PATHOLOGY OF INFECTIOUS DISEASES

In developing countries unsanitary living conditions & malnutrition lead to a massive burden of infectious diseases especially respiratory and diarrheal infections caused by viruses & bacteria. Moreover, despite vaccination & antibiotics, infectious diseases continue to have a heavy role in patients on immunosuppressive drugs or those with AIDS.

Commensals are microorganisms that live and share the host's food without causing harm e.g.

1. Bacteria living on the skin
2. Vit. K producing intestinal bacterial flora, which are normal inhabitants.

Pathogens are microorganisms that injure the host. They include; viruses, bacteria, fungi, protozoa (e.g. Entameba) & metazoa (e.g. worms).

Pathogenicity is the capacity of a particular microorganism to cause disease.

Virulence is the degree of pathogenicity. It should be noted that commonsals are potential pathogens; they may become pathogenic for e.g. in immuncompromised patients. In this situation the infections produced are called opportunistic infections**.** The site is important for e.g.

1. E. coli is a normal inhabitant of GIT but when introduced into the urinary tract through for e.g. a urinary catheter, it becomes pathogenic and leads to severe urinary infection.
2. During tooth extraction, diseased heart valves may become infected by Strept. Viridans, which are normal commensals of the mouth. Such an infection leads to serious disease (bacterial endocarditis).

Infection by definition is the presence of microorganism in a part of the body where it is normally absent & where if allowed to multiply, it stimulates a host response & cause infectious disease. The outcome depends on balance between the microorganism's aggressive mechanisms & the host defenses.

Invasion: Is the first step of causing an infection, it depends on the penetration of the hosts' tissues by micro-organisms.

Host Defenses are divided into

A. Non-specific defense mechanisms; these are operative irrespective of the nature of the pathogens

1. ***Mechanical barriers*** e.g. clean dry skin, mucous layer of the conjunctiva, respiratory & GIT mucosa. Should any one of these barriers is broken, infection occur e.g. infections are a recognized complication of burns, because the latter damage the skin barrier.

2. ***Glandular secretions***
- Acidity of sweat is bactericidal for some pathogens.
- Acidity of gastric juice is effective in killing most types of microorganism that contaminate food & water.
- Lysozyme enzymes secreted by mucous membranes can digest mucopeptide of bacterial cell wall. It is found in lacrimal, salivary & nasal glands.
- Secretary IgA antibodies found in saliva, tears, intestinal contents, respiratory tract mucus, milk & urine.

3. ***Secretion currents***
- Continuous flow of tears prevents conjunctival infection.
- Ciliated respiratory epithelial cells prevent infection. Failure of this mechanism permits influenza virus to combine with epithelial cells.
- Smoking damages respiratory epithelium predisposing to bacterial infection
- Intestinal pathogens e.g. Salmonella food poisoning leads to acute inflammation with increased peristalsis and thus diarrhoea. This is in away a defensive mechanism to get rid of the offending bacteria.
- Obstruction of urinary flow leads to stasis of the urine with subsequent urinary tract infection (UTI). This is seen for e.g. in prostatic enlargement and urinary calculi.

4. ***Phagocytosis***
- Neutrophils migrate to tonsillar crypts & macrophages migrate into the alveoli.
- Both engulf particles & microorganisms & thus play a role in preventing invasion.

B. Specific defenses (specific immunity), which are offered by the immune system & are directed against the relevant infectious agent.

The causes for decline of infections in the world include

1. Improved standards of community & personal hygiene
2. Better nutrition & housing
3. Prophylactic immunization
4. Antimicrobial chemotherapy

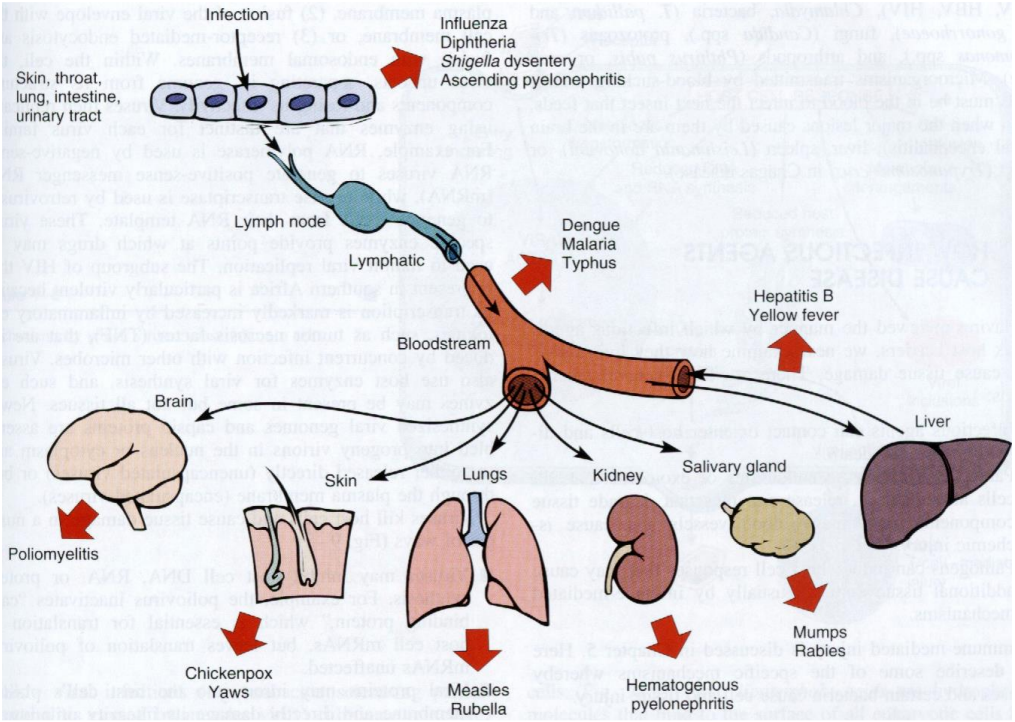
Categories of infectious agents

Organisms causing infectious diseases range in size from 20nm (poliomyelitis virus) to 10 meters (the tape worm Taenia saginata).

Taxonomic class	Sample species	Related disease
1. Viruses	Poliovirus	Poliomyelitis
2. Chlamydiae	Chlamydia trachomatis	Trachoma
3. Rickettsiae	Rickettsia prawazeki	Typhus fever
4. Mycoplasma	Mycoplasma pneumoniae	Atypical pneumonia
5. Bacteria, **Mycobacteria**	Staph. epidermidis Vibrio cholerae Strept.pneumoniae Mycobacterium tuberculosis	Wound infection Cholera Pneumonia Tuberculosis
6. Fungi	Tricophyton spp. Candida albicans Sporothrix schenkii Histoplasma capsulatum	Tinea pedis (Athlete's foot) Thrush Sporotrichosis Histoplasmosis
7. Protozoa	Giardia lamblia Tryponosoma gambiense Tryponosoma cruzi Leishmania donovani	Giardiasis Sleeping sickness Chaga's disease Kala azar
8. Helminthes	Enterobius vermicularis (pin worms)	Enterobiasis

Routes of entry, dissemination & release of microbes from the body

Microbes spread rapidly along the wet epithelial surfaces of the intestine,lung & genitourinary tract & slowly on the dry surfaces of the skin.



Release of microbes from the body

For transmission of diseases, the exit of infectious agents from the host's body is as important as their entry to it. Many of the mechanisms by which infectious microorganism are cleared from infected individual are responsible for their spread from one person to another, including skin shedding, coughing, sneezing, urination & defecation.

How infectious agents cause disease

After breaking host barriers, infectious agents injure cells & cause tissue damage by three general mechanisms

1. Infectious agent can come into contact with or enter host cells & directly cause cell death.
2. Pathogens can
- Release endotoxin or exotoxin that kill cells at a distance
- Release enzymes that degrade tissue components, or
- Damage tissues through ischemic injury.
3. Pathogens can induce host cell responses that may cause additional tissue damage, usually by immune-mediated mechanism.

Mechanisms of virus-induced injury

Viruses damage host cells by entering the cell & replicating at the host's expense.

Viral tropism; this is the tendency of a virus to infect specific cells & not others e.g. Influenza virus infect respiratory epithelial cells, similarly the hepatitis viruses A, B & C.

They have specific viral proteins (ligands) that bind to particular host proteins (receptors), e.g. HIV bind to CD_4 cells (T-helper lymphocytes). Once attached, the entire virus penetrates the cell cytoplasm. Within the cell, the virus uncoats, separating its genome from its structural proteins. Virus then replicates, using enzymes that are distinct for each virus family e.g. reverse transcriptase is used by retroviruses like HIV to generate DNA from their RNA template. Newly synthesized viral genome & capsid proteins are assembled in the nucleus or the cytoplasm & then released.

Mechanisms of Bacterial –Induced Injury

Bacterial damage to host tissue depends on the ability of the bacteria to

1. Adhere to & enter host cells or
2. Deliver toxins.

Bacteria adhere to the host cells by **adhesions**, which are molecules that bind bacteria to host cells. Next, they will inhibit protein synthesis of the target cell. This is followed by multiplication of the bacteria with lysis of the host cells.

Bacterial toxins are of two types

1- Endotoxins

These are lipopolysaccharides that are structural components of the outer cell wall of gram-negative bacteria. ***The biological activities of endotoxins include***

1. Induction of fever

2. Septic shock

3. Acute respiratory distress syndrome

2- Exotoxins

These are secreted proteins that directly cause cellular injury & determine disease manifestations. Examples include

1. ***Diphtheria toxin*** secreted by Corynebacterium diphtheriae. This toxin causes neural & myocardial dysfunction.

2. ***Tetanospasmin,*** which is a toxin secreted by Clostridium tetani that contaminate wound. This toxin causes violent muscular contraction (tetanus)

Exotoxins	Endotoxins
1- Secreted by living bacteria	Released only when bacterium dies (structural elements of bacteria)
2- Simple proteins	Complexes of phospholipids (lipid A), Polysaccharide and protein (cell wall of Gram- negative bacteria)
3-Extremely potent- Gram positive bacteria	Gram- negative bacteria
4- Vary in their biological effects	All have the same biological effects, Their active component resides in Lipid A
5- Antigenically specific and their activity Is usually neutralized by union with antibody	They are antigenically different

Special Techniques for the diagnosis of Infectious agents

Some microorganisms can be seen in H&E-stained sections such as bacterial clumps, inclusion bodies caused by herpes virus, candida, and most protozoa e.g. Entamoebae & all helminthes. However, many microorganisms can only be seen after the application of special techniques or stains.

Technique	Agent(s) detected
1. Gram stain	Most bacteria
2. Acid fast stain	Mycobacteria
3. Sliver stain	Fungi, legionella, pneumocystis
4. Periodic acid-schiff (PAS)	Fungi, amebae
5. Mucicarmine stain	Cryptococci
6. Giemsa stain	Campylobacter, malaria, leishmania
7. Antibody probes	Viruses, rickettsiae
8. Culture	All classes
9. DNA probes	Viruses, bacteria, protozoa