Chapter 5
Therapy for Fungal and Viral Infections

Chapter 5 Topics
• Fungi and Fungal Diseases
• Viruses and Viral Infections
• HIV-AIDS and Antiretroviral Agents
• Other Viral and Fungal STDs

Learning Objectives
• Understand the differences between fungi and viruses and why the drugs to treat them must have very different mechanisms of action.
• Differentiate antifungal, antiviral, and antiretroviral drugs by their indications, therapeutic effects, side effects, dosages, and administration.

Fungi and Fungal Diseases
Fungi
• Single-cell organisms
• Mushrooms, yeasts, and molds

Characteristics of Fungi
• Eukaryotic (defined nucleus): fungus, animal cell, and green plant cell
• Prokaryotic (no defined nucleus): bacteria
• Fungi differ from green plants
  – Lack chlorophyll
  – Reproduce by spores
• Fungi differ from animal cells
  – Have rigid cell wall unlike that of bacteria
Discussion
In what ways are human cells similar to fungi cells? How are they different?

Human cell membranes contain cholesterol, and cell membranes of fungi contain ergosterol.

Fungal Diseases
• Systemic fungal diseases most likely to occur in patients immunosuppressed by disease, drug therapy (corticosteroids or antineoplastics), or poor nutrition
• Fungi can cause skin and nail infections
• Women on antibiotics often need antifungal for vaginal yeast infection

Fungal Organisms and Resulting Infections
<table>
<thead>
<tr>
<th>Organism</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus</td>
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<tr>
<td>Blastomyces</td>
<td>blastomycosis</td>
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<tr>
<td>Candida (yeast)</td>
<td>candidiasis</td>
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<tr>
<td>Coccidioides</td>
<td>coccidioidomycosis</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>cryptococcosis</td>
</tr>
<tr>
<td>Histoplasma</td>
<td>histoplasmosis</td>
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</tbody>
</table>

Viruses and Viral Infections
• Virus
  – Minute infectious agent
  – Does not have all components of a cell
  – Replicate within cell by using metabolic process of host cell
  – Can only replicate within a living host cell: animal, plant, or bacteria

Virus and Bacterium
• A virus is much smaller than a bacterium.
• Image shows a virus infecting a bacterium.
Virus Characteristics

- Most viruses spread by
  - Direct contact
  - Ingestion of contaminated food and water
  - Inhalation of airborne particles
  - Exposure to contaminated body fluids/equipment

Virion
- An individual virus particle capable of infecting a living cell
- Consists of a core of genetic material, either DNA or RNA
- Capsid (protein shell) surrounds and protects nucleic acid

Virus Characteristics

- Depending on virus, capsid is
  - Covered with a membrane called an envelope
  - Not covered with an envelope
- Naked virus: a virus without an envelope

Five Stages of Viral Infection
1. Virus attaches to a cell receptor.
2. Virus penetrates cell as cell membrane indents and closes around the virus.
3. Virus escapes into the cytoplasm of the cell.
4. Virus uncoats.
   - Sheds its covering
   - Releases DNA or RNA into cell nucleus
5. Virus converts nuclear activity in the cell to viral activity and reproduces new viral particles.
   - Uses energy of host cell to infect the cell and make more virus

Blocking Viral Division
- All virus-infected cells have some characteristics different from uninfected cells
- These differences offer ways to block viral division
  - Normal cells not affected
### Discussion

Provide an example of a common viral infection and the symptoms of this condition.

The flu (influenza) with symptoms of malaise, myalgia (muscle pain), headache, chills, and fever

### Classification of Viral Infections

Viral infections classified in several ways

- **Viral duration and severity**
  - **Chronic**
  - **Acute**
  - **Slow**

- **Extent of infection within the body**
  - **Local**
  - **Generalized**

### Viral Duration and Severity

- **Acute**: quickly resolves, no latent infection. Common cold, flu
- **Chronic**: protracted course with long periods of remission interspersed with reappearance. Herpes virus infection
- **Slow**: progressive course, ends in death. HIV (AIDS)

### Viral Infection

- **Local**: affects tissues of a single system, such as the respiratory tract, eye, or skin
- **Generalized**: has spread or is spreading to other tissues by way of bloodstream or tissues of the CNS

### Viral Latency

- Virus lies dormant, then under certain conditions, reproduces and behaves like an infective agent
- Latency problem with herpes virus and HIV
- Some viruses cause normal cells to transform into cancer cells
Virus and Cell Interaction

- A virus can damage host cell by
  - Altering the cell
  - Incorporating into genetic material of host cell
  - Dividing when host cell divides
  - Killing host cell

Virus and Cell Interaction

- Most viruses have several antigens on their surface
- Antigens stimulate host to produce immunoglobulins
  - An antibody that may prevent an organism from attaching to a cell receptor or may destroy the virus

Interferon

- Some virus-infected cells respond by producing interferon
  - Substance that protects neighboring uninfected cells from viral infection
  - Inhibits viral RNA synthesis
  - Host specific

Vaccination

- Introduces a vaccine into the body to produce immunity to actual agent
- Exposes patient to a virus component or a similar strain that does not produce infection
- When vaccinated patient encounters actual virus, infection cannot develop

Discussion

Who should receive an influenza vaccine?

High-risk patients such as healthcare workers, nursing home residents, public safety workers, individuals over 65 years old, and immunocompromised patients.

Antivirals

- Antivirals are formulated to prevent virus cell replication without interfering with host cell’s normal function
**HIV-AIDS and Antiretrovirals**

- HIV is a retrovirus
  - Copies its RNA genetic information into the host’s DNA
  - Uses reverse transcriptase, a retroviral enzyme
- Antiretroviral drugs limit progression of HIV retrovirus

**Seven Classes of Antiretroviral Drugs**

- Nucleoside reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Nucleotide reverse transcriptase inhibitors (NtRTIs)
- Protease inhibitors (PIs)
- Fusion inhibitors
- Chemokine receptors
- Integrase inhibitors

**Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**

- Mimic a DNA building block to inhibit the actions of the enzyme nucleoside reverse transcriptase
- Prevents replication of HIV

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**

- Inhibit action of HIV reverse transcriptase
- Prevent formation of DNA copy of viral RNA

**Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)**

- Inhibits the activity of HIV-1 reverse transcriptase by competing with natural nucleic acid building block; NtRTIs terminate chain formation.
- Less toxicity than NRTIs

**Protease Inhibitors (PIs)**

- Inhibit protease enzyme, which cleaves certain HIV protein precursors needed to replicate virus
- Result: production of immature, noninfectious virions
- Combined with other antiretroviral drugs
Fusion Inhibitors and Chemokine Coreceptors

- Prevent HIV from attaching to immune system cells

Discussion

How do fusion inhibitors represent an advance in the treatment of HIV?
Prevents AIDS virus from entering the cell

Integrase Inhibitor

- Drug blocks enzyme integrase
- Integrase inserts DNA produced by reverse transcriptase into patient’s DNA

Responding to HIV Exposure

- Centers for Disease Control (CDC) guidelines for healthcare workers exposed to HIV
  - Post-exposure prophylaxis (PEP)
  - Begin within two hours
  - Can decrease risk of infection by 80%

Combining Antiretrovirals

- Standard care for AIDS treatment is to combine three or more drugs
- Regimens complex and difficult to follow
- Problem with compliance

Combining Antiretrovirals

<table>
<thead>
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<th>Regimen Type</th>
<th>Recommendation</th>
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<tr>
<td>standard therapy</td>
<td>NNRTI: efavirenz + lamivudine + (zidovudine or tenofovir or stavudine)</td>
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<tr>
<td>PI</td>
<td>lopinavir-ritonavir + lamivudine + (zidovudine or stavudine)</td>
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</table>
Combining Antiretrovirals

<table>
<thead>
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<th>Regimen Type</th>
<th>Recommendation</th>
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<td>alternative therapy</td>
<td>3-NRTI: abacavir + lamivudine + (zidovudine or stavudine)</td>
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<tr>
<td>post-exposure prophylaxis (PEP)</td>
<td>zidovudine + lamivudine + (indinavir or nefavir)</td>
</tr>
</tbody>
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Discussion

What is one of the biggest problems when treating HIV?

Noncompliance with drug regimen due to problematic side effects and complex dosing.

Assignments

- Complete Chapter Review activities
- Answer questions in Study Notes document
- Study Partner
  - Quiz in review mode
  - Matching activities
  - Drug tables

Chapter 6 Topics

- The Nervous System
- Anesthesia
- Pain Management
- Migraine Headaches

Learning Objectives

- Understand the central and peripheral nervous systems, their functions, and their relationship to drugs.
- Recognize different dosage forms and understand how the drug delivery system works.
- Learn how drugs affect body systems and where they work in the body.
Learning Objectives

• Understand the concepts of general and local anesthesia, and know the functions of these agents.
• Define the action of neuromuscular blocking agents in reducing muscle activity.

Learning Objectives

• Distinguish between narcotic and nonnarcotic analgesia.
• Understand the different classes of narcotics and the role of the technician in monitoring these drugs.
• Become familiar with the various types of agents for migraine headaches.

The Nervous System

• Transmits information over vast network throughout the body
• Neuron: nerve cell that transmits information
• Neurotransmitter: chemical substance released from neuron
  – Stimulates or inhibits activity in target cells, especially other neurons

Neurotransmitters Being Released from a Neuron

Divisions of the Nervous System: CNS

• Central Nervous System (CNS)
  – Consists of brain and spinal cord
  – Spinal cord receives information and sends it to brain
  – Brain evaluates information and sends a response

Divisions of the Nervous System: PNS

• Peripheral Nervous System (PNS) made up of nerves and sense organs
  – Afferent system: nerves and sense organs bring information to CNS
  – Efferent system: nerves send information from the CNS
**PNS Efferent System**

- Autonomic nervous system (ANS)
  - Involuntary activities: respiration, circulation, digestion, body temperature, metabolism, blood glucose, sweating
- Somatic nervous system
  - Voluntary activities: skeletal muscles
  - Acetylcholine only neurotransmitter between CNS and skeletal muscles

**CNS and PNS Primary Neurotransmitters**

- CNS
  - Acetylcholine (Ach)
  - Dopamine
  - Norepinephrine
  - GABA (gamma-aminobutyric acid)
  - Glutamate
  - Serotonin
- PNS
  - Acetylcholine (Ach)
  - Norepinephrine

**Autonomic Nervous System**

- Sympathetic and Parasympathetic Primary Neurotransmitters
  - Sympathetic System
    - Acetylcholine (Ach)
    - Norepinephrine
    - Dopamine
    - Glutamate
    - Epinephrine
  - Parasympathetic System
    - Acetylcholine (Ach)

**ACh and GABA**

- ACh acts on receptors in smooth and cardiac muscle, skeletal muscle, and exocrine glands
- ACh receptors blocked by anticholinergics
- GABA regulates message delivery system of the brain

**Dopamine, Epinephrine, and Norepinephrine**

- Dopamine acts on receptors in the CNS and kidneys
- Epinephrine acts on cardiac and bronchodilator receptors
- Norepinephrine acts on alpha and beta receptors
Serotonin and Glutamate

- Serotonin acts on smooth muscle and gastric mucosa
  - Causes vasoconstriction which decreases blood flow
  - Emotional responses: depression, anxiety
- Glutamate may be crucial to some forms of learning and memory

Types of Receptors

- Alpha
  - Vasoconstriction, raises blood pressure
- Beta-1
  - Increases heart rate and contractive force of the heart
- Beta-2
  - Influences bronchodilation

Discussion

What are three important types of receptors in the study of drugs?

Three important types are alpha, beta-1, and beta-2.

Drug Effects on the Nervous System

- Effects on receptors
  - Neurotransmitter binding causes cell membrane to be more permeable to various ions.
  - Activate enzyme systems that promote chemical reaction
  - Blocking, preventing transmitters from binding to receptors
    - Anticholinergics

Side Effects of Anticholinergics

- Decreased GI motility (constipation)
- Decreased sweating
- Decreased urination
- Dilated pupil and blurred vision
- Dry eyes
- Dry mouth

Anesthesia

- Allows painless and controlled surgical, obstetric, and diagnostic procedures
- Most potent anesthetics are gases or vapors
- Two classes of anesthesia: general and local
Anesthesia

- One anesthetic may be superior to another, depends on clinical situation
- Final choice based on drugs and anesthetic techniques safest for patient
- Anesthesiologist oversees administration of anesthesia during surgery

Physiologic Effects of Anesthesia

- Involves many systems
  - Nervous
  - Respiratory
  - Endocrine
  - Cardiovascular
  - Skeletal muscular
    - GI
    - Hepatic

Goals of Balanced Anesthesia

- Amnesia to eliminate patient’s memory of procedure
- Adequate muscle relaxation, no contracting of muscles
- Adequate ventilation by maintaining oxygen concentrations
- Pain control

Discussion

What are some of the indicators used to assess general anesthesia?

Some indicators include: blood pressure, hypervolemia, oxygen level, cardiac rate, tissue perfusion, and urinary output.

General Anesthetics

- General anesthesia is the unique condition of reversible unconsciousness and absence of response to painful stimuli
- Four reversible actions
  - Unconsciousness
  - Analgesia (relieving pain)
  - Skeletal muscle relaxation
  - Amnesia on recovery

Preanesthetic medications

- Control sedation
- Reduce postoperative pain
- Provide amnesia
- Decrease anxiety

Drugs often used: narcotics, benzodiazepines, phenothiazines
General Anesthetics

- Malignant hyperthermia is a serious side effect of anesthesia
  - Fever of 110°F or more
  - Life threatening
- Treatment: dantrolene (Dantrium)
  - Always check expiration date

Injectable Anesthetics

- Very lipid soluble
- Most dispensed by IV drip
- Most are controlled substances

Warning!

Injectable Anesthetics START HERE

Benzodiazepines

- Used for induction, short procedures, and dental procedures
- Used in controlling and preventing seizures induced by local anesthetics
- midozolam (Versed)
  - fastest onset of action
  - greatest potency
  - most rapid elimination

Antagonist Agents

- flumazenil (Romazicon) reverses overdoses of benzodiazepine
- naloxone (Narcan) reverse overdoses of narcotics
- All operating and emergency rooms maintain a supply of antagonists

Neuromuscular Blocking Agents

- Causes immediate skeletal muscle relaxation of short, long, and extended durations
- Used to facilitate endotracheal intubation and ensure patient does not move during surgery

Reversal of Neuromuscular Blocking Agents

- Anticholinesterase agents increase action of acetylcholine
  - Inhibits acetylcholine
  - Restores transmission of nerve signal to neuromuscular blocking agent
Local Anesthesia

- Relieves pain without altering alertness or mental function
- Affect all types of nervous tissue
- Commonly combined with other drugs
- Variety of combinations available

Dosage Forms of Local Anesthetics

- Topical: drops, sprays, lotions, ointments
- Infiltration: superficial injection
- Nerve block: injection
- IV
- Epidural: regional anesthesia
- Spinal: blocks afferent pain nerve impulses from lower part of the body

Discussion

What are the two classes of local anesthetics?
The two classes are esters and amides.

Local Anesthetics

- Esters
  - Short acting
  - Metabolized in plasma and tissue fluids
  - Excreted in urine

- Amides
  - Longer acting
  - Metabolized by liver enzymes
  - Excreted in urine

Discussion

What functions are lost with local anesthetics?
Functions that are lost include: pain perception, temperature sensation, touch, proprioception, and skeletal muscle tone.

Discussion

Under what conditions would a local anesthetic be used over a general anesthetic?
It is chosen when a well-defined area of the body is targeted.
Pain Management

• Pain is a protective mechanism to warn of damage or the presence of disease
  – Part of the normal healing process
  – Can be a disease
  – Considered the “fifth” vital sign

Discussion

What are the classifications of pain?
There are three: acute, chronic nonmalignant, and chronic malignant.

Pain Management

• Acute Pain
  – Associated with trauma or surgery
  – Warns of a problem
  – Easier to manage by treating the cause
  – Disappears when body heals
  – Has beginning and end

Pain Management

• Chronic nonmalignant pain
  – Lasts more than 3 months
  – Diagnosed or undiagnosed cause
  – May respond poorly to treatment
  – May or may not have an identifiable physical or chemical basis
  – Suffering includes a sense of helplessness and hopelessness
  – Affects all aspects of life

Pain Management

• Chronic malignant pain
  – Accompanies malignant disease
  – Often increases in severity with disease progression

Major Sources of Pain

• Source: somatic
• Areas: body framework
• Characteristics: throbbing, localized
• Treatment: narcotics, nerve blockers
Major Sources of Pain

- **Source:** visceral
- **Areas:** kidneys, intestines, liver
- **Characteristics:** aching, throbbing, sharp, gnawing, crampy
- **Treatment:** narcotics, NSAIDs, nerve blockers, antiemetics

Major Sources of Pain

- **Source:** neuropathic
- **Areas:** nerves
- **Characteristics:** burning, aching, numbing, tingling, constant
- **Treatment:** antidepressants, anticonvulsants

Major Sources of Pain

- **Source:** sympathetically mediated
- **Areas:** overactive sympathetic system
- **Characteristics:** occurring when no pain should be felt
- **Treatment:** nerve blockers

Narcotics

- Pain-modulating chemicals that cause insensitivity or stupor
- **Opiates**
  - Derived from opium or synthetic
  - Agonists of opioid receptor sites
- Main effects on CNS and GI tract
- Lesser effects on peripheral tissues

Natural Opioids

- Endorphins, enkephalins, and dynorphins
- Brain produces in response to pain stimuli
- When receptors are activated
  - Causes decreased nerve transmission
  - Sensation of pain diminished
- Opioids bind to these same receptors

Discussion

What are three effects of narcotics?

Three effects are analgesia, sedation, and euphoria and dysphoria.
Effects of Narcotics

- Analgesia: reduces pain from most sources
- Sedation: decrease anxiety and cause drowsiness
- Euphoria and dysphoria: feelings of well-being, disquiet, restlessness
- Narcotics have potential for tolerance and dependence

Patient-Controlled Analgesia Pump

- PCA pump effective means of controlling pain
- Patient regulates, within limits, amount of drug received
- Better pain control with less drug

Analgesic Ladder of Pain Relief

1. Mild to moderate pain
   - Acetaminophen or NSAID and an adjuvant
2. If adequate relief not achieved
   - NSAID plus a “weak” opioid (codeine)
3. If adequate relief not achieved
   - Strong opioid (morphine) with an adjuvant analgesic if indicated

Transdermal Patch

- Provides pain control
- Allows patient to remain more alert than with most other methods

Addiction and Dependence

- Chronic opioid therapy has low risk of addiction when used appropriately
Discussion

What is the difference between addiction and dependence?

Dependence and Addiction

- Dependence
  - Physical and emotional reliance on a drug
  - Withdrawal
- Addiction
  - Compulsive disorder

Signs of Narcotics Addiction

- Preoccupation with drugs
- Refusal of medication tapers
- Strong preference for a specific opioid
- Decrease in ability to function
- Medication often not taken as prescribed
- Tendency to rely on multiple prescribers and pharmacies to conceal behavior

Withdrawal

- Patients more successful overcoming addiction if withdrawal symptoms are handled appropriately
- Opioid antagonists have stronger attraction for receptors than analgesic agents
- Blocking opioid action may prevent withdrawal symptoms

Narcotic Analgesics

- Dose requirements vary with
  - Severity of pain
  - Individual response to pain
  - Patient’s age and weight
  - Presence of concomitant illness
- Morphine is standard against which all other narcotic analgesics are measured

Combination Drugs for Managing Pain

- Combinations of narcotics and nonnarcotics are common
  - Increases pain relief
  - Allows use of lower doses
  - Limits intake of addictive substances
  - Decreases side effects
Migraine Headaches

- Migraine Headache
  - Severe, throbbing, vascular headache
  - Recurrent unilateral headache
  - Accompanied by neurologic and GI disturbances
- 90% of migraine sufferers report nausea
- Sensitivity to light, sound, and stimulation also common

Components of Migraine

- Classic migraine components (all five not experienced by everyone)
  - Prodrome
  - Aura
  - Headache
  - Headache relief
  - Postdrome

Components of Migraine

- Prodrome: Symptom indicating onset
- Aura: Subjective sensation or motor phenomenon that precedes onset
  - Flashing lights
  - Shimmering heat waves
  - Bright lights
  - Dark holes in visual fields
  - Vision blurred, cloudy transient or loss of

Components of Migraine

- Headache and Headache Relief
  - Generally dissipates in 6 hours, but may last 1 to 2 days
- Postdrome
  - Knowing headache is gone

Cause of Migraine Headaches

- Serotonin appears involved in cause
- Decreased levels causes excessive vasodilation in cranial arteries and migraine occurs
- By stimulating serotonergic receptor, vasoconstriction occurs, alleviating migraine

Causative Factors of Migraine Headaches

- Diet
- Stress
- Depression
- Sleep habits
- Certain medications
- Hormonal fluctuations
- Atmospheric pressure
- Environmental irritants
Initial Treatment of Migraine Headaches

- At first hint of migraine, identify and eliminate triggers
  - Quiet environment and sleep may help
  - Lying down in a dark room
- For severe or debilitating and frequent attacks, drug therapy may be indicated
  - Sedative, antiemetic, and narcotic agents

Discussion

What are the two classes of migraine drug therapy?
The two classes are prophylactic therapy and abortive therapy.

Therapy for Migraine Headaches

- Prophylactic Therapy
  - Attempts to prevent or reduce recurrence
- Abortive Therapy
  - Taken after acute migraine occurs
  - Taken at first sign of a migraine or headache

Prophylactic Therapy

- Anticonvulsants
- Beta blockers
- Calcium channel blockers
- Estrogen
- Feverfew
- NSAIDs
- SSRIs
- Tricyclic antidepressants

Abortive Therapy

- Simple analgesics
- NSAIDs
- Ergotamine-containing medications
- Serotonin-containing medications

Discussion

What are some of the issues facing migraine sufferers and the medication that is used?

Some issues are nausea and vomiting, 0.5 to 2 hours of action, and side effects.
Assignments

- Complete Chapter Review activities
- Answer questions in Study Notes document
- Study Partner
  - Quiz in review mode
  - Matching activities
  - Drug tables

Chapter 7 Topics

- Depression and Mood Disorders
- Psychosis
- Anxiety
- Sleep and Sleep Disorders
- Alcoholism

Learning Objectives

- Differentiate the antidepressant, antipsychotic, and antianxiety agents.
- Be prepared to discuss the antidepressant classes, their uses, and their side effects.
- Know why and how lithium and other drugs are used in treating bipolar disorders.

- Be familiar with antipsychotics and the drugs that prevent their side effects.
- Define anxiety, learn its symptoms, and know the drugs used in its treatment.
- Recognize the course and treatment of panic disorders, insomnia, and alcoholism.

- Clinical depression is the most common severe psychiatric disorder.
- Women more likely than men to have depression.
- Depression occurs later in life in men.
### Common Symptoms of Depression

- Loss of interest in usual activities
- Low self-esteem
- Pessimism
- Self-pity
- Significant weight loss or gain
- Insomnia or hypersomnia
- Extreme restlessness
- Loss of energy
- Feelings of worthlessness
- Diminished ability to think
- Feelings of guilt
- Recurrent thoughts of death
- Suicide attempts

### Mood Disorders

- **Mania**
  - Mood of extreme excitement, excessive elation, hyperactivity, agitation, and increased psychomotor activity
- **Bipolar disorder**
  - Mood swings that alternate between major depression and mania

### Mood Disorders

- **Unipolar depression**
  - Major depression with no previous occurrence of mania
- **Post-traumatic stress disorder (PTSD)**
  - Disorder characterized by persistent, recurring fear and avoidance of the event following a traumatic event and lasting for over a month or impairing work or relationships

### Mood Disorders

- **Seasonal affective disorder (SAD)**
  - Form of depression that recurs in the fall and winter and remits in the spring and summer

### Discussion

What are the differences that may be seen in patients with unipolar and bipolar disorders?

Patients with unipolar disorder have depression symptoms. Patients with bipolar disorder have depression and mania symptoms.

### Neurotransmitters and Depression Therapy

- **Neurotransmitters**
  - Chemicals produced by nerve cells
  - Involved in transmitting information in the body
  - Important in mood disorders
- **Antidepressants**
  - Change levels of two neurotransmitters: serotonin, norepinephrine
Four Classes of Antidepressants

- Selective serotonin reuptake inhibitor (SSRI)
- Serotonin norepinephrine reuptake inhibitor (SNRI)
- Tricyclic antidepressants (TCAs)
- Monoamine oxidase inhibitors (MAOIs)

How Antidepressants Work

- SSRIs block reuptake (reabsorption) of serotonin, little effect on norepinephrine
- SNRIs increase both serotonin and norepinephrine
- TCAs prevent reuptake of serotonin and/or norepinephrine
- MAOIs inhibit enzymes that break down serotonin and norepinephrine

SNRIs

- Used when SSRIs are not effective
- Affect both serotonin and norepinephrine reuptake
- More effective for pain than drugs affecting one neurotransmitter

Cyclic Antidepressants

- Two varieties
  - 3 fused carbon rings (tricyclic)
  - 4 fused carbon rings (tetracyclic)
- Tricyclic antidepressants
  - Produce response in 50% of patients
  - Also used in bed-wetting

Discussion

Why would cyclic antidepressants be prescribed for bed wetting in children?

They may be prescribed because of their anticholinergic side effects.

Monoamine Oxidase Inhibitors (MAOIs)

- Second-line treatment because of many interactions with food and other drugs
- Most beneficial in atypical depression
- Currently used to treat conditions other than depression
**bupropion (Wellbutrin, Zyban)**
- Dopamine-uptake inhibitor
- Does not cause sedation, blood pressure changes, or ECG changes
- Maximum daily dose of 450 mg
- Approved aid to smoking cessation and SAD

**trazodone (Desyrel)**
- Prevents reuptake of serotonin and norepinephrine
- Better side effect profile than TCAs
- Ginkgo—possible interaction
- Priapism

**Bipolar Disorders Mania Episodes**
- Decreased need for sleep
- Distractibility
- Elevated or irritable mood
- Grandiose ideas
- Increase in activity
- Racing thoughts
- Pressure to keep talking
- Excessive involvement in pleasurable activities with large potential for painful consequences

**Bipolar Disorders Depressive Episodes**
- Sadness, excessive crying
- Low energy
- Loss of pleasure
- Difficulty concentrating
- Irritability
- Thoughts of death or suicide

**Discussion**
What is the drug of choice for treating bipolar disorders?
Lithium

**Discussion**
What is the two-fold objective of drug therapy for bipolar disorder?
The two objectives are to treat acute episodes and prevent subsequent attacks.
lithium (Eskalith, Lithobid)

- Drug of choice to treat
  - Bipolar disorder and acute mania
  - Prophylaxis of unipolar and bipolar disorders
- Patients taking lithium must have frequent blood tests to assess lithium levels and maintain therapeutic range.
- START HERE 11/12/14

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carbamazepine (Tegretol) or divalproex (Depakote)

- For patients who cannot tolerate lithium, either drug can be substituted:
  - carbamazepine
  - divalproex

Neurotransmitters in Schizophrenia

- Dopamine and, to lesser degree, serotonin
- Dopamine receptors in 4 pathways, including limbic system
- Limbic system
  - Controls emotions
  - Psychotic experiences when dopamine levels are excessive

Psychosis

- Antipsychotics or neuroleptics
- Schizophrenia is primary indication
  - Retreat from reality
  - Delusions
  - Hallucinations
  - Ambivalence
  - Withdrawal
  - Bizarre or regressive behavior

Antipsychotics

- Older or typical antipsychotics: many side effects, especially muscle control problems
- New or atypical antipsychotics
  - Improved efficacy and reduced side effects
  - Limit dopamine-blocking ability to the limbic system pathway
  - First-line agents

(continued)
Atypical Antipsychotics
- Improved efficacy and reduced side effects
- Better tolerated, but associated with metabolic side effects
  - Weight gain
  - Hyperglycemia
  - New-onset diabetes
  - Dyslipidemia

Anxiety
- State of uneasiness characterized by apprehension and worry about possible events
- Two types of anxiety
  - Exogenous: response to external stresses
  - Endogenous: not related to external stresses, result of abnormality in cellular function in CNS

Discussion
What is the most common self-prescribed treatment for anxiety?
Alcohol

Antianxiety Agents
- Also called sedatives
- Include both noncontrolled and controlled substances
- Benzodiazepines, buspirone, and to a lesser extent, beta blockers are most used for panic attacks

Panic Disorders
- Panic: form of intense, overwhelming, and uncontrollable anxiety
- Neither a controllable voluntary emotion nor a condition that can be ignored or wished away

Panic Disorders
- Can occur anywhere at anytime
- Criteria for diagnosis
  - Three attacks in a three-week period
  - At least four qualifying symptoms
Pathophysiology of Panic Disorders

- Result from neurochemical defect in part of the brain
- Stimuli can be excessively amplified and cause an overreaction

Treatment of Panic Disorders

- Combination of antipanic medication and behavioral therapy
- Psychotherapy preferred treatment when symptoms cause significant discomfort or impairment
- Antianxiety medications indicated for short-term treatment

Sleep and Sleep Disorders

- Sleep is fundamental to human health
- Four stages of sleep

Four Stages of Sleep

- Stage I. Somewhat aware of surroundings, relaxed, NREM
- Stage II. Unaware of surroundings, easily awakened, NREM
- Stages III and IV. Increased autonomic activity, REM with dreams, 4 to 5 times a night

Insomnia

- Difficulty falling or staying asleep, or not feeling refreshed on awakening
- Treated with hypnotics (drugs that induces sleep)
- Chronic, occasional, or short-term insomnia
- Transient insomnia not sleep disorder

Causes of Some Sleep Disorders

- Situational: job stress, hospitalization, travel
- Medical: pain, respiratory or GI problems
- Psychiatric: schizophrenia, depression, mania
- Drug induced: alcohol, sedatives, sympathomimetic agents
Treatment for Sleep Disorders

- Diagnosis and effective treatment can often eliminate need for hypnotic drugs
- For clearly defined insomnia, hypnotics used as an adjunct

Narcolepsy

- Recurring, inappropriate episodes of sleep during the daytime hours
- No known cause
- Occurs four times more in men than women

Four Characteristics of Narcolepsy

1. Patient feels sleepy during daytime and immediately enters REM sleep
2. Patient experiences cataplexy with sudden emotions
3. Sleep paralysis
4. Very vivid hallucinations at the onset of sleep

Treatment of Narcolepsy

- Nondrug Therapy
  - Lifestyle changes
- Drug Therapy
  - Stimulants
  - Tricyclic antidepressants
  - SSRIs

Treatment of Sleep Disorders

- Pharmacological: hypnotics
- Nonpharmacological
  - Normalizing sleep schedule
  - Increase physical exercise
  - Discontinue alcohol as a sedative
  - Sleep only 7 to 8 hours per 24-hour period
  - Reduce caffeine and nicotine intake
  - Eliminate any drug that could lead to insomnia

Z Hypnotics

- Preferred treatment of sleep disorders
- No seizures if drug abruptly discontinued
- Relatively short half-life
- Do not significantly impact REM sleep
**Sleep Agents**
- Should be used in conjunction with other medical therapeutics
- Take 1 hour before bedtime
- Take only a limited number of times each week
- Duration of use: 4 to 6 week period

**Alcoholism**
- Disease can be arrested, not cured
- Lifetime disease, potentially fatal
- Complex genetic disease

**Effects of Alcoholism on Metabolism**
- Alcohol is an anesthetic and can cause loss of consciousness
- Emetic action prevents death by preventing absorption of lethal concentrations
- Alcoholics metabolize alcohol rapidly, which increases tolerance

**Side Effects of Alcoholism**
- Obesity with vitamin deficiency
- Gastritis and loss of appetite
- Organic brain damage
- Alcoholic psychosis and dementia
- Cirrhosis of the liver (irreversible damage)

**Four Steps Towards Recovery from Alcoholism**
1. Acknowledge the problem
2. Limit time spent with substance abusers
3. Seek professional help
4. Seek support from recovering alcoholics

**Symptoms of Dependence on Alcohol**
- Blackouts or lapses of memory
- Concerns of family, friends, and employers about the drinking
- Doing things that cause regret
- Financial or legal problems from drinking
- Loss of pleasure without alcohol
**Symptoms of Dependence on Alcohol**
- Neglecting responsibilities
- Trying to cut down or quit drinking, but failing
- Using alone; hiding evidence
- Drinking to forget about problems
- Willingness to do almost anything to get alcohol

**Alcohol Withdrawal Symptoms**
- Agitation
- Circulatory disturbances
- Convulsions
- Delirium treatments (DTs)
- Digestive disorders
- Disorientation
- Extreme fear
- Hallucinations
- Mental disturbances
- Nausea and vomiting
- Restlessness
- Sweating
- Tremor and weakness

**Assignments**
- Complete Chapter Review activities
- Answer questions in Study Notes document
- Study Partner
  - Quiz in review mode
  - Matching activities
  - Drug tables

**Chapter 8 Topics**
- Epilepsy
- Parkinson’s Disease
- Other Central Nervous System Disorders

**Learning Objectives**
- Develop an understanding of the physiologic processes that occur in epilepsy.
- Classify seizures and the goals of their therapy.
- Understand that specific drugs are used in different classes of seizures.
Learning Objectives

• Be familiar with Parkinson’s disease and the drugs used in its treatment.
• Identify the drugs and goals of therapy for attention-deficit disorders.
• Realize that some drugs may be used for several disease states.

• Recognize drugs used to treat Alzheimer’s disease.

Epilepsy

• Common neurologic disorder with sudden and recurring (paroxysmal) seizures.
• Caused by abnormal electrical impulses in the brain.
• All epilepsy patients have seizures, but not all with seizures have epilepsy.
• 1% to 2% have chronic epilepsy.

Seizures

• Disturbances of neuronal electrical activity that interfere with normal brain function.
• Behavior change patient not aware of.
• Conscious periods may or may not be accompanied by loss of control over movement.
• Loss of body control may affect one area or entire body.

Convulsions

• Excessive firing of neurons can result in a convulsion.
  – Involuntary contraction or series of contractions of the voluntary muscles.

Causes of Seizures

• Imbalance of excitatory and inhibitory neurotransmitters.
  – GABA: excitatory
  – Glutamate: inhibitory
  – Other neurotransmitters can play a role.
• Enzymes control neurotransmitter levels.
• Disruption in enzymes = disruption of neurotransmitters.
Causes of Seizures

- Alcohol or drug withdrawal
- Epilepsy
- High fever
- Hypoglycemia, hyperglycemia
- Infection (meningitis)
- Neoplasm (brain tumor)
- Trauma or injury (head, hematoma)

Two Classes of Seizures

- Partial
  - Simple partial
  - Complex partial
- Generalized
  - Tonic-clonic (was called grand mal seizure)
  - Absence (was called petit mal seizure)
  - Myoclonic
  - Atonic

Partial Seizures

- Localized in a specific area of the brain
- Almost always results from injury to cerebral cortex
- Occurs in about 65% of people with epilepsy
- Can progress to generalized seizures

Two Classes of Partial Seizures

- Simple Partial
  - No loss of consciousness
  - May have muscle twitching or sensory hallucinations
- Complex Partial
  - Impaired consciousness
  - Confusion, blank stare, and postseizure amnesia

Generalized Seizures

- Involves both hemispheres of the brain, no specific location
- Four types
  - Tonic-Clonic
  - Absence
  - Myoclonic
  - Atonic

Tonic-Clonic Seizures

- Tonic: body becomes rigid, patient may fall, lasts a minute or less
- Clonic: starts with muscle jerks, may be accompanied by shallow breathing, loss of bladder control, and excess salivation
  - lasts a few minutes
Absence Seizures

- Interruption of activities by blank stare, rotating eyes, uncontrolled facial movements, rapid eye blinking, twitching or jerking of an arm or leg
- No generalized convulsions
- Usually lasts 30 seconds or less
- Most prevalent first 10 years of life. 50% of children have tonic-clonic as they grow older

Myoclonic Seizures

- Occurs with sudden, massive, brief muscle jerks which may throw patient down or nonmassive, quick jerks
- Consciousness is not lost
- Can occur during sleep

Atonic Seizures

- Begins with sudden loss of muscle tone and consciousness
- Patient may collapse, head drop, arm or leg may go limp
- Lasts few seconds to a minute, then patient can stand and walk again

Status Epilepticus

- Continuous tonic-clonic seizures, with or without return to consciousness
- Last at least 30 minutes
- High fever and lack of oxygen may cause brain damage or death

Discussion

What percentage of patients status epilepticus patients die, regardless of treatment?

10%

Two Goals of Antiepileptic Therapy

- Seizure control or lessen the frequency
- Prevent emotional and behavioral changes that may result from seizures
Discussion

About 30% of patients do not comply due to side effects such as sedation and loss of cognitive processes. What are some possible strategies health care providers can use to help improve drug therapy compliance?

Antiepileptic Drug Therapy

- Different seizure types require different drugs
- Start with monotherapy at low dose and increase slowly over 3 to 4 weeks
- Medication must be maintained at steady therapeutic levels
- If insufficient response, polytherapy can be considered

Antiepileptic Drug Therapy

- Newer drugs are seizure-specific
- High potential for drug interactions
- Anticonvulsants have narrow therapeutic ranges
- Minor dosage changes can result in loss of seizure control or toxicity
- Prescribers often write for the brand name

Discussion

Which neurotransmitters play the greatest role in seizures?

The neurotransmitters are glutamate (excitatory) and GABA (inhibitory).

Parkinson's Disease

- Characterized by tremor when resting, rigidity, and akinesia (absence of movement)
- Poor posture control, shuffling gait, loss of overall muscle control
- Usually affects people over 60

Physiology of Parkinson's Disease

- Parkinson's disease is result of alterations in the extrapyramidal system
  - Part of the CNS that controls motor activities
  - Made up of the basal nuclei
- Most common extrapyramidal disease
- Parkinson has no definitive test, diagnosed by symptoms
Physiology of Parkinson's Disease

- For normal muscle movement to be performed, 2 main neurotransmitters must be in balance
  - Dopamine (inhibitor)
  - Acetylcholine (ACh) (stimulator)
- In Parkinson's disease, these neurotransmitters are not in balance.

Cutaway View of the Brain

Dopamine and Parkinson Disease

- In the substantia nigra, insufficient dopamine is released to counteract effects of ACh
- This causes excessive motor nerve stimulation

Substantia Nigra

Parkinson's Disease Drug Therapy

- Improves functional ability and clinical status of patients
- Aims at symptomatic relief, does not alter disease process. No cure.
- Temporary remission
- Side effects can be a problem

Discussion

What are the two primary neurotransmitters involved in Parkinson disease and what role do they play?
The two neurotransmitters involved are Acetylcholine (excitatory) and dopamine (inhibitory).
Other Central Nervous System Disorders

- Myasthenia gravis
- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis (MS)
- Huntington’s disease
- Alzheimer’s disease
- Attention-deficit hyperactivity disorder and attention-deficit disorder

Myasthenia Gravis

- Autoimmune disorder of the neuromuscular junction
- ACh receptors are destroyed at the motor end plate
- Characterized by weakness and fatigability, especially of skeletal muscles

Motor End Plate

Presenting Signs of Myasthenia Gravis

- Ptosis (drooping eyelid)
- Diplopia (double vision)
- Dysarthria (speech)
- Dysphagia (swallowing)
- Extremity weakness
- Respiratory difficulty

Treatment of Myasthenia Gravis

- Acetylcholinesterase drugs can produce improvements in all forms of myasthenia gravis
- Drug therapy does not inhibit or reverse the immunologic flaw

Amyotrophic Lateral Sclerosis (ALS)

- Also known as Lou Gehrig’s disease
- Progressive degenerative disease of the nerves
- Muscle weakness, paralysis, and eventually death
- Cause: excessive levels of glutamate
Multiple Sclerosis (MS)
- Autoimmune disease in which myelin sheaths around nerves degenerate
- Patient loses use of muscles, and often eyesight is affected
- Some drugs can slow progression
- No cure

Huntington’s Disease
- Neurodegenerative disorder characterized by brief, repetitive, jerky, involuntary movements
- Patient may have emotional disturbances and problems thinking
- Tetrabenazine can treat condition, reducing activity of chemicals in brain

Restless Leg Syndrome
- Causes pain or unpleasant sensations in the legs
- More common in middle-aged or older adults
- May be linked to kidney disease, Parkinson’s disease, peripheral neuropathy, and iron deficiency
- Can be treated with gabapentin and Parkinson’s medication

Fibromyalgia
- Patient suffers from long-term pain across entire body
- Linked to sleep problems, fatigue, headaches, anxiety, and depression
- Most common in women ages 20 through 50
- Treatment may include ibuprofen, massage, antidepressants, muscle relaxers, or anticonvulsants

Alzheimer’s Disease
- Progressive form of dementia
- Changes personality and behavior
- No treatments can cure or reverse
- Drugs can slow the disease
- Depression often treated with antidepressants according to symptoms

Progression of Alzheimer’s Disease
1. Memory deficit, forgetfulness, misplacements of ordinary items
2. Inability to complete complex tasks
3. Complete incapacitation, disorientation, and failure to thrive
Discussion
How does Alzheimer’s disease affect patients’ families? Has the disease affected someone in your family?

Attention-Deficit Disorders
• Attention-Deficit Hyperactivity Disorder (ADHD)
• Attention-Deficit Disorder (ADD)

Attention-Deficit Hyperactivity Disorder (ADHD)
• Neurologic disorder characterized by hyperactivity, impulsivity, and distractibility
• Symptoms can persist into adult life
• Most drugs used are amphetamines and amphetamine derivatives, C-II

Discussion
Several of the diseases presented in this chapter are degenerative, and there is yet no known cure. How might this affect patients with a diagnosis of one of these conditions?

Assignments
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• Study Partner
  – Quiz in review mode
  – Matching activities
  – Drug tables