DEPRESSIVE DISORDERS can affect anyone, regardless of age, sex, ethnicity, education, income, or marital status. In this article, I’ll discuss the major types of antidepressants used to treat depressive disorders: monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), selective serotonin-norepinephrine reuptake inhibitors (SSNRIs), and several other atypical antidepressants. Let’s start with some background on how antidepressants act in the body.

Although the exact mechanism of antidepressants isn’t fully known, researchers believe they act at the synaptic gap in the central nervous system (CNS), regulating the process that breaks down the neurotransmitters norepinephrine and serotonin. Initially, researchers thought that dysfunction of only these two neurotransmitters caused major depression. But growing evidence indicates that dysregulation of other neurotransmitters (dopamine, acetylcholine, and gamma-aminobutyric acid) is also involved in the pathophysiology of major depression. Slow adaptive changes in norepinephrine and serotonin receptors may also play a part in depression symptoms.

Now let’s look at each of the antidepressant types, starting with the older drug classes, MAOIs and TCAs. These drugs aren’t considered first-line treatments for depression today because newer drugs, such as SSRIs and SSNRIs, are generally safer and less likely to cause burdensome or dangerous adverse reactions. Patients should be assessed for suicide risk before starting any antidepressant.

MAOIs: First of their kind
The first class of antidepressant developed, MAOIs inhibit the activity of monoamine oxidase, a complex enzyme system that inactivates certain neurotransmitters. As a result, the breakdown of norepinephrine, serotonin, tyramine, and dopamine at the synaptic gap is inhibited, making more of these neurotransmitters available to stimulate the CNS and relieve symptoms of depression.

In the United States, the MAOIs phenelzine (Nardil) and tranylcypromine sulfate (Parnate) may be prescribed for atypical depressions, panic disorders, social phobias, bulimia, posttraumatic stress disorder, and generalized anxiety disorder. Because an interaction with certain foods (including aged cheese, red wine, and some fruits) can cause

Tracking the ups and downs of antidepressants

Adverse reactions to these drugs prompt some patients to abandon therapy. Here’s what you need to know about them to help your patient stay on his medications and benefit from treatment.

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hypertensive crisis or stroke, patients taking MAOIs must follow strict dietary guidelines (more on this later). Other adverse reactions to MAOIs include orthostatic hypotension, weight gain, edema, change in cardiac rate and rhythm, constipation, urinary hes-tinacy, sexual dysfunction, vertigo, overactivity, mus-cle twitching, hypomania and manic behavior, insomnia, weakness, and fatigue.¹

**TCAs: Inhibiting reuptake**

Tricyclic antidepressants block the reuptake of norepinephrine and serotonin, resulting in higher levels of these neurotransmitters at the synaptic gap. A patient must take a TCA for 3 to 4 weeks to attain a therapeutic level.

Common TCAs include amitriptyline (Elavil), desipramine (Norpramine), doxepin (Sinequan), imipramine (Tofranil), and nortriptyline (Pamelor). Adverse reactions include anticholinergic effects (such as blurred vision, dry mouth, postural hypoten-sion, constipation, and urinary retention), dysrhythmias (such as sinus tachycardia and prolongation of conduction time), liver toxicity, menstrual irregularities, sexual adverse reac-tions, and lowering of the seizure threshold.

Patients should be assessed for cardiac, liver, or seizure disorders and for suicidal ideation before starting TCA therapy. Use TCAs cautiously in patients with a recent history of myocardial infarction or other cardiovascular dis-orders, narrow-angle glaucoma, or seizures. Monitor these patients closely during therapy. Pregnant women shouldn’t take TCAs. Because their combined action could be fatal, don’t use TCAs and MAOIs together.

**SSRIs and SSNRIs: Top of the line**

The theory that depression is caused by excess reuptake of neurotransmitters such as serotonin led to the development of SSRIs and SSNRIs. These drugs are recommended as first-line therapy in all depressions except psychotic depression, melancholic depression, or mild outpatient depression.¹ The SSRIs selectively block the neuronal uptake of serotonin, letting sero-tonin act as a CNS stimulant for an extended period. (The SSNRIs have the same action, and block reuptake of serotonin and norepinephrine.)

The SSRIs are citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox), fluoxetine (Prozac), paroxetine (Paxil), and sertraline (Zoloft). The SSNRIs are duloxetine (Cymbalta) and ven-lafaxine (Effexor). Both types are used (on- and off-label) for depression, some anxiety disorders, obses-sive compulsive disorder and panic disorder. These drugs may also help women with late luteal phase dysphoric disorder.³

Common adverse reactions to SSRIs and SSNRIs include agitation, anxiety, sleep disturbance, tremor, sexual dysfunction, tension headache, and autonomic reactions (dry mouth, sweating, weight change, mild nausea, and loose bowel movements). Because SSRIs and SSNRIs cause fewer anticholinergic adverse reac-tions than TCAs, patients may be more likely to stick with treatment. These drugs are also less toxic than TCAs and MAOIs, so they’re less dangerous if the patient takes an overdose.

But SSRIs and SSNRIs carry the risk of another rare but life-threatening adverse reaction: central serotonin syndrome. This condition is triggered by overactiva-tion of the central serotonin receptors caused by too-high SSRI or SSNRI dosages or by interaction between an SSRI or SSNRI and other drugs (such as MAOIs).¹ Symptoms include abdominal pain, diarrhea, delirium, myoclonus, increased motor activity, irritability, hostility, and mood change. Severe manifestations include hyperpyrexia, cardiovascular shock, and death.

If your patient develops central serotonin syndrome, stop the SSRI or SSNRI and administer cyproheptadine as prescribed to block serotonin receptors.⁴ Provide respiratory support and administer anticon-vulsants and dantrolene for muscle rigidity and tremors, as prescribed.¹

Another concern with SSRIs and SSNRIs is the increased risk of suicidal ideation, especially in patients under age 18. (Fluoxetine is the only SSRI labeled for use in patients under age 18.) These anti-depressants now carry a black-box warning stating that they should be used in children only if the clinical need outweighs the risk. Patients should be closely monitored, especially at the start of therapy.

**Novel antidepressants: New kids on the block**

In addition to SSRIs and SSNRIs, the following novel or atypical antidepressants are some of the more recent additions to the antidepressant lineup. Initially, patients typically are prescribed an SRI, SSNRI, or atypical antidepressant; if these aren’t effective, other antidepressant classes or combinations may be tried.

▪ **Bupropion** (Wellbutrin) inhibits the reuptake of serotonin, norepinephrine, and dopamine.⁵ Increased seizure risk is the drug’s most serious adverse effect; patients who have a history of seizure are at highest risk.⁶ Bupropion also is used for smoking cessation...
and can be given in tandem with SSRIs to relieve the sexual dysfunction and insomnia brought about by that group of medications.

- Trazadone (Desyrel) inhibits the reuptake of norepinephrine and serotonin and is a strong inhibitor of serotonin type 2 receptors on the postsynaptic neuron. The drug’s efficacy is comparable with the Mirtazapine 25(5):441-447, October 2005.

- TrazadoneLike prescription and OTC drugs, Patients on MAOIs www.nursing2007.com ly if they develop a sore throat, difficulty urinating, patients to call their health care provider immediate-come, or motor or autonomic changes. Teach fusion, restlessness, hypomania, hallucinations, and symptoms after the addition of a new antidepressant or dosage increase may indicate an allergic reaction or central serotonin syndrome.

What your patient needs to know
All patients should be assessed for suicidal ideation before starting an antidepressant and be warned not to stop taking a drug abruptly because of the risk of withdrawal symptoms.

Any antidepressant can cause drowsiness, dizziness, and hypotension, which generally subside after several weeks. If the problem is excessive or if it persists, the patient should report it to his health care provider. Teach him to use caution when performing tasks that require alertness, such as driving, operating machinery, or even crossing streets, until he determines how the medication affects him.

Also tell him not to drink alcohol while taking an antidepressant. Because alcohol is a depressant, it can block the antidepressant’s effects. Also warn him not to take other medications, including over-the-counter (OTC) medications, without talking to his health care provider. Here are some special considerations for specific drug types.

- Patients on MAOIs must limit foods and drugs that contain tyramine, which can interact dangerously with MAOIs and cause hypertensive crisis. Provide the patient with a handout listing these foods. Some of these foods are smoked or fermented meats; dried fish; aged cheese; certain fruits such as avocados, figs, and bananas; red wine; and yeast extracts used in Chinese cooking. Medications that can interact with MAOIs include OTC cold and allergy drugs, antihypertensive medications, opioids, and levodopa.

- Patients on SSRIs or SNRIs should be taught to seek immediate medical help if they develop signs and symptoms of central serotonin syndrome, such as changes in mental status, anxiety, agitation, confusion, restlessness, hypomania, hallucinations, coma, or motor or autonomic changes. Teach patients to call their health care provider immediately if they develop a sore throat, difficulty urinating, rashes or hives, excessive or unexplained bleeding, anorexia or weight loss, rapid heartbeat, severe headaches, fever, or general malaise. These signs and symptoms after the addition of a new antidepressant or dosage increase may indicate an allergic reaction or central serotonin syndrome.

Herbal: A popular alternative
Herbal preparations for anxiety and depression have become increasingly popular over the past several years because they’re readily available and much less expensive than prescription antidepressants. However, study results on their efficacy are mixed, and more study is needed. Like prescription and OTC drugs, herbal preparations can also cause adverse reactions and potentially life-threatening interactions.

Because they’re considered dietary supplements, herbal preparations aren’t regulated under Food and Drug Administration guidelines. Dosing, quality, stability, and purity can be inconsistent from manufacturer to manufacturer. By staying up-to-date on warnings about herbal products, you can help your patient make good choices. (See Resources below.)

Happier endings
Antidepressant drug therapy has come a long way since its inception in the late 1950s. Tell your patient to work closely with his health care practitioner to iron out any problems he may have with his medication regimen. With so many medications to choose from, his practitioner can try many other options if one drug doesn’t work well or causes unacceptable adverse reactions.

REFERENCES

RESOURCES
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