

**THE ONE WITH TREATMENT  
RESISTANT BIPOLAR DISORDER**  
JANICE LANDY MD

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**NO FINANCIAL RELATIONSHIPS  
TO DISCLOSE, BUT MAY DISCUSS  
OFF-LABEL USE OF COMMERCIAL  
PRODUCTS.**

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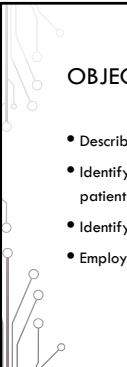
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**OBJECTIVES**

- Describe diagnostic criteria for Bipolar I Disorder
- Identify three alternatives to lithium for Bipolar I Disorder in the geriatric patient population.
- Identify side effects to commonly prescribed mood stabilizing medications.
- Employ strategies for mood stabilization in the geriatric patient population.

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**CASE-HPI**

82-year-old male with past medical history significant for HTN and Bipolar I Disorder and HTN who presents to hospital with lower extremity erythema as well as decreased need for sleep and changes in behavior.

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**CASE-HPI CONTINUED**

- Patient managed multiple decades on lithium
- Hospital admission for lithium toxicity earlier in year
  - Lithium stopped
  - Patient not immediately restarted on mood stabilizing agent (does this contradict the next slide?)
- History of prolonged admissions related to Bipolar I diagnosis

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**H&P**

- Patient had prescriptions for olanzapine and valproic acid, non-adherent
- No substance misuse
- Allergies: Tegretol
- Lives with son, enjoys gardening
- Active senior at baseline

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**MANIA**

- Grandiosity
- Decreased need for sleep
- Pressured/Increased speech
- Flight of ideas
- Distractibility
- Increased goal-directed activity
- Reckless behavior

**STANDARD APPROACH**

- Acute mania inpatient
  - Mood stabilizer
  - Atypical antipsychotic

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**LITHIUM**

- Approved for acute mania and bipolar maintenance therapy
- Mechanism-of-action unknown but activity on sodium transporters and alters metabolism of specific neurotransmitters
- Relative contraindication with renal and cardiac impairment

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**CASE-HPI CONTINUED**

- Patient admitted to medicine for cellulitis and eventually transferred to psychiatry unit
- Standard approach to treatment initiated for acute mania

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### MEDICATION OPTIONS IN ACUTE MANIA

- Mood stabilizers
- Atypical antipsychotics
- Typical antipsychotics
- Benzodiazepines

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### MEDICATION TRIALS AND EFFECTS

1. Valproic acid and risperidone-Parkinsonian side effects, intolerable, minimal sleep, agitation
2. Valproic acid and quetiapine-Parkinsonian side effects and sedation, intolerable, varying sleep minimal, agitation
3. Valproic acid and chlorpromazine (low-dose)-Varying levels of sedation, mood more stable, minimal sleep, decreased agitation, mild parkinsonian side effects
4. Valproic acid, lithium (low-dose), chlorpromazine (low-dose)-increased creatinine, mood improved, varying sleep, no agitation, mild parkinsonian side effects
5. Valproic acid, chlorpromazine (low-dose), temazepam (low-dose)-mood depressed, decreased energy, no agitation, improved sleep, mild parkinsonian side effects
6. Chlorpromazine (low-dose), temazepam-mood lability, agitation, decreased sleep, less sedation, mild parkinsonian side effects
7. Oxcarbazepine, chlorpromazine (low-dose), temazepam-improved sleep, no agitation, improved mood, adequate energy, mild parkinsonian side effects. However, developed allergic reaction
8. Lamazepam-adequate sleep, mood lability, agitation
9. Chlorpromazine-parkinsonian side effects, sedation, mood lability, varying sleep

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### VALPROIC ACID

- Acute mania and maintenance
- Blocks voltage-sensitive sodium channels and increases GABA
- CNS side effects-sedation, confusion, appetite changes, weakness
- Caution in elderly
- Multiple formations available

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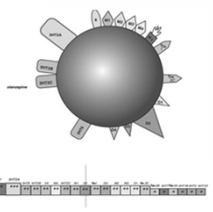
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### OLANZAPINE



The diagram shows a central sphere representing the Olanzapine molecule. It has several arrows pointing outwards, each labeled with a receptor: 5HT<sub>2A</sub>, D<sub>2</sub>, D<sub>1</sub>, D<sub>4</sub>, D<sub>5</sub>, α<sub>1</sub>, α<sub>2</sub>, and H<sub>1</sub>. Below the sphere is a horizontal bar chart showing the relative affinity of Olanzapine for these receptors. The chart indicates high affinity for 5HT<sub>2A</sub> and D<sub>2</sub>, and lower affinity for the other receptors.

- Atypical antipsychotic with mood stabilizing properties
- Ideal initial step with mood stabilizer in acute mania
- Sedation and weight gain
- Can contribute to delirium

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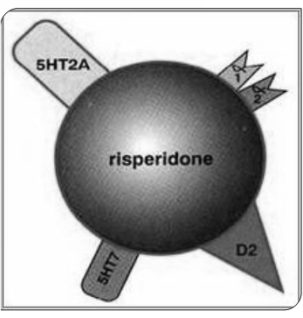
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### RISPERIDONE



The diagram shows a central sphere representing the Risperidone molecule. It has three arrows pointing outwards, labeled with receptors: 5HT<sub>2A</sub>, D<sub>2</sub>, and 5HT<sub>7</sub>. The sphere is labeled "risperidone".

- Thought dopamine and 5HT<sub>2A</sub> activity contributes to mood stabilizing effects
- Comparative increased D<sub>2</sub> activity
- Aggressive behavior and affective instability

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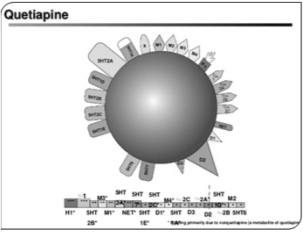
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### QUETIAPINE



The diagram shows a central sphere representing the Quetiapine molecule. It has many arrows pointing outwards, each labeled with a receptor: 5HT<sub>2A</sub>, 5HT<sub>2B</sub>, 5HT<sub>1A</sub>, 5HT<sub>1B</sub>, 5HT<sub>1C</sub>, 5HT<sub>1D</sub>, 5HT<sub>1E</sub>, 5HT<sub>1F</sub>, 5HT<sub>1G</sub>, 5HT<sub>1H</sub>, 5HT<sub>1I</sub>, 5HT<sub>1J</sub>, 5HT<sub>1K</sub>, 5HT<sub>1L</sub>, 5HT<sub>1M</sub>, 5HT<sub>1N</sub>, 5HT<sub>1O</sub>, 5HT<sub>1P</sub>, 5HT<sub>1Q</sub>, 5HT<sub>1R</sub>, 5HT<sub>1S</sub>, 5HT<sub>1T</sub>, 5HT<sub>1U</sub>, 5HT<sub>1V</sub>, 5HT<sub>1W</sub>, 5HT<sub>1X</sub>, 5HT<sub>1Y</sub>, 5HT<sub>1Z</sub>, 5HT<sub>2A</sub>, 5HT<sub>2B</sub>, 5HT<sub>2C</sub>, 5HT<sub>2D</sub>, 5HT<sub>2E</sub>, 5HT<sub>2F</sub>, 5HT<sub>2G</sub>, 5HT<sub>2H</sub>, 5HT<sub>2I</sub>, 5HT<sub>2J</sub>, 5HT<sub>2K</sub>, 5HT<sub>2L</sub>, 5HT<sub>2M</sub>, 5HT<sub>2N</sub>, 5HT<sub>2O</sub>, 5HT<sub>2P</sub>, 5HT<sub>2Q</sub>, 5HT<sub>2R</sub>, 5HT<sub>2S</sub>, 5HT<sub>2T</sub>, 5HT<sub>2U</sub>, 5HT<sub>2V</sub>, 5HT<sub>2W</sub>, 5HT<sub>2X</sub>, 5HT<sub>2Y</sub>, 5HT<sub>2Z</sub>, 5HT<sub>7</sub>, D<sub>1</sub>, D<sub>2</sub>, D<sub>3</sub>, D<sub>4</sub>, D<sub>5</sub>, α<sub>1</sub>, α<sub>2</sub>, and H<sub>1</sub>. The sphere is labeled "Quetiapine".

- Mood effects due to serotonin activity
- Weakly dopaminergic
- Decreased concerns of parkinsonian side effects
- Sedating, metabolic side effects

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### CHLORPROMAZINE

**Antipsychotic/Neuroleptics**

Chlorpromazine:  $\alpha_1 = 5-HT_2 = D_2 > D_1 > M \geq \alpha_2$   
 Haloperidol:  $D_2 > D_1 = \alpha_1 > \alpha_2 > 5-HT_2 > H_1 > M = \alpha_2$   
 Clozapine:  $D_1 = \alpha_1 > 5-HT_2 = M > D_2 = D_3 = \alpha_2; H_1$   
 Quetiapine:  $5-HT_2 = D_2 = \alpha_1 = \alpha_2; H_1$   
 Risperidone:  $5-HT_2 \gg \alpha_1 > H_1 \geq D_2 > \alpha_2 \gg D_1$   
 Sertindole:  $5-HT_2 > D_2 = \alpha_2$

- Low-potency antipsychotic
- Mood stabilizing properties
- CNS depression, cardiac risk, hypotension
- Cautious use in geriatric patients

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### GOALS OF CARE

- Stabilize
- Minimize side effects
- Minimize hospitalization time

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### APPROACH TO GERIATRIC PATIENTS

- Begin treatment with standard approach
- Consider starting at lower doses
- If standard approach fails, theory-based approach for optimal medication
- Consider using multiple medications at lower doses
- Monitor closely for side effects
- Physical therapy

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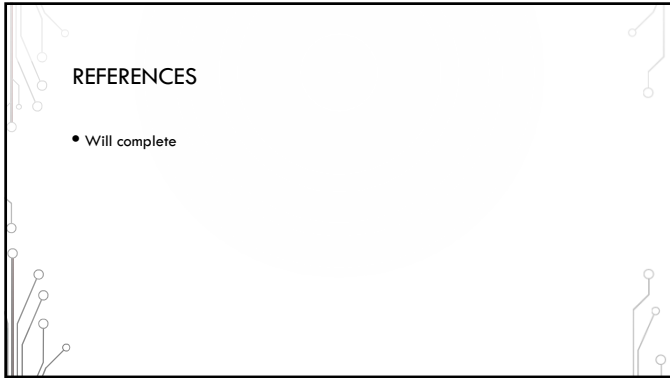
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REFERENCES

- Will complete

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QUESTIONS?

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