Antimicrobial Agents

Unit 9

Pathogens are organisms that cause disease by invading tissues or secreting toxins

Types of Pathogens: Bacterium, Virus, Protozoa, Multicellular

Types of Pathogens (Con’t): Fungi

Common Bacterial Pathogens

Anti-infective Agents

• General term to drugs effective against pathogens
• Classified by their chemical structures or by their mechanisms of action
• Act by selectively targeting a pathogen’s metabolism or life cycle

Primary Goal of Antimicrobial Therapy

• Assist the body’s defenses in eliminating a pathogen
• Bacteriocidal drugs kill bacteria
• Bacteriostatic slow their growth, allowing the body’s natural defenses to eliminate the microorganisms

General Principles

• Broad-spectrum antibiotic - one that is effective against a wide variety of different microbial species
• Narrow-spectrum antibiotic - one that is effective against a smaller group of microbes or only the isolated species

General Principles

• Resistance – ability of bacteria to oppose antimicrobial agents
• Superinfection – secondary infection due to antibiotic therapy
• Empiric therapy – based on experience
• Prophylactic therapy -preventative

Acquired resistance is a major clinical problem that is worsened by improper use of anti-infectives
General Principles
- Indications – choice of agents
- Contraindications
  - Sensitivity or allergy to any drug in the class
- Precautions
  - Antibiotics decrease effectiveness of oral contraceptive agents
  - All have the potential of causing superinfections

General Principles
- Side effects
  - Dependent on agent
  - Often GI upset, diarrhea, nausea
  - Itching, rash
- Toxicities
  - Nephrotoxicity (Vancomycin)
  - Ototoxicity (Vancomycin)
  - Liver toxicity (INH)

Associated labs
- Follow culture and sensitivity (C/S) and WBC for all antimicrobials

Culture and Sensitivity Testing
- The organism is grown and the effective antibiotics are identified
- Should be identified before anti-infective therapy is begun
- Treatment often needs to begin prior to return of labs

Mechanisms of action of antimicrobial drugs

Nosocomial Infection
- Acquired in hospital or other health care setting
- Often resistant to common antibiotics
- Two particularly serious resistant infections
  - Methicillin-resistant Staphylococcus aureus (MRSA)
  - Vancomycin-resistant enterococci (VRE)

Prevention Principles from CDC
- Prevent infections whenever possible, easier to prevent an infection, than to treat one
- Teach patient the importance of getting immunizations
- Restrict the use of antibiotics to those conditions deemed medically necessary

Prevention Principles from CDC
- Advise the patient to take anti-infectives for full length of therapy, even if symptoms disappear before the regimen is finished
• Prematurely stopping antibiotic therapy allows some pathogens to survive, thus promoting the development of resistant strains

21 Prevention Principles from CDC
• Prevent transmission of the pathogen by using proper infection control procedures
• Use standard precautions and teach patients methods of proper hygiene for preventing transmission in the home and community settings.

22 Antibiotic Agents
• Careful selection of the correct antibiotic is essential for effective pharmacotherapy and to limit adverse effects
• The penicillins are one of the oldest and safest groups of anti-infectives

23 Action of Penicillins
• Kill bacteria by disrupting their cell walls
• Chemical structure of penicillin responsible for its antibacterial activity is called the beta-lactam ring
• Resistance
  – Some bacteria secrete an enzyme, called beta-lactamase or penicillinase, which splits the beta-lactam ring
  – This structural change allows these bacteria to become resistant to the effects of most penicillins

24 Action of penicillinase

25 Modifications
• Chemical modifications to natural penicillin molecule produced drugs advantages
• Penicillinase-resistant penicillins
• Broad spectrum penicillins
• Extended-spectrum penicillins

26 Cephalosporins
• Similar in structure and function to the penicillins
• One of the most widely prescribed anti-infective classes
• Contain a beta-lactam ring
• Bacteriocidal, inhibit bacterial cell wall synthesis
• Primary therapeutic use
  – Gram-negative infections
  – Patients who cannot tolerate the less-expensive penicillins
• Cross allergy with penicillins

28 Classified by Their “Generation”
• First-generation drugs contain a beta-lactam ring, and bacteria producing beta-lactamase
will normally be resistant to these agents
• Second-generation cephalosporins are more potent and more resistant to beta-lactamase, and exhibit a broader spectrum than the first-generation drugs

29 □ Classified by Their “Generation”
• Third-generation cephalosporins generally have a longer duration of action, broader spectrum, & are resistant to beta-lactamases
• Fourth-generation drugs are more effective against organisms that have developed resistance to earlier cephalosporins

30 □

31 □ Selected Cephalosporins

32 □ Tetracyclines
• Bacteriostatic effect by inhibiting bacterial protein synthesis
• Effective against a wide range of gram-negative and gram-positive organisms
• One of the broadest spectrums of any class of antibiotics
• Drugs of choice for few diseases

33 □ Tetracyclines
• Bacteriostatic effect by inhibiting bacterial protein synthesis
• Effective against a wide range of gram-negative and gram-positive organisms
• One of the broadest spectrums of any class of antibiotics
• Drugs of choice for few diseases
  – Rocky Mountain spotted fever, typhus, cholera, Lyme disease Chlamydia, acne vulgaris

34 □ Tetracyclines
• Patient Teaching
  – Gastric distress common – take with food
  – Do not drink milk since tetracyclines bind to calcium and iron ions, decreasing the drug’s absorption by as much as 50%
  – Avoid direct exposure to sunlight due to photosensitivity
  – Contraindicated in children under 9 years because drugs may cause permanent yellow-brown discoloration of teeth

35 □

36 □ Macrolide Antibiotics
• Safe alternatives to penicillin for many infections
• Inhibit bacterial protein synthesis
• May be either bacteriocidal or bacteriostatic depending on dose and target organism
• Used for infections resistant to penicillin
  – Legionnaire’s disease, whooping cough
• Mild GI upset most common adverse effect
• No serious side effects
Aminoglycosides

- Narrow-spectrum drugs that have the potential to cause serious toxicity
- Bacteriocidal, acts by inhibiting bacterial protein synthesis
- Treatment of a number of aerobic gram-negative bacteria, mycobacteria, and some protozoan

Aminoglycosides

- Ototoxicity
  - Damage to the inner ear, causes hearing impairment, dizziness, loss of balance, persistent headache, and ringing in the ears
- Nephrotoxicity
  - Kidney damage, abnormal urinary function tests, elevated serum creatinine or blood urea nitrogen (BUN)

Fluoroquinolones

- Broad spectrum, wide clinical applications
- Relative safety
- Gram-negative pathogens
- Newer ones are significantly more effective against gram-positive microbes
- Bacteriocidal
- Inhibit bacterial DNA synthesis

Sulfonamides

- Inhibit folic acid, an essential substance in cellular metabolism
- Traditional drugs of choice for urinary tract infections
- Many resistant bacterial strains
- Newer antibiotic agents are safer

Miscellaneous Anti-infectives

A number of additional anti-infectives have distinct mechanisms of action and specific indications
Tuberculosis
The pharmacotherapy of tuberculosis requires special dosing regimens and schedules

Drug Therapy of Tuberculosis
- Mycobacteria grow slowly
- Resistance is common
  - Used for preventing the disease or treating it
- Differs from most other infections
  - Therapy for 6-12 months
- Mycobacteria have a cell wall that is resistant to penetration by anti-infective drugs
  - 2-4 antibiotics needed concurrently

Example Treatment Regime
- Initial phase: 2 months of daily therapy with isoniazid, rifampin (Rifadin, Rimactane), pyrazinamide (PZA) and ethambutol (Myambutol)
- If laboratory test results show the strain is sensitive to the first three drugs, ethambutol is dropped from the regimen
- Continuation phase: 4 months of therapy with isoniazid and rifampin, 2 to 3 times per week

Drugs For Fungal, Viral, and Parasitic Diseases

Fungal Infections
- Fungal infections are classified as superficial or systemic (see table 26-1)
- Superficial infections of the skin, nails, and mucous membranes are effectively treated with topical and oral antifungal drugs
- Systemic antifungal drugs are used for serious infections of internal organs

Antiviral Pharmacotherapy Strategies
- Viruses are infectious agents that require a host to replicate
- Prevent viral infections through the administration of vaccines
- Treat active infections with drugs such as acyclovir (Zovirax) that interrupt the virus’s replication cycle

Antiviral Pharmacotherapy Strategies
- For long-term infections, use drugs that boost the patient’s immune response
(immunostimulants) so that the virus remains in latency with the patient symptom-free

**Structure of the human immunodeficiency virus (HIV)**

**Pharmacotherapy of HIV-AIDS**
- Antiretroviral drugs do not cure HIV-AIDS
- Reduce HIV-related morbidity and prolong survival
- Improve the quality of life
- Restore and preserve natural functions of the immune system
- Maximum suppression of viral load
- Prevent the transmission from mother to child in HIV-infected pregnant patients

**Antiretroviral Drug Classification**
- Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs and NtRTIs)
  - NRTIs inhibit the action of reverse transcriptase, the viral enzyme that converts the viral RNA into viral DNA

**Antiretroviral Drug Classification**
- Nonnucleoside reverse transcriptase inhibitors (NNRTIs)
  - Bind directly to the reverse transcriptase molecule and inhibit its ability to build viral DNA
- Protease inhibitors.
  - Block the final assembly of the HIV particle

**Antiretroviral Drug Classification**
- Miscellaneous agents: Newer drugs are being developed as scientists discover more about the HIV replication cycle
  - Enfuvirtide (Fuzeon) blocks the fusion of HIV to the CD4 receptor on the lymphocyte
  - Raltegravir (Isentress) prevents HIV from inserting its genes into uninfected DNA

**Antiretroviral Drugs for HIV-AIDS (continued)**

**Herpes Virus Family**
- HSV-type 1—primarily infections of the eye, mouth, and lips, although the incidence of genital infections is increasing
- HSV-type 2—genital infections
- Cytomegalovirus (CMV)—affects multiple body systems, usually in immunosuppressed patients
- Varicella-zoster virus—shingles (zoster) and chickenpox (varicella)
- Epstein-Barr virus—mononucleosis and Burkitt’s lymphoma, a form of cancer
Antiviral Drugs for Herpes and Influenza Infections (continued)

Other Pathogens
- Protozoans - single-celled organisms
- Multicellular animals - mites, ticks, and worms
- Infections from helminths and protozoans cause significant disease worldwide
- Many of these diseases are rare in the US and Canada, travelers to Africa, Asia, and South America may acquire them overseas and return home with the infection

Drugs for Helminth and Protozoan Infections (continued)

Client Teaching
- Use of various antimicrobial agents
  - Appropriateness
- Course of treatment
- Potential side effects
- Drug interactions
- Food interactions

Concept Review
- Why does antibiotic resistance become more of a problem when antibiotics are prescribed too often?

Concept Review
- Why have the number of antifungal and antiviral drugs increased significantly over the past 15 years?

Concept Review
- If penicillins are inexpensive, why might a physician prescribe a more expensive cephalosporin or macrolide antibiotic?

Concept Review
- Why are viral infections difficult to treat with current drugs?