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--ß-LACTAM ANTIBIOTIC
      b. ACTIVITY--PEPTIDOGLYCAN CROSS-LINKING
      c. ß-LACTAMASES AND PENICILLINASES
      d. NATURAL PENICILLINS
      e. SEMI-SYNTHETIC PENICILLINS
         1) ACID STABILITY
         2) SPECTRUM
         3) RESISTANCE TO ß-LACTAMASES
   2. CEPHALOSPORINS (FROM MOLD CEPHALOSPORIUM)
      a. STRUCTURE--ALSO A ß-LACTAM ANTIBIOTIC
      b. ACTIVITY SAME AS PENICILLINS
      c. SEMI-SYNTHETIC DERIVATIVES ARE USED
   3. OTHER ß-LACTAMS
      a. IMIPENAM (PRIMAXIN) VERY BROAD SPECTRUM
      b. AZTREONAM ß-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. INFERFERON

B. VIRAL-SPECIFIC DRUGS
1. ZOVIRAX OR ACYCLOVIR -- HERPES
2. AMANTIDINE -- INFLUENZA
3. RECEIVER & 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