

**Antipsychotic Drugs**

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**ANTIPSYCHOTIC DRUGS**

- ☐ Treat
  - Schizophrenia
  - Schizoaffective disorder
  - Bipolar disorder
  - Psychotic depression
- ☐ Off-label uses
  - Insomnia
  - Tics
  - Delirium
  - Stuttering

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**ANTIPSYCHOTIC DRUGS (Cont.)**

- ☐ Discovered accidentally around 1950
- ☐ Chlorpromazine (Thorazine)
- ☐ Historically have been referred to as...

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## CLASSIFICATION SYSTEMS

- ☐ Traditional antipsychotics or first generation
- ☐ Atypical antipsychotics or second generation
- ☐ High-potency drugs
  - Fluphenazine (Prolixin)
  - Haloperidol (Haldol)
  - Thiothixene (Navane)
  - Trifluoperazine (Stelazine)

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## CLASSIFICATION SYSTEMS (Cont.)

- ☐ Moderate-potency drugs
  - Loxapine (Loxitane)
  - Perphenazine (Trilafon)
- ☐ Low-potency drugs
  - Chlorpromazine (Thorazine)
  - Thioridazine
- ☐ Low-potency drugs cause more intense anticholinergic effects
- ☐ High-potency drugs cause more EPSE

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## CLASSIFICATION SYSTEMS (Cont.)

- ☐ From 1990 to the present, the new drugs are called *atypical antipsychotics* owing to
  - Reduced risk of EPSE
  - Increased effectiveness in treating negative symptoms
  - Minimal risk of Tardive Dyskinesia (TD)
  - Reduced risk for elevated prolactin

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## CLASSIFICATION SYSTEMS (Cont.)

- ☐ Atypical antipsychotics (second-generation drugs)
  - Aripiprazole      Quetiapine
  - Clozapine        Risperidone
  - Olanzapine      Ziprasidone
  - Paliperidone
- ☐ Novel antipsychotics (third-generation drug)
  - Aripiprazole

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## NEUROCHEMICAL THEORY OF SCHIZOPHRENIA

- ☐ Positive symptoms
  - Excessive dopamine in the mesolimbic tract
- ☐ Negative symptoms
  - Too little dopamine in the mesocortical tract

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## NEUROCHEMICAL THEORY OF SCHIZOPHRENIA (Cont.)

- ☐ Increased levels of dopamine
- ☐ Antipsychotic drugs block dopamine.
- ☐ Liberation of dopamine in the mesocortical area treats negative and cognitive symptoms.

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## NEUROCHEMICAL THEORY OF SCHIZOPHRENIA (Cont.)

- ☐ Tract 1: Nigrostriatal tract is involved in movement. Traditional antipsychotic blockade can cause EPSE.
- ☐ Tract 2: Tuberoinfundibular tract modulates pituitary function. Traditional antipsychotic blockade increases prolactin levels.
- ☐ Tract 3: Mesolimbic tract involved in emotional and sensory processes. Traditional antipsychotic blockade relieves or eliminates hallucinations and delusions.

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## NEUROCHEMICAL THEORY OF SCHIZOPHRENIA (Cont.)

- ☐ Tract 4: The mesocortical tract is involved in cognitive processes. Traditional antipsychotic blockade can intensify negative and cognitive problems.
- ☐ Atypical antipsychotics can block dopamine receptors in the mesolimbic area and liberate dopamine in the mesocortical area, not obstructing the function of the nigrostriatal tract or blocking receptors in the tuberoinfundibular tract.

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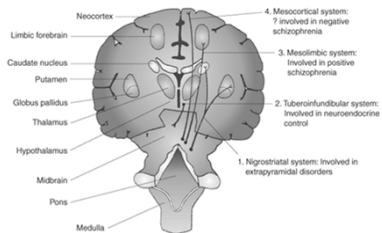
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## Dopaminergic Tracts



From Roberts GW, Leigh PN, Weinberger DR: *Neuropsychiatric disorders*, London, 1993, Wolfe Publishing.

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## PHARMACOLOGICAL EFFECTS

- ▣ Tranquilizing:
- ▣ Antipsychotic:
- ▣ Most effective in treating the positive symptoms
- ▣ Negative symptoms are less responsive to any of the antipsychotic agents.

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## SYMPTOMS MODIFIED BY ANTIPSYCHOTIC DRUGS

- ▣ Alterations in perception:
  
- ▣ Alterations in thought:
  
- ▣ Alterations in activity:
  
- ▣ Alterations in consciousness:

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## PHARMACOLOGICAL EFFECTS (Cont.)

- ▣ Alterations in personal relationships:
  
- ▣ Alterations in affect:

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### PHARMACOKINETIC HIGHLIGHTS

- ☐ Absorption: variable:
- ☐ Lipid soluble:
  - Patients who abruptly stop their medications experience an antipsychotic effect for some time.
- ☐ Highly protein-bound
- ☐ Metabolized by CYP-450 enzyme system
  - Half-life: 10 to 30 hours

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### PHARMACOKINETIC HIGHLIGHTS (Cont.)

- ☐ Impaired hepatic function...
- ☐ Cigarette smoking...
- ☐ Oral and parenteral forms are available.
- ☐ Oral administration is the preferred route.
- ☐ A few oral medications dissolve instantly.

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### PHARMACOKINETIC HIGHLIGHTS (Cont.)

- ☐ Parenteral drugs ...
- ☐ Long-acting injectable forms ...
  - Beneficial for patients who are nonadherent
    - Fluphenazine decanoate
    - Haloperidol decanoate
    - Risperidone microspheres
    - Paliperidone palmitate (Invega Sustenna)

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## ANTIPSYCHOTIC SIDE EFFECTS

- ☐ Anticholinergic
- ☐ Antiadrenergic
- ☐ Cardiac
- ☐ Extrapiramidal

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## ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ☐ **NURSING ALERT**
- ☐ Anticholinergic effects can
  - Increase intraocular pressure, aggravating narrow-angle glaucoma
  - Intensify prostatic hypertrophy, making urination even more difficult
  - Trigger arrhythmias and cause death

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## ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ☐ Antiadrenergic effects
- ☐ Orthostatic hypotension can cause falls,...
- ☐ Occurs most often in older adults
- ☐ Hypotension causes a reflex tachycardia ...
- ☐ Be sure to assess individuals ...

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## CASE STUDY

- ▣ Martha has been taking haloperidol (Haldol) 5 mg BID for many years. Her first psychotic break took place in 1983. Due to her taking the haloperidol routinely, her positive symptoms of schizophrenia have markedly reduced. Upon assessment, Martha reports some dizziness if she moves too quickly upon awakening. She has some inner jittery feelings.
- ▣ What side effects is Martha demonstrating?
- ▣ What are the nursing actions?

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## ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ▣ Common path that leads to rehospitalization
- ▣ EPSE → nonadherence → relapse → rehospitalization
- ▣ High-potency traditional antipsychotics are the most likely cause of EPSE.
- ▣ Atypical antipsychotics are least likely to cause EPSE.

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## ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ▣ Endocrine
  - Elevation of prolactin levels by traditional antipsychotics
- ▣ Metabolic syndrome or insulin resistance syndrome
  - Reduced metabolism of glucose and resistance to insulin by insulin receptors on cells
  - Type 2 diabetes

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### ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ☐ Metabolic syndrome: three or more of the following:
  - Abdominal girth greater than 40 inches in men and greater than 35 inches in women
  - Elevated triglycerides
  - Reduced high-density lipoproteins
  - Elevated blood pressure
  - Elevated fasting glucose
  - Clozapine and olanzapine most likely to cause metabolic syndrome

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### ANTIPSYCHOTIC SIDE EFFECTS (Cont.)

- ☐ Sexual
  - Caused by dopamine blockade
  - Most significant is the third phase of sexual behavior (orgasm).
- ☐ Gastrointestinal
  - Weight gain
  - Insulin resistance is an outcome and cause of excessive weight gain.
  - Carbohydrate craving

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### NURSING IMPLICATIONS

- ☐ Overdose is seldom fatal
  - Causes severe CNS depression...
  - Restlessness or agitation, convulsions...
- ☐ Use in pregnancy
  - Avoid during first trimester.
  - Can cause EPSE in some newborns
  - Can cause glucose intolerance

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### **NURSING IMPLICATIONS (Cont.)**

- ☐ Use by older adults
  - Reduce dose.
  - Heightened EPSE and anticholinergic effects
  - Higher risk for Tardive Dyskinesia (TD)
  - Do not give to older adults with dementia-related psychosis; can cause higher risk of death

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### **NURSING IMPLICATIONS (Cont.)**

- ☐ Interactions with other drugs
  - CNS depressants
  - Alcohol
  - Antihistamines
  - Antianxiety drugs
  - Antidepressants
  - Barbiturates
  - Meperidine
  - Morphine
  - Cigarette smoking

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### **PATIENT TEACHING**

- ☐ Important aspect of nursing care
- ☐ Use discretion in selecting content of educational sessions, because of patient paranoia and anxiety.
- ☐ Focus on symptoms that can be seen or felt.
- ☐ Provide a written description of drug benefits and side effects with instructions on how to cope with side effects.

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## PATIENT TEACHING (Cont.)

- ☐ Avoid hot tubs, showers, and baths to prevent hypotension and falls.
- ☐ Avoid abrupt withdrawal of drug; EPSE can occur.
- ☐ Use sunscreen to prevent sunburn.
- ☐ Take medication as prescribed.
- ☐ Report sore throat, fever, malaise, and bleeding.
- ☐ Dress appropriately for hot weather; drink plenty of water.

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## TRADITIONAL DRUGS

- ☐ Effective, higher risk for adverse effects
- ☐ Less expensive
- ☐ Low-potency traditional antipsychotics
  - Chlorpromazine (Thorazine)
    - First antipsychotic
    - Anticholinergic
    - Antiadrenergic effects
    - Sedating
    - Significant weight gain

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## TRADITIONAL DRUGS (Cont.)

- ☐ Thioridazine: A few patients respond better than any other drug. Cases of sudden death have been linked to this drug.
- ☐ Moderate-potency
  - Loxapine
  - Perphenazine
    - Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study effective as any of the atypical antipsychotics, except olanzapine
  - Loxapine inhalation power (Adasuve) recently approved to treat agitation in schizophrenia

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## TRADITIONAL DRUGS (Cont.)

- ☐ High-potency traditional antipsychotic
- ☐ Fluphenazine: Prolixin Decanoate long-acting form can be given IM every 2 to 3 weeks
- ☐ Haloperidol: causes more EPSE and fewer anticholinergic side effects
  - Used for older adults and pediatric patients
  - Parenteral haloperidol assists with aggressive behavior
  - Haloperidol decanoate long-acting form IM every 2 to 4 weeks

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## ATYPICAL ANTIPSYCHOTIC DRUGS

- ☐ Different mechanism of action than traditional drugs and a greater effect on negative symptoms
  - Block 5-HT<sub>2A</sub> receptors, which liberates dopamine
  - Faster “on-off” the D<sub>2</sub> receptor
  - Can modulate the mesolimbic function without a significant effect of the nigrostriatal tract

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## NEGATIVE EFFECTS OF ATYPICAL ANTIPSYCHOTICS

- ☐ Metabolic dysregulation: metabolic syndrome
  - Obesity
  - Diabetes
  - Hyperlipidemia
  - Hypertensive

It is important for nurses to monitor patients for potential metabolic syndrome and report to the prescribing clinician.

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## CLOZAPINE

- ☐ Introduced in the United States in 1990
- ☐ Serious side effect: agranulocytosis
- ☐ Use in individuals with severe schizophrenia who have not responded to other antipsychotic drugs
- ☐ Causes significant anticholinergic effects: orthostasis, sedation, weight gain, and sexual dysfunction
- ☐ Primarily metabolized by CYP-450 1A2; smoking decreases level of clozapine

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### PROTOCOL FOR CLOZAPINE THERAPY

- ☐ Institute therapy only if WBC is above 3500/mm<sup>3</sup> and ANC is 2000/mm<sup>3</sup> or higher .
- ☐ Monitor WBC weekly.
- ☐ If counts are normal for 6 months, monitor level every 2 weeks.
- ☐ If counts are normal for 1 year, monitor level every 4 weeks.
- ☐ Discontinue drug if WBC drops below 3000/mm<sup>3</sup> or ANC drops below 1500/mm<sup>3</sup> .
  - Monitor counts daily.
  - If no infection is present, resume drug when counts return to normal.
- ☐ Permanently discontinue drug if WBC drops below 2000/mm<sup>3</sup> or ANC drops below 1000/mm<sup>3</sup>.

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## CLOZAPINE (Cont.)

- ☐ Side effects: dose-related seizures and excessive salivation
- ☐ Myocarditis—patients need to report dyspnea, fever, chest pain, palpitations, tachycardia, and other symptoms of heart failure immediately.
- ☐ Fatal overdose

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### **RISPERIDONE AND PALIPERIDONE**

- ❑ Risperidone (Risperdal) has greater affinity for D2 receptors and similar antagonism of 5-HT 2A receptors
- ❑ Favorable receptor profile both positive and negative symptoms
- ❑ Well-tolerated drug
- ❑ Decreased anticholinergic side effects
- ❑ No agranulocytosis, tardive dyskinesia (TD), or neuroleptic malignant syndrome (NMS)

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### **RISPERIDONE AND PALIPERIDONE (Cont.)**

- ❑ Risperidone blocks alpha-1 and H1 receptors, resulting in orthostatic hypotension, sedation, appetite stimulation
- ❑ Higher doses of EPSE and hyperprolactinemia
- ❑ Side effects: insomnia, agitation, headache, anxiety, and rhinitis
- ❑ Long-acting IV available
- ❑ Paliperidone (Invega) part of risperidone family; extended release and IM forms

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### **OLANZAPINE**

- ❑ Olanzapine (Zyprexa): blocks 5-HT 2A and D2 receptors
- ❑ High affinity for cholinergic, H1, and alpha-1 receptors, causing anticholinergic effects of sedation, weight gain, and orthostasis
- ❑ Normalizes N-methyl-D-aspartate (NMDA) receptor function in glutaminergic system, which blocks some signs and symptoms of schizophrenia

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## OLANZAPINE (Cont.)

- ❑ Side effects: few incidents of EPSE
- ❑ Weight gain
- ❑ Effective in treating acute mania
- ❑ FDA-approved for monotherapy for bipolar disorder
- ❑ Long-acting IM available

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## CASE STUDY

- ❑ Jack has been on olanzapine for the last 6 months. He has experienced a rapid weight gain of 75 pounds and is upset that this is occurring.
- ❑ What nursing assessment is indicated?
- ❑ What nursing interventions can assist this patient?

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## QUETIAPINE

- ❑ Quetiapine (Seroquel): similar to clozapine, lower affinity for D2 receptors than for 5-HT<sub>2A</sub>
- ❑ Few anticholinergic side effects
- ❑ Orthostatic hypotension
- ❑ Sedation
- ❑ Appetite stimulation
- ❑ Effective for both positive and negative symptoms

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### QUETIAPINE (Cont.)

- ❑ Few incidents of EPSE
- ❑ Does not significantly increase prolactin levels
- ❑ Improves cognitive function
- ❑ Titrate slowly over 4 to 5 days.
- ❑ Taken orally, intranasally, IV
- ❑ Provides anxiolytic and sedative effects

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### ZIPRASIDONE

- ❑ Ziprasidone (Geodon): effective for both positive and negative symptoms
- ❑ Few EPSE
- ❑ Few anticholinergic side effects
- ❑ Mild antihistamine effects
- ❑ Side effects: nausea, dyspepsia, abdominal pain, constipation, somnolence, insomnia, coryzal symptoms (head cold)

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### ZIPRASIDONE (Cont.)

- ❑ Less weight gain
- ❑ Linked to potential cardiac problems due to lengthening of QTc interval
- ❑ Low potential for drug–drug interaction
- ❑ IM is available
- ❑ Absorption increased when ziprasidone is given with food
- ❑ Decreases anxiety and depressive symptoms

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A patient is learning about her new medication, ziprasidone (Geodon). What can the nurse teach this patient that will increase absorption?

- A. Take the medication without any food.
- B. Take the medication with graham crackers.
- C. Take the medication with fruit juice.
- D. Take the medication with food.

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### ARIPIPIRAZOLE

- ☐ Aripiprazole (Abilify): dopamine system stabilizer, which balances the dopamine system by increasing dopamine in brain areas where there is a deficiency and decreasing dopamine where dopamine is overactive
- ☐ Reduces positive symptoms
- ☐ Patients feel better, more energy
- ☐ Negative symptoms subside

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### ASENAPINE

- ☐ Asenapine (Saphris): sublingual tablet, ineffective if swallowed
- ☐ Used for the treatment of both acute schizophrenia and bipolar disorder
- ☐ Low cause of EPSE; may have some cases of akathisia
- ☐ Effective in treatment of cognitive and negative symptoms

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## ILOPERIDONE

- ❑ Iloperidone (Fanapt): related to risperidone
- ❑ Metabolite of risperidone
- ❑ Can precipitate EPSE, prolactin elevation, and hyperprolactinemia
- ❑ Weight gain
- ❑ Sedation
- ❑ Orthostasis

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## LURASIDONE

- ❑ Lurasidone (Latuda): absorption improved when taken with food (similar to ziprasidone)
- ❑ Good side effect profile
- ❑ Few instances of dizziness, orthostatic hypotension, cognitive problems, sedation, or weight gain reported

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## NEW THEORY OF SCHIZOPHRENIA

- ❑ Glutamate hypothesis
- ❑ Explains both positive and negative symptoms of schizophrenia
- ❑ Glutamate does not pass the blood-brain barrier.
- ❑ Requires an obligate co-agonist
- ❑ Ongoing research on co-agonists

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