

Week 1

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Chapter 79

1. Itraconazole Drug Interactions

- **Mechanism:** Itraconazole inhibits the CYP3A4 enzyme, leading to potential interactions with many other drugs.
- **Examples of Common Medications and Interactions:**
 - **Statins (e.g., simvastatin):** Increased risk of myopathy and rhabdomyolysis. Consider avoiding or switching to a non-interacting statin like pravastatin.
 - **Calcium Channel Blockers (e.g., verapamil, diltiazem):** Risk of congestive heart failure due to additive negative inotropic effects.
 - **Warfarin:** Increases INR and bleeding risk. Requires close INR monitoring if used concurrently.
- **Clinical Recommendations:** Evaluate the need for itraconazole when patients are on interacting drugs. Consider alternative antifungals or adjust doses.

2. Therapeutic Uses of Caspofungin

- **Primary Indications:**
 - **Invasive Candidiasis:** Effective against most *Candida* species, especially useful for *C. glabrata* and *C. krusei*, which are resistant to azoles.
 - **Invasive Aspergillosis:** Second-line option for patients who cannot tolerate or do not respond to amphotericin B or voriconazole.
- **Example Medications:** Caspofungin (Cancidas).
- **Dosing and Duration:** 70 mg loading dose, then 50 mg daily; duration depends on infection severity and response to therapy.

3. Griseofulvin Indications

- **Common Uses:** Dermatophyte infections, especially when caused by *Microsporum* and *Trichophyton* species.
- **Indications:**
 - **Tinea Capitis:** Often used in children as it is effective against scalp infections.
 - **Tinea Corporis and Tinea Cruris:** Alternative option when topical treatments are ineffective.
- **Example Medications:** Griseofulvin (Grifulvin V, Gris-PEG).
- **Clinical Considerations:** Requires several weeks to months of therapy depending on the location and severity of the infection.

4. Oral Terbinafine Indications

- **Primary Indications:**
 - **Onychomycosis:** Effective for fungal nail infections due to dermatophytes.
 - **Tinea Capitis:** Also used for scalp ringworm, especially in children.
- **Example Medications:** Terbinafine (Lamisil).
- **Dosing:** For onychomycosis, typically 250 mg daily for 6 weeks (fingernails) to 12 weeks (toenails).
- **Advantages:** Fungicidal activity against dermatophytes with high success rates in nail infections.

5. Azole Use in Older Adults

- **Commonly Used Azoles:** Fluconazole (Diflucan), Itraconazole (Sporanox), Voriconazole (Vfend), and Posaconazole (Noxafil).
- **Age-Specific Considerations:**
 - **Fluconazole:** Relatively safe but may require renal dose adjustment.
 - **Itraconazole:** Monitor for heart failure, especially in those with pre-existing cardiac conditions.
 - **Voriconazole:** Associated with visual disturbances; use cautiously in patients with ocular issues.
- **Clinical Recommendations:** Use the lowest effective dose, monitor liver function tests, and avoid polypharmacy where possible to reduce adverse effects and interactions.

6. Pharmacokinetics of Amphotericin B

- **Administration:** Typically administered via IV infusion due to poor oral bioavailability.
- **Distribution:** Binds extensively to tissues; penetrates poorly into the cerebrospinal fluid.
- **Example Medications:**
 - **Conventional Amphotericin B (Fungizone):** Higher nephrotoxicity risk.
 - **Liposomal Amphotericin B (AmBisome):** Better tolerated and preferred in patients at risk for kidney injury.
- **Half-Life:** Ranges from 15 days to several weeks due to slow tissue release.
- **Clinical Implications:** Monitor renal function and electrolytes closely, especially potassium and magnesium levels.

7. Treatment Choice for Systemic Mycoses

- **Options Based on Infection Type:**
 - **Histoplasmosis, Blastomycosis, and Coccidioidomycosis:** Often treated with itraconazole or amphotericin B for severe cases.

- **Aspergillosis:** Voriconazole is the preferred first-line agent; caspofungin as an alternative.
- **Cryptococcosis:** Amphotericin B with flucytosine for initial treatment, followed by fluconazole for maintenance.
- **Examples:**
 - **Amphotericin B** for life-threatening systemic infections.
 - **Fluconazole** for less severe infections or for step-down oral therapy after initial amphotericin B treatment.
- **Considerations:** Therapy duration varies widely, from weeks to several months, based on infection and patient immune status.

8. Drug Interaction with Itraconazole

- **Reiteration of Important Interactions:**
 - **Benzodiazepines (e.g., midazolam):** Prolonged sedation; avoid combination or reduce dose.
 - **Antiarrhythmic Drugs (e.g., quinidine):** Risk of QT prolongation and arrhythmias.
- **Patient Counseling:** Educate patients on potential side effects, such as dizziness or increased bleeding risk, if taking anticoagulants.

9. Adverse Effects of Caspofungin

- **Most Common Adverse Effects:** Fever, chills, headache, and gastrointestinal disturbances.
- **Serious Adverse Effects:**
 - **Hepatotoxicity:** Monitor liver enzymes in patients on prolonged therapy.
 - **Infusion Reactions:** Can include rash, pruritus, and histamine-mediated symptoms; slow infusion or premedicate if necessary.
- **Monitoring:** Regular liver function tests are recommended during treatment.

10. Tinea Pedis Treatment

- **Topical Options:**
 - **Terbinafine (Lamisil):** Applied daily for 1-2 weeks.
 - **Clotrimazole (Lotrimin):** Used twice daily for 2-4 weeks.
- **Oral Options (for refractory cases):**
 - **Oral Terbinafine:** 250 mg daily for 2-4 weeks.
 - **Oral Fluconazole:** 150 mg weekly for up to 6 weeks.

- **Patient Education:** Encourage patients to keep feet dry and avoid tight footwear to prevent recurrence.

11. Amphotericin B: Minimizing Nephrotoxicity

- **Preventive Measures:**
 - **Hydration:** Saline loading (500 mL IV normal saline before and after administration) can reduce kidney damage.
 - **Liposomal Formulation:** AmBisome or other lipid-based formulations have lower nephrotoxicity.
- **Monitoring:** Regular renal function tests (creatinine, BUN) and electrolyte monitoring (especially potassium and magnesium).
- **Example Protocol:** For severe infections, start with 0.3-0.5 mg/kg/day and adjust based on response and side effects.

12. Griseofulvin Indications

- **Common Dermatophyte Infections Treated:**
 - **Tinea Capitis:** Commonly treated in pediatric populations.
 - **Tinea Corporis and Tinea Pedis:** Used when first-line topical treatments fail.
- **Example Dosage:** 500 mg daily for adults; for children, weight-based dosing.
- **Adverse Effects:** Headache, gastrointestinal upset, photosensitivity. Advise patients to avoid sun exposure.

13. Azole Use in Older Adults

- **Examples and Adjustments:**
 - **Fluconazole:** Requires renal dose adjustment; generally safe but monitor for hepatic toxicity.
 - **Itraconazole and Voriconazole:** Use cautiously due to potential for heart failure and visual disturbances, respectively.
- **Monitoring:** Baseline liver function tests, periodic ECGs for QT prolongation, and routine checks for adverse effects.
- **Polypharmacy Consideration:** Reduce the risk of drug-drug interactions by using a single azole agent and avoiding concurrent CYP450 inhibitors.

Chapter 80

1. Oseltamivir (Tamiflu) Mechanism of Action (MOA)

- **MOA:** Oseltamivir is a neuraminidase inhibitor that blocks the neuraminidase enzyme on the surface of influenza viruses. This inhibition prevents the release of newly formed virus particles from infected cells, limiting the spread of the virus within the respiratory tract.

- **Virus Specificity:** Effective against influenza A and B strains, helping to reduce the duration and severity of symptoms if administered early in the infection.

2. Oseltamivir (Tamiflu) Administration

- **Dosage Forms:** Available as oral capsules and an oral suspension for patients who have difficulty swallowing capsules.
- **Standard Dosing:**
 - **Treatment:** 75 mg twice daily for 5 days for adults and children over 13, with weight-based dosing in younger children.
 - **Prophylaxis:** 75 mg once daily for 7-10 days for exposed individuals, especially during influenza outbreaks in settings like nursing homes.
- **Timing:** Most effective when started within 48 hours of symptom onset. May still benefit high-risk patients if initiated later.

3. Oseltamivir (Tamiflu) Indications

- **Primary Indications:**
 - **Treatment of Acute Uncomplicated Influenza:** For patients who have had symptoms for less than 48 hours, reducing symptom duration and complication risk.
 - **Prophylaxis:** For patients exposed to influenza (e.g., close contacts, healthcare workers), particularly valuable for high-risk groups such as the elderly and immunocompromised.
- **High-Risk Populations:** Indicated for individuals at high risk for influenza complications, including those with chronic illnesses (e.g., asthma, diabetes) or weakened immune systems.

4. Acyclovir: Route of Administration Considerations

- **Routes:** Acyclovir is available in oral, intravenous (IV), and topical formulations.
- **Oral Acyclovir:** Typically used for mild to moderate infections, including genital herpes, shingles, and chickenpox.
- **Intravenous Acyclovir:** Indicated for severe infections, such as herpes encephalitis, neonatal herpes, or severe varicella in immunocompromised patients. IV administration requires careful monitoring of renal function to avoid nephrotoxicity.
- **Topical Acyclovir:** Less effective than oral or IV forms, generally reserved for mild mucocutaneous herpes lesions in immunocompromised patients.

5. Purpose of Annual Flu Vaccine

- **Preventive Purpose:** Annual vaccination is the most effective way to prevent influenza and reduce the severity of illness if infection occurs.
- **Public Health Benefit:** Helps reduce influenza transmission within communities, especially protecting vulnerable populations (e.g., elderly, young children, pregnant women, immunocompromised).

- **Vaccine Composition:** Updated yearly to match circulating influenza strains (usually two A strains and one or two B strains), based on global surveillance.
- **Duration of Immunity:** Immunity wanes over time, so annual vaccination is recommended for sustained protection.

6. Flu Vaccine: Contraindications

- **Absolute Contraindications:**
 - **Severe Allergy to Previous Flu Vaccine:** Includes anaphylaxis or severe allergic reactions to any component of the vaccine.
 - **Egg Allergy (Severe):** Patients with severe egg allergy may require a recombinant or cell-based vaccine. However, most flu vaccines can be safely administered with observation for minor egg allergies.
- **Precautions:**
 - **History of Guillain-Barré Syndrome (GBS):** Patients who developed GBS within 6 weeks of a previous flu vaccine should discuss the risks with their healthcare provider.
 - **Moderate or Severe Illness with Fever:** Defer vaccination until recovery.

7. Palivizumab Indications

- **Primary Indication:** Prevention of severe respiratory syncytial virus (RSV) infection in high-risk infants and young children.
- **At-Risk Populations:**
 - **Premature Infants:** Especially those born before 29 weeks gestation.
 - **Infants with Chronic Lung Disease:** Particularly those under 24 months receiving medical therapy for lung disease.
 - **Infants with Congenital Heart Disease:** Particularly those with hemodynamically significant heart disease.
- **Administration:** Monthly intramuscular injections during RSV season (typically fall through spring) in high-risk patients.

8. Acyclovir Indication

- **Primary Indications:**
 - **Herpes Simplex Virus (HSV) Infections:** Used for genital herpes, herpes labialis (cold sores), and herpes encephalitis.
 - **Varicella-Zoster Virus (VZV) Infections:** Treats varicella (chickenpox) and herpes zoster (shingles) in immunocompetent and immunocompromised patients.
- **Prophylactic Use:** Acyclovir is used in immunocompromised patients to prevent recurrent HSV infections, especially post-transplant or during chemotherapy.

9. Acyclovir Mechanism of Action (MOA)

- **MOA:** Acyclovir is a nucleoside analog that interferes with viral DNA synthesis. Once phosphorylated, it incorporates into viral DNA, causing chain termination and halting viral replication.
- **Selectivity:** Targets viral thymidine kinase more than human cells, which limits its activity to infected cells and reduces toxicity.
- **Spectrum of Activity:** Most effective against HSV-1 and HSV-2, with moderate activity against VZV.

Chapter 81

1. Protease Inhibitors (PIs): Mechanism of Action (MOA)

- **MOA:** Protease inhibitors block the action of the HIV-1 protease enzyme, preventing the cleavage of polyproteins into functional viral proteins. This inhibition results in the production of immature, non-infectious viral particles.
- **Common Examples:** Atazanavir (Reyataz), Darunavir (Prezista), Ritonavir (often used to boost levels of other PIs).
- **Therapeutic Impact:** PIs effectively reduce viral load when used as part of combination antiretroviral therapy (cART), leading to improved immune function.

2. Protease Inhibitors (PIs): Adverse Effects

- **Common Side Effects:**
 - *Gastrointestinal Issues:* Nausea, vomiting, diarrhea are common with most PIs.
 - *Metabolic Disturbances:* Lipodystrophy (fat redistribution), hyperlipidemia, and insulin resistance.
 - *Elevated Liver Enzymes:* Risk of hepatotoxicity, especially in patients co-infected with hepatitis.
- **Long-Term Risks:** Increased risk of cardiovascular disease due to lipid abnormalities and insulin resistance.

3. Protease Inhibitors (PIs): Prescribing Considerations

- **Boosting:** PIs are often “boosted” with ritonavir or cobicistat to enhance their levels in the bloodstream, allowing for lower dosing and increased efficacy.
- **Drug Interactions:** Significant CYP450 interactions, which require careful review of the patient’s other medications.
- **Adherence:** Consistent dosing is crucial due to potential for rapid viral resistance; patients must be counseled on the importance of adherence.

4. Integrase Strand Transfer Inhibitors (INSTIs): Mechanism of Action (MOA)

- **MOA:** INSTIs inhibit the HIV integrase enzyme, preventing the integration of viral DNA into the host cell’s genome. This action blocks viral replication early in the infection cycle.

- **Examples:** Dolutegravir (Tivicay), Bictegravir (found in Biktarvy), Raltegravir (Isentress).
- **Therapeutic Benefit:** Often used in first-line treatment due to high potency, rapid viral suppression, and minimal drug interactions.

5. Integrase Strand Transfer Inhibitors (INSTIs): Adverse Effects

- **Common Side Effects:**
 - *Gastrointestinal Distress:* Diarrhea, nausea, abdominal pain.
 - *Central Nervous System (CNS) Effects:* Insomnia, headache, and, rarely, depression or anxiety.
- **Rare Side Effects:** Hypersensitivity reactions, including rash and, in very rare cases, rhabdomyolysis.
- **Considerations in Pregnancy:** Dolutegravir has been associated with a potential risk of neural tube defects if used early in pregnancy.

6. Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Mechanism of Action (MOA)

- **MOA:** NRTIs mimic natural nucleosides and are incorporated into viral DNA by reverse transcriptase. Once incorporated, they terminate DNA chain elongation, preventing viral replication.
- **Examples:** Tenofovir disoproxil fumarate (TDF), Tenofovir alafenamide (TAF), Lamivudine (3TC), Abacavir (ABC).
- **Significance:** NRTIs form the backbone of most cART regimens and are often combined with other antiretroviral classes.

7. Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Adverse Effects

- **Class-Related Toxicities:**
 - *Mitochondrial Toxicity:* Leading to lactic acidosis and hepatic steatosis (more common with older NRTIs like stavudine and didanosine).
 - *Renal Toxicity and Bone Mineral Density Loss:* Associated primarily with tenofovir disoproxil fumarate (TDF).
- **Drug-Specific Side Effects:**
 - *Abacavir (ABC):* Risk of hypersensitivity reaction in patients with the HLA-B*5701 allele.
 - *Zidovudine (AZT):* Can cause bone marrow suppression, leading to anemia and neutropenia.

8. Chemokine Receptor 5 (CCR5) Antagonists: Mechanism of Action (MOA)

- **MOA:** CCR5 antagonists bind to the CCR5 receptor on host cells, preventing HIV from entering the cell. This action blocks the virus's entry into CCR5-tropic HIV strains.
- **Example:** Maraviroc (Selzentry).