ASK THE PHARMACIST:
PSYCHIATRIC MEDICATION
TIPS & CLINICAL PEARLS

Azita Alipour, PharmD, BCPP, BCGP
Assistant Professor - Psychiatric Pharmacy
Marshall B. Ketchum University, College of Pharmacy
NAMI Santa Cruz Meeting
January 15, 2020
Disclosures

- The speaker does not have any conflicts of interest to disclose
- The speaker will discuss off-label uses of medications
Overview

- How to maximize your appointment time with the doctor
- Understanding how the medications work and what to expect
- Special considerations with specific medications
- Side effects
- The importance of adhering to your medications
Ask Questions

- What can I expect from taking the medication?
- What am I using the medication for?
- How soon will the medication start working?
ANTIDEPRESSANTS
Depression Symptoms

- D = Depressed mood
- S = Sleep
- I = Interest
- G = Guilt
- E = Energy
- C = Concentration
- A = Appetite
- P = Psychomotor
- S = Suicide
Monoamine neurotransmitter (NT) regulation at the neuronal level. NTs carry messages between cells. Each NT generally binds to a specific receptor, and this coupling initiates a cascade of events. NTs are reabsorbed back into nerve cells by reuptake pumps (ie, transporter molecules) at which point they may be recycled for later use or broken down by enzymes. For their primary mechanism of action, most antidepressants are thought to inhibit the transporter molecules and allow more NT to remain in the synapse. (Reproduced from Mind Over Matter. NIH Publication No. 09-7423. The National Institute on Drug Abuse, National Institutes of Health, U.S. Department of Health and Human Services. Printed 2009.)
Antidepressants

- **Selective serotonin reuptake inhibitors (SSRIs)**
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
  - Fluvoxamine (Luvox)

- **Serotonin norepinephrine reuptake inhibitors (SNRIs)**
  - Venlafaxine (Effexor)
  - Desvenlafaxine (Pristiq)
  - Duloxetine (Cymbalta)
  - Levomilnacipran (Fetzima)

- **Dopamine Norepinephrine Reuptake Inhibitor (DNRI)**
  - Bupropion HCL (Wellbutrin)

- **Monoamine oxidase inhibitors (MAOIs)**
  - Phenelzine
  - Selegiline

- **Tricyclic antidepressants (TCAs)**
  - Amitriptyline
  - Imipramine

- **Others**
  - Mirtazapine (Remeron)
  - Trazodone (Desyrel)
  - Vilazodone (Viibryd)
  - Vortioxetine (Trintellix)
First-line Antidepressant options for MDD

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin norepinephrine reuptake inhibitors (SNRIs)
- Bupropion
- Mirtazapine
<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Effect Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>First few days</td>
<td>Improvement in sleep &amp; appetite</td>
</tr>
<tr>
<td>1-3 weeks</td>
<td>Increased activity and sex drive, self-care habits improve, concentration, memory, thinking, and movement normalize</td>
</tr>
<tr>
<td>6-8 weeks</td>
<td>Relief of depressive mood, begin to experience pleasure, feel less helpless, thoughts of suicide</td>
</tr>
</tbody>
</table>
Antidepressant Related Sexual Side Effects

- Can be a side effect of some antidepressants
- Conflicting evidence has been reported as to frequency

Antidepressants with lower risk: Bupropion, mirtazapine

Antidepressant Discontinuation Syndrome

- Some risk factors include:
  - Short half-life antidepressant
    - Paroxetine, venlafaxine
  - Skip/miss doses
  - Taking for ≥ 8 weeks

- Onset usually within 1 week after decrease dose or discontinue the antidepressant

Discontinuation Syndrome Symptoms

- Headache
- Dizziness
- Diarrhea
- Parasthesia
- Lethargy
- “Electric Shock – Like” Feeling
- Fever, Chills, Sweating
- Nausea/Vomiting
- Insomnia

Antidepressant Selection Based on Target Symptoms

- **Fatigue/low energy**: Fluoxetine
- **Lack of appetite**: Paroxetine
- **Poor Concentration**: Bupropion
- **Insomnia**: Mirtazapine, Trazodone

**Target Symptoms**
- Depression
- Fatigue/low energy
- Lack of appetite
- Poor Concentration
- Insomnia

**Antidepressants**
- Mirtazapine
- Trazodone
- Bupropion
- Fluoxetine
- Paroxetine

## Antidepressant Selection Based on Co-morbid Condition

<table>
<thead>
<tr>
<th>Co-morbid Condition</th>
<th>Antidepressants which may be Preferred Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety Disorder</td>
<td>SSRI, SNRI</td>
</tr>
<tr>
<td>Breast Cancer (Tamoxifen)</td>
<td>Venlafaxine, mirtazapine, citalopram, escitalopram</td>
</tr>
<tr>
<td>Elderly</td>
<td>SSRIs, SNRIs, mirtazapine</td>
</tr>
<tr>
<td>Hypertension</td>
<td>SSRI</td>
</tr>
<tr>
<td>Obesity</td>
<td>Bupropion, vilazodone</td>
</tr>
<tr>
<td>Pain Syndromes</td>
<td>SNRIs</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Sertraline</td>
</tr>
<tr>
<td>Sexual Dysfunction</td>
<td>Bupropion, mirtazapine</td>
</tr>
<tr>
<td>Smoker</td>
<td>Bupropion</td>
</tr>
</tbody>
</table>

Serotonin Syndrome

- Patient Presentation

![Diagram showing symptoms of Serotonin Syndrome]

- Mydriasis
- Agitation
- Diaphoresis

- Hyperreflexia (greater in lower extremities)
- Tremor (greater in lower extremities)
- Clonus (greater in lower extremities)
- Increased bowel sounds; may have diarrhea
- Tachycardia
- Autonomic instability; often hypertensive

Black Box Warning - Suicidality

- Antidepressants increased the risk compared with placebo of suicidal thinking and behavior (suicidality) in short-term studies in children, adolescents, and young adults with major depressive disorder (MDD) and other psychiatric disorders.

- Short-term studies did not show an increase in the risk of suicidality with antidepressants compared with placebo in adults older than 24 years.

- Appropriately monitor and closely observe patients of all ages who are started on antidepressant therapy for clinical worsening, suicidality, or unusual changes in behavior.

- Medication guide is required for all antidepressants each time dispensed.

Question:
Can you become addicted to a antidepressant?
Antipsychotics approved in Depression

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Indications used in depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abilify</td>
<td>Aripiprazole</td>
<td>Adjunctive to antidepressants for MDD</td>
</tr>
<tr>
<td>Symbyax</td>
<td>Fluoxetine/Olanzapine</td>
<td>Treatment-Resistant Depression (TRD) in adults</td>
</tr>
<tr>
<td>Seroquel XR</td>
<td>Quetiapine</td>
<td>Adjunctive to antidepressant for MDD</td>
</tr>
<tr>
<td>Rexulti</td>
<td>Brexipiprazole</td>
<td>Adjunctive to antidepressants for MDD</td>
</tr>
</tbody>
</table>

**Pearls:**
- Olanzapine associated with most metabolic adverse effects
  - Increased blood pressure, blood sugars and cholesterol
- Olanzapine & quetiapine most sedating vs aripiprazole activating
Esketamine (Spravato)

- **Approved Indication:** Adjunctive to antidepressant for Treatment-Resistant Depression (TRD)

- **TRD Definition in Esketamine Clinical Trials:**
  - At least two adequate (at least 6 weeks and at adequate dose) antidepressant trials

https://www.fda.gov/media/121378/download
Esketamine (Spravato)

- Most common adverse effects:

- Dissociation
- Dizziness
- Nausea
- Sedation
- Vertigo
- Hypoesthesia
- Anxiety
- Lethargy
- Blood Pressure Increased
- Vomiting
- Feeling Drunk

[www.fda.gov](http://www.fda.gov) Spravato Package insert
Esketamine (Spravato)

Only administered in healthcare settings which can monitor the patient for at least 2 hours

Healthcare settings & pharmacies & need to be specially certified

Patient enrollment in registry to review post-marketing data on risks and safe use

https://www.fda.gov/media/121378/download

ANTIPSYCHOTICS
Four Dopamine Pathways

- **Mesocorticol**
  - Cognition, social function

- **Mesolimbic**
  - Positive Symptoms
    - EX: Hallucinations, Delusions

- **Nigrostriatal**
  - Movement

- **Tuberoinfundibular**
  - Prolactin
Antipsychotics

First Generation “Typical” Antipsychotic

Second Generation “Atypical” Antipsychotic

D2 receptor antagonists

Serotonin-Dopamine Antagonist

5-HT2A
### Antipsychotic Target Symptoms

- Agitation/anxiety
- Hostility
- Insomnia
- Suspiciousness
- Mutism
- Preoccupations
- Loose associations
- Social withdrawal
- Inappropriate affect
- Delusions
- Hallucinations
Antipsychotic Response time

- **1st week:** ↓ agitation, hostility, aggression and improved sleep and appetite

- **2 – 4 weeks:** ↓ paranoia, hallucinations and more organized thinking

- **6 – 12 weeks:** ↓ delusions, improvement in (-) symptoms, ongoing improvements in (+) symptoms

- **3 – 6 months:** cognitive symptoms improve (with atypical antipsychotics)
Antipsychotic Discontinuation Effects

**Discontinuation syndromes**: (usually appear within days of stopping)

- Nausea
- Vomiting
- Diarrhea
- Diaphoresis
- Cold sweats
- Muscle aches and pains
- Insomnia
- Anxiety
- Confusion
# First Generation Antipsychotics (FGAs)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine®</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Mellari®</td>
</tr>
<tr>
<td>Mesoridazine</td>
<td>Serentil®</td>
</tr>
<tr>
<td>Molindone</td>
<td>Moban®</td>
</tr>
<tr>
<td>Loxapine</td>
<td>Loxitane®</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>Trilafon®</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Navane®</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>Stelazine®</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Haldol®</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>Prolixin®</td>
</tr>
</tbody>
</table>
Extrapyramidal Adverse Effects

- Acute dystonic reactions
- Pseudoparkinsonism
- Akathesia
- Tardive Dyskinesia
Second Generation Antipsychotics

- Clozapine (Clozaril®)- 1990
- Risperidone (Risperdal®)- 1994
- Olanzapine (Zyprexa®)- 1996
- Quetiapine (Seroquel®)- 1997
- Ziprasidone (Geodon®)- 2001
- Aripiprazole (Abilify®)- 2002

- Lurasidone (Latuda®)- 2013
- Asenapine (Saphris®)- 2015
- Iloperidone (Fanapt®)- 2009
- Brexipiprazole (Rexulti®)- 2016
- Cariprazine (Vraylar®)- 2015

Brand name only
- High cost
When is clozapine indicated?

- Treatment-resistant Schizophrenia
  - Failed at least two adequate trials of antipsychotics
- Aggressive
- Suicidal
Weight Gain

- **Mechanism not fully understood**
  - 5-HTc antagonism
  - H₁ antagonism
  - Insulin & leptin levels affected

- **Clozaril & Zyprexa**
  - up to 12 kg in 1 yr
Food Effects

- **Latuda**
  - Take with at least a 350 calorie meal

- **Geodon**
  - Take with at least a 500 calorie meal
Question:

Can antipsychotics be used as mood-stabilizers?
What is a mood stabilizer?

- Commonly defined as an agent which treats a phase of bipolar disorder (depression and/or mania) without causing either

  +

- Must prevent episodes from occurring (maintenance or prophylaxis)

- Antidepressants are **NOT** mood stabilizers
MOOD STABILIZERS
Bipolar Disorder

- Cyclical illness with alternating periods of

  Mania/Hypomania  Euthymia  Depression

Diagnostic and Statistical Manual of Mental Disorders – Fifth Ed. 2013
Pharmacologic Treatment

- Lithium

- **Anti-Epileptic Drugs** (AEDs)
  - Valproic Acid (VPA) / Divalproex sodium
  - Carbamazepine (CBZ)
  - Lamotrigine
  - Others?

- **First Generation Antipsychotics** ("Typicals")
- **Second Generation Antipsychotics** ("Atypicals")
Lithium History

- Arguably the **GOLD STANDARD** of bipolar disorder treatment

- First used in the 1800s as medicinal treatment for:
  - Gout
  - Neurological ailments
  - GI ailments
  - Table salt substitute

- In 1949 Cade described successful treatment of mania
- In 1970 FDA approved for treating acute mania
- In 1974 FDA approved for prophylaxis of bipolar disorder

Lithium

Some common adverse effects:
- Feeling tired, difficulty concentrating
- Nausea/heartburn
- Weight changes
- Skin changes

Examples of side effects you should report right away:
- Loss of balance
- Slurred speech
- Visual disturbances (ex: double vision)
- Nausea, vomiting, stomach ache
- Watery stools, diarrhea (more than twice a day)
- Abnormal general weakness or drowsiness
- Marked trembling, muscle twitches, jaw shaking

Counseling Points to Consider

**Important considerations:**

- Important to keep yourself well hydrated
- Limit number of caffeinated (ex: coffee) liquids you drink
- Avoid nonsteroidal anti-inflammatory drugs (ex: Ibuprofen, Motrin, Advil) as they can affect the blood level of lithium and result in toxicity.
- If you have the flu, especially if vomiting or diarrhea occur, check with your doctor regarding your lithium dose.
- Use extra care in hot weather and during activities that cause you to sweat heavily.
Pharmacologic Treatment

- Lithium

- Anti-Epileptic Drugs (AEDs)
  - Valproic Acid (VPA) / Divalproex sodium
  - Carbamazepine (CBZ)
  - Lamotrigine
  - Others?

- First Generation Antipsychotics (“Typicals”)
- Second Generation Antipsychotics (“Atypicalsc”)
SLEEP MEDICATION
## Insomnia Signs and Symptoms

<table>
<thead>
<tr>
<th>Subjective</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep Complaints</strong></td>
<td>• Difficulty falling asleep&lt;br&gt;• Maintaining sleep&lt;br&gt;• Waking multiple times during the night&lt;br&gt;• Waking too early</td>
</tr>
<tr>
<td><strong>Daytime Complaints</strong></td>
<td>• Non-restorative sleep&lt;br&gt;• Excessive daytime sleepiness (EDS) or fatigue&lt;br&gt;• Malaise&lt;br&gt;• Difficulty concentrating&lt;br&gt;• Memory impairment</td>
</tr>
</tbody>
</table>
Insomnia Etiology/Risk Factors

**Gender**
- 55-60% of patients are female (may be as high as 2:1)

**Environmental**
- Ex: Noise, light, extremes of temperature

**Situational Stress**
- Ex: work, finances, major life events
Non-Pharmacologic – Stimulus Control

<table>
<thead>
<tr>
<th>Stimulus Control Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Establish regular times to wake up and to go to sleep</td>
</tr>
<tr>
<td>2. Sleep only as much as necessary to feel rested</td>
</tr>
<tr>
<td>3. Go to bed only when sleepy. Avoid long periods of wakefulness in bed. Use the bed only for sleep or intimacy; do not read or watch television in bed.</td>
</tr>
<tr>
<td>4. Avoid trying to force sleep; if you do not fall asleep within 20-30 minutes leave the bed and perform a relaxing activity (ex: read, listen to music) until drowsy. Repeat this as often as necessary</td>
</tr>
<tr>
<td>5. Avoid blue spectrum light from television, smart phones, tablets, and other mobile devices.</td>
</tr>
<tr>
<td>6. Avoid daytime naps</td>
</tr>
<tr>
<td>7. Schedule worry time during the day. Do not take your troubles to bed</td>
</tr>
</tbody>
</table>
Non-Pharmacologic – Sleep Hygiene

**Sleep Hygiene Recommendations**

1. Exercise routinely (three to four times weekly) but **NOT** close to bedtime because this can increase wakefulness.

2. Create a comfortable sleep environment by **avoiding temperature extremes**, loud noises, and illuminated clocks in the bedroom.

3. *Discontinue or reduce the use of alcohol, caffeine, and nicotine*

4. **Avoid drinking large quantities of liquids in the evening** to prevent nighttime trips to the restroom.

5. Do something relaxing and enjoyable before bedtime.
Treatment Options

Non-pharmacological management

Short-intermediate acting BZD receptor agonist
-or
NBRA (Sonata, Ambien, Lunesta)
-or
Ramelteon

Sedating antidepressants (ex: Trazadone, Remeron), especially with concurrent depression or anxiety

BZD = Benzodiazepines
NBRA = Non-benzodiazepine Receptor Agonist

Question:

Which over the counter medications/herbals can help with sleep?
OTHER
(IF TIME)
Question:

Any quick acting medications to help with anxiety that are not controlled substances?
Question:

What are some anti-craving medications used to prevent relapse to smoking cigarettes, alcohol, or opioid use?
Anti-Craving/Deterrent Medications

**Alcohol Use Disorder**
- Acamprosate (Campral)
- Naltrexone (Revia, Vivitrol)
- Disulfiram (Antabuse)

**Opioid Use Disorder**
- Methadone
- Buprenorphine (Suboxone)
- Naltrexone (Revia, Vivitrol)
Contents of Tobacco Smoke

- Greater than 7000
  - Nicotine
  - Carbon monoxide
  - Carcinogens
  - Toxins

Ammonia
Sulfur Dioxide
Acetone
Hydrogen Cyanide
Cadmium
Arsenic

Methane
Swamp Gas
Bleaching agent
Gas chamber
Car Batteries
Rat poison

How do these chemicals get in there?

## Health Consequences of Cigarette Smoke

### Four big categories of disease with tobacco smoking

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Pulmonary Damage</th>
<th>Vascular Damage</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal aortic aneurysm</td>
<td>Acute respiratory illness</td>
<td>Cerebrovascular disease Stroke</td>
<td>AML</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>Upper respiratory tract</td>
<td>Peripheral vascular disease</td>
<td>Bladder</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Lower respiratory tract</td>
<td>Other organs involved</td>
<td>Cervical</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>Chronic respiratory illness</td>
<td></td>
<td>Esophageal</td>
</tr>
<tr>
<td></td>
<td>Chronic obstructive pulmonary disease</td>
<td></td>
<td>Gastric</td>
</tr>
<tr>
<td></td>
<td>Respiratory symptoms</td>
<td></td>
<td>Kidney</td>
</tr>
<tr>
<td></td>
<td>Poor asthma control</td>
<td></td>
<td>Laryngeal</td>
</tr>
<tr>
<td></td>
<td>Reduced lung function</td>
<td></td>
<td>Lung</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Oral cavity and pharyngeal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pancreatic</td>
</tr>
</tbody>
</table>

**Health Benefits of Smoking Cessation**

**Minutes to days:**
- Lower BP, lower CO, better stamina, smell/taste, lower heart attack risk

**1 year**
- Excessive risk of CHD decreases to half that of a continuing smoker

**1 to 9 months**
- Lung ability to clear mucus increases, coughing, sinus congestion, fatigue, and shortness of breath decrease, and cilia regain normal function in the lungs, increasing the ability to handle mucus, clear lungs and reduce infection

**1 to 3 months:**
- Circulation improves, lung function increases

**10 years**
- Rate of death from lung cancer drops to half that of a continuing smoker. Cancer risk for mouth, throat, esophagus, bladder, kidney, pancreases decrease

**5 years**
- Stroke risk is reduced to that of a nonsmoker 5 to 15 years after quitting

**15 years:**
- CHD risk is similar to that of a nonsmoker

**CO = Carbon Monoxide**
Combating Smoking Triggers

Strategies to Combat Triggers
Anti-Craving for Nicotine

- **Nicotine Replacement Products**
  - Lozenge
  - Gum
  - Patch
- Bupropion (**Zyban**)
- Varenicline (**Chantix**)
Questions?

Azita Alipour, PharmD, BCPP, BCGP
Assistant Professor

Email: aalipour@ketchum.edu