

## Antipsychotic Drugs Anti Mania Drugs

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### Lecture Objectives

- The student will understand:
- Drugs used to treat mania and psychosis
  - ◆ Lithium
  - ◆ Traditional antipsychotics
  - ◆ Atypical antipsychotics
  - ◆ Anticholinergics

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### Lecture Objective cont:

- The student will understand:
  - ◆ The mechanism of action of the drugs
  - ◆ The side effects of the drugs
  - ◆ The nursing responsibilities
  - ◆ Patient teaching

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## Lithium Carbonate

- Mechanism of action
  - ◆ Lithium is a positively charged ion
  - ◆ Measured in mEq/L of blood
  - ◆ Similar to sodium and potassium
  - ◆ Mechanism of action not understood
  - ◆ May alter electrical activity of neurons

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## Mechanism of action cont.

- ◆ Overexcitement of neurons in some part of brain and may be component of bipolar disorder
- ◆ Alteration in electrical activity explains some of the untoward and toxic effects of lithium

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## Mechanism of action cont.

- ◆ By altering electrical conductivity, lithium represents a potential threat to all body functions that are regulated by electrical activity
- ◆ Lithium has the lowest therapeutic index of all psychiatric drugs

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### Mechanism of action cont.

- ◆ Therapeutic index— the ratio of lethal dose to the effective dose
- ◆ Blood level that can cause death is not far removed from effective level of drug which is true for lithium (Therapeutic window)

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### Mechanism of action cont.

- ◆ Sodium and potassium play strong role in maintaining fluid balance and distribution of fluids in body compartments
- ◆ Many disturbances in body fluids are caused by lithium

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### Indications for use

- Antimania drug
- Lithium— prototypical antimanic drug
- Effective in 90% of clients with pure manic symptoms; mania and grandiosity
- May prevent or modify future manic episodes and protect against future depressive episodes

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### Indications for use cont.

- Less effective in:
- Patients who not are truly bipolar
- Rapid cyclers

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### Effectiveness of Lithium

- Most effective in reducing symptoms of:
  - ◆ Grandiosity and elevated mood
  - ◆ Flight of ideas
  - ◆ Irritability
  - ◆ Anxiety

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### Effectiveness of Lithium cont.

- Less effective in reducing:
  - ◆ Insomnia
  - ◆ Psychomotor excitation
  - ◆ Assaultive behavior
  - ◆ Distractibility; difficulty concentrating

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## Lithium levels

- Therapeutic level
  - ◆ Initial 0.8 to 1.4mEq/L
  - ◆ Maintenance 0.4 to 1.0mEq/L
  - ◆ Narrow range between therapeutic and toxic levels (narrow therapeutic window)
  - ◆ Frequent need for blood levels

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## Therapeutic levels cont.

- ◆ Levels should never exceed 1.5mEq/L
- ◆ Many conditions can move patient from therapeutic to toxic levels
- ◆ What is therapeutic for one patient may be toxic for another

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## Contraindications of Lithium

- Cardiac, renal or thyroid disease
- Pregnancy and breast feeding
- Dementia and neurological disorders
- Myasthenia gravis
- Children under age 12

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## Side Effects of Lithium

- Side effects related to blood levels
- Expected side effects 0.4 to 1.0mEq/L
  - ◆ *Fine* hand tremor
  - ◆ Mild thirst
  - ◆ Polyuria
  - ◆ Mild nausea
  - ◆ Weight gain

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- Early signs of toxicity  $\leq 1.5\text{mEq/L}$ 
  - ◆ Nausea
  - ◆ Vomiting
  - ◆ Diarrhea
  - ◆ Muscle weakness
  - ◆ Thirst
  - ◆ Slurred speech
  - ◆ Polyurea

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## Side effects cont.

- Advanced signs of toxicity 1.5-2.0 mEq/L
  - ◆ *Coarse* hand tremor
  - ◆ Persistent GI disturbances
  - ◆ EEG changes
  - ◆ Mental confusion
  - ◆ Incoordination
  - ◆ Resembles CVA

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### Side effects cont.

- Severe toxicity 2.0-2.5 mEq/L
  - ◆ Severe hypotension
  - ◆ Severe polyuria
  - ◆ Serious EEG changes
  - ◆ Stupor
  - ◆ Coma
  - ◆ Death r/t pulmonary complications

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### Treatment of Toxicity

- No known antidote
- Hemodialysis may be used
- Urea, manitol, and aminophylline may hasten excretion
- Gastric lavage

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### Patient Teaching

- Diuretics contraindicated
- Drink 6-8 glasses H<sub>2</sub>O daily (1500-3000ml)
- Do not restrict sodium—4-5 Gms daily
- Take with food
- Report nausea, vomiting, diarrhea

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**Patient teaching cont.**

- Monitor blood levels as ordered
- Monitor weight
- Check renal and thyroid function
- Do not take over the counter meds
- Consider support group
- Avoid excessive use of caffeine and colas

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**Patient Teaching cont.**

- Monitor cardiac status
- Driving and heavy machinery with caution
- Avoid activities that cause sodium depletion
- Use contraception
- Lithium levels should be drawn 8-12 hours after last dose

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**Alternative Antimanic & Mood  
Stabilizing Drugs**

- Anticonvulsants
  - ◆ Carbamazepine (Tegretol)
  - ◆ Valproic acid (Depakene, Depakote)
  - ◆ Gabapentin (Neurontin)
  - ◆ Lamotrigine (Lamictal)
  - ◆ Topiramate (Topamax)

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### Alternative Drugs continued

- ◆ Anxiolytics
  - ◆ Clonazepam (Klonopin)
  - ◆ Lorazepam (Ativan)

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### Alternatives continued

- Atypical Antipsychotics
  - ◆ Clozapine (Clozaril)
  - ◆ Olanzapine (Zyprexa)
  - ◆ Ziprazadone (Geodon)
  - ◆ Aripiprazole (Abilify)
  - ◆ Quetiapine (Serequel)

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### Alternatives continued

- Calcium channel blockers
  - ◆ Verapamil
  - ◆ Flunarizine
  - ◆ Nimodipine

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## Standard Antipsychotic Drugs

- Mechanism of action
  - ◆ Block dopamine (DA) receptors in basal ganglia
  - ◆ This produces many DA related side effects (SEs)
  - ◆ Dopamine modulates and fine tunes motor activity

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## Mechanism of action cont.

- ◆ DA regulates & inhibits prolactin release
- ◆ Antipsychotics block muscarinic receptors, acetylcholine and nor-epinephrine (NE)
- ◆ Results in antiparasymphathetic effects and orthostatic hypotension

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## Indications for use

- Schizophrenia
  - ◆ Altered thought processes
  - ◆ Sensory perceptual alteration
  - ◆ Reduce relapse
  - ◆ Reduce violent and aggressive behavior
  - ◆ Improve ADL's and sleep patterns

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### Side Effects of Typical Antipsychotics

- Anticholinergic symptoms
- Extrapyramidal side effects (EPS)
  - ◆ Dystonia
  - ◆ Akathisia
  - ◆ Akinesia
  - ◆ Pseudoparkinsonism
  - ◆ Tardive dyskinesia (TD)
  - ◆ Neuroleptic malignant syndrome (NMS)

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### Extrapyramidal Side Effects cont.

Acute Dystonic Reactions

- Occur early in TX
- Involuntary ms.—posture, gait, ocular movements
- Oculogyric crisis: eyes roll upward
- Torticollis: contracted cervical ms. produce neck torsion
- Laryngeal-pharyngeal dystonias: assoc. w/gagging, cyanosis, resp. distress & asphyxia
  - ◆ Life-threatening—immediate intervention
  - ◆ All dystonic conditions respond to IM anticholinergic drugs

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### Extrapyramidal Side Effects cont

- Akathisia
  - ◆ Subjective & objective restlessness
  - ◆ May present as agitation
  - ◆ Disappears when drug is stopped
  - ◆ Anticholinergic agents—Artane & Cogentin
  - ◆ Benzodiazepines (BZDs)—Ativan, Valium, Klonopin
  - ◆ Propranolol (Inderal)

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## EPSEs Continued

- Akinesia
  - ◆ Absence of or impairment of movement
  - ◆ Bradykinesia—slowing of movements
  - ◆ Lack spontaneity in movement or speech

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## EPSE Continued

- Parkinsonism
  - ◆ Tremors, rigidity, bradykinesia
  - ◆ Similar to neg. sx. of schizophrenia
  - ◆ Anticholinergic agents

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## Extrapyramidal Side Effect cont.

- Tardive Dyskinesia (TD)
  - ◆ Manifests in 6-24 mos.
  - ◆ May continue when drug is discontinued
  - ◆ Abnormal involuntary movements of face, tongue, trunk, & extremities
    - ◆ Lip smacking, teeth grinding, tongue rolling or protrusion, tics & diaphragmatic movements which may impair breathing

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## EPSE Continued

- Tardive Dyskinesia continued
  - ◆ Early detection (AIMS)
  - ◆ Treatment
    - ◆ Bromocriptine (Parlodel)
    - ◆ Clonazepam (Klonopin)
    - ◆ Vitamin E
    - ◆ Clozapine (Clozaril)

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## Cardiovascular Side Effects

- Hypotension & orthostatic hypotension
- Tachycardia
- Treatments
  - ◆ Hold drug systolic <80mmHg
  - ◆ TED stockings
  - ◆ Cardiac workup
  - ◆ Give haloperidol (Haldol)

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## Miscellaneous Side Effects

- Dermatologic changes
- Photosensitivity
- Endocrine changes
- Weight gain
- Sedation

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### Rare Side Effects

- Aganulocytosis
  - ◆ Treatment
  - ◆ Notify physician and withhold dose
  - ◆ Monitor lab work
  - ◆ High mortality rate

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### Rare Side Effects cont.

- Cholestatic jaundice
  - ◆ Treatment
  - ◆ Stop drug, bedrest
  - ◆ High carb diet, high protein diet
  - ◆ Liver function tests

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### Neuroleptic Malignant Syndrome NMS

- Cardinal symptoms
- Mental changes
- Rigidity (Lead pipe)
- Hyperthermia (up to 108F)
- Diaphoresis
- Tachypnea
- Autonomic Dysfunction
  - Hypotension, tachycardia, sweating, salivation,  
urinary incontinence

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## NMS continued

- Other signs & symptoms
  - ◆ Agitation, hyperreflexia, impaired breathing, muteness, pallor
  - ◆ Laboratory findings
    - ◆ Elevated CPK
    - ◆ Hyperkalemia
    - ◆ Hyponatremia
    - ◆ Metabolic acidosis
    - ◆ Elevated WBCs

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## EPSEs Continued NMS continued

- Risk factors
  - ◆ Young adulthood      Dehydration
  - ◆ Male sex              Dx of alcoholism
  - ◆ OBS                    Previous brain injury
  - ◆ EP disorder (PD)      Iron deficiency
  - ◆ Nonschizophrenic illness      Catatonia
  - ◆ High-potency drugs      Prolonged restraint
  - ◆ Lithium coadministration
  - ◆ Poorly controlled EPSEs
  - ◆ Withdrawal from anticholinergics

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## Treatment of NMS

- Stop drug and transfer to ICU
- Treat symptoms
- Bromocriptine (Parlodel)
- Dantrolene (Dantrium)
- Amantadine (Symmetrel)
- Antipyretics
- Heparin
- Hydration and electrolyte balance

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**NMS Treatment cont.**

- Treat arrhythmias
- Monitor LOC
- Medic Alert Bracelet

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**Common Standard  
Antipsychotics**

- Chlorpromazine (Thorazine)
- Thioridazine (Mellaril)
- Fluphenazine (Prolixin)
- Trifluoperazine (Stelazine)
- Haloperidol (Haldol)
- Perphenazine (Trilafon)
- Thiothixene (Navane)

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**Depot Drugs**

- Haloperidol deconate     Haldol
- Fluphenazine deconate     Prolixin
- Fluphenazine enanthate     Prolixin

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## Atypical Antipsychotics

- Treat both positive and negative signs and symptoms of schizophrenia
- No dopamine blockade
- Improved quality of life r/t improved social skills and ADL's

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## Atypical Antipsychotics

- Clozapine (Clozaril)
  - ◆ Common side effects
  - ◆ Tachycardia
  - ◆ Sedation
  - ◆ Hypotension
  - ◆ Hypersalivation
  - ◆ Sedation

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## Clozapine (Clozaril) side effects cont.

- Serious Side Effects
  - ◆ Agranulocytosis 1-2% incidence
  - ◆ Seizures 3% incidence related to dosage
  - ◆ Very costly drug to administer
  - ◆ Weekly blood work

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### Risperadone (Risperdal)

- No agranulocytosis
- Low EPS
- Can alleviate tardive dyskinesia
- Dosages of 6mg/day are associated with low side effect profile
- Dosages of 10mg/day are associated with increased side effects

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### Risperidone side effects

- Insomnia, agitation, anxiety
- Orthostatic hypotension
- Weight gain
- EPS
- Headache
- Rhinitis

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### Olanzapine (Zyprexa)

- Once a day dosing, long half life
- Greater compliance
- No cardiac or hematological problems

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### Olanzapine side effects

- Weight gain—can be excessive
- Metabolic syndrome:
  - ◆ Elevated glucose, cholesterol, triglycerides
- Other side effects similar but milder than risperidone

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### Anticholinergics

- Anticholinergics:
  - ◆ Treatment of EPS
  - ◆ Treatment of NMS
- Benztropine (Cogentin) most common
- trihexphenidyl (Artane) abuse potential due to mood elevation

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### Anticholinergics cont.

- Side Effects:
  - ◆ Dry mouth
  - ◆ Urinary retention
  - ◆ Constipation
  - ◆ Blurred vision
  - ◆ Impotence

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## Acute Dystonic Reactions

- First drug treatment:
  - ◆ Benzotropine (Cogentin) 1-2 mg IM
  - ◆ Second Choice:
    - ◆ Diphenhydramine HCL (Benadryl) 25-50 mg. IM (Note well: This protocol is different than what is stated in Varcarolis)

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## Additional Notes:

- Patients with schizophrenia who have existing cardiac disease should have a thorough cardiac work-up periodically. Drug of choice of major antipsychotics is haloperidol (Haldol) because of its low anticholinergic properties. Preferred treatment is with atypical antipsychotics.
- Patient taking traditional neuroleptics need periodic eye exams due to vision changes

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## Additional Notes cont:

- Atypical Antipsychotics:
- Disadvantages:
  - ◆ Weight gain that can lead to risk of cardiovascular disease, diabetes and hypertension
  - ◆ All but ziprasidone (Geodon) and aripiprazole (Abilify) cause weight gain
  - ◆ Result in poor self-esteem and noncompliance
  - ◆ Expense

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**Additional Notes cont:**

- For patients who tend to cheek their meds many of the major antipsychotics and atypical antipsychotics are available in liquid form. A drug of choice is olanzepine (Zyprexa Zydis). A new injectable form of resperadone (Resperdal) is Resperadone Consta.

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