

## The Treatment of Depression

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## Principles of Depression

- Affects almost 7% of the population
- Fourth leading cause of disease burden worldwide
- 15% of the population with MDD commit suicide
- Up to two thirds of patients have another episode within one year

## MDD

- Patients are under diagnosed due poor recognition of symptoms by themselves or staff
- Stopping medication due to side effects or perceived need to decrease dose leads to failure on therapy
- Up to 2/3 of patients do not find adequate relief even after trying several antidepressants according to STAR D study

## STAR-D Study

- Studied group of patients with MDD
- Premise: find most successful therapy (ies)
- Interesting findings

## Characteristics of Depression


- Five or more symptoms present nearly every day during same 2 week period:
  - A. Depressed mood
  - B. Markedly diminished interest or pleasure
  - C. Significant change in weight or appetite
  - D. Insomnia or hypersomnia
  - E. Fatigue or loss of energy
  - F. Feeling of worthlessness or excessive or inappropriate guilt

## Characteristics of Depression

- Five or more symptoms
  - G. Decreased ability to think or concentrate, or inability to make decisions
  - H. Recurrent thought of death, or thoughts of suicide

	<h2>Major Types of Depression</h2>
	<ul style="list-style-type: none"> <li>■ MDD</li> <li>■ Dysthymic Disorder</li> <li>■ Adjustment disorder with depressed mood</li> <li>■ Bipolar disorder</li> <li>■ SAD</li> <li>■ Depression related to hormone imbalance</li> </ul>


	<h2>Characteristics of Depression</h2>
	<ul style="list-style-type: none"> <li>■ Symptoms cause clinically significant distress or impairment in social and/or occupational functioning</li> <li>■ Symptoms need to be evaluated as not to be due to substance abuse or medical conditions</li> <li>■ Symptoms should not be better attributed to normal bereavement patterns</li> </ul>

	<h2>What does this look like?</h2>
	<ul style="list-style-type: none"> <li>■ In persons with I/DD, depressed mood may be described by others as irritable, grouchy, assaultive, self injurious behavior, spitting, yelling, swearing, property destruction or increase in ritualistic behaviors</li> <li>■ Facial expressions: sad, not able to show animation or smile</li> <li>■ Crying or if severe disease unable to cry</li> </ul> 


	<h2>What does this look like?</h2>
	<ul style="list-style-type: none"> <li>■ Neglect of personal appearance: untidy clothes, uncombed hair</li> <li>■ Body movements and voice: hesitant or delayed</li> <li>■ Poverty of speech: how long it takes and little comes out, sparse, long pauses</li> <li>■ Slowness of mental activity</li> <li>■ Anxious or agitated depression: restlessness, hand wringing, signs of tension such as scratching and picking at the skin</li> </ul>

	<h2>What does this look like?</h2>
	<ul style="list-style-type: none"> <li>■ Pessimism</li> <li>■ Low self esteem</li> <li>■ Expecting the worst and negative expectations</li> <li>■ Self blame</li> <li>■ Difficulty in making decisions</li> <li>■ Body aches and pains</li> <li>■ Weakness and fatigue</li> </ul>

	<h2>What does this look like?</h2>
	<ul style="list-style-type: none"> <li>■ Sleeping too much or too little</li> <li>■ Not wanting to eat</li> <li>■ Not wanting to be involved in activities or workshop</li> <li>■ Isolation</li> <li>■ Slowness of body functions such as salivation, bowel activity and menses</li> <li>■ Early wakening and feeling of exhaustion in the morning</li> </ul>

<b>Depressing Drugs</b>	
<ul style="list-style-type: none"> <li>■ Anticonvulsants</li> <li>■ Barbiturates</li> <li>■ Benzodiazepines</li> <li>■ Beta blockers</li> <li>■ Calcium channel blockers</li> <li>■ Corticosteroids</li> <li>■ Hormones</li> <li>■ Levodopa and amantadine</li> <li>■ Zovirax</li> </ul>	

<b>Depressing Diseases</b>	
<ul style="list-style-type: none"> <li>■ Asthma</li> <li>■ Cancer</li> <li>■ Chronic fatigue syndrome</li> <li>■ Coronary artery disease and heart attacks</li> <li>■ Diabetes</li> <li>■ Parkinson's Disease</li> </ul>	

<b>Definitions</b>	
<ul style="list-style-type: none"> <li>■ Neurons</li> <li>■ Axon</li> <li>■ Dendrite</li> <li>■ Synthesis (from food we eat)</li> <li>■ Neurotransmitters (DA, NE, Ser)</li> <li>■ Storage Vesicle (store and protect)</li> <li>■ Synapse</li> <li>■ Pre-synaptic (autoreceptors)</li> <li>■ Post-synaptic receptors</li> <li>■ Reuptake mechanism</li> </ul>	

<b>Neurotransmitters</b>	
<ul style="list-style-type: none"> <li>■ Serotonin: problems with serotonin are associated with depressed mood, anxiety, insomnia, OCD, SAD, and violence <ul style="list-style-type: none"> <li>- 5HT-1A and 5HT-2A</li> </ul> </li> </ul>	

<b>Neurotransmitters</b>	
<ul style="list-style-type: none"> <li>■ Dopamine: Disruption in dopamine related to problems with attention, motivation, alertness, increased apathy, and difficulty in experiencing pleasure</li> <li>■ D2</li> </ul>	

<b>Neurotransmitters</b>	
<ul style="list-style-type: none"> <li>■ Norepinephrine: disorders in norepinephrine are associated with lack of energy, decreased alertness, and lethargy</li> <li>■ GABA: major calmative neurotransmitter</li> </ul>	

<b>Chemicals as Neurotransmitters</b>	
	<ul style="list-style-type: none"> <li>■ It should be found in pre-synaptic neurons</li> <li>■ Enzymes necessary for its synthesis must be found in the neuron</li> <li>■ There should be a mechanism for terminating its action</li> <li>■ Direct action post-synaptically should be equivalent to stimulation of the pre-synaptic neuron</li> </ul>


<b>Chemicals as Neurotransmitters</b>	
	<ul style="list-style-type: none"> <li>■ When the pre-synaptic neuron is stimulated, the synaptic cleft should contain the neurotransmitter</li> <li>■ Drugs interfering with the synthesis or reaction at the postsynaptic membrane should block the effects of pre-synaptic stimulation</li> <li>■ Drugs blocking the action of the inactivating enzyme should prolong the transmitter's action</li> </ul>

<b>Antidepressants</b>	
	<ul style="list-style-type: none"> <li>■ Why do they take so long to work effectively and maximally? <ul style="list-style-type: none"> <li>- If you understand preceding slide you understand why it may take 4-6 weeks prior to activation</li> <li>- No dosage changes sooner than this (with exception of mine based on experience only!)</li> </ul> </li> </ul>

<b>Mechanisms of Action</b>	
	<ul style="list-style-type: none"> <li>■ May prevent reuptake of the neurotransmitter</li> <li>■ May affect degradation enzymes</li> <li>■ May work pre-synaptically</li> <li>■ May work post-synaptically</li> <li>■ May involve one or more neurotransmitters</li> </ul>

<b>Medications</b>	
	

<b>Tricyclic Antidepressants</b>	
	<ul style="list-style-type: none"> <li>■ The most widely used class of antidepressants prior to SSRI class</li> <li>■ More general effects on neurotransmitters, less refined</li> <li>■ Out of favor because overdose can be fatal</li> <li>■ May be prescribed when other classes have not worked</li> </ul>

<b>Tricyclic Side Effects</b>	
<ul style="list-style-type: none"> <li>■ Orthostatic hypotension (watch elderly)</li> <li>■ Weight gain</li> <li>■ Dry mouth</li> <li>■ Blurred vision</li> <li>■ Constipation</li> <li>■ Sweating</li> <li>■ Sexual dysfunction</li> </ul>	

<b>Tricyclics</b>	
<ul style="list-style-type: none"> <li>■ Anafranil (chlomipramine) 75-300mg</li> <li>■ Ascendin (amoxapine) 150-600mg</li> <li>■ Elavil (amitriptyline) 75-300mg</li> <li>■ Ludiomil (maprotiline) 75-225mg</li> <li>■ Norpramin (desipramine) 75-300mg</li> <li>■ Pamelor (nortriptyline) 50-150mg</li> <li>■ Sinequan (doxepin) 150-300mg</li> <li>■ Surmontil (trimipramine) 75-300mg</li> <li>■ Tofranil (imipramine) 75-300mg</li> <li>■ Vivactil (protriptyline) 15-60mg</li> </ul>	

<b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b>	
<ul style="list-style-type: none"> <li>■ Came on the market in 1980s</li> <li>■ The most popular antidepressant <ul style="list-style-type: none"> <li>– Side effects are less severe than older agents</li> <li>– Consequences of overdose are less severe</li> </ul> </li> <li>■ Often first choice in antidepressant</li> </ul>	

<b>SSRI Usage</b>	
<ul style="list-style-type: none"> <li>■ Major depressive disorder</li> <li>■ Dysthymia</li> <li>■ SAD</li> <li>■ Mixed depression and anxiety</li> <li>■ Anxiety related disorders</li> <li>■ Premenstrual syndrome</li> <li>■ Eating disorders</li> <li>■ Some types of chronic pain</li> </ul>	

<b>SSRIs Pharmacology</b>	
<ul style="list-style-type: none"> <li>■ They “clog the pump” which normally tells first neuron to pump some of the released serotonin back into the cell as a measure of checks and balances</li> <li>■ Therefore increased amount of serotonin hangs out in the synapse available for usage</li> <li>■ Takes 1-4 weeks to become effective, 4-6 weeks before true evaluation of effectiveness</li> <li>■ No dosage or drug changes should take place sooner than 1 month</li> </ul>	

<b>SSRIs Side Effects</b>	
<ul style="list-style-type: none"> <li>■ Increased anxiety</li> <li>■ Fatigue</li> <li>■ Upset stomach</li> <li>■ Insomnia</li> <li>■ Apathy</li> <li>■ Lack of sexual interest</li> <li>■ Inability to obtain orgasm</li> </ul>	

<b>SSRIs Side Effects</b>	
	<ul style="list-style-type: none"> <li>■ Dizziness</li> <li>■ Sweating</li> <li>■ Tremors</li> <li>■ Dry mouth</li> <li>■ Headache</li> <li>■ Weight loss</li> <li>■ Weight gain</li> </ul> <p>■ Side effects worse during the first couple of weeks and diminish with time</p>

<b>Monitoring Medications</b>	
	<ul style="list-style-type: none"> <li>■ Seldom if ever are blood levels necessary or recommended</li> <li>■ Evaluation of effectiveness based on clinical picture</li> <li>■ Evaluate potential side effects and make specific comment(s) on whether they appear, to what extent, and precautions taken to counter side effects</li> <li>■ Discuss troublesome side effects with clinician</li> </ul>

<b>SSRI cautions</b>	
	<ul style="list-style-type: none"> <li>■ Bipolar disease and increased activation of manic state</li> <li>■ Abrupt discontinuation: flu-like symptoms, vivid dreams and problems with sleep</li> <li>■ Black Box Warning for children and adolescents</li> <li>■ Avoid MAOIs</li> </ul>

<b>SSRIs</b>	
	<ul style="list-style-type: none"> <li>■ Celexa (citalopram) usual dosage 10-60mg, may have fewer interactions with other drugs, and not particularly stimulating or sedating</li> <li>■ Lexapro (Escitalopram) usual dosage 10-20mg, chemically similar to Celexa, may work faster</li> </ul>

<b>SSRIs</b>	
	<ul style="list-style-type: none"> <li>■ Luvox ( fluoxetine) usual dosage 50-300mg, generally more sedating than the others, the first to be approved for OCD</li> <li>■ Paxil (paroxetine) usual dosage 20-60mg somewhat sedating, more drug interactions, weight gain, an more pronounced withdrawal symptoms</li> <li>■ Paxil CR usual dosage 12.5-62.5mg</li> </ul>

<b>SSRIs</b>	
	<ul style="list-style-type: none"> <li>■ Prozac (fluoxetine) usual dosage 10-80mg, stimulating, may cause insomnia if taken late in the day, some report increase in anxiety, least withdrawal symptoms due to liver enzyme inhibition, but more drug interactions</li> <li>■ Zoloft (sertraline) usual dosage 50-200mg not as stimulating or sedating</li> </ul>

	<p><b>Serotonin / Norepinephrine Reuptake Inhibitors (SNRIs)</b></p> <ul style="list-style-type: none"> <li>■ Cymbalta (duloxetine) usual dosage 30-120mg, although seldom effective &gt;60mg, often used for pain</li> <li>■ Effexor (venlafaxine) usual dosage 75-375mg may have quicker action so good for severe depression, fewer drug interactions than most, may increase blood pressure in higher dosages</li> <li>■ Effexor XR as above</li> </ul>
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	<p><b>Serotonin-2 antagonists Reuptake Inhibitors (SARIs)</b></p> <ul style="list-style-type: none"> <li>■ Desyrel (trazodone) usual dosage 150-400mg sedating side effects, used mostly along with other antidepressants as a sleep aid</li> <li>■ Serzone (nafazodone) usual dosage 100-600mg may be sedating and help with anxiety 1 case liver failure resulting in death / transplant 250,000-300,000pt yrs, avoid if active liver disease</li> </ul>
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	<p><b>Noradrenergic / specific Serotonergic antidepressant (NaSSA)</b></p> <ul style="list-style-type: none"> <li>■ Enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors</li> <li>■ Remeron (mirtazapine) usual dosage 15-45mg help when insomnia is a problem, may cause weight gain</li> </ul>
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	<p><b>Norepinephrine / Dopamine Reuptake Inhibitor (NDRI)</b></p> <ul style="list-style-type: none"> <li>■ Welbutrin (bupropion) usual dosage 150-450mg less likely to cause weight gain or sexual dysfunction, may initially increase anxiety, not for those with seizures</li> <li>■ Welbutrin SR (2 x daily dosing)</li> <li>■ Welbutrin XL (1 x daily dosing)</li> </ul>
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	<p><b>MAO Inhibitors</b></p> <ul style="list-style-type: none"> <li>■ First antidepressants marketed</li> <li>■ Discovered in the 1950's serendipitously by chemist looking for treatment for TB</li> </ul>
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	<p><b>MAO Pharmacology</b></p> <ul style="list-style-type: none"> <li>■ Monoamine: neurotransmitters</li> <li>■ Oxidase: enzyme that breaks down monoamines</li> <li>■ MAO inhibitors: destroy this enzyme</li> <li>■ Allow for increased amount of neurotransmitters</li> <li>■ Work on norepinephrine, dopamine and serotonin</li> </ul>
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	<b>MAO I side effects</b>
	<ul style="list-style-type: none"> <li>■ Dangerous sudden increase in blood pressure which may lead to death, cerebral hemorrhage</li> <li>■ Avoid tyramine, which also increases blood pressure</li> <li>■ Tyramine is a natural substance found in the body and food products, tyramine forms as proteins break down as they age</li> </ul>

	<b>Foods with Tyramine</b>
	<ul style="list-style-type: none"> <li>■ Aged sausages</li> <li>■ Beer</li> <li>■ Red wine</li> <li>■ Avocados</li> <li>■ Aged cheese</li> <li>■ Smoked fish</li> <li>■ Soy products</li> </ul>

	<b>Drug Interactions</b>
	<ul style="list-style-type: none"> <li>■ Other antidepressants</li> <li>■ Most drugs for colds and asthma</li> <li>■ Drugs for the treatment of diabetes</li> <li>■ Blood pressure medications</li> <li>■ Some pain killers</li> </ul>

	<b>MAO Inhibitors</b>
	<ul style="list-style-type: none"> <li>■ Marplan (isocarboxazid) 10-40mg</li> <li>■ Nardil (phenelzine) 45-90mg</li> <li>■ Parnate (tranylcypromine) 30-60mg</li> <li>■ Emsam patch (selegiline transdermal) bypasses the GI tract, and at 6 and 9mg no dietary restrictions, but use tyramine free diet at 12 mg</li> </ul>

	<b>Antipsychotics</b>
	<ul style="list-style-type: none"> <li>■ Abilify (aripiprazole) 5-10mg, start at 2mg and increase to 5mg then 10mg, then 15 or 20mg as needed</li> <li>■ Adjunctive treatment for major depressive disorder</li> <li>■ Has minimal tendency to cause weight gain, metabolic side effects, sedation or movement disorders</li> <li>■ Side effects and drug interactions: see atypical antipsychotics</li> </ul>

	<b>Questions?</b>
	

	<b>Contact Information</b>
	<ul style="list-style-type: none"><li>■ Nanette R Wrobel, RPh <a href="mailto:Nwrobel@palrx.com">Nwrobel@palrx.com</a> Pharmacy Alternatives</li><li>or Come by our booth for a card</li><li>or I have been a member and attending DDNA conferences for 16 years, so DDNA national has my contact information as well</li></ul>