# GENERAL PATHOLOGY OF INFECTIOUS DISEASES

-Infectious diseases are an important health problem in the worldwide despite the availability of effective vaccines and antibiotics for many types of infections .

-In low-income countries, limited access to healthcare, unsanitary living conditions, and malnutrition contribute to a massive burden of infectious diseases .

-Lower-respiratory infections, HIV/AIDS, and diarrheal diseases are the top three causes of death in developing countries, and malaria and tuberculosis are among the top ten .

-Infectious diseases are important causes of death among children, older adults, individuals with chronic debilitating diseases and immunodeficiency states (e.g., AIDS), and in patients receiving immunosuppressive drugs .

-There are a relationships  between microorganisms and humans . without our normal gut flora, we would be at risk for vitamin K deficiency and the normal vaginal flora prevent recurrent Candida ("yeast") infections .

The majority of these relationships are :-

*1-* ***Symbiosis*** (of benefit to both partners) or,

2-***Commensal*** (the microorganisms that live and shares the host's food without causing harm).

*** Pathogens** :- are microorganisms that injure the host .they include bacteria , viruses , fungi , protozoa , and parasites (or worms) .

*** pathogenicity**:- the capacity of the organism to cause disease.

*** Virulence** :- is the degree of pathogenicity .

*** Opportunistic infections**:- the commensal microorganisms become pathogenic in immuncompromised patients.

e.g.

1- E. coli is a normal flora (inhabitant) in GIT but when enter the urinary tract it becomes pathogenic and lead to sever urinary infection .

2- during tooth extraction , heart valves may become infected by Streptococcus viridance which are normal commensal of the mouth . such an infection leads to serious disease (bacterial endocarditis ) .

***infection** :- is the presence of microorganism in a part of the body where its normally absent and where if allowed to multiply ,it stimulate a host immune response and cause infectious disease . the outcome depends on balance between the microorganisms aggressive mechanisms and the host defenses .

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

When microbes cause disease, the nature and extent of the disease depend on (1) the *virulence* (or pathogenicity) of the microorganism and (2) the *response of the host.*

# Host Defenses are divided in to :-

**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 and GIT mucosa. If any one of these barriers is broken , infection may occur e.g. infection are a recognized complication of burns , because the burn 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 micro-organisms that contaminate food and water .
- Lysozyme enzymes secreted by mucous membranes can digest mucopeptide of bacterial cell wall . Its found in lacrimal , salivary , and nasal glands .

**3- Secretion current**

- Continuous secretion of tears prevents conjunctival infection .
- Ciliated respiratory epithelial cells prevent infection . failure of this mechanism permits influenza virus to combine with epithelial cells. Smoking damage to respiratory epithelium predisposing to bacterial infection .
- Increase peristalsis movement of the intestine and diarrhea during intestinal pathogen e.g. salmonella this is a defending mechanism to get ride of the offending bacteria .
- Obstruction of urinary flow lead to stasis of the urine lead to subsequent urinary tract infection this seen in prostatic enlargement and urinary calculi .

**4-Phaocytosis**

- Neutrophils migrate to tonsillar crypts and macrophage migrate in to the alveoli.
- Both engulf particles and micro organisms and prevent invasion .

**B- Specific defenses which are by immune system directed against infectious agents .**

# Categories of infectious agents

Agents that cause infectious diseases range in size from 20-nm poliovirus to the 10-m tapeworm.

| **Taxonomic class** | **Sample Species** | **Related Disease** |
|---|---|---|
| Viruses | Poliovirus | Poliomyelitis |
| Chlamydiae | *Chlamydia trachomatis* | Trachoma, urethritis |
| Rickettsiae | *Rickettsia prowazekii* | Typhus fever |
| Mycoplasmas | *Mycoplasma pneumoniae* | Atypical pneumonia |
| Bacteria | *Staphylococcus aureus*<br>*Vibrio cholera*<br>*Streptococcus pneumonia*<br>*Mycobacterium tuberculosis* | Wound<br>Cholera<br>Pneumonia<br>Tuberculosis |
| Fungi | *Trichophyton* sp. | Tinea pedis (athlete's foot) |
| Protozoa | *Giardia lamblia* | Giardiasis |
| Helminths | *Enterobius vermicularis*<br>*Wuchereria bancrofti*<br>*Trichinella spiralis* | Enterobiasis<br>Filariasis<br>Trichinosis |

# 1-Viruses

Viruses are obligate intracellular organisms that depend on the host cell's metabolic machinery for their replication.

-They consist of a nucleic acid genome surrounded by a protein coat (**called a capsid**) that encased in a lipid membrane.

- Viruses may be classified by their nucleic acid genome (DNA or RNA, but not both), the shape of the capsid (icosahedral or helical), the presence or absence of a lipid envelope , the mode of replication , the preferred host cell type for replication (called tropism), or the type of pathology they cause .

- Some viral particles aggregate within infected cells and form characteristic **inclusion bodies**, which may be seen with the light microscope and are useful for diagnosis for example, **cytomegalovirus** and **herpesviruses** , **smallpox and rabies viruses .** many viruses **(e.g., poliovirus)** do not produce inclusions **.**

- Because viruses are smaller than the limits of light microscopic resolution (20-300 nm in size), they are best visualized by electron microscopy .

**- Viruses can cause illnesses in several ways :-**

*Many viruses cause transient illnesses (e.g., colds, influenza ).

*Other viruses persist within cells of the host for years, either continuing to multiply (e.g hepatitis B virus ) or stay in nonreplicating form **(termed latent infection)** with the potential to be reactivated later . For example, herpes zoster virus, the cause of chickenpox **.**

*Some viruses are transform the host cell into a benign or malignant (e.g., human papillomavirus induced benign warts and cervical carcinoma) .

## 2-Bacteria

Bacteria are prokaryotes means they have a **cell membrane** but lack membrane-bound nuclei and other membrane-enclosed organelles . Most bacteria are bounded by a **cell wall** consisting of peptidoglycan surrounding the cell membrane .

There are two common forms of bacterial cell wall structure: a thick wall surrounding the cell membrane that retains crystal violet stain (Gram-positive) or a thin cell wall sandwiched between two phospholipid bilayer membranes ( these do not retain crystal violet stain and are thus Gram-negative ) .

Bacteria are classified by **Gram staining** (positive or negative) , **shape** (e.g., spherical called cocci ; rod-shaped called bacilli), and their **requirement for oxygen** (aerobic or anaerobic) . Motile bacteria have flagella that long helical filaments extending from the cell surface that rotate and move the bacteria. Some bacteria possess pili , that can attach bacteria to host cells or extracellular matrix .

Many bacteria remain extracellular when they grow in the host, while others survive and replicate either outside or inside of host cells (**facultative intracellular bacteria)** and some grow only inside host cells (**obligate intracellular bacteria** ) .

## 3- Chlamydiae, Rickettsia , and Mycoplasmas

Chlamydia and Rickettsia are obligate intracellular bacteria that replicate inside membrane bound vacuoles in epithelial and endothelial cells, respectively . These bacteria get their energy source, ATP, from the host cell. **Chlamydia trachomatis** is the infectious cause of female sterility and blindness .Rickettsiae injure the endothelial cells , causing ahemorrhagic vasculitis , visible as a rash, but they also may injure the central nervous system (CNS), with potentially fatal outcome, as in **Rocky Mountain spotted fever** and **epidemic typhus**. Rickettsiae are transmitted by arthropod vectors, including lice , ticks and mites .

Mycoplasma are unique among extracellular bacterial pathogens that they do not have a cell wall.

## 4-Fungi

Fungi are eukaryotes that possess thick, chitin-containing cell walls and ergosterol-containing cell membranes. Fungi can grow either as rounded yeast cells or as slender, filamentous hyphae .

Fungi may cause superficial or deep infections.

***Superficial infections** typically involve the skin, hair, or nails. Fungal species that cause superficial infections are called **dermatophytes**. Infection of the skin is called **tinea** such tinea pedis is “athlete’s foot” and a tinea capitis is scalp ringworm. Certain fungi invade the subcutaneous tissue, causing abscesses or granulomas sometimes called **mycetomas** **.**

***Deep fungal infections** can spread systemically and invade tissues, destroying vital organs in immunocompromised hosts, but usually resolve or remain latent in normal hosts.

## 5-Protozoa

Protozoa, single-celled eukaryotes that are major causes of disease and death in developing countries. The protozoa can replicate

- **Intracellularly** in many cell types (e.g., Plasmodium in erythrocytes , Leishmania in macrophages) or

- **Extracellularly** in the urogenital system, intestine, or blood. **urogenital system** is Trichomonas vaginalis is a sexually transmitted protozoan that can colonize in female vagina and male urethra .

The most prevalent **intestinal protozoans** is Entamoeba histolytica and Giardia lamblia *are ingested as nonmotile cysts in contaminated food or water and become motile trophozoites that attach to intestinal epithelial cells .*

**Blood-borne protozoa** (e.g., Plasmodium, Trypanosoma, and Leishmania) replicate within insect vectors before transmission to new human hosts .

Toxoplasma gondii is acquired either through contact with oocyst-shedding kittens or by eating cyst-ridden, undercooked meat .

## 6-Helminths

Parasitic worms are highly differentiated multicellular organisms with complex life cycles; most alternate between sexual reproduction in the definitive host and asexual multiplication in an intermediary host or vector. depending on the species, humans may harbor adult worms (e.g., Ascaris lumbricoides), immature forms (e.g., Toxocara canis), or asexual larval forms (e.g., Echinococcus species).

Helminths comprise three classes :

- Roundworms (nematodes)
-Flatworms (cestodes)
-Flukes (trematodes)

## 7- Ectoparasites

Ectoparasites are insects (lice, bedbugs, fleas) , or arachnids ( mites, ticks, spiders) that cause disease by biting or by attach to and live on or in the skin .

At the site of bites, mouth parts may be found with infiltrate of lymphocytes, macrophages, and eosinophils .

These parasites may produce disease by direct tissue damage or indirectly by serving as the vectors for transmission of infectious agents.

**Routes of Entry of Microbes**

Microbes can enter the host through breaches in the skin , by inhalation or ingestion, or by sexual transmission .

**Spread and Dissemination of Microbes within the Body**

Some microorganisms proliferate locally, at the site of initial infection, whereas others penetrate the epithelial barrier and spread to distant sites by way of the lymphatics , the blood, or nerves .

**Microbes can spread within the body in several ways :-**

**1-Lysis and invasion** Some extracellular organisms secrete lytic enzymes which destroy tissue and allow direct invasion. For example, S. aureus secretes hyaluronidase , which degrades the extracellular matrix between host cells .

**2-Through blood and lymph** Some microorganisms may be spread either in extracellular fluid or within host cells or transported in the plasma .

**3- Cell-to-cell transmission**. some organisms as viruses spread locally from cell to cell by replication and release of infectious virions .

but others may propagate from cell to cell by causing fusion of host cells, or by transport within nerves ( rabies virus and varicella-zoster virus).

Microbes spread rapidly along the wet epithelial surfaces of intestine ,lung and genitourinary tract and slow on the dry surface of the skin .

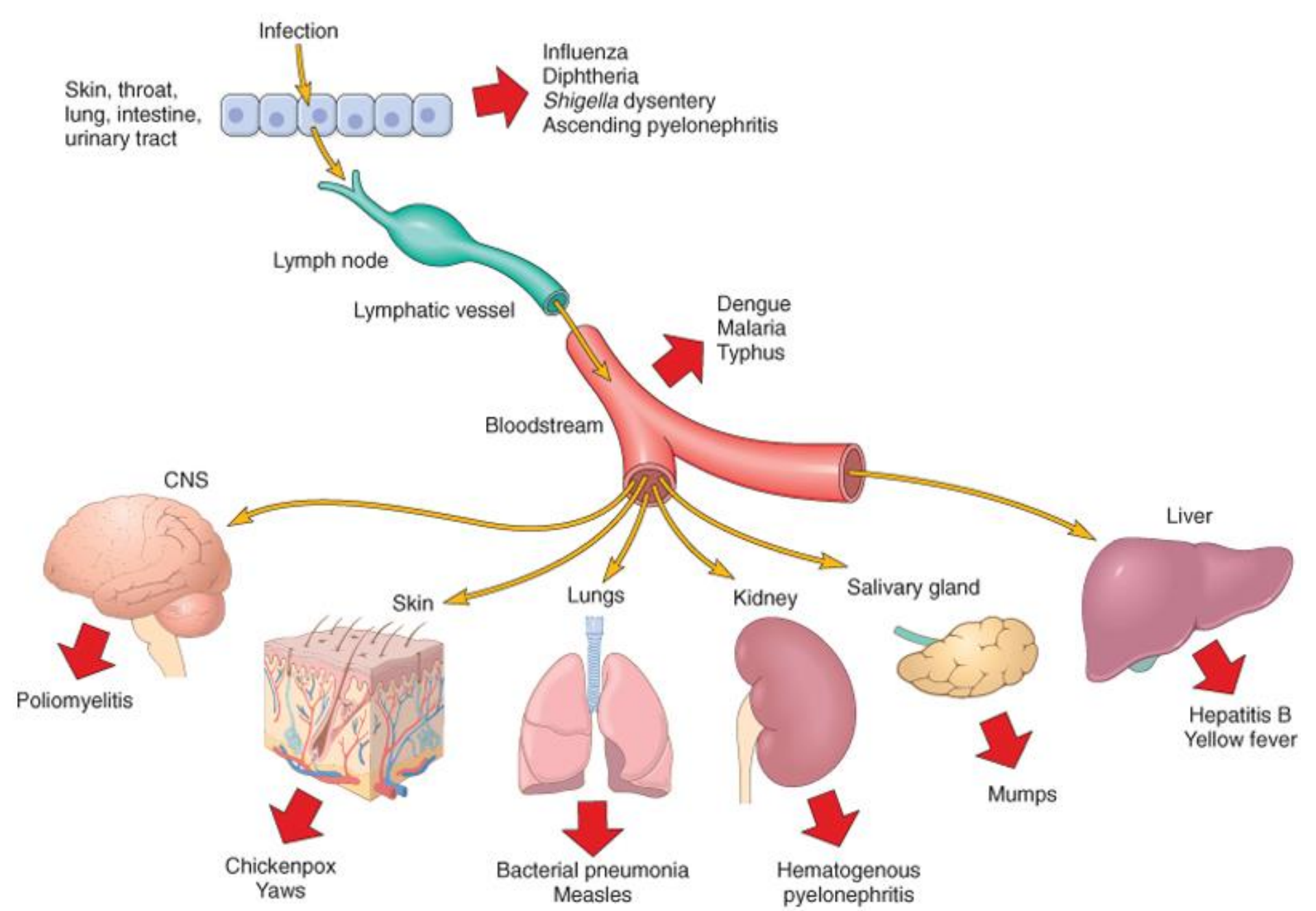




Figure 9-4 Entry and dissemination of microbes. (Adapted from Mims CA: The Pathogenesis of Infectious Disease. Orlando, Academic Press, 1987.)

**Transmission of microbes**

For transmission of disease , the mode of exit of microorganisms from the host is as important as the original entry.

Transmission may occur through skin , oral secretion, respiratory secretion , stool, blood , urine , genital tract and vertical transmission (Transmission of infectious agents from mother to fetus ).

Some pathogens may be spread even though the host is asymptomatic .

**Microorganisms can be transmitted** from person to person, by direct contact.

**Transmission** of microbes from animals to humans (**called zoonotic infections**), either by direct contact with or by eating the infected animal products or indirect by an invertebrate vector such as insects (i.e., mosquitoes ) , ticks, or mites that either spread infection or occasionally serve as hosts for microbial replication and development .

**How microorganisms cause disease**

Infectious agents establish infection and damage tissues by any of three mechanisms :-

1- infectious agent can contact with or enter host cells and directly cause death of cell .

2-infectious agent can

- release toxins that kill cells at a distance .

- release enzymes that degrade tissue components, or damage blood vessels and cause ischemic necrosis .

3- infectious agent can induce host immune responses that may cause additional tissue damage .

# Mechanisms of Viral Injury

Viruses can directly damage host cells by entering them and replicating . The manifestations of viral infection are determined by the tropism of the virus for specific tissues and cell types .

**Viral tropism** is tendency of a virus to infect certain cells and not others e.g influenza virus infect respiratory epithelial cells . similarly hepatitis A , B, and C virus infect liver .

Viral tropism is determined by several factors :-

**1-Host-cell receptors for virus.** Viruses possess specific surface proteins ( ligand ) that bind to host cell surface proteins (receptor) . Many viruses enter the cells by use normal host cell receptors . Thus, HIV gp120 binds to CD4 ( T helper lymphocytes) .

**2- Physical characteristics of host tissues.** Host environment such as chemicals and temperature, contribute to tissue tropism **.** For example ,

-**Enteroviruses** replicate in the intestine because they can resist inactivation by acids, bile, and digestive enzymes .

**-Rhinoviruses** infect cells only within the upper-respiratory tract because they replicate optimally at the lower temperatures characteristic for this site .

## Viruses can kill host cells in several ways:-

**1- Direct cytopathic effects .** Viruses can kill host cells by preventing synthesis of critical host macromolecules, by producing degradative enzymes and toxic proteins, or by inducing apoptosis .

**2- Anti-viral immune responses.** Viral proteins expressed on host cell surfaces are recognized as foreign by the immune system and T lymphocytes may attack virus-infected cells .

**3- *Transformation of infected cells* into benign or malignant tumor cells.** Different oncogenic viruses (Human PapillomaViruses HPV and Epstein-Barr virus ) can stimulate cell growth .

**4-Inhibition of host cell DNA, RNA, or protein synthesis**. they may cause cell death, or they may lead to cellular dysfunction .

**5- Damage to plasma membranes**. Viral proteins can insert into host plasma membranes and thereby alter their integrity .

**6-Damage the cells involved in antimicrobial defense**, leading to secondary infections. For example, viral damage to respiratory epithelium predisposes to subsequent bacterial pneumonia, and HIV depletion of CD4+ helper T lymphocytes leads to opportunistic infections .

**Mechanisms of Bacterial Injury**

Bacterial damage to host tissues depends on :-

(1)the ability of bacteria to adhere to host cells,

(2) their ability to invade cells and tissues,

(3) their ability to deliver toxins that damage cells and tissues .

Bacteria adhere to the host cells by adhesion molecules called **adhesins** , which are molecules that bind bacteria to host cells or extracellular matrix , next they will inhibit protein synthesis of target cell. This followed by multiplication of bacteria with lysis of host cells .

**Bacterial toxins :-** Any bacterial substance that contributes to illness can be considered **a toxin are two types:-**

**1- Endotoxin** is a lipopolysaccharide that is a major component of the outer cell wall of gram-negative bacteria.

**The biological activity of endotoxins include :-**

1- induction of fever.

2- septic shock .

3-acute respiratory distress syndrome

4- disseminated intravascular coagulation

**2-Exotoxins** are secreted proteins that directly cause cellular injury and disease are include :-

**1-Enzymes. Bacteria secrete enzymes (proteases, hyaluronidases, coagulases, fibrinolysins).**

**2-Superantigens**

**3-Neurotoxins Clostridium botulinum and Clostridium tetani inhibit release of neurotransmitters, resulting in paralysis.**

**4-Enterotoxins affect the gastrointestinal tract causing nausea and vomiting**

| **Exotoxins** | **Endotoxins** |
| --- | --- |
| 1- Secreted by living bacteria | 1-Released when the bacteria dies |
| 2- Simple protein | 2-Polysaccharide and protein |
| 3- Produced by Gram positive bacteria | 3- Produced by Gram negative bacteria |
| 4- Vary in their biological effects | 4-Have the same biological effects |

**Immune evasion by microbes**

The micro organism escapes humeral and cellular immune responses of the host by :-

**1-Remaining inaccessible** (e.g. residing within the host cells) .

**2- Antigenic variation.** Some microbes can evade immune responses by varying the antigens they express. microbes use many strategies that involve genetic mechanisms for generating antigenic variation.

**3- Antimicrobial peptides,** including **defensins , cathelicidins**, These peptides bind the bacterial membrane and form pores, lead to killing the bacterium . Some Bacterial avoid killing by making surface molecules that resist binding of antimicrobial peptides.

4-The carbohydrate capsule on the surface of many bacteria makes them resistant to phagocytosis also the Proteins on the surface of bacteria include as proteins A and M inhibit phagocytosis by killing phagocytic cells .

**5- Suppressing the host immune response** (e.g., by inhibiting MHC expression and antigen presentation )

## Inflammatory Responses to Infection

### 1-Mononuclear and Granulomatous Inflammation

Diffuse mononuclear infiltrates are a common feature of all chronic inflammatory processes in response to viruses , intracellular bacteria, or intracellular parasites. In addition helminths provoke chronic inflammatory responses .

### 2-Cytopathic-Cytoproliferative Response

These reactions are usually produced by viruses . The lesions are characterized by cell necrosis or cellular proliferation, usually with sparse inflammatory cells.

### 3-Necrotizing Response

Clostridium perfringens and other organisms secrete powerful toxins can cause rapid and severe necrosis and tissue damage is the dominant feature.

### 4-Chronic inflammation and scarring

Many infections cause chronic inflammation, which can either resolve with healing or lead to scarring.