NR566 Midterm Study Guide

Week 1: Chapters 79, 80, 81, and 83

Chapter 79: Antifungal Drugs

Pharmacokinetics of Amphotericin B (polyene antifungal class; available in IV form)

- Drug of choice to be used as a broad spectrum for most systemic mycoses
- Minimizing Nephrotoxicity
    - Dose exceeding 4G likely to cause renal impairment
        - Should be administered for the shortest time possible (typically 6-8 weeks, up to 3-4 months) and only for a life- threatening condition.
        - Contraindicated in patients with severe renal impairment. Itraconazole

(Sporanox); azole antifungal class; available in PO form

- Alternative to amphotericin B as a broad spectrum for systemic and superficial mycoses with less toxicity.
- Drug Interactions:
    - Decreased Itraconazole absorption when used with PPIs, H2 antagonists, and antacids
        - Administer 1 hour before Itraconazole or 2 hours after.
    - As a CYP3A4 inhibitor, Itraconazole can increase serum levels of drugs such as cisapride, pimozide, dofetilide, and quinidine -> increased risk of fatal ventricular dysrythmias.
        - Also increases cyclosporine, digoxin, warfarin and sulfonylurea serum levels.
- Do not treat superficial mycoses in patients with HF/other cardiac

dysfunction. Caspofungin (Cancidas); echinocandin antifungal agent

- Indications: narrow spectrum IV antifungal for use against aspergillus and candida species
    - With invasive aspergillosis that is unresponsive to Amphotericin B or Itraconazole
    - Systemic candida infections (candidemia and candida-related peritonitis, pleural space infections, and intraabdominal abscesses).
- Adverse Effects
    - Histamine Response - rash, facial flush, pruritis, anaphylaxis, or a sense of warmth
    - Phlebitis at injection-site
    - Common - Fever, headache, rash, nausea, or vomiting. Griseofulvin (Gris-

PEG); other antifungal class

- Indications: treatment of superficial mycoses; PO administration
    - Dermatophytic infections of the skin, hair, and nails.
    - Is NOT active against Candida species or systemic mycoses. Terbinafine (Lamisil);

allylamine antifungal agent

- Oral Terbinafien Indications – use against dermatophytes (highly effective) and against Candida species (less effective)
    - Specifically systemic fungal infections like tinea and

onychomycosis. Azole Use in Older Adults

- Reduced gastric hydrochloric production (achlorhydria) is greater in older adults which can make absorption of some antifungal agents unpredictable.
- Practice of medication reconciliation is important due to many drug interactions such as changed

plasma levels of medications (warfarin, phenytoin, and oral hypoglycemic agents) that are increased by azoles.

- Consider cognitive ability to safely self-administer medications without skipping or doubling doses.
- Consider altered pharmacokinetics based on age-related changes. Tinea Pedis Treatment
- One of the four types of "ring worm" or dermatophytic fungal infections.
    - Ring worm of the foot, also known as "athletes' foot".
- Responds well to topical antifungal therapy
- Patient education:
    - Wear absorbent cotton socks
    - Change their shoes often
    - Dry their feet after bathing Treatment Choice

for Systemic Mycoses

- 1st Choice Amphotericin B; 2nd Choice

Itraconazole Chapter 80: Antiviral Drugs

Acyclovir (Zovirax); available topically, orally, or intravenously

- MOA: inhibits viral DNA synthesis by activating acyclo−guanosine monophosphate (GMP) which is then converted to acyclo−guanosine triphosphate (GTP) that inhibits viral DNA polymerase. GTP also becomes incorporated into the viral DNA, blocking further DNA chain growth.
- Indications: first-choice agent for most infections caused by the herpes simplex virus (HSV-1 & HSV-2), varicella-zoster virus (VZV), and cytomegalovirus (CMV)
- Route of administration considerations
    - Topical – may cause burning or stinging
    - Oral – safe during pregnancy and can be used to prevent HSV-2 near term
    - IV – can cause renal failure; avoid in patients with pre-existing renal disease or those who are dehydrated.

Oseltamivir (Tamiflu); neuraminidase inhibitor antiviral class

- MOA: inhibits the neuraminidase enzyme on the surface of the influenza virus which prevents the release of new viral particles from infected cells -> halting the spread of infection within the body.
- Indications – prevent and treat influenza A and B infections, H1N1 (swine flu), and H5N1 (avian flu).
- Administration
    - Begin treatment as soon as symptoms begin
    - Dose depends on severity, condition and patient response.
    - Discontinue 2 days prior to receiving the influenza vaccine since it will decrease the immune response.
    - Take with food to reduce GI upset
    - Available in oral formulations either via tablet or suspension.
    - For influenza prevention, the dosage is half than treatment dose.
        - Candidates include those exposed to the flu or nursing home

residents. Palivizumab (Synagis); monoclonal antibody

- Indications: for preventing RSV infection in premature infants and in young children with chronic lung disease

Influenza Vaccine

- Purpose of annual vaccination:

- Influenza viruses are constantly evolving, so the influenza vaccines must continuously change too. Manufacturers produce a new vaccine directed against the three (trivalent) or four (quadrivalent) strains of influenza virus deemed most likely to cause disease during the upcoming flu season each year.

- Contraindications:
  - People at high risk for flu complications:
    - Pregnant women should not receive the live influenza vaccine but can have the inactivated vaccine.
    - Current recommendations have one main contraindication - a severe allergic reaction to influenza vaccine or a vaccine component.

Chapter 81: Antiretroviral Drugs

NRTIs

- MOA: prodrugs that inhibit HIV replication by suppressing synthesis of viral DNA
- Adverse Effects - are associated with mitochondrial toxicity since NRTIs can disrupt synthesis of mitochondrial DNA and impair mitochondrial function:
  - Lactic Acidosis as lactic acid accumulates due to dysfunctional mitochondria that cannot break down lactic acid.
    - Nausea, malaise, fatigue, anorexia, and hyperventilation (blowing off carbon dioxide can reduce acidosis)
    - Most likely to occur with NRTIs, didanosine and stavudine, and come with Black Box Warning.
  - Hepatic Steatosis since there is a decreased breakdown of fatty acids by mitochondria leading to fatty deposits in the liver.
  - May also lead to pancreatitis and myopathies.

Protease Inhibitors (PIs)

- MOA: prevent HIV maturation by blocking the HIV enzyme protease. This maturation is necessary for HIV to infect CD4 cells -> immature forms are noninfectious.
- Adverse Effects:
  - Hyperglycemia and the development of diabetes
  - Lipodystrophy (fat redistribution)
  - Elevation of serum transaminases
  - Decreased cardiac conduction velocity
  - Can also increase bleeding in patients with hemophilia.
- Prescribing Considerations
  - Increased risk of bone loss – take Calcium and Vitamin D
  - St John's Wort reduces serum levels of PIs
  - PIs, Indinavir and fosamprenavir, may cause kidney stones Integrase Strand Transfer

Inhibitors (INSTIs)

- MOA: target HIV by terminating the integration of HIV into DNA. Integrase is one of three viral enzymes needed for HIV replication and inserts HIV genetic material into the DNA of CD4 cells.
  Inhibition of integrase prevents insertion of HIV DNA -> stops HIV replication.
  - Integrase inhibitors are combined with other antiretroviral agents to treat adults infected with HIV-1.
- Adverse Effects:
  - Few adverse effects, but commonly patients may have dizziness and insomnia.

- Depression and SI have been noted in patients with previous psychiatric issues.

Chemokine Receptor 5 Antagonists (CCR5 Antagonists)

- MOA: block entry of HIV into CD4 T-cells

Chapter 83: Anthelmintics

Albendazole (Albenza); first choice anthelmintic drug

- MOA: inhibits polymerization of tubulin and hence prevents the formation of cytoplasmic microtubules. As a result, microtubule- dependent uptake of glucose is prevented.
- Drug of choice for infestation with hookworms, pinworms, whipworms, Chinese liver flukes, giant roundworms, and pork roundworms, the cause of trichinosis.

Mebendazole (Emverm or Vermox)

- MOA: prevents uptake of glucose by susceptible intestinal worms. This glucose deprivation results in immobilization followed by slow death.
  - It does not influence glucose uptake or utilization by humans
- Drug of choice for most intestinal round worms and clears infestation with pinworms, hookworms, and giant roundworms.
- Broad spectrum of action makes it useful for treatment of mixed

infestations. Enterobiasis (“Pin worm”)

- Treatment Choices:
  - Albendazole, Mebendazole, and Pyrantel Pamoate

Week 2: Chapters 70, 71, 72, 73, 74, 75, and 76

Chapter 70

Antibiotics

- Determining Drug Susceptibility
  - Narrow-spectrum antibiotics - active against only a few species of microorganisms; preferred over broad-spectrum.
  - Broad-spectrum antibiotics - active against a wide variety of microbes.
  - Sensitivity testing is not always needed and is indicated only when the infecting organism is one in which resistance is likely.
    - Ex: microbes like group A streptococci are highly susceptible to penicillin G, therefore sensitivity testing is not necessary
    - In contrast, when resistance is common, as it is with S. aureus and gram-negative bacilli, tests for drug sensitivity should be performed.
  - Most tests currently used are based on one of three methods: disk diffusion, serial dilution, or gradient diffusion.

- Lifespan Considerations of Infants
  - Highly vulnerable to drug toxicity due to underdeveloped kidney and liver functioning -> eliminate drugs slowly.
  - Use of sulfonamides in newborns can produce kernicterus, a severe neurologic disorder caused by displacement of bilirubin from plasma proteins
- Antibiotic Stewardship
  - Prophylactic Use
    - Common in severe infections pending test results

- Choose treatment based on clinical evaluation and knowledge of which