Lecture Objectives:

1. Be able to explain the mechanism of action of antipsychotics (neuroleptics, major tranquilizers), antiparkinsonians, anxiolytics (minor tranquilizers), antidepressants, stimulants, and antimanics.
2. Include patient and family education while planning and implementing care for patients taking psychotropic medications.
3. Know the generic and trade name of the prototype medications within each category and the most common psychotropic medications within each category.
4. Describe common side effects of psychotropic medications, be prepared to instruct patients regarding these side effects, and know the most appropriate nursing care and medical treat for each.
5. Distinguish between characteristics of extrapyramidal symptoms, tardive dyskinesia, and neuroleptic malignant syndrome.
6. Be prepared to apply, as necessary, the “Nursing Implications” as delineated in Davis Drug Guide, 9th edition.
7. Know the definition of terms in the “Terms to Know” section of this guide.

Terms to Know:

1. Psychotropic or psychoactive - Drugs that change or alter moods and thoughts of the persons who have difficulty responding to reality. These medications affect the CNS.
2. Neurotransmitter - Highly specialized chemical substances that are involved in the transport of information across the synaptic gap.
3. Prototype - 1) The original type or form of a drug that is typical of later medications; 2) the drug that is most characteristic of the classification.
4. Physiological action - Usual or expected effect of the drug; how the drug exerts it’s effect at the tissue or cellular level.
5. Side effect - A consequence other than that for which a drug or other agent is used. Can be an adverse effect. Some drugs are used just for their side effects.
6. Extrapyramidal - Outside the pyramidal tracts. The pyramidal tract is a motor nerve tract that extends from the brain down the spinal cord. This tract controls and coordinates the
posture, stature, supporting, and locomotion mechanisms.

NOTE: the reference for the exams is your Davis Drug Guide.

LECTURE OUTLINE

I. Introduction
   A. Drug therapy can complement other procedures and therapies. It is not a quick fix or miracle drug.
   B. Drugs do not treat the patient’s personal, social, or environmental responses to the mental illness.
   C. Side effects and adverse reactions of drug therapy add another level of concern and need for expertise and judgment in nursing care.

II. Role of the nurse
   A. Patient assessment - what meds the patient is on and what side effects he is having on admission or when you first see him.
   B. Coordination of treatment modalities.
   C. Psychopharmacological drug administration.
   D. Monitoring all drug effects, both therapeutic and adverse.
   E. Medication education for both patient and family.

III. General information regarding pharmacokinetics
   A. In general, most psychoactive drugs should be discontinued by a tapering method.
   B. Children tend to metabolize drugs more rapidly than adults, although children exhibit a variable response.
   C. The elderly and newborns are particularly sensitive to psychotropic drugs. Drug distribution, hepatic metabolism, and renal clearance are all affected by age.
   D. If a pregnant woman takes psychoactive drugs, the unborn infant may experience drug effects and even withdrawal symptoms at birth unless the baby is detoxified from the drug.
   E. Newborns whose mothers are taking psychoactive drugs should not be breast-fed.

IV. Drug interactions
   A. In general, polypharmacy in psychiatric care should be used only when necessary and with caution.
   B. Guidelines for polypharmacy
      1. Identify specific target symptoms for each drug.
      2. If possible, start with one drug and evaluate effectiveness and side effects before adding a second drug.
3. **Be alert for adverse drug interactions.**
4. Consider the effects of a second drug on the absorption and metabolism of the first drug.
5. Consider the possibility of additive side effects.
6. Change the dose of only one drug at a time and evaluate results.
7. Be aware of increased risk of medication errors.
9. Be aware of decreased patient adherence in the aftercare setting when medication regimen is complex.
10. In follow-up treatment, eliminate as many drugs as possible and establish the effective dose of the drugs used.
11. Patient education programs regarding concomitant drug regimens must be particularly clear, organized and effective.
12. Patient follow-up contacts should be more frequent.

V. Biological basis of psychopharmacology
   
   A. The **synapse** is a narrow gap separating 2 neurons (the presynaptic cell and the post-synaptic cell) at a transmission site. During neurotransmission the chemical **neurotransmitter** is released from a storage vesicle in the presynaptic cell, crosses the synapse, and is recognized by the receptor on the postsynaptic cell membrane (binds with the receptor).
   
   B. **Receptors** are the cellular recognition sites for specific molecular structures such as neurotransmitters, hormones, and many drugs. Their action is selective for specific chemicals.
   
   C. Neurotransmitters - chemical messengers that travel from one brain cell to another.
   
   D. At the synapse, neurotransmitters act as receptor activators (agonists) or inhibitors (antagonists) and trigger complex biological responses within the cell.
   
   E. The remaining chemical in the synapse is either reabsorbed (through uptake) and stored by the presynaptic cell or it is metabolized (inactivated by enzymes, one of which is monoamine oxidase).
   
   F. Many psychiatric disorders are thought to be related to a dysfunction of the neurotransmitters.
      1. Excess dopamine - schizophrenia
      2. Deficiency of norepinephrine, serotonin, and others - depression and mania.
      3. Decreased gamma-aminobutyric acid (GABA) - anxiety and panic attacks.
   
   G. Dysfunction (dysregulation) can be affected by **drugs** in the following manner:
      1. Release - more neurotransmitter is released into the synapse from the storage vesicles in the presynaptic cells.
      2. Blockade - the neurotransmitter is prevented from binding to the post-
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synaptic receptor.

3. Receptor sensitivity change - the receptor becomes more or less responsive to the neurotransmitter.

4. Reuptake inhibition - the presynaptic cell does not reabsorb the neurotransmitter well, leaving more neurotransmitter in the synapse and therefore enhancing or prolonging its action.

5. Interference with storage vesicles - the neurotransmitter is either released again into the synapse (more neurotransmitter) or released to metabolizing enzymes (less neurotransmitter).

6. Precursor chain interference - the process that makes the neurotransmitter is either facilitated (more is synthesized) or disrupted (less is synthesized).

7. Synaptic enzyme interference - less neurotransmitter is metabolized, so more remains available in the synapse and the presynaptic neuron.

8. Examples:
   a. Antipsychotic drugs block dopamine from the receptor site.
   b. Tricyclic antidepressants, selective serotonin reuptake inhibitors, and several other antidepressants block the reuptake of norepinephrine or serotonin and regulate the areas of the brain that manufacture these chemicals.
   c. Monoamine oxidase inhibitors prevent enzymatic metabolism of norepinephrine and serotonin.
   d. Benzodiazepines potentiate GABA.
   e. Some antidepressants and antipsychotics block specific serotonin receptors.

VI. Adverse side effects of antipsychotics

A. General information

1. The greatest hazard of neuroleptics (antipsychotics) involves the development of adverse side effects such as extrapyramidal reactions and tardive dyskinesia.

2. The risk of extrapyramidal symptoms is highest for clients with long-term use of older neuroleptic medications.

3. Risperidone and clozapine and other newer antipsychotic medications are frequently referred to as “atypicals.” The side effects for these agents involve other systems, such as the hematological system (e.g. agranulocytosis for clozapine).

4. A thorough understanding of side effects is essential for both the client and his family to alleviate anxiety, promote cooperation, and gain early treatment for side effects that occur.

B. Movement disorders
1. Neuroleptic malignant syndrome
   a. **Life threatening.** Can occur after a single dose of neuroleptic medication but is more common within the first 2 weeks of daily administration or may occur with an increase in dosage.
   b. Symptoms - severe muscular rigidity, altered consciousness, stupor, catatonia, hyperpyrexia, and labile pulse and blood pressure. Symptoms can occur for up to 2 weeks after medication is discontinued.
   c. Treatment - immediate **discontinuation** of the medication and hospitalization to stabilize acute symptoms. Supportive treatment in the **hospital** may include dopaminergic agonists such as Parlodil (bromocriptine) and Symmetric (amantadine).

2. Tardive dyskinesia (TD)
   a. Results from prolonged use of neuroleptics and is **the most serious side effect of long-term use of neuroleptics because it is often irreversible and the symptoms tend to be severely disabling.** The risk of development increases with cumulative dose and duration of treatment.
   b. Symptoms - earliest may be fine, wormlike movements of the tongue or increased blinking; others are involuntary choreoathetotic movements affecting the face, tongue movements and tongue protrusion, perioral, buccal, and masticatory muscle movements, to include sucking, smacking lips, or chewing jaw movements (rabbit syndrome). The neck, torso, and extremities may also be involved.
   c. Treatment - decreasing or discontinuing neuroleptic medication. **Best treatment is prevention** - i.e., regular reevaluation of drug dosage and assessment for beginning side effects. Withdrawal dyskinesia can occur. The symptoms are the same as for TD but tend to resolve within a few weeks.

C. Extrapyramidal side effects
1. Acute dystonic reactions - generally occur within 5 days of initial administration of neuroleptic medication or after dose increases. Untreated, dystonic reactions can last minutes to hours. Reversible.
   a. Symptoms - muscle hypertonicity with tonic contractions of muscles in the mouth and torso that can last from minutes to hours; more often associated with high-potency neuroleptics (e.g. haloperidol), oculogyric crisis (eyes rolling upward and unable to move downward).
   b. Treatment - IM administration of diphenhydramine 25 mg. Or benztropine, or concomitant use of these two. Resolution is usually rapid. Medication may also be given orally if patient can
swallow.

2. Parkinsonism - (also known as pseudoparkinsonism) - maximum risk for developing symptoms occurs between 5 and 30 days after initiating neuroleptic medications.
   a. Symptoms - rigid masklike facial expressions, tremor, cogwheel rigidity, drooling, shuffling gait, finger and hand tremors.
   b. Treatment - diphenhydramine or benztropine or trihexyphenidyl. Symptoms resolve within days.

3. Akinesia - the most serious form of parkinsonism
   a. Symptoms - diminished spontaneity, few gestures, apathy, difficulty initiating activities, may be difficult to differentiate from schizophrenia. Clients appear depressed, social adjustment is compromised.
   b. Treatment - see #2 above.

4. Akathisia - usually occurs within 5 to 60 days after initiation of neuroleptic medication. Is a cause of noncompliance.
   a. Symptoms - uncomfortable restlessness, feelings of tenseness in the lower extremities with an irresistible urge to move them, inability to sit still, foot tapping, excitement, agitation, hyperactivity. Clients feel restless.
   b. Treatment - changing to different neuroleptic or decreasing dose; also, trihexyphenidyl, propranolol, benzodiazepines, clonidine.

VII. Classifications
A. Antipsychotics - also known as neuroleptics, many also called major tranquilizers. Side effects may include movement defects such as Parkinson’s type symptoms, akinesia, akathisia, and tardive dyskinesia, sedation, anticholinergic effects, orthostatic hypotension, and failure to ejaculate. Chlorpromazine is the prototype. Caution: These medications should not be administered when CNS depression is evident, blood dyscrasias exist, in patients with Parkinson’s disease, or those with liver, renal, or cardiac insufficiency.
1. Traditional (1st generation)
   a. Phenothiazines
      (1) chlorpromazine
      (2) mesoridazine
      (3) thioridazine
      (4) perphenazine
      (5) prochlorperazine
      (6) trifluoperazine
   b. Thioxanthenes - thiothixene
   c. Butyrophenones - haloperidol
   d. Dihydroindolone - molindone
e. Dibenzoxazepine - loxapine

2. Atypical - fewer side effects than typical antipsychotics - they treat both positive and negative symptoms of schizophrenia.
   a. Dibenzodiazepine - clozapine
   b. Benzisoxazole - risperidone
   c. Thienobenzodiazepine - olanzapine
   d. Dibenzothiazepine - quetiapine

B. Antiparkinsonians
   1. Anticholinergics
      a. Benztropine - DOES NOT TREAT TARDIVE DYSKINESIA
      b. Trihexyphenidyl
   2. Antihistamine - diphenhydramine - has more side effects than benztropine
   3. Dopaminergic agonists
      a. Amantadine - relief of EPS
      b. Bromocriptine - treatment of neuroleptic malignant syndrome

C. Antidepressants - norepinephrine, serotonin, and/or dopamine are the neurotransmitters that seem to be deficient in depression. The treatment goal is to increase the amount OR the effectiveness of the neurotransmitters. The prototype is amitriptyline. **Caution:** these medications are contraindicated during the acute recovery phase of MI and angle-closure glaucoma. **Also,** use with caution in the elderly and those with hepatic, renal and cardiac insufficiency.
   1. Tricyclic antidepressants (TCAs) - very effective. However, sedation and anticholinergic effects can be unwelcome side effects.
      a. Amitriptyline
      b. Amoxapine
      c. Clomipramine
      d. Desipramine
      e. Doxepin
      f. Imipramine
      g. Nortriptyline
      h. Protriptyline
      i. Trimipramine
   2. Heterocyclics
      a. Bubropion
      b. Maprotiline
      c. Mirtazapine
      d. Trazodone
   3. SSRIs - selective serotonin reuptake inhibitors - some also used to treat OCD, bulimia, panic disorder, alcoholism, anorexia, and ADHD. They block the reuptake of serotonin. Seem to show comparable efficacy while
not presenting the anticholinergic and sedating side effects that limit client compliance of tricyclics and heterocyclics. The prototype is fluoxetine.

a. Citalopram  
b. Fluoxetine  
c. Paroxetine  
d. Sertraline

4. Non-selective reuptake inhibitors  
a. Nafazodone  
b. Venlafaxine - has been useful in severely depressed and melancholic clients

5. Monoamine oxidase inhibitors (MAOIs) - the neurotransmitters norepinephrine, epinephrine, dopamine and serotonin as well as many different food substances and other drugs are monoamines. Monoamine oxidase is an enzyme that destroys these monoamines. MAOIs prevent the destruction of monoamines by inhibiting the action of monoamine oxidase. Since the neurotransmitters aren’t destroyed, there is more chemical substance present to allow for synaptic transmission. However, not only are serotonin and dopamine not destroyed by the MAOs, neither are the other neurotransmitters, and this can cause major side effects and problems from other drugs. To prevent acute hypertensive reactions, many foods and drugs containing tyramine must be restricted. MAOIs may also be used for PTSD, SAD, and panic disorder, to include night terrors.

a. Isocarboxazid  
b. Phenelzine  
c. Tranylcypromine

D. Anxiolytics - antianxiety, panic attacks, alcohol withdrawal - GABA seems to inhibit neurons in many parts of the brain and reduce anxiety. The prototype is diazepam. **Caution:** these medications are CNS depressants and should not be taken in combination with other CNS depressants. They are contra-indicated in pregnancy, narrow-angle glaucoma, shock, and coma. Also, the elderly and depressed patients.

1. Benzodiazepines - some of these medications are predominantly hypnotics, whereas others reduce anxiety without being as soporific. Can cause respiratory depression, coma, and death, especially in the presence of other CNS depressants. Safety is also an issue.

a. Alprazolam  
b. Chlordiazepoxide  
c. Clonazepam  
d. Clorazepate  
e. Diazepam  
f. Lorazepam
g. Oxazepam

2. Propanediols - anxiety
   a. Meprobamate

   a. Buspirone

   a. Propranolol

E. Mood stabilizers
1. Antimanics - mechanism of action not fully understood. It is similar in structure to sodium and potassium and may alter electrical conduction in the body. Side effects, therefore, may be very serious. Polyuria, polydipsia, and edema may result and are a frequent reason for noncompliance. The serum blood level must be observed closely; blood serum level has a narrow range of safety. The therapeutic level for acute mania is 1.0 to 1.5. Symptoms of toxicity (>1.5) are listed in Townsend and Davis. Levels of 3.5 and above may lead to cardiovascular collapse.
   a. Lithium carbonate
   b. Lithium citrate

2. Anticonvulsants - these alter electrical conductivity and apparently reduce the excitement of the manic phase and reduce mood swings.
   a. Carbamazepine - may also be used to treat rage reactions and resistant schizophrenia
   b. Clonazepam - structurally a benzodiazepine - sedates
   c. Valproic acid
   d. Oxcarbazepine

3. Calcium channel blockers - action unclear
   a. Verapamil

F. Central nervous system stimulants - Caution: these medications should not be used in clients with arteriosclerosis or other cardiovascular disease.
1. Amphetamines - treatment of narcolepsy, ADHD, and, sometimes, obesity. CNS stimulation from release of norepinephrine in central noradrenergic neurons of cerebral cortex, reticular activating system (RAS), and brain stem. Perhaps dopamine released at higher doses.
   a. Amphetamine sulfate
   b. Dextroamphetamine sulfate
   c. Methamphetamine HCl

2. Anorexigenics - treatment of obesity - exact mechanism of action unclear
   a. Benzphetamine
b. Diethylpropion

c. Mazindol

d. Phendimetrazine

e. Phentermine

f. Sibutramine

3. Miscellaneous - treatment of ADHD in children, narcolepsy; methylphenidate used for treatment of depression in elderly, cancer, and poststroke clients. Actions similar to amphetamines.

a. Methylphenidate

b. Permoline