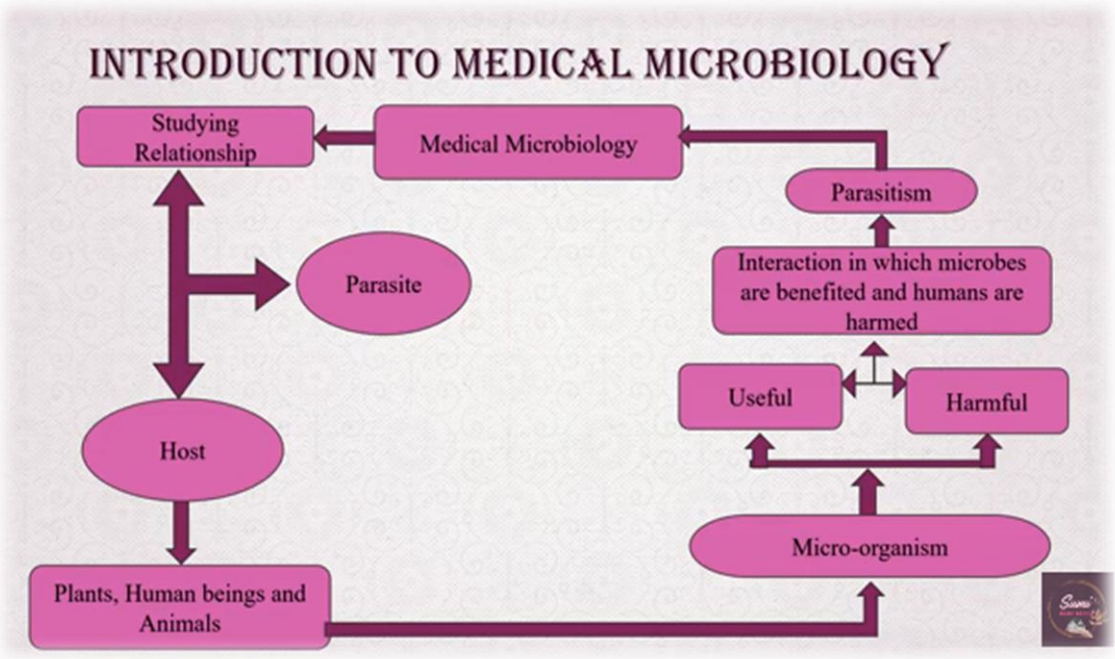
Introduction to Medical Microbiology



A. What is Medical Microbiology?

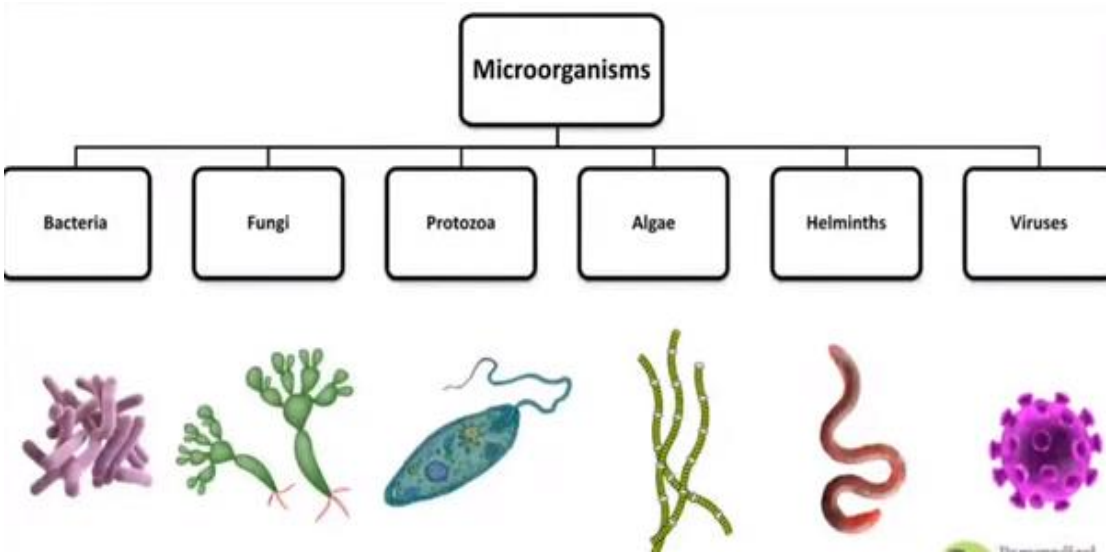
Medical Microbiology is an integrative scientific discipline that applies the principles of microbiology to medical practice, focusing on microbial pathogens and their impact on human health. the scope of this field encompasses four cornerstone activities that define the life cycle of an infectious disease:

1. **Pathogenesis:** The study of the molecular and cellular mechanisms by which microbes cause disease. This involves understanding virulence factors and their interaction with host defenses.
2. **Diagnosis:** The development and use of rapid, accurate laboratory methods to identify the causative agent. This includes bacterial culture, microscopy, serological tests, and molecular techniques like **Polymerase Chain Reaction (PCR)**.
3. **Treatment:** The study of antimicrobial agents (antibiotics, antiviral, antifungal) and their mechanisms of action, coupled with predicting their efficacy through susceptibility testing and monitoring the emergence of **Antimicrobial Resistance (AMR)**, which the World Health Organization (WHO) cites as one of the top global public health threats.

4. **Prevention:** The development and implementation of strategies to prevent the spread of infection, including vaccination programs, hospital infection control, and public health measures.

B. Classification of Microorganisms of Medical Importance:

Clinicians classify pathogens into four main groups, each requiring distinct diagnostic and therapeutic approaches:



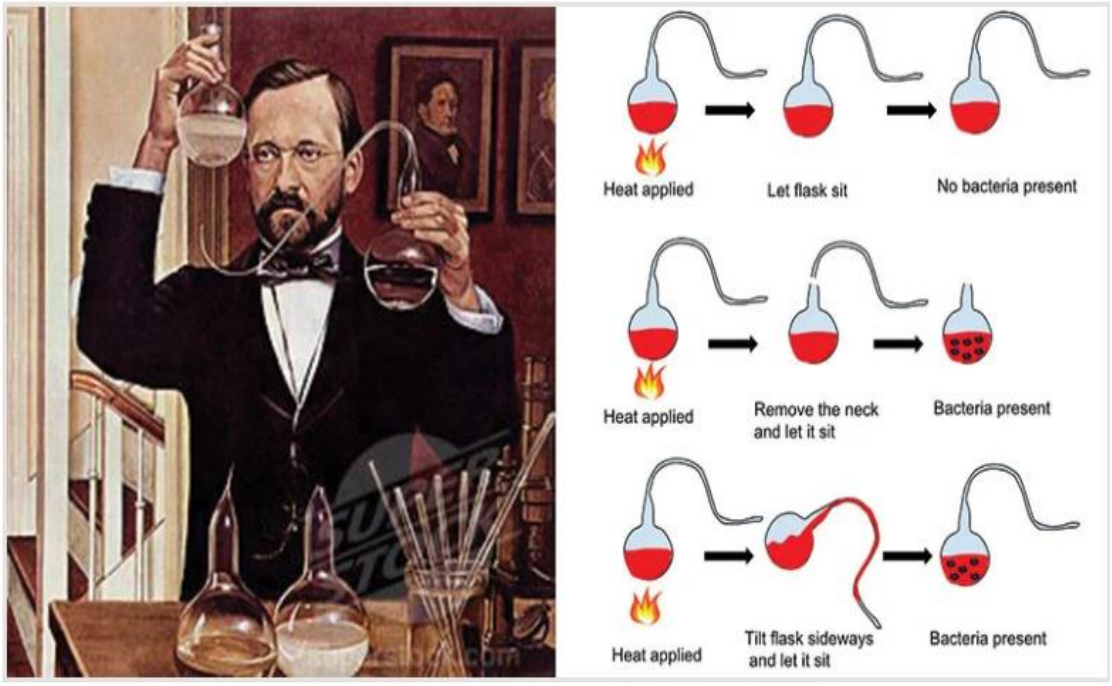
1. **Bacteria:** Single-celled, **prokaryotic** organisms (lacking a membrane-bound nucleus). They reproduce by binary fission. They are classified based on Gram stain, morphology, and metabolic requirements.
2. **Viruses: Acellular, obligate intracellular parasites**. They consist of genetic material (DNA or RNA) surrounded by a protein coat (capsid). They cannot replicate outside a host cell.
3. **Fungi: Eukaryotic** organisms (with a true nucleus) with chitin in their cell walls. They include yeasts (unicellular) and molds (multicellular).
4. **Parasites: Eukaryotic** organisms that live at the expense of the host. They are divided into:

- **Protozoa:** Unicellular, motile organisms (e.g., *Plasmodium* spp. causing malaria).
- **Helminths:** Multicellular worms (e.g., tapeworms, roundworms).

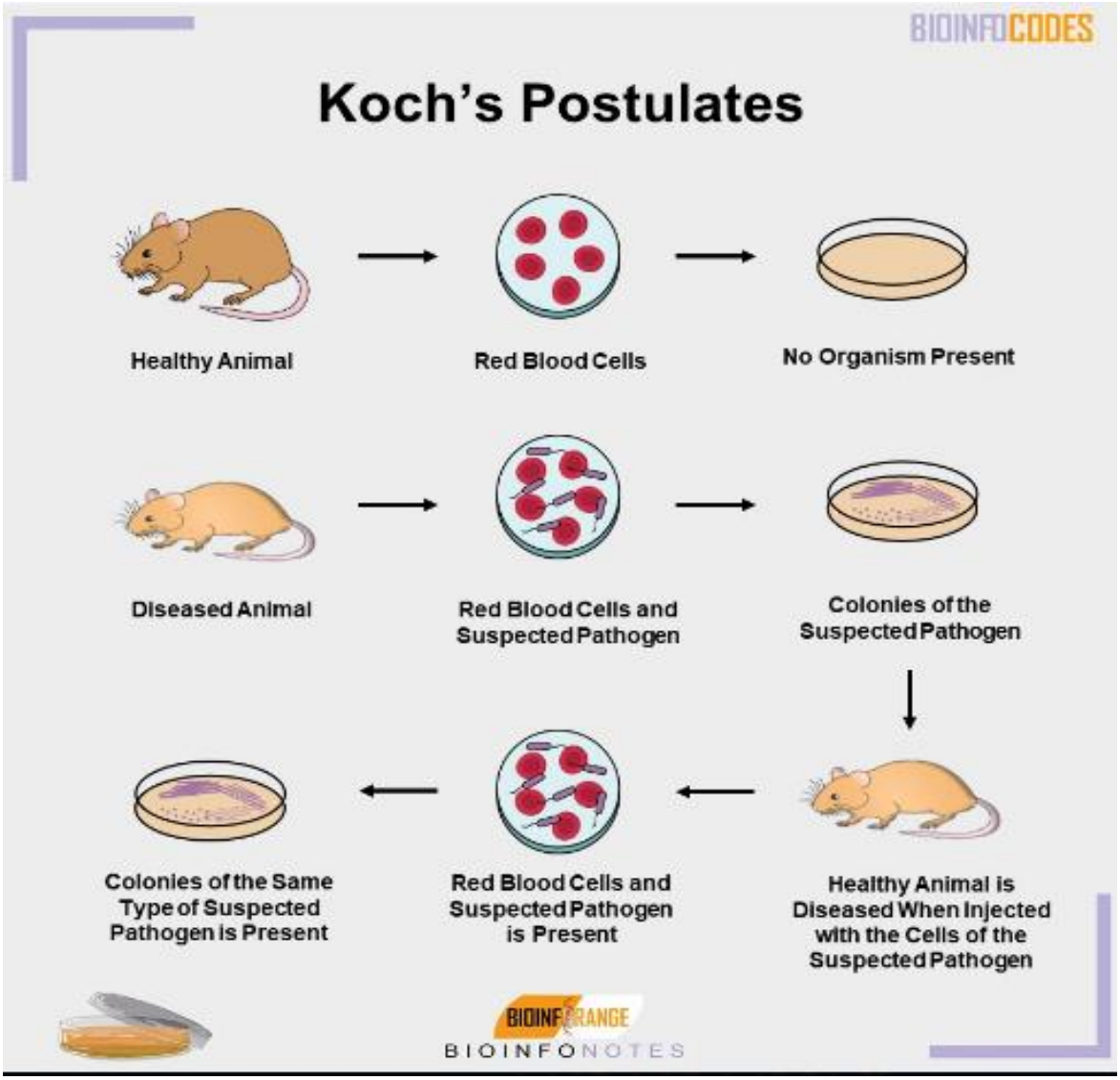
Historical Significance

The **Germ Theory of Disease** was a pivotal paradigm shift in medical history, replacing ancient theories like the miasma theory or spontaneous generation. Below are the contributions of key scientists in greater scientific detail:

- **Louis Pasteur (1822-1895):** Beyond disproving spontaneous generation, Pasteur established the concept of **"aseptic technique"** and demonstrated that fermentation and putrefaction were caused by microbes from the air. He developed **pasteurization** for food preservation. In immunology, he developed attenuated (weakened) vaccines against **anthrax** and **rabies**, ushering in the modern era of immunology.



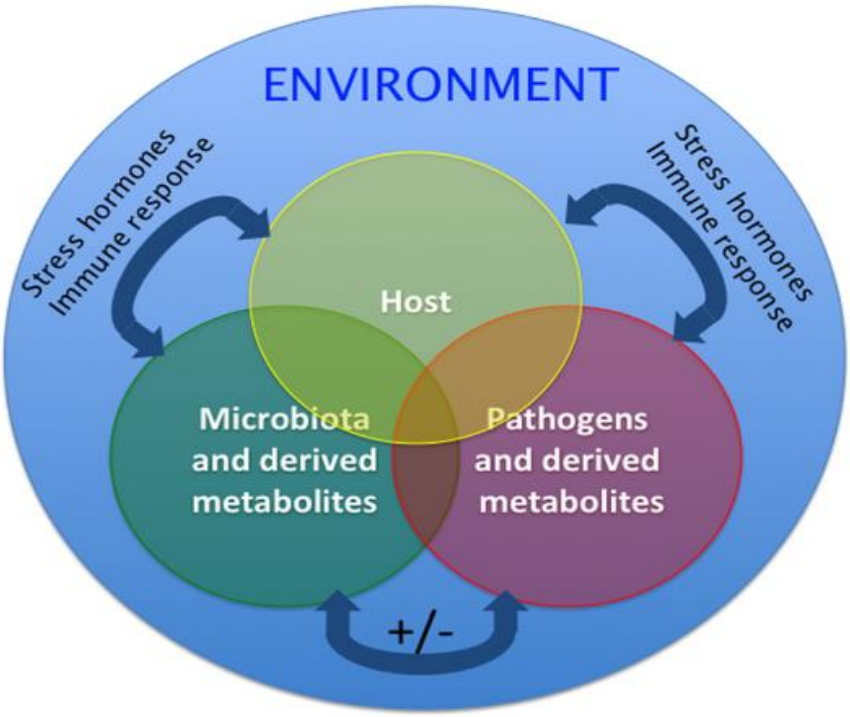
- **Robert Koch (1843-1910):** Established **"Koch's Postulates,"** which provided a rigorous methodological framework to prove a causal relationship between a specific microbe and a specific disease. In his laboratory, he developed fundamental techniques still used today, such as **bacterial staining** and methods for **culturing bacteria on solid media** (like agar). He received a Nobel Prize for discovering the **tubercle bacillus**.



- **Limitations of Koch's Postulates in the Modern Era:** While Koch's Postulates remain foundational, scientific progress has revealed their limitations in several scenarios, including:
  - **Uncultivable Pathogens:** Such as Hepatitis B virus or the slow-growing *Mycobacterium tuberculosis*.
  - **Asymptomatic Carriers:** Where an individual harbors the microbe without showing disease (e.g., carriers of *Salmonella Typhi*).
  - **Multifactorial Diseases:** Resulting from the interaction of multiple microbes or between a microbe and a host's genetic predisposition.
- **Beyond Koch and Pasteur:** The discoveries of **Alexander Fleming (Penicillin)** and **Joseph Lister (Antiseptic Surgery)** led to a dramatic reduction in mortality from infections, paving the way for 20th-century medicine.

The Microorganism-Host Interaction

Pathogenesis cannot be understood without appreciating the ecological context in which microbes interact with the human body. This relationship is a spectrum, not a binary state of disease or no disease.



1. Normal Human Microbiota (Normal Flora):

This term refers to the complex microbial communities that permanently colonize the human body. Recent research, the number of microbial cells in the human body is roughly comparable to the number of human cells, making it a virtual "organ" with vital functions:

- **Protective Functions:**
  - **Competition for Space and Nutrients:** The normal microbiota competes with pathogens for adhesion sites on epithelial cells and for nutrient sources, a mechanism known as **"Microbial Antagonism."** Example: *Lactobacillus* in the vagina inhibits the growth of *Candida albicans*.
  - **Production of Antimicrobial Substances:** Some microbiota produce antibiotic-like substances (Bacteriocins) that kill closely related strains.
- **Developmental and Immunological Functions:**
  - The normal microbiota stimulates the development of **Gut-Associated Lymphoid Tissue (GALT)**, a primary immune defense line.

- It helps "educate" the immune system to distinguish between harmless antigens (food, commensals) and harmful ones (pathogens), reducing the incidence of allergic and autoimmune diseases.

- **Metabolic Functions:**
  - They ferment indigestible dietary fibers to produce Short-Chain Fatty Acids (e.g., Butyrate), which nourish colon cells.
  - They synthesize Vitamin K and B vitamins like Biotin.

2. Transient Colonization: This is the temporary presence of microbes on the body (from the environment) that does not lead to permanent colonization due to competition from the normal microbiota or physiological defense mechanisms (like stomach acidity or respiratory ciliary movement).

3. Infection vs. Disease:

It is crucial to distinguish between these two concepts:

- **Infection:** The entry and multiplication of a microbe within a host. **Infection does not necessarily lead to disease.** Many infections are **subclinical**.
- **Disease:** The tissue or functional damage resulting from infection, accompanied by clinical signs and symptoms.

The transition from infection to disease depends on a **delicate balance between three factors**, as illustrated by the "**Epidemiologic Triangle**":

1. The **virulence and number** of the pathogen.
2. The **susceptibility and immune status** of the host.
3. The **environment** (e.g., malnutrition, stress, vector presence).

Molecular Mechanisms of Microbial Virulence

Virulence is a quantitative measure of the severity of disease caused by a microbe. Virulence is achieved through **"Virulence Factors,"** which are genetic traits that enable a microbe to cause disease. They can be categorized by function:

1. Attachment and Invasion:

- **Adhesins:** Molecules on the microbe's surface (e.g., **Pili**, **Fimbriae**, surface proteins) that bind to specific receptors on host cells. This specific binding is the critical first step in establishing infection. Example: Pili of

Uropathogenic *E. coli* (UPEC) that bind to **uroplakin** receptors on uroepithelial cells.

- **Invasion Factors:** Enable the microbe to penetrate tissue barriers. Example: The enzyme **Hyaluronidase** breaks down hyaluronic acid in connective tissue, known as a "spreading factor." Similarly, **Coagulase** enzymes form a blood clot that protects bacteria from the immune system.

2. Immune Evasion:

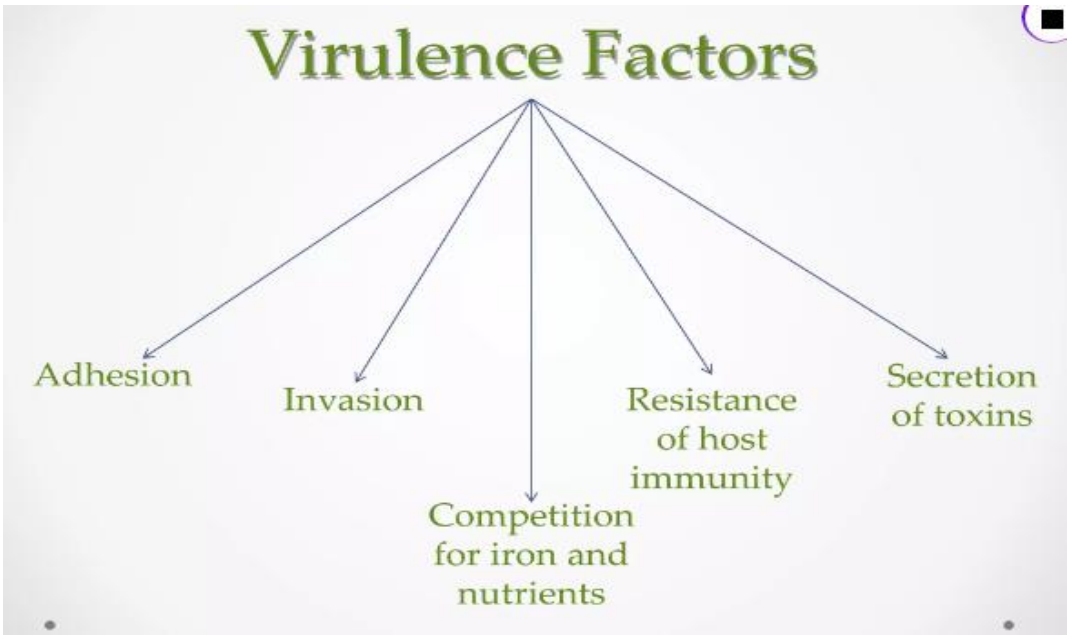
- **Capsule:** A polysaccharide layer surrounding the cell wall of some bacteria (e.g., *Streptococcus pneumoniae*, *Bacillus anthracis*). The capsule prevents **phagocytosis** by white blood cells by inhibiting recognition by phagocytic receptors.
- **Antigenic Variation:** The microbe's ability to periodically change its surface proteins to avoid recognition by antibodies the host produced in a previous infection. This is highly evolved in **Influenza virus** (antigenic drift/shift) and the parasite ***Trypanosoma brucei***.
- **Intracellular Survival:** Some microbes (e.g., *Mycobacterium tuberculosis*, *Legionella pneumophila*) are engulfed by phagocytes but develop mechanisms to survive and multiply inside these cells, using them as a "Trojan horse" for dissemination.

3. Toxins: These are virulence factors that cause direct damage to the host. They are divided into two main classes:

- **Exotoxins:**
  - **Nature:** Potent proteins **secreted** by living bacteria (both Gram-positive and Gram-negative).
  - **Effect:** Often highly specific, affecting particular cellular functions.
  - **Examples:**
    - **Neurotoxins:** Such as Tetanospasmin (from *Clostridium tetani*), which blocks inhibitory neurotransmitter release, causing muscle spasms. Botulinum toxin (Botox) causes flaccid paralysis.
    - **Enterotoxins:** Such as Cholera toxin (from *Vibrio cholerae*), which triggers massive secretion of water and electrolytes into the intestine, causing profuse watery diarrhea.
- **Endotoxins:**
  - **Nature:** Not proteins, but a component of the **Lipopolysaccharide (LPS)** found **exclusively in the outer membrane of Gram-negative bacteria**.
  - **Release:** Released when the bacterium lyses (dies), divides, or is attacked by antibiotics.

- **Effect:** Cause generalized, non-specific systemic responses. They bind to **TLR4 receptors** on immune cells, triggering the release of potent inflammatory **cytokines** like **TNF-α** and **IL-1**, leading to:

- **Fever**
- **Hypotension** (low blood pressure)
- **Disseminated Intravascular Coagulation (DIC)**
- **Septic Shock**, a life-threatening condition.



What Are Pathogens?

Scientific Definition: Pathogens are biological agents capable of causing disease in a host organism. These agents include microorganisms (bacteria, viruses, fungi, protozoa) and more complex parasitic organisms (helminths), as well as non-cellular agents like prions.

1. Bacteria: Prokaryotic Pathogens

1.1 Fundamental Characteristics

Cellular Structure:

- Prokaryotic cells lacking membrane-bound organelles
- Typical size: 1-10 micrometers
- Cell wall containing peptidoglycan
- 70S ribosomes
- Circular chromosomal DNA + accessory plasmids

Classification Systems:

- **Gram stain classification:**
  - Gram-positive: Thick peptidoglycan layer
  - Gram-negative: Thin peptidoglycan layer with outer membrane
- **Shape-based classification:**
  - Cocci (spherical)
  - Bacilli (rod-shaped)
  - Spiral forms

1.2 Bacterial Pathogenesis

Virulence Factors:

- **Adhesion factors:** Pili, fimbriae, adhesion proteins
- **Invasion factors:** Enzymes facilitating tissue penetration
- **Toxins:**

- Exotoxins: Secreted proteins (e.g., tetanus, cholera toxins)
- Endotoxins: LPS components of gram-negative cell walls

- **Immune evasion mechanisms:**

- Capsules preventing phagocytosis
- Antigenic variation
- Biofilm formation

1.3 Clinical Significance

Major Bacterial Pathogens:

- **Gram-positive pathogens:**

- Staphylococcus aureus (skin infections, MRSA)
- Streptococcus pneumoniae (pneumonia, meningitis)

- **Gram-negative pathogens:**

- Escherichia coli (UTIs, gastroenteritis)
- Pseudomonas aeruginosa (opportunistic infections)

2. Viruses: Obligate Intracellular Parasites

2.1 Fundamental Characteristics

Basic Structure:

- Non-cellular entities, 20-300 nanometers
- Nucleic acid core (DNA or RNA)
- Protein capsid
- Some possess lipid envelopes
- No independent metabolism

Classification:

- **By nucleic acid:**
  - DNA viruses (e.g., Herpesviruses, Poxviruses)
  - RNA viruses (e.g., Influenza, HIV)
- **By structure:**
  - Enveloped viruses
  - Non-enveloped viruses

2.2 Viral Replication Cycle

Stages of Infection:

1. **Attachment:** Binding to specific host cell receptors
2. **Entry:** Membrane fusion or endocytosis
3. **Uncoating:** Release of viral nucleic acid
4. **Replication:** Synthesis of viral components
5. **Assembly:** Formation of new virions
6. **Release:** Budding or cell lysis

2.3 Viral Pathogenesis

Mechanisms of Cellular Damage:

- Direct cytopathic effects
- Immune-mediated damage
- Transformation to malignant cells
- Latent and persistent infections

Host Response:

- Innate immune responses (interferons, NK cells)
- Adaptive immune responses (antibodies, CTLs)
- Immunopathological reactions

Comparative Analysis: Bacteria vs. Viruses

Characteristic	Bacteria	Viruses
Cell Structure	Prokaryotic cells	Non-cellular
Size	1-10 micrometers	20-300 nanometers
Genetic Material	DNA + plasmids	DNA or RNA
Reproduction	Binary fission	Host-dependent
Metabolism	Independent	None
Ribosomes	70S	Absent
Antibiotic Sensitivity	Yes	No

3. Fungi: Eukaryotic Pathogens

Main Forms:

Form	Characteristics	Examples
Yeasts	Single-celled, reproduce by budding	Candida albicans
Filamentous Fungi	Multicellular, form hyphae	Aspergillus species
Dimorphic Fungi	Transition between forms depending on conditions	Histoplasma species

Pathogenic Factors:

- Ability to grow at 37°C
- Production of keratin-degrading enzymes
- Morphological transition from yeast to filamentous form
- Resistance to phagocytosis

4. Parasites: From Protozoa to Helminths

A. Protozoan Parasites:

Type	Characteristics	Diseases
Flagellates	Move using flagella	African Sleeping Sickness
Amoebae	Move using pseudopodia	Amoebic Dysentery
Ciliates	Move using cilia	Balantidiasis

B. Helminth Parasites:

Type	Characteristics	Diseases
Nematodes	Cylindrical, non-segmented body	Ascariasis, Filariasis
Platyhelminths	Flat, segmented body	Schistosomiasis, Liver Flukes

Microbial Taxonomy

- **Systematics:** is the term used to define the study of the diversity of life and the relationships between organisms.
- **Taxonomy:** tends to be restricted to the theory and practice of classifying organisms.
- **Classification:** attempts to group organisms according to their similarity.
- **TAXON:** A group or category of related organisms.

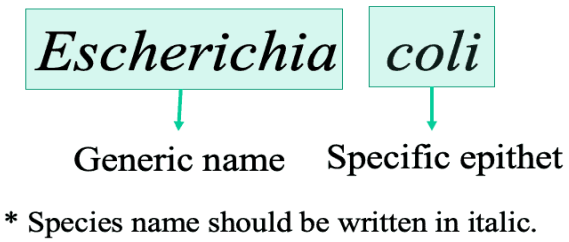
There are two key characteristics of taxa:

1. Members of lower-level taxa (e.g., Species) are more similar to each other than are members of higher-level taxa (e.g., Kingdom or Domain).
2. Members of specific taxa are more similar to each other than any are to members of different specific taxa found at the same hierarchical level (e.g., Humans are more similar to apes – a comparison between species – than either is similar to, for example, *Escherichia coli*). Thus, once you know that two individuals are members of the same **taxon**, you can infer certain similarities between the two organisms.

Binomial Nomenclature

- Organisms are named using binomial nomenclature (viruses are exceptions).
- Binomial nomenclature employs the names of the two-level taxa, **Genus** and **Species**, to name a species.
- Binomial nomenclature includes the following rules:
  i. Genus comes before species (e.g., *Escherichia coli*).
- ii. Genus name is always capitalized (e.g., *Escherichia*).
- iii. Species name is never capitalized (e.g., *coli*).

- iv. Both names are always either *italicized* or underlined (e.g., *Escherichia coli*).
- v. The genus name may be used alone, but not the species name (i.e., saying or writing "*Escherichia*" alone is legitimate while saying or writing "*coli*" is not).



* Species name should be written in italic.

Example of Bacterial Hierarchical Classification:

- **Domain:** Bacteria
- **Kingdom:** Bacteria
- **Phylum/Division:** Proteobacteria
- **Class:** Zymobacteria
- **Order:** Enterobacterales
- **Family:** Enterobacteriaceae
- **Genus:** *Escherichia*
- **Species:** *coli*
- **Scientific name:** *Escherichia coli*

Bacteria

Bacteria are single-celled prokaryotic microorganisms, and their DNA is not contained within a **separate nucleus** as in **eukaryotic** cells. They are approximately 0.1–10.0 µm in size and exist in various shapes, including **spheres (cocci)**, **curves**, **spirals**, and **rods (bacilli)**.

Bacterial Classification

Bacterial classification depends on the following characteristics:

1. Morphology and arrangement
2. Staining
3. Cultural characteristics
4. Biochemical reactions
5. Antigenic structure
6. Base composition of bacterial DNA.

The morphology and staining of bacteria are the commonly used characteristics to classify bacteria.

Morphology of Bacteria

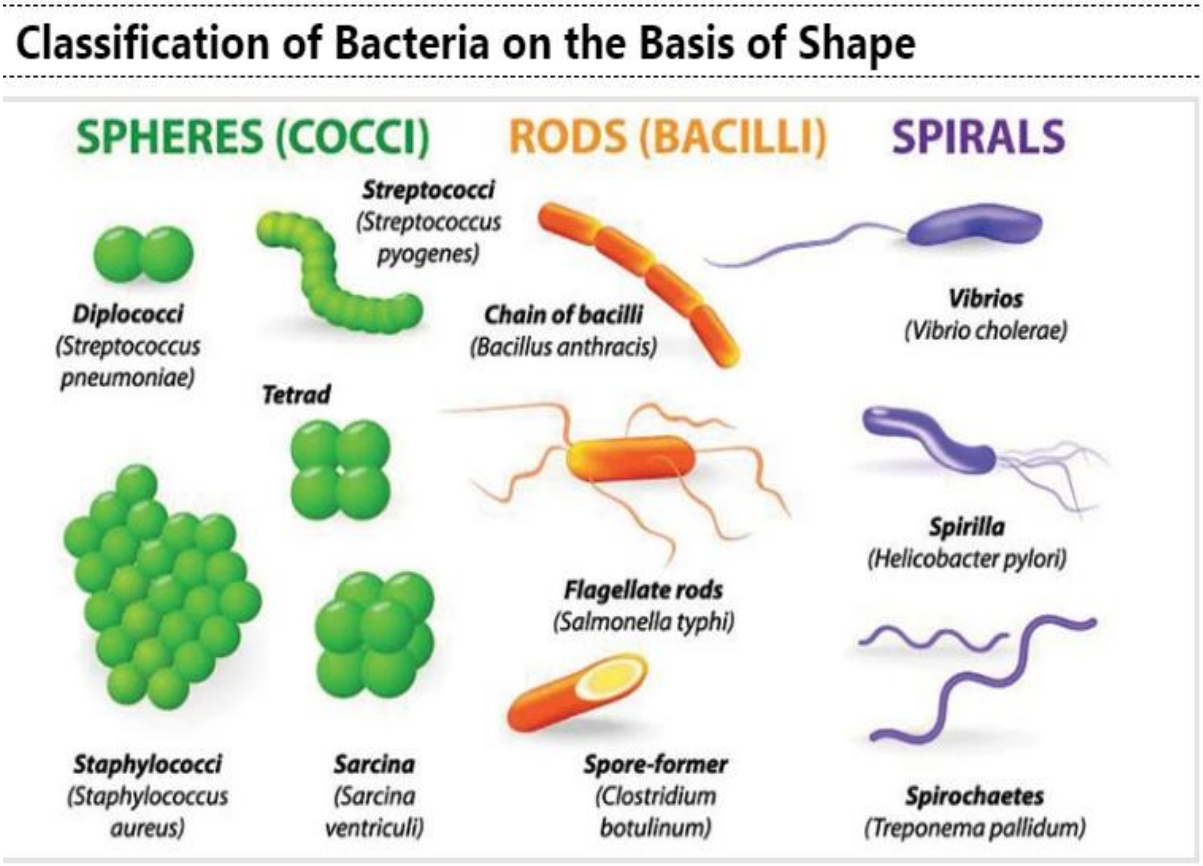
When bacteria are visualized under a light microscope, the following morphologies are seen:

1. **Cocci (singular coccus):** Round or oval bacteria measuring about 0.5-1.0 µm in diameter. They are found as single cells, in pairs, chains, or clusters.
2. **Bacilli (singular bacillus):** Stick-like bacteria with rounded, tapered, square, or swollen ends; with a size measuring 1-10 µm in length by 0.3-1.0 µm in width.
3. **Coccobacilli (singular coccobacillus):** Short rods.
4. **Spiral:** Spiral-shaped bacteria with regular or irregular distances between twists. E.g., Spirilla and spirochetes.

Depending on the arrangement, bacteria can be classified into:

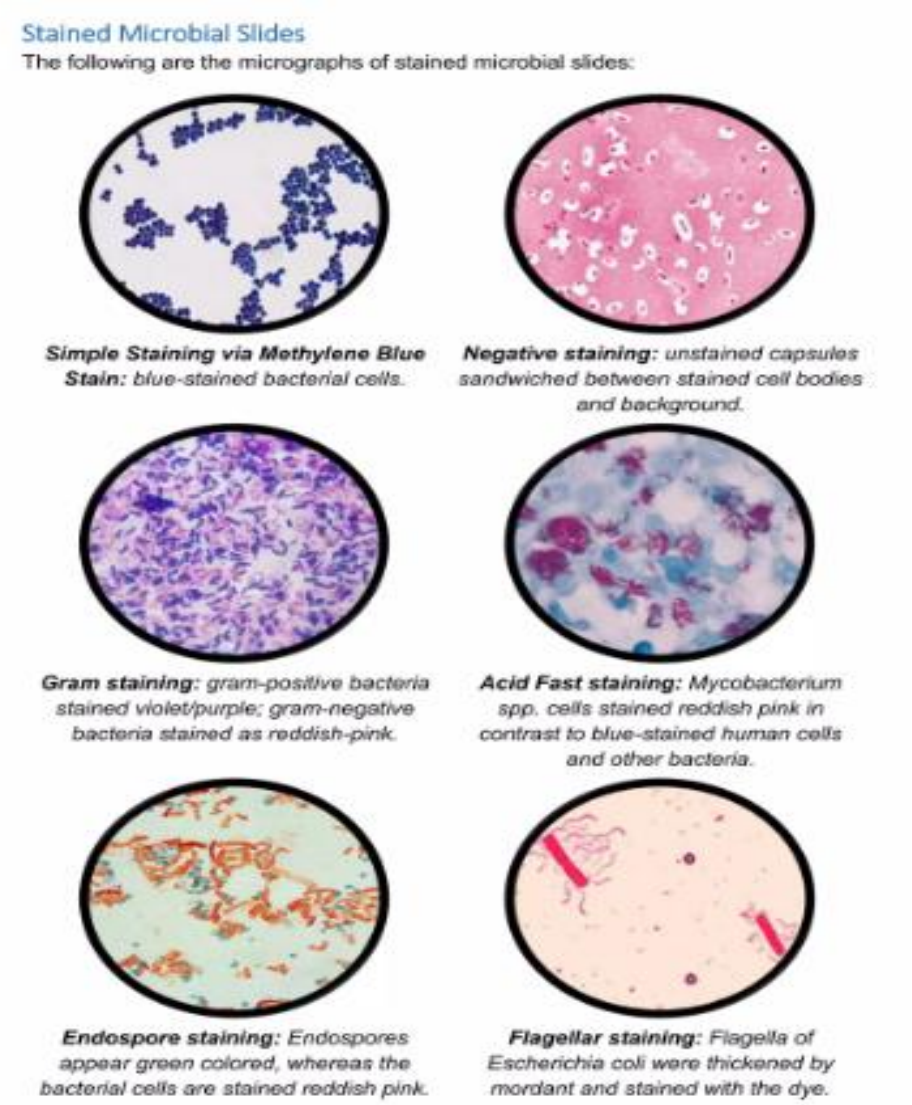
- **Single cell** (coccus, bacillus, and curved or spiral)

- **Diplococci:** Cocci arranged in pairs.
- **Streptococci:** Cocci arranged in chains.
- **Staphylococci:** Cocci arranged in clusters.
- **Streptobacilli:** Bacilli arranged in chains.
- **Tetrads:** Cocci arranged in groups of four cells.
- **Cubic:** Cocci arranged in a cube-like structure.



Staining of Bacteria

- Bacterial staining is the process of coloring colorless bacterial structural components using stains (dyes).
- Staining reactions are made possible because of the physical phenomena of capillary osmosis, solubility, adsorption, and absorption of stains or dyes by cells of microorganisms.



Types of Microbiological Stains:

- **Basic stains**
- **Acidic stains**
- **Neutral stains.**

Bacterial Staining Methods include:

- **Simple stain** (e.g., Methylene blue stain)
- **Differential stain** (e.g., Gram stain, Acid-fast stain)

- **Special stain** (e.g., Spore stain, Flagellar stain).

According to the **Gram-stain** technique, bacterial cells are classified into:

- **Gram-positive bacteria:** Appear **purple** in color.
- **Gram-negative bacteria:** Appear **pink** in color.

Some bacterial cells cannot be stained with the Gram stain due to differences in the structure of the bacterial cell wall; thus, they must be stained with other techniques such as the **Acid-Fast stain**.

Normal Flora (Microbiota)

The term "**normal flora**" refers to the diverse community of microorganisms that colonize the skin and mucous membranes of healthy individuals. These microorganisms maintain a symbiotic relationship with their human hosts and play crucial roles in maintaining health and preventing disease.

Types of Microbial Colonization:

- **Resident Microbiota:** Consists of fixed microbial types that regularly inhabit specific body sites. These organisms demonstrate stable colonization and can rapidly reestablish themselves if disturbed.
- **Transient Microbiota:** Comprises microorganisms acquired from the environment that temporarily inhabit body surfaces. These organisms typically persist for hours to weeks without causing disease or establishing permanent colonization.

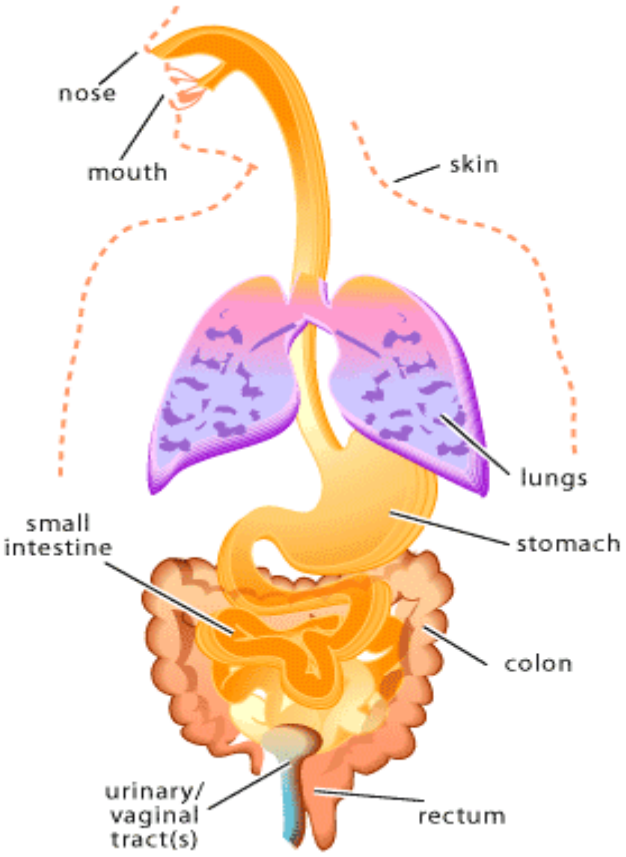
Distribution and Composition by Body Site:

1. **Skin Microbiota:**
   - Primary colonizers: *Staphylococcus epidermidis* (dominant) *Propionibacterium acnes*, *Corynebacterium* species
   - Significant pathogens: *Staphylococcus aureus* (nasal carriage), *Candida albicans*
   - Ecological factors: Varies by skin region (moist, dry, sebaceous)
2. **Ocular Microbiota:**
   - Predominant organisms: *Staphylococcus epidermidis*, *Staphylococcus aureus*, diphtheroids, *Streptococcus pneumoniae*
   - Protective mechanisms: Lysozyme in tears, blinking action, continuous tear flow
3. **Oropharyngeal Microbiota:**
   - Key inhabitants: Viridans streptococci group (*S. sanguinis*, *S. mutans*, *S. mitis*)
   - Clinical significance: Major cause of subacute bacterial endocarditis
   - Additional residents: *Neisseria* species, *Haemophilus* species, anaerobes
4. **Gastrointestinal Microbiota:**
   - Stomach: Sparse colonization due to acidic environment (pH ~2.0)
   - Small intestine: Moderate colonization with facultative organisms
   - Colon: Dense and diverse population (10^11-10^12 CFU/gram contents)
   - Major constituents: *Bacteroides fragilis*, *Escherichia coli*, *Enterococcus faecalis*, anaerobic cocci
5. **Vaginal Microbiota:**
   - Dominant organisms: Lactobacillus species (*L. acidophilus*, *L. crispatus*)
   - Protective function: Maintain acidic pH (3.8-4.5) through lactic acid production

- Clinical importance: Prevents overgrowth of *Candida albicans* and other pathogens

6. **Urethral Microbiota:**

- Primary colonizers: *Staphylococcus epidermidis*, diphtheroids
- Gender differences: Female urethra more susceptible to colonization by fecal flora.
- Clinical relevance: *Escherichia coli* colonization predisposes to urinary tract infections.



Beneficial Functions and Host Interactions:

1. **Colonization Resistance:**

- Physical occupation of ecological niches and binding sites
- Competition for essential nutrients and growth factors

- Creation of unfavorable microenvironments for pathogens

2. **Antimicrobial Activities:**

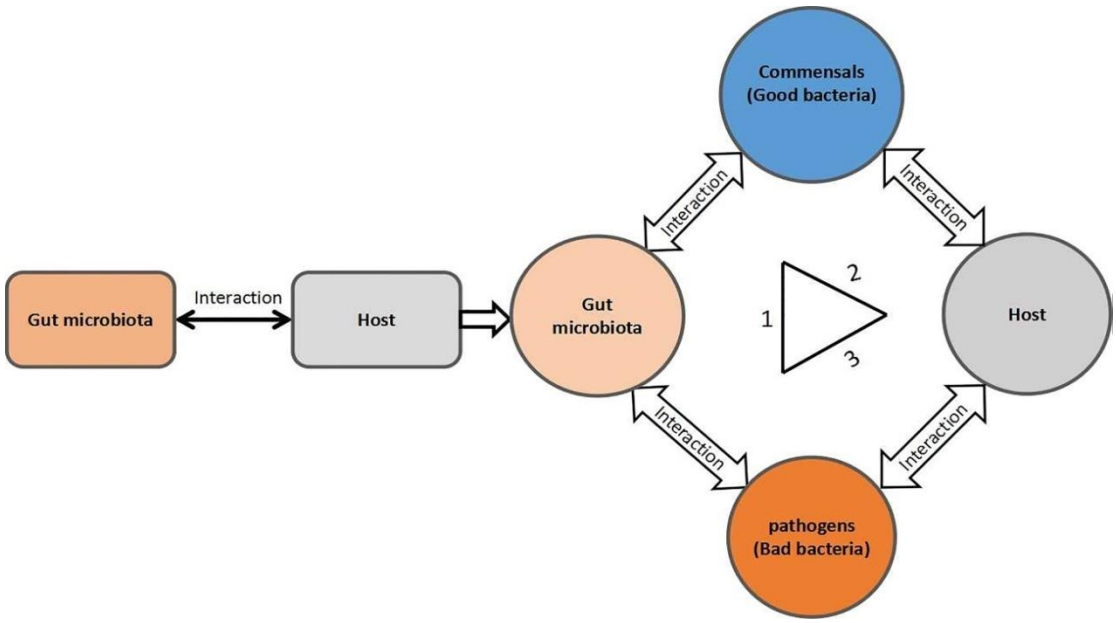
- Production of bacteriocins and other inhibitory substances
- Generation of metabolic byproducts (short-chain fatty acids) that inhibit pathogen growth
- Modulation of local pH to create unfavorable conditions for competitors

3. **Immune System Development:**

- Stimulation of innate immune responses through pattern recognition receptors
- Education and maturation of adaptive immune system components
- Maintenance of immunological memory and tolerance

4. **Metabolic Contributions:**

- Synthesis of essential vitamins (Vitamin K, B12, biotin, folate)
- Enhancement of nutrient absorption and energy harvest
- Metabolism of dietary compounds and xenobiotics
- Production of short-chain fatty acids with systemic effects.



Bacterial Structure

General Prokaryotic Properties:

- Simpler than eukaryotic cells but with a more complex **cell envelope**.
- Contain both DNA and RNA.
- Replicate by binary fission.
- Possess a rigid **cell wall** (with few exceptions).
- Grow in artificial media and are sensitive to antimicrobial agents.

Levels of Bacterial Structure:

1. **Cell Envelope:** Cell wall & cell membrane.
2. **Internal Elements:** Nucleoid, ribosomes, cytoplasmic granules.
3. **External Elements:** Flagella, pili, glycocalyx (capsule/slime layer).

The Cell Envelope

The cell envelope is a complex structure that defines the interaction between the bacterium and its environment. Its composition is the basis for the **Gram stain**.

The Cell Wall

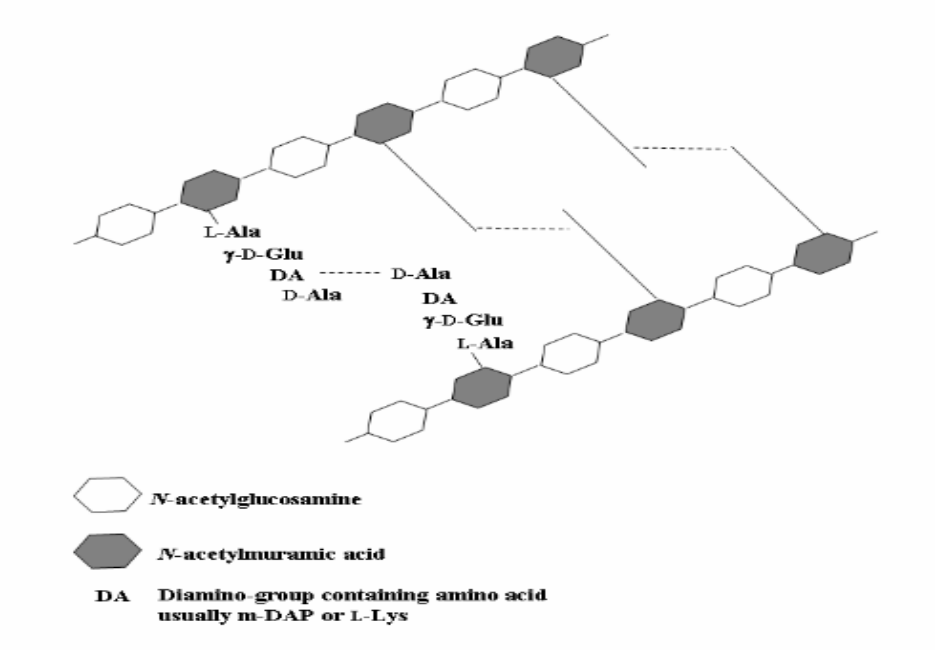
Function:

- Maintains cell shape and prevents osmotic lysis.
- Major site of antibiotic attack (e.g., Penicillins, Cephalosporins).
- Contributes to pathogenicity.

The Universal Component: Peptidoglycan

- **Composition:** Also known as **murein** or **mucopeptide**. A complex, mesh-like polymer.

- **Structure:**
  - **Backbone:** Alternating N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) linked by β(1→4) bonds.
  - **Tetrapeptide Side Chains:** Attached to NAM.
  - **Peptide Cross-Bridges:** Link tetrapeptide chains, providing strength.
- **Medical Importance:** Target of beta-lactam antibiotics (e.g., Penicillin) which inhibit cross-linking. Lysozyme in human tears and mucus cleaves the NAG-NAM backbone.



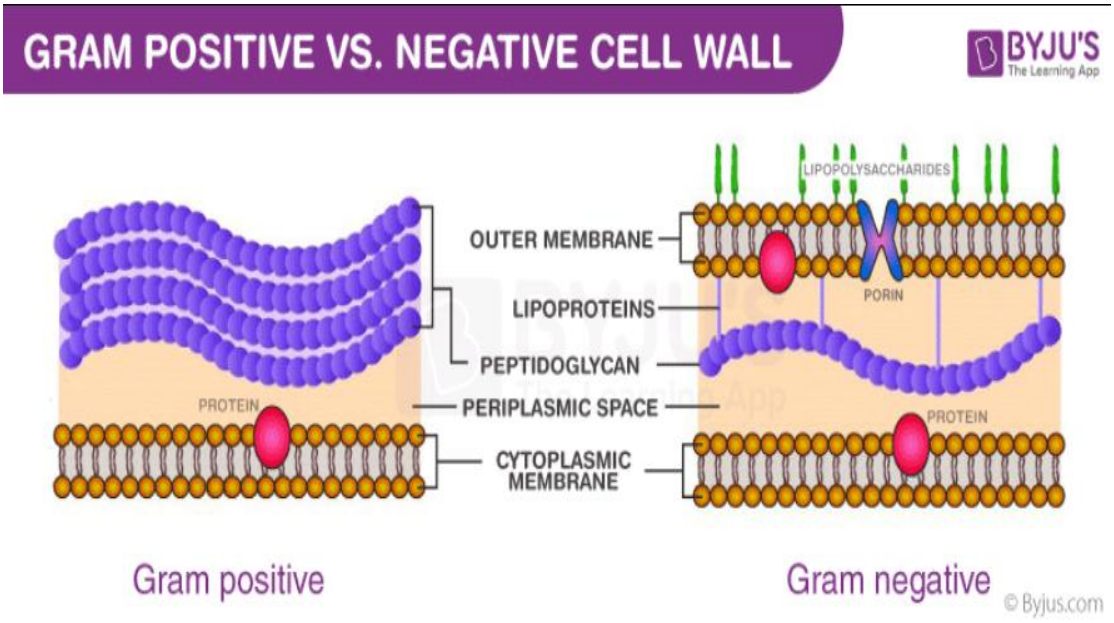
Gram-Positive Cell Wall

- **Thick, Multi-layered Peptidoglycan:** Forms 30-100 nm thick layer.
- **Teichoic and Teichuronic Acids:**
  - Polymers of glycerol phosphate or ribitol phosphate embedded in the peptidoglycan.
  - **Medical Importance:** Major surface antigens; help in adhesion to host tissues; regulate cell wall growth.

Gram-Negative Cell Wall

A more complex, multi-layered structure.

1. **Outer Membrane:**
   - **Inner Leaflet:** Phospholipids.
   - **Outer Leaflet: Lipopolysaccharide (LPS)**.
   - **Porins:** Protein channels that allow passive diffusion of small molecules.
2. **Thin Peptidoglycan Layer:** Located in the **periplasmic space**.
3. **Periplasmic Space:** A gel-like compartment containing proteins, enzymes (e.g., beta-lactamases), and the peptidoglycan.

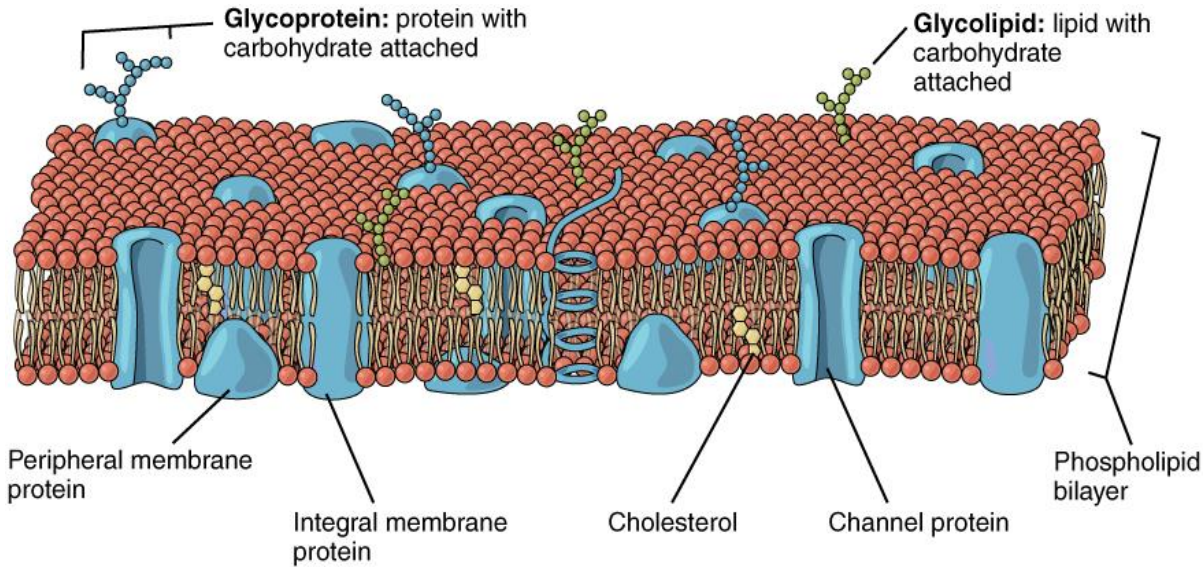


Lipopolysaccharide (LPS) - The Endotoxin

- **Location:** Outer leaflet of the outer membrane in Gram-negative bacteria.
- **Components:**
  - **Lipid A:** The **toxic component (Endotoxin)**. Anchors LPS in the membrane. Causes fever, shock, and DIC.
  - **Core Polysaccharide:** Conserved structure.
  - **O-Specific Polysaccharide (O Antigen):** Highly variable; used for serotyping (e.g., *E. coli* O157:H7).
- **Medical Importance:** LPS release during bacterial lysis can trigger a potent, life-threatening systemic inflammatory response (septic shock).

Cell (Cytoplasmic) Membrane

- **Structure:** A **fluid mosaic** of phospholipids and proteins. It is a delicate tri-laminar unit membrane.
- **Composition:** ~60% protein, 20-30% lipid, 10-20% carbohydrate.
- **Functions:**
  - Selective permeability and transport.
  - Energy production (electron transport chain).
  - Synthesis of cell wall components.
- **Medical Importance:** Target for antibiotics like Daptomycin and Polymyxins.

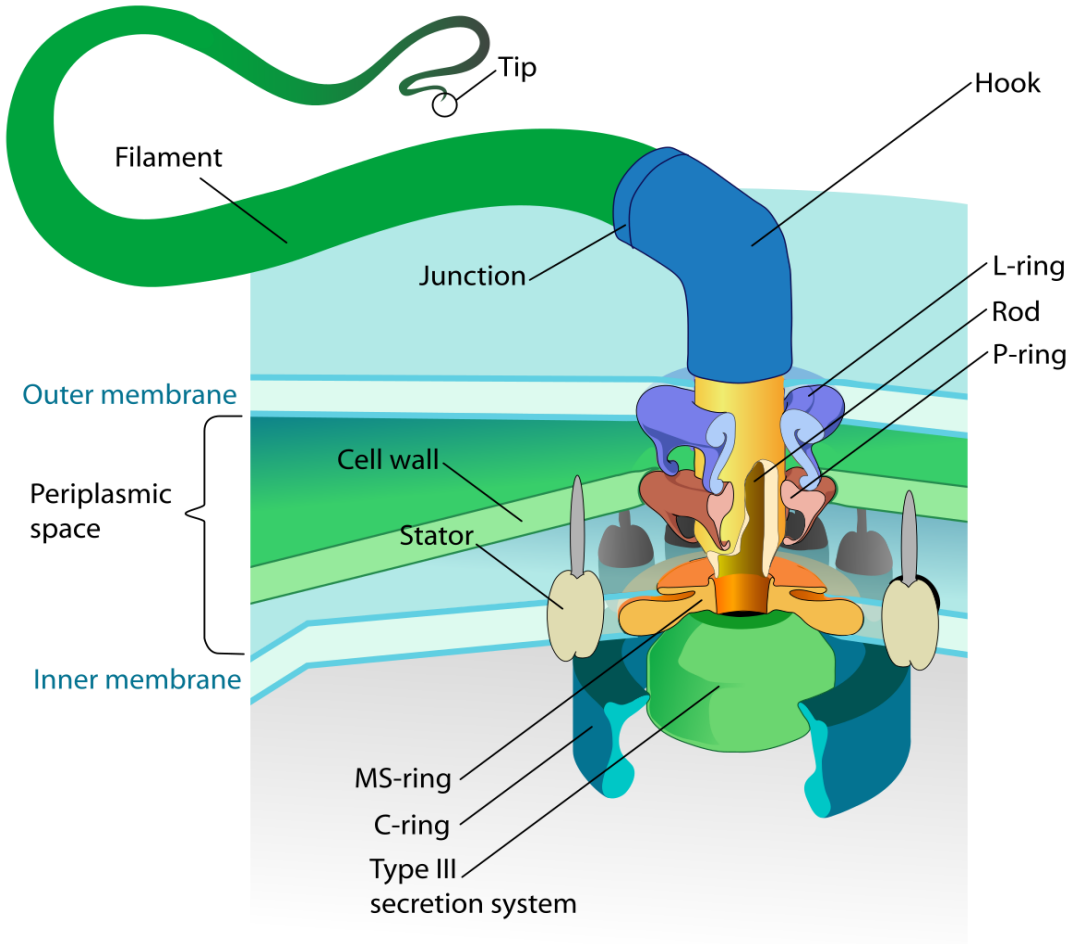


External Structures: Glycocalyx, Capsule, and Slime Layer

- **Glycocalyx:** An inclusive term for polysaccharide-containing material outside the cell.
- **Capsule:** A **condensed, well-defined** layer that excludes particles (e.g., India ink). A key virulence factor.
- **Slime Layer:** A **loose, unorganized** secretion.
- **Medical Importance:**
  - **Antiphagocytic:** Prevents ingestion by immune cells.
  - **Adhesion:** Aids in forming biofilms on tissues and devices.
  - **Vaccine Target:** Capsular polysaccharides are used in vaccines (e.g., Pneumococcal vaccine).

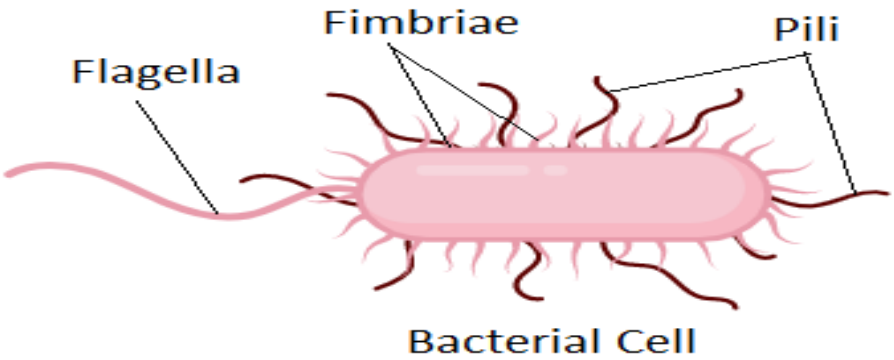
External Structures: Flagella

- **Function:** Thread-like, proteinaceous appendages for **motility**.
- **Structure:** Composed of flagellin protein; consists of a filament, hook, and basal body.
- **Arrangement Patterns (Taxonomically Important):**
  - **Monotrichous:** Single polar flagellum.
  - **Lophotrichous:** Tuft of polar flagella.
  - **Amphitrichous:** Flagella at both ends.
  - **Peritrichous:** Flagella distributed over the entire cell.
- **Medical Importance:**
  - **H Antigens:** Highly antigenic; used in serotyping.
  - **Virulence:** Essential for spread and chemotaxis.



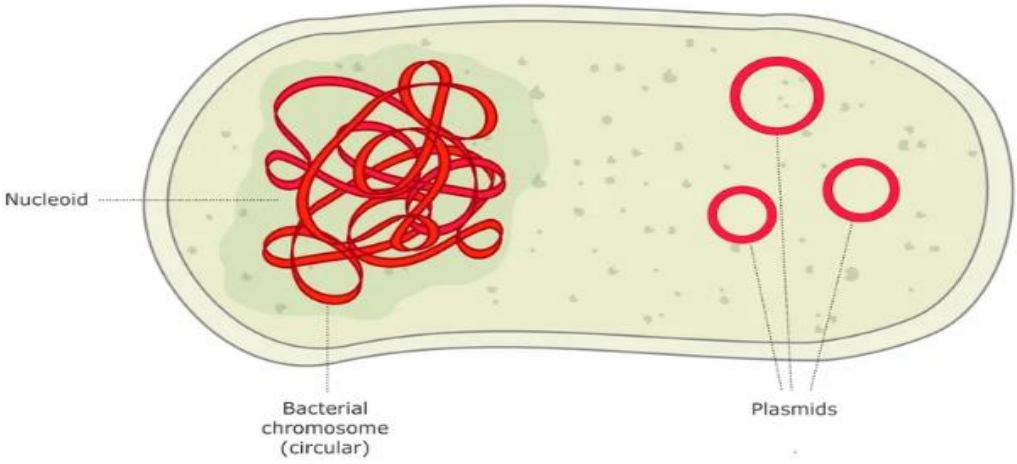
External Structures: Pili and Fimbriae

- **Fimbriae:** Short, fine, hairlike appendages. Primarily for **adherence** to surfaces and host tissues (a critical virulence factor).
- **Pili (Sex Pili):** Longer, fewer. Used for **conjugation** (transfer of DNA, including antibiotic resistance genes).
- **Type IV Pili:** A special class that can mediate **twitching motility** and adhesion.
- **Medical Importance:** Antigenically distinct; targets for potential vaccines and adhesin-blocking therapies.



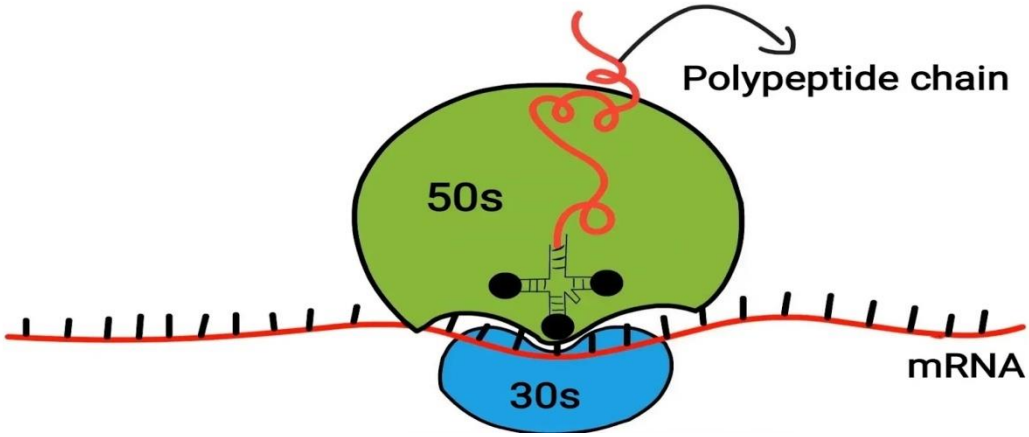
The Nucleoid & Plasmids

- **Nucleoid:**
  - An irregularly shaped region containing the **single, circular, double-stranded DNA chromosome**.
  - **Supercoiling & NAPs:** The chromosome is compacted by supercoiling and Nucleoid-Associated Proteins to fit inside the cell.
- **Plasmids:**
  - Small, circular, **extrachromosomal DNA** molecules.
  - Replicate independently.
  - Often carry genes for **antibiotic resistance, toxins, and virulence factors**.
  - **Episomes:** Plasmids that can integrate into the chromosome.
  - **Curing:** The loss of a plasmid from a cell.



Ribosomes

- **Structure: 70S** ribosomes, composed of a **50S** and a **30S** subunit.
- **Function:** Site of protein synthesis (translation).
- **Medical Importance:** The structural difference from human ribosomes (80S) is exploited by antibiotics:
  - **Aminoglycosides & Tetracyclines:** Target the 30S subunit.
  - **Macrolides & Clindamycin:** Target the 50S subunit.



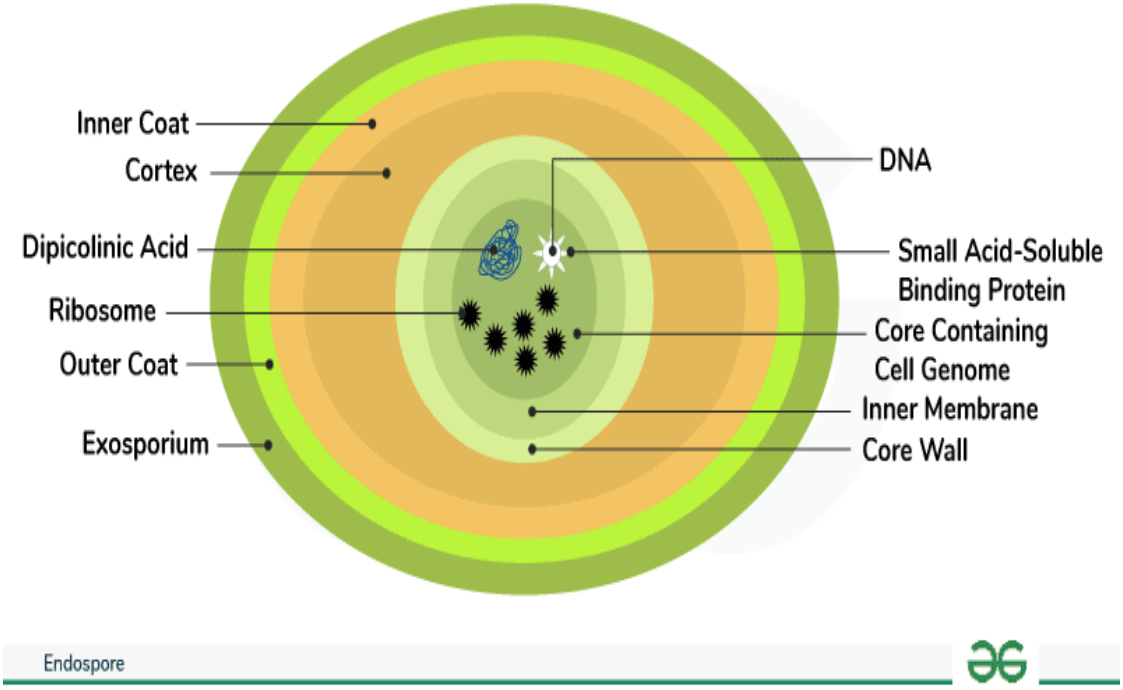
Endospores

- **Formation:** Dormant, highly resistant structures formed by *Bacillus* and *Clostridium* under stress (sporulation).
- **Resistance:** Extremely resistant to heat, desiccation, chemicals, and radiation.

- **Structure:**

1. **Core:** Contains DNA, ribosomes, and energy molecules.
2. **Spore Wall:** Inner membrane layer.
3. **Cortex:** Thick, modified peptidoglycan.
4. **Coat:** Keratin-like, proteinaceous layer.
5. **Exosporium:** Outer, delicate layer.

- **Medical Importance:** Cause of diseases like anthrax and tetanus .



Bacterial growth

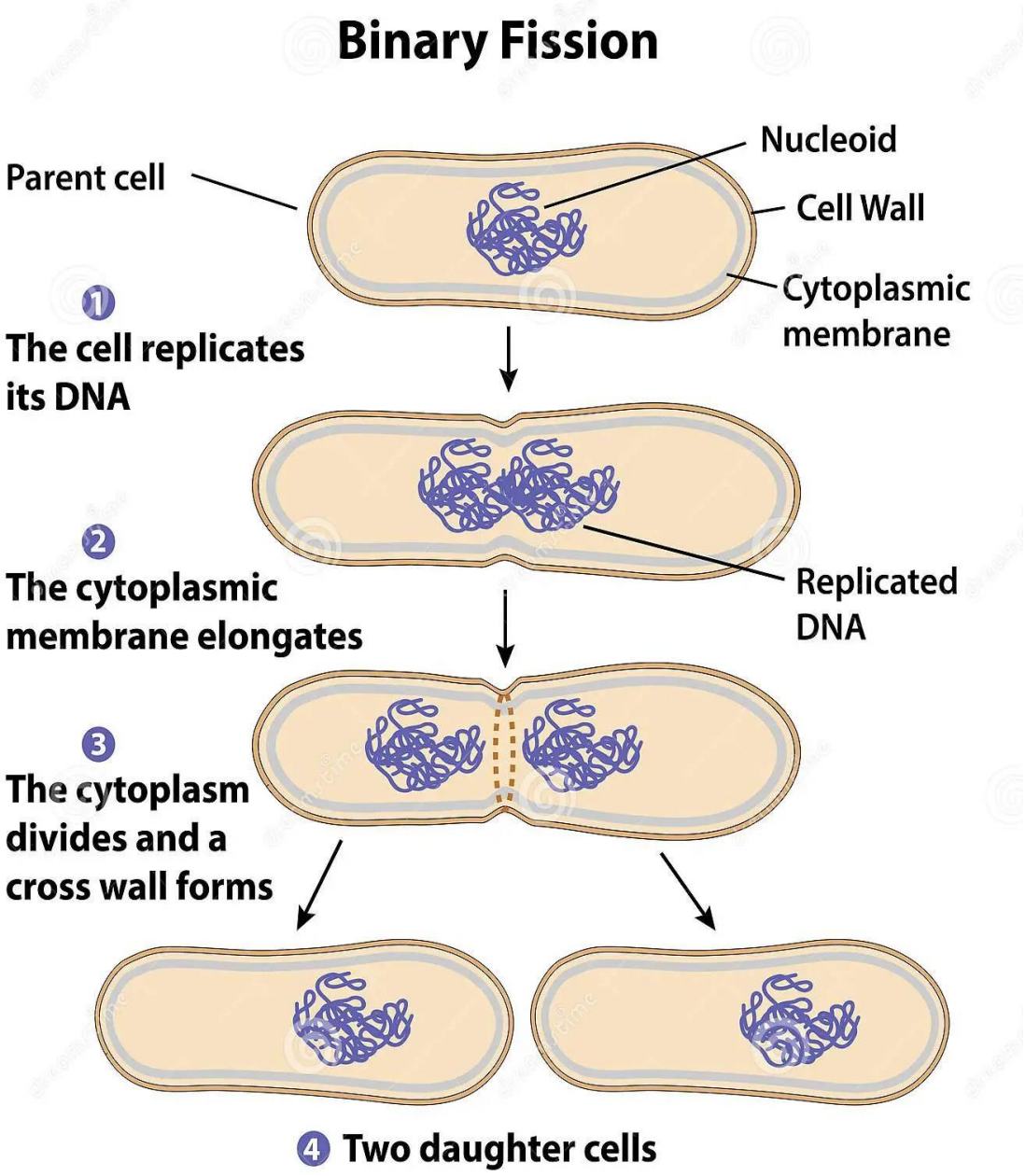
- **Bacterial growth** is the regular increase in all cell components, leading to an increase in cell size and subsequent division into two identical cells via **binary fission**.
- In a population context, growth is defined as an increase in the number of individuals in the bacterial population, measured by cell density or mass.

Mechanism of Bacterial Cell Division

Most bacteria reproduce by **transverse binary fission**, which occurs in the following stages:

1. **Elongation**: Increase in cell length through the synthesis of the cell wall and plasma membrane.
2. **Replication of Genetic Material (DNA)**.
3. **Formation of the Septum**: The cell wall grows inward at the midpoint of the cell.
4. **Separation of the Two Cells**: They may separate immediately or remain attached for a period.

- **Generation Time**: The time required for one cell to divide into two. It varies depending on the bacterial species and environmental conditions (from minutes to days).



Factors Preventing Binary Fission

These factors prevent the formation of the division septum:

- Soap, bile salts, ultraviolet radiation, antibiotics, nutrient deficiency, mutations.

Bacterial Growth Curves

When bacteria are transferred to a closed liquid nutrient medium, they pass through four distinct phases:

1. **Lag Phase**:

- A period of adaptation and acclimatization; no cell division occurs.
- The cell synthesizes new enzymes and prepares for growth.

2. **Log / Exponential Phase**:

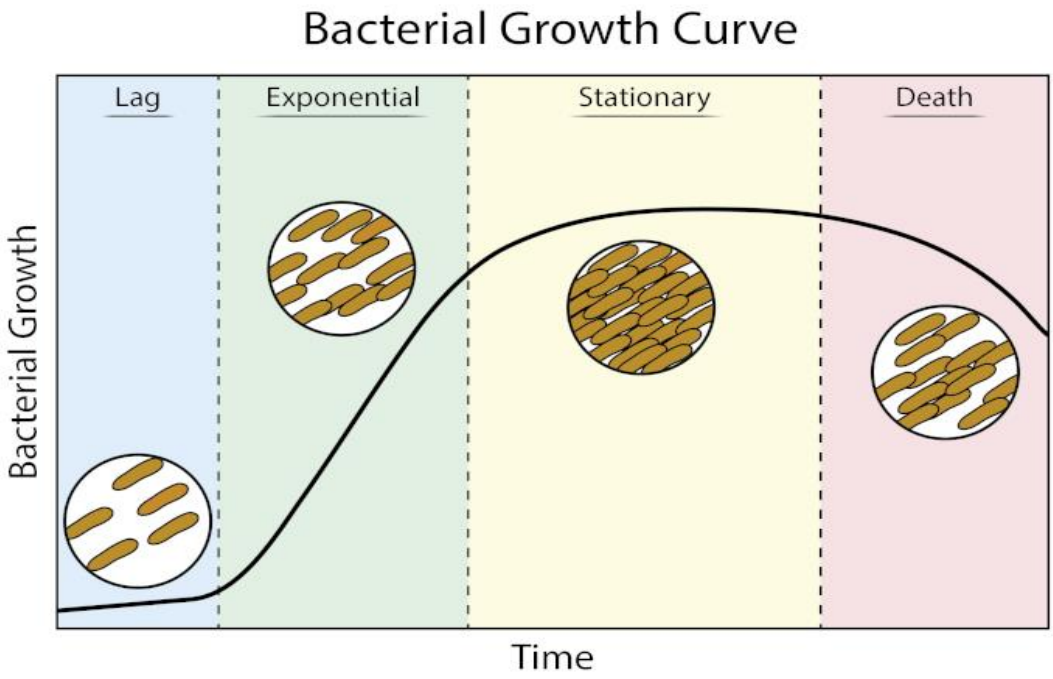
- Growth and division occur at a constant maximum rate.
- The relationship between the logarithm of the cell number and time is linear.
- Cells are uniform, small in size, and sensitive to physical and chemical factors.

3. **Stationary Phase**:

- The number of living cells balances with the number of dead cells due to:
  - Depletion of nutrients.
  - Accumulation of toxic waste products.
- Spores may form, and morphological changes occur to resist harsh conditions.

4. **Death Phase**:

- The number of dead cells exceeds the number of living cells.
- Death occurs at a constant logarithmic rate.



Growth Calculation Equations

- Number of generations (n): $n = 3.3 \times \log(\frac{N_1}{N_0})$
- Generation time (G): $G = \frac{t}{n}$

  Where:
- N_0: Initial number of cells.
- N_1: Number after time (t).
- t: Total time.
- n: Number of generations.

Special Types of Growth

1. **Synchronous Growth**: All cells divide simultaneously (for research purposes).
2. **Diauxic Growth**: Sequential use of two carbon sources.
3. **Continuous Culture**:

- **Chemostat**: Controls the bacterial growth rate by the flow of fresh medium.
- **Turbidostat**: Controls cell density using optical devices.

Methods for Measuring Bacterial Growth

First: Direct Methods

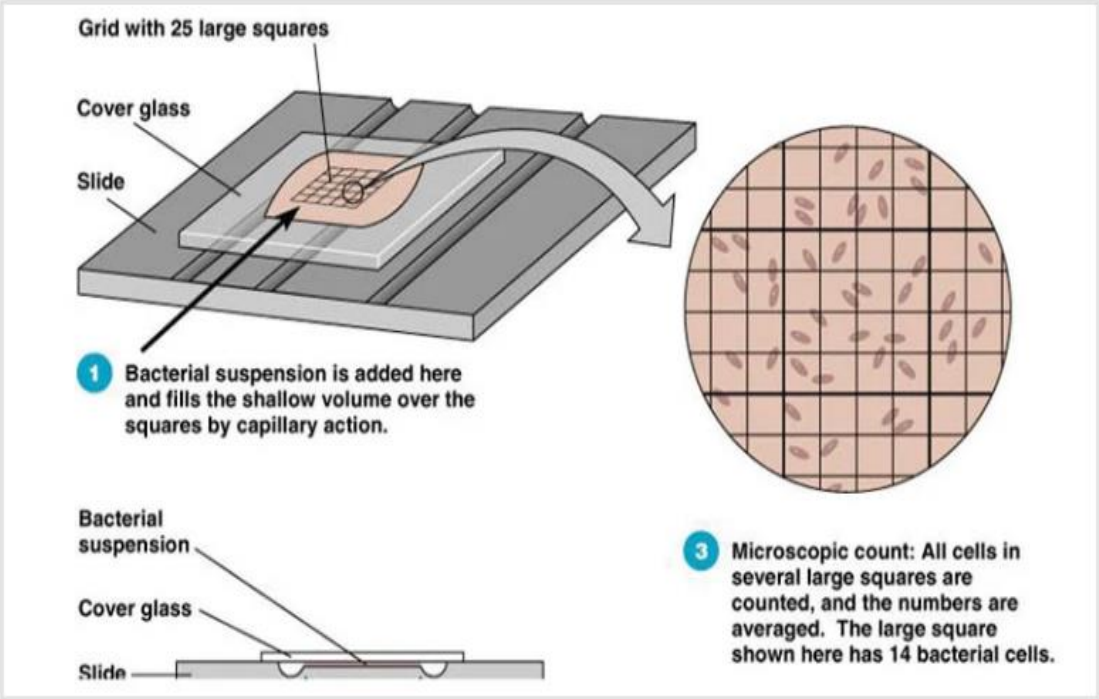
1. **Microscopic Cell Count (Breed Method)**.
2. **Cell Counting using a Counting Chamber (Petroff-Hausser Chamber)**.
3. **Membrane Filtration**.
4. **Electronic Cell Counters**.

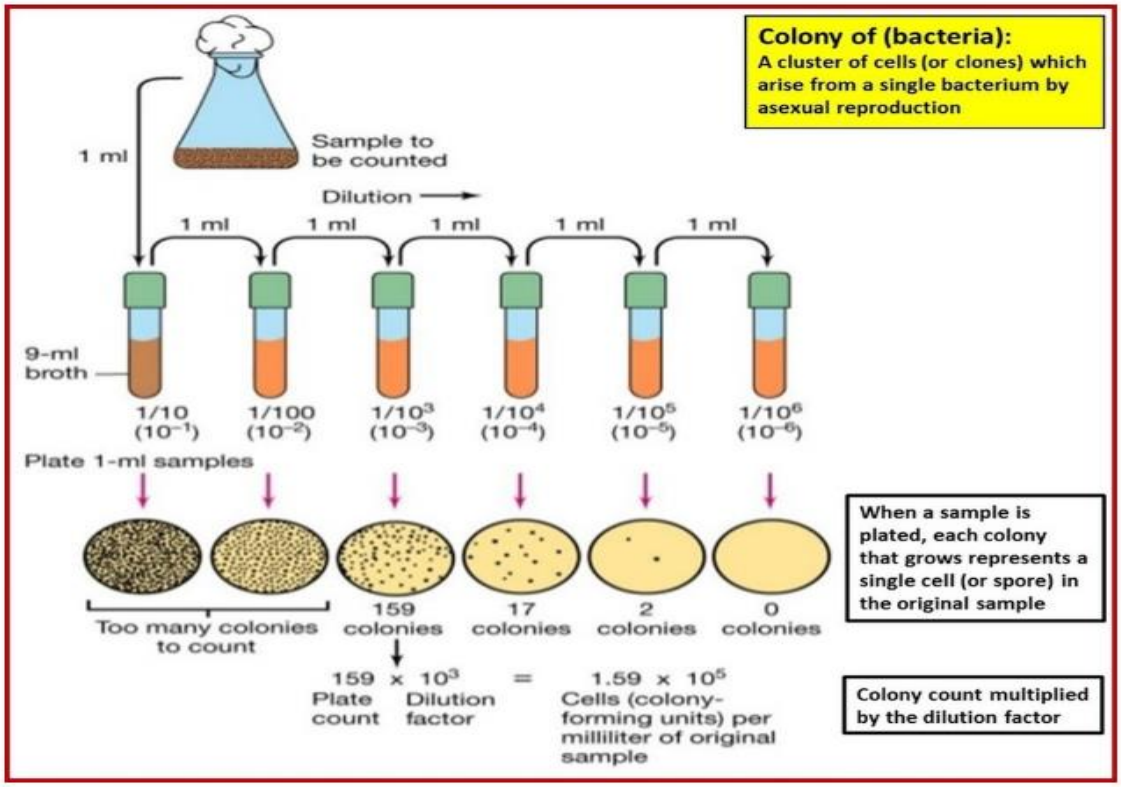
Advantages: Speed, relative accuracy.

Disadvantages: Cannot distinguish between live and dead cells.

Second: Indirect Methods

1. **Chemical Methods**: Measuring nitrogen content, protein, nucleic acids.
2. **Measuring Dry Cell Weight**.
3. **Measuring Turbidity** using a Spectrophotometer.
4. **Serial Dilution Method** for estimating the viable count.
5. **Colony Count** on Agar media (the standard method for viable count).


Grid with 25 large squares
Cover glass
Slide
1 Bacterial suspension is added here and fills the shallow volume over the squares by capillary action.
Bacterial suspension
Cover glass
Slide
3 Microscopic count: All cells in several large squares are counted, and the numbers are averaged. The large square shown here has 14 bacterial cells.


Colony of (bacteria):
A cluster of cells (or clones) which arise from a single bacterium by asexual reproduction
1 ml
Sample to be counted
Dilution
1 ml
1 ml
1 ml
1 ml
1 ml
9-ml broth
1/10 (10⁻¹)
1/100 (10⁻²)
1/10³ (10⁻³)
1/10⁴ (10⁻⁴)
1/10⁵ (10⁻⁵)
1/10⁶ (10⁻⁶)
Plate 1-ml samples
Too many colonies to count
159 colonies
17 colonies
2 colonies
0 colonies
When a sample is plated, each colony that grows represents a single cell (or spore) in the original sample
159 x 10³ = 1.59 x 10⁵
Plate count
Dilution factor
Cells (colony-forming units) per milliliter of original sample
Colony count multiplied by the dilution factor

Bacterial Genetics

Why Study Bacterial Genetics?

Bacteria are ideal models for genetic studies due to their:

- **Small size** and rapid reproduction rate.
- **Genetic uniformity** of clonal populations.
- **Ease of manipulation** in laboratory cultures.

Genetic Structure in Bacteria

The genetic material of bacteria is organized into two main components:

1. The Bacterial Chromosome

- A single, circular, double-stranded DNA molecule.
- Located in a region not enclosed by a membrane, called the **nucleoid**.
- Contains all the essential genes for bacterial life, metabolism, and reproduction.

2. Plasmids

- Small, circular, double-stranded DNA molecules that exist independently of the chromosome.
- **Not essential for routine survival**, but they provide significant selective advantages.
- They carry genes for:
  - **Antibiotic resistance** (R factors).
  - **Virulence factors** (e.g., toxins, adhesion factors, capsules).
  - **Degradation of complex compounds** (e.g., hydrocarbons).
  - **Conjugation** (e.g., the Fertility factor, F plasmid).

- A bacterial cell can harbor multiple different plasmids and can replicate and transfer them to other bacteria.

Mechanisms of Genetic Transfer between Bacteria (Horizontal Gene Transfer)

Horizontal Gene Transfer (HGT) refers to the movement of genetic material between contemporary bacteria within the same generation, as opposed to vertical transmission (from parent to offspring). HGT is the key reason behind the rapid evolution and adaptability of bacteria.

There are three principal mechanisms:

1. Transformation

- **Definition:** The process by which bacteria take up free, extracellular DNA from their environment and incorporate it into their own chromosome.
- **Mechanism:**

1. DNA is released into the environment from dead or lysed bacterial cells.
2. A recipient bacterium that is **competent** takes up this DNA fragment.
3. Some bacteria are naturally competent (e.g., *Streptococcus pneumoniae*), while others become competent under specific conditions like starvation.
4. The incorporated DNA can then recombine into the recipient's chromosome.

- **Significance:**
  - A crucial mechanism for the spread of resistance genes.
  - Historically demonstrated by Griffith's experiment showing the transfer of the capsule-forming gene in *S. pneumoniae*.
  - Extensively used in laboratories for genetic engineering to introduce desired genes into bacteria.

2. Conjugation

- **Definition:** The direct cell-to-cell transfer of genetic material through a specialized protein tube called a **pilus**.
- **Mechanism:**

1. The donor cell (which possesses a conjugative plasmid, like the **F plasmid**) produces a pilus.
2. The pilus attaches to a recipient cell (F^-), forming a cytoplasmic mating bridge.
3. A copy of the F plasmid is transferred to the recipient, converting it into a donor (F^+) cell.
4. In **High-frequency recombination (Hfr)** strains, the F plasmid is integrated into the bacterial chromosome. During conjugation, the Hfr strain can transfer portions of the chromosomal DNA to the recipient.

- **Significance:**
  - The **most common mechanism** for the spread of antibiotic resistance genes, especially among Gram-negative bacteria (e.g., *E. coli*, *Salmonella*, *Pseudomonas*).
  - Allows for the transfer of large segments of DNA, including chromosomal genes.

3. Transduction

- **Definition:** The transfer of bacterial DNA from one cell to another using a **bacteriophage (phage)** as a vector.
- **Mechanism:**

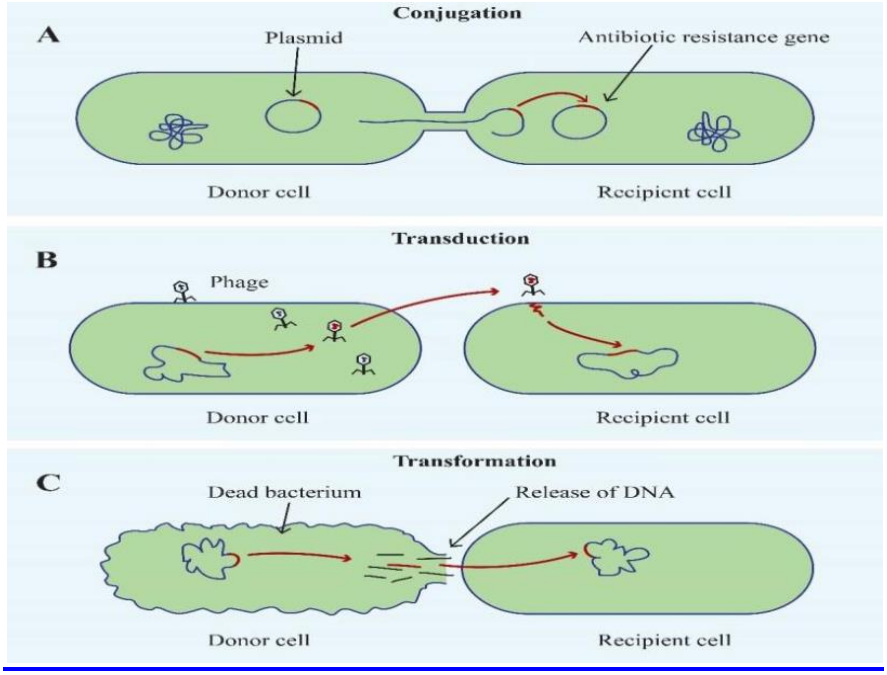
1. A phage infects a donor bacterial cell and degrades the host's DNA.

2. During the assembly of new phage particles, a fragment of the bacterial DNA may be mistakenly packaged into a phage capsid instead of the viral DNA.
3. This phage particle, called a transducing particle, is released and infects a new recipient cell.
4. The bacterial DNA is injected into the recipient and can recombine into its chromosome.

- **Types:**
  - **Generalized Transduction:** Any random fragment of donor bacterial DNA can be transferred.
  - **Specialized Transduction:** Only specific bacterial genes adjacent to the phage's integration site in the donor chromosome are transferred.

Significance:

- Responsible for the spread of potent toxins. A classic example is the Shiga toxin in *E. coli* O157:H7, which was acquired through transduction.
- Occurs in various bacteria like *E. coli*, *Bacillus*, and *Staphylococcus*.



Mutations and Genotypic Changes

- **Mutation:** A stable, heritable change in the nucleotide sequence of the DNA.
- **Types of Bacterial Mutations:**

1. **Antibiotic or disinfectant resistance.**
2. **Altered production of enzymes or toxins** (increasing or decreasing virulence).
3. **Auxotrophic mutations** (inability to synthesize an essential nutrient, requiring it in the growth medium).
4. **Morphological changes** (loss of capsule, spores, or flagella).

- **Causes of Mutations:**

  - **Spontaneous mutations:** Occur naturally during DNA replication.
  - **Induced mutations:** Caused by mutagens such as UV radiation, X-rays, or chemical agents (e.g., base analogs).

Pathogenicity of bacteria:

The inherent ability of a microorganism to cause disease. It is defined as the structural and biochemical mechanisms that enable microbes to cause disease, or the infectious process that leads to the development of signs and symptoms of disease.

1. **Pathogen:**

   A microorganism (such as a bacterium, virus, fungus, or parasite) that has the ability to cause damage in host tissues and produce disease.

2. **Infection:**

   The presence and multiplication of a microbe within a host. This does not necessarily lead to apparent disease.

Scientific Classification of Pathogens

1. **Primary Pathogen:**

   A microbe capable of causing disease in a healthy host with normal immune defenses, regardless of the host's resident **microbiota**. *Example:* ***Mycobacterium tuberculosis***.

2. **Opportunistic Pathogen:**

   A microbe that typically does not cause disease in healthy individuals but causes disease in situations that compromise the host's defenses. Susceptible individuals include:

- The immunocompromised (elderly, infants, chemotherapy patients, AIDS).
- Those with a breach of protective barriers (burns, wounds, surgery).

- Those with an imbalance in the normal microbiome. *Example:* ***Pseudomonas aeruginosa***.

Virulence Factors

Virulence: The quantitative measure of the severity of disease caused by a microbe. It is determined by **virulence factors**, which are molecules produced by bacteria that enhance their efficiency in causing disease.

Roles of Virulence Factors:

1. Aid in host **invasion**.
2. Cause direct tissue **damage**.
3. Evade host defenses (**evasion**).

Key Virulence Factors:

1. Adherence Factors:

- **Description:** Hair-like protein appendages (**Pili** or **Fimbriae**) on the bacterial surface.
- **Function:** Bind to specific receptors on host cell surfaces (usually mucosal membranes), enabling the bacteria to **colonize** the host and resist removal.

2. Capsule:

- **Description:** A sticky, polysaccharide layer surrounding the bacterial cell wall.
- **Function:** Acts as an **antiphagocytic** factor by preventing phagocytic cells from recognizing and engulfing the bacteria.

3. Tissue-Degrading Enzymes:

- **Function:** Facilitate the spread of bacteria through host tissues by breaking down structural components.

- **Examples:**

- **Hyaluronidase:** Degrades hyaluronic acid in connective tissue.
- **Collagenase:** Breaks down collagen.
- **Lipase** and **Elastase:** Degrade lipids and elastin.

4. **Toxins:** Molecules that cause direct damage to host cells. They are divided into:

- **Endotoxins:**

- **Nature: Lipopolysaccharides (LPS)**, which are an integral part of the outer membrane of **Gram-negative** bacteria.
- **Release:** Released only upon bacterial lysis (death) or during division.
- **Effect:** Triggers a strong immune response (e.g., fever, septic shock) but its effect is non-specific.

- **Exotoxins:**

- **Nature:** Potent **proteins** secreted by both Gram-positive and Gram-negative bacteria during their growth.
- **Effect:** Highly specific and potent.
- **Types:**

- **Cytotoxins:** Destroy specific types of cells (e.g., *Staphylococcus* toxins).
- **Enterotoxins:** Affect intestinal cells, causing diarrhea (e.g., Cholera toxin).
- **Neurotoxins:** Interfere with nerve function (e.g., Botulinum and Tetanus toxins).

5. **Invasion Factors:**

- **Description:** Surface proteins or enzymes (sometimes called "**Invasins**").
- **Function:** Allow bacteria to invade non-phagocytic host cells and spread within tissues.

6. **Siderophores:**

- **Description:** Small molecules with a very high affinity for iron.
- **Function:** Compete with host proteins (e.g., transferrin, lactoferrin) for iron, an essential nutrient for bacterial growth inside the host.
- *Example:* ***Pseudomonas aeruginosa***.

Sources of Infection

1. Endogenous Source:

The source of infection is the microbiota already present on or within the host, which seize an opportunity to become pathogenic.

2. Exogenous Source:

The pathogen enters the patient's body from the surrounding environment.

- **Sources:** Other infected persons, animals, contaminated water or food, surfaces, medical devices.

Stages of Infection Initiation (Steps of Pathogenesis)

1. Transmission & Portal of Entry:

- **Direct Route:** Physical contact, droplet spread (from coughing, sneezing).
- **Indirect Route:** Airborne (dried droplets), vehicle-borne (food, water), vectors (insects).

2. Colonization:

The establishment and multiplication of bacteria at their site of entry (e.g., respiratory, digestive, or urinary tract).

3. **Adherence:**

   The firm attachment of bacteria to host cells using adherence factors (Pili) that bind to specific cell receptors.

4. **Invasion:**

   The ability of bacteria to penetrate epithelial barriers and spread to deeper tissues, aided by degradative enzymes and invasion factors.

5. **Toxigenesis:**

   The production and release of toxins (endotoxins or exotoxins) that cause direct damage to cells and tissues, either locally or at distant sites via the bloodstream.

6. **Evasion of Host Defenses:**

   Sophisticated mechanisms that allow bacteria to survive and spread, such as:

- The **Capsule** for resisting phagocytosis.
- Secretion of enzymes that degrade antibodies (e.g., Protease).
- **Antigenic Variation** to avoid recognition by the immune system.
- **Intracellular Growth** to evade humoral immunity.

Classes of Antibacterial Agents

A fundamental classification is based on **spectrum of activity**:

- **Narrow-spectrum:** Primarily active against a limited group (e.g., Gram-positives only).
- **Broad-spectrum:** Active against a wide range of bacteria (e.g., both Gram-positives and Gram-negatives).

Major Classes Based on Cellular Target

1. Inhibitors of Cell Wall Synthesis

These drugs are selectively toxic because human cells lack a cell wall. Their target is the peptidoglycan layer.

- **Beta-Lactams:** Characterized by a beta-lactam ring. They bind to Penicillin-Binding Proteins (PBPs), inhibiting the final cross-linking step of peptidoglycan synthesis.
  - **Penicillins:** (e.g., Penicillin G, Amoxicillin, Methicillin).
  - **Cephalosporins:** (e.g., Cefazolin [1st gen], Ceftriaxone [3rd gen]).
  - **Carbapenems:** (e.g., Meropenem) – very broad spectrum.
  - **Monobactams:** (e.g., Aztreonam) – active against Gram-negatives only.
- **Glycopeptides:** (e.g., Vancomycin). Bind directly to the D-Ala-D-Ala terminus of peptidoglycan precursors, blocking polymerization. Crucial for treating serious Gram-positive infections like MRSA.

2. Inhibitors of Protein Synthesis

These drugs target the bacterial ribosome (70S), which is structurally different from the human ribosome (80S).

- **Targeting the 30S Ribosomal Subunit:**
  - **Aminoglycosides:** (e.g., Gentamicin, Amikacin). Bind irreversibly to the 30S subunit, causing misreading of mRNA and inhibiting initiation. Bactericidal.
  - **Tetracyclines:** (e.g., Doxycycline). Bind reversibly to the 30S subunit and block tRNA attachment. Bacteriostatic.
- **Targeting the 50S Ribosomal Subunit:**
  - **Macrolides:** (e.g., Azithromycin, Erythromycin). Block the translocation step. Bacteriostatic.
  - **Others:** Chloramphenicol (inhibits peptide bond formation); Lincosamides (e.g., Clindamycin).

3. Inhibitors of Nucleic Acid Synthesis

- **Quinolones/Fluoroquinolones:** (e.g., Ciprofloxacin, Levofloxacin). Inhibit DNA gyrase (topoisomerase II) and topoisomerase IV, enzymes essential for DNA supercoiling and replication. Bactericidal.
- **Rifampin:** Inhibits bacterial DNA-dependent RNA polymerase by binding to its beta-subunit, blocking transcription initiation.

4. Antimetabolites

- **Sulfonamides & Trimethoprim:** Inhibit sequential steps in bacterial folate synthesis, an essential cofactor for nucleotide synthesis.
  - **Sulfonamides:** Compete with PABA (para-aminobenzoic acid) for the enzyme dihydropteroate synthase.
  - **Trimethoprim:** Inhibits dihydrofolate reductase.
  - Often used in combination (Co-trimoxazole) for a synergistic effect.

5. Agents Affecting the Cell Membrane

- **Polymyxins:** (e.g., Colistin). Act like detergents, disrupting the outer and cytoplasmic membranes of Gram-negative bacteria. Bactericidal.
- **Daptomycin:** A lipopeptide that inserts into and depolarizes the cytoplasmic membrane of Gram-positive bacteria.

Key Clinical Concepts

- **Bactericidal vs. Bacteriostatic:** Cidal agents *kill* bacteria (required in endocarditis, meningitis, neutropenia). Static agents *inhibit growth*, relying on host immunity for clearance.
- **Pharmacodynamics (PD):** The relationship between drug concentration and antibacterial effect.
  - **Time-Dependent Killing:** Efficacy depends on the time the drug concentration remains above the Minimum Inhibitory Concentration (MIC) (e.g., Beta-lactams, Vancomycin). Dosing strategy: Frequent dosing or continuous infusion.
  - **Concentration-Dependent Killing:** Efficacy depends on the peak concentration achieved relative to MIC (e.g., Aminoglycosides, Fluoroquinolones). Dosing strategy: Higher, less frequent doses.
- **Therapeutic Index:** The ratio between toxic dose and therapeutic dose. Drugs with a low therapeutic index (e.g., Aminoglycosides) require careful monitoring.

General Characteristics and Classification of Viruses

1. What Are Viruses?

Viruses are **obligate intracellular pathogens** with a unique nature:

- **Not cells:** They lack cellular organelles and cannot perform independent metabolism.
- **Simple structure:** Composed of nucleic acid (DNA or RNA) surrounded by a protein coat (capsid).
- **Obligatory replication within a living cell:** They are entirely dependent on the host cell's machinery for replication.
- **Extremely small size:** Ranging from 20-300 nanometers.

2. General Characteristics of Viruses

A. Basic Structure

1. **Viral Genome:**
   - **Type:** Either DNA or RNA (never both in one virus).
   - **Form:** Linear or circular; single-stranded or double-stranded.
   - **Size:** Ranges from a few thousand to hundreds of thousands of nucleotides.
2. **Capsid:**
   - **Function:** Protects the genome and is involved in virus attachment to the host cell.
   - **Structure:** Composed of repeated protein subunits called **capsomeres**.
   - **Symmetry Types:**
     - **Icosahedral:** e.g., Herpesviruses, Poliovirus.
     - **Helical:** e.g., Measles virus, Mumps virus.

- **Complex:** e.g., Bacteriophages, Poxviruses.

3. **Viral Envelope:**

- **Origin:** Acquired from the host cell membranes (plasma membrane, endoplasmic reticulum, nuclear envelope).
- **Components:** A lipid bilayer containing **viral glycoproteins** essential for cell attachment and entry.
- **Significance:** Enveloped viruses are more sensitive to disinfectants and environmental conditions than non-enveloped (naked) viruses.

4. **Viral Enzymes:**

- Some viruses carry specific enzymes crucial for their life cycle, such as:

- **Reverse Transcriptase** in retroviruses (e.g., HIV).
- **RNA-dependent RNA polymerase** in negative-sense RNA viruses.

B. Biological Characteristics

1. **Tissue Tropism:** The virus's ability to infect specific cell types (e.g., Hepatitis B virus infects hepatocytes).
2. **Host Range:** The spectrum of host organisms a virus can infect.

3. The Scientific Classification System for Viruses (According to ICTV).

The **International Committee on Taxonomy of Viruses (ICTV)** relies on multiple criteria:

1. Type of genetic material (DNA or RNA).
2. Genome structure (ss/ds, linear/circular, segmented/non-segmented).
3. Strategy of replication.
4. Capsid symmetry (Icosahedral, Helical, Complex).
5. Presence or absence of a viral envelope.

6. Physicochemical properties (size, buoyant density, stability).

Taxonomic Hierarchy:

Realm → Phylum → Class → Order → Family → Genus → Species.

Examples of Medically Important Virus Families:

- **DNA**
  Viruses: *Herpesviridae* (Herpes), *Adenoviridae*, *Poxviridae* (Smallpox).
- **RNA**
  Viruses: *Orthomyxoviridae* (Influenza), *Paramyxoviridae* (Measles, Mumps), *Coronaviridae*, *Retroviridae* (e.g., HIV).

4. Practical Classification of Viruses in Clinical and Laboratory Medicine

For diagnostic, therapeutic, and epidemiological purposes, viruses are classified based on practical criteria:

A. Based on Clinical Symptoms and Site of Infection:

1. **Respiratory Viruses:** e.g., Rhinovirus, Influenza virus, SARS-CoV-2.
2. **Enteric Viruses:** e.g., Rotavirus, Norovirus.
3. **Dermatotropic/Mucosal Viruses:** e.g., HSV, HPV, Varicella-Zoster virus.
4. **Neurotropic Viruses:** e.g., Poliovirus, Rabies virus.
5. **Blood-borne/Sexually Transmitted Viruses:** e.g., HBV, HCV, HIV.

B. Based on Modes of Transmission:

- Respiratory, fecal-oral, direct contact, blood transfusion, vertical transmission (mother to fetus).

C. Based on Preventative Strategy:

- Viruses with effective vaccines (e.g., Measles, Mumps, Polio, Hepatitis B).
- Viruses without widely effective vaccines yet (e.g., HIV, HCV).

5. Case Study: SARS-CoV-2 as an Applied Model

- **ICTV Classification:**

Realm: *Riboviria*

Order: *Nidovirales*

Family: *Coronaviridae*

Genus: *Betacoronavirus*

Species: *Severe acute respiratory syndrome-related coronavirus*

- **Structural Characteristics:**
  - **Genome:** Positive-sense single-stranded RNA (+ssRNA).
  - **Capsid:** Helical, contained within an envelope.
  - **Envelope:** Contains prominent glycoproteins, chiefly the **Spike (S) protein**.
- **Clinical Relevance of Classification:**

Understanding its family (*Coronaviridae*) helped predict some properties (e.g., respiratory transmission) and identify the Spike protein as a primary target for vaccines and therapeutics.