* Brief anatomy & Physiology
* Defense mechanisms
* Diseases & Pathogens & symptoms.

* ... tonsil
- located laterally in oropharynx
* lingual tonsil
- located at the base of tongue.

MB 331 (I)

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Functional perspective

1. Respiratory system

a. Conducting zone b. Respiratory zone

The respiratory system is divided into two parts: the upper respiratory system and the lower respiratory system.

The upper respiratory system consists of the nose, the pharynx (throat), and structures associated with them, including the middle ear and the auditory (eustachian) tubes. Ducts from the sinuses, and nasolacrimal ducts from the lacrimal (tear forming) apparatus, empty into the nasal cavity. The auditory tubes from the middles ear empty into the upper portion of the throat.

Defense mechanisms: The upper respiratory system has several defenses against airborne pathogens. **Coarse hairs** in the nose filter large dust particles from the air. The nose is lined with a **mucous membrane** that contains numerous mucous secreting cells and **cilia**. The upper portion of the throat also contains a ciliated mucous membrane. The **mucous** moistens inhaled air and traps dust and microorganisms, especially particles larger than 4 to 5 μm. The cilia help remove these particles by moving them toward the mouth for elimination.

Pharyngeal tonsils

At the junction of the nose and the throat are masses of **lymphoid tissue**, the **tonsils** and **adenoids**, which contribute immunity to certain infections. Occasionally however, these tissues become infected and help spread infections to the ears via the auditory tubes. Because the nose and the throat are connected to the sinuses, naso-lacrimal apparatus, and middles ear, infections spread from one region to another.

The lower respiratory system consists of the larynx (voice box), trachea (wind pipe), bronchial tubes, and the alveoli as sacs that make up the lung tissue; within them, oxygen and carbon dioxide are exchanged between the lungs and blood. Our lungs contain more than 300 million alveoli, with an absorptive area of about 90 square meters. The double- layered membrane covering the lungs in the pleura. A ciliated mucous membrane lines the lower respiratory system down to the smaller bronchial tubes and helps prevent microorganisms from reaching the lungs.

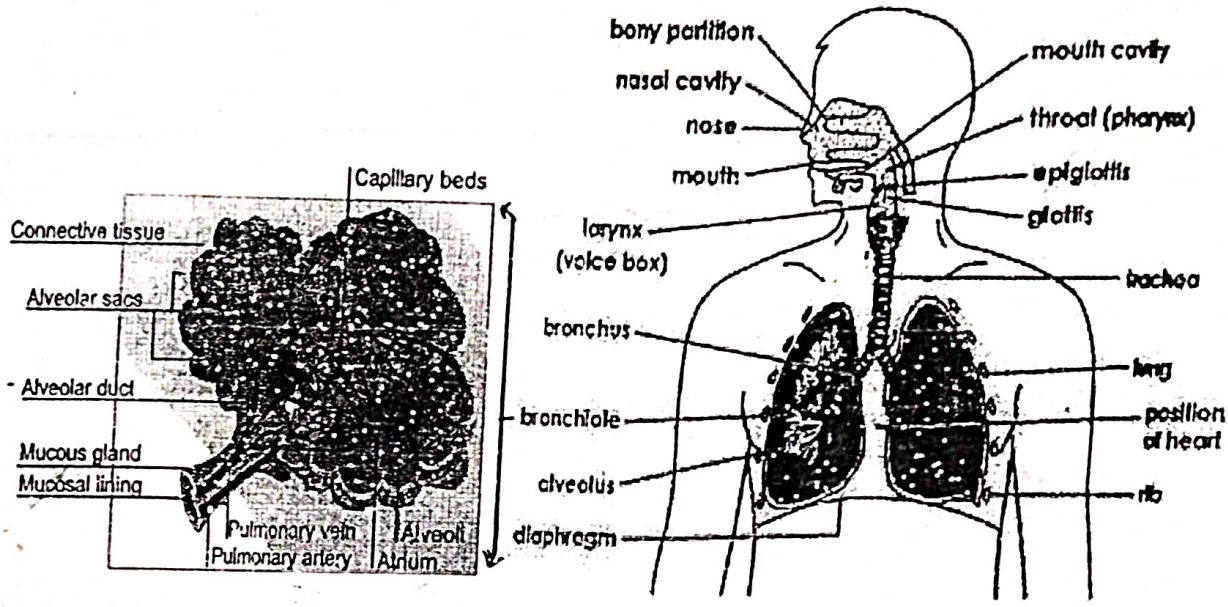
Particles trapped in the larynx, trachea, and larger bronchial tubes are moved by up toward the throat by ciliary action called the **ciliatory escalator.** If microorganisms naturally reach the lungs, phagocytic cells called alveolar macrophages usually locate, ingest, and destroy most of them. IgA antibodies in such secretions as respiratory mucous, saliva and tears also help protect mucosal surfaces of the respiratory system from many pathogens. Thus, the body has several mechanisms for removing the pathogens that cause air-borne infections.

A number of potentially pathogenic microorganisms are part of the normal microbiota in the upper respiratory system. However, they usually do not cause illness because the predominant microorganisms of the **normal microbiota** suppress their growth by competing with them for nutrients and producing inhibitory substances.

By contrast, the lower respiratory tract is nearly sterile – although, the trachea may contain a very few bacteria because of the normally efficient functioning of the ciliatory escalator in the bronchial tubes.

~~Fig: Structure of Respiratory system~~

Fig: Structure of Respiratory system:



Common diseases/microbial pathogens and symptoms:

The respiratory system is the site of many common infections, some of them mentioned here:

(1) **Pharyngitis:** It is common inflammation of mucous membrane (2) of throat, or **sore throat**. When the larynx is the site of infection, the condition called **laryngitis**, which affects our ability to speak. It is caused by *Streptococccus pneunoniae* or *S. pyogenes* or viruses often in combination. Streptococcal pharyngitis is (Strept throat) is characterized by local inflammation and a fever.

The microbes that cause Pharyngitis also can cause inflamed tonsil, or **tonsillitis** (lymph nodes in the neck region become enlarged and tender). (3)

(4) The nasal sinuses are cavities in certain cranial bones that open into the nasal cavity. They have a mucous membrane lining that is continuous with that of the nasal cavity. When a sinus becomes infected with organisms such as *S. pneumonia* or *Haemophilus influenzae*, the mucous membrane become inflamed, and there is a heavy nasal discharge of mucus. This condition called **sinusitis**. If the opening by which leaves the sinus becomes blocked, internal pressure can cause **pain** or a **sinus headache**.

Probably the most threatening infectious disease of the upper respiratory system is **epiglottitis** (5) inflammation of the epiglottis. Epiglottitis is a rapidly developing disease that can result in death within a few hours. It is caused by opportunistic pathogens, usually *H. influenzae* type b.

Airborne pathogens make their first contact with body's mucous membranes as they enter the upper respiratory system.

(6) **Scarlet fever** is infectious condition called when the *S. pyogenes* strains causing streptococcal Pharyngitis produces an erythrogenic (reddening) toxin. The toxin causes a **pinkish-red skin rash** (which is probably the skins hypersensitivity reaction to the circulating toxin) and a **high fever**. The **tongue** has spotted **strawberry** like appearance and then, when it loses its upper membrane, becomes very red and enlarged.

A general feeling of being unwell

7) **Diphtheria:** The disease is caused by *Corynebacterium diphtheriae*. The disease begins with a sore throat and fever, followed by general **malaise** and **swelling of neck**. Characteristic of diphtheria is a tough **grayish membrane** that forms in the throat in response to infection. It contains fibrin, dead tissue and bacterial cells and can totally block the passage of air to the lungs (**Asphyxia**). Asphyxia

8) **Otitis Media:** If is one of the complications of the common cold, or of any infection of the nose or throat infecting the **middle ear**, which leads to **earache**. The pathogens cause the formation of **pus**, which built up pressure against the eardrum and causes it to become **inflamed** and painful. The most commonly isolated pathogen is *S. pneumonia*. Others include *H. influenzae, S. pyogenes, S. aureus, Moraxella catarrhalis* and viruses also.

Asphyxia.

- **Viral diseases of upper respiratory system:**

1) **The common cold:** A number of different viruses are involved in the etiology of the common cold – includes- Rhinoviruses, Coronoviruses, and several other viruses. Symptoms of common cold include **sneezing, excessive nasal discharge,** and **congestion**. The infection can easily spread from the throat to the sinuses, the lower respiratory system, and the middle ear, leading to **complications of laryngitis** and **Otitis media**. The uncomplicated cold usually is **not** accompanied by **fever**.

Common diseases/ pathogens of lower Respiratory systems: The lower system can be infected by many of the same bacteria and viruses that infect the upper respiratory system. As the bronchi become involved, bronchitis, or bronchiolitis, develops. A sever complication of bronchitis is pneumonia, in which the pulmonary alveoli become involved.

- **Bacterial diseases of lower respiratory system:** Inflammation of mucus membrane

1) **Pertussis:** Infection by *Bordetella perussis* results in pertussis (the name pertussis is derived from the latin – per = throughly, and tussis=cough) or whooping cough. Primary a childhood disease, pertussis can be quite severe. The initial stage called the catarrhal resembles a common cold. Prolonged series of coughing characterize the paroxysmal stage, or second stage. When ciliary action is compromised, mucous accumulates, and the infected person desperately attempts to cough up these mucous accumulations. Gasping for air between coughs causes a **whooping sound**, hence the informal name of the disease. **Coughing episodes** occur several times a day for **1-6 weeks**. The convalescence stage, the third stage, may last for months. Because **infants** are less capable of copping with the effort of coughing to maintain the airway, irreversible **damage to the brain** occasionally, occurs and **mortality rate** in this group is relatively **high**. In adults, pertussis often manifests itself only as a **persistent cough** and is unrecognized.

3 Stages

Catarrha
paroxysma
convalescen

Catarrha

2) **Tuberculosis:** Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. Most healthy people will defeat a potential infection with activated macrophages, especially if the infecting dose is low. If the bacilli are not destroyed the phagocytes tend to protect them from antibodies and other immune defense mechanisms and may survive and multiply within the phagocytes. Macrophages and other defensive cells accumulate at the infection site, forming a surrounding layer. This leads to a walled-off lesion called a **tubercle** (meaning lump of knob), a characteristic that gives the disease its name. Most surrounding macrophages are not very successful in destroying bacteria but release enzymes and cytokines that cause a lung damaging **inflammation**.

Fever, cough with blood, nausea, etc are some common symptoms.

Weight loss, night sweats.

3) **Bacterial Pneumonias:** The term pneumonia is applied to many pulmonary infections, most of which are caused by bacteria. Pneumonia caused by *Streptococcus pneumonia* is the most common and therefore referred to as typical pneumonia. Pneumonias caused by other microorganisms which include fungi, protozoa, viruses, as well as other bacteria, are termed **atypical pneumonia**.

Pneumonias are also named after the portions of the lower respiratory tract they affect. For example; if caused *S. pneumonia,* it is called **lobar pneumonia,** when lobes of the lung infected. **Bronchopneumonia** indicates that the alveoli of the lungs, adjacent to the bronchi are infected. **Pleurisy** is often complication of various pneumonias in which the pleural membranes become painfully inflamed.

Pneumococcal Pneumonia: Caused by *S. pneumoniae*. It also causes otitis media, meningitis, and septicemia. Pneumococcal pneumonia involves both bronchi and alveoli. Symptoms include- high fever, breathing difficulty, and chest pain. The lungs have reddish appearance because blood vessels are dilated. In response to infection, alveoli fill with some RBCs, polymorphonuclear leucocytes (PMNs) and fluid from surrounding tissues. The sputum is often rust colored.

4) ***Haemophilus influenzae* pneumonia:** Patients with such conditions as alcoholism, poor nutrition, cancer or diabetes are especially susceptible.

5) **Mycoplasmal Pneumonia:** *Mycoplasma pneumoniae* is the causative agent. This infection is endemic and is common cause of pneumonia in young adults and children. Mild symptoms which persists for three weeks or longer include low **fever, cough,** and **headache**.

6) **Legionellosis:** (Legionnaires' disease): It is caused by gram negative rod, *Legionell pneumophila*. The disease is characterized by **high fever, cough,** and general symptoms of pneumonia.

7) **Psittacosis (Ornithosis):** The term psittacosis is derived from the diseases associated with psittacine birds such as parakeets and other parrots. The disease can be contracted from other birds also such as pigeons, chickens, ducks, and turkeys. Therefore the more general term ornithosis also used for it. The causative agent is *Chlamydia psittaci,* a gram negative, **obligate intracellular** bacterium.

Psittacosis is a form of pneumonia that usually causes fever, headache and chills.

8) **Chlamydial pneumonia:** Recent outbreaks of respiratory illness found to be caused by chlamydail organisms. Originally the pathogen was considered a strain of *C. psittaci,* but now it has assigned the species name *Chlamydia pneumonia* and the disease is known as Chlamydial pneumonia. Clinically it resembles mycoplasmal pneumonia.

9) **Q fever:** Characterized by a fever (lasting for 1/2 weeks), **chills, chest pain, severe headache,** and other evidence of pneumonia type of infection. Causative agent_ *Coxiella burnetii,* a rickettsia.

Viral diseases of lower respiratory system: It can occur as a complication of influenza, measles, or even chickenpox. A number of enteric and other viruses have been shown to cause pneumonia.

1) **Respiratory Syncytial Viruses (RSV):** It is the most common cause of viral respiratory disease in infants. The name is derived from its characteristic of causing cell fusion (cyncytium formation) in cell culture. The symptoms are **coughing and wheezing** that last for more than a week.

2) **Influenza: (Flue):** characterized by **chills, fever, headache** and general **muscular aches**. Recovery normally occurs in a few days, and cold like symptoms appear as the fever subsides. It is caused by influenza virus that consists of eight weakly linked RNA segments enclosed by an inner layer of protein

and outer lipid bilayer. Embedded in the lipid bilayer are numerous projections that characterize the virus. There are two types of projections (spikes): hemagglutinins (H) and neuraminidases (N). Viral strains are identified by variation in the H and N spike antigens (eg. - H_2N_1,H_1N_1, etc).

Fungal diseases of the lower Respiratory System:

1) **Histoplasmosis:** If superficially resembles tuberculosis. The lungs are most likely to be initially infected; the pathogen may spread in the blood and lymph, causing lesions in almost all organs of the body. **Symptoms are poorly defined** and mostly subclinical, and the disease passes for a minor respiratory infection. Causative organism is *Histoplasma capsulatum*, is a dimorphic fungus; that has yeast like morphology in tissue growth, and, in soil or artificial media, it forms a filamentous mycelium carrying reproductive conidia. Human acquires infection from airborne conidia produced. H. capsulatum.

2) **Coccidioidomycosis:** The causative agent is *Coccidioides immitis*, a dimorphic fungus. The spores are found in dry, alkaline soils. Most infections are not apparent, and almost all patients recover in a few weeks. Symptoms include chest pain, and perhaps **fever, coughing** and weightless.

3) **Pneumocystis pneumonia:** It is caused by *Pneumocystis corinii*. The disease occurs through the world and can endemic in hospitals. Pathogen is found in healthy human lungs but causes diseases among immunocompromised patients. They form a thick-walled cyst in which spherical intracystic bodies successively divide as a part of sexual life cylcle. Eventually the cyst ruptures and releases them, and each body develops into a vegetative cell.

4) **Blastomycosis: (North American Blastomycosis):** It is caused by fungus *Blastomyces dermatitidi*, a dimprphic fungus, found most often in the Mississippi Velley. The infection begins in the lungs and can spread rapidly. Cutaneous ulcers commonly appear and there is extensive abscess formation and tissue destruction.

5) **Other fungal infections:** Many other opportunistic fungi can cause respiratory diseases, particularly in immunocompromised host or when there is exposure to massive number of spore. Aspergillosis is an important example; it is transmitted by the spores of *Aspergillus fumigatus* and other species of Aspergillus.

Similar pulmonary infections result when individuals are exposed to spores of mold of genera such as Rhizopus and Mucor.

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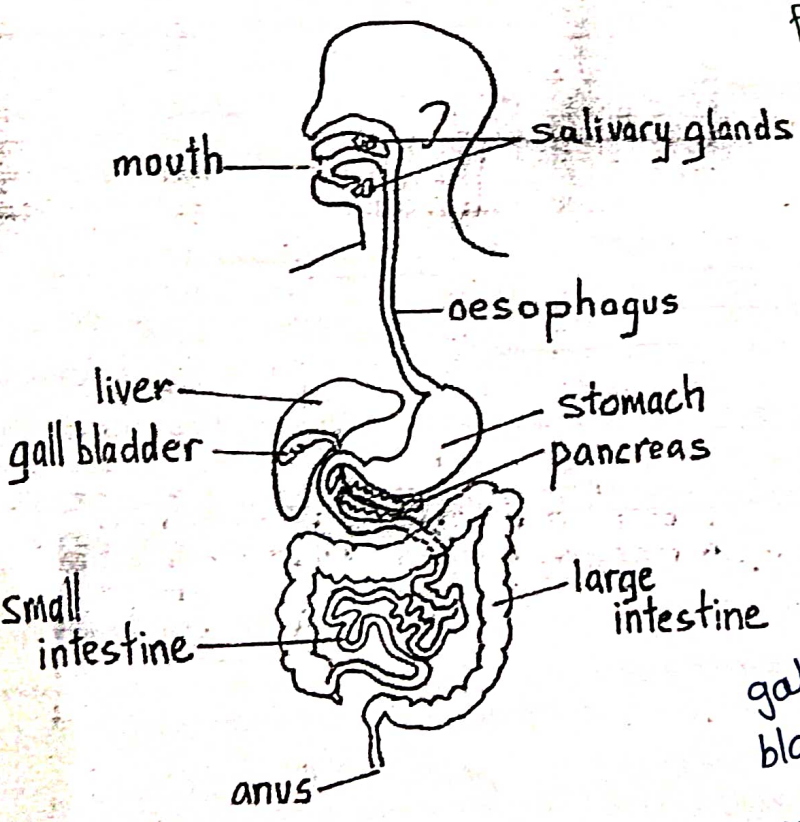
2. Gastrointestinal system

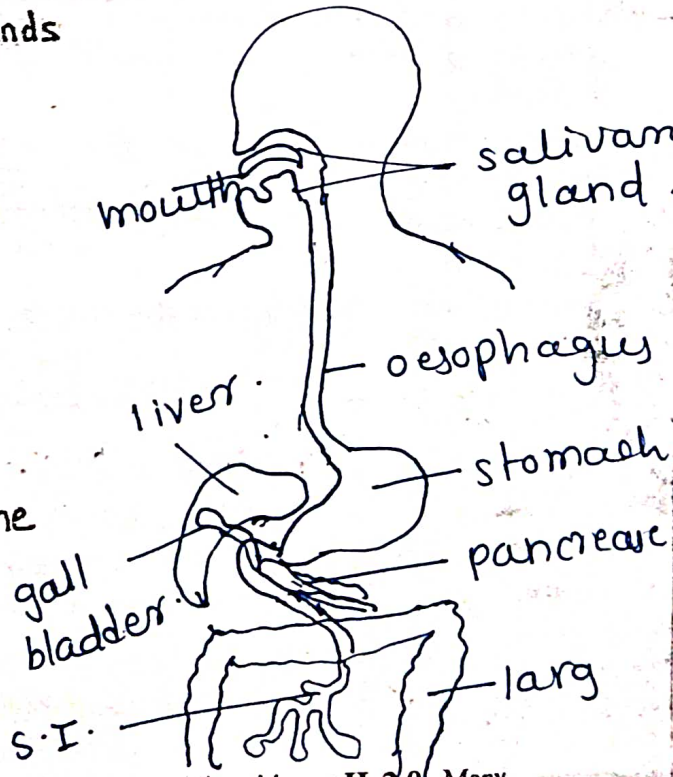
The gastrointestinal system (digestive system) may be divided into two groups of organs. One is **gastrointestinal tract (GIT)** or alimentary canal, essentially a tube like structure that includes the **mouth, pharynx** (throat), esophagus (food tube), **stomach, small intestine,** and **large intestine**. The other group of organs, the **accessory structures**, consists of the **teeth, tongue, salivary glands, liver, gall bladder,** and **pancreas**. Except the teeth and tongue, the accessory organs lie outside the GIT and produce secretions that are conveyed by ducts into it.

The purpose of digestive system is to digest foods- that is to break them down into small molecules that can be taken up and used by body cells. In a process called absorption, these end products of digestion pass from the small intestine into the blood or lymph for distribution to body cells. The food moves through large intestine where water, vitamins, and nutrients are absorbed from it. Over the course of an average life span, about 25 tons of food passes through the digestive system. The resulting undigested solids, called **feces**, are eliminated from the body through anus. Intestinal gas, or **flatus**, is a mixture nitrogen from swallowed air and microbially produced carbon dioxide, hydrogen, and methane. On an average, we produce 0.5- 2.0 liters of flatus every day.

Fig: Gastrointestinal System



Flatus = intestinal gas



Defense mechanisms:

a) Stomach acidity: The gastric fluid present in the stomach is quite acidic with a **pH 2.0**. Many bacteria that enter stomach are killed in such an environment. The acidity in stomach can **reduce** or **eliminate pathogenic microorganisms** or toxins before they reach intestine.

b) Normal microbiota/flora: Bacteria heavily populate most of the digestive system. In the mouth, each milliliter of saliva can contain millions of bacteria. The stomach and small intestine have relatively few microorganisms because of the **hydrochloric acid** produced by the stomach and the **rapid movement** of the food through the **small intestine**. By contrast large intestine has enormous microbial populations exceeding 100 million bacteria per gram of feces (up to 40% of fecal mass is microbial cell material). The population of large intestine is composed mostly of the genera **Lactobacillus** and **Bacteroides (Probiotics)**, and facultative anaerobes, such as *E. coli, Enterobacter sp., Klebsiella sp.* and *Proteus spp.*

Probiotics are the live microorganisms which confer health benefits (**pathogen inhibition**/colonization resistance, **enhance immunity** /intestinal integrity and mobility, **reduces intestinal inflammations** and mutagenic or carcinogenic compounds, etc.) to the host.

More than 400 species of microorganisms (normal flora) live in adult GI tract. This flora can provide **resistance** to **colonization by many pathogens**. In healthy individual, host tissue and normal GI tract flora operate in harmony.

c) The GI tract Immune system: The GI tract has its own immune system which helps to keep body healthy by **reducing absorption** of some large molecules (e.g. **toxins**), or **reducing colonization** of epithelium by **pathogens without affecting normal flora**. The intestinal wall contains **lymphocytes** and **antibody producing cells** that fight infection. Generally only organisms that can attach to the intestinal lining cause problem. Otherwise microorganisms are swept out by motility of GI tract (http://www.mass.gov/eohhs/docs/dph/environmental/foodsafety/ref-manual/chap-3.pdf).

d) Bile acids and digestive enzymes: Bile acids are produced in the liver and assist digestion and absorption of fat. They inhibit growth of many pathogens. However intestinal commensals remain unaffected.

Digestive enzymes are active through GI tract, and inhibit or inactivate variety of pathogens. E.g. lysozyme in saliva kills and digests microbes.

Common microbial diseases/ pathogens of GI system:

Bacterial infections of mouth-

1) **Dental caries (Tooth decay):** The teeth are unlike any other exterior surface of the body. They are hard, and they do not shed surface cells. This allows the accumulation of masses of microorganisms and their products. These **accumulations**, called **dental plaque**, are intimately involved in the formation of **dental caries** or **tooth decay.**

Oral bacteria convert sucrose and other carbohydrates into lactic acid, which in turn attacks the tooth enamel. The most important **cariogenic** (caries causing) bacterium is *Streptococcus mutans.* S. mutans

The initiation of caries depends on the attachment of *S. mutans*, or other streptococci, to the tooth. Within minutes, freshly brushed tooth become coated with a pellicle (thin film) of proteins from saliva and within a couple of hours, cariogenic bacteria become established on this pellicle and begin to produce gummy polysaccharide of glucose molecules called dextran. Accumulation of bacteria and dextran adhering to the teeth make up dental plaque.

Although saliva contains nutrients that encourage growth of bacteria, it also contain antimicrobial substances like lysozyme that offers protection to exposed tooth surface. Some protection is also provided

Crevicular fluid. - crivicular fluid.

by **crecicular fluid**, tissue exudates that flow into the gingival crevice. It protects teeth by virtue of its flushing action and its phagocytic cells and immunoglobulin contents.

Localized acid production within deposits of dental plaque results in a gradual softening of the external enamel. (Enamel low in fluoride is more susceptible to the effects of the acid. This is the reason for fluoridation of water and toothpastes).

2) **Periodontal diseases:** Periodontal disease is a term for conditions characterized by inflammation and degradation of structures that support the teeth (cementum).

i) Gingivitis: In many cases of periodontal disease, the infection is restricted to the gums, or gingivae. This infection, called gingivitis, is characterized by bleeding gums while brushing the teeth. Streptococci, Actinomyces, and anaerobic gram negative bacteria predominant in these infections.

ii) Periodontitis: Gingivitis can progress to a chronic condition called periodontitis, which is responsible for tooth lose in older adults. The gums are inflamed and bleed easily. Sometimes pus is formed. Different types of *Porphyromonas species* are found in these infections; damage to tissue is done by an inflammatory response to the presence of these bacteria.

iii) Acute necrotizing ulcerative gingivitis, also termed **Vincents disease** or **Trench mouth,** is one of the more common serious mouth infection. The disease causes pain that make normal chewing difficult. **Foul breath (halitosis)** also comprises the infection. *Prevotella intermedia* is the bacterium usually associated with it.

Prevotella intermedia

- **Bacterial diseases of the lower digestive system:**

Diseases of the digestive systems are of two types: 1) infections and 2) intoxication

An infection occurs when a pathogen enters the GI tract and multiplies. Infections are characterized by a delay in the appearance of GI disturbance while the pathogen increases in number or affects the invaded tissue. **There is also usually a fever, one of the body's general responses to an infective organism.**

Some pathogens, cause diseases by forming toxins that affect GI tract. Intoxication is caused by the ingestion of such a preformed toxin. Most intoxications such as that caused by *Staphylococcus aureus* are characterized by a very sudden appearance of symptoms of a **GI disturbance**, fever, is less often one of the symptoms.

Both infections and intoxications often cause **diarrhea.** Severe diarrhea accompanied by **blood or mucus** is called **dysentery.** Also, both are frequently accompanied by **abdominal cramps, nausea,** and **vomiting.** The general term **gastroenteritis** is applied to diseases causing **inflammation of the stomach and intestinal mucosa.**

In developing countries, diarrhea is a major factor in infant mortality. The cause of diarrhea may be any of several pathogens, most common cause is **rotaviruses**, but enterotoxigenic *E.coli* and *Shigella species* are responsible.

1) **Staphylococcal Food Poisoning (Staphylococcal Enterotoxicosis):** A very common cause of gastroenteritis is Staphylococcal food poisoning, an intoxication caused by ingesting an enterotoxin produced by *S. aureus*. It produces several toxins that damage tissues or increase its virulence. A population of about 1 million bacteria per gram of food will produce enough enterotoxin to cause illness. Custards, cream pies, and ham are examples of high risk foods.

The toxin quickly triggers the brains vomiting reflux center, **abdominal cramps** and usually **diarrhea** then ensue.

2) **Shigellosis** (bacillary dysentery): It is a severe form of diarrhea caused by species of genus Shigella. There are four species of Shigella that causes dysentery- *S. sonnei, S. dysenteriae, S. flexneri,* and *S. boydii.* The virulent **toxin** (Shiga toxin) produced by these bacteria destroy tissue in **intestinal mucosa, causing severe diarrhea** with **blood** and **mucus in the stool.**

3) **Salmonellosis** (salmonella gastroenteritis): It is caused by species of genus Salmonella (gram negative motile rods). The Salomonellae first **invade the intestinal mucosa** and multiply there. They can some timed manage to pass through the intestinal mucosa to the **lymphatic** and cardiovascular **system** and from there to other organs. The **fever** associated with Salmonella infections might be from **endotoxin** released by lysed cells. There is fever associated **with nausea, abdominal pain and cramps,** and **diarrhea.**

4) **Typhoid fever**: Some Salmonella are much more resistant than others. The most virulent, *S. typhi* causes the bacterial infection typhoid fever. The incubation period is much longer than that of salmonellosis, normally about two weeks. The patient first suffers from a **high** fever of 40°C (104°F) and **frontal headache. Diarrhea** occurs only during the second or third week and the fever tends to decline. Unlike salmonellosis, the bacteria do not multiply in the intestinal cells; they differ by continuing to [illegible] phagocytic cells. Then they become **disseminated in** the body and can be isolated form blood, [illegible] In severe cases, **perforations** of the intestinal walls can occur.

[illegible] agent is *Vibrio cholerae,* a slightly curved, gram negative rod with polar [illegible] small intestine and produces an **enterotoxin** that results in **secretions** of chlorides, [illegible] and water. These excess electrolytes and water excreted take a "rice water" appearance of [illegible] The sudden loss of these fluids and electrolytes causes **shock, collapse** and often **death.**

Gastroenteritis:

1) **Vibrio Gastroenteritis:** *Vibrio parahaemolyticus* is found in salt water estuaries, morphologically similar to *V. cholerae* but is **halophilic** and requires 2% or more NaCl for optimum growth. It is most common cause of gastroenteritis in Japan. Symptoms include **abdominal pain, vomiting, burning sensation in stomach** and **watery stool.**

2) ***Escherichia coli* gastroenteritis:** *E. coli* is normally harmless, but certain strains can be pathogenic. They produce toxins that cause gastrointestinal disturbances collectively called *E. coli* gastroenteritis.

3) **Campylobacter Gastroenteritis:** It is caused by *Campylobacter jejuni.* Clinically it is characterized by **fever, cramping abdominal pain, diarrhea** with **blood** and **mucus** present in the stool.

4) **Helicobacter peptic ulcer disease:** *Helicobacter pylori* is responsible for most cases of **peptic ulcer.** This syndrome include **gastric** and **duodenal ulcer.**

Viral diseases of the digestive system:

1) **Mumps:** The target of the mumps virus is the **parotid glands** located just below and in front of the ears. Mumps typically begins with **painful swelling** of one or both **parotid glands.** Mumps is characterized by **inflammation** and swelling of the parotid glands, **fever,** and pain during swallowing. After onset of symptoms, the **testes can become inflamed.** Sterility is possible but rare. Other complications include **meningitis,** inflammation of the **ovaries.**

2) **Cytomegalovirus (CMV) infusion disease:** It is caused by a cytomegalovirus (CMV), a Herpes virus that causes **nuclear inclusions** and **swelling**, or **cytomagaly** of the host cells. The official name for the virus is human Herpesvirus 5.

3) **Hepatitis:** Hepatitis is an **inflammation of liver (and dysfunctioning of liver)**. At least five different viruses (hepatitis A virus, hepatitis B, hepatitis C, hepatitis D, hepatitis E, ~~and hepatitis D~~). Hepatitis is also an occasional result of infections by other viruses such as EB (Epstein Bar) virus or CMV.

- **Fungal diseases of GI tract:** Claviceps purpurea

1) **Ergot poisoning**: Some mycotoxins are produced by *Claviceps purpurea*, a fungus causing smut infections on grain crops. These mycotoxins cause ergot poisoning or **ergotism**, which results from the ingestion of rye or other cereal grains, contaminated with the fungus. The toxin can **restrict blood flow** in **the limbs**, and **gangrene** results. It may also cause **hallucinogenic** symptoms.

2) **Aflatoxin poisoning:** Aflatoxin is a mycotoxin produced by the fungus *Aspergillus flavus*, a common mold. Aflatoxin **contributes** to **cirrhosis** of the liver and **cancer** of the liver. → irreversible scarring / fibrosis of liver

- **Protozoan Diseases:**

1) **Giardiasis:** *Giardia lamblia* is a flagellated protozone that is able to attach firmly to human intestinal wall, causes giardiasis – a **prolonged diarrheal** disease. It is characterized by **malaise, nausea, flatulence, weakness, weight loss**, and **abdominal cramp.**

2) **Amoebic dysentery (Amoebiasis):** It is spread mostly by food or water contaminated by the protozoan amoeba *Entamoeba hystolytica*. It is severe **dysentery** and the feces characteristically contain **blood** and **mucus**.

- **Helminthic Diseases:**

1) **Tapeworm infections:** *Taenia saginata, Taenia solium,* are typical tapeworm whose lifecycle extends through three stages. *T. saginata* , can live in **human intestine** for 25 years and reaches a length of 6 meters, or longer, seldom causes significant symptoms beyond a **vague abdominal discomfort**.

- **Nematode Infections:**

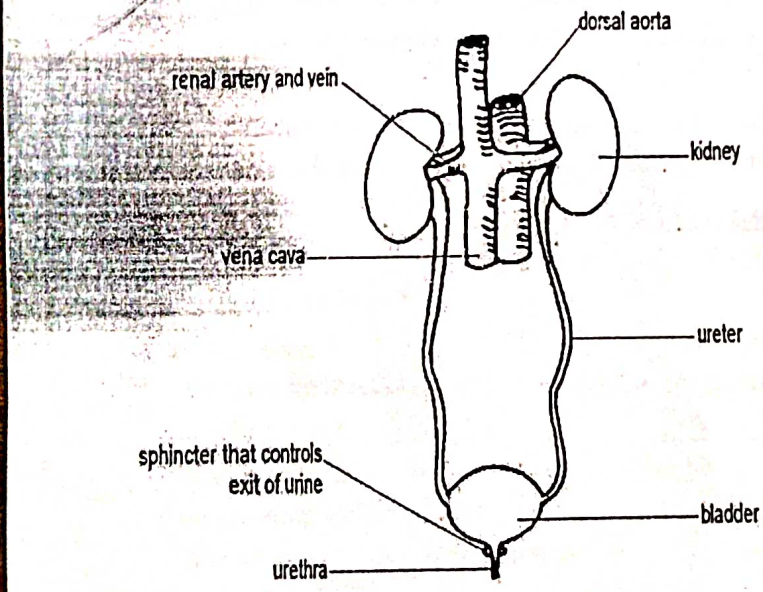
1) **Hookworm infections:** The hookworm attaches to the intestinal wall and feeds on **blood** and **tissue** rather than on partially digested food, so the presence of large members of worms can lead to **anemia** and **lethargic behavior.**

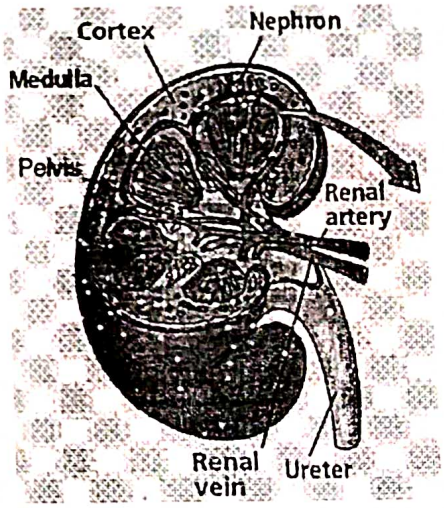
3. Kidney (Urinary) and Genital (Reproductive) system:

Urinary system: The urinary system consists of two kidneys, two ureters, and a single urinary bladder urethra. Certain wastes, collectively called urine, are removed from the blood as it circulates through the kidneys. This urine passes through the ureters into the urinary bladder, where it is stored prior to elimination from the body through the urethra. In the female the urethra conveys only urine to the exterior. In male, the urethra is a common tube for both urine and seminal fluid.

Defense mechanisms: Where the ureters enter the urinary bladder, valves prevent the backflow of urine to the kidneys. This mechanism helps shield the kidneys form lower urinary tract infections. In addition, the acidity of urine has some antimicrobial properties. The flushing action of urination tends to remove potentially infectious microbes; all these mechanisms offer and contribute to defense mechanisms giving check to microbes.

Fig: Urinary system; Kidney:





dysuria
pyum

Common diseases/pathogens:

1) **Cystitis:** It is a common inflammation of the urinary bladder in females. Symptoms often include **dysuria** (difficult, painful, urgent urination) and **pyuria** (presence of leucocytes in urine). In either gender, most are due to infection by *E. coli*, and *Staphylococcus saprophyticus*.

2) **Pyelonephritis:** Cystitis (untreated) may progress to pyelonephritis, an inflammation of one or both kidneys. Symptoms are **fever** and **flank or back pain**. In females it is often a complication of lower urinary tract infection. Causative agent is *E. coli*.

3) **Leptospirosis:** It is primary a disease of domestic wild or animals, but it can pass to humans and sometimes causes severe kidney or liver disease. Causative agent is *Leptospira interrogans*. After an incubation period (1-3 weeks), **headache, muscular aches, chills, and fever** rapidly appear. Several days

interrogans

later, the acute symptoms disappear and the temperature returns to normal. A few days later, however, a second episode of fever may occur.

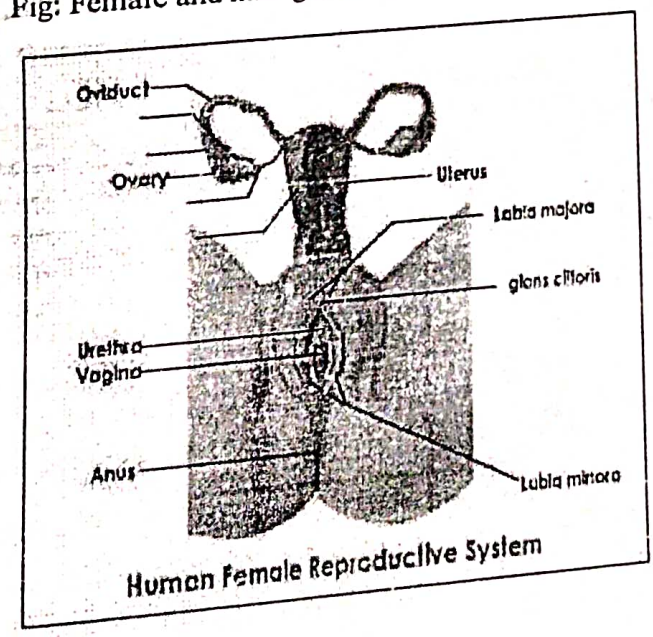
Genital (Reproductive) system:

Female genital (reproductive system): It consists of two ovaries, two uterine (fallopian) tubes, the uterus- including the cervix, the vagina, and external genitals.

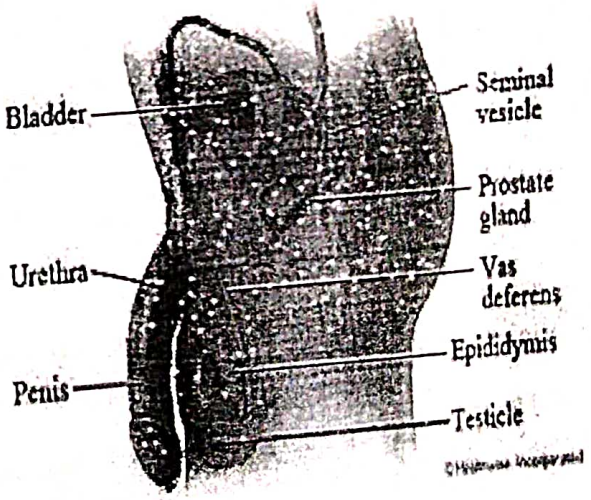
The ovaries produce female sex hormones and ova (eggs). When an ovum is released during the process of ovulation, it enters a uterine tube, where fertilization may occur if viable sperms are present. The fertilized ovum (zygote) descends the tube and enters the uterus. It implants in the inner wall and remains there while it develops into an embryo and, later, a fetus. The external genitals (vulva) include the clitoris, labia, and glands that produce a lubricating secretion during copulation.

Male genital (reproductive) system: It consists of two testes, a system of ducts, accessory glands, and the penis. The testes produce male sex hormones and sperms. To exit the body, sperm cell passes through a series of ducts: the epididymis, ductus (vas) deferens, ejaculatory duct, and urethra.

Fig: Female and male genital system



Human Female Reproductive System



Defense mechanisms:

Normal microbiota of the urinary and reproductive systems: Normal urine is sterile, but it may become contaminated with members of skin microbiota near the end of its passage through the urethra.

In the female genital system, the normal microbiota of the vagina is influenced by sex hormones and offers some protection. For example, within a few weeks after birth, the female infant's vagina is populated by **lactobacilli**. This population grows because **estrogens** are transferred from maternal to fetal blood and cause glycogen to accumulate in the cells lining the vagina. Lactobacilli convert the glycogen to lactic acid, and the pH of the vagina becomes acidic. This glycogen- lactic acid sequence provides the condition under which acid- tolerant normal microbiota grow in the vagina.

The physiological effects of estrogens diminishes several weeks after birth, and other bacteria, including corynebacteria and variety of cocci and bacilli, become established and dominate the microbiota. As a result, the pH of the vagina becomes neutral until puberty. At puberty, estrogen levels increase, lactobacilli again dominate, and the vagina again become acidic. In the adult, a disturbance of this ecosystem by an increase in glycogen (caused by oral contraceptives or pregnancy, for example), or elimination of the normal microbiota by antibiotics can lead to vaginitis. When the female reaches menopause, estrogen levels again decrease, the composition of the microbiota returns to that of childhood, and the pH again becomes neutral. Pregnancy and menopause are factors that increase the risk of urinary tract infections, which are probably related to lowered acidity. The use of spermicides, which may inhibit lactobacill, is also associated with urinary tract infections.

The male urethra is normally sterile, except for a few contaminating microbes near the external opening.

Common diseases/ pathogens:

Most diseases of the reproductive systems are transmitted by sexual activity and are therefore called sexually transmitted diseases (STDs) or venereal diseases (VDs). Neissena gonorrhoeae.

1) **Gonorrhoea:** It is caused by the gram negative diplococcus *Neisseria gonorrhoeae*. Males become aware of infection by **painful urination** and a discharge of **pus-containing** material from the **urethra**. In some instances, the urethra is scarred and particularly blocked. **Sterility** can result when the testes become infected or when the ductus deferens blocked by scar tissue. Neissena gonorrhoeae.

Very few women are aware of the early stages of the infection. Later in the course of the disease, there might be **abdominal pain** from complications such as **pelvic inflammatory disease.**

In both males and females, untreated gonorrhea can become a serious, systemic infection. Complications of gonorrhea **can involve joints, heart**-gonorrheal **endocarditis, meningitis**- gonorrheal meningitis, **eyes, pharynx** or other parts of body.

Gonorrheal eye infections occur most often in new borne. If the mother is infected, the eye of infant can become infected as it passes through the birth canal. This condition, **ophthalmia neonatorum**, can result in **blindness.** ophthalmia neonatorum.

2) **Nongonorrheal urethritis (NGU):** It is also known as nonspecific urethritis (NSU), refers to any inflammation of the urethra not caused by *Neisseria gonorroeae*. Symptoms include **painful urination** and a **watery discharge**. The pathogen associated is *Chlamydia trachomatis*. Chlamydia trachomd

3) **Pelvic Inflammatory Diseases (PID):** It is collective term for any extensive bacterial infection of the female pelvic organs, particularly the **uterus, cervix, uterine tubes** or ovaries. fallopean tubes

PID is often caused by *N. gonorrhoeae*. Infection of the **uterine** tubes or **salpingitis**, is the most serious form of PID. It can result in **scaring** that block the passage of ova from the ovary to the uterus, possibly causing **sterility**. salpingitis.

4) **Syphilis:** It is caused by *Treponema pallidum*, a weak staining, and gram negative spirochete. In primary stage of disease, the initial sign is a small, hard-based chancre, or sore, which usually appear at the site of infection. The chancre is painless, and serous exudates are formed in the center. painless genital ulcer.

Several weeks after the primary stage, the disease enters the secondary stage, characterized by (mainly) skin rashes. Other symptoms often observed are- loss of patches of hair, malaise, and mild fever. The

Hisseria gonorrhoea

* Syphilis:- 3 distinct stages:-

(1) 1° / early stage:- Chancre / Sores
painless genital ulcers.
Average 3 weeks of exposure.
Even without treatment, they heal with 6 weeks with s

(2) 2° stage:- It might last one to three months.
begins within 6 weeks & 6 months after exposure.
Skin rashes typically on palms of the hands & soles of the feet.
Other symptoms include moist warts in the groin
white patches on inside of the mouth, swollen lymph glands
fever, weight loss.
like 1° syphilis, it will also resolve without treatment.

(3) latent syphilis :- The infection lies dormant (Inactive) without causing symptoms.

(4) 3° syphilis:- If the infection is not treated, it may then progress to a stage characterized by severe problems in heart brain & nerves that can result in paralysis, blindness, deafness, dementia & even death.

dementia → problems with thinking, behaviour memory.

symptoms of secondary syphilis usually subside after a few weeks, and the disease inters a latent period, during which there are no symptoms (although serological tests are positive). In some of cases the disease reappears in tertiary stage in which most of symptoms are due to body's immune reactions, of cell mediated nature to surviving spirochetes. Inflammatory response causes **lesions** called gummas, **rubbery masses of tissue** that appear on many organs and sometimes on the external skin.

5) **Gardnerella Vaginosis:** Inflammation of the vagina due to infection, or vaginitis, is most commonly caused by one of three organisms. The fungus *Candida albicans*, the protozoa *Tricomonas vaginalis*, or the bacterium *Gardnerella vaginalis*, a gram variable rod. The condition is characterized by a pronounced fishy odor of a frothy vaginal discharge, which is usually copious.

Viral diseases of the genital system:

1) **Genital herpes:** A much published STD is genital herpes, usually caused by herpes simplex virus types 2 (HSV-2). • genital pain & sores

Genital herpes lesions appear after an incubation period of one week cause a burning sensation. After this, vesicle appears. In both sexes, urination can be painful and walking is quite uncomfortable, the patient is even irritated by clothing.

2) **Genital warts:** Warts are caused by viruses known as **Papillomaviruses.** Some warts are extremely large and 'warty' in appearance, with fingerlike projections resembling cauliflower: others are smooth or flat. Several serotypes are associated with a progression to cancer. Warts can cause pains & discomfort & itching.

3) **AIDS:** AIDS is viral disease caused by HIV-1 and HIV-2 that is frequently transmitted by sexual contact. Initially, with flulike illness and later as its effects are on immune system recurrent certain viral and bacterial infections (like- Herpes, pneumonitis, diarrhea, etc) are the progression of the infection. large lymph nodes, fever, weight loss

Fungal diseases of the reproductive system:

1) ***Candida albicans*** is the cause of oral candidiasis, or thrush. It is also responsible for NGU in males and for valvovaginal candidiasis, which is the most common cause of vaginitis.

The lesions of valvovaginal candidiasis resembles those of thrush but produce more irritation, severe itching; a thick yellow, cheesy discharge, and yeasty or no odor.

2) **Trichomoniasis:** The anaerobic protozoan *Trichomonas vaginalis* is normal inhabitant of the vagina in femalesand of the urethra in many males. If the normal acidity of the vagina is disturbed, the protozoan may overgrow and cause trochominiasis. In response to infection, the body accumulates leukocytes at the infection site. The resulting discharge is profuse, greenish-yellow, and characterized by a foul odor, accompanied by irritation and itching.

Latent period:- A period between exposure & infection. Since the orgm is in 'latent' stage without clinical symptoms or signs of infection in host.

Incubation period:- The period between exposure & onset of clinical symptoms.

→ means to shiver & trembling in fear.

* Kuru :- · Very rare disease found among people from New Guinea who practiced a form of Cannibalism in which they ate brains of dead people as a part of funeral ritual.

Kuru causes brain & nervous tissue changes similar to CJD a similar disease in cow as BSE

- It mainly affects 'cerebellum' - the part of brain responsible for coordination & balance.
- Prions are abnormal or misfolded proteins.
- They aren't living organisms & don't reproduce.
- They are inanimate & misshapen proteins that multiply in the brain & form clumps hindering normal brain processes.
- Disease is contracted by eating infected brain or coming in contact with wounds & sores of someone who is infected.

4. Nervous system:

The human nervous system is organized into two divisions: the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS consists of brain, and the spinal cord. As the control centre for the entire body, the CNS picks up sensory information from the environment, interprets the information, and sends impulses that coordinate the body activity. The PNS consists of all the nerves that branch off from the brain and spinal cord. These peripheral nerves are the lines of communication between the central nervous system and the various parts of the body, and the external environment.

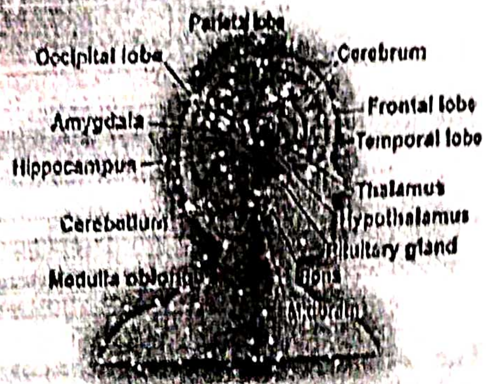
Defense/ protection:

Both the brain and the spinal cord are covered and protected by three continuous (inner) membranes called **meninges.** These are - the outermost **dura-mater,** the **middle archnoid,** and the **outer most pia-mater.** Between the pia-mater and archnoid mater is a space called the sub-archnoid space, in which an adult has 100-160 ml. of cerebrospinal fluid (**CSF**) circulating. Because CSF has low levels of **complement** or **circulating antibodies** and few **phagocytes,** bacteria can multiply in it with a few checks.

An important feature of the brain is **blood-brain barrier (BBB).** Certain capillaries permit some substances to pass from the blood into the brain but restrict others. Theses capillaries are less permeable than others within the body and are therefore more selective in passing materials.

Drugs cannot cross the BBB unless they are lipid-soluble (glucose and many amino acids are not lipid-soluble. But they can cross the barrier because special transport systems exists for them). The lipid soluble antibiotic Chloramphenicol enters the blood rapidly. Inflammation of the brain tend to alter the BBB in such a way as to allow antibiotics to cross that would not be able to cross if there were no infection.

Brain/Central Nervous System



Glial cells Non-neuronal cells that provide support to neurons, ... participate in signal transduction, destroy pathogens & remove dead neurons.

Jyotsna

Even though the CNS has considerable protection, it can still be invaded by microorganisms in several ways. For example, microorganisms can gain access through trauma such as a skull or backbone fracture, or through a medical procedure such as a spinal tap to obtain a sample of CSF for diagnosis. Some microorganisms can also move along peripheral nerves. But the most common routes of CNS invasion are the blood stream and lymphatic system, when inflammation alters permeability of the BBB.

* Poliomyelitis :
- A highly contagious disease.
- Children younger than 5 yrs old are more likely to contract it.

Protozoan disease:-

1) African Trypanosomiasis:-
- Sleeping sickness.
- Caused by Trypanosoma brucei gambiense or T. b. rhodesiense Flagellates that are injected by the bite of tsetsefly.
- Early stages trypanosomae → found in blood.
  late stages → CSF
- Decrease in physical activity & mental acuity (sharpness of mind).
- Untreated host → enters coma & death may occur.

2) Naegleria Meningoencephalitis:-
- Naegleria fowleri, protozoan (amoeba).
- Common victims → children who swim in ponds/streams.
- Intial infection is to nasal mucosa & later it proliferates in brain.

Naegleria fowleri

Caused by Prions - Naegleriameningoencephalitis Naeg. fowleri

- Prions → self replicating proteins with no detectable nucleic acid
- Theses diseases are having long incubation periods & progress slow CNS damage is insidious (subtle way) & progressive without fever & inflammation seen in encephalitis.
- Autopsies show the characteristic spongiform degeneration of brain

1) Sheep scrapie :-
- Infected animal scrapes itself against fences & walls until areas on its body are raw.
- During a period of several weeks/months, the animal finally looses its motor control & dies
- In humans CJD (Creutzfeldt-Jakob disease).

2) Kuru :- Apparently it is related to the practice of smearing brain tissue onto the body during cannibalistic rituals.

3) Mad cow disease :- bovine spongiform encephalopathy

① Common diseases/ Pathogens:

Meningitis:- Most patients suffering from any type of meningitis complain of a **headache** and have symptoms of **nausea** and **vomiting**. Convulsions and coma accompany the infection in many cases. Meningitis can be caused by different types of pathogens, including viruses, bacteria, fungi, and protozoa. Viral meningitis mostly caused by echoviruses in more common than bacterial meningitis.

Only three bacterial species cause more than 70% of the meningitis cases. These are the gram positive diplococcus *Strptococcus pneumonia* and the gram negative *Neiserria meningitidis* and *Hemophilus influenzae*. All these possess a capsule that protects them from the phagocytosis as they replicate rapidly in the blood stream, from which they might enter the CSF.

② Tetanus: It is caused by *Clostridium tetani*. The symptoms of tetanus are caused by an extremely potent neurotoxin, - **tetanospasmin**, that is released upon death and lysis of the growing bacteria.

Symptoms: The tetanus neurotoxin blocks the relaxation pathways so that both opposing sets of muscles contract, resulting in the characteristic **muscle spasms**. The muscles of jaw are affected preventing the mouth from opening, a condition known as **lock jaw**. In extreme conditions, spasms of the back muscles cause the head and neck to bow backward, a condition called **opisthotonos**.

③ Botulism: It is a form of food poisoning, caused by *Clostridium botulinum*, an obligatory anaerobic, endospore forming, gram positive rod.

Symptoms: Individuals suffering from botulism undergo a progressive **flaccid paralysis** and may die from **respiratory** and **cardiac failure**. Nausea but no fever, may precede the neurological symptoms that includes; **double or blurred vision, difficulty in swallowing** and general **weakness**.

Viral infections (diseases):

① Poliomyelitis (Polio): It is best known as a cause of **paralysis**. The great majority of cases is asymptomatic or cause mild symptoms, such as **headache, sore throat, fever**, and **nausea**, which are often interpreted as mild meningitis or influenza. The polio is caused by poliovirus.

② Rabies: It is acute infectious disease that usually results in **fetal encephalitis**. The causative agent is the rabies virus, a **rhabdovirus** having a bullet shape.

Symptoms: The primary symptoms are mild and varied. When the CNS becomes involved, the patient tends **alternate** between periods of **agitation** and **intervals of calm**. At this time, a frequent symptom is **spasms** of the **muscles of the mouth and pharynx** that occur when patient swallows liquid. In fact, even the mere sight or thought of water can set off the spasms- thus the common name- **hydrophobia.**

Fungal diseases:

***Cryptococcus neoformans* meningitis (cryptococcoisis):** The CNS is seldom invaded by fungi. However, one pathogenic fungus is - *Cryptococcus neoformans* causes cryptococcoisis.

Inhalation of *Cryptococcus neoformans* initially causes infection of lungs, frequently subclinical. However, it can spread through bloodstream to the other parts of body, including the brain and meninges. The disease is usually expressed as chronic meningitis, which is often progressive and fatal if untreated.

(4) Listeriosis:-

- Listeria monocytogenes
- Infects a type of leukocyte "monocytes".
- It is ingested by phagocytic cells but isn't destroyed.
- Unusual capacity of moving directly from one macrophage to adjacent one.
- It mainly affects adults who are immunocompromised, pregnant.
- Has a special affinity for growth in CNS.
- As it infects placenta it has ability to cross cell to cell & hence cross the barrier of placenta & cause fetus infection. Stillbirths & abortions are at high rate.

(5) Leprosy:-

Leprae.

- Mycobacterium lepsae, the only bacterium grows in PNS
- Hansen's disease.
- Organ - growth temp. optimum 30°C
- A very long generation time of about 12 days.
- Armadillos → valuable experimental animal.
- 2 forms of leprosy:-

Armadillos

① Tuberculoid form:- Characterized by regions of the skin that has lost sensation & are surrounded by a border of nodules. This form occurs in persons with good/effective immune reactions.

② lepromatous (progressive) form of leprosy:- Skin cells are infected & disfiguring nodules form all over the body. Persons have at least effective CMI. Mucous membranes of nose tend to become affected & a lion faced appearance is associated with this type of leprosy.

- It is known to affect skin, peripheral nerves, mucosal surfaces of upper respiratory tract & the eyes.
- Skin lesion are most common. Can be single or multiple & usually less pigmented than normal surrounding skin.
- A variety of skin lesions may be seen but macules (flat), papules (raised) or nodules are common.
- loss of sensation, thickened nerves because of this damage to nerves, muscles to which they are attached might be weaked
- Positive skin smears