that is spherical or oval.

b- Some divide by fission that can either be even (سطحي) or uneven cell division (budding).

c- *Candida albicans* ; sometimes produces buds that fail to isolate into daughter cells and are called pseudohyphae (الهايفات الكاذبة).These can resemble hyphae and penetrate (أختراق) deeper tissue.

d- Colonies on agar can resemble bacterial colonies, especially staph colonies.

e- Can use oxygen or organic compounds as final electron acceptor (can do aerobic respiration and fermentation).

3- Dimorphic Fungi

Some fungi, especially pathogenic fungi, exhibit two forms of growth – yeast like fungi and moldlike fungi. Examples of human pathogens those are dimorphic are

1- *Histoplasma capsulatum*
2- *Coccidioides immitis*, Valley Fever

Fungi: Nutritional Adaptations

Differ from bacteria in the following ways:

1- Grow best at pH 5.0.
2- Almost all molds are aerobic; most yeasts are facultative anaerobes.
3- Most fungi are more resistant to osmotic pressure (can grow in high sugar or salt concentration).
4- Fungi can grow on substances with low moisture.
5- Require less nitrogen than bacteria.

Fungi: Economic Effect of Fungi

1- unwanted effects (الأضرار)

a- Spoilage of food. Grow where bacteria cannot. Fruit, grains, vegetables, jams/jellies.
b- Plant pathogens

– **Dutch elm disease;** carried by bark beetles devastated US tree population

– **Chestnut blight Disease;** imported from China (1904) killed nearly all chestnut trees in US

2- Benefits (الفوائد)

a- *Saccharomyces cerevisiae;* Used to make bread, wine and beer. Genetically engineered protein products e.g. Hepatitis B vaccine

b- Biological control of pests (الآفات).

c- Medications such as antibiotic and anticancer.

Lecture Ten; Pathogenic fungi, types and identification

Over the last decade the fungal infections increasing, these infections are occurring as nosocomial infections and in people with compromised immune system.

Fungi: Medically Important Division of Fungi (الفطريات الطبية)

1- **Anamorphs (Deuteromycota, fungi imperfecti) الفطريات الناقصة**

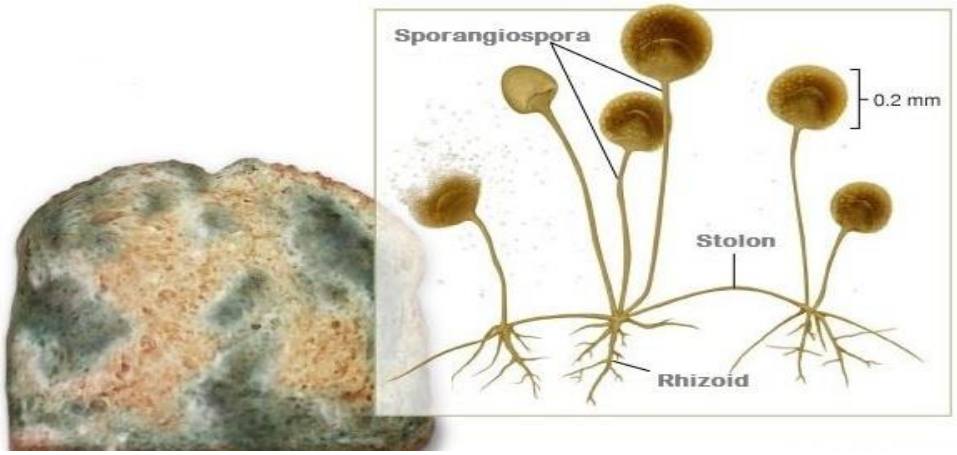
a- Placed here if they have not been found to **produce sexual spores** (telomorph); produce asexual chlamydospores, arthrospores, conidiospores, or budding.

b- Have septate hyphae (الهايفة مقسمة او تحوي حواجز) . Most are anamorph (asexual) phases of Ascomycota and a few are Basidiomycota. Example: Coccidioides immitis

2- **Zygomycota**

a- Saprophytic molds (الاعفان الرمية التغذية) that have nonseptate hyphae and produce sporangiospores (asexual) and zygospores (sexual).

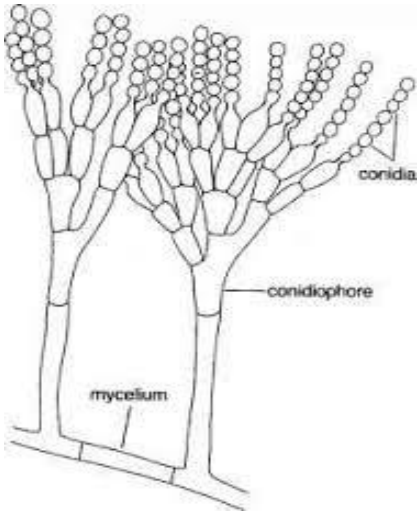
b- Life cycle: Sexual spores are zygospore – A large spore enclosed in a thick wall. Examples: *Mucor* and *Rhizopus*



3- **Ascomycota**

a- Includes molds with septate hyphae and some yeast.

b- Life cycle – Asexual spores are usually conidiospores produced in long chains from the cinidiophore. While, sexual spore is ascus with ascospores Examples: *Aspergillus* and *Histoplasma capsulatum*



Ascomycota

4- **Basidiomycota** – Mushrooms

Life cycle: Have septate hyphae and produce basidiospores; some produce conidiospores. Example: *Cryptococcus neoformans* (anamorph).

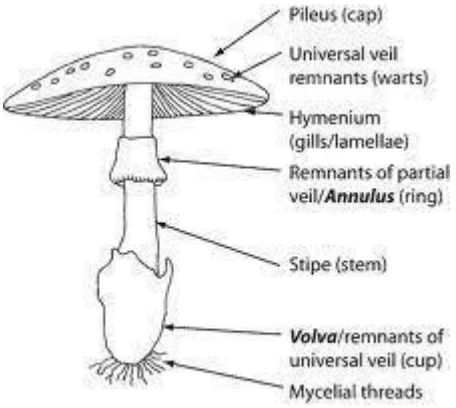


Fig. 1A

Type of Fungal Diseases (أمراض الفطريات)

There are approximately 1.5 million different species of fungi on Earth, but only about 300 of those are known to produce diseases. Fungal diseases are often caused by fungi that are common in the environment. Fungi are everywhere, in soil and on plants and trees as well as on human skin.

Most of Fungi do not caused human's disease. However some of them do cause serious diseases. Any fungal infection called **mycosis [mycosis are generally chronic disease (long-lasting) because fungi grow slowly].** Fungi cause a wide range of diseases, divided into five groups according to the degree of tissue involvement and mode of entry into the host.

1- **Superficial infection (الأصابات السطحية)**

Superficial fungal infections; Are fungi which attack tissues on the surface of the human body, which include the skin, nails, and hair. **They most often occur in moist areas, such as between the toes, in the crotch, or in the mouth**.

The symptoms produced by infection with different types of fungi varies, these infections generally causes itching, reddened skin, and inflammation. Some

superficial skin infections are mild and produce few or no symptoms. Others are more irritating. Superficial fungal infections are rarely life threatening, but they may cause considerable discomfort or embarrassment

Superficial fungal infections are somewhat infectious and pass from person to person through direct contact or, less commonly, through clothes or contact with surfaces of other objects in the environment.

a- Subcutaneous mycoses (تحت الجلدية) are fungal infections beneath the skin caused by saprophytic fungi that live in soil and vegetative. Example: *Sporothrix schenckii* (rose thorns).

b- Cutaneous mycoses (dermatophytes) (الجلدية) affect keratin-containing tissues such as hair, nails, and skin. Example: *Microsporum* (ringworm).

1- are ringworm

2- athlete's foot

3- jock itch

c- Yeast infections includes Candidiasis are usually found;

a- On the skin,

b- On the head of the penis

c- In the mouth

d- In the vagina

e- Around the nails.

d- Opportunistic mycoses (المتحينة للفرص) caused by normal microbial or fungi that are not usually pathogenic (is generally harmless in its normal habitat). Examples

a- Mucormycosis (Rhizopus and Mucor).

b- Aspergillosis (Aspergillis).

c- Candidiasis (Thrush) – *Candida albicans.*

2- Systemic infection (Systemic mycoses) (الأصابات الجهازية)

Systemic infections; are fungal infections deep within the body and attacked many tissues and internal organs. They often start in the lungs, but in severe cases may spread to the blood, heart, brain, kidneys, liver, or other parts of the body. Examples: Histoplasmosis and Coccidioidomycosis.

Systemic fungal infections often are chronic and develop slowly, taking weeks or months to become a problem. Symptoms are sometimes similar to those of the common cold, but sometimes, especially in people with weakened immune systems, symptoms may be sudden and severe, requiring hospitalization. Symptoms may include cough, fever, chills, night sweats, anorexia (loss of appetite), weight loss, general fatigue, and depression.

Example of some fungal diseases

1- Tinea Infections

Common Superficial fungal infections of the skin, hair and nails, these infections known by the medical term tinea (ringworm), can occur almost anywhere on the body. In general antifungal creams or sprays are often effective for limited infections. But some of these infections, such as scalp ringworm, typically require treatment with a prescription medication to kill the fungus.

Ringworm infections are conveniently divided into categories, based on the part of the body that was infected:

a- **Tinea capitis**: Ringworm of the scalp, eyebrow and lashes.

b- **Tinea corporis**: Ringworm of the body.

c- **Tinea cruris**: Ringworm of the groin, perineum and perianal region. Infections are commonly referred to as "**jock itch**".

d- **Tinea unguium**: Ringworm of the nail.

e- **Tinea barbae**: Ringworm of the beard.

f- **Tinea pedis**: Ringworm of the feet. Infections are commonly referred to as **athlete's foot**.

g- **Tinea manuum**: Ringworm of the hand.

2- Candidiasis

Candidiasis is a common type of fungal infection caused by different yeast species in the Candida family. Candida yeast grows on moist surfaces of the body and is a common cause of vaginal infections. It can also cause an infection of the mouth or throat, known as **thrush**. Candida rarely invades the bloodstream and spreads to other areas of the body. People with a weaken immune system are most susceptible to systematic candidacies, which can be life-threatening.

3- Aspergillosis

Aspergillosis:- Disease caused by *Aspergillus fumigatus* parasitizes animals, especially birds, infecting mainly lungs, through inhalation of spores, and causing heavy mortality

A spergillus is a common fungus found in soil, decaying plants, air conditioning vents and dust. Aspergillus spores can be inhaled with air into the nose and lungs. In general, Aspergillus spores cause no harm. However, some people in particular people taking medicines that suppress the immune system. Aspergillus can grow in the lungs causing fungal disease called aspergillomas. In some cases, Aspergillus

moves from the lungs to the bloodstream causing a widespread, life-threatening infection.

4- Coccidioidomycosis (Systemic mycosis**)**

Coccidioidomycosis also known as Valley Fever; is a fungal disease caused by Coccidioides. This fungus inhabits dry areas, such as Arizona, Nevada, western Texas, central California and some areas of New Mexico. Inhalation of dust contaminated with Coccidioides spores introduces the fungus to the lungs. In most cases infected with Coccidioides have no symptoms. In those who develop symptomatic illness, headache, fever, muscle aches, cough and skin rash are common. Although most people recover from coccidioidomycosis within a few weeks, some develop a persistent lung infection or systemic invasion in which the fungi travel to and infect other parts of the body.

5- Histoplasmosis (Systemic mycosis**)**

Histoplasma capsulatum causes the fungal infection known as histoplasmosis. Bat and bird droppings stimulate the growth of *H. capsulatum* in the soil. Caves inhabited by bats, bird roosts and waste from poultry houses often harbor *Histoplasma*. *Histoplasma* spores are inhaled when digging or moving contaminated soil. Most people infected with *H. capsulatum* do not become ill. However, some people experience **a respiratory illness** characterized by a dry

cough, fever, loss of appetite, muscle and chest pain. Uncommonly, this respiratory illness becomes chronic, causing progressive lung damage over months to years. Rarely, Histoplasma fungi enter the bloodstream and infect other organs

Laboratory identification

1- Identification by fungal culture of specimens: blood, pus, CSF, sputum, tissue biopsies, skin scrapings, nail clippings on media that encourages fungal growth e.g. Standard media such as sabouraud agar, potato dextrose agar.

2- Identification by the morphology of conidia structures and carbonhydrate assimiliation tests.

3- Fungal Staining – methylene blue staining or wet prep using KOH to dissolve tissue material

4- Antigen testing to test for antigen present in the wall of fungus e. g crytococcal antigen, galactomannan used in serum and CSF samples.

Lecture Eleven; Introduction of virology, characterization, types of viruses

Introduction:

The virus is the smallest an infectious non-living particle that cannot survive on its own. It is considered to be non-living because it cannot exist purely by itself. It has no enzymatic system necessary for its multiplication. It requires a host cell to replicate itself and uses the host cell replication and protein synthesis machinery to create progeny of its own. Viral hosts include all organisms ranging from microorganisms like bacteria to highly evolved species like animals and humans. Viruses are not cellular and are referred to as particles with a size ranging from 20-300 nm.

A Virion:- A virus in its infectious state is called a virion.

Viriod : Viroids are much smaller than viruses and are also considerably simpler, for they consist of no more than a single strand of RNA

Prion : The prions are exclusively composed of glycoprotein called prion protein (PrP). They contain no nucleic acid

Evolution of viruses: نشوء أو تطور الفيروسات

There are three hypothesis for the evolution and nature of the viruses:

1- Viruses may be originated from (wild) cellular genes which have gone out of control.
2- They may be initiated by a retrogressive development from a pathogenic bacteria with loss of enzyme system necessary for independent replication .
3- Viruses are independent unicellular creatures had the ability to activate the infected cells for protein synthesis.

Structure of viruses

All viruses composed of

1- N**ucleic acid: (the genome**). Either DNA or RNA not both.

2- P**rotein: capsid** that covers the genome. Together this is called the **nucleocapsid**.

3- Envelope: Many viruses have a lipoprotein **bilayer** that encloses the capsid. This layer is called the ***envelope* or *glycoprotein coat,*** and consist of two lipid layers interspersed with proteins and is usually derived from **the modified host cell membrane**.

The entire intact virus is called the virion.

The structure and composition of these components can vary widely. The nucleic acid is either single or double stranded. All DNA viruses are double stranded (DS) except Parvoviruses and all RNA viruses are SS except Reoviruses.

The capsid is responsible for

1- the protection of the nucleic acid.
2- assists in the adhesion of the virus to the infected cell.
3- It has the antigenic character, i. e: the capsid protein activates the immune system to develop antibodies.

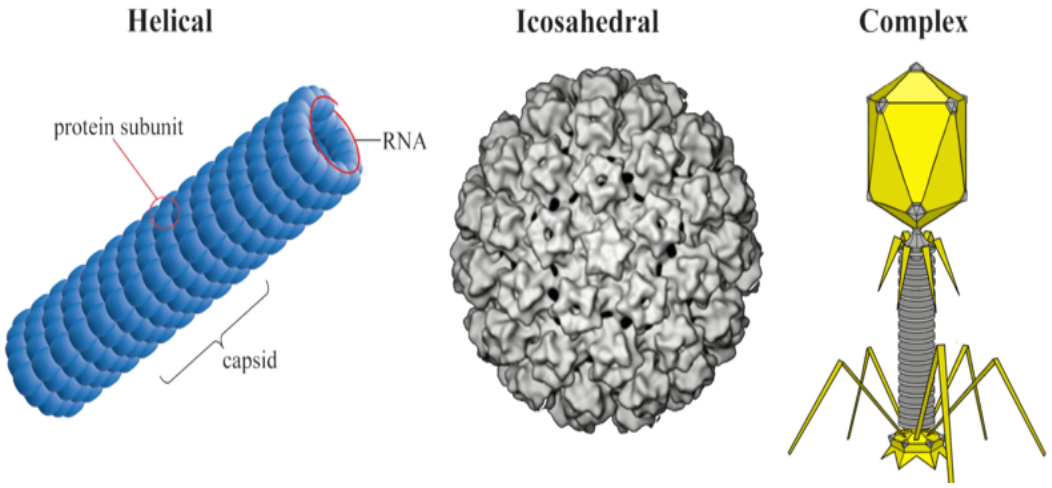
1- **<u>Helical Capsids</u>**: The first and best studied example is the plant tobacco mosaic virus (TMV), which contains a Single strand (SS) RNA genome and a protein coat made up of a single, 17.5 kd protein. This protein is arranged in a helix around the viral RNA, with 3 nt of RNA fitting into a groove in each subunit. Helical capsids can also be more complex, and involve more than one protein subunit.

Several families of animal virus contain helical nucleocapsids, including the *Orthomyxoviridae* (influenza), the *Paramyxoviridae* (bovine respiratory

syncytial virus), and the *Rhabdoviridae* (rabies). All of these are enveloped viruses.

2- **Icosahedral Capsids**: In these structures, the subunits are arranged in the form of a hollow, quasi spherical structure, with the genome within. **An icosahedron is defined as being made up of 20 equilateral triangular faces arranged around the surface of a sphere. They display 2-3-5 fold symmetry.** Since proteins are not equilateral triangles, each face of an icosahedron contains more than one protein subunit.

4- **Complex capsid**: Some virus are more complex, being composed of several separate capsomere with separate shape and symmetry. Have no symmetry due to complexity of their capsid structure. Eg. Pox virus, Bacteriophage.



The name of viral groups is taken according to:

1- The disease caused. Such as FMD virus and HIV.

2- The place of discovery: Bunya virus (Kenyan village).

3- Shape of the virion: corona virus (crown-like), and rotavirus (wheel-like).

4- Abbreviated from the full name: Reo = respiratory enteric orphan, Papova = papilloma polyoma vaculating agent.

5- Size: picornavirus, pico = small (Latin).

6- Associated with the scientist name: Romarov, Pous sarcoma virus.

7- Presence of some characteristics: Retroviruses contains reverse transcriptase enzyme which is responsible of RNA transcription to DNA.

Multiplication of viruses

All of the dynamic events associated with the virus (transcription & replication of genomes) occurs within the living host cell. All DNA viruses multiply inside the host cell nucleus (except pox virus) and all RNA viruses multiply in the cytoplasm.

Steps of multiplication:

1- Attachment:

The virion attaches to the cell membrane through a selective specific receptors. Presence or absence of virion receptors in the cell membrane justifies the cell affinity to the virus.

2- Penetration:

Occurs either by fusion (without capsid0 or viropexis (engulfment of the virion) or direct inoculation through pores of the cell membrane. So, the virion has not yet been ensured to enter the cell as nucleocapsid or not.

3- Transcription:

It means the duplication of the nucleic acid of the virus. That occurs by transfer of the genomes from the nucleic acid to a messenger RNA which reach the cellular ribosomes for synthesis of protein to from a new strand.

4- Assembly:

Assembly occurs in a definite site in the cell, either in the nucleus or in a certain site in the cytoplasm (viroplasm or virus factory) which differs from a species to another. The nucleus and the capsid might be formed separately or at the same time.

5- Release:

Depends upon the virus species and the nature of invaded cell. Excessive multiplication of the virus leads to the lysis and rupture of the cell. Virions then invade new cells through membrane pores.

Diagnostic Procedures of Viral Diseases

Since the viral isolation is not quite successful, the principal of the use of antigen antibody reaction is the best mean for diagnosis of different viral disease. It is applied by different serological procedures differ in their sensitivity and specifity.

1- Virus neutralization:

Some antibodies interact with virions and neutralize there activity. This test is the most sensitive and specific test. Antibodies used only interact against selective serotype of virus, it shows a little or no cross interaction with other viruses.

2- Haemagglutination inhibition:

Antibodies can inhibit haemagglutination by blocking the antigen of the virus responsible for this phenomenon. It depends upon adding antigen to serially diluted

sera and erythrocytes. The high titer is the least cell agglutination occurred in. this test is highly sensitive, highly specific except in Togo viruses.

This test is preferable for that it is simple, inexpensive and rapid.

3- Gel diffusion:

The antigen antibody reaction can be detected by observation of precipitation reactions in semisolid gels. The diffusion depends upon the molecular weight of the antigen. Although the test is highly specific, but it is less sensitive that it gives no idea about the titer of the antigens.

5- Complement fixation:

Complement is an assisting substance which has the property of lysis of sheep RBCs with haemolysin. It is added to the antigen-antibody complex, incubated at 24C overnight. The test is of low sensitivity and specifity.

5- Immunofluorecence:

This test is based on the observation of the refractory greenish-blue fluorecein dye under the electron microscope.

A/ Direct Immunofluorecence:

Virus antigen is mixed with fluorecein-tagged antiviral serum. Fluorescent lamb adsorbs all blue and violet light, the specimen appears black except the area in which fluorecein is emitting greenish-yellow light.

B/ Indirect Immunofluorecence:

More sensitive and more specific. It differs from the above that the interaction occurs through an intermediate conjugated antigammaglobulin, which is obtained by injection of human globulin in goat or rabbit.

B/ Indirect Immunofluorecence:

More sensitive and more specific. It differs from the above that the interaction occurs through an intermediate conjugated antigammaglobulin, which is obtained by injection of human globulin in goat or rabbit.

Pathogenesis of viral diseases

Pathogenesis means:- Entry of the virus to the animal body, it's mode of spread from the portal of entry to the target organ, the sites of primary and secondary multiplication and the mechanism of tissue damage and disease.

Influenza virus:

In human influenza, the virus enters the respiratory tract as air borne droplets. Multiplication occurs in the nasopharynx 1 – 2 days before and after the onset of the disease. Viremia has been reported in few patients. Neuraminidase is an enzyme secreted by the influenza virus which lowers the viscosity of the mucous film in the respiratory tract, expose the cellular surface receptors and promotes the spread of the virus containing fluid to the lower tract.

Hepatitis viruses

There are 5 main hepatitis viruses, referred to as types A, B, C, D and E. These 5 types are of greatest concern because of the illness and death they cause and the potential for outbreaks and epidemic spread. In particular, types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer.

Hepatitis A

Hepatitis A is caused by an infection with the hepatitis A virus (HAV). This type of hepatitis is most commonly transmitted by consuming food or water contaminated by feces from a person infected with hepatitis A.

Hepatitis B

Hepatitis B is transmitted through contact with infectious body fluids, such as blood, vaginal secretions, or semen, containing the hepatitis B virus (HBV). Injection drug use, having sex with an infected partner, or sharing shavers with an infected person increase your risk of getting hepatitis B.

Hepatitis C

Hepatitis C comes from the hepatitis C virus (HCV). Hepatitis C is transmitted through direct contact with infected body fluids, typically through injection drug use and sexual contact.

Hepatitis D

Also called delta hepatitis, hepatitis D is a serious liver disease caused by the hepatitis D virus (HDV). HDV is contracted through direct contact with infected

blood. Hepatitis D is a rare form of hepatitis that only occurs in conjunction with hepatitis B infection. The hepatitis D virus can't multiply without the presence of hepatitis B. It's very uncommon in the United States.

Hepatitis E

Hepatitis E is a waterborne disease caused by the hepatitis E virus (HEV). Hepatitis E is mainly found in areas with poor sanitation and typically results from ingesting fecal matter that contaminates the water supply., hepatitis E have been reported in the Middle East, Asia, Central America, and Africa, according to the

	Hepatitis A virus (HAV)	Hepatitis B virus (HBV)	Hepatitis C virus (HCV)	Hepatitis D virus (HDV)	Hepatitis E virus (HEV)
Viral genome	RNA	DNA	RNA	RNA	RNA
Transmission	Faecal-oral route	Blood and other body fluids	Blood	Blood and other body fluids	Faecal-oral route
Incubation period	14–28 days	30–180 days	14 days –6 months	HDV requires HBV for replication	14–70 days
Diagnosis	• Anti-HAV-specific AB • HAV RNA	• HBV surface protein • Anti-HBV-specific AB	• Anti-HCV-specific AB • HCV RNA	• Anti-HDV-specific AB • HDV RNA	• Anti-HEV-specific AB • HEV RNA
Possible chronic infection	No	Yes	Yes	Yes	Yes
Vaccine	Yes	Yes	No	No	Yes (in China only)

AB, antibody; DNA, deoxyribonucleic acid; RNA, ribonucleic acid

Acquired Immune Deficiency Syndrome (AIDS)

The Human Immunodeficiency Virus (HIV) causes AIDS. The virus attacks the immune system and leaves the body susceptible to a variety of life-threatening illnesses and cancers.

Common bacteria, yeast, parasites, and viruses that ordinarily do not cause serious disease in people with fully functional immune systems can cause fatal illnesses in people with AIDS.

HIV has been found in saliva, tears, nervous system tissue, blood, semen (including pre-seminal fluid, or "pre-cum"), vaginal fluid, and breast milk. However, only blood, semen, vaginal secretions, and breast milk have been proven to transmit infection to others.

Transmission of the virus occurs:

1- Through sexual contact
2- Through blood -- via blood transfusions or needle sharing.
3- From mother to child -- a pregnant woman can passively transmit the virus to her fetus.
4- Other transmission methods are rare and include accidental needle injury, artificial insemination with donated semen, and through a donated organ.

People at highest risk

1- homosexual or bisexual
2- intravenous drug users who share needles,
3- infants born to mothers with HIV
4- people who received blood transfusions or clotting products between 1977 and 1985 (prior to standard screening for the virus in the blood).

Acquired Immune Deficiency Syndrome (AIDS) is the final and most serious stage of HIV disease, which causes severe damage to the immune system About 47 million people worldwide have been infected with HIV since the start of the epidemic.

Stages of ADS infection

AIDS begins with HIV infection. People infected with HIV may have no symptoms for ten years or longer, but they can still transmit the infection to others during this symptom-free period. Meanwhile, their immune system gradually weakens until they develop AIDS.

Stage 1: Acute HIV infection

Within 2 to 4 weeks after infection with HIV, people may experience a flu-like illness, which may last for a few weeks. This is the body's natural response to infection. When people have acute HIV infection, they have a large amount of virus in their blood and are very contagious.

Stage 2: Clinical latency (HIV inactivity or dormancy)

This period is sometimes called asymptomatic HIV infection or chronic HIV infection. During this phase, HIV is still active but reproduces at very low levels.

Stage 3: Acquired immunodeficiency syndrome (AIDS)

AIDS is the most severe phase of HIV infection. People with AIDS have such badly damaged immune systems that they get an increasing number of severe illnesses, called opportunistic illnesses.

Lecture Twelve; Introduction of Parasites

Introduction to Medical Parasitology

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; the host is an organism which supports and harbor's the parasite.

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- Temporary parasite - is one that visit the host only for a short period of time.

7- A zoonotic parasite- that primarily infects animals and is transmittable to humans.

8- Opportunistic parasite- that is capable of producing disease in an immune deficient host (like AIDS and cancer patients) e.g. Toxoplasma gondii.

9- Permanente parasite- that lives on its host until maturity e.g. Enteric amebas.

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- Paratenic host – a host that serves as a temporary refuge and vehicle for reaching an obligatory host, usually the definitive host, and it's not necessary for the completion of the parasites life cycle.

4- Reservoir host – a host that makes the parasite available for the transmission to another host and is usually not affected by the infection.

5- Natural host – a host that is naturally infected with certain species of parasite.

6- 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

1- Mutualism - both organisms are benefited

2- Commensalism - in which one partner benefits from the association, but the host is no harmed.

3- 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.

Vector: Animal that serve as a carrier of parasites.

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.

B/ Indirect Immunofluorecence:

More sensitive and more specific. It differs from the above that the interaction occurs through an intermediate conjugated antigammaglobulin, which is obtained by injection of human globulin in goat or rabbit.

Lecture Thirteen; Protozoa, *Entamoeba histolytica*

Protozoa: are eukaryotic, unicellular microorganisms, which lack cell wall.

Characteristics of Protozoa: The major distinguishing characteristics is

1- They do not have cell wall; some however, possess a flexible layer, a pellicle, or a rigid shell of inorganic materials outside the cell membrane.
2- They have the ability during their entire life cycle or part of it to move by locomotor organelles or by a gliding mechanism.
3- They have heterotrophic mode of nutrition, whereby the free-living forms ingest particulates, such as bacteria, yeast and algae, while the parasitic forms derive nutrients from the body fluids of their hosts.
4- They reproduce primarily by asexual means, although in some groups sexual modes also occur.

Classification of Protozoa:

The classification of protozoa is mainly based on their means of locomotion. They are subdivided into the following four classes.

1- Sarcodina: Motility is due to the streaming of ectoplasm, producing protoplasmic projections called pseudopodia (false feet). Examples: Entamoeba histolytica.
2- Mastigophora: Locomotion is effected by one or more whip-like, thin structures called flagella. Examples: Giardia lamblia.
3- Ciliophora: Locomotion is carried out by means of short hair-like projections called cilia Examples: Balantidium coli.
4- Sporozoa: Unlike the above three classless of protozoa, members of the class sporozoa do not have locomotor organelles in their mature stage; however, immature forms exhibit some type of movement. All the members of this group are parasites. Examples: Plasmodium spp.

Amoeba or Rhizopoda Class

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.

Their reproduction is through binary fission, e.g. splitting of the trophozoite or through the development of numerous trophozoites with in the mature multinucleated cyst.

Motility is accomplished by extension of pseudopodia (“false foot”)

Entamoeba histolytica

Disease: amoebic dysentery.

Habitat: large intestine.

Geographical distribution: worldwide.

Infective stage: Quadranucleated (mature 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 evenly 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 10-20μm. 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.

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 may occur. 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: non pathogenic, 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:

*Examination of a fresh dysenteric faecal specimen or rectal scraping for trophozoite stage. (Motile amoebae containing red cells are diagnostic of amoebic dysentery).

* Examination of formed or semiformed faeces for cyst stage. (Cysts indicate infection with either a pathogenic E.histolytica or non-pathogenic *E.dispar.)*

Lecture Fourteen; Flagellate, Giardia, Trichomonase

PROTOZOA

Flagellates

Blood & tissue flagellates

Trypanosoma species.

Leishmania species.

Intestinal flagellates

Giardia lamblia

urogenital flagellates

Trichomonas vaginalis

Amoebas - Entamoeba histolytica

Cliliophora - Balantidium coli

Coccidian - Toxoplasma gondii, Plasmodium spp

contaminated with cyst (Quadranucleated cyst).

Pathogenic Flagellates

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:

I- Luminal or digestive or intestinal flagellates: Giardia lamblia

II- Genital flagellates: Trichomonas vaginalis

III- 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

Morphological features: the life cycle consists of two stages, the trophozoite and cyst. The trophozoite is 9-12 μm long and 5-15μm 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 8-12μm long and7-10μm wide, thick-walled with four nucleus and several internal fibera. Each cyst gives rise to two trophozoites during excystation in the intestinal tract.

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: Examination of diarrhoeal stool- trophozoite or cyst, or both may be recovered in wet preparation. In examinations of formed stool (e.g. in asymptomatic carriers) only cysts are seen.

Life cycle of Giardia lamblia

Trophozoite and cyst of Giardia lambilia

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.

Important 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.

Trophozoite of Trichomonas vaginalis

Life cycle of Trichomonas vaginalis

Pathogenesis: The trophozoite is found in the urethra & vagina of women and the urethra & prostate gland of men. After introduction by sexual intercourse, proliferation begins which results in inflammation & large numbers of trophozoite

in the tissues and the secretions. The onset of symptoms such as vaginal or vulval 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.

Lecture Fifteen; Blood Flagellates, Lishmania

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. 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 Species

Leishmania Species	*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* *2-Leishmania braziliensis* (american Leishmaniasis
Clinical disease	Veseral Leishmaniasis kala-azar (black	Cutaneous leishmaniasis	Mucocutaneous

	sickness) or dumdum fever	***(Oriental sore)***	Leishmaniasis **(chiclero ulcer)**
Habitat	Reticuloendothelial system (liver, spleen and bone marrow)	skin inside macrophages of endothelial cells of the capillaries of the infected site	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.

Life cycle of Leishmania

Promasitgote & amasigote forms of Leishmania

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.

Lecture Sixteen; Sporozoa, Plasmidium, Toxoplasma

COCCIDIA (SPOROZOA)

I-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. The genus Plasmodium that are the causes of malaria.

There are four species of malaria normally 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.

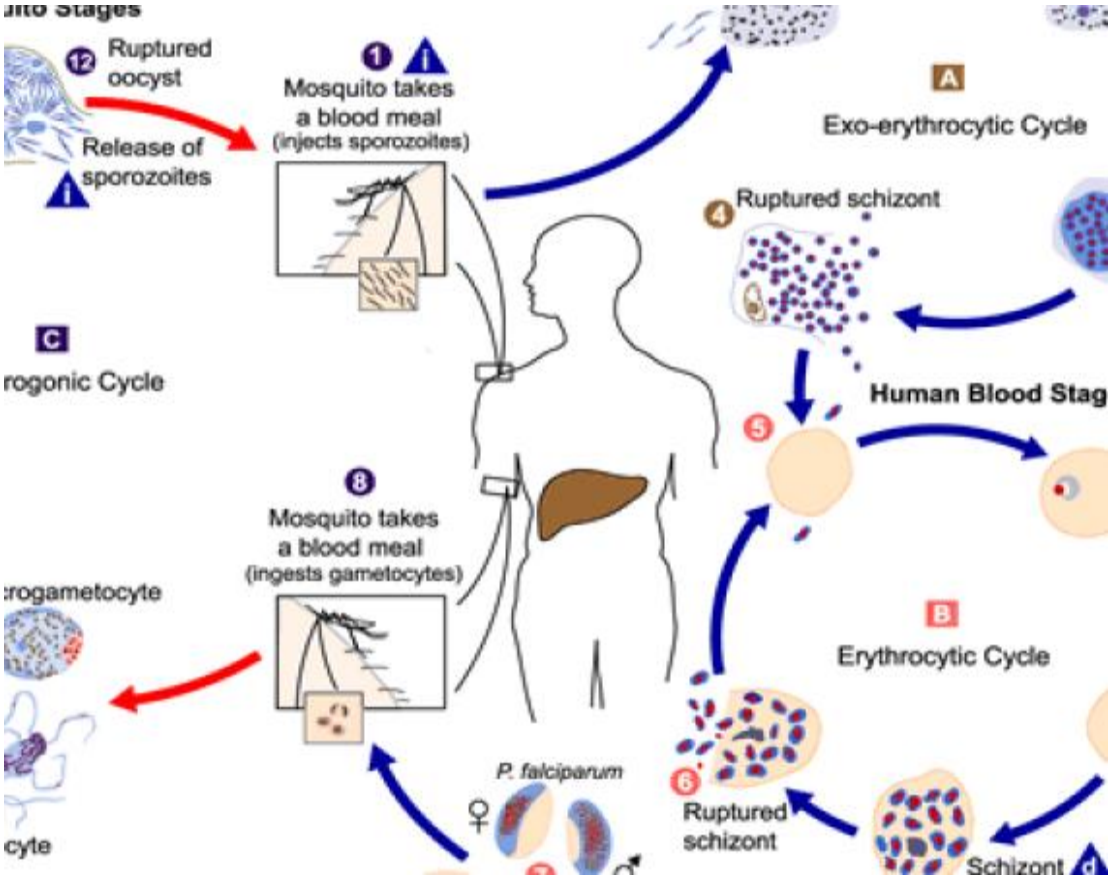
Vector: female anopheles mosquitoes.

Infective stage: 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 and asexual stage (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 passes in four stages:

Three in man:-

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

One in mosquito - Sporogony

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

Pre- Erythrocytic and Erythrocytic schizogony - 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. So malaria transmitted by blood transfusion reproduces only erythrocytic cycle.

Gametogony

Some merozoites that invade RBC's develop into sexual stages (male and female gametocytes). These undergo no further development until taken by the mosquito.

Sporogony (extrinsic cycle in mosquito)

When a female Anopheles mosquito vector bites an infected person, it sucks blood containing the different stages of malaria parasite. All stages other than gametocytes are digested in the stomach.

The microgametocyte undergoes ex-flagellation. The nucleus divides by reduction division into 6-8 pieces, which migrate to the periphery. At the same, time 6-8 thin filaments of cytoplasm are thrust out, in each passes a piece of chromatin. These filaments, the microgametes, are actively motile and separate from the gametocyte. The macrogametocyte by reduction division becomes a macrogamete. Fertilization occurs by entry of a micro gamete into the macro gamete forming a zygote. The zygote changes into a worm like form, the ookinete, which penetrates the wall of the stomach to develop into a spherical oocyst between the epithelium and basement membrane. The oocystes increase in size. 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. Now the mosquito is infective the sporogonous cycle in the mosquito takes 8-12 days depending on Temperature.

Trophozoite: On entry into an erythrocyte, the merozoite again transforms into a trophozoite. It is grow stage of parasite in the red blood cells of human. Gametes: Reproductive elements, male and female. Gametocytes: Precursors of the sexual forms of the malaria parasite, which differentiate into either male or female gametes within the stomach of the mosquito. Hypnozoite: The form of the malaria parasite that remains dormant in the liver. Merozoite: The form of the malaria parasite that invades red blood cells. Oocyst: A stage of the malaria parasite within

the mosquito which is produced when male and female gametes combine. Ookinete: The actively moving zygote of the malarial organism that penetrates the mosquito stomach to form an oocyst under the outer gut lining. Schizont: The mature form of the malaria parasite within red blood cells that ruptures and releases merozoites. Sporozoite: The infectious actively moving form of the malaria parasite, which is injected into people by mosquitoes. Zygote: The diploid cell resulting from union of a male and a female gamete. Schizogony: a process of asexual reproduction of parasite occur in human. Sporogony: a process of sexual reproduction of parasite occur in female anopheles mosquitoes.

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:

1- *P. falciparum*: occur with few weeks or months and die out usually within a year.
2- *P. vivax*: occur mostly in the first year and die within 3 years of the original infection.
3- *P. malariae*: persist for several years.
4- *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.

***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, 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.

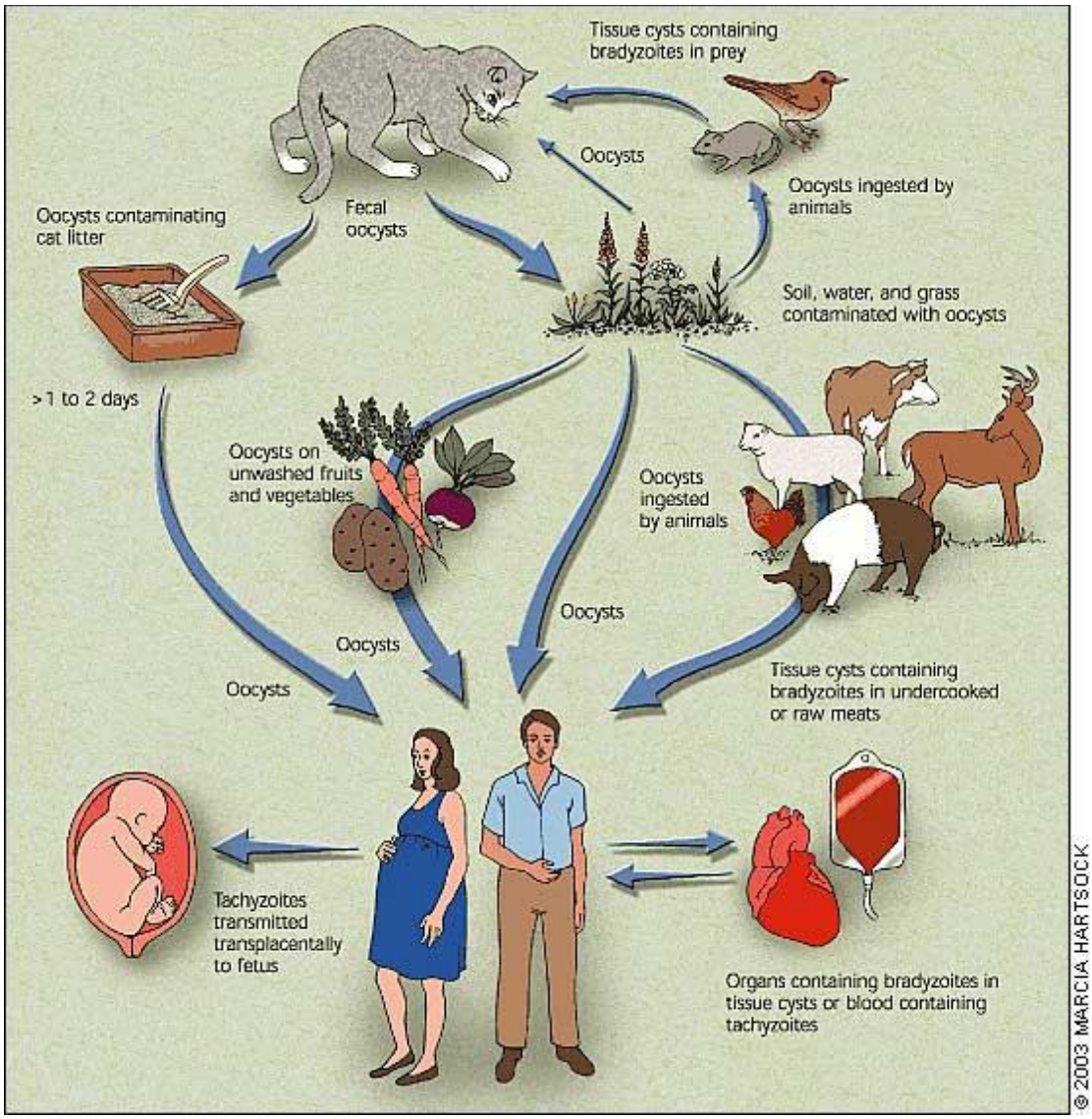
Morphology of toxoplasma: toxoplasma are small, crescent in shape measuring 2-3x4-7μ with Central nucleus, usually with one end rounded and the other end pointed.

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: the life cycle of Toxoplasma gondii starts, when oocysts (resting form of the parasite) exit the final host (cat) in the feces. Millions of oocysts are shed for as long as three weeks after infection. Oocysts sporulate and become infective within a few days in the environment. The

oocysts are found only in the feces of domestic and wild cats. Birds, humans and other intermediate hosts get infected after ingesting water or food contaminated with the cat feces. (Healthy cats can get infected this way, too.) In the gut oocysts transform into tachyzoites(actively multiplying) which are about 4–8 μm long and 2–3 μm wide. They travel to other parts of the body via bloodstream and further develop into tissue cyst bradyzoites(slowly multiplying) in muscle and neural tissue. bradyzoites are about 5–50 μm in diameter. They are commonly found in skeletal muscles, brain, myocardium and eyes where they can remain many decades. If a cat (or a human) eats the intermediate host, the tissue cysts get ingested and the parasite activates in the small intestine.



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- Animal inoculation

4-blood and cerebrospinal fluids findings in toxoplasmosis.

Lecture Seventeen; Helminthology, Introduction of Helminthes Cestodes (Tapeworms) *Taenia saginata* and *Taenia solum*

Medical Helminthology علم الديدان الطبي

Medical helminthology: Is concerned with the study of helminthes or worms. هو العلم الذي يدرس الديدان

Helminthes: Are trophoblastic metazoa (multi-cellular organisms). عباره عن كائنات متعددة الخلايا

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

1- Cestodes (Tape worms) الديديان المسطحة
2- Trematodes (Flukes)
3- Nematodes (Round worms) الديدان الأسطوانية

The Trematodes and Cestodes are groups of flat worms.

Differences between Cestodes, Trematodes, and Nematodes Cestodes

Characters	Cestodes	Trematodes	Nematodes
Shape	Tape-like; تشبه الشريط Segmented مقسمة	Leaf-like; تشبه الورقة Unsegmented غير مقسمة	Enlongated, cylindric اسطوانية متطاولة Unsegmented
Sexes	Not separated, غير مقسمة Hermaphrodite خنثية (monoecious)	Not separate (monoecious) except schistosomes which are diecious ثنائية الجنس	Separated (diecious)
Head	Suckers,ممصات often with hooks اشواك	Suckers, without hooks	No Suckers, no hooks, well developed buccal capsule تجويف فموي in some species
Alimentary Canal القناة الهضمية	absent	Present but incomplete; no anus موجودة ولكن غير كاملة لعدم وجود فتحة المخرج	Present and complete; anus present

Body Cavity تجويف الجسم	absent	absent	present

Cestodes (Tapeworms)

Features of Tapeworm: صفات الديدان الشريطية

1- Tapeworms are hermaphroditic.الديدان الشريطية خنثية

(الدودة تحمل الأعضاء الجنسية الذكرية والأنثوية في نفس الدودة)

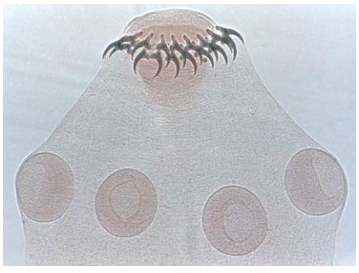
2- They consist of an anterior أمامي attachment organ or scolex and a chain

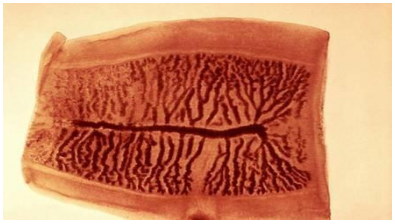
3- Segments (proglottids القطعة الحبلى) also called strobilla.

4- It has suckers ممصات 5- It has rosetellum خطم

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

Taenia Tapeworm: comparison مقارنة between taenia species Taenia saginata Taenia solium

Characters	***Taenia saginata***	***Taenia solium***
Geographical Distribution	Worldwide عالمي الانتشار	Europe, central America, Ethiopia
Common Name	Beef tapeworm الدودة الشريطية البقرية	Pork tapeworm الدودة الشريطية الخنزيرية
Disease	Taeniasis	Taeniasis
Habitat	Intestinal tract الأمعاء الدقيقة	Intestinal tract
Intermediate Host	Beef الأبقار	Pigs الخنازير
Final Host	Human	Human
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 دائرية 2mm in diameter, 4 suckers, without Hooklets اشواك 	Globular كروي , 1mm in diameter, 4 suckers ممصات , with Hooklets 

Gravid Segmentالحبلى	2 wide, 20 mm long	8 mm wide, 13 mm long
Uterus Branch عدد تفرعات الرحم	15-30 	5-10
Egg	Rounded, 2-3 µm in diameter hexacanth embryo جنين سداسي الأشواك surrounded with thick striated wall	Roundedدائرية, 2-3 µm in diameter hexacanth embryo جنين سداسي الأشواك surrounded with thick striated wall

Mode of transmission:

Humans become infected with taenia tapeworm by: يصبح الشص مصاب بالديدان الشريطية

1- ingesting inadequately cooked beef with cysticercus bovis larvae, تناول طعام غير مطهو بصورة جيدة محي على اليرقاتcontaining an invaginated protoscolex (*Taenia saginata*).

2- 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. **Final host**: Human which harbours تحوي the adult worm.

2. **Intermediate host**: Cattle المواشي or pigs which harbours the larval stage.

3- The **adult worm** lives in the small intestine of human.

4- The eggs or gravid segments are passed out with the faeces on the ground. تخرج البيوض والقطع الحبلى مع فضلات النصان المصاب الى الأرض

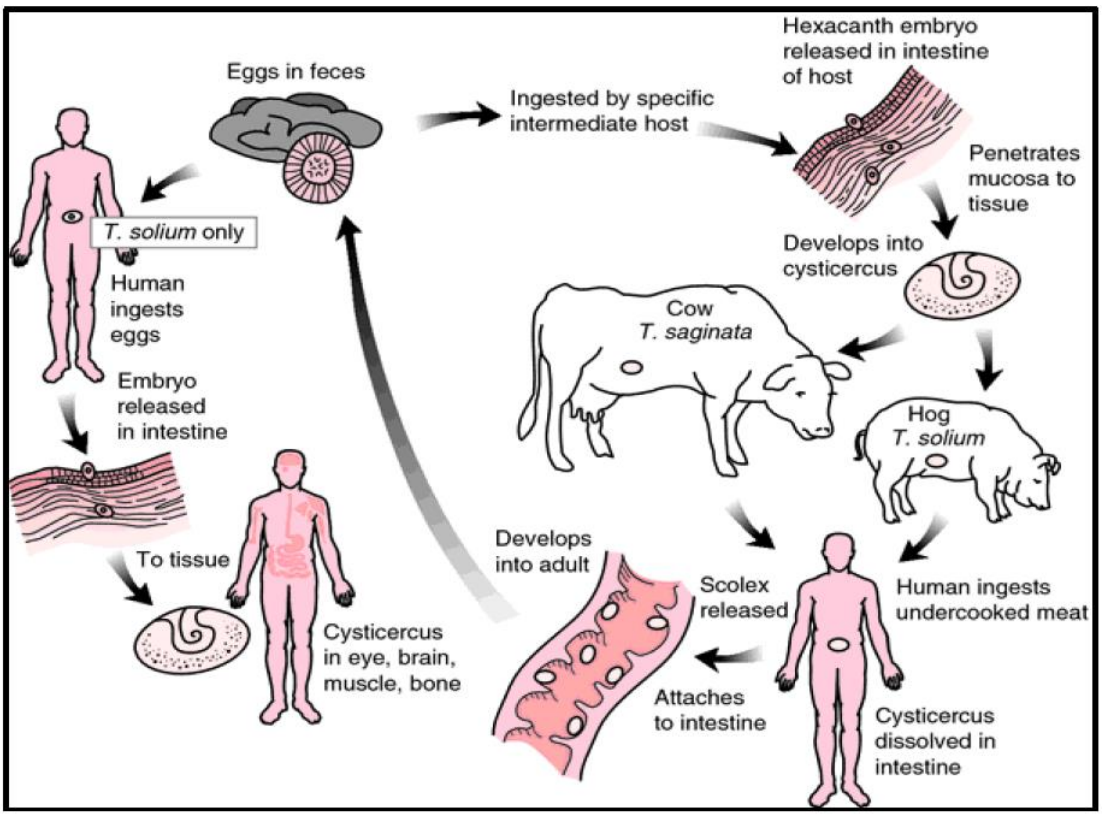
5- The **animals swallow these eggs** during grazing in the field. الحيوانات تتناول البيوض خلا تغذيتها على العشب

6- On reaching the alimentary canal of the intermediate host عند وصولها اى القناة الهضمية للمضيف الوسطي, the radially striated walls of the eggs rupture and oncosheres are liberated. تخرج اليرقات من البيوض

7- These penetrate تخترق the gut wall with the aid بمساعدة of their hooks من خلال أشواكها and gain entrance تنجح في الوصول into the portal vessels الأوعية الدموية البوابية or mesenteric المساريقية lymphatics then to the systemic circulation ومنها الى الدورة الدموية الجهازية.

8- The **naked oncospheres** are filtered out from the circulating تترشح من الدورة الدموية blood into the muscular tissues الى الأنسجة العضلية .

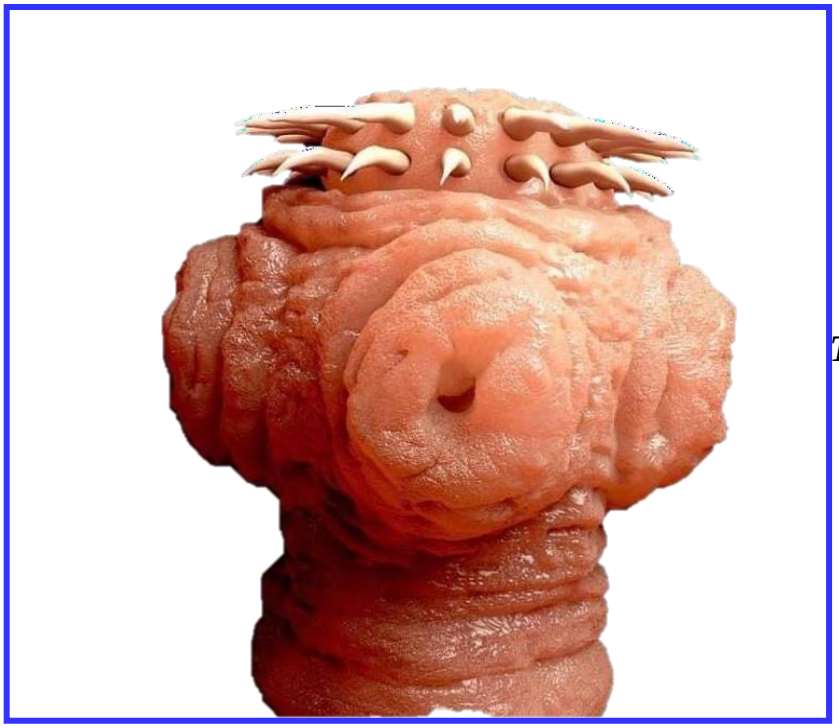
9- Ultimately they settle down in the muscular tissue and undergoes further development. تستقر في العضلات وتعاني من تطورات اخرى لتصبح معدية



Clinical Presentation: ***Taenia saginata*** **taeniasis** produces only mild abdominal symptoms اعراض متوسطة الشدة. The most striking feature consists of the passage of proglottids خروج القطع الحبلى. Occasionally, appendicitis or cholangitis can result from migrating proglottids احيانا التهاب الزائدة ناتج عن هجرة القطع الحبلى .

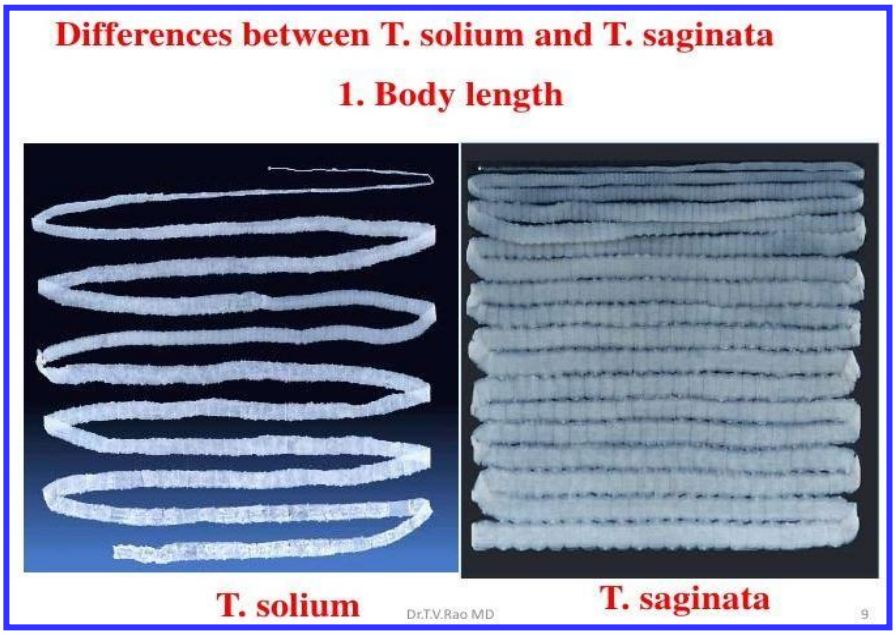
Taenia solium **taeniasis** is **less** frequently symptomatic than ***Taenia saginata*** **taeniasi**s. The main symptom is often the passage of proglottids. Infected persons may complain of epigastric pain, abdominal discomfort, diarrhea, weight loss, hunger sensation, vomiting.

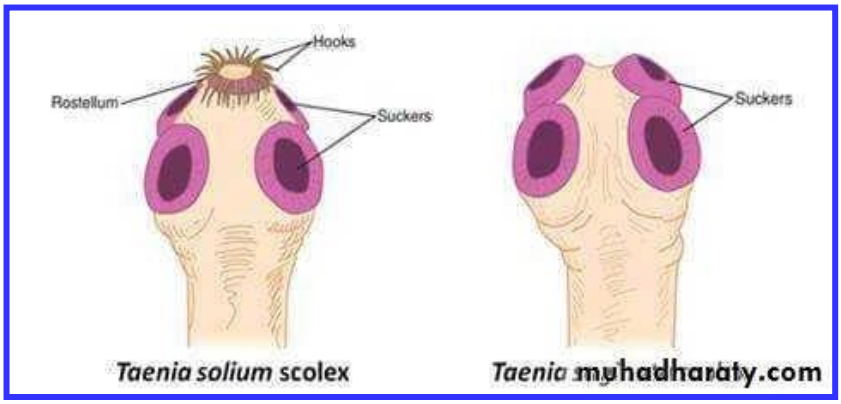
Laboratory Diagnosis Diagnosis of intestinal taeniasis can be made by recovery of the characteristic ova in the stool. However, the ova of T. solium and T. saginata are identical and diagnosis is made by the recovery of the segments or scolex.



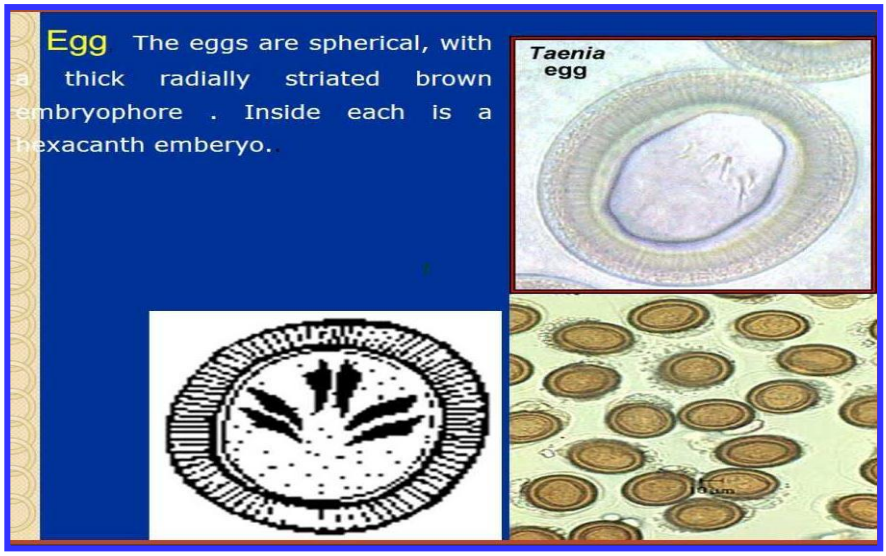
Taenia saginata

Taenia solium





Heads of Taenia spp



Taenia eggs

Lecture Eighteen; Echinococcus granulosus

Echinococcus granulosus

Common name: dog tape worm دودة الكلب الشريطية

Disease: Echinococcosis or hydatid cyst مرض الأكياس المائية

Geographical distribution: warm climate countries المناطق الحارة

Habitat: small intestine الأمعاء الدقيقة

Infective stage: eggs

Final host: dog and other carnivore الكلاب وآكلات اللحوم

Intermediate host: human, cattle المواشي , sheep الأغنام

Mode of infection طريقة انتقال العدوى: Ingestion of eggs by the

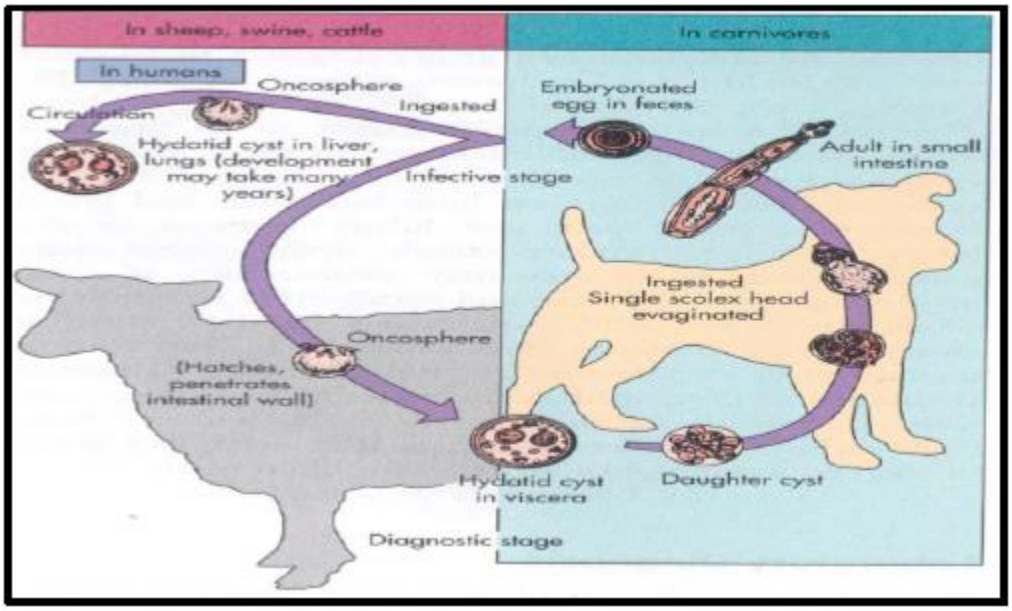
1- Ingestion of water or vegetables polluted ملوثة by infected dog feces فضلات الكلاب المصابة.
2- Handling or caressing infected dogs حمل الكلاب المصابة where the hairs are usually contaminated with eggs عادة يكون الشعر محمل ببيض الدودة .

Morphology: The adult worm measures 3-6 mm in length (up to 1 cm). It has scolex رأس , neck عنق and strobillaخطم . Adult worms live in small intestine of

(final) definitive host (dog). Human is an intermediate host carrying the hydatid cyst الكيس المائي (larva) اليرقة.

Life cycle: Oncosphere البيضة الحاوية على الجنين hatch in duodenum or small intestine into embryos (oncosphere) which:

1- Penetrate wall تخترق جدار الأمعاء
2- Enter portal veins الوريد البوابي
3- Migrate تهاجر via portal blood supply to organs: eg: lungs, liver, brain etc., thus, causing extra intestinal infections الأصابة خارج الأمعاء
4- In these organs, larvae develop into hydatid cysts.
5- The cysts may be large, filled with clear fluid and contain characteristic protoscolices (immature forms of the head of the parasite الشكل غير الناضج لرأس الدودة).
6- These mature into developed scolices, which are infective for dogs.



Clinical features:

Asymptomatic بدون أعراض infection is common شائع , but in symptomatic patients أما إذا كانت الإصابات ذات أعراض

1- It may cause cough - with hemoptysis in lung hydatid disease. تسبب سعال إذا كانت الإصابة في الرئة
2- Hepatomegaly تضخم الكبد - with abdominal pain and discomfort عدم راحة في منطقة الكبد
3- Pressure -from expanding cyst الضغط على المنطقة المصابة نتيجة توسع الكيس
4- Rupture of cyst - severe allergic reaction - anaphylaxis. في حالة انفجار سوف يسبب حساسية شديدة

Diagnosis: التشخيص

1- X-ray or other body scans بواسطة الأشعة او السونار.
2- Demonstration of protoscolices in cyst after operation التحري عن وجود الرؤس داخل الكيس بعد اجراء العملية
3- Serology test: indirect heamagglutination test, complement fixation test, latex agglutination. الفحوصات اسيرولوجية المختلفة
4- Casoni´s test: it is skin test made up by injection 0.2ml of filtered, sterile, diluted fluid of hydatid cyst intradermal عبارة عن حقن0.2 ml من سائل الكيس المفلتر تحت الجلد. Positive results appears by characteristic reading احمرار of skin within 10-20 minutes of injection الحقن.

Lecture Nineteen; *Hymenolepis Nana*

Hymenolepis Nana

Common name: Dwarf Tapeworm Disease مرض الدودة الشريطية القزمية: Hymenolepiasis

Geographical distribution: warm climate countries المناطق الحارة

Habitat: small intestine

Infective stage: eggs

Final host: Human

Mode of infection: طريقة انتقال العدوى

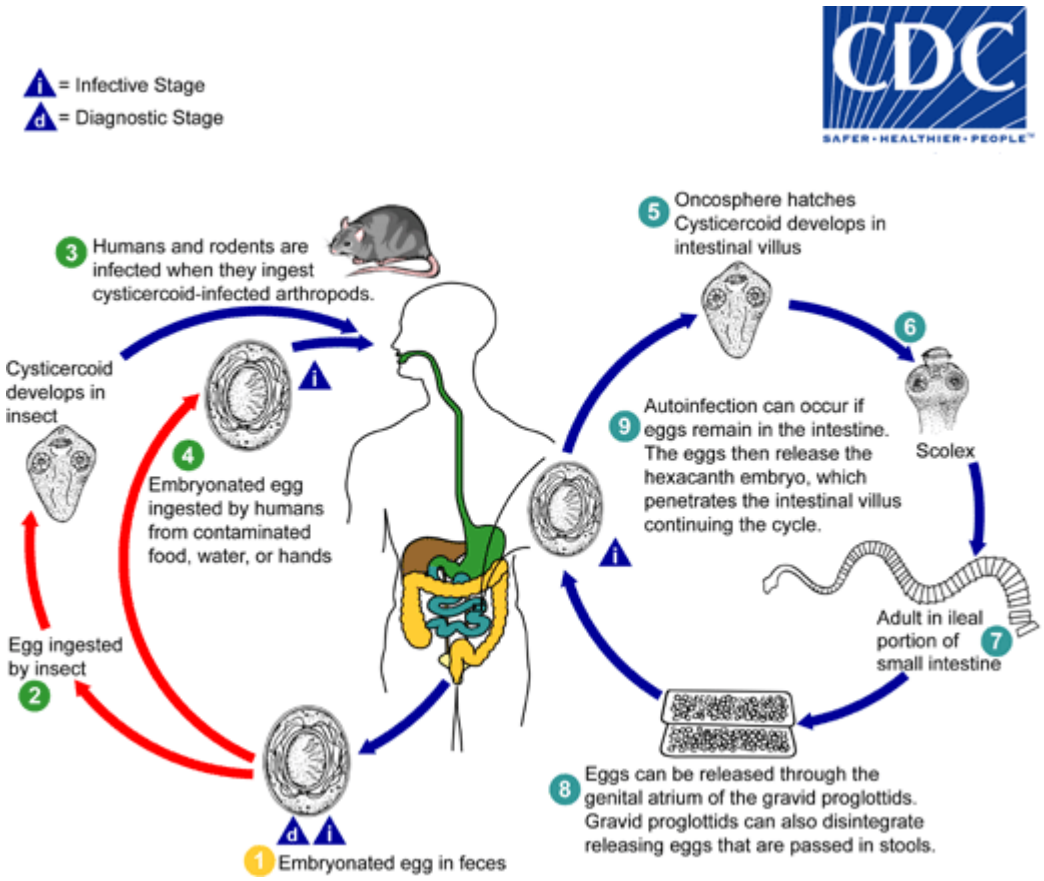
1. Ingestion of egg with contaminated raw vegetables الخضروات النيئة .

2. Direct infection from a patient to patient. مباشر من الشخص المريض

3. Auto infection الإصابة الذاتية : the eggs of *H. nana* are infective as soon as they are passed with feces by the patient. البضة تصبح معدية بعد خروجها مع البراز مباشرة وقد ترجع لتصيب نفس الشخص

Morphology: Adult worm measures 1-3 cm in length. It is made up of head (scolex) رئس, neck عنق and segmented body جسم الدودة . The head carries four

suckers and a rostellum armed with one row of hooks صف واحد من الأشواك . The segments of the body قطع جسم الدودة are divided into mature القطعة الناضجة and gravid segments القطع الحبلى. 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 أشواك ذات ستة أجنة within a rigid membrane جدار صلب (the embryosphere). This embryosphere has two polar thickening or knobs حليمات from which project 4-8 long, thin filaments called polar filaments تدعى اسواط طويلة نحيفة الأسواط القطبية.



Life cycle of *Hymenolepis Nana*

Pathogenicity: Light infections produce no symptoms الأصابات الخفيفة بدون اعراض. In fairly heavy infections الأصابة بأعداد كبيرة جدا, children may show lack of appetite فقدان الشهية, abdominal pain الآم في منطقة البطن and diarrhea اسهال.

Life Cycle: The lifecycle of *H. nana* does not require an intermediate host لاتحتاج الى مضيف وسطي, complete development occurring within the villi الزغابات 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. **Laboratory diagnosis**: Diagnosis is based on recovery and identification of the characteristic ova in feces التحري عن البيضة في البراز . Adult worms and proglottids are rarely seen in stool samples الدودة البالغة من النادر رؤيتها في براز الشخص المصاب.

Lecture Twenty; Nematodes (Round Worms)

Nematodes (Round Worms)

Ascaris lumbricoides

Disease: ascariasis Habitat: small intestine

Common name: roundworms infective stage: fertilize egg which contain larvae

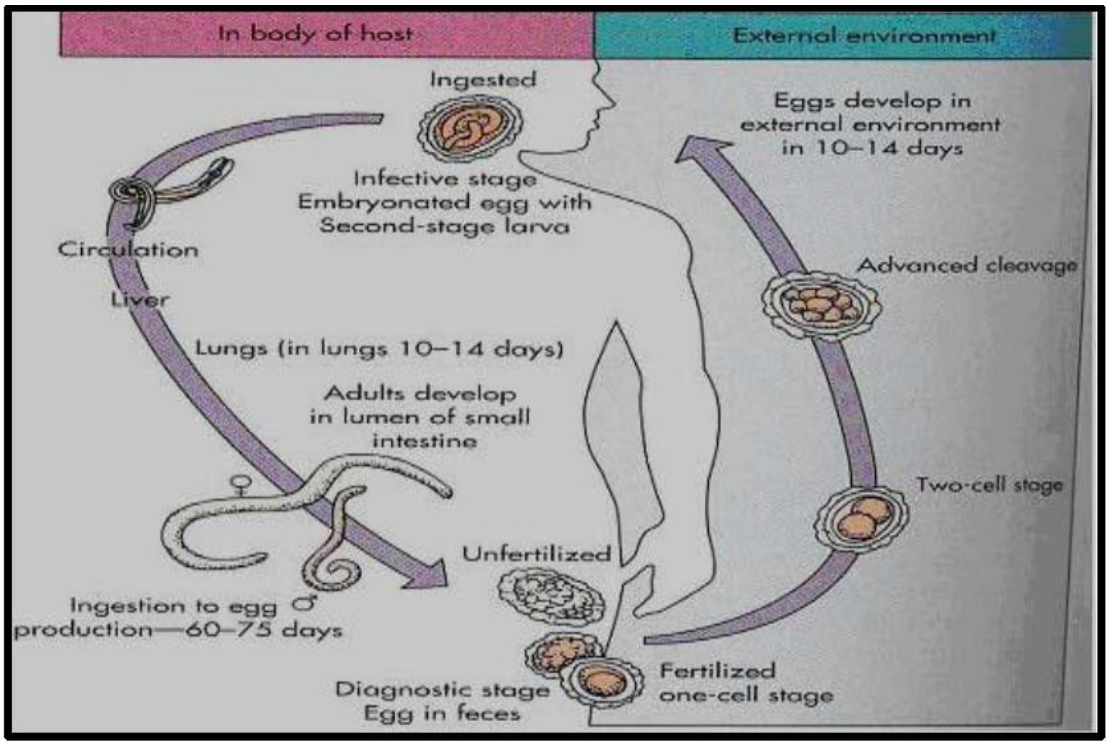
Final host: man and not required to intermediate host

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.



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 sputu

Lecture Twenty One; Schistosomes

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. This condition is important for transportation.

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

Morphology of Schistosomes: the Schistosomes are long and cylenderical 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 urinary bladder (S. haematobium). The eggs pass into the lumens and organs and are evacuated in the feces (S. mansoni) 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.

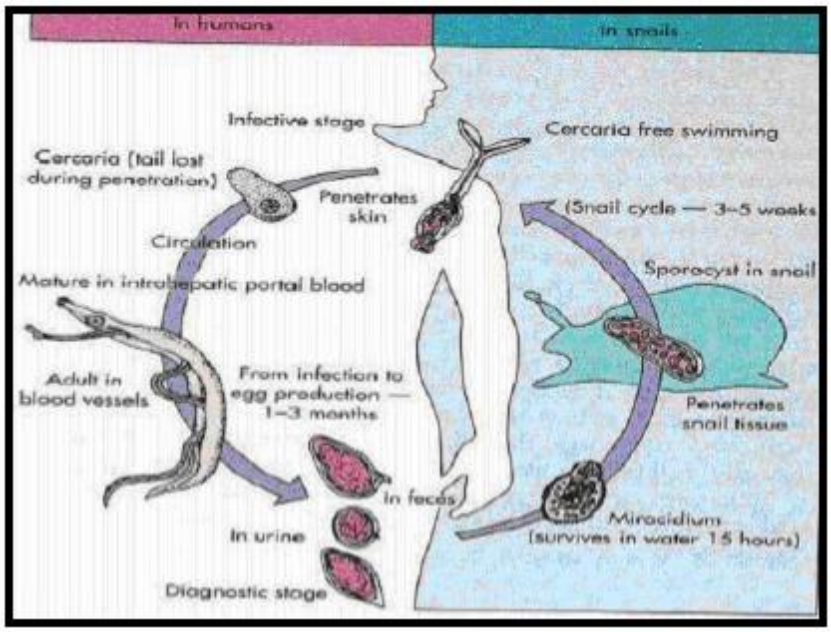
Within the intrahepatic portion of the portal system, the worms feed and grow to maturity.

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. 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.

S. haematobium causes squamous cell carcinoma in the bladder.

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:

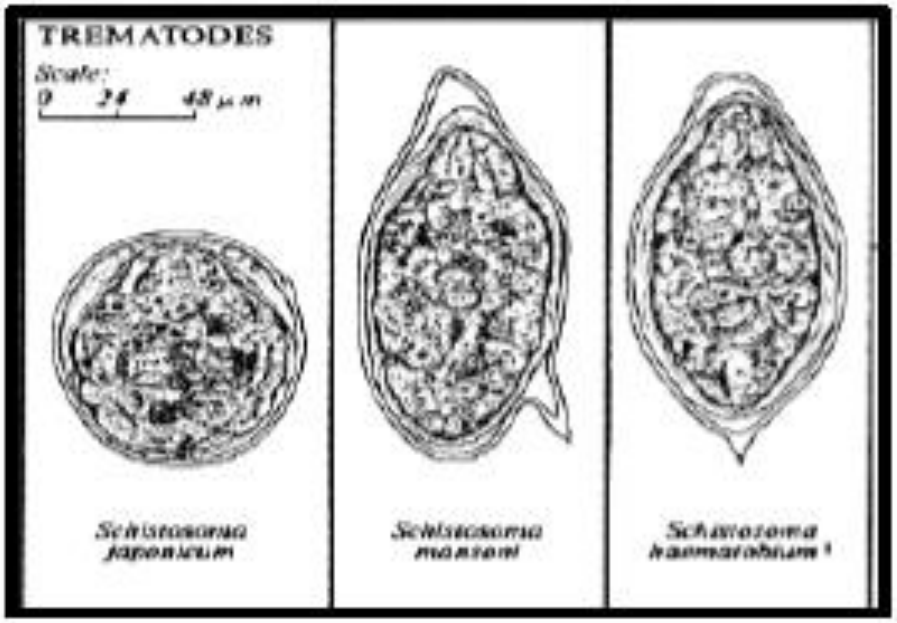
***S. mansoni*:** ♦ Microscopic examination of the stool for eggs after concentration by sedimentation

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.



Lecture Twenty Two; Immune system, organs of immune systems

Immune system

The term immunity comes from the Latin word immunitas, means protection from legal prosecution. **Immunity refers to protection from disease and other pathogens.** The cells and molecules responsible for immunity are called **immune system** and their efforts in regards to any etiological agent are called **immune responses**. Normally the immune responses are elicited against the foreign substances but occasionally to the self molecules and are referred as autoimmune responses. **Immunology is a branch of life-science which deals with the cellular and molecular events occurring in the body after encounters of micro-organisms and other foreign substances**.

The history of immunology is quite old. In ancient China, people often used skin lesions of patients recovered from small pox to cure small pox in young children. The first successful record of vaccination came from the work of **Edward Jenner's** efficacious vaccination against smallpox. Jenner observed that milkmaid who had recovered from cowpox never showed any symptom of smallpox. Following this observation he inoculated the cowpox pustules into the arm of a young boy who later did not show full progressive smallpox symptoms. Small pox

was the first disease that was eradicated worldwide by vaccination. Recently the science of immunology has grown up by the advent of new molecular biology tools. Advances such as recombinant DNA technology, immunohistochemistry, monoclonal antibody production and x-ray crystallography have changed the immunology to a broader area.

Immune system

Immune **system is the system of specialized cells and organs that protects an organism from any attack or invasion by any foreign body**. Immune system is made up of a complex and vital network of cells and organs. All these organs are called **lymphoid organs** because they are concerned with the growth, development, and deployment of lymphocytes. Thus, immune system is also sometimes called the **lymphoid system** and the tissues associated are called **lymphoid organs.** Depending upon the function, these can be of two types: primary lymphoid organs and secondary lymphoid organs. **The Primary lymphoid organs** include thymus and bone marrow, where maturation of lymphocytes takes place, whereas **secondary lymphoid organs** include lymph nodes, spleen, and various mucosal associated lymphoid tissues (MALT), which trap antigen and provide sites for interaction between mature lymphocytes and antigen.

The blood vessels and lymphatic vessels are important parts of the lymphoid system as they interconnect the organs of the immune system and carry the lymphocytes to and from the different areas in the body causing systemic immunity. On the other hand mucosal associated lymphoid tissues give mucosal immunity.

Innate and adaptive immunity

Defence against microbes includes an early response action called **innate immunity** and a later response called as **adaptive immunity.**

Innate immunity is also called **natural or native** immunity and provides first line of defense against any microbial infection in human body. It usually involves many cellular and biochemical events that react to microbes and their products in order to clear them from the body. The main.

Components of innate immune system are

1- Barriers – skin and outer epithelial surface.

2- Scavenger cells – neutrophils, macrophages, dendritic cell and natural killer cells.

3- Complement system

4- Cytokines

5- Chemical mediators of inflammation

Microbial agents and pathogens contain some molecules over their surface that act as foreign substance for the body and are collectively called as **pathogen associated molecular pattern** (PAMP). PAMP's are recognized by specific proteins and biochemical molecules produced by cells of innate immunity and these recognition molecules are called as **pattern recognition receptors**. The innate immune responses are produced against the specific structures present over the microbes and are common to many of them. Thus, they cannot distinguish the minute differences among microbes.

In contrast, adaptive immunity is stimulated by constant exposure of infectious agents. The most characteristic feature of adaptive immunity is **memory** against the repetitive exposure of same pathogen. Furthermore, it has a capacity to distinguish between fine differences among microbes and hence also called as **specific immunity**. As specific immunity is gathered by constant exposure to the foreign agent, it is better termed as **acquired immunity**.

The central components of adaptive immunity are

1- Lymphocytes and their secreted products e.g. **antibodies**

2- Foreign substances that trigger specific immune responses and are identified by lymphocytes or antibodies are called as **antigens**.

Almost all the higher organisms have well developed mechanisms for defending against the microorganisms. Innate and adaptive system work together as they are

the components of host integrated system. However there are many microbes that have developed and adapted to resist the innate immunity and hence more robust mechanisms are required for their expulsion. Innate and adaptive immune systems are interlinked; stimulation of anyone against the foreign substances instigates the other and hence functions cooperatively.

The mechanism of innate immunity provides an initial defense against the infection. Adaptive immune responses develop later and consist of lymphocytes.

Cells of the immune system Cells of the immune system are present as circulating cells in the blood and lymph. They are distributed to almost every organ and tissue of the animal body.

1- Macrophages and Phagocytes- They are present in virtually every tissue and organ of the body and respond instantaneously to the entering pathogens.

The major function of macrophage are

a- Ingest and kill the microbes.

b- Ingest and clear dead cells and unused cells.

c- They secrete cytokines upon activation.

d- They serve as antigen presenting cells to display the antigens to the T lymphocyte.

e- They also help in angiogenesis (formation of blood vessels).

2- Neutrophils- These are the granulocytes present in the blood stream and are the first line of the defense in the body. They are the most abundant cells present in the blood stream. They are about 12-15 μm in diameter with projection on their surface

3- Mononuclear phagocytes- They play a central role in the innate and adaptive immune system. They are formed by precursor hematopoietic cells and are called monocytes. Once enter into the circulation they are called macrophages.

4- Mast cells- These are derived from bone marrow cells and contain histamine and other chemical mediators of allergic diseases. Mast cells express the receptors for IgE and IgG antibodies. They also provides defense against helminth infection.

5- Basophils- They are structurally and functionally similar to mast cells and mediate allergic conditions. The granules of basophils contain acidic proteins which bind to basic dyes (hematoxylin)

6- Eosinophils- They are granulocytes present in the blood and contains the enzyme required to damage the cell wall of the parasite. The granules of the eosinophils contain the basic proteins which bind to acidic dye (eosin).

7- Dendritic cells- They are the specialized antigen presenting cells which captures the microbes and microbial antigens, and transport them to lymphoid

tissues to be recognized by lymphocytes. They activate the naive T cells and form a bridge between innate and adaptive immune response. They are widely distributed into many organs and epithelial surface. Plasmacytoid dendritic cells are the subpopulation of dendritic cells involved in the recognition of the virus infected cells.

8- Naïve lymphocytes- The lymphocytes that are not previously encountered with antigens are called as Naïve lymphocytes. They trigger the adaptive immune response after encountering with the antigen.

9- Lymphocytes- These are the cells of the adaptive immune system. There are two subsets of the lymphocytes.

a- B lymphocyte- Involved in the production of the antibodies (bursa of Fabricius derived lymphocyte). The two major subsets of the B lymphocytes are follicular B cells and marginal B cells.

b- T lymphocyte- Involved in the production of cellular immune response.

Organs of immune system

Immune organs divided to the central or **primary organs include Bone**

marrow and **thymus, where the** B and T lymphocytes produce respectively. And **peripheral** or **secondary** lymphoid organs such as **spleen** and **lymph node where the** B and T lymphocytes are complete its functional maturation.

1- Bone marrow

Bone marrow is the major site for the generation of circulating RBC, granulocyte, monocytes and B cells. All the cells are formed in the bone marrow by the process of **hematopoiesis** by hematopoietic stem cells (HSC) during fetal stage. Majority of the B cell maturation takes place in the bone marrow, but the final maturation completes in the secondary lymphoid organs (spleen). T cell maturation occurs entirely in the thymus while NK cell maturation occurs entirely in the bone marrow.

2- Thymus

The thymus gland is the site for the maturation of T lymphocytes. It is situated in the anterior side of mediastinum and bilobed in shape. The thymus is divided into outer cortex which is densely filled with T lymphocyte and inner medulla which are sparse in lymphocyte population. Interleukin- 7, secreted by the cortical cells is responsible for the development of T lymphocytes.

3- spleen

Spleen is also called as grave yard of red blood cells. It is made up of **red pulp**

which is full of blood cells and **white pulp** rich in lymphocyte. The white pulp helps to stimulate adaptive immune response against blood borne antigens. The white pulp area is divided into T cell and B cell zone. The T cell zone is also the resident area for mature dendritic cells which activates the naïve T cells upon antigen stimulation. Follicular dendritic cells reside in the B cell zone and activate the humoral immune response.

4- **lymph node**

5- are the organs that carry the lymph and help in the activation of adaptive immune response. The segregation of B and T lymphocyte depends on the cytokines secreted by the lymph node.

6- **Other lymphoid tissues** Skin, gastrointestinal mucosa, and respiratory epithelium mucosa have their own lymph nodes. The lymphoid tissues associated with the gastrointestinal tract are called **gut associated lymphoid tissues** (GALT) while bronchial mucosa associated lymphatic tissues are called **mucosa associated lymphoid tissues** (MALT).

Lecture Twenty Three; Antigen and Antibody

ANTIGENS

Antigens are any substances that are capable, under appropriate conditions, of inducing the formation of antibodies and reacting specifically with the antibodies so produced.

S.N.	Antigen	Antibody
1	Generally proteins but can be lipids, carbohydrates or nucleic acids.	Antibodies are proteins.
2	Triggers the formation of antibodies.	Variable sites has the antigen binding domain.
3	There are three basic kinds of antigens. (Exogenous, Endogenous and Autoantigens)	There are five basic kinds of antibodies. (Immunoglobulins M, G, E, D and A)
4	The region of the antigen that interacts with the antibodies is called epitopes.	The variable region of the antibody that specially binds to an epitope is called paratope.
5	Cause disease or allergic reactions.	Protects the body by immobilization or lysis of antigenic material.

They react with both T-cell recognition receptors and with antibodies. These antigenic molecules may have several antigenic determinants, called epitopes, and

each epitope can bind with a specifi c antibody. Thus, a single antigen can bind to many different antibodies with different binding sites

Some low-molecular-weight molecules called haptens are unable to evoke an immune response but can react with existing antibodies. These molecules need to be coupled to a carrier molecule to be antigenic. For some molecules such as drugs, the molecule needs to be conjugated to a carrier. The carrier may be a host protein. The tertiary structure of the molecule as well as the amino acid sequence is important in determining antigenicity. Certain structures such as lipids and DNA are generally poor antigens.

Most antigens are either thymus dependent or thymus-independent antigens. Thymus-dependent antigens require T-cell participation: Most proteins and foreign red cells are examples of these molecules. Thymus-independent antigens do not require T-cell participation for antibody production. Instead, they directly stimulate specifi c B lymphocytes by cross linking antigen receptors on the surface of B cells. These molecules produce primarily

IgM and IgG2 antibodies and do not stimulate long-lasting memory cells. Most bacterial polysaccharides (found in bacterial cell walls) fall into this category. Certain polysaccharides, such as LPS (lipopolysaccharide), not only induce specifi c B-cell activation but also can act as a polyclonal B-cell stimulant.

Antibody

Antibodies, also called immunoglobulins, Y-shaped molecules are proteins manufactured by the body that help fight against foreign substances called antigens. Antigens are any substance that stimulates the immune system to produce antibodies. Antigens can be bacteria, viruses, or fungi that cause infection and disease. Following are some of the differences between Antigen and Antibody:

The basic structure of the antibody molecule is consists of a four-chain structure divided into two identical heavy (H) chains with a molecular weight of 25 kDa. Each chain is composed of domains of 110 amino acids and is connected in a loop by a disulfide bond between two cysteine residues in the chain. The amino acid N-terminal domains of the heavy and light chains include the antigen-binding site. The amino acids of these variable domains vary between different antibody molecules and are thus known as the variable (V) regions. Most of these differences reside in the hyper variable areas of the molecule and are usually only six to ten amino acid residues in length. When the hypervariable regions in each chain come together along with the counterparts on the other pair of H and L chains, they form the antigen-binding site. This part of the molecule is unique to the molecule and is known as the idiotype determinant. In any individual, 106 to 107 different antibody molecules can be composed from 103 different heavy and light chains of the variable regions. The part of the molecule next to the V region is

called the constant (C) region made up of one domain in the light chain (C1) and three or four in a heavy chain (CH). A Cl chain may consist of either

two kappa (κ) or two lambda (λ) chains but never one of each. Of all the human antibody molecules, approximately 60%, are κ chains and 40% contain λ chains. Although there are no known differences in the functional properties of κ and λ chains, there are several different types of the CH domain. These differences are refl ected in determining the class (isotype) of the antibody and thereby the physiological function of a particular antibody molecule

Lecture twenty four; Antibody and Antigen Reactions

Antibody and Antigen Reactions

Basic characteristics of antigen-antibody reactions are Immunoagglutination and Immunoprecipitation

The antigen-antibody reactions are reactions between specific antigens and matching antibodies that occur in a laboratory under controlled conditions (*in vitro*). These reactions form the basis of immunological tests **or immunoassays** used for determining the presence of a variety of antigens or antibodies in samples.

ANTIBODY - The molecule present in serum and other body fluids which mediates humoral immunity, and which can bind specifically to an antigen. Serum which contains antibodies (directed against one or more antigens) is termed an antiserum.

ANTIGEN - A molecule which can be specifically bound by an antibody (typically a protein or carbohydrate recognized as "foreign").

Since antibodies can bind with high specificity many different antigens, such as structural molecules of microbes and their secreted products or products of

immune and other cells (e.g. cytokines, hormones, etc.), these methods have a wide range of application in laboratory diagnostics in different fields of medicine (biochemistry, immunology, microbiology, endocrinology, hematology, etc.), as well as in research.

Antigen-antibody reactions are sometimes referred to as serological reactions, based on the fact that serum is commonly used sample in these reactions.

Antigen-antibody reactions can be seen as if they were equations with one unknown variable. In other words, based on the known variable (antigen or antibody) and the final result of the reaction (presence or absence of antigen-antibody complex

Anti-immunoglobulin antibodies are sometimes also referred to as the secondary antibodies, considering the fact that the antibodies that bind directly to an antigen are, so called, primary antibodies. also allow determining their class, which can help in diagnosis of many diseases.

In general, there are two ways how the immune complexes may be detected in these tests:

1- Antigens and antibodies, under some conditions, tend to to form large complexes that can be detected by bare eye or using photometers (The extent of complex formation depends on the antigen characteristics

2- It is also possible to label one of the reagents, usually antibodies, with an appropriate marker (e.g. fluorescent dye), that can be detected upon completion of reaction (regardless of the size of the formed complex) by bare eye or using a specific equipment.

In some cases (e.g. when a deficiency of humoral immunity is suspected), it is necessary to measure the total amount of particular class of immunoglobulins in a serum of a patient (IgG, IgM or others), irrelevant of their specificity, and this amount is expressed as a concentration **Immunoagglutination**

Immunoagglutination (often simply called agglutination) is a laboratory diagnostic test based on the reaction between a particular antigen and the matching specific antibody, wherein the antigen is insoluble, or represent an integral part of a large insoluble particle (e.g. red blood cells, bacteria or inert particles). In this reaction, a large number of antibody and antigen molecules cross-link (agglomerate) in a big branched immune complexes and, as a result, aggregate called agglutinate is formed that can be detected by the naked eye (or optionally with the magnifying glass). Hemagglutination is a specific form of agglutination that involves red blood cells. All antibody isotypes can agglutinate antigens, but IgM antibodies have the most prominent capacity for agglutination, since they are pentamers and have 10 binding sites for antigen. In addition to the class of antibody, the effectiveness of agglutination is influenced by the amount of antigen and antibodies in the reaction.

Optimal agglutinate formation occurs when the amounts of antigen and antibody are approximately equal (so called zone of equivalence). If either the antigen or the antibody is in excess, they will react, but very small complexes will form that do not clump to form visible agglutination resulting in false negative result. The lack of agglutination at high concentrations of antibodies is traditionally called prozone effect (or prozone phenomenon). This problem can be solved by diluting the tested sample, which reduces the amount of antibodies, so that the equivalence between the antigen and the antibody can be achieved.

Immunoagglutination can be direct or indirect (indirect is sometimes termed passive). In direct immunoagglutination, the antigen (antigenic determinant) is an integral part of a large particle (e.g. bacterial surface molecule) that is directly agglutinated by antibodies, while in indirect immunoagglutination the antigen is a soluble molecule passively adsorbed or chemically attached to the surface of a large insoluble particle (erythrocytes, polystyrene inert particles or latex microbeads) that becomes passive carrier of this antigen.

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One of the most important applications of direct immunoagglutination is in determination of blood types. In addition, immunoagglutination (both direct and indirect) has been used in microbiology for the diagnosis of many infectious

diseases, on the basis of detection of specific antibodies or antigens in the patient's samples (e.g. serum or cerebrospinal fluid). Indirect immunoagglutination is also used for detection of various autoantibodies that may occur in many autoimmune diseases.

A Coombs test (or antiglobulin test) is a special form of immunoagglutination used for the detection of anti-erythrocyte antibodies **Immunoprecipitation**

Immunoprecipitation (also called precipitin reaction or precipitin test) is a laboratory diagnostic test based on the precipitation (deposition) of the soluble antigen by the matching specific antibody (often called precipitin) due to the formation of large insoluble immune complexes. The result of the reaction is a precipitate, which can be easily detected (usually with the bare eye) and its formation only occurs when optimal concentration ratio of antigen and antibody (approximately equal amounts) is achieved (the zone of equivalence). In the case of antigen or the antibody excess, the reaction between them will occur but the small soluble complexes form (so called microprecipitates) that remain in the solution. Although invisible for naked eye, these complexes can still be detected using the appropriate device, such as nephelometer (see below).

Lecture twenty five; Hypersinsitivity

Hypersensitivity Reactions

Introduction

Under some circumstances, immunity, rather than providing protection,

produces damaging and sometimes fatal results. Such harmful reactions are known collectively as Hypersensitivity or allergic reactions.

Hypersensitivity reactions differ from protective immunity only in that they are exaggerated or inappropriate and damaging to the host. The cellular and molecular mechanisms of the two types of reaction are virtually identical. Hypersensitivity reactions are of four classes, designated type I, II, III and 1V,

	Type I	**Type II**	**Type III**	**Type IV**	
Immune reactant	IgE, TH2 cells	IgG	IgG	T cells	
Antigen	Soluble antigen	Cell surface antigen	Soluble antigen	Soluble antigen	Cell associated antigen
Effector mechanism	Mast-cell activation	Complement FcR cells (phagocytes, NK cells	Complement Phagocytes	Macrophage activation	Cytotoxicity
Example	Allergic, rhinitis, asthma, systemic anaphylaxis	Some drug allergies (e.g. penicillin) transfusion reaction	Serum, sickness Systemic lupus erythematosus	dermatitis, graft rejection, rheumatoid arthritis	Contact dermatitis graft rejection diabetes mellitus

Type I: Immediate or anaphylactic reaction

Allergens are antigens that induce IgE mediated reactions in susceptible individuals who also referred to as atopic individuals, while atopy "i.e., uncommon" is frequently used to referred to conditions which manifest type I hypersensitivity such as bronchial asthma and eczema.

Mechanism

All normal individuals can make IgE antibody specific for a variety of

antigens but only few of them develops clinical symptoms.

Why some individuals develop allergy?

We do not yet understand what causes some individuals to become allergic to a substance while others do not. Some of the important factors include:

1- The MHC genotype plays a role in determining susceptibility to allergy,

2- Differences in mucosal permeability may restrict the effect of allergens

lodging on the mucosal surface,

3- Allergic sensitization in a susceptible individual may result from failure of IgE Control mechanisms.

Immune therapy

Allergists use carefully controlled and repeated exposure to the allergen to desensitize the patients, which is believed to gradually divert the response to one dominated by production of IgG and IgA antibodies specific for the allergen.

Type II: Cytolytic or Cytotoxic Reactions

Mechanism

Binding of the specific Ab directly to an antigen on the surface of a cell

produces damage to that cell through **two major pathways**. **In the first pathway,** antibody (usually IgM, but also IgG) activates the entire complete complement sequence and eventual lysis of the cell. In the **second pathway (usually IgG**) serve to engage receptors on phagocytic cells for Fc and C3b. These lead to phagocytosis and destruction of the cell by macrophages and neutrophils.

Examples of diseases caused by type II hypersensitivity

1- **Transfusion reactions:**

The simplest form of cytotoxic reactions is seen after transfusion of ABO

incompatible blood.

2- **Rh incompatibility reactions:**

Antibodies against Rh antigens can be damaging to new-born babies. In brief, a Rhesus negative (Rh-) mother may be immunized by the transplacental passage of red cells from the baby and may make antibodies against Rh+ cells of her (usually first) baby who has inherited the Rh antigen (or factor) from his father. Any subsequent Rh+ babies she might have may be damaged by these antibodies which can cross the placenta, bind to the baby's erythrocytes, activate complement and lyse the cells causing anemia.

Fortunately, this hemolytic disease of the new-born is now understood, and is controllable and can be largely avoided by preventing sensitization of the mother in the first place. This is done by a process known as passive immunization.

3- Autoimmune reaction:

As a consequence of certain infectious diseases or for other, still unknown reactions, some people produce Ab against their own red cells. This antibody, on binding to the red cells, destroy them by lysis or phagocytosis via receptors for Fc and C3b. This may lead to progress anemia.

Type III: Immune Complex Reactions

Mechanism

Immune complexes are generated in every antibody response. The

pathogenic potential of immune complexes is determined in part by their size. Walls of certain tissue sites, and it is here that they cause tissue damage or immunocomplex disease. Immune complexes can activate platelets and basophils via Fc receptors to release vasoactive amines which cause endothelial cell retraction and increased vascular permeability leading to complex deposition,

Examples of type III hypersensitivity reactions

1- Arthus reaction:

It is a skin reaction seen as an area of redness and swelling which is maximal 6 hours after intradermal injection of antigen. It is caused by IgG When a sensitized individual has IgG antibodies directed against an antigen immune complexes can be generated locally by injection of the antigen into the skin, IgG antibody that has diffused into the tissues forms immune complexes locally.

2- Infection associated immune complex disease:

In a number of infectious diseases such as malaria, leprosy, viral hepatitis and bacterial endocarditis, there may be times during the course of the infection when large amounts of antigen and antibodies exist simultaneously and cause

the formation of immune aggregates that are deposited in various locations. Thus some of the symptoms of these diseases may include a component

Type IV: Cell Mediated Hypersensitivity Reactions

Nomenclature

The nomenclature of this type of hypersensitivity response has varied over the years, according to historic usage. Originally the response was termed the tuberculin reaction. Subsequently, the delayed nature of the onset of these responses, has led to their collective designation as delayed-type hypersensitivity (DTH) reactions. With the discovery that all these reactions are mediated by T cells, they are now classified as T cell-mediated or simply cellmediated immunity.

Lecture Twenty Six; Autoimmunity and Autoimmune Diseases

Autoimmunity and Autoimmune Diseases

Normally the function of immune system in our body is to recognize foreign elements and to destroy these before they could harm us either by humoral immune response (specific antibody formation) or cell mediated immune response by activation and clonal expansion of T cells.

Thus the immune system defends the body against infections and certain other diseases by identifying, attacking, and destroying germs and other foreign substances. **Sometimes the immune system makes a mistake and starts attacking the body's own tissues or organs. This is called autoimmunity.** There are many autoimmune diseases one example being type 1 diabetes in which the Islets cells (produce Insulin) in the pancreas are destroyed by the immune system.

An autoimmune disease is a case of mistaken identity; it is an abnormal condition in which the body reacts against constituents of its own tissues. The result may be simple hypersensitivity reaction and or autoimmune disease when the body begins attacking its own healthy tissues. About 5 % to 7 % of adults suffer from autoimmune diseases and two thirds of these are females. Somehow left handed people are more prone the reason for this is not known.

This failure to differentiate between self and non self may result due to some extraneous environmental factors like some viral infections and exposure to some mutagenic agents; can be due to the breakdown and failure of immune regulation and due to some aberration in the genes. Whatever the reason the result is autoimmune disease which may involve a particular organ when it is called an organ specific disease (e.g. Addison's disease involving Adrenal

Example of Autoimmunity there is an immune response to one's own tissue antigens. This type of body response results in a disease state characterized by a specific antibody or cell-mediated immune response against the body's own tissues (autoantigens). **So, we can say that autoimmunity is the breakdown of mechanisms responsible for self tolerance and induction of an immune response against components of self.**

The immunological mechanism of the body is dependent on two major factors:

1- the inactivation and rejection of foreign substances and
2- the ability to differentiate between the body's own antigens ('self') and foreign ('non self').

It is not yet known exactly what causes the body to fail to recognize self proteins as its own and to react to them as if they were foreign resulting in autoimmunity

and may be autoimmune diseases. Prominent examples include celiac disease, diabetes mellitus type 1 (IDDM), sarcoidosis, systemic lupus erythematosus and **many others.**

The autoimmune diseases can be divided into systemic, localized and haemolytic disorders, depending on tissue/cells affected and the clinico-pathologic features

1- **Systemic autoimmune diseases:-** These diseases are associated with auto antibodies to antigens which are not tissue specific. One example can be polymyositis, Another example is rheumatoid arthritis (RA).

Rheumatoid arthritis

– Systemic lupus erythematosus (SLE)

– Scleroderma

– Primary Sjogrens's syndrome

– polymyositis

2- Organ specific or localized autoimmune diseases:- As the name indicates in these cases the autoimmunity involves a particular

organ. One best studied organ **is thyroid and e**xamples are

1- H**ashimoto's** disease which affects thyroid gland causing lymphadenoid goitre and the other is

2- **Graves** disease causing thyrotoxicosis. Anti thyroglobulin antibodies are produced in both these cases and these can be shown in sera of the patients by various tests. However, **the pathology in the two is different and so are the resulting symptoms.**

In Hashimoto' goitre there is hypothyroidism and in Graves disease there is hyperthyroidism. Another example is Addison's disease in which the adrenal glands are affected. There is lymphocytic infiltration of the adrenal glands and production of antibodies directed against zona glomerulosa.

3- Other diseases

include autoimmune disease of eyes, brain, skin and many others.

In organ specific autoimmune diseases the implicated antigens and the autoimmunity are restricted to specific organs in the body

4- Haemolytic autoimmune diseases:

Auto antibodies are formed against RBCs leading to autoimmune haemolytic anaemia; auto antibodies may form against platelets resulting in autoimmune thrombocytopaenia; and formation of anti leucocyte antibodies resulting in autoimmune leucopaenia and so on.

CAUSES OF AUTOIMMUNE DISEASES

To understand why normally immune response does not occur against our own tissue antigens. This is due to "Tolerance to self antigens" which is acquired by various mechanisms. Failure in immune recognition of self and injury of self tissues (autoimmunity) results from a loss of self tolerance.

Mechanisms of self tolerance

One mechanism is that the clones of lymphocytes which act against self antigens are deleted. This is the "clonal deletion" theory. Clonal deletion is mediated by ubiquitous self antigens. The second is inactivation of developing lymphocytes so our immune system becomes self tolerant, no activation of immunity against self antigens as specific lymphocytes are either deleted or inactivated. Clonal inactivation can be mediated by tissue-specific antigens.

Mechanisms of breakdown of self tolerance resulting in autoimmunity:

There may be loss of "Self Tolerance" germinal centers due to some genetic aberration or some environmental factors.

MHC (Major Histocompatibility complex) molecules normally should present the peptide (antigen) at optimal level to T cells for immune response to occur.

Gene mutation/s leads to one or more autoimmune diseases.

Autoimmune diseases are associated with particular MHC genotypes. Sometimes there may be more than one gene involved and the result is complex autoimmune diseases.

Environmental factors which can cause breakdown of self tolerance include pathogens (bacterial, viral and others), drugs, hormones, and toxins.

These are just a few ways that can cause autoimmunity.

1- Drugs
2- Drug induced lupus
3- Toxins
4- Example: Toxic Oil Syndrome
5- Hormones
6- Example: Endometriosis and preeclampsia are both thought to be autoimmune in nature