ANTI DEPRESSANTS

(From Lippincott)

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The symptoms of depression are feelings of sadness and hopelessness, as well as the inability to experience pleasure in usual activities, changes in sleep patterns and appetite, loss of energy, and suicidal thoughts.
Mania is characterized by the opposite behavior: enthusiasm, anger, rapid thought and speech patterns, extreme self confidence, and impaired judgment.
Most clinically useful antidepressant drugs potentiate, either directly or indirectly, the actions of norepinephrine and/or serotonin (5-HT) in the brain.

DRUG CLASS	DRUG NAMES	MOA	THERAPEUTIC USE	DURATION OF ACTION	ADVERSE EFFECTS	OTHER POINTS
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram Escitalopram Fluoxetine Fluvoxamine Paraxetine Sertraline	- SSRIs block the reuptake of serotonin, leading to increased concentrations of the neurotransmitter in the synaptic cleft. -SSRIs have little blocking activity at muscarinic, α-adrenergic, and histaminic H1 receptors	-SSRIs have largely replaced TCAs and monoamine oxidase inhibitors (MAOIs) as the drugs of choice in treating depression -Antidepressants, including SSRIs, typically take at least 2 weeks to produce significant improvement in mood, and maximum benefit may require up to 12 weeks or more -A number of other psychiatric disorders also respond favorably to SSRIs, including obsessive–compulsive disorder, panic disorder, generalized anxiety disorder, posttraumatic stress disorder, social anxiety disorder, premenstrual dysphoric	-Peak levels are seen in approximately 2 to 8 hours on average -The majority of SSRIs have plasma half-lives that range between 16 and 36 hours -	-headache -sweating -anxiety and agitation, -gastrointestinal (GI) effects (nausea, vomiting, diarrhea), -weakness and fatigue - sexual dysfunction -changes in weight -sleep disturbances (insomnia and somnolence) -associated with hyponatremia, especially in the elderly and patients who are volume depleted or taking diuretics. -Sexual dysfunction, which may include loss of libido, delayed ejaculation, and anorgasmia, is common with the SSRIs.	-relatively safe even in overdose - Dosages of the SSRIs should be reduced in patients with hepatic impairment

			disorder, and bulimia nervosa (only fluoxetine is approved for bulimia). -Paroxetine and fluvoxamine are generally more sedating than activating, and they may be useful in patients who have difficulty sleeping. Conversely, patients who are fatigued or complaining of excessive somnolence may benefit from one of the more activating SSRIs, such as fluoxetine or sertraline. -Fluoxetine, sertraline, and fluvoxamine are approved for use in children to treat obsessive–compulsive disorder, and fluoxetine and escitalopram are approved to treat childhood depression.	Fluoxetine half life = 50 hours -halflife of S-norfluoxetine (active metabolite of Fluoxetine) is quite long, averaging 10 days.	(bupropion or mirtazapine has fewer sexual side effects) - Antidepressants should be used cautiously in children and teenagers, because about 1 out of 50 children report suicidal ideation as a result of SSRI treatment. -Overdose with SSRIs does not usually cause cardiac arrhythmias, with the exception of citalopram, which may cause QT prolongation -All SSRIs have the potential to cause serotonin syndrome, especially when used in the presence of a MAOI or other highly serotonergic drug. Serotonin syndrome may include the symptoms of hyperthermia, muscle rigidity, sweating, myoclonus (clonic muscle twitching), and changes in mental status and vital signs -All of the SSRIs have the potential to cause a discontinuation syndrome after their abrupt withdrawal (Fluoxetine has the lowest risk) Possible signs and symptoms of SSRI discontinuation syndrome include headache, malaise, and flu-like symptoms, agitation and irritability, nervousness, and changes in sleep pattern	

Serotonin norepinephrine reuptake inhibitors (SNRIs)	Desvenlafaxine Duloxetine Levomilnacipran Venlafaxine	-inhibit the reuptake of both serotonin and norepinephrine -Venlafaxine is a potent inhibitor of serotonin reuptake and, at medium to higher doses, is an inhibitor of norepinephrine reuptake. -Duloxetine inhibits serotonin and norepinephrine reuptake at all doses.	-effective in treating depression in patients in whom SSRIs are ineffective. - GI side effects are common with duloxetine, including nausea, dry mouth, and constipation. Insomnia, dizziness, somnolence, sweating, and sexual dysfunction are also seen. Duloxetine may increase blood pressure or heart rate.		-The most common side effects of venlafaxine are nausea, headache, sexual dysfunction, dizziness, insomnia, sedation, and constipation. At high doses, there may be an increase in blood pressure and heart rate	-Duloxetine is extensively metabolized in the liver to inactive metabolites and should be avoided in patients with liver dysfunction.
Atypical anti depressants	Bupropion	-Bupropion is a weak dopamine and norepinephrine reuptake inhibitor	Bupropion is used to alleviate the symptoms of depression. It is also useful for decreasing cravings and attenuating withdrawal symptoms of nicotine in patients trying to quit smoking.		Side effects may include dry mouth, sweating, nervousness, tremor, and a dosedependent increased risk for seizures. It has a very low incidence of sexual dysfunction.	Use of bupropion should be avoided in patients at risk for seizures or those who have eating disorders such as bulimia
	Mirtazapine	Mirtazapine enhances serotonin and norepinephrine neurotransmission by serving as an antagonist at presynaptic α2 receptors. Additionally, some of the antidepressant activity may be related to antagonism	-Mirtazapine is markedly sedating, which may be an advantage in depressed patients having difficulty sleeping		-It is sedating because of its potent antihistaminic activity, but it does not cause the antimuscarinic side effects of the TCAs, or interfere with sexual function like the SSRIs. -Increased appetite and weight gain frequently occur	

		at 5-HT2 receptors.				
	Nefazodone Trazodone	-weak inhibitors of serotonin reuptake. -Their therapeutic benefit appears to be related to their ability to block postsynaptic 5-HT2a receptors.	-Trazodone is commonly used off-label for the management of insomnia. -Trazodone has been associated with priapism, and nefazodone has been associated with a risk for hepatotoxicity.		Both agents also have mild to moderate α1 receptor antagonism, contributing to orthostasis and dizziness.	
	Vilazodone	Vilazodone is a serotonin reuptake inhibitor and a 5-HT1a partial agonist			The adverse effect profile of vilazodone is similar to the SSRIs, including a risk for discontinuation syndrome if abruptly stopped.	
	Vortioxetine	Vortioxetine utilizes a combination of serotonin reuptake inhibition, 5-HT1a agonism, and 5-HT3 and 5-HT7 antagonism	Treat depression		The common adverse effects include nausea, vomiting, and constipation, which may be expected due to its serotonergic mechanisms	
Tricyclic anti depressants (TCAs)	Amitriptyline Amoxapine Clomipramine Desipramine Doxepin Imipramine Maprotiline Nortriptyline Protriptyline Trimipramine	- TCAs block norepinephrine and serotonin reuptake into the presynaptic neuron -TCAs also block serotonergic, α-adrenergic, histaminic, and muscarinic receptors. -Amoxapine also	-The TCAs elevate mood, improve mental alertness, increase physical activity, and reduce morbid preoccupation in 50% to 70% of individuals with major depression. -TCAs are effective in treating moderate to severe depression. -Some patients with panic disorder also respond to TCAs.	-The onset of the mood elevation is slow, requiring 2 weeks or longer	-Blockade of muscarinic receptors leads to blurred vision, xerostomia (dry mouth), urinary retention, sinus tachycardia, constipation, and aggravation of angle-closure glaucoma -These agents affect cardiac conduction similarly to quinidine and may precipitate life-threatening arrhythmias in	-readily penetrate into the CNS. -should be used with caution in patients with bipolar disorder, even during their depressed state, because antidepressants may cause a

		blocks 5-HT2 and dopamine D2 receptors	- Imipramine has been used to control bed-wetting in children older than 6 years of age; however, it has largely been replaced by desmopressin and nonpharmacologic treatments (enuresis alarms). - The TCAs, particularly amitriptyline, have been used to help prevent migraine headache and treat chronic pain syndromes (for example, neuropathic pain) in a number of conditions for which the cause of pain is unclear. - Low doses of TCAs, especially doxepin, can be used to treat insomnia.		an overdose situation. - The TCAs also block α-adrenergic receptors, causing orthostatic hypotension, dizziness, and reflex tachycardia. - Imipramine is the most likely, and nortriptyline the least likely, to cause orthostatic hypotension. - Sedation may be prominent, especially during the first several weeks of treatment, and is related to the ability of these drugs to block histamine H1 receptors. - Weight gain is a common adverse effect of the TCAs. - Sexual dysfunction occurs in a minority of patients, and the incidence is lower than that associated with the SSRIs	switch to manic behavior. -TCAs have a narrow therapeutic index (for example, five- to sixfold the maximal daily dose of imipramine can be lethal). -TCAs may exacerbate certain medical conditions, such as benign prostatic hyperplasia, epilepsy, and preexisting arrhythmias
Monoamine Oxidase Inhibitors (MAOIs)	Isocarboxacid Phenelzine Selegiline Tranylcypromine	The MAOIs may irreversibly or reversibly inactivate the enzyme MAO, permitting neurotransmitters to escape degradation and, therefore, to accumulate within the presynaptic neuron and leak into the synaptic space.	-Selegiline is also used for the treatment of Parkinson's disease. It is the only antidepressant available in a transdermal delivery system - The MAOIs are indicated for depressed patients who are unresponsive or allergic to TCAs and SSRIs or who experience strong anxiety. - A special subcategory of depression, called atypical depression, may respond		- Selegiline and tranylcypromine have an amphetamine-like stimulant effect that may produce agitation or insomnia. - Individuals receiving a MAOI are unable to degrade tyramine obtained from the diet. Tyramine causes the release of large amounts of stored catecholamines from nerve terminals, resulting in a hypertensive crisis, with signs and symptoms such as occipital	-Use of MAOIs is limited due to the complicated dietary restrictions required while taking these agents -SSRIs should not be coadministered with MAOIs. -Both SSRIs and MAOIs require a washout period of

		These drugs inhibit not only MAO in the brain but also MAO in the liver and gut that catalyzes oxidative deamination of drugs and potentially toxic substances, such as tyramine, which is found in certain foods. The MAOIs, therefore, show a high incidence of drug–drug and drug–food interactions.	preferentially to MAOIs.		headache, stiff neck, tachycardia, nausea, hypertension, cardiac arrhythmias, seizures, and, possibly, stroke. Patients must, therefore, be educated to avoid tyramine-containing foods. (Phentolamine and prazosin are helpful in the management of tyramine-induced hypertension.) - Other possible side effects of treatment with MAOIs include drowsiness, orthostatic hypotension, blurred vision, dry mouth, and constipation.	at least 2 weeks before the other type is administered, with the exception of fluoxetine, which should be discontinued at least 6 weeks before a MAOI is initiated
Tx OF MANIA AND BIPOLAR DISORDERS	Lithium		-Lithium salts are used acutely and prophylactically for managing bipolar patients. - Lithium is effective in treating 60% to 80% of patients exhibiting mania and hypomania.		-. Common adverse effects may include headache, dry mouth, polydipsia, polyuria, polyphagia, GI distress (give lithium with food), fine hand tremor, dizziness, fatigue, dermatologic reactions, and sedation. - Adverse effects due to higher plasma levels may indicate toxicity and include ataxia, slurred speech, coarse tremors, confusion, and convulsions. - Thyroid function may be decreased and should be monitored.	- The therapeutic index of lithium is extremely low, and lithium salts can be toxic. -Unlike other mood stabilizers, lithium is renally eliminated, and though caution should be used when dosing this drug in renally impaired patients, it may be the best choice in patients with hepatic impairment.

	OTHER DRUGS Carbamazepine Lamotrigine Valproic acid		- approved as mood stabilizers for bipolar disorder.			

Monoamine oxidase (MAO) is a mitochondrial enzyme found in nerve and other tissues, such as the gut and liver. In the neuron, MAO functions as a “safety valve” to oxidatively deaminate and inactivate any excess neurotransmitters e.g. norepinephrine, dopamine, and serotonin that may leak out of synaptic vesicles when the neuron is at rest.