Learning Objectives
- Identify principal anti-anxiety agents and describe mechanism of action, therapeutic effects and adverse effects; compare advantages and disadvantages between classes

Overview
- Anxiety disorders are the most common mental illness in the US (~15% of adults are affected)
  - “Normal” anxiety: feeling of alarm or worry, short term, does not impair function
  - “Abnormal” anxiety: prolonged, affects function (i.e. social and/or work life)

Categories of Anxiety
- Acute Stress Disorder
- Generalized anxiety disorder (GAD)
- Anxiety disorder due to medical condition or substance-induced

Anxiety Disorders:
- Specific Phobia
- Panic disorder
- Agoraphobia
- Social anxiety disorder (phobia)
- Post traumatic stress disorder (PTSD)
- Obsessive compulsive disorder (OCD)

Drugs used to treat anxiety
- Benzodiazepines: Potentials GABA via BZ binding site associated with GABA<sub>a</sub> receptor
- Azapirone (e.g., buspirone): 5-HT<sub>1A</sub> receptor partial agonist
- Antidepressants
  - Tricyclic
  - Selective 5-HT re-uptake inhibitors (SSRI)
  - Other: e.g. venlafaxine
- Monoamine Oxidase Inhibitors
- Beta-Blockers
  - β Adrenergic receptors central and peripheral, sympathetic response

Benzodiazepines
- Mechanism: Benzodiazepines do not directly activate the receptor/channel, but increase the frequency of Cl<sup>-</sup> channel opening produced by GABA
- Safety probably results from binding properties: benzodiazepines do not have an effect on their own, but require GABA.

![Diagram of benzodiazepine effects](image)
Benzodiazepine drugs

Anxiety:
- Alprazolam (Xanax) intermediate
- Diazepam (Valium) long-acting
- Lorazepam (Ativan) intermediate

Benzodiazepines: Therapeutic uses
- Anxiety: general anxiety and panic disorders
- Pre-surgical

Major Side Effects of Benzodiazepines
- CNS depression: fatigue, drowsiness, muscle weakness, ataxia
- Potentiates effects of other CNS depressants
- Tolerance and Dependence

Respiration: hypnotic doses of benzodiazepines don’t depress respiration, although higher doses may have some effects. Care should be taken in children, those with impaired liver or lung function; may have additive effects with other CNS depressants such as opioids or alcohol

Cardiovascular: orthostatic hypotension, tachycardia

Buspirone (Buspar)
- Mechanism: 5-HT1A agonist
- No hypnotic, anti-convulsant or muscle relaxant effects
- Advantages: minimal abuse liability, no tolerance or dependence
- Does not potentiate effects of CNS depressants
- No sedation or impairment of performance
- No cross-tolerance with BZs
- No tolerance or withdrawal
- No abuse potential
- Disadvantages: Requires approx. a week to become effective
- Therapeutic use: Indicated for GAD
- Useful as SSRI augmentation for panic, social phobia, depression
- Adverse Effects: Nausea, Headache, Insomnia, nervousness, Restlessness, Dizziness, lightheadedness

Selective Serotonin Re-uptake Inhibitors
- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)
- Dosing for OCD is higher than for depression
- Once daily dosing

Serotonin-Norepinephrine Reuptake Inhibitor
- Venlafaxine XR (Effexor-XR) 75-300 mg/d
- Indicated for GAD; effective for panic disorder, social phobia, PTSD, OCD
- Typical side effects
- GI distress, jitteriness, headaches, sexual disturbance
- Non-addicting

Beta-adrenergic antagonists (propranolol): used for situational or social phobias with autonomic symptoms
- Physiologic component of anxiety:
- Tachycardia, palpitations, tremor, sweating
- No CNS depression
- Non-addicting, no drowsiness
- Do not use in asthma, diabetes;
- Monitor BP, pulse
- Helpful for performance anxiety:
  - Propranolol 10 mg prn

MAO inhibitors
- Inhibits the degradation of catecholamines and serotonin
- Side effects: light-headedness, neurological symptoms, weight gain, sexual dysfunction, edema
- Dietary restrictions/Hypertensive crisis; “cheese reaction”
- Risk of lethal overdose and toxicity
- Generally reserved for refractory cases
- Efficacy: Best for Panic Disorders and Social Phobias

ANTIANXIETY AGENTS

<table>
<thead>
<tr>
<th>Generic Names</th>
<th>Trade Names</th>
<th>Daily Dosage (mg/day)</th>
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<tbody>
<tr>
<td>BENZODIAZEPINES</td>
<td></td>
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</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Librium, others</td>
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<td>Diazepam</td>
<td>Valium, others</td>
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<td>Oxazepam</td>
<td>Serax, others</td>
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<tr>
<td>Chlorazepate</td>
<td>Tranxene, others</td>
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<td>Lorazepam</td>
<td>Ativan</td>
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<td>Centrax</td>
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<td>Alprazolam</td>
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<td>AZAPIRONES</td>
<td>Buspirone</td>
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<td>ANTIDEPRESSANTS</td>
<td>SSRI</td>
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<td>Venlafaxine</td>
<td>Effexor</td>
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<td>Drug</td>
<td>Generalized Panic disorder</td>
<td>Social phobia (generalized)</td>
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<td>Bzs</td>
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<tr>
<td>Beta blockers</td>
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