Chapter 30

Antidepressant agents
Major depressive disorder (MDD) is characterized by depressed mood most of the time for at least 2 weeks and/or loss of interest or pleasure in most activities. In addition, depression is characterized by disturbances in sleep and appetite as well as deficits in cognition and energy. Thoughts of guilt, worthlessness, and suicide are common.

Major depression is commonly associated with a variety of medical conditions—from chronic pain to coronary artery disease. Coronary artery disease, diabetes, and stroke appear to be more common in depressed patients, and depression may considerably worsen the prognosis for patients with a variety of comorbid medical conditions.
2. Pathophysiology of Major Depression

A. Neurotrophic Hypothesis

- Decrease of brain-derived neurotrophic factor (BDNF) in association with stress and pain
- Loss of volume in structures such as the hippocampus in patients
- BDNF into the midbrain, hippocampus, and lateral ventricles of rodents has an antidepressant-like effect in animal models
- All known classes of antidepressants are associated with an increase in BDNF levels in animal models with chronic administration
2. Pathophysiology of Major Depression

B. Monoamines and other neurotransmitters

- A deficiency in the amount or function of cortical and limbic serotonin (5-HT), norepinephrine (NE), and dopamine (DA).

- All classes of antidepressants appear to enhance the synaptic availability of 5-HT, norepinephrine, or dopamine.
2. Pathophysiology of Major Depression

B. Monoamines and other neurotransmitters
2. Pathophysiology of Major Depression

C. Neuroendocrine

- Abnormalities in the HPA axis in patients with MDD.

- MDD is associated with elevated cortisol levels

- Both exogenous glucocorticoids and endogenous elevation of cortisol are associated with mood symptoms and cognitive deficits similar to those seen in MDD.
3. Basic Pharmacology of Antidepressants

A. Selective Serotonin Reuptake Inhibitors (SSRIs)

- SSRIs are the most common antidepressants in clinical use
- Major depression
- Panic disorder, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD) and Pain disorders
3. Basic Pharmacology of Antidepressants

B. Serotonin-norepinephrine Reuptake Inhibitors

- SNRIs: venlafaxine, and duloxetine

- Tricyclic Antidepressants (TCAs)

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![Diagram](image)
3. Basic Pharmacology of Antidepressants

C. 5-HT\textsubscript{2} Antagonists

5-HT\textsubscript{2} antagonists at the 5-HT2 receptor:

- trazodone and nefazodone

for Major Depression and Anxiety Disorders
3. Basic Pharmacology of Antidepressants

D. Tetracyclic and unicyclic antidepressants

Functions similar to TCAs, at the present time, TCAs and Tetracyclic antidepressants are used primarily in depression that is unresponsive to more commonly used antidepressants such as the SSRIs or SNRIs.
4. Clinical Pharmacology of Antidepressants

A. Clinical Indications

- **DEPRESSION**
  - Recurrence in a lifetime (approximately 85%)
  - Long-term maintenance treatment if they have had two or more serious MDD episodes in the previous 5 years or three or more serious episodes in a lifetime.

- **ANXIETY DISORDERS**
  - A number of SSRIs and SNRIs have been approved for all the major anxiety disorders, including PTSD, OCD, social anxiety disorder, GAD, and panic disorder.

- **PAIN DISORDERS**
  - Medications that possess both norepinephrine and 5-HT reuptake blocking properties are often useful in treating pain disorders.

- **PREMENSTRUAL DYSPHORIC DISORDER**

- **SMOKING CESSATION**

- **EATING DISORDERS**
  - Antidepressants appear to be helpful in the treatment of bulimia but not anorexia.
4. Clinical Pharmacology of Antidepressants

B. Adverse Effects

- **Selective Serotonin Reuptake Inhibitors**
  - **Gastrointestinal symptoms**: Increased serotonergic activity in the gut is commonly associated with nausea, gastrointestinal upset, diarrhea

- **Serotonin-Norepinephrine Reuptake Inhibitors and Tricyclic Antidepressants**
  - **Gastrointestinal symptoms as SSRI**
  - **Increased blood pressure and heart rate**
  - **CNS activation**: insomnia, anxiety, and agitation.

- **5-HT2 Antagonists**
  - sedation and gastrointestinal disturbances
4. Clinical Pharmacology of Antidepressants

C. Overdose

- The most common method used in suicide attempts, and antidepressants, especially the TCAs, are frequently involved.

- Induction of lethal arrhythmias, including ventricular tachycardia and fibrillation. In addition, blood pressure changes and anticholinergic effects including altered mental status and seizures.
The End

Thank You