8.7: Antidepressants

Antidepressants are used to treat depression and other mental health disorders, as well as other medical conditions such as migraine headaches, chronic pain, and premenstrual syndrome. Antidepressants increase levels of neurotransmitters in the CNS, including serotonin (5-HT), dopamine, and norepinephrine. Treatment is based on the belief that alterations in the levels of these neurotransmitters are responsible for causing depression.[1]

This module will discuss four classes of antidepressants: tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs). TCAs and MAOIs are referred to as first-generation antidepressants because they were first marketed in the 1950s. SSRIs, SNRIs, and other miscellaneous medications such as bupropion are called second-generation antidepressants and are popular because of fewer side effects like sedation, hypotension, anticholinergic effects, or cardiotoxicity.[2]

Black Box Warnings are in place for all classes of antidepressants used with children, adolescents, and young adults for a higher risk of suicide. All patients receiving antidepressants should be monitored for signs of worsening depression or changing behavior, especially when the medication is started or dosages are changed.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) were one of the original first-generation antidepressants. Due to the popularity of SSRIs and SNRIs, TCAs are now more commonly used to treat neuropathic pain and insomnia.

Mechanism of Action

Amitriptyline is an antidepressant with sedative effects. Its mechanism of action is not known. Amitriptyline inhibits the membrane pump mechanism responsible for uptake of norepinephrine and serotonin in adrenergic and serotonergic

[1] https://med.libretexts.org/Bookshelves/Nursing/Nursing_Pharmacology_(OpenRN)/08%3A_Central_Nervous_System/8.07%3…
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neurons. This interference with reuptake of norepinephrine and/or serotonin is believed to underlie the antidepressant activity of amitriptyline.

**Indications for Use**

TCAs are used to treat depression, neuropathic pain, and insomnia.

**Nursing Considerations Across the Lifespan**

TCAs are often administered at bedtime due to sedating effects and are contraindicated with MAOIs.

Geriatric patients are particularly sensitive to the anticholinergic side effects of tricyclic antidepressants. Peripheral anticholinergic effects include tachycardia, urinary retention, constipation, dry mouth, blurred vision, and exacerbation of narrow-angle glaucoma. Central nervous system anticholinergic effects include cognitive impairment, psychomotor slowing, confusion, sedation, and delirium. Elderly patients taking amitriptyline may be at increased risk for falls. Elderly patients should be started on low doses of amitriptyline and observed closely.

After prolonged administration, abrupt cessation of treatment may produce nausea, headache, and malaise. The dose should be gradually tapered, but transient symptoms may still occur.

**Adverse/Side Effects**

Adverse effects of TCAs are a result of their blockade effects on various receptors, often resulting in anticholinergic adverse effects such as constipation, urinary retention, and drowsiness. Blockage of adrenergic and dopaminergic receptors can cause cardiac conduction disturbances and hypotension. Histaminergic blockage can cause sedation, and serotonergic blockade can alter the seizure threshold and cause sexual dysfunction.

Black Box Warnings are in place for all classes of antidepressants used with children, adolescents, and young adults for a higher risk of suicide. Patients receiving antidepressants should be monitored for signs of worsening depression or changing behavior, especially when the medication is started or dosages are changed.

**Overdosage**

Death may occur from overdosage with this class of drugs. Multiple drug ingestion (including alcohol) is common in deliberate tricyclic antidepressant overdose. If overdose occurs, consult with a Certified Poison Control Center (1-800-222-1222) or go to www.poisonhelp.org/help for the latest recommendations.

**Patient Teaching & Education:** Due to the increased risk of suicidality with antidepressants, patients and their family members or caregivers should be instructed to immediately report any sudden changes in mood, behaviors, thoughts, or feelings. Potential side effects discussed above should be reviewed.\[3\] [4] [5]

Now let's take a closer look at the medication grid for amitriptyline in Table 8.7a.\[6\] [7] [8]

<table>
<thead>
<tr>
<th>Class/Subclass</th>
<th>Prototype/Generic</th>
<th>Administration Considerations</th>
<th>Therapeutic Effects</th>
<th>Adverse/Side Effects</th>
</tr>
</thead>
</table>

Table 8:7a Amitriptyline Medication Grid
| Tricyclic | amitriptyline | Black Box Warning: Increased risk of suicidality  
Taper dose when discontinuing; do not stop abruptly  
Monitor orthostatic blood pressures and consider fall risk precautions | Based on indication: decrease feelings of depression, chronic pain, or insomnia | 
Immediate report signs or symptoms of suicidality  
Anticholinergic effects  
Hypotension  
May lengthen QT interval; risk for arrhythmias  
Sedation  
Sexual dysfunction  
Altered seizure threshold |

### Selective Serotonin Reuptake Inhibitor (SSRI)

Selective Serotonin Reuptake Inhibitors (SSRIs) are a second-generation antidepressant and have fewer side effects than TCAs and MAOIs. Fluoxetine and citalopram are commonly used SSRIs.

**Mechanism of Action**

SSRIs inhibit the reuptake of serotonin.

**Indications for Use**

SSRIs are primarily used to treat depression, but are also used to treat obsessive compulsive disorder, bulimia, panic disorder, posttraumatic stress disorder, other forms of anxiety, premenstrual syndrome, and migraines.

**Nursing Considerations Across the Lifespan**

The onset of fluoxetine’s antidepressant effect develops slowly for up to 12 weeks.

Use with caution in patients who are taking other CNS medications or who have liver dysfunction. This drug is contraindicated with MAOIs. Monitor for increased suicide ideation in all populations, as well as for the development of serotonin syndrome. Patients should avoid grapefruit juice due to its effect on the CYP3A4 enzyme that affects the bioavailability of the medication.

**Adverse/Side Effects**
Black Box Warnings are in place for all classes of antidepressants used with children, adolescents, and young adults for a higher risk of suicide. Patients receiving antidepressants should be monitored for signs of worsening depression or changing behavior, especially when the medication is started or dosages are changed.

The development of a potentially life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs, particularly with concomitant use of serotonergic drugs, drugs that impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Symptoms of serotonin syndrome may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form, can resemble neuroleptic malignant syndrome (NMS), which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms.

Other side effects include rash; mania; seizures; decreased appetite and weight; increased bleeding associated with the concomitant use of fluoxetine and NSAIDs, aspirin, warfarin, or other drugs that affect coagulation; hyponatremia; anxiety; and insomnia.

Abrupt discontinuation may cause several adverse effects, so a gradual reduction in the dose rather than abrupt cessation is recommended whenever possible.

**Patient Teaching & Education**

Patients should be careful to take medications as directed. Abrupt discontinuation may cause anxiety, insomnia, and increased nervousness. Additionally, orthostatic blood pressure changes are common during medication therapy. Patients may also be increasingly drowsy or exhibit some confusion. Use of SSRI medications with alcohol or other CNS depressant drugs should be avoided.

Patients, family, and caregivers should monitor patients carefully for suicidality. Other side effects include possible decreased libido, urinary retention, constipation, and increased photosensitivity.

<table>
<thead>
<tr>
<th>Class/Subclass</th>
<th>Prototype/Generic</th>
<th>Administration Considerations</th>
<th>Therapeutic Effects</th>
<th>Adverse/Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>fluoxetine</td>
<td>Black Box Warning: Monitor for increased risk of suicidality</td>
<td>Based on indication: primarily decreases feelings of depression</td>
<td>Immediately report signs/symptoms of increased suicidality or serotonin syndrome</td>
</tr>
<tr>
<td></td>
<td>citalopram</td>
<td>Do not stop abruptly; taper dose when discontinuing</td>
<td>Contraindicated with</td>
<td>Rash, mania, seizures, decreased appetite and weight, increased bleeding, hyponatremia, anxiety, and insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Critical Thinking Activity 8.7

A 32-year-old female visits the nurse practitioner with concerns about “feeling tired all the time,” “having difficulty concentrating,” “problems sleeping,” and “just generally feeling down.” The nurse practitioner prescribed fluoxetine.

The patient tells the nurse, “One of my friends told me I have to be careful or I might get serotonin syndrome if I take medication.”

1. What places a patient at risk for serotonin syndrome, and what symptoms should the nurse teach the patient about this condition?

2. The nurse knows that anyone starting an antidepressant is at risk for suicidal thoughts. How should the nurse therapeutically discuss this potential adverse effect with the patient?

3. What potential common side effects should the nurse discuss with the patient?

The patient states, “I can’t wait to feel better again. How soon will this medication work?”

4. What is the nurse’s best response?

Note: Answers to the Critical Thinking activities can be found in the “Answer Key” sections at the end of the book.
Serotonin Norepinephrine Reuptake Inhibitor (SNRI)

Venlafaxine is an example of a Serotonin Norepinephrine Reuptake Inhibitor (SNRI).

**Mechanism of Action**

Venlafaxine inhibits the reuptake of serotonin and norepinephrine, with weak inhibition of dopamine reuptake.

**Indications for Use**

SNRIs are indicated for treatment of a major depressive disorder.

**Nursing Considerations Across the Lifespan**

SNRIs are contraindicated with MAOIs or within 14 days of use of an MAOI. Dosage adjustment is required for use in patients with renal and/or liver disease. Elderly patients are at greater risk for developing hyponatremia. Use with caution with other serotonin medications.

**Adverse/Side Effects**

Black Box Warnings are in place for all classes of antidepressants used with children, adolescents, and young adults for a higher risk of suicide. Patients receiving antidepressants should be monitored for signs of worsening depression or changing behavior, especially when the medication is started or dosages are changed.

SNRI medication may cause sustained increase in blood pressure. Other side effects include serotonin syndrome, insomnia, anxiety, decreased appetite, weight loss, mania, hyponatremia, increased bleeding (especially with the concomitant use of fluoxetine and NSAIDs, aspirin, warfarin, or other drugs that affect coagulation), elevated serum cholesterol, somnolence, and nausea. [16]

**Patient Teaching & Education**

Patients should be careful to take medications as directed. The dose should be tapered prior to discontinuation. Patients may also be increasingly drowsy or dizzy. Use of SNRI medications with alcohol or other CNS depressant drugs should be avoided. Patients, family, and caregivers should monitor patients carefully for suicidality.

Now let’s take a closer look at the Medication Grid for venlafaxine in Table 8.7c.[17]
Gradually reduce dose when discontinuing when possible

Use with caution with patients with liver or renal disease

<table>
<thead>
<tr>
<th>syndrome</th>
<th>Elevated BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Mania</td>
<td>Hyponatremia</td>
</tr>
<tr>
<td>Increased bleeding</td>
<td>Elevated cholesterol</td>
</tr>
<tr>
<td>Somnolence</td>
<td>GI: Nausea and constipation</td>
</tr>
</tbody>
</table>

**Monoamine Oxidase inhibitors (MAOI)**

Monoamine oxidase inhibitors (MAOIs) are a first-generation antidepressant. Tranylcypromine is an example of a MAOI. A significant disadvantage to MAOIs is their potential to cause a hypertensive crisis when taken with stimulant medications or foods containing tyramine.

**Mechanism of Action**

The mechanism of action of tranylcypromine tablets as an antidepressant is not fully understood, but is presumed to be linked to potentiation of monoamine neurotransmitter activity in the central nervous system resulting from its irreversible inhibition of the enzyme monoamine oxidase (MAO).[^18] MAO inactivates norepinephrine, dopamine, epinephrine, and serotonin. By inhibiting MAO, the levels of these transmitters rise.[^19]

**Indications for Use**
Tranylcypromine is indicated for the treatment of major depressive disorder in adult patients who have not responded adequately to other antidepressants. The drug may also be used to treat Parkinson’s disease.

**Nursing Considerations Across the Lifespan**

Serious interactions with several medications, as well as foods and beverages containing tyramine, have been reported; check drug labelling before administering. Safety has not been established with the pediatric population. The elderly population is at increased risk for postural hypotension and serious adverse effects. Abuse and dependence have been reported. Withdrawal effects can continue for several weeks after discontinuation.

**Adverse/Side Effects**

Black Box Warnings are in place for all classes of antidepressants used with children, adolescents, and young adults for a higher risk of suicide. Patients receiving antidepressants should be monitored for signs of worsening depression or changing behavior, especially when the medication is started or dosages are changed.

Use with caution due to the risks of hypertensive crisis, serotonin syndrome, and increased suicidality. **Hypertensive crisis** is defined by severe hypertension (blood pressure greater than 180/120 mm Hg) with evidence of organ dysfunction. Symptoms may include occipital headache (which may radiate frontally), palpitations, neck stiffness or soreness, nausea or vomiting, sweating, dilated pupils, photophobia, shortness of breath, or confusion. Either tachycardia or bradycardia may be present and may be associated with constricting chest pain. Seizures may also occur. Intracranial bleeding, sometimes fatal, has been reported in association with the increase in blood pressure. See more information about serotonin syndrome in the “SSRI” section.

Other potential side effects include mania, **orthostatic hypotension**, hepatotoxicity, seizures, hypoglycemia in diabetic patients, decreased appetite and weight loss, dizziness, headache, drowsiness, and restlessness. Patients should be advised it may impair ability to operate machinery or drive. MAOIs should be discontinued if hepatotoxicity occurs.

**Patient Teaching & Education**

Patients should be careful to take medications as directed. They should avoid abrupt cessation of therapy to avoid withdrawal symptoms. Patients should avoid alcohol, other CNS depressants, and tyramine-containing products for two weeks after therapy is discontinued. Patients should be advised regarding the signs of hypertensive crisis and to immediately report headache, chest or throat tightness, and palpitations to the provider.

Now let’s take a closer look at the medication grid for tranylcypromine in Table 8.7d.

<table>
<thead>
<tr>
<th>Class/Subclass</th>
<th>Prototype/Generic</th>
<th>Administration Considerations</th>
<th>Therapeutic Effects</th>
<th>Adverse/Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAOI</td>
<td>tranylcypromine</td>
<td>Black Box Warning: Monitor for hypertensive crisis and increased suicide ideation</td>
<td>Based on indication: decreased feelings of depression or decreased symptoms of Parkinson's disease</td>
<td>Increased suicidality, Hypertensive</td>
</tr>
<tr>
<td>Avoid foods containing tyramine</td>
<td></td>
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<td>----------------------------------</td>
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<td></td>
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<tr>
<td>Many drug interactions</td>
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<tr>
<td>Monitor BP</td>
<td></td>
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</tr>
<tr>
<td>Do not stop abruptly; taper dose when discontinuing</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue if hepatotoxicity</td>
<td></td>
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</tr>
</tbody>
</table>

- Crisis
- Serotonin syndrome
- Mania
- Orthostatic hypotension
- Hepatotoxicity
- Seizures
- Hypoglycemia in diabetic patients
- Decreased appetite and weight loss
- CNS: dizziness, headache, drowsiness, and restlessness
- May impair ability to operate machinery or drive
