

# PLAGUES IN MAN

## ANTIBIOTICS & ANTIVIRAL DRUGS

- I. INTRODUCTION AND HISTORICAL PERSPECTIVE
  - A. CHEMOTHERAPEUTIC AGENTS
    - 1. SYNTHETIC DRUGS
    - 2. ANTIBIOTICS
  - B. THE "MAGIC BULLET"
    - 1. PAUL EHRLICH & CHEMOTHERAPY--1900
      - a. QUININE FOR MALARIA
      - b. DISCOVERED SALVARSAN (SYPHILIS)
    - 2. FLEMING AND PENICILLIN--1927
      - a. ANTIBIOSIS AND ANTIBIOTICS
      - b. PENICILLIUM NOTATUM INHIBITS S. AUREUS
    - 3. DOMAGK & TREFOUEL -- PRONTOSIL AND SULFONAMIDES--1935
    - 4. FLOREY & CHAIN -- DEVELOPED PENICILLIN--1940 (WWII)
    - 5. WAKSMAN -- SURVEYED ACTINOMYCETES - STREPTOMYCIN--1944
    - 6. THE HUNT WAS ON:
      - a. STREPTOMYCES SPECIES
      - b. BACILLUS SPECIES
      - c. FUNGI
- II. PROPERTIES OF ANTIMICROBIAL DRUGS
  - A. SELECTIVE TOXICITY
  - B. ANTI-ALLERGENIC (NO OTHER TOXIC REACTIONS)
  - C. WATER SOLUBLE AND STABLE--PENETRATE & LONG LASTING
  - D. LOW PATHOGEN RESISTANCE
- III. SPECTRUM AND ACTION OF ANTIMICROBIAL DRUGS
  - A. BROAD AND NARROW SPECTRUM
  - B. BACTERICIDAL OR BACTERIOSTATIC
  - C. CELL WALL ANTIBIOTICS
    - 1. PENICILLINS
      - a. STRUCTURE-- $\beta$ -LACTAM ANTIBIOTIC
      - b. ACTIVITY--PEPTIDOGLYCAN CROSS-LINKING
      - c.  $\beta$ -LACTAMASES AND PENICILLINASES
      - d. NATURAL PENICILLINS
      - e. SEMI-SYNTHETIC PENICILLINS
        - 1) ACID STABILITY
        - 2) SPECTRUM
        - 3) RESISTANCE TO  $\beta$ -LACTAMASES
    - 2. CEPHALOSPORINS (FROM MOLD CEPHALOSPORIUM)
      - a. STRUCTURE-ALSO A  $\beta$ -LACTAM ANTIBIOTIC
      - b. ACTIVITY SAME AS PENICILLINS
      - c. SEMI-SYNTHETIC DERIVATIVES ARE USED
    - 3. OTHER  $\beta$ -LACTAMS
      - a. IMIPENAM (PRIMAXIN) VERY BROAD SPECTRUM
      - b. AZTREONAM  $\beta$ -LACTAMASE RESISTANT
      - c. COMBINATIONS-AUGMENTIN (AMOXICILLIN & CLAVULANATE) AND TIMENTIN
    - 4. VANCOMYCIN (STAPH AND STREP ONLY)
    - 5. BACITRACIN (TOPICAL APPLICATIONS ONLY)
  - D. PROTEIN SYNTHESIS ANTIBIOTICS
    - 1. AMINOGLYCOSIDES
      - a. STREPTOMYCIN & GENTAMICIN
      - b. AMINO SUGARS & AMINO INOSITOL
      - c. BINDS TO 30S RIBOSOMAL PROTEIN (S12)
      - d. BACTERICIDAL
      - e. SOMEWHAT TOXIC (RENAL AND NERVE)

2. TETRACYCLINES
    - a. POLYCYCLIC COMPOUNDS
    - b. BIND TO 30S SUBUNIT -- BLOCK A SITE
    - c. LOW TOXICITY (BUT RESISTANCE)
    - d. NOT FOR CHILDREN -- STAINS TEETH (& BONE)
  3. CHLORAMPHENICOL
    - a. SMALL MOLECULE--PENETRATES ALL TISSUES
    - b. BINDS TO 50S SUBUNIT
    - c. BROAD SPECTRUM
    - d. SERIOUS SIDE-EFFECTS -- APLASTIC ANEMIA
  4. ERYTHROMYCIN (MACROLIDE ANTIBIOTICS)
    - a. LARGE LACTONE RING
    - b. BINDS TO 50S SUBUNIT (L15--PEPTIDYL TRANSFERASE)
    - c. BROAD SPECTRUM--OFTEN SUBS FOR PENICILLIN
    - d. ORALLY ADMINISTERED (CHILDREN)
- E. ANTIMETABOLITES
1. SULFONAMIDES -- FIRST WAS SULFANILAMIDE
    - a. SYNTHETIC DRUGS
    - b. INHIBIT FOLIC ACID SYNTHESIS (MIMIC PABA)
  2. TRIMETHOPRIM
    - a. INHIBITS DHF REDUCTASE
    - b. USED WITH SULFONAMIDE--SULFAMETHOXAZOLE  
[Bactrim and Septra]
  3. OTHERS
    - a. ISONIAZID--FOR TB
    - b. ETHAMBUTOL--FOR TB and DAPSONE--FOR LEPROSY
- F. NUCLEIC ACID ANTIBIOTICS
1. QUINOLONES "CIPRO" -- TOPOISOMERASE ACTIVITY
  2. RIFAMYCINS INHIBIT RNA POLYMERASE
- G. MEMBRANE ACTIVE ANTIBIOTICS
1. POLYENES--AMPHOTERICIN B (ANTIFUNGAL)
  2. IMIDAZOLES--MICONAZOLE & KETOCONAZOLE (ANTIFUNGAL)
- VI. ANTIVIRAL DRUGS
- A. NONSPECIFIC DRUGS
    1. DNA & RNA SYNTHESIS INHIBITORS
      - a. NUCLEOSIDES
      - b. CHAIN TERMINATORS
    2. INTERFERON
  - B. VIRAL-SPECIFIC DRUGS
    1. ZOVIRAX OR ACYCLOVIR - HERPES
    2. AMANTIDINE - INFLUENZA
    2. RELENZA & TAMIFLU - INFLUENZA
    3. AZT *et al* - HIV-1
    4. PROTEASE INHIBITORS - HIV-1
  - C. MODE OF ACTION
    1. INHIBIT NA REPLICATION
      - a. INHIBIT ENZYME
      - b. CHAIN TERMINATORS
    2. INHIBIT VIRAL ENZYMES
    3. DRUG ACTIVATION BY VIRAL ENZYMES
  - D. RESISTANCE