Principles of anti-microbial therapy

Chemotherapy:

- Refers to synthetic chemicals used to destroy infectious organisms, including **antibacterial, antiviral, antifungal, and anti-parasitic agents**.
- Also includes **antineoplastic (anticancer) agents**.
- **Selective toxicity** allows these drugs to harm microorganisms without significantly affecting the host.

Antibiotics:

- Natural products secreted by organisms to inhibit or kill others.
- Categories: **antibacterial, antifungal, and anticancer** antibiotics.
- **Chemical modifications** can enhance potency, efficacy, or spectrum.

Antibacterial Drugs: Classification

1. **By Spectrum:**
    - **Narrow-spectrum**: Targets gram-positive (e.g., penicillin G) or gram-negative bacteria (e.g., polymyxins).
    - **Broad-spectrum**: Effective against both (e.g., chloramphenicol, tetracyclines).
2. **By Action:**
    - **Bactericidal**: Kills bacteria (e.g., for immune-compromised patients or severe infections).
    - **Bacteriostatic**: Inhibits growth, requiring host defense to eliminate bacteria.
3. **By Mechanism of Action:**
    - Inhibition of:
        - **Cell wall synthesis**: e.g., β-lactams, vancomycin.
        - **Cell membrane function**: e.g., polymyxins.
        - **Protein synthesis**: e.g., tetracyclines, macrolides.
        - **Metabolism**: e.g., sulfonamides.
        - **Nucleic acid synthesis**: e.g., fluoroquinolones, rifampin.

Antibacterial Resistance

Genetic Causes:

- **Chromosomal mutations**: Often less pathogenic.
- **Plasmids (R-plasmids)**: Transfer resistance genes between bacteria via:
    - **Conjugation**: Cell-to-cell contact.
    - **Transduction**: Transfer via bacteriophages.

- **Transformation**: Uptake of free DNA.

Mechanisms:

- **Bacterial enzymes** that inactivate the drug. Examples: B - lactamases inactivate penicillins, adenylating and acetylating enzymes inactivate aminoglycosides.
- **Decreased entry of the drug** into the bacterial cell as aminoalvcosides or **increased efflux of drug out** of the cell as with tetracycline.
- **Alteration of the binding site for the drug** changing the aminoglycoside binding site or deleting it or changing the penicillin binding protein.
- **Development of alterative metabolic pathway** as sulfonamide resistence.
- **Natural resistance:** Some bacteria have no cell wall and cell wall inhibitors can't affect these bacteria. Microorganisms that are metabolically inactive may be resistant to drugs e.g. mycobacteria. TB

Antimicrobial Drug Combinations

Indications for Combinations:

- Broaden antimicrobial spectrum.(severely ill patents , sever infection"endocarditis,meningitis"
- Treat polymicrobial infections (e.g., abscesses).
- Prevent resistance (e.g., tuberculosis).
- Enhance synergy

Examples of Synergy:

1. Blocking sequential metabolic steps: Trimethoprim-sulfamethoxazole.
2. Enzyme inactivation protection: Clavulanic acid with amoxicillin.
3. Enhanced uptake: Penicillins with aminoglycosides.

Chemoprophylaxis

- Preventive use of antibiotics for:
  - High-risk contacts (e.g., meningitis, gonorrhea).
  - Recurrence prevention (e.g., syphilis, rheumatic fever).
  - Immunocompromised patients (e.g., post-transplant,chemotherapy).
  - Prevent bacterial endocarditis in patients with valve disease.
  - Prevent wound infections in surgical operations.

Adverse Reactions of Antibiotics

1. **Toxicity**: Organs (e.g., kidneys, liver) may be affected.
2. **Hypersensitivity**: Allergic reactions.
3. **Superinfection**:
    - Occurs when normal flora is disrupted by broad-spectrum antibiotics.
    - Leads to proliferation of resistant microorganisms (e.g., *Pseudomonas*, *Enterobacteriaceae*).
    - Can cause serious new infections.

Misuse of Antibiotics

- Common issues include:
    - Treating non-bacterial infections (e.g., viral infections).
    - Improper drug use (e.g., wrong dose or duration).
    - Improper choice of antibiotics.
    - Neglecting surgical drainage of pus.
    - Development of bacterial resistance

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