# PSYCHIATRY
# REVIEW FOR NURSES


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## Course Objectives

At the end of this course, you will be able to:

- Describe the role of neurotransmitters in the brain and how they relate to mental health
- Conceptualize the difference between anxiety, depression, bipolar disorder, borderline personality disorder and schizophrenia
- Identify medications used to treat psychiatric disorders
- Manage acute psychiatric symptoms and medication reactions

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# AGENDA

- Introduction
- Phases of Illness
- The Brain & Neurotransmitters
- Pharmacokinetics & Pharmacodynamics
- Anxiety & Pharmacology
- Borderline Personality Disorder & Treatment
- Depressive Disorders, Mood Disorders & Pharmacology
- Catatonia
- Psychosis, Schizophrenia & Pharmacology
- Untoward or Adverse Effects, Side effects, and Treatment of Acute Agitation

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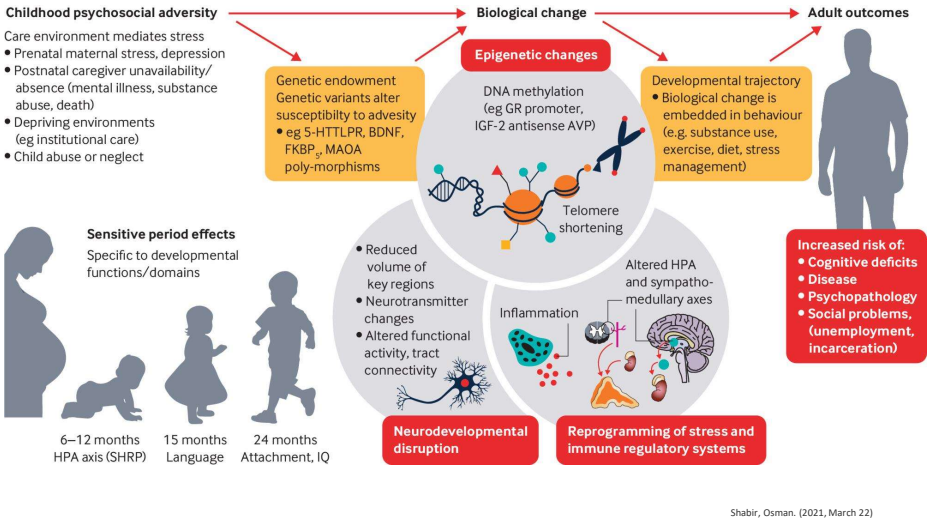
# Introduction

Our goal is to educate patients about their mental health diagnosis and what they can do to be a more active and knowledgeable participant in their own care. We have learned mental illness is complicated. This is a brief snapshot of the interconnectedness of the disease, before we dive into some of the specifics of mental illness and its treatment. Many mental health disorders have multifactorial causes – some genetic and some environmental.




Shabir, Osman. (2021, March 22)

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# Phases of illness continuum

## Acute Phase

GOAL: Prevent harm, manage aggressive behaviors, reduce positive symptoms, return patient to baseline functioning, work with SW for community resources, work on treatment goals

Medications may be started, or current meds adjusted

RN Interventions: Implement continuous monitoring of responses, provide ongoing education about medication's expected benefits (or response) and expected side effects to the patient, as well as the family

## Stabilization Phase

GOAL: Minimize stress and enhance adaptation, continued reduction in symptoms and recovery of functioning

Medication may need to be adjusted and optimized

RN Interventions: Continue to monitor response and side effects, provide information to patient and family, help patient learn self-management skills

## Maintenance Phase

GOAL: Ensure that symptom remission or control is sustained. Patient is asked to report increases in symptoms or relapses, and any adverse effects from medications

Medication adherence

RN interventions: Monitor weight, BMI, blood glucose, lipids, and other factors depending on individual patient

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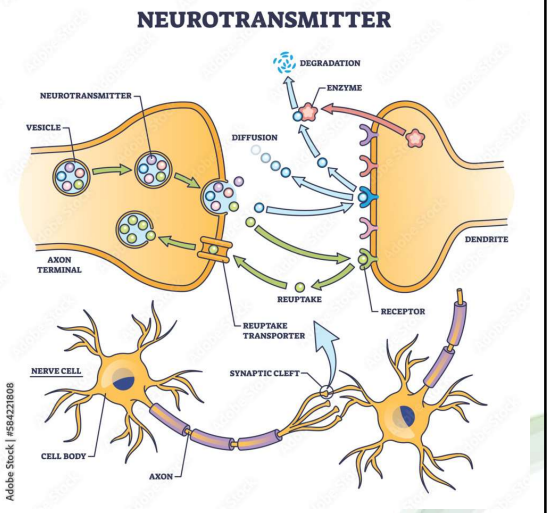
# Neurons & Neurotransmitters in the Brain

- The brain is composed of approximately 100 billion neurons (nerve cells that conduct electrical impulses)
- Most communication among structures of the brain and among the brain and other body parts comes from neurons
- Neurons come in different shapes and sizes, but they all carry out 3 types of physiological actions
  - Responding to stimuli
  - Conducting electrical impulses
  - Releasing chemicals called neurotransmitters once impulse reaches the end of the neuron
- **What are neurotransmitters?** Neurotransmitters are an endogenous chemical messenger that facilitate communication between nerve cells, or neurons. The neurotransmitter crosses the synapse and attaches to receptors on another neuron's surface
- Neurotransmitters play a vital role in modulating and balancing neural signals, which in turn helps maintain brain function
  - For example, they help regulate autonomic responses (breathing, heart rate) & physiological functions (learning, mood, fear, pleasure, happiness)
  - Some have inhibitory effects, while some have excitatory or modulating effects
- Theoretically, alterations of these chemicals are the basis of psychiatric illness
- It is the interaction between neurotransmitter and receptor that is a major target of drugs used to treat psychiatric disease




https://www.simplypsychology.org/neurotransmitter.html

(Guy-Evans, 2023)



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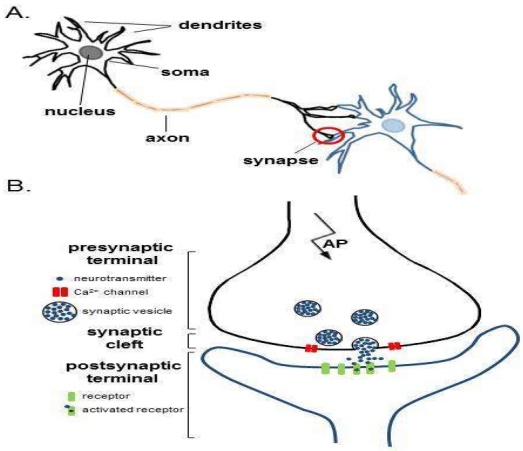
# What is neurotransmission?




Neurons (nerve cells) need to communicate with each other to send messages via neurotransmitters. When the signals travel through a neuron and reach the end of that neuron, they can't travel on their own to the next one. The neuron must trigger the release of neurotransmitters, which then carry the signals across the synapses. The action potential (an electrical impulse) triggers the synaptic vesicles of the pre-synaptic neuron to release neurotransmitters. These neurotransmitters diffuse across the synaptic cleft and bind to specialized 'receptor' sites on the post-synaptic neuron. This process is known as **neurotransmission.** The next target cell could be a nerve cell, muscle cell, or gland.

Anatomy of Neurons. A. Two connected neurons. Neurons have a soma that contains a nucleus, an axon, and a dendritic tree. A single synapse (red circle) is formed at the point where an axon's neuron (black) connects to another neuron's dendrite, soma, or axon (blue). B. A magnified view of a single synapse. On the arrival of an action potential at the presynaptic terminal, calcium triggers the release of neurotransmitters from the synaptic vesicles into the synaptic cleft. Neurotransmitters diffuse across the synaptic cleft to activate postsynaptic receptors. Contributed Image by Karin Aubrey

Sheffler ZM, Reddy V, Pillarisetty LS. (2023).

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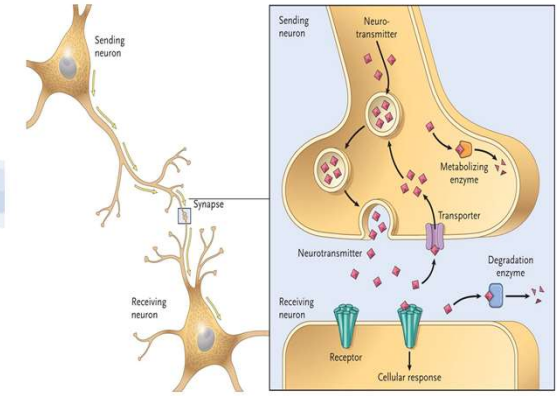


https://www.physio-pedia.com/Neurotransmitters

## Why does this matter?

Psychotherapeutic drugs produce a wide range of effects on receptors. Each neurotransmitter has several receptor types, and each given receptor type might have various subtypes with different actions. For example, one drug can have multiple actions in different areas of the brain and spinal cord, depending on the distribution of the neurotransmitter pathways and receptors . Neurotransmission can also be affected by illicit drugs such as marijuana, cocaine, and heroin. For example, heroin binds to the opioid receptors and triggers the release of very high levels of dopamine. Over time tolerance will develop, and the brain won't function the way it did before starting the drug. Each neurotransmitter has a specific mechanism for enzymatic destruction, or in other words, inactivation after it has completed its chemical action. Here are some key terms to re-familiarize yourself with.

**Receptors**: cellular components to which a drug binds and initiates its effect

- Agonist = mimic effects of neurotransmitters naturally found in the human brain
- Antagonist = block the neurotransmitters, thereby obstructing the action
- Inverse agonist = exert the opposite effect of agonists
- Partial agonist = bind to agonist recognition site but trigger a lower response than full agonist

**Ion channels:** exist for many ions ( sodium, potassium, chloride, calcium): Unlike ions, neurotransmitters don't pass from neuron to another. Instead, the neurotransmitter interacts with the receptor, causing it to change configuration. The effects of this "gating" action depend upon the neurotransmitters action (excitatory or inhibitory)

**Enzymes**: proteins important for drug metabolism (i.e. monoamine oxidase is an enzyme – after the neurotransmitter is released into the synaptic cleft and reacts with the receptor, it is pumped back into the terminal where MAO can destroy it)

**Transport pumps**: involved in the reuptake of neurotransmitters for reabsorption. The synapse must be clear and the end of the signal.

Boto, T., & Tomchik, S. M. (2019). Hutchinson, K. (2015).

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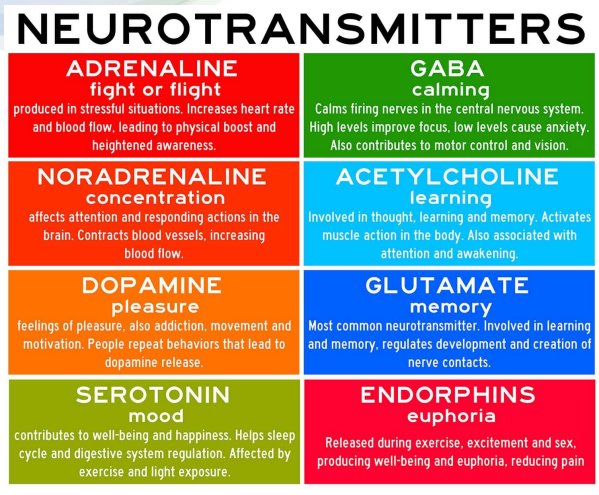
Scientists know of at least 60 distinct neurotransmitters in the brain and suspect there may be more. Neurotransmitters are multi-faceted and complex. They can work with one another or against one another. The table below lists a few different neurotransmitters that are most familiar in psychiatric practice. The next slide will show in more detail the neurotransmitter, the receptor sites associated with the neurotransmitter, the effects on the body, and the association with mental health.

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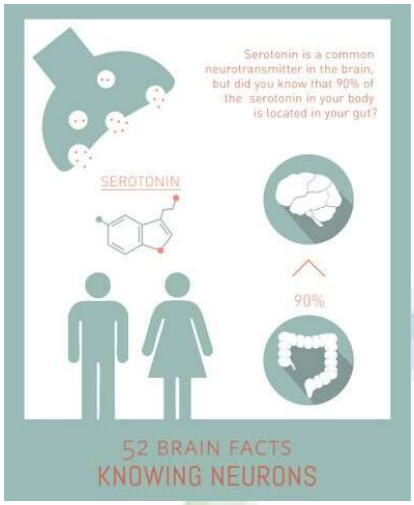


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# Neurotransmitters and Receptors

| Neurotransmitters | Receptors | Effects/Comments | Association with Mental health |
|---|---|---|---|
| **Monoamines** | | | |
| **Dopamine (DA)** | D1, D2, D3, D4, D5 | -Involved in fine muscle movement<br>-Involved in integration of emotions and thoughts<br>-Involved in decision making<br>-Stimulates hypothalamus to release hormones (sex, thyroid, adrenal) | Decreased levels seen in:<br>Parkinson's disease<br>Depression<br><br>Increased levels seen in :<br>Schizophrenia<br>Mania |
| **Norepinephrine (NE)(noradrenaline)** | α1, α2, β1, β2 | -Level in brain affects mood<br>-Attention & arousal<br>-Stimulates sympathetic branch of autonomic nervous system for "fight or flight" in response to stress | Decreased levels seen in:<br>Depression<br><br>Increased levels seen in:<br>Mania<br>Anxiety states<br>Schizophrenia |
| **Serotonin (5-HT)** | 5-HT1, 5-HT2, 5-HT3, 5-HT4, others | -Plays a role in sleep regulation, hunger, mood states, and pain perception<br>-Hormonal activity<br>-Plays a role in aggression & sexual behavior | Decreased levels seen in:<br>Depression |
| **Histamine** | H1, H2 | -Involved in alertness<br>-Involved in inflammatory response<br>-Stimulates gastric secretion | Decreased levels seen in:<br>Sedation<br>Weight gain<br>Increased levels:<br>Anxiety |

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# Neurotransmitters and Receptors continued

| Neurotransmitters | Receptors | Effects/Comments | Association with Mental health |
|---|---|---|---|
| **Amino Acids** | | | |
| **γ-Aminobutyric acid** (GABA) | $GABA_A$<br>$GABA_B$ | -Plays a role in **inhibition "off";** reduces aggression, excitation, and anxiety<br><br>-May play a role in pain perception<br><br>-Has anti-convulsant and muscle-relaxing properties<br><br>-May impair cognition and psychomotor functioning | Decreased levels seen in:<br>Anxiety disorders<br>Schizophrenia<br>Mania<br>Huntington's Disease<br><br>Increased levels:<br>Reduction of anxiety |
| **Glutamate** | NMDA, AMPA | -Most abundant amino acid in your brain<br><br>-Is **excitatory "on"** – primary role is to excite other neurons so that they'll carry out their functions<br><br>-AMPA plays a role in learning and memory | Decreased levels (NMDA):<br>Psychosis<br>Increased levels (NMDA):<br>Prolonged increased state can be neurotoxic<br>Neurodegeneration in Alzheimer's disease<br>ALS, HIV, Stroke/TBI, Chronic pain |

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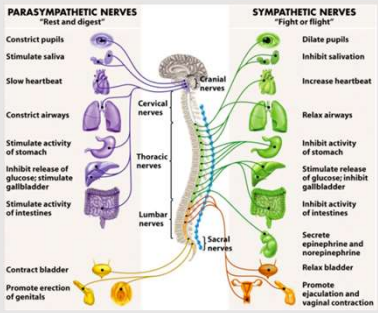
# Neurotransmitters and Receptors continued

| Neurotransmitters | Receptors | Effects/Comments | Association with Mental health |
|---|---|---|---|
| **Cholinergics** | | | |
| **Acetylcholine (ACh)** | Nicotinic<br>Muscarinic (M1, M2, M3) | -Plays a role in learning, memory<br><br>-Regulates mood: mania, sexual aggression<br><br>-Affects sexual and aggressive behavior<br><br>-Stimulates parasympathetic nervous system, "rest & digest" | Decreased levels:<br>Alzheimer's disease<br>Huntington's disease<br>Parkinson's disease<br><br>Increased levels:<br>Depression |



https://www.diffen.com/difference/Parasympathetic_nervous_system_vs_Sympathetic_nervous_system

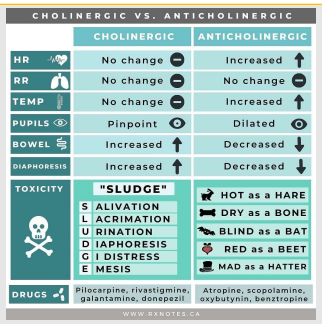
What is Anticholinergic Burden?

Remember that the autonomic nervous system has two sides: the sympathetic & parasympathetic system.

When we REST our body relies on this "rest and digest" system which includes the neurotransmitter Acetylcholine. Memory tip SLUDGE (chart to the right shows the effects of drugs on body systems).***It is also involved in cognitive function.**

Anticholinergic medications are involved with the "fight or flight", sympathetic nervous system. Anticholinergic medications block the activity of acetylcholine. They can cause dry eyes (blurry vision), dry mouth, urinary retention, constipation, and mental confusion. When these symptoms persist, they have the potential to lead to serious health problems. The combination of medications with anticholinergic properties can cause significant problems, especially in the elderly.

(Aiken et al., 2022)

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# Psychiatric medications aim to target specific neurotransmitter receptors with the help of medications.

On the next few slides we will briefly review pharmacodynamics and pharmacokinetics before diving into specific diagnoses and medications.

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## Pharmacokinetics
### How the body moves a drug throughout the body (Absorption, Distribution, Metabolism, Excretion)

**ABSORPTION:**

- Oral: Convenient but can cause GI upset. Absorbed thru small bowel, passing into the portal (liver or hepatic) circulation. Most psychotropic drugs are partially metabolized by the cytochrome P450 (CYP450) enzymes as the drugs pass through the liver, "first-pass metabolism"
- Sublingual, IM, or IV: bypasses liver absorption (first pass) and goes directly to systemic circulation

**DISTRIBUTION:**

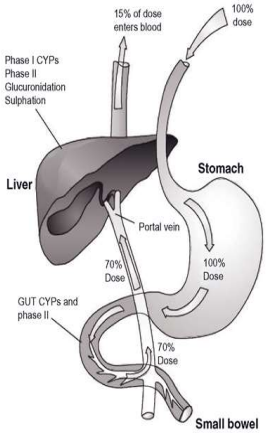
- After drugs go thru the liver they enter the systemic circulation, where they are distributed to organs in direct proportion to their fat and protein content
- Most psychotropic drugs are highly lipophilic ("love fat") and highly protein bound (attach to proteins)
- Lithium is mostly distributed in body water (plasma, interstitial fluid and intracellular fluid)
- The unbound (free) proteins then readily pass the blood brain barrier

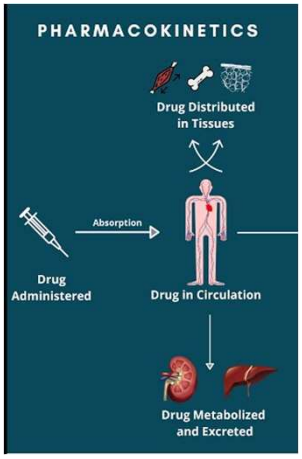
**METABOLISM**:

- The breaking down of a drug so it can be eliminated from the body. Most psychotropic drugs undergo extensive biotransformation in the liver in two phases (Phase I and Phase II).
- Older adults typically lose or have decreased Phase 1 metabolism, while children and adolescents typically have the highest Phase 1 metabolism.
- The purpose of CYP metabolism is to make fat=soluble molecules more water-soluble so that they can be eliminated via kidneys

**EXCRETION**:

- Elimination refers to the removal of a drug from the body. The kidney is the most important organ for drug elimination




Zhao, M., Ma, J., Li, M., Zhang, Y., Jiang, B., Zhao, X., Huai, C., Shen, L., Zhang, N., He, L., & Qin, S. (2021).

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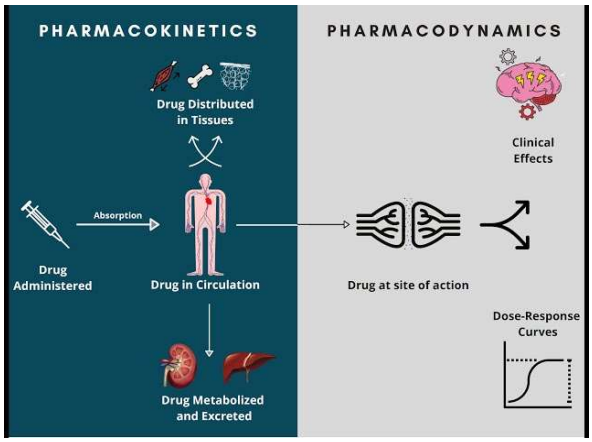
# Factors that can affect pharmacokinetics

- Hepatic CYP450 interactions can induce or inhibit the metabolism to certain drugs, changing the desired concentration levels (example: nicotine is an inducer of CYP450 enzymes, so if a heavy nicotine user quits smoking, they may require a lower dose of the drug)
- Hepatic disease: drugs that have high first-pass effects can result in elevated or toxic plasma drug levels
- Renal disease or drugs that reduce renal clearance (example: NSAIDS with Lithium may increase serum concentration of lithium)
- Most psychotropic drugs are lipid-soluble, so when lean body mass is lost and body fat concentration increases, the lipid soluble psychotropic drugs distribute widely in fat tissue. This can lead to unexpectedly prolonging drug actions
- Malnutrition, wasting, and aging affect the amount of free-circulating drug that is bound to proteins in the bloodstream
- Cardiovascular disease and reduced cardiac output can affect both renal and hepatic drug clearance
- People with gastric bypass should not have extended-release medications because it can cause limited absorption
- In general, older adults are more susceptible to adverse drug effects and interactions (particularly cardiac)

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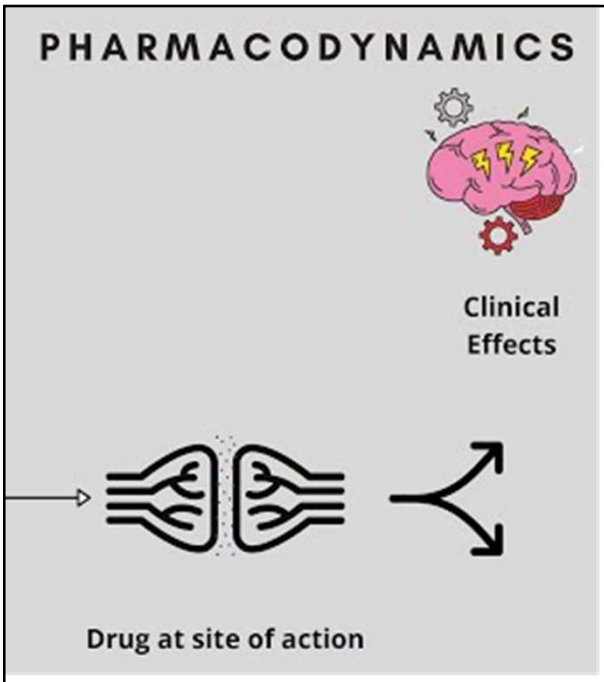


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## Pharmacodynamics refers to what the "drug" does to the body

In a perfect world, a psychiatric drug would relieve the mental disturbance of the patient without causing additional cerebral (mental) or somatic (physical) effects

However, because all activities of the brain involve actions of neurons, neurotransmitters, and receptors, these are the targets of pharmacological intervention.

As stated earlier, most psychotropic drugs act by either increasing or decreasing the activity of certain neurotransmitter-receptor systems.

Moving forward we will focus on specific mental illness diagnoses, possible causes, nursing interventions, associated pharmacology, and side effects and/or adverse effects

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## Anxiety & Related Disorders

- Characterized by fear and worry that leads to dysfunction by interfering with the ability to make a decision
- Persistent, excessive fear or worry in situations that are not life threatening
- **<u>First line treatment is SSRIs or SNRIs</u>**
- More prevalent in females than males except for OCD and social anxiety disorder

| | | |
|---|---|---|
| Panic disorder | Generalized Anxiety Disorder | Phobias |
| Obsessive Compulsive Disorder | Body Dysmorphic Disorder | Hoarding |
| Trichotillomania | Excoriation | Separation Anxiety Disorder |
| Posttraumatic Stress Disorder | Acute Stress Disorder | Adjustment Disorder |

(Hutchinson, 2015), (NAMI, 2023)

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## Anxiety Causes

- Alterations in amygdala function
  - Especially in OCD
- Low GABA levels
  - For example, ETOH and benzodiazepines lower anxiety by GABA receptor modulation. Anxiety increases when those substances are removed.
- Hypothalmic-Pituitary-Adrenal (HPA) axis dysfunction
  - Chronic response to stress with increased circulating levels of cortisol
- Unconscious childhood trauma
- Learned response through modeling of parents or peers
- Genetic
- Part of a syndrome with medical or substance related conditions
  - Hyperthyroidism, ADHD, ETOH/Benzodiazepine withdrawal

(Hutchinson, 2018), (Varcarolis, 2018)

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## **Goal**: Decrease the cardiovascular manifestations triggered by chronic or acute anxiety. Most medications act directly or indirectly on the GABA system.

| SSRIs | Benzodiazepines | Tricyclics | Miscellaneous | Nonpharmacological management |
|---|---|---|---|---|
| • First line treatment for medications<br>• Steady state requires 4-6 weeks<br>• Low risk of dependency, however, depending on half-life dose, must be tapered gradually | • High potential for abuse, addiction, diversion, acute withdrawal, can be fatal<br>• Rapid onset of action and can be used "as needed"<br>• Commonly prescribed to reduce 'activating' effects of SSRIs during titration<br>• The shorter the half life the more severe the withdrawal and rebound anxiety | • Many drug-drug interactions<br>• May cause anticholinergic adverse effects<br>• Overdose potential<br>• Monitor EKG, avoid in patients with cardiac disease | • Beta blockers as needed (taper if consistently taken)<br>• Gabapentin: can be taken as needed, wide therapeutic range<br>• Buspirone: must be taken consistently for 8 weeks for anxiolytic effects<br>• Hydroxyzine: may be useful as "PRN" but generally considered second line in anxiety disorders related to side effects and lack of efficacy for usual comorbid disorders | • Preferred treatment for anxiety<br>• CBT<br>• Support groups<br>• Aroma therapy<br>• Exercise<br>• Animal-assisted therapy (emotional support animals) |

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(Carlat & Puzantian, 2020)

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# Hydroxyzine (Atarax, Vistaril)

- **FDA Indication**: Generalized anxiety disorder (GAD); pruritis; pre-anesthetic sedative
- **Off-label uses**: Other anxiety disorders; insomnia; anxiety and agitation related to opioid withdrawal
- **Mechanism of Action**:
- Competes with histamine for H1-receptor sites in the gastrointestinal tract, blood vessels, and respiratory tract (Simons 1994)
- Very low affinity for acetylcholine receptors (means patient will have less anticholinergic effects)
- Has anti-serotoninergic effects which cause it to decrease anxiety (more than other anti-histamines)

(Simons & Simons, 1994), (Guaiana, 2010), (Sawantdesai, 2016)

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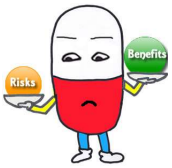
# Nursing Considerations for Hydroxyzine (Atarax, Vistaril)




**Side effects**:
- Sedation, somnolence, daytime grogginess, dry mouth, constipation

***watch for delirium in elderly patients

**Serious but rare side effects**:
- QT prolongation

**Patient teaching:**
- Hydroxyzine easily crosses the blood-brain barrier and can produce an effect quickly, usually in 15-30 minutes
- Beware of anticholinergic effects, especially in patients who take many doses throughout the day
- Good non-addictive option for rapid acting anxiolytic

Interesting fact:
There are two versions of hydroxyzine; Atarax and Vistaril. Popular opinion is that Vistaril may have greater solubility or lipophilicity which makes it better for anxiety and sedation while Atarax is better for itching, but this is a myth

(Simons & Simons, 1994)

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# Benzodiazepines

- Clonazepam (Klonopin)
- Diazepam (Valium)
- Alprazolam (Xanax)
- Lorazepam (Ativan)

**FDA Indication:** Dependent on specific drug and listed below

**Off-label uses:** All the drugs listed have off-label uses for acute mania or psychosis; catatonia

**Mechanism of Action:**

- Benzodiazepines potentiate the effects of gamma-amino-butyric acid (GABA) in the brain by binding to benzodiazepine receptors
- Inhibits neurotransmission in the limbic system and cortex
- Benzodiazepines are effective for all types of anxiety. Ideally should be used short term or as needed, and at the lowest dose. Should be avoided in those with substance abuse disorder or risk
- Benzodiazepines help people feel calm, and quickly (as quick as 30 minutes)

**Medications:**

- Intermediate acting benzos treat more acute anxiety symptoms:
  - Alprazolam (FDA indications: GAD; panic disorder)
  - Lorazepam (FDA indications: GAD; status epilepticus (IV route))
- Long-acting benzos treat more chronic anxiety disorders, seizures and ETOH/benzo withdrawal:
  - Clonazepam (FDA indications: seizure disorders; panic disorder)
  - Diazepam (FDA indications: GAD; alcohol withdrawal; seizures; muscle spasms)

**All of the above have off-label uses for acute mania or psychosis and catatonia**

(Carlat & Puzantian, 2020, pp. 87-94)

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# Nursing Considerations for Benzodiazepines

**Side effects: sedation, confusion, daytime grogginess, ataxia (without coordination) and decreased cognitive function**

**Serious but rare side effects:**

- **Paradoxical reactions, especially in elderly and patients with brain injury (anxiety, agitation, talkativeness, loss of impulse control, irritability)**
- **Anterograde amnesia (can't create new memories)**
- **Increased fall risk**
- **Respiratory depression (Avoid the use of alprazolam (xanax) and clonazepam (klonopin) in patients who have severe pulmonary disorders and/or sleep apnea**

**Patient teaching:**

- **Not recommended for elderly patients due to risk of developing dementia and falls**
- **Cessation of use after 3-4 months of daily use may cause withdrawal symptoms**
- **Antacids may delay absorption**
- **Flumazenil used for overdose of benzodiazepines**

**Benzodiazepine withdrawal: a withdrawal from a normal dosage of benzodiazepine treatment has the potential to result in several symptomatic patterns that typically peak around week 2 and have potential to last up to several months or even years if not properly addressed.**

**Withdrawal symptoms typically characterized by:**

- **Sleep disturbances**
- **Irritability**
- **Increased tension and anxiety (rebound anxiety typically lasts 1-4 days after d/c)**
- **Panic attacks**
- **Hand Tremors**
- **Difficulty concentrating**
- **Nausea & dry retching**
- **Palpitations**
- **Muscle stiffness**
- **Host of perceptual changes**

(Carlat & Puzantian, 2020, pp. 87-94)

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# Buspirone (BuSpar)

**FDA Indication**: Generalized Anxiety Disorder (GAD)

**Off-label uses**: Treatment-resistant depression; anxiety symptoms in depression

**Mechanism of Action**:

- Serotonin 5-HT1A receptor partial agonist
- The underlying mechanism of why it translates into clinical results is unknown, but it has been repeatedly proven to work as well as benzodiazepine treatment in GAD

(Carlat & Puzantian, 2020, p. 91)

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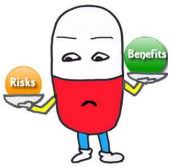
# Nursing Considerations for Buspirone (BuSpar)




**Side effects**:

- Dizziness, nervousness, nausea, jitteriness, headache

**Serious but rare side effects**:

- None to report

**Patient teaching:**

- Unlike benzodiazepines, Buspirone typically does not make patients sleepy or sluggish
- May be less effective or ineffective in patients who have previously responded to benzodiazepines
- Avoid use with MAOI's; caution with serotonergic agents due to additive effects and risk for serotonin syndrome
- Has only shown efficacy in GAD, not PTSD, OCD, or panic disorder

(Carlat & Puzantian, 2020, p. 91)

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# Off label medication used to treat anxiety & related disorders

**When you are anxious your brain makes more of the chemical's noradrenaline and adrenaline. Some of these drugs help with the physical symptoms of anxiety but DO NOT TREAT underlying anxiety.**

**Propranolol (Inderal)**

- FDA: Hypertension; angina; post-MI cardioprotection; atrial fibrillation; migraine prophylaxis; essential tremor
- Off label uses: Performance anxiety, tremor due to medication side effects (especially Lithium); akathisia (inability to sit still)
- Mechanism of Action: Non-selective beta-1 and beta-2 adrenergic receptor antagonist
- Side effects: Dizziness, fatigue, bradycardia, and hypotension
- Propranolol reduces some of the somatic symptoms of anxiety (tremor, sweating, flushing, tachycardia) due to beta blockage

**Gabapentin (Gralise, Horizant, Neurontin)**

- FDA: Partial seizures; post-herpetic neuralgia; restless leg syndrome
- Off label uses: Anxiety disorders; withdrawal from alcohol or benzodiazepines; alcohol dependence
- Mechanism of Action: Blocks voltage-dependent calcium channels and modulates excitatory neurotransmitter release
- Side Effects: Dizziness, somnolence, ataxia, weight gain
- Gabapentin is structurally related to GABA but it does not bind with GABA-A or GABA-B receptors, and it does not appear to influence synthesis or uptake of GABA

(Carlat & Puzantian, 2020, pp. 96-128)

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# Off label medication used to treat anxiety in combination with PTSD, nightmares, and/or severe insomnia

**Clonidine (Catapres, Kapvay)**

- FDA: Hypertension; ADHD (children ages 6-17)
- Off label uses: Conduct disorder; Tourette's and motor tics; pervasive developmental disorders; migraine prophylaxis; opioid withdrawal. We see it used with PTSD, nightmares, and severe insomnia.
- Mechanism of Action: Centrally acting, selective alpha-2 adrenergic agonist
- Side effects: Dry mouth, somnolence, dizziness, constipation, fatigue, headache
- Risk of nervousness, anxiety, and possibly rebound hypertension 2-4 days after abrupt discontinuation. Taper dose in no more that 0.1mg/day decrements, every 3-7 days.

**Prazosin (Minipress)**

- FDA: Hypertension
- Off label uses: PTSD
- Mechanism of Action: Alpha-1 adrenergic receptor antagonist
- Side Effects: Somnolence, dizziness, headache, weakness
- Serious but rare: Orthostasis and syncope; prolonged erections and priapism
- Caution with other antihypertensive agents, diuretics and PDE5 inhibitors (eg, Viagra) that may have additive hypotensive effects

(Carlat & Puzantian, 2020, pp. 17-95)

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## N-Acetylcysteine (NAC) for Obsessive Compulsive Disorder

**FDA Indication**: None

**Off-label uses**: OCD; trichotillomania; nail biting; skin picking

**Mechanism of Action**:

- NAC is derived from the amino acid cysteine, a precursor of a key brain antioxidant, glutathione
- Works as a glutamate modulator, which may have effects on inflammatory mediators, neurotransmission, neuroplasticity, oxidative stress, and mitochondrial dysfunction

**Side effects**:

- Usually well tolerated, but can cause n/v/d, cramping, and flatulence

**Serious but rare side effects**:

- May exacerbate asthma

**Patient teaching:**

- NAC is most recognized for use in Acetaminophen overdose
- Most patients develop tolerance to GI symptoms
- No long-term data

(Carlat & Puzantian, 2020, p. 139)

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## Borderline Personality Disorder Memory Tip "I DESPAIR"

**I**dentity: Inconsistent sense of self and purpose

**D**ysphoria: Pattern of experiencing primarily negative emotions

**E**motional Instability: Sudden and drastic swings off emotion (affective lability)

**S**uicide/Self Harm: Non suicidal self-injury (cutting), chronically suicidal

**P**sychosis Like and Dissociative Sx: AH, paranoia, delusions, dissociative experiences (transient, occurs in times of severe stress and are vague)

**A**nger: Frequent feelings of anger, antagonism and hostility

**I**mpulsivity: Leads to substance abuse, unsafe sex, job loss, reckless driving, running away, lashing out at others, self-harm

**R**elationships: short lived, unstable, frantic efforts to avoid abandonment, sensitive to interpersonal rejection, intolerant of being alone

(Heldt, 2018)

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# Borderline Personality Disorder

**Epidemiology**

- 10% of the population shows symptoms that cause dysfunction
- Equal rates in men and women
- Symptoms most often begin in adolescence

**Prognosis**

- 50% of people who initially meet criteria for the diagnosis no longer do by 2 years
- 85% do not meet criteria after 10 years (even without treatment)
- Complete remission is rare (some level of persistent dysfunction remains)
- Lower than average rates of employment
- Decreased life satisfaction
- Effective treatment leads to better life outcomes and decrease in symptoms

(Heldt, 2018)

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# Borderline Personality Disorder Treatment

- Treatable condition, psychotherapy most effective modality
- Dialectical Behavior Therapy (DBT)
  - Most studied
  - Includes skills such as mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness
  - Can be costly
  - Time intensive
  - Long waiting lists
  - Sometimes difficult to access due to geographic distance
- Good Psychiatric Management model and Mentalization based treatment have been shown to be as effective as DBT

(Heldt, 2018)

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# Borderline Personality Disorder Treatment Plan

Diagnosis: Provides a framework for the multiple concerns and a treatment plan for how to move forward to improve symptoms

Educate: Educate on causes and good prognosis

Life outside of treatment:

- Encourage patient to work or volunteer and develop healthy interpersonal relationships
- Avoid medications: A higher number of meds is associated with lower chance of clinical improvements. If meds are used, they should treat specific symptoms such as insomnia or impulsivity
- Prioritize treatment of Borderline Personality Disorder over depression, anxiety, PTSD
- Safety Plan
- Expect change: Provide education of disorder and treatment guidance in exchange for their commitment to work towards change

(Heldt, 2018)

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# Evidence Based Practice Tips for Borderline Personality Disorder

- Inpatient hospitalization should be avoided, if possible, due to regression that occurs
- Make clear treatment plan early in hospitalization that patient and treatment team and patient agree on
- Be prepared to discharge if patient does not follow treatment plan
- Nursing staff should be aware of their own counter transference reactions, becoming overly involved with the patient, and having very clear personal boundaries
- Observe patient's behavior frequently. Avoid appearing watchful or suspicious
- Encourage patient to seek out a staff member if they are unable to keep themselves safe
- If a patient does self-harm, care for them in a matter-of-fact manner. Do not give positive reinforcement
- Encourage patient to talk about feelings they were having before behavior occurred, with the goal of problem solving to prevent self-harm in the future
- Give positive reinforcement when attempts to appropriately express anger are made
- Try to redirect violent behavior r/t anxiety to appropriate physical outlets
- Use show of force when needed to indicate to patient that there is control over the situation
- Use medications to calm as needed (Zyprexa, Vistaril, Benzodiazapines, Haldol)
- When patient is a time of extreme stress, they should not be left alone d/t extreme fear of abandonment (may need 1:1 if actively self-harming)

(Fagin, 2004), (Hunt, 2018), (Bodner et al., 2015), (Heldt, 2018)

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# Evidence Based Practice Tips for Borderline Personality Disorder

- Caring for patients with borderline personality disorder can be very challenging. Nursing staff should have a plan of care that is consistently followed. When consistency in the treatment team is not demonstrated, staff may become split into one group that believes that the patient is manipulative and needs firm limits and another group that becomes overprotective and tolerant beyond reasonable limits (Fagin, 2004).
- Counter transference occurs when a nurse transfers their personal thoughts and feelings onto a patient. Examples of this are becoming critical, taking on an "advising" tone, over supporting the patient, agreeing with the patient too often, changing the topic or distancing themselves from the patient (Hunt, 2003).
- An example of this behavior is when a nurse repeatedly fails to confront a patient who is not following the treatment agreement. The nurse may be doing this because they believe they must have a positive relationship with all their patients. When a nurse recognizes counter transference is taking place, they must confront their own behavior and realizing how this belief is causing them to not address important issues in a patient with borderline personality disorder. Counter transference may lead to disruption of the team and the patient does not receive the type of nursing care they need to result in a decrease in symptoms.
- Studies have shown that it is common for nurses to have negative attitudes and low empathy towards patients who have borderline personality disorder. One study shows a direct correlation between the amount of patients with borderline personality disorder a nurse has cared for and an increase of negative attitude. A theory is that it stems from lack of knowledge/education in caring for this population and having to interact intensively with these patients on a very frequent basis throughout their shift. This study also references the frequency of counter transference among nurses and patients with borderline personality disorder. (Bodner et al., 2015).

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# DEPRESSIVE & MOOD DISORDERS

Depression is the most common mental illness and among the most treatable. The literature shows that major depression will affect 1 in 6 men and 1 in 4 women in their lifetime. Depression is characterized by a group of symptoms with a theme of melancholy. The patient is unable to meet Maslow's hierarchy of needs: physiological, psychosocial, safety, and belonging. (Townsend, Morgan, 2018)

There are many different theories regarding the etiology of depression:

**Monoamine Dysregulation Theory**:

- Monoamines are the neurotransmitters (serotonin (5HT), norepinephrine (NE), and dopamine(DA))
- This theory hypothesizes that depression is caused by a deficit or reduction in one or more of the monoamines

**Dysregulation of the HPA Axis Theory:**

- This theory focuses on depression and stress response systems, particularly the HPA Axis (Hypothalmic-pituitary-adrenal). The HPA Axis appears to be a main site where genetic, hormonal, and environmental influences converge in mood disorder etiology. The body's adrenal glands release the hormone cortisol which activates the SNS response. If stressors remain high for long periods of time with concomitantly high cortisol levels, then major damage can occur biochemically, physiologically, anatomically, and

**Vitamin D Deficiency Theory:**

- Vitamin D exerts neurological benefits on cognition, memory and mood. Vitamin D may be deficient among people who develop mood disorders (Farrington & Moller, 2013)

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# MAJOR DEPRESSIVE EPISODE/MAJOR DEPRESSIVE DISORDER & SUBTYPES

- Persistent depressive disorder, formerly dysthymia
- Adjustment Disorder (life changes, situational depression)
- Seasonal Affective Disorder (fall and winter)
- Postpartum Depression (within the first 10 days postpartum that lasts at least 2 weeks)

- Persistent sadness for greater than two weeks
- Lack of pleasure in and interest in activities a person previously enjoyed
- Affects many areas of life:
  - Affective: hopeless, worthless, anhedonia
  - Behavioral: psychomotor retardation or agitation, verbal communication and hygiene decreased, social isolation
  - Cognitive: self-blame, SI, recurrent thoughts of death
  - Physical: body slowdown, sleep disturbances, weight loss or gain, insomnia, fatigue

**DSM Criteria:**

Major depressive disorder (unipolar depression)
- Requires at least two weeks of depression/loss of interest and majority of the additional depressive symptoms, with one or more major depressive episodes

Persistent depressive disorder (dysthymia)
- Ongoing low-grade depression of at least 2 years' duration for more days than not and does not meet the criteria for major depression
- A major depressive episode can occur as a comorbidity

(Halter, 2018), (Hutchinson, 2015)

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# SELECTIVE SEROTONIN REUPTAKE INHIBITORS ( SSRI'S)

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Paroxetine (Paxil)
- Sertraline (Zoloft)
- Fluvoxamine (Luvox)

**FDA Indications (all except Fluvoxamine)**: Major depression

**FDA indications for OCD ONLY (Age 8+):** Fluvoxamine (Luvox)

**Off-label uses**: Depends on specific drug

**Mechanism of Action**:

Increases levels of serotonin in the brain. The drug blocks the reabsorption of serotonin into neurons, which makes more serotonin available to improve transmission of messages between neurons

(Carlat & Puzantian, 2020)

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# Nursing Considerations & Teaching for SSRI's

**Side effects**:

Severity depends on different medications. Nausea/ diarrhea, insomnia/agitation, sedation, weight gain, QT prolongation (Citalopram causes biggest QT prolongation)

**All drugs**: sexual dysfunction.

Paroxetine (Paxil): anticholinergic s/e and orthostatic hypotension in addition

**Serious but rare side effects**:

Hyponatremia (mainly elderly, thought to be secondary to development of SIADH), GI bleeding (especially when combined with NSAIDs such as Ibuprofen).

**Patient teaching:**

- A therapeutic response for anxiety can occur in the first two weeks
- Full therapeutic benefit of anti-depressant properties doesn't occur until 8 weeks
- A decrease in OCD symptoms takes at least 12-16 weeks
- Sexual side effects are a common reason for discontinuation. Sometimes adding Wellbutrin can help
- Risk for Serotonin syndrome (next slide)

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(Carlat & Puzantian, 2020)

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# Serotonin Syndrome

**Symptoms:**

**H: Hyperthermia**

**A: Autonomic instability**

**R: Rigidity**

**M: Myoclonus**

**Treatment:**

- Stop the medication
- Cyproheptadine, Methysergide, Propanolol
- Benzodiapines
- Admission to ICU as needed
- Oxygen
- IV fluids
- Ventilator and paralytics

(Hutchinson, 2015); (Simon, Keenaghan, 2023)

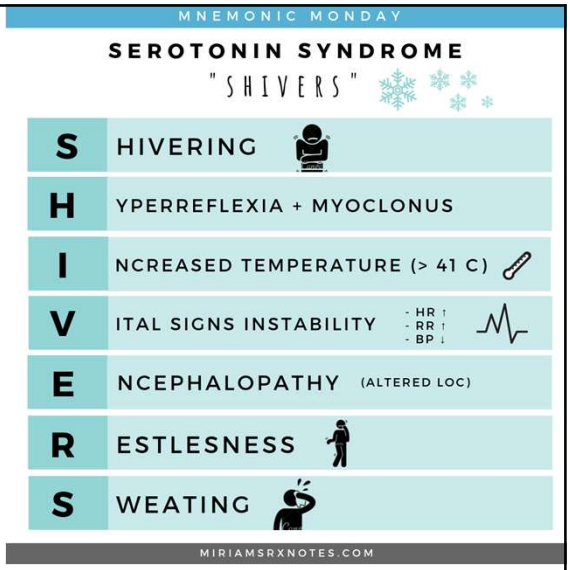


Image retrieved from https://rxnotes.ca/signs-symptoms/serotonin-syndrome-2/

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## Dual Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

Venlafaxine (Effexor) | Desvenlafaxine (Pristiq) | Duloxetine (Cymbalta)

**FDA Indication**:

- Desvenlafaxine (Pristiq): MDD
- Venlafaxine (Effexor): MDD, GAD, social anxiety disorder, panic disorder
- Duloxetine (Cymbalta): MDD, GAD, diabetic peripheral neuropathic pain, fibromyalgia, chronic musculoskeletal pain (OA and chronic back pain)

**Mechanism of Action**:

SNRIs increase the availability of both serotonin and norepinephrine by inhibiting the reuptake of both

(Carlat & Puzantian, 2020)

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## Nursing Considerations and Teaching for Dual Serotonin and Norepinephrine Reuptake Inhibitors SNRI's


**Side effects**:

Most Common Side Effects: Nausea/diarrhea, insomnia/agitation, sexual dysfunction (less than SSRIs), weight gain; increased blood pressure and pulse, and sweating

**Serious but rare side effects**:

- Venlafaxine & Desvenlafaxine: Sustained dose-related hypertension
- Duloxetine (Cymbalta): Rare cases of hepatic failure, can worsen liver problems, may cause orthostatic hypotension or syncope especially in first week & after dose increases. Urinary retention.

**Patient teaching:**

- Frequently used in patients with pain and fatigue
- Avoid if history of heavy alcohol use or chronic hepatic disease
- Monitor blood pressure periodically for Venlafaxine and Desvenlafaxine.
- SNRIs can increase bleeding, especially when combined with Ibuprofen, ASA and blood thinners
- Slight risk for Serotonin syndrome.

(Carlat & Puzantian, 2020)

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# Tricyclic Antidepressants (TCAs)

Imipramine (Tofranil) | Desipramine (Norpramin) | Amitryptyline (Elavil) | Nortriptyline (Pamelor) | Clomipramine (anafranil)

**FDA Indication**: Major depression, OCD (Clomipramine only)

**Off-label uses**: HA, neuropathic pain, anxiety disorders, fibromyalgia, insomnia, cataplexy

**Mechanism of Action**:

- Blocks the reuptake (reabsorption) of both serotonin and norepinephrine (desired action of the drug)
  - Also blocks acetylcholine, histamine, alpha-adrenergic and sodium channels (causes unwanted side effects)

(Carlat & Puzantian, 2020)

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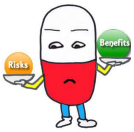
# Nursing Considerations & Teaching for TCAs




**Side effects:**

Sedation, weight gain, orthostatic hypotension, dizziness, vertigo, dry mouth, constipation, urinary retention, blurred vision

**Serious but rare side effects:**

Seizure, cardiac effects including orthostasis, arrhythmias, QT prolongation, AV block

**Patient/Nurse teaching:**

- Expected clinical response: sleep and energy improvements may occur within the first 1-2 weeks, full effects take 3-4 weeks
- Baseline EKG if history of cardiac disease (due to s/e)
- Annual LFT's, CBC, Thyroid function studies
- Patients often have adherence issues due to unwanted side effects
- Contraindicated in older adults related to potential cardiac effects
- High toxicity in overdoses (caution in suicidal patients)
- Abrupt discontinuation of TCAs will result in withdrawal syndrome

(Carlat & Puzantian, 2020)

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# Monoamine Oxidase Inhibitors (MAOIs)

- Phenelzine (Nardil)
- Tranylcypromine (Parnate)
- Isocarboxazin (Marplan)

**FDA Indication**: Major depression

**Off-label uses**: Treatment-resistant depression; panic disorder; social anxiety disorder

**Mechanism of Action**:

- Inhibits the MAO enzyme from breaking down serotonin, norepinephrine and dopamine (monoamines); which allows for more availability of those monoamines in the synapses when depolarization happens
- Takes 3-6 weeks before efficacy
- Because of dietary restrictions, MAOIs were mostly replaced with SSRIs

(Carlat & Puzantian, 2020)

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# Nursing Considerations & Teaching for MAOI's


**Side effects**:

Dizziness, headache, orthostatic hypotension, dry mouth, constipation, drowsiness, tremor, sweating, sexual side effects, peripheral edema, weight gain

**Serious but rare side effects**:

Hypertensive crisis

**Patient teaching:**

- Avoid with other anti-depressants, serotonergic agents, stimulants, disulfiram, and meperidine
- Do not use within 5 weeks of fluoxetine discontinuation or two weeks of another antidepressant discontinuation
- Needs to be discontinued 10 days prior to elective surgery
- Antihypertensives may exaggerate hypotensive effects
- Avoid use with foods or supplements high in tyramine, tryptophan, phenylalanine, or tyrosine (examples: aged cheese, air-dried or cured meats such as salami, fava or broad bean pods, tap/draft beers sauerkraut, soy sauce, or spoiled foods.

(Carlat & Puzantian, 2020)

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# Other Antidepressants

| SARI (Serotonin Antagonist and Reuptake Inhibitor) | NaSSA (Noradrenaline and specific serotonergic antidepressants) | NDRI (Norepinephrine–dopamine reuptake inhibitor) |
|---|---|---|
| • Trazodone (Desyrel) is generally used in lower doses for treatment of insomnia because it causes sedation<br>• Men must be advised of the risk of priapism<br>• Patients should be aware of the risk of orthostatic hypotension | • (Mirtazapine) Remeron makes serotonin and norephinephrine more available<br>• Indicated for patients with depression, insomnia and anxiety<br>• Advise patients of highly sedating effects and risk of falls<br>• Can cause significant weight gain<br>• Less sexual side effects | • Buproprion (Wellbutrin) inhibits reputake of both dopamine and norephinephrine<br>• Used as treatment of depression and as an augmenting agent with other antidepressants<br>• No sexual side effects<br>• Can lower seizure threshold in persons with history of seizures disorder or bulimia |

(Carlat & Puzantian, 2020)

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# Mood Disorders

## Bipolar 1 Disorder:

Criteria: At least one manic episode that may have been preceded by or followed by a hypomanic or major depressive episode. Requires hospitalization for stabilization

- Manic Episode: irritable mood or elevated energy lasting 7 days with at least three of the following symptoms:
  - Distractibility
  - Indiscretions/impulsivity
  - Grandiosity
  - Flight of ideas
  - Decreased need for sleep
  - Talkativeness (pressured/uninterruptible)

## Bipolar 2 Disorder:

Criteria: At least one hypomanic episode and one major depressive episode

- Hypomania criteria:
  - Distinct period of elevated mood or irritability lasting 4 days and three mania symptoms
  - Change in mood and function is observable by others
  - Doesn't warrant hospitalization

## Cyclothymic Disorder:

Periods of hypomanic symptoms and depressive episodes that do not meet full criteria for hypomania and depressive disorder, but is severe enough to cause social and occupational impairment

- 15-50% risk that it will develop into bipolar 1 or bipolar II disorder

(Marzoni, Neff, 2021), (Zakhari, 2022)

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# Treatment of Bipolar Disorder

- Medications
  - Lithium
  - Atypical Antipsychotics: Abilify, Saphris, Vraylar, Latuda, Zyprexa, Symbayax, Seroquel, Risperdal, Geodon
  - Anticonvulsants: Tegretol, Depakote, Lamictal
- Psychotherapy
- ECT: Used in patients with severe bipolar depression
  - Strongest prognostic factors are older age, absence of OCD and personality disorders, people not treated with Lamotrigine
- Light Therapy:
  - Bright light therapy can help with depression, dark light therapy can help decrease mania symptoms
- Transcranial Magnet Therapy
  - Currently being researched as a treatment for bipolar depression

(Marzoni, Neff, 2021), (Zakhari, 2022)

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# Treatment of Acute Mania

- Goal: Ensure safety of patient and others by achieving rapid control of agitation, impulsivity, and aggression
- Interventions:
  - Lithium is first line drug if appropriate for patient
  - Antipsychotics to manage psychosis, aggression and agitation
  - Benzodiazepines to manage anxiety
  - Staff set limits in a firm, nonthreatening and neutral manner to prevent further escalation and provide safe boundaries for patient and others
  - Be consistent in approach and expectations
  - Maintain low level of stimuli in patient's environment
  - Remind patient to eat; monitor intake and offer high calorie protein drinks and finger foods as needed
  - Encourage rest periods and promote environment conducive to sleep
  - Monitor patient's hygiene and intervene as needed

(Halter, 2018)

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# Lithium (Eskalith, Lithobid)

**FDA Indication**:
- Acute mania; bipolar disorder (maintenance) in children and adults

**Off-label uses**:
- Bipolar depression; treatment resistant depression; neutropenia; vascular headache

**Mechanism of Action**:
- Alters neuronal sodium transport
  - Drugs that INCREASE lithium levels: "**N**o **ACE** in the **H**ole" (**N**SAIDs, **ACE** inhibitors, and **H**CTZ)
  - Excess sweating can increase levels
  - Low sodium diet can increase levels
  - Caffeine may decrease levels

**Bottom Line:** Lithium is the gold standard for bipolar disorder

(Carlat & Puzantian, 2020)

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## Nursing Considerations & Teaching for Lithium

**Side effects**: Nausea/diarrhea (take with meals, split dosing, switch to ER), fine tremor (lower dose or use propranolol), polyuria/excessive thirst (dose all at bedtime), memory problems, weight gain, hypothyroidism (9x more common in women), acne or worsening psoriasis, benign increase in WBC

**Serious but rare side effects**: Chronic use may result in diminished renal concentrating ability (nephrogenic diabetes insipidus); usually reverses when discontinued. Cardiac: bradycardia, cardia arrythmia, flattened or inverted T waves, sinus node dysfunction

**Lithium Toxicity:**
- Serum levels above 1.5 meq/L; but may see signs at lower levels, especially in elderly
- Symptoms: nausea, vomiting, diarrhea, ataxia, stupor, coma, seizures, dysarthria, fasciculations, clonus
- Can cause interstitial nephritis, arrythmia, sick sinus syndrome, hypotension, T wave abnormalities, bradycardia
- Treatment: IV NaCl, hemodialysis, propranolol for tremors

**Patient teaching:**
- Lithium serum levels, thyroid function tests and renal indices need to be checked regularly (Check every one to two weeks initially, then every 3 to 6 months. Increased monitoring frequency with dose changes or when adding a medication that affects the kidneys)
- Overdose can be fatal
- Toxicity is dose dependent
- High rates of withdrawal
- Educate about drugs & food/drink that increase and/or decrease levels

(Carlat & Puzantian, 2020)

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# Mood Stabilizers

**FDA Indication**: Bipolar disorder, seizures
**Mechanism of Action**: Sodium channel blocker

| | |
|---|---|
| Valproic Acid (Depakene, Depakote) | Valproic acid is a first choice antimanic agent for acute manic episodes. It has a faster onset of response and better adverse effect profile compared to lithium, fewer drug interactions than carbamazepine, and efficacy for rapid cycling and relapse prevention<br>**Off label uses**: Bipolar maintenance; impulse control disorders; violence and aggression |
| Carbamazepine (Tegetrol) | Carbamazepine is not used first-line for bipolar disorder due to its side effect profile and high likelihood of significant drug interactions<br>**Off label uses**: Bipolar maintenance; impulse control disorders; violence and aggression |
| Lamotrigine (Lamictal) | Lamotrigine is a good choice for maintenance treatment of bipolar disorder, especially to prevent depressive episodes. The drug has a good side effect profile. Main disadvantage is the very slow titration schedule related to risk of Steven-Johnson syndrome<br>**Off label uses**: Bipolar depression; neuropathic pain; major depression |

(Carlat & Puzantian, 2020)

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# Mood Stabilizers Nursing Considerations & Teaching


***Valproic acid (Depakene, Depakote):***

**Side effects**: Somnolence, hair loss, nausea, fatigue, dizziness, tremor, thrombocytopenia (up to 24% of patients; dose-related; reversible)
**Serious but rare side effects**: Hepatotoxicity - rare idiosyncratic reaction, not dose related. Asymptomatic elevated liver levels. PCOS in about 10% of women. Hyperammonemia, encephalopathy (sometimes fatal). Pancreatitis (rare but potentially fatal)

**Patient teaching:** Teratogenic, serum levels need to be monitored, titrate to serum level of 50-125 mcg/mL

***Carbamezepine (Tegretol):***

**Side effects**: Dizziness, somnolence, nausea, headache

**Serious but rare side effects**: Hematologic abnormalities including agranulocytosis, aplastic anemia, neutropenia, leukopenia, thrombocytopenia, and pancytopenia. Severe reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome are rare but can be fatal

**Patient teaching:** Slower titration mitigates adverse effects, serum levels need to be monitored, dose may need to be changed over time, high potential for significant drug interactions, avoid use with oral contraceptives (lowers serum levels) and with clozapine (additive risk of agranulocytosis)

***Lamotrigine (Lamictal, Lamictal XR):***

**Side effects**: Dizziness, headache, nausea, sedation, benign rash (7%)

**Serious but rare side effects**: Skin reactions (black box warning): Severe, potentially life-threatening skin rashes requiring hospitalization reported. Toxic epidermal necrolysis, and angioedema

**Patient teaching:** Very slow titration schedule, discontinue at first sign of rash, majority of steven-johnson cases occur in the first 8 weeks, but isolated cases may occur beyond 8 weeks. Caution with oral contraceptives (may decrease levels)

(Carlat & Puzantian, 2020)

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## Catatonia

(need 3 or more symptoms for diagnosis)

- Stupor (no psychomotor activity)
- Catalepsy (passive induction of a posture held against gravity)
- Waxy flexibility (slight, even resistance to positioning by examiner)
- Mutism (no or very little verbal response)
- Negativism (opposition or no response to instructions)
- Posturing (spontaneous and active maintenance of a posture against gravity),
- Mannerisms (odd caricature of normal actions),
- Stereotypy (repetitive, abnormally frequent, non-goal directed movement)
- Agitation not influenced by external stimuli
- Grimacing
- Echolalia (mimicking speech)
- Echopraxia (mimicking movements)

(Burrow et al, 2023)

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## Catatonia Treatment

- Exclude medical causes
- Lorazepam challenge - titrate to symptom relief
  - Decrease as tolerated, may take months
- If symptoms do not respond to benzodiazepines in one week; ECT can be used
- Lorazepam is effective in approximately 80% of cases

(Burrow et al, 2023)

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# What is schizophrenia?

- A chronic mental illness characterized by at least two of the following symptoms persisting longer than 6 months: positive symptoms (delusions, hallucinations, disorganized speech and behavior), negative symptoms (apathy, social isolation and diminished affect), and cognitive impairment
- At least one of the two symptoms must be delusions, hallucinations or disorganized speech
- Diagnosis is made after the exclusion of other possible conditions
  - Substances, mood disorders, bipolar disorder with psychotic features, or other medical conditions

(Rahman, Lauriello, 2016)

| Prodromal Phase | Active Psychosis | Residual Phase |
|---|---|---|
| • Characterized by odd beliefs, ideas of reference, unusual perceptual experiences, negative symptoms, and deterioration of function prior to the onset of active psychosis<br>• 80-90% of people have a prodromal period that lasts up to a year before a major psychotic episode (possible symptoms: anxiety, obsessive thoughts, mild paranoia, auditory hallucianations and compulsive behaviors | • Symptoms: delusions, hallucinations, disorganized speech, grossly disorganized behavior, and negative symptoms | • Persistent functional impairment, abnormalities in affect, impaired cognition, and impaired communication<br>• Every patient is different. Some might only have one episode, and some have them repeatedly thoughout their life |

(Zakhari, 2022)

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# Symptoms of schizophrenia

| Positive symptoms: (the presence of something that should not be present) | Negative Symptoms: (the absence of something that should be there) | Cognitive symptoms: | Affective Symptoms: |
|---|---|---|---|
| • Auditory Hallucinations<br>• Command Hallucinations<br>• Delusions<br>• Disorganized speech<br>• Bizarre behaviors | • Anhedonia<br>• Avolition (low motivation)<br>• Asociality<br>• Apathy<br>• Alogia (poverty of speech)<br>• Affect (flat, blunted) | • Concrete thinking<br>• Impaired memory<br>• Impaired information processing<br>• Impaired executive functioning | • Unstable, erratic, labile mood<br>• Depression<br>• Suicidality |

(Heldt, 2018)

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**Slide 57**

**EA0** Schizophrenia is difficult to define with one sentence. The DSM-5 has detailed criteria for the diagnosis of  schizophrenia. There is no specific test to diagnose someone with schizophrenia. The diagnosis is made after other conditions are ruled out. These include substances, mood disorders, schizoaffective disorders, bipolar disorder with psychotic features or other medical conditions. If the patient has autism or a communication disorder there are additional criteria.

Emily M. Allred, 2023-10-27T21:59:03.068

# Incidence & Prevalence of Schizophrenia

- 1% of the general population has Schizophrenia
- Male to female ratio is 1.4:1
- Females are generally diagnosed at ages 25-35
  - More associated dysphoria & paranoid delusions with comorbid hallucinations
- Males are generally diagnosed at ages 18-25
  - More prevalent negative symptoms, worse prognosis, more hospitalizations, less responsive to meds
- 20% of people with Schizophrenia attempt suicide and 5-6% of people complete suicide
- People with Schizophrenia are 2-3 more times likely to die early than the general population
- Estimated that 15-20% of the homeless population has schizophrenia (NAEH, 2014), (Rahman, Lauriello, 2016)
- Up to 90% of people with schizophrenia use nicotine
- 40-50% of people with schizophrenia have a substance use disorder at some point during their illness

(Zakhari, 2022)

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# Genetics and Schizophrenia

- 80% of the risk of schizophrenia comes from genetic and epigenetic factors. However, many people who have a relative with schizophrenia will not develop schizophrenia
  - Studies show a strong genetic propensity for schizophrenia. The risk of heritability is estimated to be 2% for third-degree relatives, 9% for first-degree relatives, 27% for children of two affected parents, and 50% for monozygotic twins. The risk of disease proves to be 6 to 10 times higher than the general population for an adopted child whose biological parent is a schizophrenic" (Trifu, 2020).
- Over 100 loci in the human genome are associated with increased risk of schizophrenia
- Genetic research has not yielded a clear cause of Schizophrenia

(Zakhari, 2022)

# Environmental Factors and Schizophrenia

**Prenatal Stressors**

- Infections while pregnant, inflammation, being born in late winter/early spring, father older than the age of 35, low folate levels, hypoxia during birth process

**Psychological Stressors**

- Childhood sexual abuse, chronic poverty, immigration
- Increased levels of cortisol from stress causes changes in the brain

**Environmental Stressors**

- Toxins (ex. Tetrachloroethylene), living in urban areas
- Cannabis use disorder
- Low Omega 3 and Omega 6 polyunsaturated fatty acids have been found to be low in the brains of people with schizophrenia. (Fatty acid supplements are being researched for the possibility of lowering the conversion of "at risk" to developing schizophrenia. Fatty acids help maintain ACH and serotonin stability by reducing inflammation and free radicals in the brain (Halter, 2018)

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# Neurobiological

Because so much about schizophrenia is unknown, the neurobiological components of the disorder are complex, in large part because nearly everything is based on theory

- Dopamine Theory: Formed in 1975 when Haldol was found to bind to dopamine 2 receptors and psychotic symptoms were decreased.
- NMDA Receptors: Formed when NMDA receptor agonists such as ketamine and PCP were noted to produce symptoms of schizophrenia (Nakazawa, 2020).
- Role of serotonin, GABA and acetylcholine: studies are showing that all of these neurotransmitters are affected in people with schizophrenia.
- Brain imaging differences in patients with schizophrenia: people with schizophrenia have enlarged ventricles and cortical tissue loss of about 5% of brain volume.
- Synaptic Pruning: A process of pruning of synapses occurs in people's brains between the ages of 2 to 10 years old. There is a hypotheses that over pruning of these synapses causes schizophrenia (Sakai, 2020).
- Illegal substances have helped increase the understanding of Schizophrenia. Amphetamines and cocaine can induce psychosis in people without schizophrenia and bring on schizophrenia. When someone uses PCP, their behavior can resemble schizophrenia.

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# Prognosis for schizophrenia

Medications and psychosocial interventions can significantly help decrease symptoms & improve quality of life.

Usually mild or severe residual symptoms are left leading to varying degrees of dysfunction and disability.

Less Positive Prognosis:

- Slow onset of disorder (more than 2 or 3 years)
- Younger age at onset
- Higher premorbid level of social adjustment
- Longer duration between first symptoms and first treatment
- Longer periods of untreated illness
- High levels of "expressed emotions" in home environment
- Higher levels of negative symptoms
- Males
- Substance abuse

- Treatment-Resistant Schizophrenia: after several FGA trials, 10% to 30% of patients with schizophrenia still do not show much improvement in their symptoms, and another 30% to 60% report either insufficient or partial improvement or unacceptable side effects from antipsychotic therapy (Patel et al, 2014).

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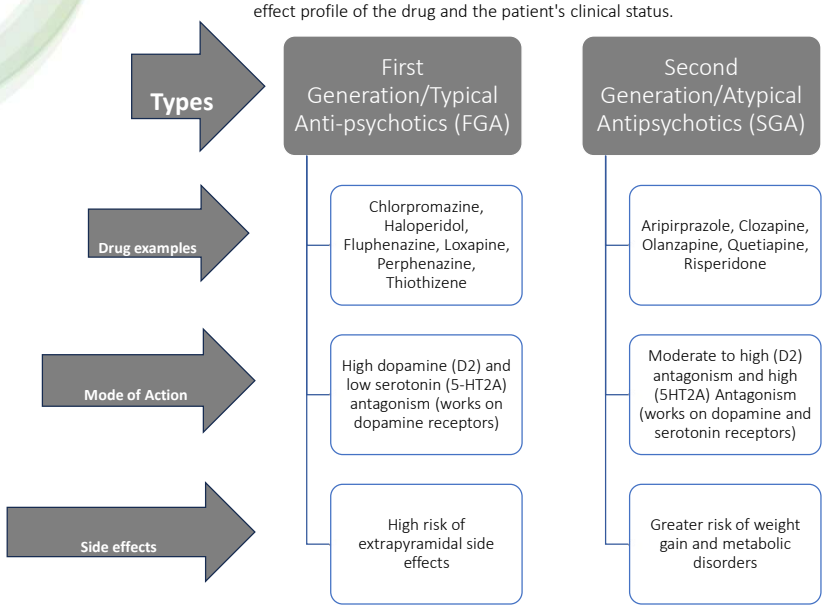
# First & Second-Generation Antipsychotic Drugs – A brief overview

All antipsychotics, except for Clozapine (used for treatment resistant schizophrenia), have similar clinical effectiveness. The drug of choice depends on the side effect profile of the drug and the patient's clinical status.




(Carlat & Puzantian, 2020)

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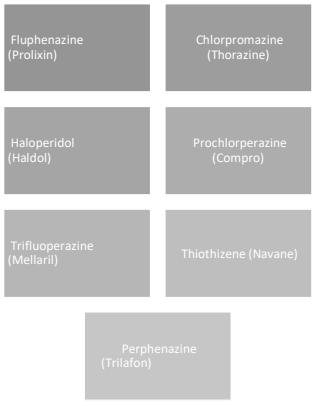
# First Generation Antipsychotics (FGA), also called Typical Antipsychotics




**FDA Indication**: Treatment of schizophrenia, Psychosis, Tourette's, Severe behavior problems

**Off-label uses**: Chemo induced nausea, Delirium

## Mechanism of Action:

Works by blocking dopamine (dopamine antagonists) in the brain -> generally reducing or eliminating positive symptoms of psychosis. However, these drugs tend to block dopamine in dopamine pathways that serve other brain areas as well, resulting in untoward or adverse effects

Clinical effects:

- 30 - 60 minutes - some aggressive behaviors may improve
- 7 - 10 days - antipsychotic action takes place
- 4 - 6 weeks - full therapeutic effect occurs

(Carlat & Puzantian, 2020)

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# Second Generation Antipsychotics (SGA), also called Atypical Antipsychotics

| | | | |
|---|---|---|---|
| Aripiprazole (Abilify) | Asenapine (Saphris) | Olanzapine (Zyprexa) | Risperidone (Risperdal) |
| Palperidone (Invega) | Clozapine (Clozaril) | Lurasidone (Latuda) | Ziprasidone (Geodon) |

- **FDA Indication**: Schizophrenia, Bipolar Disorder (mania/mixed), Agitation, Irritability r/t autism
- **Off-label uses**: Depression, Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder, Personality Disorders, Tourette's syndrome, Autism, and agitation in Dementia (Maglione, 2011)
- **Mechanism of Action**: Decrease positive, negative and cognitive effects by blocking dopamine (D2) receptors as well as serotonin receptor antagonist (5-HT2A)
- **Clinical effects:**
  - 30 - 60 minutes - some aggressive behaviors may improve
  - 7-10 days - antipsychotic action takes place
  - 4-6 weeks - full therapeutic effect occurs

(Carlat & Puzantian, 2020)

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# Clozapine (Clozaril, FazaClo, Versacloz)

- **Bottom Line:** The only drug with convincing evidence to help treatment-resistant schizophrenia. Providers typically consider using it after 2 failed trials of other antipsychotics
- **FDA Indication**: Treatment-resistant Schizophrenia; reduction in risk of suicide in schizophrenia and schizoaffective disorder
- **Off-label uses**: Treatment-resistant bipolar disorder; treatment-resistant aggression and violence
- **Mechanism of Action**: Dopamine D2 & serotonin 5-HT2A receptor antagonist
- **Monitoring:**
  - Fasting glucose, lipids
  - Before starting clozapine, ensure absolute neutrophil count (ANC) >1500; different parameters for benign ethnic population
  - Repeat ANC weekly for first 6 months, then every 2 weeks from 6 months to 12 months, then monthly after 12 months
  - Therapeutic response generally occurs between 350 ng/ml-450 ng/ml.
- **Side Effects:**
  - Most common: sedation, orthostatic hypotension, hypersalivation (place towel on pillow), weight gain (15-30 pound average weight gain after 1 year), constipation (risk of toxic megacolon if untreated), tachycardia (can treat with propranolol)
  - Serious but rare: Potentially life-threatening neutropenia (1%-2%); periodic ANC testing must occur

(Carlat & Puzantian, 2020)

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# Long-Acting Injectable (LAI) Antipsychotics

- **Bottom Line:** Patients who are non-adherent with oral medication are likely to do better on LAI's, if they will agree to LAI.
- **Potential Advantages:**
  - Ensure otherwise non-adherent patients have robust serum levels of antipsychotics
  - More consistent serum levels over time compared to oral medications
  - Family, friends, and Healthcare team spend less time struggling with patients about medication adherence
  - Patient is not being sent home with large quantities of pills which could result in intentional and/or unintentional overdose
- **General notes**:
  - Ensure patient has taken oral medication form and tolerated
  - LAI's can take several months to reach full therapeutic effect
  - Providers may continue oral overlap depending on LAI chosen
  - LAI's should never be given on a patient who has a history of neuroleptic malignant syndrome (NMS)
- **LAI Options**:
  - Typical antipsychotics
    - Fluphenazine (Prolixin Deconate) & Haloperidol (Haldol Decanoate)
  - Atypical antipsychotics
    - Aripiprazole (Abilify Maintena), Aripiprazole lauroxil (Aristada), Olanzapine (Zyprexa Relprevv), Paliperidone palmitate monthly (Invega Sustenna), Paliperidone palmitate every 3 months (Invega Trinza), Risperidone (Risperdal Consta), Risperidone (Perseris)

(Carlat & Puzantian, 2020)

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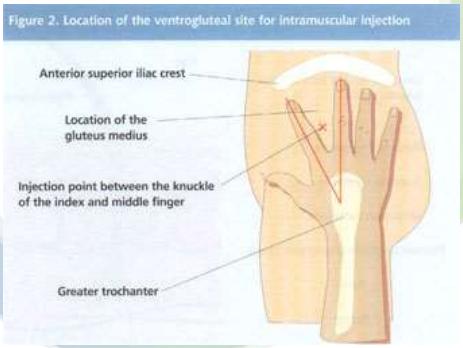
# Long-Acting Injectable (LAI) Antipsychotics




**General Administration Notes**:

- Most LAI's are administered by deep IM injection
- Preferable to give medication into deep ventrogluteal muscle (of the hip) and not subcutaneous fatty tissue (delays absorption significantly)
- Ventrogluteal muscle is easily located and free of major blood vessels and nerves
- Z-track technique should be used when fluphenazine or haloperidol deconate to gluteal muscle. You can use the Z-track technique with other drugs to ensure deep IM administration and minimize or prevent drug leakage.
- Longer needles should be used in obese patients
- Administer dose immediately after suspending and/or shaking to avoid settling or needle occlusion (refer to specific product information)
- Do not massage the injection site! Advise patients to not massage injection site. Massaging site promotes dispersal into fatty tissue.
- Maximum recommended volume to be administered:
  - Gluteal: 3 mL
  - Deltoid: 2 mL

(Carlat & Puzantian, 2020)

Photo obtained from: https://www.inmo.ie/MagazineArticle/PrintArticle/5676

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# Untoward or Adverse Effects

Side effects can be distressing to patients and can be a source of nonadherence to the medication regime.

Some side effects are potentially fatal.

The next few slides will go over possible untoward or adverse effects.


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**Gynecomastia & Galactorrhea**:
Antipsychotics antagonize D2 receptor sites resulting in increased levels of prolactin leading to gynecomastia (enlarged breast tissue) and galactorrhea (expression of milk from mammary glands in breast)

**Photosensitivity:**
Increased sensitivity to sunlight might place patient at increased risk for sunburn

**Hypotension:**

Most common with second generation antipsychotics. Frequently is accompanied by orthostatic tachycardia. Symptoms occur when medication is initially started or when dose is increased. Usually regulates itself within a few days

**Anticholinergic Side Effects:**
FGA's cause Anticholinergic (ACh) side effects by blocking muscarinic cholinergic receptors: urinary retention, dilated pupils, constipation, blurred near vision, tachycardia, dry mucous membranes, reduced peristalsis, cognitive impairment

**METABOLIC SYNDROME:**

**How it happens:** The cause is not completely clear but second-generation antipsychotics are associated with increased appetite and altered metabolism. Research shows cholinergic muscarinic M3 receptors (M3R) are expressed on pancreatic beta cells and in the brain where they influence insulin secretion and may regulate other metabolic hormones via the vagal innervation of the GI tract. Clozapine and Olanzapine are the medications carrying the highest risk of developing metabolic syndrome.

**Symptoms**: Abdominal obesity, insulin resistance, dyslipidemia, HTN

**Treatment**: Metformin, active monitoring of weight, food intake and physical activity

(Carlat & Puzantian, 2020)

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# Extrapyramidal side effects (EPS)

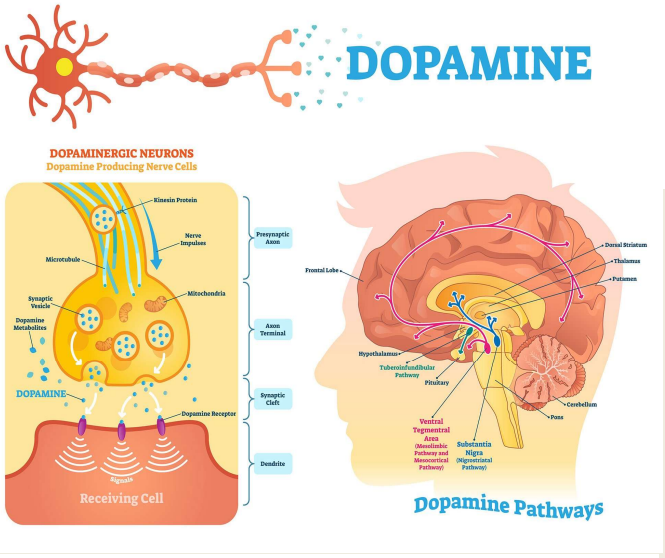


Image from: https://www.dreamstime.com/illustration/dopamine-vector.html

- No antipsychotic medication can directly target the 'positive' symptoms of schizophrenia without influencing other pathways. Patients need to be advised of possible short-term and long-term movement disorders that may result from decreased dopamine in the nigrostriatal pathways, which results in EPS.

The Nigrostriatal pathway is responsible for motor planning of purposeful movement. Decreased dopamine can results in extrapyramidal side effects; Acute Dystonic Reaction, Pseudoparkinsonism, Akathisia, and Tardive Dyskinesia

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## ACUTE DYSTONIC REACTION:

**How it happens:** Idiosyncratic, unpredictable; 50% occur within 48 hours

**Symptoms:** abnormal muscle tonicity and spasms such as of eyes (oculogyric crisis), face (glossopharyngeal spasms), head, neck (wry neck or torticollis), and back (spasms)

**Treatment:** Notify LIP. Anticholinergics such as benztropine (Cogentin); 1-2 mg IM, Antihistamines such as diphenhydramine (Benadryl) (50 mg IM), Maintain patent airway, be prepared to give multiple doses over the next 24 hours. Both options are effective; Benztropine may be slightly more effective and cause less drowsiness

## AKATHISIA:

**How it happens:** Occurs early in therapy, dose dependent

**Symptoms:** Extremely distressing neurological syndrome characterized by an inability to sit still, motor restlessness, an overwhelming sense of terror

**Treatment:** Notify LIP. Reduce antipsychotic dose or change. Propranolol, Benztropine.

Link to Barnes Akathisia rating scale: Microsoft Word - Barnes Akathisia Scale.doc (simpleandpractical.com)

(Carlat & Puzantian, 2020)

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## PSEUDOPARKINSONISM:

**How it happens:** Develops slowly (days to weeks)

**Symptoms:** Muscle stiffness, cogwheel rigidity, shuffling gait, stooped posture, drooling, slow resting tremor

**Treatment:** Notify LIP. Reduce antipsychotic dose or change. Amantadine.

## TARDIVE DYSKINESIA (TD):

**How it happens:** Develops in months to years after chronic use of antipsychotic drugs

**Symptoms:** Affects the muscles of the face, mouth, tongue (periorbital areas), fingers, and toes with a presentation of lip-smacking, grimacing, tongue movements, and writhing movements of the fingers and toes

**Treatment:** Notify LIP. Regular monitoring with the AIMS scale will aid early symptom detection; Dose and/or med change, Botox, Amantadine

(Carlat & Puzantian, 2020)

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# Dangerous Antipsychotic Side Effects:

- Anticholinergic toxicity: Characterized by flushing, anhidrosis, dry mucous membranes, dilated pupils, altered mental status, fever, urinary retention
  - Treat with benzodiazepines for agitation and supportive care for other symptoms
- Prolongation of the QT interval: Usually no symptoms. Occasionally patient may faint or have seizures. Concern is it can cause torsade de pointes which can be a fatal arrhythmia.
  - Adjust or discontinue medication that is causing it
  - Transfer symptomatic patient to ED
- Liver impairment: In acute settings, this is usually picked up with elevated liver enzymes. In extreme cases, a patient may have acute liver failure
  - Discontinue medication
- Agranulocytosis: Often asymptomatic. May have fever, sore throat, joint pain, sepsis
  - Discontinue drug causing it and treat with broad spectrum antibiotics

(Carlat & Puzantian, 2020)

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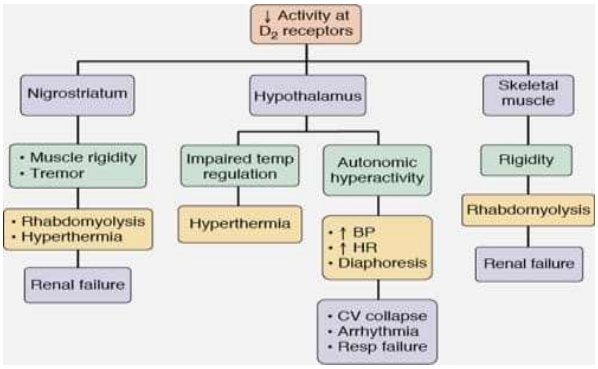
# Neuroleptic Malignant Syndrome (NMS)

**A life-threatening, neurological disorder associated with introduction/increase in dose of dopamine receptor antagonists OR rapid withdrawal of dopaminergic agents**




**Symptoms:**
- High fever
- Sweating
- Unstable blood pressure
- Stupor
- Muscle rigidity
- Autonomic dysfunction

**Interventions:**
- Life threatening emergency with a 10-20% mortality rate
- Discontinue any anti-psychotic drug
- Transfer to ICU for supportive care
- IV fluids
- Aggressive management of fever
- Benzodiazepines for agitation
- Medications (efficacy is unclear and disputed)
  - Dantrolene
  - Amantadine
  - Bromocriptine

Image provided by: Neuroleptic Malignant Syndrome - Assignment Point (Wijdicks EFM, 2022)

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# Treatment of Acute Agitation

- Communication
- Adjust environment as able
- Medications
  - Haldol 2.5-10 mg IM or
  - Haldol 5 mg IM plus Lorazepam 2 mg IM or
  - Zyprexa 10 mg IM
  - In elderly patients, reduce dose of antipsychotic in half.
  - Move to a different class (FGA vs SGA) when 1st class is ineffective or excessive doses are required
- Seclusion
- Restraints

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# Conclusion

The psychiatric mental health nurse strives to do what is best for the patient, to respect the patient's autonomy as a guiding principle in all ethical considerations, and to avoid coercive measures. It is our hope that this course will help the RN feel more prepared to provide patients with evidence-based care and knowledge.

Thank you for taking the course.

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