

Name: Ethanol

Class: Alcohol

Mech.: Disordering of lipid memb. → perturbs fxns of ion-channels & other proteins. May augment GABA med. synaptic inhib & Cl⁻ influx. High conc → ↑ Cl⁻ permeability w/o GABA mediation.

Absorption: Rapidly, and usu. completely, absorbed from mouth, stomach, small intestine.

Dist.: Rel. uniform distribution throughout all tissues and fluids.

Metab.: 90-98% completely oxid. Zero order kinetics: 7-15 gram (1 drink)/hr. Mostly oxid. in liver by alcohol dehydrogenase. Resulting acetaldehyde oxid by mitoch. aldehyde dehydrog.

Excretion, t_{1/2}: 2-10% not oxidized (excreted via lungs and kidneys).

Tox./S.E.s: **CNS**—depressant (additive w/other depressants); **Heart**—↓ contractility, arrhythmia;

Smooth Musc—vasodilation. May inhib. metab. of other drugs. Resp. depression, hypoglycemia.

Chronic S.E.s: **Liver/GI**—liver fat accum, hepatitis, fibrosis, cirrhosis; ↑ gastric & pancreatic secretion & mucosal damage → ↑ risk of gastritis and pancreatitis, aggravation of PUD. **Nerv. sys**—symm. periph. nerve injury, memory loss, sleep disturbances, psychoses.

Blood—mild anemia (↓ prolif. of marrow cells), ↑ HDL/LDL ratio (↓ risk of CHD).

CV—cardiomyopathy, arrhythmia. **Fetal Alcohol Synd.** **Sex**—impotence, sterility, testicular atrophy, gynecomastia, ↓ estrogen metab. ↑ **Cancer risk**—mouth, pharynx, larynx, esophagus, liver, breast. **Alcohol W/drawal Synd.**

Utility: Solvent for drug admin., nerve blocking agent for pain relief, antidote for methanol and ethylene glycol poisoning.

Special Features: Induces cyt. P450. Acute tolerance can occur.

Name: Disulfiram (Antabuse)

Class: Aversive Agent

Mech.: Irreversibly inactivates aldehyde dehydrogenase.

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}: Effective for 2-3 days.

Toxicity/S.E.s: Dizziness, metallic taste, nausea, headache, skin reactions.

Utility: Used to treat alcoholism. When alcohol is ingested, blood acetaldehyde concentrations rise, producing hangover symptoms of flushing, headache, nausea, vomiting, and hypotension.

Special Features:

Name: Methylphenidate (Ritalin)

Class: CNS Stimulant

Mech.: CNS Mech. = Release of DA, NE, & 5HT from nerve terminals. Some blockade of reuptake of DA, NE, & 5HT. Weak inhib. of MAO. Produces elev. of mood, euphoria, ↑ alertness, ↓ sense of fatigue, ↓ food intake, periph. sympathomimetic effects.

Absorption: Oral → good bioavail.

Dist.: Crosses BBB.

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Irritability & manic behavior (large doses). Prolonged use → toxic psychosis (looks like paranoid schiz.). Produces psych dependence (depression on w/drawal). **C/I:** hyperthyroidism, mod-severe hypertension, hist. of drug abuse, glaucoma, hist. of hypersens. or idiosync. to sympathomimetic amines.

Utility: Treat ADHD, narcolepsy.

Special Features: Not metab. by COMT. Decreased metab. by MAO.

Name: Cocaine (Various)

Class: CNS Stimulant (Indirect Sympathomimetic Agent)/Local Anesth (Ester)

Mech.: Inhib. reuptake of catecholamines (DA, NE, 5HT) → prolonged action. Local anesthetic properties from block of Na⁺ & Ca²⁺ channels → ↓ rate of rise of action potential, failure to propagate action potential, eventual conduction block. Smaller, unmyelinated fibers are more easily blocked and remain blocked longer.

Absorption: : Rapidly absorbed IV & oral. IV absorption can be limited w/a vasoconstrictor. Rapid topical absorption at mucous membranes.

Dist.: Rapidly dist. to highly perfused organs (i.e., brain, liver, kidney, heart)

Metab.: Rapidly metab. by plasma pseudocholinesterases. Med. duration of anesth action.

Toxicity/S.E.s: Fever, nausea, vomiting, confusion, headache. Neurosis, paranoia, frank psychosis. Tolerance, but not as strong as opiates. Acute toxicity → hypertension, stroke, seizures, cardiac arrhythmias. Very strong psych. dependence. Mild physical dependence. W/drawal → ↑ appetite, fatigue, depression.

Utility: Used in ENT surgery to produce local anesthesia, hemostasis, vasoconstriction. Crack = smokable version.

Special Features: Does not require concomitant application of a vasoconstrictor. Twice the potency of procaine. Produces elevation of mood, euphoria, ↑ self-esteem, ↑ energy, ↓ sense of fatigue. Moderate dose → ↑ HR, ↑ BP.

Name: Dextroamphetamine (Dexedrine)**Class:** CNS Stimulant**Mech.:** CNS Mech = Release of DA, NE, & 5HT from nerve terminals. Some blockade of reuptake of DA, NE, & 5HT. Weak inhib. of MAO. Produces elev. of mood, euphoria, ↑ alertness, ↓ sense of fatigue, ↓ food intake, periph. sympathomimetic effects.**Absorption:** Oral → good bioavail.**Dist.:** Crosses BBB.**Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Irritability & manic behavior (large doses). Prolonged use → toxic psychosis (looks like paranoid schiz.). Produces very strong psych. dependence (depression on w/drawal), mild phys. dependence. **C/I:** hyperthyroidism, mod-severe hypertension, hist. of drug abuse, glaucoma, hist. of hypersens. or idiosync. to sympathomimetic amines.**Utility:** Treat narcolepsy, ADHD, short term Rx of exogenous obesity.**Special Features:** Not metab. by COMT. Decreased metab. by MAO.**Name: Caffeine****Class:** Xanthine**Mech.:** Mobilizes Ca²⁺ stores. Inhibition of phosphodiesterase → ↑ cAMP. Antagonizes adenosine receptors. Causes ↓ drowsiness, ↓ fatigue, faster/clearer thought flow, improved motor performance, ↓ reaction time, cardiac stim., bronchodilation, mild diuresis, gastric acid secretion.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Restlessness, insomnia, tremors, seizures, mild diuresis, cardiac stim., gastric acid secretion.**Utility:** OTC CNS stimulants.**Special Features:****Name: Strychnine****Class:** Convulsant**Mech.:** Competitive glycine receptor antagonism. ↑ neuron excitability due to selective block of inhib. impulses (i.e., interf. w/recurrent Renshaw cell inhib. at skeletal muscle motor neurons). Sim. to tetanus toxin.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Tightness of neck and jaw muscles. Symm. tonic convulsions (aggravated by sensory stim.). Resp. paralysis. Impaired resp. → hypoxia → medullary paralysis → death.**Utility:** Pesticide/rodenticide.**Special Features:** Treat poisoning w/IV diazepam, insulation from sensory input, and respiratory support.**Name: Doxapram (Dopram)****Class:** Analeptic**Mech.:** Direct stim. of medullary resp. centers → stimulation of respiration. May stim. resp. via reflex effect on periph. chemoreceptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Large doses → tonic-clonic seizures.**Utility:** Occasionally used to treat acute resp. failure assoc. w/COPD. Prev. used to treat resp. depression assoc. w/CNS depressant overdose. No longer recommended for this use due to high potential for seizures.**Special Features:**

Name: Procaine (Novocain)**Class:** Local Anesthetic (Ester)**Mech.:** Blocks Na^+ & Ca^{2+} channels \rightarrow \downarrow rate of rise of action potential, failure to propagate action potential, eventual conduction block. Smaller, unmyelinated fibers are more easily blocked and remain blocked longer.**Absorption:** Rapidly absorbed IV & oral. IV absorption can be limited w/a vasoconstrictor. Rapid topical absorption at mucous membranes.**Dist.:** Rapidly dist. to highly perfused organs (i.e., brain, liver, kidney, heart).**Metab.:** Rapidly metab. by plasma pseudocholinesterases.**Excretion, $t_{1/2}$:** Short duration of action.**Toxicity/S.E.s:** Progressive CNS effects—agitation leading to convulsions, generalized CNS and resp. depression, CV depression, death. Rare hypersens. rxns assoc. w/histamine release.**Utility:** Surface anesthesia, infiltration anesth., field block anesth., nerve block anesth., IV regional anesth., spinal anesth., epidural anesth.**Special Features:** Rel. low potency. Sometimes used w/epinephrine to prolong action and decrease system toxicity.**Name: Benzocaine****Class:** Local Anesthetic (Ester)**Mech.:** Blocks Na^+ & Ca^{2+} channels \rightarrow \downarrow rate of rise of action potential, failure to propagate action potential, eventual conduction block. Smaller, unmyelinated fibers are more easily blocked and remain blocked longer.**Absorption:** Topical use only.**Dist.:****Metab.:** Absorbed benzocaine is rapidly metab. by plasma pseudocholinesterases.**Excretion, $t_{1/2}$:****Toxicity/S.E.s:** Too slowly absorbed to produce serious systemic toxicity..**Utility:** Sustained anesthetic effect when applied to wounds and ulcerated surfaces.**Special Features:****Name: Lidocaine (Xylocaine)****Class:** Local Anesthetic (Amide)**Mech.:** Blocks Na^+ & Ca^{2+} channels \rightarrow \downarrow rate of rise of action potential, failure to propagate action potential, eventual conduction block. Smaller, unmyelinated fibers are more easily blocked and remain blocked longer.**Absorption:** Rapidly absorbed IV & oral. IV absorption can be limited w/a vasoconstrictor. Rapid topical absorption at mucous membranes.**Dist.:** Rapidly dist. to highly perfused organs (i.e., brain, liver, kidney, heart).**Metab.:** Metab. by liver microsomal enzymes.**Excretion, $t_{1/2}$:** Med. duration of action.**Toxicity/S.E.s:** Progressive CNS effects—agitation leading to convulsions, generalized CNS and resp. depression, CV depression, death.**Utility:** Surface anesthesia, infiltration anesth., field block anesth., nerve block anesth., IV regional anesth., spinal anesth., epidural anesth.**Special Features:** 4x as potent as procaine. Sometimes used w/epinephrine to prolong action and decrease system toxicity.**Name: Bupivacaine (Marcaine)****Class:** Local Anesthetic (Amide)**Mech.:** Blocks Na^+ & Ca^{2+} channels \rightarrow \downarrow rate of rise of action potential, failure to propagate action potential, eventual conduction block. Smaller, unmyelinated fibers are more easily blocked and remain blocked longer.**Absorption:** Rapidly absorbed IV & oral. IV absorption can be limited w/a vasoconstrictor. Rapid topical absorption at mucous membranes.**Dist.:** Rapidly dist. to highly perfused organs (i.e., brain, liver, kidney, heart). Placental transfer inversely related to level of protein binding. 95% protein bound. \therefore most preferred obstetric agent.**Metab.:** Metab. by liver microsomal enzymes.**Excretion, $t_{1/2}$:** Long duration of action.**Toxicity/S.E.s:** Progressive CNS effects—agitation leading to convulsions, generalized CNS and resp. depression, CV depression, death.**Utility:** Surface anesthesia, infiltration anesth., field block anesth., nerve block anesth., IV regional anesth., spinal anesth., epidural anesth.**Special Features:** 16x as potent as procaine. Sometimes used w/epinephrine to prolong action and decrease system toxicity.

Name: Nitrous Oxide

Class: General Anesthetic (Anesthetic Gas)

Mech.: Stabilizes membranes of excitable tissue → inhibition of action potential (primarily pre-synaptic blockade of synaptic transmission).

Absorption: Inhaled. Poor blood solubility → **Rapid onset of effect (Blood/gas partition coefficient = 0.47)**. High conc. required for effect (MAC = 101).

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.:

Excretion, t_{1/2}: Primarily unmetab. excretion via lungs.

Toxicity/S.E.s: Low arrhythmia potential. **Low level of cardiac depression.**

Utility: Used as an adjunct to potentiate anesthesia.

Special Features: Non-irritating, non-flammable. **No circulatory depression.** Cannot be used alone to produce general anesthesia. Good analgesic. Poor muscle relaxant.

Name: Halothane (Fluothane)

Class: General Anesthetic (Halogenated Hydrocarbon)

Mech.: Stabilizes membranes of excitable tissue → inhibition of action potential (primarily pre-synaptic blockade of synaptic transmission).

Absorption: Inhaled. High blood solubility → Rel. slow onset of effect (BGPC = 2.3). MAC = 0.77.

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Some liver metab.

Excretion, t_{1/2}:

Toxicity/S.E.s: High level of cardiac depression. Depresses circulation. May produce fatal hepatitis. Med. high potential for arrhythmia. **Avoid repeated exposure.**

Utility: Induces general anesthesia.

Special Features: **Non-irritating**, non-flammable. Satisfact. analgesia and muscle relaxation.

Name: Isoflurane (Forane)

Class: General Anesthetic (Halogenated Hydrocarbon)

Mech.: Stabilizes membranes of excitable tissue → inhibition of action potential (primarily pre-synaptic blockade of synaptic transmission).

Absorption: Inhaled. Interm. blood solubility → Interm. onset of effect (BGPC = 1.4). MAC = 1.40.

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Very little liver metab. (2%).

Excretion, t_{1/2}:

Toxicity/S.E.s: Moderately irritating. **Low level of cardiac depression.** Depresses circulation. **Low potential for arrhythmia.**

Utility: Induces general anesthesia.

Special Features: **Lowest toxicity of the volatile liquids.** Non-flammable. Satisfact. analgesia, good relaxation.

Name: Desflurane (Suprane)

Class: General Anesthetic (Halogenated Hydrocarbon)

Mech.: Stabilizes membranes of excitable tissue → inhibition of action potential (primarily pre-synaptic blockade of synaptic transmission).

Absorption: Inhaled. Low blood solubility → **Rapid onset of effect** (BGPC = 0.42). MAC = 6-7.

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Some liver metab.

Excretion, t_{1/2}:

Toxicity/S.E.s: Moderately irritating. Low level of cardiac depression. Depresses circulation. Low potential for arrhythmia.

Utility: Induces general anesthesia.

Special Features: Produces rapid induction/awakening. Non-flammable. Satisfact. analgesia, good relaxation.

Name: Thiopental (Pentothal)

Class: General Anesthetic (IV Induction Agent)

Mech.:

Absorption: IV → rapid onset of effect.

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Hepatic metab.

Excretion, t_{1/2}: Rapidly diffuses out of brain and redistributes to other tissues (1^o terminator of action) → short duration of effect. But **long t_{1/2}**.

Toxicity/S.E.s: Dose-dependent CV depression. Mod. resp. depression.

Utility: Induces general anesthesia.

Special Features: No analgesia. Still one of most common agents used.

Name: Midazolam (Versed)

Class: General Anesthetic (IV Induction Agent) (BZD)

Mech.:

Absorption: IV

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.:

Excretion, t_{1/2}: **Short duration of effect. Moderate t_{1/2}.**

Toxicity/S.E.s: Slight CV depression. Minimal resp. depression.

Utility: Induces general anesthesia.

Special Features: No analgesia. Causes high incidence of amnesia, so freq. given before induction of general anesthesia.

Name: Propofol (Diprivan)

Class: General Anesthetic (IV Induction Agent)

Mech.:

Absorption: IV

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Hepatic metab.

Excretion, t_{1/2}: Short duration of effect. **Short t_{1/2}.**

Toxicity/S.E.s: Some CV depression. Mod. resp. depression.

Utility: Induces general anesthesia.

Special Features: No analgesia.

Name: Fentanyl

Class: General Anesthetic (IV Opioid)

Mech.:

Absorption: IV

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.:

Excretion, t_{1/2}: Short duration of effect. Short t_{1/2}.

Toxicity/S.E.s: Slight CV depression. Resp. depression (mild-apnea).

Utility: Induces general anesthesia.

Special Features: Excellent analgesia.

Name: Ketamine (Ketalar)

Class: General Anesthetic (IV Anesthetic Agent)

Mech.: Blocks membrane effects of glutamic acid at NMDA receptors. Related to PCP.

Absorption: IV

Dist.: Dissolves in blood. Organs w/high perfusion are most affected.

Metab.: Hepatic metab.

Excretion, t_{1/2}: Urinary & biliary excretion. Short duration of effect. Mod. t_{1/2}.

Toxicity/S.E.s: **CV stimulation. Minimal resp. depression.** Emergence phenomena include disorientation, sensory & perceptual illusions, and vivid dreams (prior admin. of diazepam reduces incidence).

Utility: General anesthetic. Also inducing agent.

Special Features: Excellent analgesia.

Name: Diazepam (Valium)

Class: Antianxiety-Sedative-Hypnotic Agent (Benzodiazepine) (Antiepileptic-Status)

Mech.: Acts on BZD receptors closely coupled to GABA_A receptors → enhancement of GABA inhib. action via ↑ freq. of Cl⁻ channel opening.

Absorption: Oral → rapid absorption (large variability in indiv. responsiveness). IV for seizures & conscious sedation, but may cause pain & phlebitis. IM → poor bioavailability (avoid).

Dist.: Protein binding 99%. High lipid solubility. Rapid CNS dist. Accum. in fat.

Metab.: Liver microsomal N-dealkylation/hydroxylation, then conjug → inactive glucuronides. No induction of hepatic microsomal enzymes.

Excretion, t_{1/2}: Urine—mostly metabolized. Long—50-150 hr. Active metabolites.

Toxicity/S.E.s: All dose-related. **Acute**—excessive depression of CNS fxns (drowsiness, sleep, confusion, disorientation, ataxia, slurred speech, nystagmus, mild amnesia, dementia). May also cause aggression, hyperactivity, delirium, insomnia. Large doses or mixture w/depressants (e.g., EtOH) may cause resp. depression, coma, hallucinations, nightmares, confusion.

Chronic—impaired thinking/memory, weight gain/loss. May exacerbate depression. Habituation & physical dependence → w/drawal syndrome. Abrupt discontinuation → risk for convulsion (but less risk than w/newer BZDs). Symptoms have long latency (5+ days). Metab. ↓ in elderly and by cimetidine. **Overdose** → serious resp. depression (rarely fatal w/support). Psych & phys depend.

Utility: Anxiety, insomnia, relief of alcohol w/drawal symptoms, anesthesia. Sedation—all BZDs are DOCs for sedation. Anticonvulsant—a DOC (IV) for status epilepticus or drug-induced seizures. Skeletal muscle relaxation—spasms, tetanus, orthopedic manipulations.

Name: Triazolam (Halcion)

Class: Antianxiety-Sedative-Hypnotic Agent (Benzodiazepine)

Mech.: Acts on BZD receptors closely coupled to GABA_A receptors → enhancement of GABA inhib. action via ↑ freq. of Cl⁻ channel opening.

Absorption: Oral → rapid absorption (large variability in indiv. responsiveness).

Dist.: Protein binding ≥50%. CNS.

Metab.: Liver microsomal N-dealkylation/hydroxylation, then conjug → inactive glucuronides. No induction of hepatic microsomal enzymes.

Excretion, t_{1/2}: Urine—mostly metabolized. Short—3-5 hr. Active metabolites.

Toxicity/S.E.s: Acute—excessive depression of CNS fxns (drowsiness, sleep, confusion, disorientation, ataxia, slurred speech, nystagmus, mild amnesia, dementia). Early morning awakening, rebound insomnia. May also cause aggression, hyperactivity, delirium, insomnia. Large doses or mixture w/depressants (e.g., EtOH) may cause resp. depression, coma, hallucinations, nightmares, confusion. **Chronic**—impaired thinking/memory, weight gain/loss. Habituation & physical dependence → w/drawal syndrome. Abrupt discontinuation → risk for convulsion (greater risk than w/older BZDs). Metab. ↓ in elderly and by cimetidine. **Overdose** → serious resp. depression (rarely fatal w/support). Psych & phys dependence.

Utility: **Insomnia**, anxiety, alcohol w/drawal. Sedation—all BZDs are DOCs for sedation.

Special Features: Newer BZD (shorter t_{1/2}, greater potency).

Name: Alprazolam (Xanax)

Class: Antianxiety-Sedative-Hypnotic Agent (Benzodiazepine)

Mech.: Acts on BZD receptors closely coupled to GABA_A receptors → enhancement of GABA inhib. action via ↑ freq. of Cl⁻ channel opening.

Absorption: Oral → rapid absorption (large variability in indiv. responsiveness).

Dist.: Protein binding ≥50%. CNS.

Metab.: Liver microsomal N-dealkylation/hydroxylation, then conjug → inactive glucuronides. No induction of hepatic microsomal enzymes.

Excretion, t_{1/2}: Urine—mostly metabolized. Short—12-15 hr. Active metabolites.

Toxicity/S.E.s: Acute—excessive depression of CNS fxns (drowsiness, sleep, confusion, disorientation, ataxia, slurred speech, nystagmus, mild amnesia, dementia). Early morning awakening, rebound insomnia. May also cause aggression, hyperactivity, delirium, insomnia. Large doses or mixture w/depressants (e.g., EtOH) may cause resp. depression, coma, hallucinations, nightmares, confusion. **Chronic**—impaired thinking/memory, weight gain/loss. Habituation & physical dependence → w/drawal syndrome. Abrupt discontinuation → risk for convulsion (greater risk than w/older BZDs). Metab. ↓ in elderly and by cimetidine. **Overdose** → serious resp. depression (rarely fatal w/support). Psychological and physical dependence.

Utility: **Panic/depression.** Anxiety, insomnia, alcohol w/drawal. Sedation—all BZDs are DOCs for sedation.

Special Features: Newer BZD (shorter t_{1/2}, greater potency).

Name: Flurazepam (Dalmane)**Class:** Antianxiety-Sedative-Hypnotic Agent (Benzodiazepine)**Mech.:** Acts on BZD receptors closely coupled to GABA_A receptors → enhancement of GABA inhib. action via ↑ freq. of Cl⁻ channel opening.**Absorption:** Oral → rapid absorption (large variability in indiv. responsiveness).**Dist.:** Protein binding ≥50%. CNS.**Metab.:** Liver microsomal N-dealkylation/hydroxylation, then conjug → inactive glucuronides. No induction of hepatic microsomal enzymes.**Excretion, t_{1/2}:** Urine—mostly metabolized. Long—24-100 hr. Active metabolites.**Toxicity/S.E.s: Acute**—excessive depression of CNS fxns (drowsiness, sleep, confusion, disorientation, ataxia, slurred speech, nystagmus, mild amnesia, dementia). May also cause aggression, hyperactivity, delirium, insomnia. Large doses or mixture w/depressants (e.g., EtOH) may cause resp. depression, coma, hallucinations, nightmares, confusion. **Chronic**—impaired thinking/memory, weight gain/loss. Habituation & physical dependence → w/drawal syndrome. Abrupt discontinuation → risk for convulsion (less risk than w/newer BZDs). Metab. ↓ in elderly and by cimetidine. **Overdose** → serious resp. depression (rarely fatal w/support). **ALL BZDs**—Use caution w/↑ age, pregnancy, EtOH/subst. abuse, depression, driving/dangerous machinery, use of other CNS depressants, narcolepsy, hypersensitivity, chronic use > 1 wk- 1 month (except for epilepsy). Psych & phys dependence.**Utility:** Anxiety, insomnia, alcohol w/drawal. Sedation—all BZDs are DOCs for sedation.**Special Features:** Older BZD (longer t_{1/2}, less potency).**Name: Flumazenil (Romazicon)****Class:** Benzodiazepine Antagonist**Mech.:** Competitive antagonist for BZD receptor → antagonism of BZD CNS effects, including respiration depression.**Absorption:** IV**Dist.:** CNS**Metab.:****Excretion, t_{1/2}:** Duration of action 1-4 hr. ∴ repeated admin. often required.**Toxicity/S.E.s:** Can precipitate severe abstinence synd. in BZD-dependent patients.**Utility:** Treat CNS depressant effects of BZD overdose.**Special Features:****Name: Buspirone (Bu Spar)****Class:** Antianxiety-Sedative-Hypnotic Agents (Selective Antianxiety Agent)**Mech.:** Agonist for 5-HT_{1A} and D₂ receptors.**Absorption:** Oral → rapid absorption.**Dist.:****Metab.:** Extensive 1st-pass metab. (hepatic hydroxylation & dealkylation) → metabolites that may have slight activity.**Excretion, t_{1/2}:** 2-4 hr.**Toxicity/S.E.s:** Wide safety margin. Dizziness, insomnia, nervousness, nausea, headache, myoclonic jerks, chest pain, tinnitus, fatigue. Lower incidence of CNS S.E.s than w/BZDs, but higher incidence of GI S.E.s. Coadmin. w/haloperidol → ↑ serum haloperidol. W/MAO inhib. may cause ↑ BP.**Utility:** Short-term relief of anxiety w/o signif. sedation, drowsiness, or amnesia.**Special Features:** No synergistic/additive effect w/other antianxiety or hypnotic agents. No CNS depression. No known potential for tolerance, dependence, abuse, or withdrawal. May take more than a week for anxiolytic effects to develop.**Name: Phenobarbital****Class:** Antianxiety-Sedative-Hypnotic Agent (Barbiturate) (Antiepileptic:Tonic-Clonic)**Mech.:** Potentiates GABA transmission by interacting w/GABA receptor → ↑ duration of channel opening. High doses → direct activation of Cl⁻ channel → global CNS synaptic depression & block of sustained high freq. repetitive firing..**Absorption:****Dist.:** 40-60% protein binding.**Metab.:** Hepatic metab → inactive metabolites. Signif. induction of hepatic microsomal enzymes → ↑ potential for drug interactions.**Excretion, t_{1/2}:** 46-136 hr (adults), 37-173 hr (kids).**Toxicity/S.E.s: Dose-dependent** depression of CNS fxn (mild sedation → sleep → coma → coma w/resp. depression → death), cognitive impairment, hyperactivity, ataxia, changes in sleep patterns. **Non-dose-rel.**—lethargy, ↓ attention span, osteopenia. **Idiosync.**—allergic dermatitis, Stevens Johnson synd., serum sickness rxn, granulocyte suppress. Chronic use of doses 2x-4x hypnotic dosage → tolerance & psych/phys. dependence. W/drawal symptoms include grand mal seizures and DTs and are potentially lethal.**Utility:** Alt. treatment for gen. tonic-clonic & partial seizures. Alt. treatment of status epilepticus. Rarely used as backup to other sedative-hypnotic drugs. Suicide.**Special Features:** Long-acting agent

Name: Pentobarbital**Class:** Antianxiety-Sedative-Hypnotic Agent (Barbiturate)**Mech.:** Potentiates GABA transmission by interacting w/GABA receptor. High doses → direct activation of Cl⁻ channel → global CNS synaptic depression.**Absorption:****Dist.:****Metab.:** Hepatic metab → inactive metabolites. Signif. induction of hepatic microsomal enzymes → ↑ potential for drug interactions.**Excretion, t_{1/2}:****Toxicity/S.E.s:** Dose-dependent depression of CNS fxn (mild sedation → sleep → coma → coma w/resp. depression → death). Chronic use of doses 2x-4x hypnotic dosage → tolerance & psych/phys. dependence. W/drawal symptoms include grand mal seizures and DTs and are potentially lethal.**Utility:** Rarely used as backup to other sedative-hypnotic drugs. Suicide.**Special Features:** Short-acting agent**Name: Chloral hydrate****Class:** Antianxiety-Sedative-Hypnotic Agent**Mech.:** Sim. to barbiturates**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:****Utility:** Used in hospitals, nursing homes, pediatric dental settings. Mickey Finn.**Special Features:** Rarely used.**Name: Zolpidem (Ambien)****Class:** Antianxiety-Sedative-Hypnotic Agent**Mech.:** Binds to BDZ receptors, although it's not structurally related to BDZs.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Tolerance and physical dependence rarely develop.**Utility:** Short-term treatment of insomnia. As effective as BZDs in prolonging total sleep time and shortening sleep latency. Little effect on sleep stages.**Special Features:****Name: Diphenhydramine (Benadryl)****Class:** H₁-Histamine Antagonist (OTC)**Mech.:** Competitive inhib. of histamine and histamine receptor interaction.**Absorption:****Dist.:** Enters CNS**Excretion, t_{1/2}:****Toxicity/S.E.s:** Sedation (not in everyone). Taken w/alcohol → enhanced CNS depression. Local anesthetic activity. Acute poisoning in kids → complex CNS excitatory and depressant effects (convulsions, hyperpyrexia). Topical use = highest risk of sensitization, ∴ shouldn't be applied topically.**Utility:** Treat allergic rxns (e.g., hay fever). Prevent motion sickness. Can be used for morning sickness. Treat PD symptoms (esp. geriatric patients).**Special Features:** Most effective if taken prophylactically. Can't reverse effects once histamine has bound to receptor. Therapeutically effective dose related to amount of antigen.

Name: Morphine**Class:** Opioid (Alkaloid)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching).**Absorption:** IM, subcut., mucous membranes, intrathecal, oral (1st pass metab → low oral:parenteral potency)**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine. Duration of analgesia—4-5 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Utility:** Analgesia. Intrathecal for post-surg. pain → long duration of action, few side effects.**Special Features:** High maximum efficacy. High addiction/abuse liability. Psych. dependence.**Name: Codeine****Class:** Opioid (Alkaloid)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching).**Absorption:** IM, subcut., mucous membranes, oral (high oral:parenteral potency).**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine. Duration of analgesia—3-4 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Utility:** Antitussant. Analgesia.**Special Features:** Low maximum efficacy. Medium addiction/abuse liability. Psych. dependence.**Name: Heroin****Class:** Opioid (Semi-synthetic)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching). Init. ↓ of adenylate cyclase in locus coeruleus & symp. pregang. neurons. Tolerance develops.**Absorption:** IM, subcut., mucous membranes, oral, smoking.**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal (prob. med. by hyperactive adenylate cyclase) → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Special Features:** High addiction/abuse liability. Psych. dependence.**Name: Dextromethorphan****Class:** Opioid (Semi-synthetic) (OTC)**Mech.:** Agonist of opioid receptors → depression of CNS cough center.**Absorption:** Oral.**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine.**Toxicity/S.E.s:** High doses → hallucinations. Potentially fatal interactions with MAOIs.**Utility:** Antitussant.**Special Features:** Minimal addiction/abuse liability.

Name: Methadone (Dolophine)**Class:** Opioid (Synthetic-Analgesic) (Withdrawal Suppressant)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching).**Absorption:** IM, subcut., oral (high oral:parenteral potency).**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine. Duration of analgesia—4-6 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Utility:** Treatment of physical dependence to other opioids, esp. heroin (less severe w/drawal synd.). Analgesia. Migraine relief.**Special Features:** High maximum efficacy. High addiction/abuse liability. Psych. dependence.**Name: Meperidine (Demerol)****Class:** Opioid (Synthetic-Analgesic)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching).**Absorp.:** IM, subcut., oral (1st pass metab → med. oral:parenteral potency).**Metab.:** Hepatic conjug. → polar metabolites. **Excretion, t_{1/2}:** Urine. Duration of analgesia—2-4 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression; MAO inhib → hyperpyrexia, coma, convulsions.**Utility:** Analgesia.**Special Features:** High maximum efficacy. High addiction/abuse liability. Psych. dependence. Less severe constipation, effect on smooth muscle. Less predictable miosis.**Name: Propoxyphene (Darvon)****Class:** Opioid (Synthetic-Analgesic)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uteral muscle tone, histamine release (hypotension, urticaria, itching).**Absorption:** Oral**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine. Duration of analgesia—4-5 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Utility:** Limited analgesia (no more than aspirin in usu. therapeutic dose, but augments the effects of aspirin & acetaminophen).**Special Features:** Very low maximum efficacy (limited analgesia). Low addiction/abuse liability.**Name: Pentazocine (Talwin)****Class:** Opioid (Synthetic-Analgesic)**Mech.:** Mixed agonist-antagonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), sedation, resp. depression.**Absorption:** IM, subcut, oral (1st pass metab → med. oral:parenteral potency).**Metab.:** Hepatic conjug. → polar metabolites. **Excretion, t_{1/2}:** Urine. Duration of analgesia—3-4 hr.**Toxicity/S.E.s:** CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Tolerance (up to 100x) to analgesia, sedation, resp. depression.Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. Precipitates w/drawal synd. Large doses → dysphoria & hallucinations. **Drug****interactions**—sedative hypnotics → severe CNS/resp. depression;

phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.

Utility: Analgesia. Orig. thought to lack abuse liability.**Special Features:** Mod. maximum efficacy. Low addiction/abuse liability.

Name: Fentanyl (Innovar)**Class:** Opioid (Synthetic-Analgesic)**Mech.:** Agonist of opioid receptors. Causes analgesia (↑ threshold for pain, ↓ subjective rxn), antitussive effects, euphoria/dysphoria (atypical), sedation (rarely stimulation), resp. depression, miosis, n/v, ↓ body temp., ↑ ACTH/PRO/GH, ↓ LH/TSH (hormone effects usu. non-consequential), occasionally hypotension, constipation, ↑ biliary/ureteral/bladder muscle tone, ↓ uterine muscle tone, histamine release (hypotension, urticaria, itching).**Absorption:** Parenteral, transdermal patch, lollipop.**Metab.:** Hepatic conjug. → polar metabolites.**Excretion, t_{1/2}:** Urine. Duration of analgesia—1-1.5 hr.**Toxicity/S.E.s:** Histamine release → asthma in suscept. patients. Use w/caution w/compromised resp. patients. CO₂ retention → ↑ intracranial pressure (may mask signs of head injury). Poisoning → coma, severe resp. depression, pinpoint pupils. Rapid onset of tolerance (up to 100x) to analgesia, euphoria/dysphoria, sedation, n/v, resp. depression, cough suppression. Physical dependence—abrupt w/drawal → rhinorrhea, lacrimation, chills, goose pimples, hyperventilation, mydriasis, myalgia, vomiting, diarrhea, anxiety, hostility (but it's not fatal). Also psychological dependence. **Drug interactions**—sedative hypnotics → severe CNS/resp. depression; phenothiazines/tricyclic antidepressants → ↑ sedation, freq. resp. depression.**Utility:** Analgesia. Induction of general anesthesia.**Special Features:** Very high maximum efficacy. High addiction/abuse liability. Psych. dependence.**Name: Tramadol (Ultram)****Class:** Opioid (Synthetic-Analgesic)**Mech:** Low affinity binding of tramadol to mu-opioid receptors and higher affinity binding of the M1 metabolite. Opioid effects only partially antagonized by naloxone. Also inhibits reuptake of norepinephrine and serotonin.**Absorption:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Sim. to opioids—dizziness, somnolence, nausea, constipation, sweating, & pruritus. Unlike opioids, significantly less respiratory depression, no histamine release. At therapeutic doses, no effect on heart rate, left-ventricular function, or cardiac index. Some orthostatic hypotension. Seizures. Use w/caution w/CNS depressants, MAO inhibitors. May trigger opioid w/drawal symptoms.**Utility:** Analgesia.**Special Features:** Inhib. reuptake of NE and 5HT.**Name: Loperamide (Imodium)****Class:** Opioid (Antidiarrheal) (OTC)**Mech.:** Increased gastric tone → delayed gastric emptying. Increase tone and decreased propulsive peristaltic waves in large intest. → decreased gut motility. Effects due to inhib. of ACh release by neurons in the intest. wall. Naloxone sensitive. Anti-secretory effect (non-naloxone sensitive).**Absorption:** Oral**Dist.:** 90% → GI tract and liver. Very little CNS.**Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** ↓ peristalsis → ↓ evacuation of bacteria and toxins.**Utility:** Antidiarrheal.**Special Features:** No abuse liability. Preferred anti-diarrheal of the opioids. Less potential for analgesia, respiratory depression, and addiction than other opioids. Much safer than other opioids. Longer lasting effects than**Name: Diphenoxylate-Atropine (Lomotil)****Class:** Opioid (Antidiarrheal)**Mech.:** Increased gastric tone → delayed gastric emptying. ↑ tone and ↓ propulsive peristaltic waves in large intest. → ↓ gut motility. Effects due to inhib. of ACh release by neurons in the intest. wall. Naloxone sensitive.**Absorption:** Oral**Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Recommended dose → dizziness, drowsiness, mild euphoria.

Excessive doses → pronounced euphoria, potentially serious respiratory depression (may not be evident until 12-30 hr later). ↓ peristalsis → ↓ evacuation of bacteria and toxins. Use w/great caution in kids. Potentiates effects of barbiturate, tranquilizers, alcohol, other narcotics. Hypertensive crisis w/MAOI.

Utility: Antidiarrheal.**Special Features:**

Name: Naloxone (Narcan)

Class: Opioid Antagonist

Mech.: Competitive inhib. at opioid receptors.

Absorption: IV

Dist.:

Metab.:

Excretion, t_{1/2}: Duration of action ~ 1 hr.

Toxicity/S.E.s:

Utility: Treat opioid poisoning.

Special Features: May require intermittent dosing, as half life is so short.

Name: Naltrexone (Trexan)

Class: Opioid Antagonist

Mech.: Competitive inhib. at opioid receptors.

Absorption: Oral

Dist.:

Metab.:

Excretion, t_{1/2}: Long duration of action.

Toxicity/S.E.s:

Utility: "Maintenance" drug for opioid addicts in rehab. programs. May also decrease alcohol craving in chronic alcoholics.

Special Features:

Name: Clonidine (Catapres)

Class: Centrally Acting Antiadrenergic Agent/Opioid Withdrawal Suppressant

Mech.: Stim. inhib. α_2 receptors in central cardiovasc pathways involving EPI or NE. α_2 are G-protein coupled to inhibit adenylyl cyclase →
↓ cAMP → ↓ central symp. activity.

Absorption:

Dist.: Act at medullary and spinal sites.

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Prominent sedation, dry mouth.

Utility: Treat hypertension. DOC for treating opioid w/drawal (probably substitutes for opioid depression of adenylate cyclase in locus coeruleus & pregang. symp. neurons. No abstinence synd. when withdrawn.

Special Features: Direct α_2 activation. Very potent (<0.5 mg/day).

Name: Sumatriptan (Imitrex)

Class: Anti-Migraine (Serotonin Agonist)

Mech.: Stim 5-HT_{1D} receptors → cranial vasoconstriction → ↑ resistance in carotid arteriovenous anastomoses and shunts w/minor effects on systemic and coronary artery vasculature.

Absorption: Subcut. (96% bioavailability) → peak plasma conc. in 5-20 min. Response in 10-30 min; 10-13 hour duration. Oral (14% bioavailability) → clinical response in 30-60 min.

Dist.:

Metab.: 80% metab.

Excretion, t_{1/2}: 2 hr.

Toxicity/S.E.s: Pain, swelling, redness at injection site. Feeling of heaviness, tightness in chest (injection). Neuro symptoms (tingling, warm/burning sensation). Rare vasospasm in patients w/coronary artery disease (→ angina, MI). 34-46% headaches recur in 24-48 hr.

Utility: Partial/complete relief of migraine headache in 80% w/in 2 hr (subcut). Relieves n/v, photophobia, phonophobia.

Special Features: Oral effective. w/few side effects at lowest doses.

Name: Ergotamine**Class:** Anti-Migraine (Serotonin Agonist)**Mech.:** Partial agony at 5-HT₂ vascular receptors & partial agonist at α-adrenergic receptors (can act as a blocker) → vasoconstriction (cerebral vasc. most sensitive), uterine smooth muscle contraction, n/v, diarrhea.**Absorption:** IV, IM, oral, sublingual, rectal, & inhaler.**Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Most common = GI (n/v, diarrhea). Most dangerous = vasospasm from overuse/overdose (intense & prolonged, but can be blocked w/α blockers). Drowsiness.**Utility:** Treat migraines.**Special Features:** Most effective when given during prodrome period. Often combined w/caffeine to facilitate absorption.**Name: Dihydroergotamine****Class:** Anti-Migraine (Serotonin Agonist)**Mech.:** Partial agony at 5-HT₂ vascular receptors & partial agonist at α-adrenergic receptors (can act as a blocker) → vasoconstriction (cerebral vasc. most sensitive), uterine smooth muscle contraction, n/v, diarrhea.**Absorption:** IV. Investigational use intranasally & orally.**Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Most common = GI (n/v, diarrhea). Most dangerous = vasospasm from overuse/overdose (intense & prolonged, but can be blocked w/α blockers). Drowsiness.**Utility:** Treat migraines.**Special Features:** Lower direct smooth muscle, vasospasm, and serotonin effects and more selective α receptor blockade than ergotamine.**Name: Methysergide (Sansert)****Class:** Anti-Migraine (Serotonin Agonist)**Mech.:** Partial agony at 5-HT₂ vascular receptors & partial agonist at α-adrenergic receptors (can act as a blocker) → vasoconstriction (cerebral vasc. most sensitive), uterine smooth muscle contraction, n/v, diarrhea.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Weight gain, peripheral edema, fibrosis (retroperitoneal, pleuropericardial, subendocardial). Concurrent use of ergot alkaloids, β adrenergic blockers, erythromycin, or dopamine → ↑ risk of arterial spasm & occlusion. Occasional central stim. & hallucinations.**Utility:** Migraine prevention. Reserved for recurrent, refractory, severe migraine, as fibrosis is assoc. w/prolonged use.**Special Features:** Relatively ineffective in treatment of impending/active migraines. Useful as a prophylactic.**Other Migraine Drugs****β Blockers:** Propranolol, timolol, nadolol, metoprolol for continuous prophylaxis. S.E.s include fatigue, depression, orthostatic hypotension. C/I in asthmatics & congestive heart failure patients.**Ca²⁺ Channel Blockers:** Verapamil & flunarazine → moderately efficacious prophylaxis.**Analgesics: Fiorinal:** aspirin + caffeine + butalbital. **Midrin:** acetaminophen + isometheptene (sympathomimetic) + dichloralphenazone (sedative). **NSAIDs**, esp. naproxen sodium (but ↓ gastric motility during acute attack may interfere w/absorption). **Butorphanol** (opioid agonist antagonist) nasal spray. **Methadone** (IM). Overuse may cause a headache ("analgesic rebound").

Name: Phenytoin (Dilantin)**Class:** Antiepileptic Agent (Tonic-Clonic/Complex-Partial)**Mech.:** Blocks voltage-dependent Na⁺ channels → inhib. of sustained high-freq repetitive neuron firing.**Absorption:****Dist.:** 69-96% protein binding.**Metab.:****Excretion, t_{1/2}:** 10-34 hr (adults), 5-140 hr (kids).**Toxicity/S.E.s: Dose-related**—nystagmus, cognitive impairment, incoordination, dyskinesias, seizure exacerbation. **Non-dose-related**—hirsutism, coarsening of facial features, exacerbation of acne, gingival hyperplasia, osteopenia, neuropathy, folate deficiency anemia. **Idiosync.**—allergic dermatitis, fetal drug effects, hepatic failure, serum sickness rxn, SLE-like rxn, hyperglycemia, aplastic anemia, granulocyte suppression. Drug interactions (↑ w/carbamazepine, felbamate; ↓ w/valproic acid).**Utility:** A DOC for generalized tonic-clonic seizures. A DOC for 1° & 2° generalized partial and complex-partial seizures.**Special Features:****Name: Valproate (Depakote, Depakene)****Class:** Antiepileptic Agent (Absence/Tonic-Clonic/Complex-Partial)**Mech.:** Multiple. Reduces T-channel Ca²⁺ currents → ↑ seizure threshold. May enhance GABAergic neurotransmission. Inhib. sustained high freq. repetitive neuron firing.**Dist.:** 80-95% protein binding.**Excretion, t_{1/2}:** 6-15 hr (adults), 8-15 hr (kids).**Toxicity/S.E.s: Dose-rel.**—GI upset, ↑ liver enzymes, tremor, hyperammonemia, initial somnolence, behavioral changes. **Non-dose-rel.**—weight gain, nausea, hair loss, changes in hair texture. **Idiosync.**—Reye-like synd., fetal drug effects, hepatic failure (esp. kids <2 y.o. on mult. drug therapy), pancreatitis, coma, stupor. Drug interactions (↓ w/carbamazepine, phenobarbital, phenytoin; ↑ w/felbamate).**Utility:** A DOC for uncomp. gen. absence. A DOC for gen. tonic-clonic seizures. DOC for atypical absence, myoclonic & atonic epilepsy. Treat 1° & 2° gen. partial & complex-partial seizures. Treatment of bipolar disorder and mgt. of aggression or violence (off-label).**Special Features:****Name: Carbamazepine (Tegretol)****Class:** Antiepileptic Agent (Tonic-Clonic/Complex-Partial)**Mech.:** Blocks voltage-dependent Na⁺ channels → inhib. of sustained high-freq repetitive neuron firing.**Absorption:****Dist.:** 66-89% protein binding.**Metab.:****Excretion, t_{1/2}:** 14-27 hr (adults), 8-28 hr (kids)**Toxicity/S.E.s: Dose-related**—double vision, blurred vision, vertigo, cognitive impairment, lethargy, behavioral changes, dyskinesias, cardiac condxn disturbances. **Non-dose-rel.**—diarrhea, fluid retention.**Idiosync.**—granulocyte suppression, allergic dermatitis, Stevens-Johnson synd., aplastic anemia, hepatic & kidney failure. Signif. drug interactions (↓ w/phenobarbital, phenytoin, primidone, felbamate).**Utility:** A DOC for generalized tonic-clonic seizures. A DOC for 1° & 2° generalized partial and complex-partial seizures. Treatment of pain assoc. w/true trigeminal neuralgia (off-label). Management of acute mania and maintenance of bipolar affective disorder (off-label).**Name: Ethosuximide (Zarontin)****Class:** Antiepileptic Agent (Absence)**Mech.:** Reduces T-channel Ca²⁺ currents → ↑ seizure threshold.**Absorption:****Dist.:** 0% protein binding.**Metab.:****Excretion, t_{1/2}:** 20-60 hr (adults & kids)**Toxicity/S.E.s: Dose-related**—anorexia, nausea, fatigue, headache. **Non-dose-rel.**—blood-dyscrasia, SLE-like rxn, hepatitis.**Utility:** A DOC for uncomplicated absence.**Special Features:**

Name: Clonazepam (Clonopin)
Class: Benzodiazepine (Antiepileptic: Absence)
Mech.: Acts on BZD receptors closely coupled to GABA_A receptors → enhancement of GABA inhib. action via ↑ freq. of Cl⁻ channel opening.
Absorption:
Dist.: **Metab.:** **Excretion, t_{1/2}:**
Toxicity/S.E.s: All dose-related. **Acute**—excessive depression of CNS fxns (drowsiness, sleep, confusion, disorientation, ataxia, slurred speech, nystagmus, mild amnesia, dementia). May also cause aggression, hyperactivity, delirium, insomnia. Large doses or mixture w/depressants (e.g., EtOH) may cause resp. depression, coma, hallucinations, nightmares, confusion. **Chronic**—impaired thinking/memory, weight gain/loss. Habituation & physical dependence → w/drawal syndrome. Abrupt discontinuation → risk for convulsion. Metab. ↓ in elderly and by cimetidine. **Overdose** → serious resp. depression (rarely fatal w/support). Development of tolerance.
Utility: Alt. to ethosuximide and valproate for uncomp. absence. Alt. to valproate for atypical absence. Limited use due to development of tolerance.
Special Features:

Name: Felbamate (Felbatol)
Class: Antiepileptic Agent (Complex-Partial)
Mech.: Multiple. Blocks voltage-dependent Na⁺ channels → inhib. of sustained high-freq repetitive neuron firing. Modulates strychnine-insens. glycine receptor. May enhance GABAergic neurotransmission.
Absorption: Oral → 100% bioavail.
Dist.: 22-25% protein binding
Metab.: 50% hepatic, 50% renal. **Excretion, t_{1/2}:** 20-23 hr (adults)
Toxicity/S.E.s: Most serious—aplastic anemia, acute hepatic failure. **Patients & physicians both required by FDA to sign info/consent form.** Most common—anorexia, n/v, insomnia, headache. Drug interactions—↓ w/phenytoin, carbamazepine.
Utility: Not DOC for anything. Monotherapy or adj. therapy of partial seizures in patients ≥ 14 y.o. Adj. therapy of partial & gen. seizures assoc. w/Lennox-Gastaut synd.
Special Features: Broad-spectrum anticonvulsant. Effective as add-on & monotherapy. But multiple drug interactions, signif. S.E.s w/initial dosing, & increased risk of aplastic anemia & acute hepatic failure diminish its charm.

Name: Gabapentin (Neurontin)
Class: Antiepileptic Agent (Complex-Partial)
Mech.: Unknown. Transp. into brain. Binds to unique specific receptor. Appears to inhibit Na⁺-med. sustained firing. ↑ brain GABA levels.
Absorption: Oral → 60% bioavailability. Actively absorbed by l-amino acid transport system. Dose-dependent decrease in absorption at doses > 600 mg.
Dist.: <10% protein binding.
Metab.:
Excret. t_{1/2}: Almost 100% excret. unchanged by kidney (∝ to creatinine clearance). 5-7 hr (adults).
Toxicity/S.E.s: Somnolence, dizziness, ataxia, fatigue, nystagmus, headache, tremor, diplopia, n/v. **No drug interactions.**
Utility: Adj. therapy of partial seizures, including secondarily generalized. Management of neuropathic pain (off-label).
Special Features: Cleanest (regarding drug interactions) antiepileptic drug. Low toxicity profile. However, there is limited clinical experience w/it against

Name: Lamotrigine (Lamictal)
Class: Antiepileptic Agent (Complex-Partial)
Mech.: Inhib. release of glutamate. Inhib Na⁺-med. sustained firing.
Absorption: Oral → 100% bioavailability.
Dist.: Protein binding 55%
Metab.: Primarily hepatic metab.
Excretion, t_{1/2}: Long t_{1/2}.
Toxicity/S.E.s: **Most common**—somnolence, dizziness, headache, blurred vision, diplopia, ataxia, n/v. **Less common**—rash (mild-severe), esp. w/concurrent use of valproic acid. Drug interactions—↓ w/phenytoin, carbamazepine; ↑ w/valproic acid. ∴ When administering w/valproic acid, start w/low dose (25 mg/d), then titrate up.
Utility: Adj. therapy of partial seizures, including secondarily generalized. Possible alt. for generalized absence.
Special Features: Long t_{1/2}, low toxicity profile, defined therapeutic range, different mech. of action. But metab. affected by concurrent antiepileptic therapy, and experience w/monotherapy is limited.

Name: L-Dopa**Class:** Antiparkinsonian Agent (Precursor)**Mech.:** Inactive. Converted to dopamine in the brain by L-aromatic acid decarboxylase.**Absorption:** Oral. Absorbed from small intest. via non-specific AA transport system. Absorption slowed if other AAs present (i.e., if taken w/food).**Dist.:****Metab.:** MAO-B, COMT**Excretion, t_{1/2}:****T/S.E.s: Wearing off**—decreased length of effect. Each dose effective for only 1-2 hr., followed by rapid return of motor deficits. Possibly controllable w/↑ dose & frequency of dosing.**Dyskinesias**—excessive & abnormal involuntary movements (dystonia, esp. upon waking w/low plasma levels; choreiform dyskinesia occurs during peak levels). **On/off phenom.**—In late PD, patient rapidly fluctuates btwn. having no beneficial effect from L-Dopa to having good mobility (but often w/signif. dyskinesia). **Others**—hallucinations & confusion (clozapine may help), cardiac arrhythmias (rare), life-threatening hypertension & pyrexia if coadmin. w/non-specific MAO inhibitor, may exacerbate/ppt. melanoma in predisposed patients. C/I w/closed-angle glaucoma. Vit. B₆ may ↓ efficacy.**Utility:** Treat Parkinson's Disease symptoms. May initially produce complete improvement in rigidity, bradykinesia, & tremor.**Features:** Must be admin. w/a peripheral decarboxylase inhibitor—carbidopa (carbidopa/L-Dopa = **Sinemet**), benserazide.**Name: Bromocriptine (Parlodel)****Class:** Antiparkinsonian Agent (DA agonist)**Mech.:** Full agonist at D2 receptors, partial agonist at D1 receptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:** 3-7 hr.**Toxicity/S.E.s:** High incidence. Dyskinesias, orthostatic hypotension, hallucinations, confusion, psychosis (C/I w/history of psychosis), anorexia, n/v, cardiac arrhythmias, (C/I w/recent MI), painless digital vasospasm (avoid w/periph. vascular disease).**Utility:** Relieve symptoms of Parkinson's Disease. Reduce on/off fluctuations and induce on/off effect less frequently.**Features:** Longer duration of action than L-Dopa. Doesn't depend on residual dopamine neurons. ∴ May be more useful in late PD. May be as effective as L-Dopa in patients that respond well to L-Dopa, but patients unresponsive to L-Dopa are poor candidates for bromocriptine treatment.**Name: Pergolide (Permax)****Class:** Antiparkinsonian Agent (DA agonist)**Mech.:** Full agonist at D1 & D2 receptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:** 3-7 hr.**Toxicity/S.E.s:** Dyskinesias, orthostatic hypotension, hallucinations, confusion, psychosis (C/I w/history of psychosis), anorexia, n/v, cardiac arrhythmias, (C/I w/recent MI), painless digital vasospasm (avoid w/periph. vascular disease).**Utility:** Relieve symptoms of Parkinson's Disease. Reduce on/off fluctuations and induce on/off effect less frequently.**Features:** Longer duration of action than L-Dopa. Doesn't depend on residual dopamine neurons. ∴ May be more useful in late PD.**Name: Selegiline (Deprenyl, Eldepryl)****Class:** Antiparkinsonian agent (MAO-B Inhibitor)**Mech.:** Low doses → selective inhibition of MAO-B → prolonged action of endogenous DA and L-Dopa effects.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Mild wearing off & on/off phenomena. However, long-term use may → shorter time to develop adverse responses to L-Dopa. In late PD, coadmin. w/L-Dopa may → exacerbation of adverse L-Dopa effects. C/I in patients taking meperidine (→ stupor, rigidity, agitation, hyperthermia).**Utility:** Relieves symptoms of Parkinson's Disease.**Special Features:** Doesn't diminish freq. of late PD problems nor postpone their development.

Name: Trihexyphenidyl (Artane)**Class:** Antiparkinsonian Agent (Anticholinergic)**Mech.:** Antagonizes muscarinic receptors, somehow producing alleviating effects.**Absorption:** Oral**Dist.:****Metab.:****Excretion, t_{1/2}:** Duration of action 6-12 hr.**Toxicity/S.E.s:****Utility:** Relieves symptoms of Parkinson's Disease. May be esp. useful in treating prominent tremor & early morning dystonia. Little effect on bradykinesia. Useful in treatment of Parkinsonian syndromes produced by antipsychotic medications.**Special Features:** Benefit is often short-lived (3-4 months). 20-30% symptomatic improvement in 50-75% of patients.**Name: Amantadine (Symmetrel)****Class:** Antiviral/Antiparkinsonian Agent**Mech.:** Blocks a late stage in assembly of influenza A virus**Absorption:** Well absorbed orally.**Distribution:****Metab.:****Excretion, t_{1/2}:** Excreted unchanged in urine.**Toxicity/S.E.s:** CNS toxicity (nervousness, confusion, hallucinations, insomnia, depression, confusion). Overdose → toxic psychosis. Freq. livedo reticularis (skin mottling). Peripheral edema, freq. nausea. C/I w/hist. of seizures or congestive heart failure. Amantadine>rimantadine**Utility:** Treat influenza A. Treat Parkinson's Disease symptoms → improvement of akinesia, rigidity, tremor, gait disturbances, & total disability in ~ 50% of patients (mech. unknown). Use alone or w/L-Dopa for PD.**Features:** Can be used prophylactically for influenza A. For PD, sustained improvement may last up to 30 months, but may also be short lived (1-3 months). For PD, as good as or better than anticholinergics.**Name: Tolcapone****Class:** Antiparkinsonian (COMT Inhibitor)**Mech.:** Inhib. COMT → ↑ plasma conc. of L-Dopa → ↑ free L-Dopa in brain → ↑ DA in brain.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Nausea (from ↑ peripheral DA), ↑ dyskinesia.**Utility:** Treat symptoms of Parkinson's Disease. Increases duration of response to L-Dopa, decreases required daily dose of L-Dopa.**Special Features:****Name: Entacapone****Class:** Antiparkinsonian (COMT Inhibitor)**Mech.:** Inhib. COMT → ↑ plasma conc. of L-Dopa → ↑ free L-Dopa in brain → ↑ DA in brain.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Nausea (from ↑ peripheral DA), ↑ dyskinesia.**Utility:** Treat symptoms of Parkinson's Disease. Increases duration of response to L-Dopa, decreases required daily dose of L-Dopa.**Special Features:**

Name: Baclofen (Lioresal)**Class:** Muscle Relaxant (Centrally Acting)**Mech.:** GABA_B agonist → inhib. of neurotrans. release → ↓ release of glutamate from Ia afferents & upper motor neurons.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Sedation (much less than diazepam), ↑ seizure activity in epileptics, dizziness, blurred vision, muscle weakness, ataxia.**Utility:** Preferred drug for treatment of spasticity assoc. w/ALS, spinal cord trauma, multiple sclerosis, & cerebral palsy.**Special Features:****Name: Dantrolene (Dantrium)****Class:** Muscle Relaxant (Peripherally Acting)**Mech.:** Decreases excitation-contraction coupling in muscle fibers by interfering w/release of Ca²⁺ from sarcoplasmic reticulum.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Muscle weakness, sedation. Chronic treatment occasionally → hepatitis.**Utility:** Treat spasticity due to spinal cord injury, cerebral palsy, multiple sclerosis, stroke, amyotrophic lateral sclerosis. Treat malignant hyperthermia. Treat neuroleptic malignant syndrome (efficacy prob. not due to block of Ca²⁺ release).**Special Features:** A hydantoin derivative.**Name: Chlorpromazine (Thorazine)****Class:** Psychopharmacological Agents (Antipsychotic) (Aliphatic Phenothiazine Derivative)**Mech.:** Blocks DA (esp. in limbic areas, CTZ, GI), muscarinic, α-adrenergic, H1 histaminic, & 5-HT₂ receptors.**Absorption:** Oral, suppository (emesis) **Dist.:** **Metab.:** **Excretion, t_{1/2}:****Toxicity/S.E.s:** Early onset extrapyramidal disorders—pseudo-Parkinsonism, akathisia, acute dystonias (dosage reduction or anticholinergics help). Late onset extrapyram. disorder—tardive dyskinesia (can be irreversible). Hyperprolactinemia, amenorrhea, infertility. Antimuscarinic effects. Orthostatic hypotension, impotence (α). Sedation (H1). Weight gain. Allergic agranulocytosis. Neuroleptic malignant synd.—hyperpyrexia, catatonia, excessive muscle rigidity, altered mental status, ANS instability; incidence 1%, mortality 15%. For NMS stop Rx, admin. dantrolene (muscle relaxant) & dopamine agonists (e.g., bromocriptine). Drug interactions—may potentiate actions of other CNS depressants.**Utility:** Treat schizophrenia, manic episodes, intractable hiccough. Treat emesis from drugs, radiation, uremia, pain, post-op, emotional, GI irritation, cancer chemotherapy. Preanesthetic.**Features:** Drug holidays important to reduce tendency for tardive dyskinesia and test for continued need. Big problem w/non-compliance. Limit doses to min. side effects. No potential for abuse.**Name: Haloperidol (Haldol)****Class:** Psychopharmacological Agents (Antipsychotic) (Butyrophenone Derivative)**Mech.:** Blocks DA (esp. in limbic areas), muscarinic, α-adrenergic, H1 histaminic, & 5-HT₂ receptors.**Absorption:** **Dist.:** **Metab.:** **Excretion, t_{1/2}:****Toxicity/S.E.s:** High incidence of extrapyramidal toxicity. Early onset extrapyramidal disorders—pseudo-Parkinsonism, akathisia, acute dystonias (dosage reduction or anticholinergics help). Late onset extrapyram. disorder—tardive dyskinesia (can be irreversible). Hyperprolactinemia, amenorrhea, infertility. Antimuscarinic effects. Orthostatic hypotension, impotence (α). Sedation (H1). Weight gain. Allergic agranulocytosis (esp. w/clozapine (1-2%)). Neuroleptic malignant synd.—hyperpyrexia, catatonia, excessive muscle rigidity, altered mental status, ANS instability; incidence 1%, mortality 15%. For NMS stop Rx, admin. dantrolene (muscle relaxant) & dopamine agonists (e.g., bromocriptine). Drug interactions—may potentiate actions of other CNS depressants.**Utility:** Treat schizophrenia, Tourette's syndrome, manic episodes, intractable hiccough, emesis. Preanesthetic.**Features:** Drug holidays important to reduce tendency for tardive dyskinesia and test for continued need. Big problem w/non-compliance. Limit doses to min. side effects.

Name: Clozapine (Clozaril)**Class:** Psychopharmacological Agents (Antipsychotic) (Dibenzodiazepine Deriv.)**Mech.:** Blocks 5HT₂, H1, α receptors. High D1 affinity, relatively low D2 affinity. Also acts on muscarinic and histaminic receptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Sedation, seizures, antimuscarinic, activity, agranulocytosis (bone marrow toxicity). Close monitoring required (i.e., blood tests every couple of weeks). Drug interactions—w/some BZDs may cause death.**Utility:** Treat schizophrenia, esp. patients w/tardive dyskinesia.**Special Features:** Little, if any, tendency for extrapyramidal disorders. May even reverse them. More effective than other antipsychotics in relieving neg. symptoms of schizophrenia.**Name: Imipramine (Tofranil)****Class:** Psychopharmacological Agents (Tricyclic Antidepressant)**Mech.:** Blocks NE and 5HT uptake. Also prominent muscarinic blockade.Possible mechs include down-reg. of brain α₂ and 5HT₂ receptors or decreased number of β brain receptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Sedation, postural hypotension, excess sweating, marked decrease in REM sleep. Block antihypertensive effects of guanethidine. Enhance effects of some sympathomimetics. Can be extremely toxic when combined w/MAO inhbs (but can also be done safely). Potentiates effects of alcohol and other CNS depressants. Overdoses → coma, seizures, hypotension, depressed resp., arrhythmias.**Utility:** Treat endogenous depression, enuresis, chronic pain, panic rxns, phobic anxiety.**Special Features:** TCAs preferred over MAOIs for initial treatment of endogenous depression. Severely depressed patients should never be given more than a 1 week supply of a TCA (danger of overdose).**Name: Amitriptyline (Elavil)****Class:** Psychopharmacological Agents (Tricyclic Antidepressant)**Mech.:** Blocks NE and 5HT uptake. Also prominent muscarinic blockade.Possible mechs include down-reg. of brain α₂ and 5HT₂ receptors or decreased number of β brain receptors.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Prominent sedation, postural hypotension, excess sweating, marked ↓ in REM sleep. Anticholinergic effects. Block antihypertensive effects of guanethidine. Enhance effects of some sympathomimetics. Can be extremely toxic when combined w/MAO inhbs (but can also be done safely). Potentiates effects of alcohol and other CNS depressants.

Overdoses → coma, seizures, hypotension, depressed resp., arrhythmias.

Utility: Treat endogenous depression, enuresis, chronic pain, panic rxns, phobic anxiety.**Special Features:** TCAs preferred over MAOIs for initial treatment of endogenous depression. Severely depressed patients should never be given more than a 1 week supply of a TCA (danger of overdose).**Name: Phenelzine (Nardil)****Class:** Psychopharmacological Agents (Antidepressant) (MAOI) (Hydrazine Deriv.)**Mech.:** Inhib. of MAO → central build-up of NE, 5HT, DA.**Absorption:****Dist.:****Metab.:****Excretion, t_{1/2}:****Toxicity/S.E.s:** Headache, drowsiness, dry mouth, weight gain, postural hypotension (central α₂), sexual disturbances, liver damage, hyperpyrexia. Interactions w/TCAs, dextromethorphan, meperidine, and tyramine can be fatal.**Utility:** Treat depression.**Special Features:** Usu. prescribed as alt. only when other drugs are ineffective.

Name: Tranylcypromine (Parnate)

Class: Psychopharmacological Agents (Antidepressant) (MAOI) (Non-Hydrazine Deriv.)

Mech.: Inhib. of MAO → central build-up of NE, 5HT, DA.

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Headache, drowsiness, dry mouth, weight gain, postural hypotension (central α_2), sexual disturbances, liver damage, hyperpyrexia. Interactions w/TCAs, dextromethorphan, mepiridine, and tyramine can be fatal.

Utility: Treat depression.

Special Features: Usu. prescribed as alt. only when other drugs are ineffective.

Name: Fluoxetine (Prozac)

Class: Psychopharmacological Agents (Antidepressant) (SSRI)

Mech.: Blocks reuptake of serotonin.

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Anxiety, insomnia, restlessness, GI distress.

Utility: Treat depression.

Special Features:

Name: Sertraline (Zoloft)

Class: Psychopharmacological Agents (Antidepressant) (SSRI)

Mech.: Blocks reuptake of serotonin.

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Anxiety, insomnia, restlessness, GI distress.

Utility: Treat depression.

Special Features:

Name: Lithium Carbonate

Class: Psychopharmacological Agents (Mood Stabilizer)

Mech.: Unknown, but may involve electrolyte/ion transport, enhanced reuptake of tryptophan → ↑ brain 5HT levels, inhib. of phosphatidyl inositol 2nd messenger system, ↓ DA & NE turnover, or ↑ synth. of ACh.

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Low TI (plasma levels must be monitored). Edema, sedation, fine tremor (treat w/propranolol), polyuria, thirst, gastric upset, mild diarrhea. Serious = coarse tremor, vomiting, profuse diarrhea, ataxia, cardiac arrhythmias, seizures, coma, death. ↓ thyroid fxn, but usu. asympt. Diuretics → Na⁺ depletion → ↑ Li⁺ conc.

Utility: Prophylaxis for bipolar illness. Acute severe mania is more quickly controlled w/neuroleptics. Combination therapy often required.

Special Features:

Name: Scopolamine (Transderm-Scop)

Class: Tertiary M₂-Muscarinic Antagonist

Mech.: Bind to muscarinic receptors and competitively inhib. ACh interaction.

Absorption: Oral, transdermal, parenteral.

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Drowsiness, blurred vision, dry mouth, urinary retention, tachycardia, constipation, cycloplegia. Mostly avoided w/transdermal application.

Utility: Prevent motion sickness (transdermal patch). Give parenterally in advance to counteract nasty anesthesia side effects (cardiac slowing, salivation, bronchial secretions).

Features: In addition to atropine-like anti-musc properties, also produces central depressant and anti-motion sickness effects. Best if admin. prophylactically.

Name: Dimenhydrinate (Dramamine)

Class: Antiemetic (H₁-Histamine Antagonist) (OTC)

Mech.: Competitive inhib. of histamine and histamine receptor interaction.

Absorption: Oral, suppository.

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Drowsiness (marked in some patients). Mild anticholinergic effects.

Utility: Prevent motion sickness. Can be used for morning sickness. Vertigo.

Special Features: Best if admin. prophylactically.

Name: Promethazine (Phenergan, Remsed)

Class: Antiemetic (H₁-Histamine Antagonist) (OTC)

Mech.: Competitive inhib. of histamine and histamine receptor interaction.

Absorption: Oral, suppository.

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: More drowsiness than other antihistamines. Mild anticholinergic effects.

Utility: Prevent motion sickness. Can be used for morning sickness. Vertigo.

Special Features: May be effective in motion sickness when other antihistamines are not. Best if admin. prophylactically.

Name: Metoclopramide (Reglan)

Class: Antiemetic

Mech.: Cholinomimetic action → ↑ GI motility. Potent DA antagonism → blockade of DA receptors in CTZ and GI. Prob. also depresses vomiting center.

Absorption: Oral

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Somnolence, nervousness, dystonic rxns. Some Parkinsonism & tardive dyskinesia. Some prolactin release.

Utility: Antiemetic, esp. w/cancer chemotherapy, and emergency surgery/labor to prevent aspiration of gastric contents.

Special Features: Best if admin. prophylactically.

Name: Prochlorperazine (Compazine)

Class: Antiemetic (Phenothiazine)

Mech.: Blocks DA receptors in CTZ and GI tract. Probably also depresses vomiting center somewhat.

Absorption: Oral, suppository.

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Drowsiness, hypotension. Hypersens—blood dyscrasias, jaundice, skin rashes. Dystonias, dyskinesias, Parkinsonism (more often than w/chlorpromazine).

Utility: Antiemetic for drugs, radiation, uremia, pain, post-op, emotional, GI irritation, cancer chemotherapy. Also very effective for intractable hiccoughs.

Special Features: Best if admin. prophylactically.

Name: Ondansetron (Zofran)

Class: Antiemetic (5HT₃ Antagonist)

Mech.:

Absorption: IV

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s:

Utility: Treat nausea/vomiting due to cancer chemotherapy.

Special Features: Best if admin. prophylactically.

Name: Dronabinol (Marinol, THC)

Class: Antiemetic (Cannabinoid)

Mech.:

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: High doses → impaired motor fxn. Mild tolerance, mild phys. dependence, psych. dependence. W/drawal → mild anorexia, insomnia, irritability. Acute intoxication → hallucinations, delusions, paranoia, anxiety.

Utility: Treat nausea & vomiting assoc. w/cancer chemotherapy. Best if admin. prophylactically. Taken to produce relaxed euphoria, impaired attention, fantasy state, impaired depth perception.

Features: Hashish = Unadulterated resin from Cannabis plants. Smoked or eaten. Far more potent than marijuana. Involved in the etymology of "assassin" (An ancient Muslim sect regularly killed its enemies after eating/smoking hashish → hashshashin).

Name: Ipecac

Class: Emetic

Mech.:

Absorption: Oral.

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s:

Utility: Induces vomiting.

Special Features: Do not use to treat poisoning due to convulsants (e.g., TCAs). Seizures may occur → ↑ risk of aspiration.

Name: LSD

Class: Hallucinogen

Mech.:

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Mild tolerance, psychological dependence. No physical dependence, no w/drawal syndrome. Acute intoxication → severe sensory disturbances, panic, impaired org. of thinking, organic brain syndrome, flashbacks.

Utility: Euphoria w/more stimulation than relaxation.

Special Features:

Name: Phencyclidine (PCP)

Class: Hallucinogen

Mech.:

Absorption:

Dist.:

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Impaired judgment, aggressive behavior, hostility. Mild tolerance, psychological dependence. No physical dependence, no w/drawal syndrome. Acute intoxication → muscle rigidity, convulsions, coma, psychosis, delirium, paranoia.

Utility:

Special Features:

Name: Methamphetamine (Desoxyn, various street names)

Class: CNS-Active Sympathomimetic Agent (Indirect)

Mech.: Release of DA, NE, & 5HT from nerve terminals. Some blockade of reuptake of DA, NE, & 5HT. Weak inhib. of MAO. Produces elev. of mood, euphoria, ↑ alertness, ↓ sense of fatigue, ↓ food intake, periph. sympathomimetic effects.

Absorption: Oral → good bioavail.

Dist.: Crosses BBB.

Metab.:

Excretion, t_{1/2}:

Toxicity/S.E.s: Neurosis, paranoia, frank psychosis. Tolerance, but not as strong as opiates. Acute toxicity → hypertension, stroke, seizures, cardiac arrhythmias. Very strong psych. dependence. Mild physical dependence. W/drawal → ↑ appetite, fatigue, depression.

Utility: Treat narcolepsy, ADHD. Off-label uses. Ice = smokable version.

Special Features: Not metab. by COMT. Decreased metab. by MAO. Higher ratio of CNS/PNS actions than amphetamine.

“I want, once and for all, *not* to know many things.

Wisdom sets limits to knowledge too”.

- Friedrich Nietzsche