

ASK THE PHARMACIST: **PSYCHIATRIC MEDICATION TIPS & CLINICAL PEARLS**

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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 am I using the medication for?

What can I expect from taking the medication?

How soon will the medication start working?



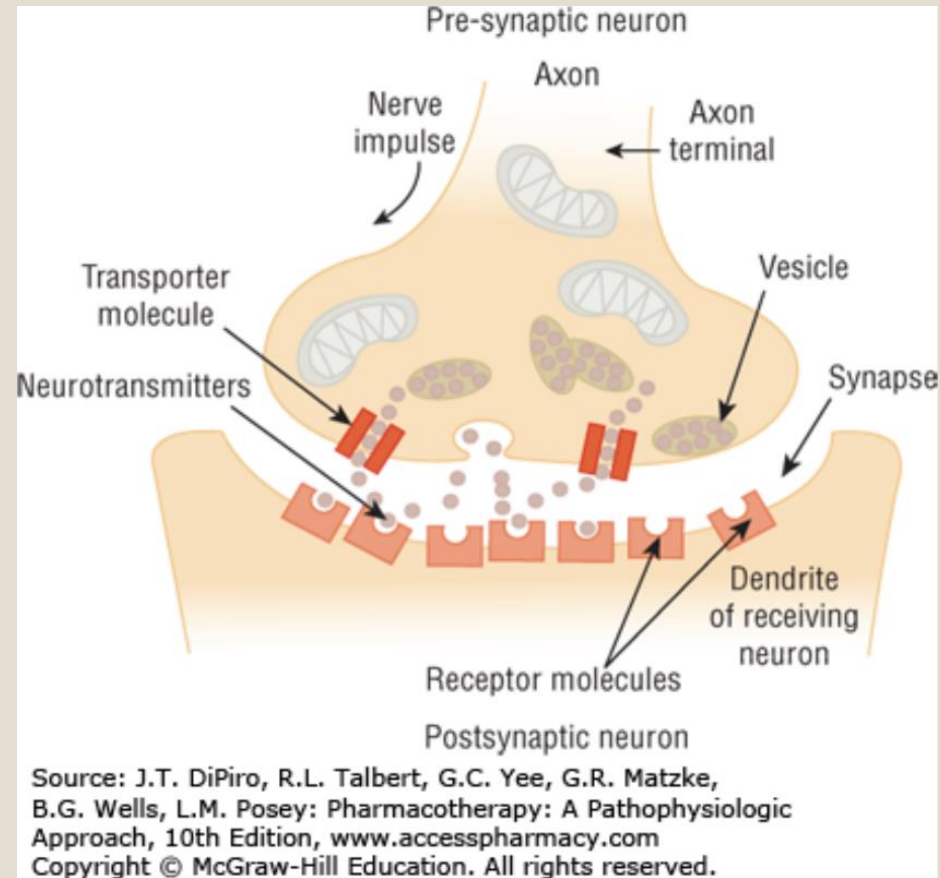


ANTIDEPRESSANTS

Depression Symptoms

- ❖ **D = Depressed mood**
- ❖ **S = Sleep**
- ❖ **I = Interest**
- ❖ **G = Guilt**
- ❖ **E = Energy**
- ❖ **C = Concentration**
- ❖ **A = Appetite**
- ❖ **P = Psychomotor**
- ❖ **S = Suicide**

Etiology



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)

Others

- Mirtazapine (Remeron)
- Trazodone (Desyrel)
- Vilazodone (Viibryd)
- Vortioxetine (Trintellix)

- **Monoamine oxidase inhibitors (MAOIs)**

- Phenelzine
- Selegiline

- **Tricyclic antidepressants (TCAs)**

- Amitriptyline
- Imipramine

First-line Antidepressant options for MDD

- **Selective serotonin reuptake inhibitors (SSRIs)**
- **Serotonin norepinephrine reuptake inhibitors (SNRIs)**
- **Bupropion**
- **Mirtazapine**



Time to Onset of Antidepressant Effects

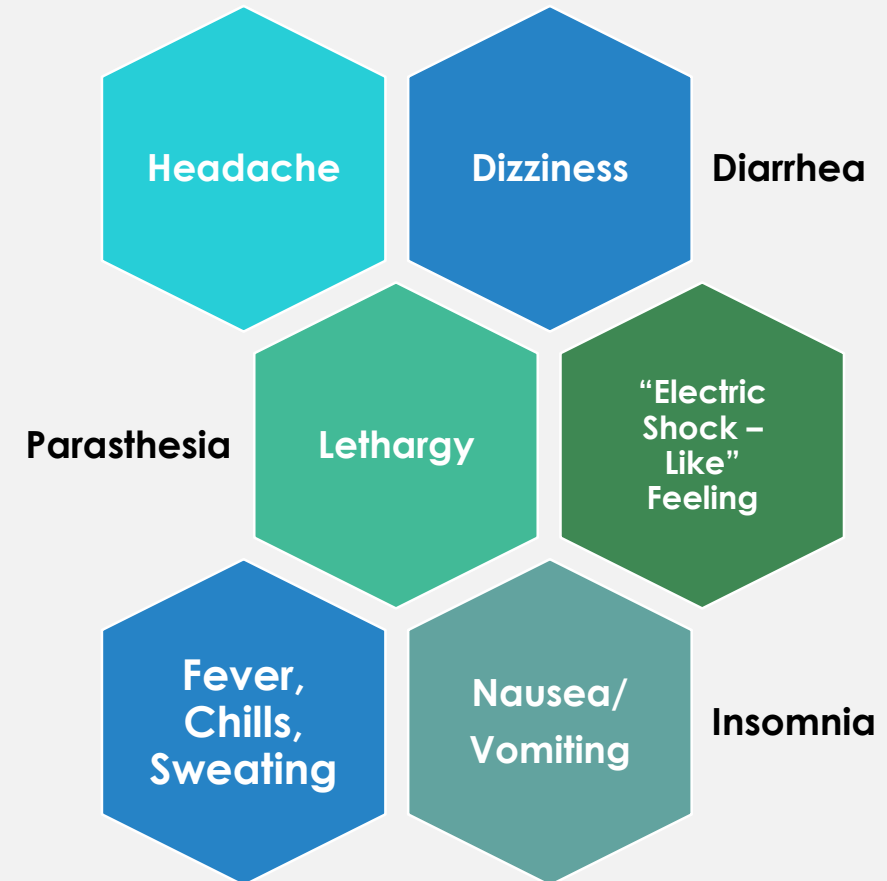
After initiate or increase dose	
First few days	Improvement in sleep & appetite
1-3 weeks	Increased activity and sex drive, self-care habits improve, concentration, memory, thinking, and movement normalize
6-8 weeks	Relief of depressive mood , begin to experience pleasure, feel less helpless, thoughts of suicide

Antidepressant Related Sexual Side Effects

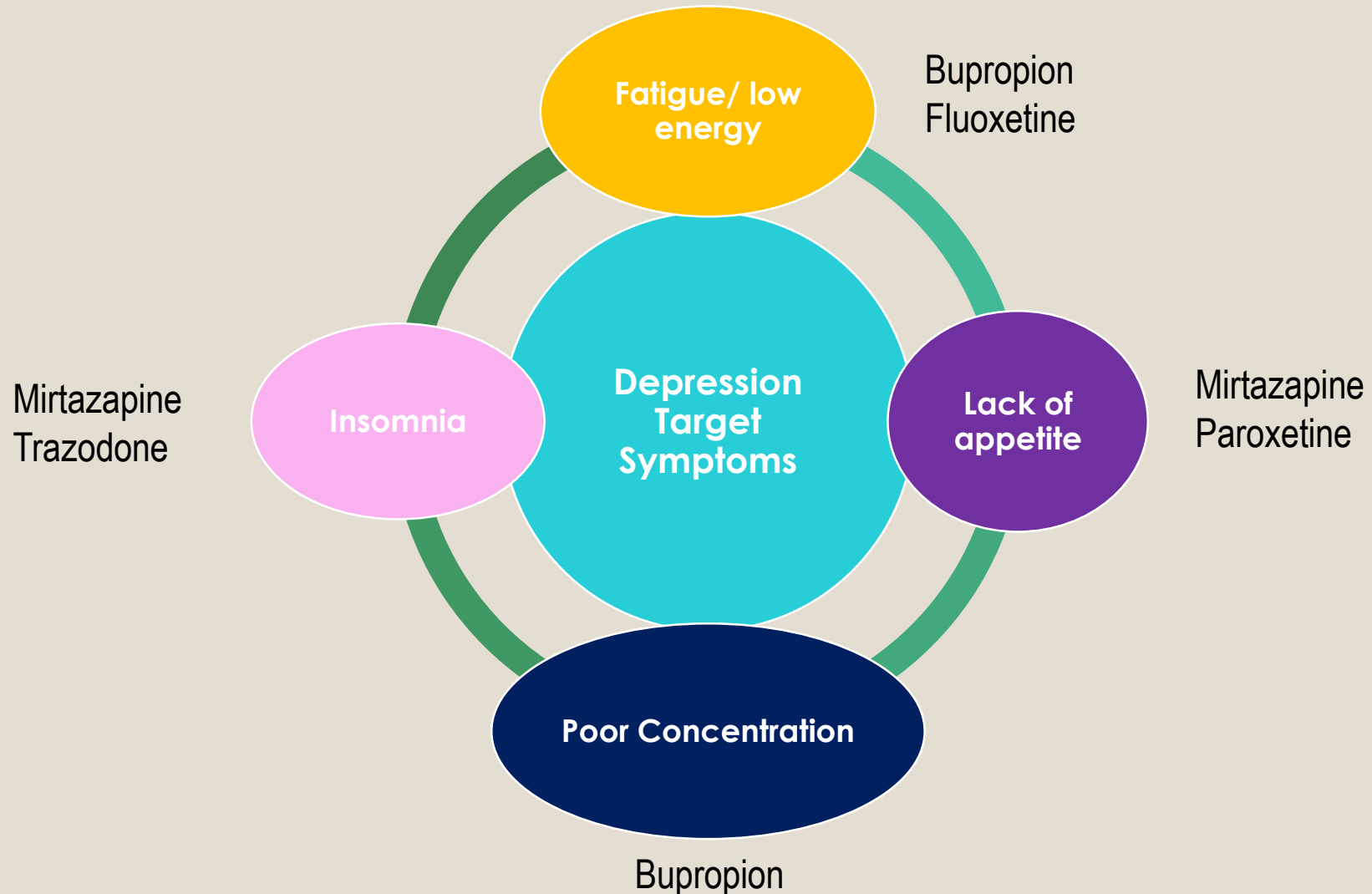
- Can be a side effect of some antidepressants
- Conflicting evidence has been reported as to frequency
 - **Antidepressants with lower risk: Bupropion, mirtazapine**

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



Antidepressant Selection Based on Target Symptoms



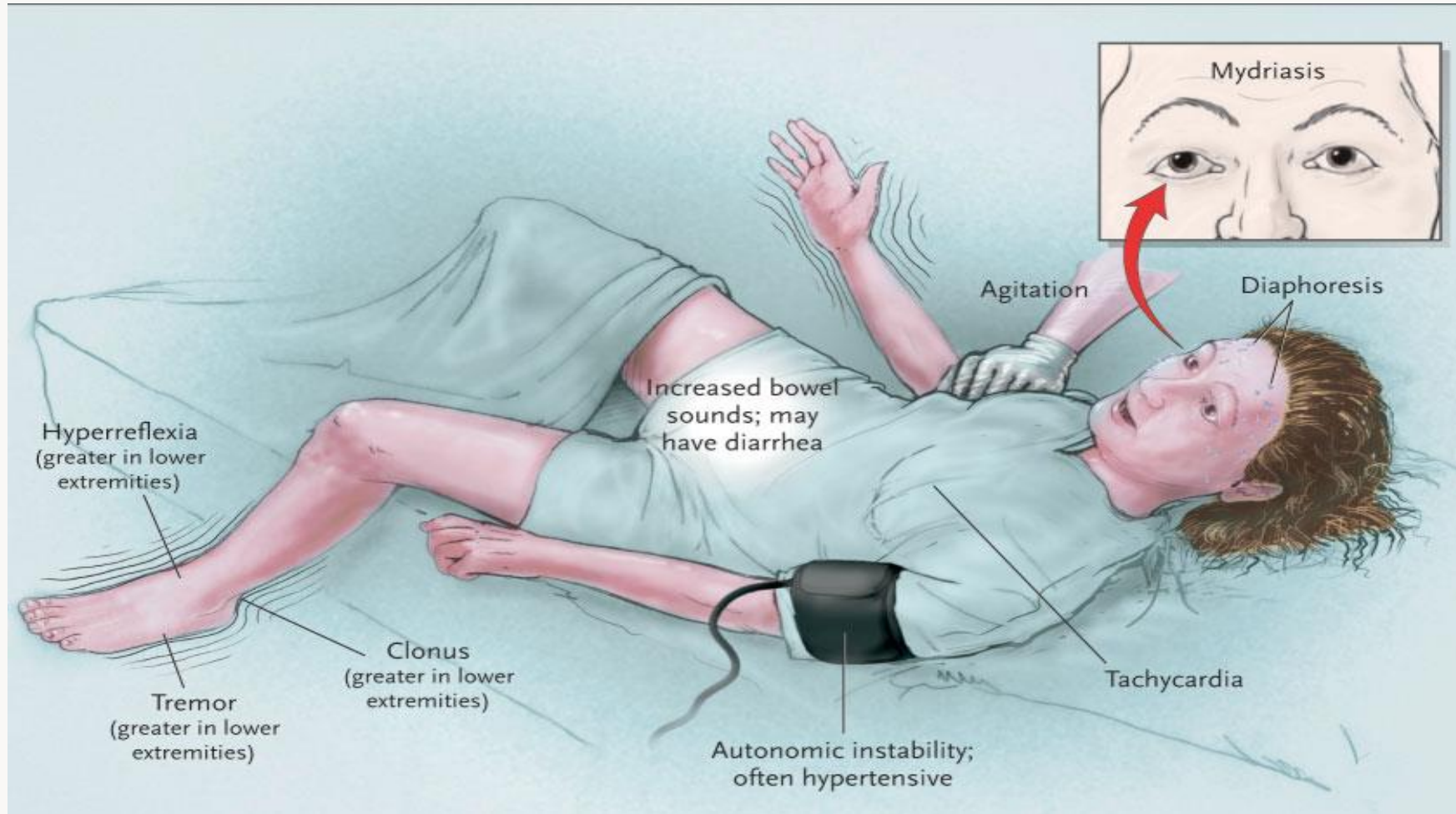
Antidepressant Selection Based on Co-morbid Condition

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

American Psychiatric Association. [Internet] Practice Guideline for the Treatment of Patients With Major Depressive Disorder. [accessed 1 June 2015]. Available from: <http://www.psychiatryonline.com/pracGuide/PracticePDFs/MDD2e>
PL Detail-Document, Choosing and Switching Antidepressants. Pharmacist's Letter/Prescriber's Letter. July 2014.

Serotonin Syndrome

- o Patient Presentation



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 an antidepressant?

Antipsychotics approved in Depression

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

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



Esketamine (Spravato)

- Most common adverse effects:

Dissociation

Vertigo

**Blood Pressure
Increased**

Dizziness

Hypoesthesia

Vomiting

Nausea

Anxiety

Feeling Drunk

Sedation

Lethargy

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



ANTIPSYCHOTICS

Four Dopamine Pathways

Mesocortical

Cognition, social function

Mesolimbic

Positive Symptoms
EX: Hallucinations,
Delusions

Nigrostriatal

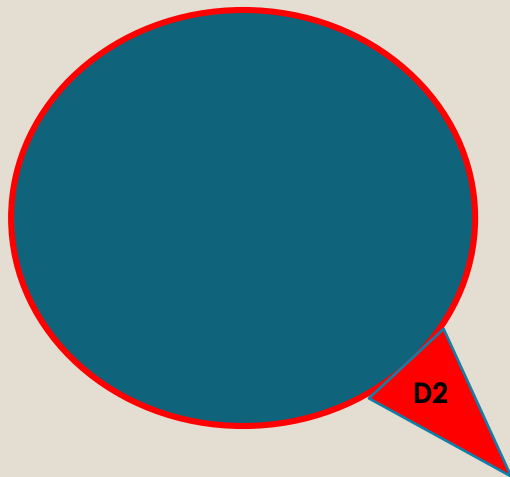
Movement

Tuberoinfundibular

Prolactin

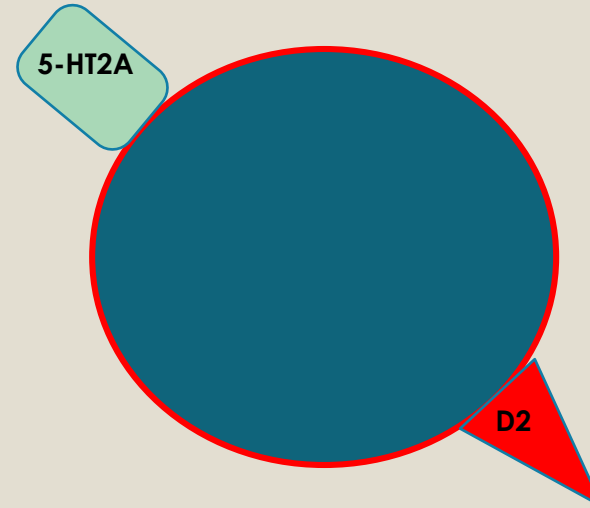
Antipsychotics

First Generation “Typical” Antipsychotic



**D2 receptor
antagonists**

Second Generation “Atypical” Antipsychotic



**Serotonin-Dopamine
Antagonist**

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)

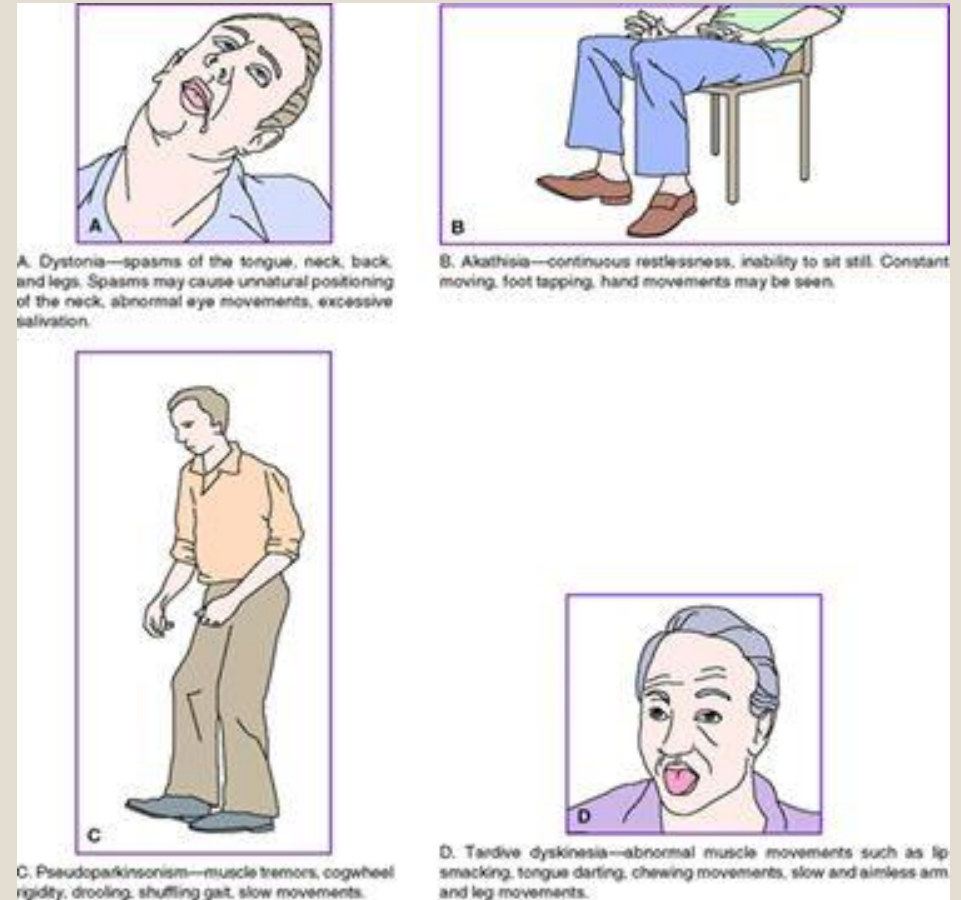
- Nausea
- Vomiting
- Diarrhea
- Diaphoresis
- Cold sweats
- Muscle aches and pains
- Insomnia
- Anxiety
- confusion

First Generation Antipsychotics (FGAs)

Generic	Brand
Chlorpromazine	Thorazine®
Thioridazine	Mellaril®
Mesoridazine	Serentil®
Molindone	Moban®
Loxapine	Loxitane®
Perphenazine	Trilafon®
Thiothixene	Navane®
Trifluoperazine	Stelazine®
Haloperidol	Haldol®
Fluphenazine	Prolixin®

Extrapyramidal Adverse Effects

- Acute dystonic reactions
- Pseudoparkinsonism
- Akathisia
- 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



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 flue, 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

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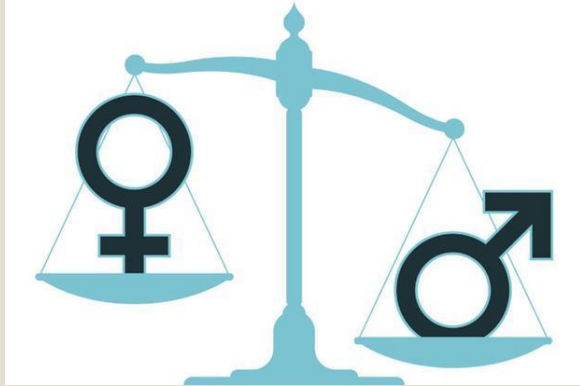
SLEEP MEDICATION

Insomnia Signs and Symptoms

Subjective	
Sleep Complaints	<ul style="list-style-type: none">• Difficulty falling asleep• Maintaining sleep• Waking multiple times during the night• Waking too early
Daytime Complaints	<ul style="list-style-type: none">• Non-restorative sleep• Excessive daytime sleepiness (EDS) or fatigue• Malaise• Difficulty concentrating• Memory impairment



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

Stimulus Control Procedures

1. Establish regular times to wake up and to go to sleep
2. Sleep only as much as necessary to feel rested
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.
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
5. Avoid blue spectrum light from television, smart phones, tablets, and other mobile devices.
6. Avoid daytime naps
7. Schedule worry time during the day. Do not take your troubles to bed

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



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



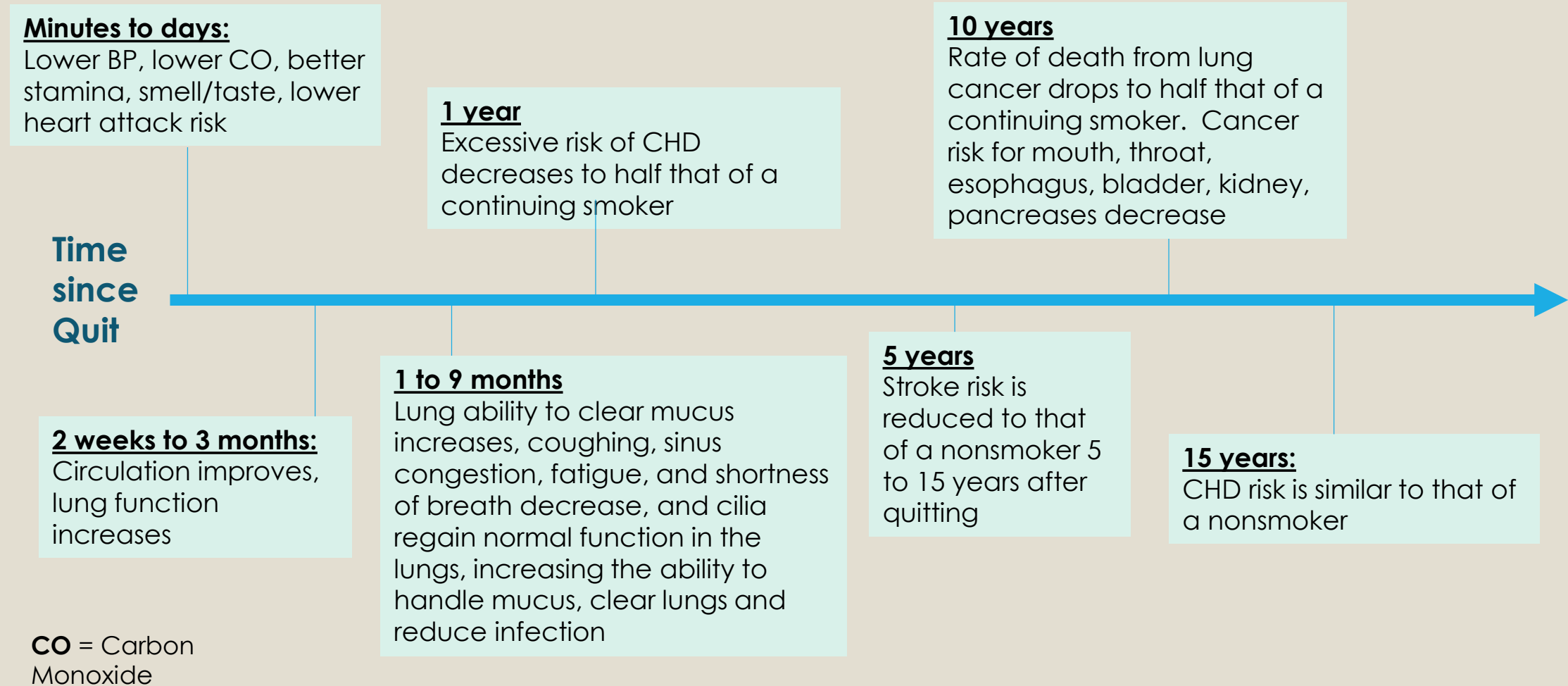
How do these chemicals get in there?

Health Consequences of Cigarette Smoke

Four big categories of disease with tobacco smoking

Cardiovascular	Pulmonary Damage	Vascular Damage	Cancer
<ul style="list-style-type: none">Abdominal aortic aneurysmCoronary heart diseaseCerebrovascular diseasePeripheral arterial disease 	<ul style="list-style-type: none">Acute respiratory illnessUpper respiratory tractLower respiratory tractChronic respiratory illnessChronic obstructive pulmonary diseaseRespiratory symptomsPoor asthma controlReduced lung function	<ul style="list-style-type: none">Cerebrovascular disease StrokePeripheral vascular diseaseOther organs involved  	<ul style="list-style-type: none">AMLBladderCervicalEsophagealGastricKidneyLaryngealLungOral cavity and pharyngealPancreatic 

Health Benefits of Smoking Cessation



Combating Smoking Triggers



Strategies to Combat Triggers

Anti-Craving for Nicotine

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

Questions?

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