

"Psychiatry for USMLE"

Section 3: Pharmacology

Psychotherapy Approaches

| Type | Mechanism / Use |
|--------------------------------------|--|
| Behavioral therapy | Change maladaptive behaviors (e.g., systematic desensitization) |
| Cognitive behavioral therapy (CBT) | Identify distorted thoughts, improve coping, emotional control (alcohol triggers, anxiety, depression) |
| Dialectical behavioral therapy (DBT) | Borderline personality disorder, emotion regulation |
| Interpersonal therapy | Improve interpersonal relationships and communication |

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| Motivational interviewing | Resolve ambivalence, enhance intrinsic motivation (substance use, weight loss) |
| Supportive therapy | Provide empathy, maintain hope/optimism |

⚡ CNS Stimulants

- Drugs: Methylphenidate, dextroamphetamine, methamphetamine, lisdexamfetamine
 - Mechanism: ↑ catecholamines (dopamine, norepinephrine) in synaptic cleft
 - Clinical Use: ADHD, narcolepsy, binge-eating disorder
 - Adverse Effects: Nervousness, agitation, insomnia, anorexia, tachycardia, hypertension, tics, weight loss
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🧩 Antipsychotics

Classification & Mechanism

| Class | Drugs | Mechanism | Notes |
|-----------------------|--|--|---|
| Typical (1st-gen) | Haloperidol, Pimozide, Trifluoperazine, Fluphenazine, Thioridazine, Chlorpromazine | D2 receptor blockade | Primarily treat positive symptoms of schizophrenia; high EPS risk; high-potency = more neurologic SEs; low-potency = more anti-HAM |
| Atypical (2nd-gen) | Clozapine, Olanzapine, Risperidone, Quetiapine, Aripiprazole, etc. | D2 + 5-HT ₂ blockade; Aripiprazole = D2 partial agonist | Treat positive & negative symptoms; clozapine for treatment-resistant cases or suicidality |

Clinical Use

- Schizophrenia, bipolar disorder with psychosis, Tourette syndrome, OCD, Huntington disease
- Clozapine: treatment-resistant psychosis, persistent suicidality

Adverse Effects

- Anti-HAM: Sedation, dry mouth, constipation, orthostatic hypotension
- Metabolic: Weight gain, dyslipidemia, hyperglycemia (especially clozapine, olanzapine)
- Endocrine: Hyperprolactinemia → galactorrhea, oligomenorrhea, gynecomastia
- Cardiac: QT prolongation
- Neurologic: EPS (ADAPT), NMS
- Ophthalmologic: Corneal deposits (chlorpromazine), retinal deposits (thioridazine)
- Hematologic / Others: Clozapine → agranulocytosis, seizures, myocarditis

Extrapyramidal Symptoms (EPS) – ADAPT

| Timeframe | Type | Treatment |
|------------|--|------------------------------|
| Hours–days | Acute dystonia (spasms, oculogyric crisis) | Benztropine, diphenhydramine |

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| Days-months | Akathisia (restlessness) | β -blockers, benztropine, benzodiazepines |
| Days-months | Parkinsonism (bradykinesia, rigidity) | Benztropine, amantadine |
| Months-years | Tardive dyskinesia (chorea, orofacial) | Benzos, botulinum toxin, valbenazine, deutetrabenazine |

Lithium

- Mechanism: Modulates neurotransmission (\downarrow excitatory, \uparrow inhibitory) and second messengers (G proteins).
- Clinical Use: Mood stabilizer for bipolar disorder (acute mania & relapse prevention).
- Adverse Effects (LiTHIUM mnemonic):
 - L \rightarrow Low thyroid (hypothyroidism)

- I → Insipidus (nephrogenic diabetes insipidus → polyuria)
 - T → Teratogenic (Ebstein anomaly)
 - H → Hypothyroidism (repeated for emphasis)
 - I → Increased calcium (mild hypercalcemia)
 - U → Unwanted movements (tremor)
 - Notes:
 - Narrow therapeutic window → monitor serum levels
 - Mostly renal excretion; reabsorbed at PCT via Na^+ channels
 - Drugs increasing toxicity: thiazides, ACE inhibitors, NSAIDs
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Buspirone

- Mechanism: Partial 5-HT_{1A} receptor agonist
- Clinical Use: Generalized anxiety disorder (non-sedating, non-addictive)

- Onset: 1-2 weeks
 - Advantages: No alcohol interaction (vs benzodiazepines)
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Antidepressants Overview

1. SSRIs (Selective Serotonin Reuptake Inhibitors)

- Drugs: Fluoxetine, Paroxetine, Sertraline, Fluvoxamine, Citalopram, Escitalopram
- Mechanism: Inhibit serotonin reuptake
- Clinical Use: Depression, GAD, panic disorder, OCD, bulimia, binge-eating, social anxiety, PTSD, premenstrual dysphoric disorder, premature ejaculation
- Adverse Effects: GI upset, sexual dysfunction, SIADH, serotonin syndrome, mania if bipolar

2. SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors)

- Drugs: Venlafaxine, Desvenlafaxine, Duloxetine, Levomilnacipran, Milnacipran
- Mechanism: Inhibit S-HT & NE reuptake
- Clinical Use: Depression, GAD, neuropathic pain (Duloxetine, Milnacipran → fibromyalgia), venlafaxine → social anxiety, panic, PTSD, OCD
- Adverse Effects: ↑ BP, insomnia, sedation, nausea, sexual dysfunction

3. Tricyclic Antidepressants (TCAs)

- Drugs: Amitriptyline, Nortriptyline, Imipramine, Desipramine, Clomipramine, Doxepin, Amoxapine
- Mechanism: Inhibit S-HT & NE reuptake
- Clinical Use: MDD, neuropathic pain, migraine prophylaxis, OCD (clomipramine), nocturnal enuresis (imipramine)
- Adverse Effects: Sedation, α 1-blocking effects → hypotension, anticholinergic → tachycardia, urinary retention, dry mouth; prolonged QT; 3° TCAs worse anticholinergic than 2°

- Toxicity (Tri-C's): Convulsions, Coma, Cardiotoxicity (Na⁺ channel blockade); treatment: NaHCO₃

4. MAO Inhibitors

- Drugs: Tranylcypromine, Phenelzine, Isocarboxazid, Selegiline (MAO-B selective)
- Mechanism: Nonselective MAO inhibition → ↑ NE, S-HT, dopamine
- Clinical Use: Atypical depression, anxiety, Parkinson disease (selegiline)
- Adverse Effects: CNS stimulation, hypertensive crisis (tyramine-rich foods)
- Contraindications: SSRIs, TCAs, St. John's wort, meperidine, dextromethorphan, pseudoephedrine, linezolid
- Notes: Wait 2 weeks after stopping MAOIs before starting serotonergic drugs or resuming normal diet

● Atypical Antidepressants

| Drug | Mechanism | Clinical Use | Key Adverse Effects / Notes |
|-------------|---|---|--|
| Bupropion | NE + DA reuptake inhibitor | MDD, smoking cessation | Stimulant effects: tachycardia, insomnia; seizures in bulimia/anorexia; ↓ sexual side effects & weight gain |
| Mirtazapine | $\alpha 2$ -antagonist → ↑ NE & S-HT; S-HT _{2/3} antagonist; H1 antagonist | MDD (esp. with insomnia/underweight) | Sedation, ↑ appetite & weight, dry mouth |
| Trazodone | S-HT ₂ , $\alpha 1$, H1 antagonist; weak S-HT reuptake inhibitor | Insomnia (antidepressant at high doses) | Sedation, nausea, priapism, orthostatic hypotension |
| Vilazodone | S-HT reuptake inhibitor + S-HT _{1A} partial agonist | MDD | Headache, nausea, diarrhea, anticholinergic; serotonin syndrome risk if combined with other serotonergic drugs |

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| Vortioxetine | S-HT reuptake inhibitor + S-HT1A agonist + S-HT3 antagonist | MDD | Nausea, sexual dysfunction, sleep disturbances, anticholinergic; serotonin syndrome risk if combined with other serotonergic drugs |
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Pharmacotherapy for Smoking Cessation

| Therapy | Mechanism | Key Points / Adverse Effects |
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| Nicotine Replacement Therapy (patch, gum, lozenge) | Nicotinic ACh receptor agonist | Relieves withdrawal; long-acting patch + short-acting forms can be combined; headache, oral irritation |
| Varenicline | Nicotinic ACh receptor partial agonist | Reduces withdrawal & reward effect; adverse: GI discomfort, sleep disturbance |

Medically Supervised Opioid Withdrawal / Relapse Prevention

| Drug | Mechanism / Use | Key Points / Adverse Effects |
|---------------|--|---|
| Methadone | Long-acting oral opioid agonist | Used for supervised withdrawal or maintenance therapy |
| Buprenorphine | Partial opioid agonist (sublingual film) | Suppresses withdrawal & maintenance; can precipitate withdrawal if given too soon after full agonist |
| Naloxone | Short-acting opioid antagonist | IM, IV, or nasal spray; reverses acute opioid overdose (respiratory & CNS depression) |
| Naltrexone | Long-acting oral opioid antagonist | Prevents relapse after detox; also helps alcohol/nicotine cessation and weight loss ("naltrexone for the long trex back to sobriety") |

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