

## DRUGS ACTING ON THE CENTRAL NERVOUS SYSTEM (21)

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### **Introduction to Pharmacology of the Central Nervous System**

Understanding how drugs affect the central nervous system depends upon an integral knowledge of neuroanatomy, biochemistry, physiology, and basic pharmacological principles. A core medical curriculum in pharmacology of the central nervous system requires at least 25 hours.

## Neurotransmitters, Neuromodulators, and Receptors

Recommended Curriculum Equivalent: 1.5 hr

### Learning Objectives

#### Physiology, pathophysiology and therapeutic actions

List the major neurotransmitters in the brain, their predominant anatomical pathways, and their associated relevant disorders.

Compare and contrast G protein coupled receptors and ligand-gated ion channels and describe the major effector systems coupled to various G-proteins.

Describe how synaptic function changes in response to chronic administration of agonists, antagonists and uptake blockers. Describe the processes of receptor sensitization and desensitization and provide examples of how these processes may be induced.

Identify the molecular, cellular, and biochemical sites where drugs can act to affect neuronal function.

Define the blood brain barrier and list the considerations that determine whether a drug will gain access to the central nervous system.

### Endogenous Agents

Primary agents	Secondary agents
ADENOSINE TRIPHOSPHATE (ATP)	adenosine
ACETYLCHOLINE (ACH)	aspartate (Asp)
DOPAMINE (DA)	beta-amyloid
5-HYDROXYTRYPTAMINE (5-HT)	beta-endorphin
GAMMA-AMINOBUTYRIC ACID (GABA)	bradykinin
GLUTAMATE	brain derived neurotrophic factor
NOREPINEPHRINE	epinephrine
SUBSTANCE P	dynorphins
	enkephalins
	glycine
	histamine
	leptin
	nerve growth factor (and other growth factors)
	nitric oxide

<b>General Anesthetics</b>			
<b>Recommended Curriculum Equivalent: 1.5 hr</b>			
<b>Drug Classes and Drugs to consider</b>			
<b>Inhalational</b>		<b>Intravenous</b>	
Primary agents	Secondary agents	Primary agents	Secondary agents
DESFLURANE ISOFLURANE NITROUS OXIDE (N <sub>2</sub> O) SEVOFLURANE	halothane	ETOMIDATE FENTANYL KETAMINE MIDAZOLAM MORPHINE PROPOFOL THIOPENTAL	alfentanil methohexital remifentanil sufentanil
<b>Learning Objectives</b>			
<p><b>Physiology, pathophysiology and therapeutic actions</b>  Define the terms “general anesthesia” and “balanced anesthesia.”  State the objectives of general anesthesia, characteristics of an ideal anesthetic, and the stages of general anesthesia.</p>			
<p><b>Mechanism of action</b>  List the current theories of the mechanisms of action of inhalation anesthetics, of intravenous anesthetics.</p>			
<p><b>Pharmacokinetics</b>  Compare the available inhalation anesthetics with respect to their pharmacokinetics properties including biotransformation.  Explain how the solubility of a gas in a liquid is defined. List the conditions that must be specified to determine the concentration of gas in the liquid phase.  Describe how the physical properties of inhalation anesthetics influence the rate of equilibration of anesthetic in the inspired air to anesthetic in alveoli, blood, brain, muscle and fat. Explain how this information is related to onset and recovery from inhalation anesthesia.  Compare and contrast commonly used intravenous induction agents--describe relative roles of distribution and metabolism in determining duration of action and how duration of action may change with repeated administration.</p>			
<p><b>Adverse effects, drug interactions and contraindications</b>  List and explain the complications that may ensue with the use of Nitrous Oxide as a direct result of the high concentrations at which it is administered and its solubility in blood relative to that of nitrogen.  Describe malignant hyperthermia, list some common triggering agents, and discuss its prevention and treatment.  Describe the utility and adverse effects of drugs commonly used as pre-anesthetic medications or in combination with inhalation anesthetics to create a "complete or balanced anesthetic". Include opioids, benzodiazepines, neuromuscular blocking agents and atropinics in your discussion. Indicate how the concomitant use of these drugs may affect the concentrations of inhaled anesthetics used to maintain the anesthetic state.  Describe the pharmacological effects of the drugs in each class on pulmonary, cardiovascular, endocrine, renal, and CNS function (aside from anesthesia).</p>			

**Therapeutic uses**

Compare and contrast commonly used intravenous induction agents—their speed of onset, and duration of action. Describe the relative roles of distribution and metabolism in determining duration of action and how duration of action may change with repeated administration of an intravenous anesthetic.

Define MAC (minimal alveolar concentration), name the physical property of an inhalation anesthetic that correlates best with its MAC, and explain how the concept of MAC is used in anesthesiology.

Discuss relative advantages and disadvantages of intravenous vs. inhalation anesthesia.

Discuss the factors involved in choosing an anesthetic protocol, including the relative advantages and disadvantages of inhalation and intravenous anesthesia.

<b>Local Anesthetics</b>	
<b>Recommended Curriculum Equivalent: 1 hr</b>	
<b>Drugs to consider</b>	
Primary agents	Secondary agents
BENZOCAINE BUPIVACAINE COCAINE LIDOCAINE PROCAINE ROPIVACAINE	tetracaine prilocaine
<b>Learning Objectives</b>	
<p><b>Physiology, pathophysiology and therapeutic actions</b></p> <p>Explain how the actions of clinically used anesthetics might be influenced by the frequency of impulse transmission in peripheral nerves, size and class of the peripheral axons, pH, and by the vascularity of the injected area.</p> <p>Discuss the relevance of isoforms of the voltage-gated sodium channel to the development of new local anesthetics.</p> <p>Describe the ionic basis of the action potential.</p>	
<p><b>Mechanism of action</b></p> <p>Discuss the mechanism of action of local anesthetics.</p>	
<p><b>Adverse effects, drug interactions and contraindications</b></p> <p>List the common adverse effects of local anesthetics and indicate appropriate treatments should they occur.</p> <p>List the significant differences between amide and ester-type local anesthetics.</p>	
<p><b>Therapeutic uses</b></p> <p>Describe the common routes of administration of local anesthetics. List anesthetics that cannot be used topically, that cannot be used for infiltration. Explain why these routes are not effective.</p> <p>Describe methods used to restrict local anesthetics to a desired site of action and indicate how these methods reduce adverse effects.</p> <p>Discuss epidural and intrathecal administration of selected opioids and local anesthetics.</p>	

<b>Opioid Analgesics, Agonist-antagonists, and Antitussives</b>			
<b>Recommended Curriculum Equivalent: 3 hr</b>			
<b>Drug Classes and Drugs to consider</b>			
<b>Agonists</b>		<b>Agonist/Antagonists and Antagonists</b>	
Primary	Secondary	Primary	Secondary
CODEINE FENTANYL HYDROCODONE MEPERIDINE METHADONE MORPHINE OXYCODONE TRAMADOL	diphenoxylate heroin l-alpha-acetyl- methadol loperamide d-propoxyphene combinations - opioids plus acetaminophen and ASA	BUPRENORPHINE NALOXONE NALTREXONE	buprenorphine- naloxone butorphanol nalbuphine nalorphine nalmefene pentazocine
<b>Learning Objectives</b>			
<p><b>Physiology, pathophysiology and therapeutic actions</b> Describe the pharmacological effects and sites of action of the prototype opioid agonist morphine, and its utility in relieving different types of pain. Discuss potential therapeutic actions of opioids aside from analgesia in CNS and other organ systems including cardiovascular, respiratory and GI. Discuss the salient differences in pharmacology between morphine and each of the following agonists: meperidine, fentanyl, methadone, and oxycodone.</p>			
<p><b>Mechanism of action</b> Explain the molecular mechanism of action of each drug in each drug class.</p>			
<p><b>Pharmacokinetics</b> Describe the pharmacokinetic processes affecting morphine, absorption, distribution, metabolism, excretion and how these are relevant to its therapeutic use. Describe the distribution of opioids in the body, including their ability to cross the blood-brain barrier and the placenta. List opioid agonists that are metabolized to morphine and indicate the salient differences in their pharmacology from that of morphine.</p>			
<p><b>Adverse effects, drug interactions and contraindications</b> List adverse effects of morphine on CNS, cardiovascular, GI-biliary, respiratory and genitourinary systems. List and explain the major drug interactions of morphine. List the contraindications for morphine and its surrogates. Describe the characteristics of opioid tolerance and dependence. Describe the opioid abstinence syndrome and how it differs from that for sedative-hypnotics. Discuss abuse liability for opioids and how it differs among the various drugs. Describe the signs and symptoms of morphine and heroin overdose and how they are managed. Define precipitated abstinence and indicate under what circumstances it might occur following the clinical use of opioid analgesics or antagonists.</p>			

**Therapeutic uses**

Present the clinical indications for the opioids and opioid antagonists and explain the basis for their use.

Contrast the analgesic effects of morphine with those of the nonsteroidal antiinflammatory drugs, with those of antidepressants, and with those of carbamazepine and gabapentin, particularly in relation to the treatment of neuropathic pain conditions. Discuss the rationale for using mixtures of opioid analgesics and NSAIDs.

Explain how agonist-antagonists and partial agonists differ in their utility and adverse effect profile when compared to morphine.

Discuss the salient differences between naloxone and naltrexone and how these are reflected in clinical use of these drugs. Discuss how the combination of naloxone with opiate analgesics in oral and sublingual preparations permits opiate action, yet decreases abuse liability.

Explain the rationale for using methadone to treat heroin abusers. List the aspects of methadone's pharmacokinetics and pharmacodynamics that make it useful for this purpose. Discuss the salient differences between maintenance therapy with methadone and buprenorphine.

**Antitussives****Recommended Curriculum Equivalent: 0.5 hr****Drug Classes and Drugs to consider**

Primary	Secondary
CODEINE DEXTROMETHORPHAN HYDROCODONE	guaifenesin

**Drugs Used in the Treatment of Motor Disorders and Centrally Acting Muscle Relaxants**

**Recommended Curriculum Equivalent: 1 hr**

**Drugs to consider**

Primary	Secondary
ALPRAZOLAM AMANTADINE BACLOFEN BENZTROPINE BROMOCRIPTINE CARBIDOPA DANTROLENE DIAZEPAM DOPAMINE ENTACAPONE L-DOPA LORAZEPAM OXAZEPAM PRAMIPEXOLE RASAGILINE ROPINEROLE SELEGILINE (deprenyl)	apomorphine cabergoline chlorazepate chlordiazepoxide cyclobenzaprine haloperidol tizanidine trihexyphenidyl

**Learning Objectives**

**Physiology, pathophysiology and therapeutic actions**

Describe the major anatomical pathways and neurotransmitter systems involved in control of motor function.

Discuss current hypotheses about the etiology and pathophysiology of Parkinson's disease.

Describe Huntington's Chorea and discuss drugs available for its treatment and their effectiveness.

Discuss the pathophysiological basis of rigidity, spasticity, muscle spasm (if not previously discussed under motor dysfunction) and the classes of agents that are used to promote skeletal muscle relaxation (baclofen/GABAB receptors, tizanidine/alpha2 adrenergic receptors).

**Mechanism of action**

Describe the molecular mechanism of action of each primary drug.

**Adverse effects, drug interactions and contraindications**

Discuss the adverse effect profile of levodopa and how it is altered by combination with carbidopa.

Compare and contrast the adverse effect profile of ergot and non-ergot dopamine agonists.

### **Therapeutic uses**

Describe the rationale for the use of levodopa in Parkinson's disease and the rationale for its use in combination with peripheral L-amino acid decarboxylase inhibitor. Discuss how the drug combination alters levodopa's therapeutic and adverse effect profiles.

Differentiate the two major classes of direct DA receptor agonists used for chronic control of Parkinson disease indicate how they are used therapeutically and how their therapeutic actions compare to that of levodopa.

Discuss the use of other classes of drugs in treating Parkinson's disease: anticholinergics, MAO inhibitors, COMT inhibitors, amantadine.

Discuss drugs that can cause parkinsonism and other movement disorders, and how these drug-induced disorders can be treated.

List drugs useful for treatment of spasticity and compare and contrast the mechanisms of action and adverse effects of benzodiazepines, baclofen, cyclobenzaprine and dantrolene when used for this purpose.

<b><u>Antiseizure drugs</u></b>	
<b>Recommended Curriculum Equivalent: 2 hr</b>	
<b>Drugs to consider</b>	
Primary	Secondary
CARBAMAZEPINE DIAZEPAM ETHOSUXIMIDE GABAPENTIN LAMOTRIGINE LORAZEPAM PHENOBARBITAL PHENYTOIN TIAGABINE TOPIRAMATE VALPROIC ACID	clonazepam fosphenytoin levetiracetam primidone zonisamide
<b>Learning Objectives</b>	
<p><b>Physiology, pathophysiology and therapeutic actions</b> Describe the pathophysiology of seizures, and the types and prevalence of epilepsy. Discuss briefly each of the following with respect to their possible relevance to the initiation and spread of seizure activity: mirror foci, kindling, post-tetanic potentiation, long-term potentiation, paroxysmal depolarizing shift, and channelopathies.</p>	
<p><b>Mechanism of action</b> List the major classes of antiseizure antiepileptic drugs, the seizure types against which they are effective, their cellular mechanisms of action, and how these actions might be relevant to their roles as antiseizure agents.</p>	
<p><b>Pharmacokinetics</b> Describe the pharmacokinetic factors relevant to appropriate therapy with antiseizure drugs. Explain why the clearance of phenytoin changes with dose. Discuss the rationale for the common practice of monitoring plasma concentrations of many antiepileptic drugs.  List the antiseizure medications that induce hepatic enzymes and describe the consequences treatment of epilepsy and for interactions with drugs used for other conditions.</p>	
<p><b>Adverse effects, drug interactions and contraindications</b> List and describe the adverse and teratogenic effects of the major antiseizure drugs.</p>	
<p><b>Therapeutic uses</b> Describe the use of antiseizure medications. Define status epilepticus and explain how it is managed pharmacologically. Discuss the therapeutic use of antiseizure drugs for conditions other than epilepsy, including their use as analgesics and as mood stabilizers.</p>	

<b><u>Drugs Used In Affective Disorders</u></b>	
<b>Recommended Curriculum Equivalent: 1.5 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
<b>Antidepressants</b>	
Primary	Secondary
AMITRIPTYLINE BUPROPION DULOXETINE ESCITALOPRAM FLUOXETINE NORTRIPTYLINE PAROXETINE SELEGILINE SERTRALINE TRAZODONE TRANLYCYPROMINE VENLAFAXINE	citalopram clomipramine desipramine fluvoxamine imipramine mirtazapine phenelzine
<b>Drugs for manic-depressive (bipolar) disorder</b>	
Primary	Secondary
CARBAMAZEPINE LITHIUM CARBONATE VALPROIC ACID ATYPICAL ANTIPSYCHOTICS: ARIPIPRAZOLE OLANZAPINE PALIPERIDONE QUETIAPINE RISPERIDONE ZIPRASIDONE	clonazepam clozapine levetiracetam primidone zonisamide
<b>Learning Objectives</b>	
<p><b>Physiology, pathophysiology and therapeutic actions</b> Describe the concept of behavioral affect, the current neurochemical theories regarding affect and how it can be altered by drugs. Define depression and list its symptoms, signs and causes. Define bipolar disorder and its subtypes, and describe its signs and symptoms and its natural history. Describe manic episodes.</p>	
<p><b>Mechanism of action</b> List the major classes of antidepressant drugs and their primary cellular targets. (Tricyclic ADs, SSRIs, SNRIs, atypical antidepressants, and MAO inhibitors). Discuss the mechanisms that could account for the delay in therapeutic actions of antidepressants. Describe the major theories explaining the presumed mechanisms of action of drugs useful for treating bipolar disorder (lithium, anticonvulsants, antipsychotics). List effects of lithium on CNS neurotransmitter systems.</p>	

**Pharmacokinetics**

Contrast the pharmacokinetics of the different classes of antidepressant drugs.

Discuss the importance of active metabolite formation, and how pharmacokinetics is relevant to switching from one medication to another.

Discuss the pharmacokinetics of lithium and its relationship to the following: alteration in dietary sodium, effects of exercise, use of diuretics, monitoring of plasma lithium levels, and treatment of lithium overdose.

**Therapeutic uses**

Discuss the utility of the various classes of antidepressants for other indications:

Obsessive compulsive disorder, panic disorder, post-traumatic stress disorder (PTSD), neuropathic pain, smoking cessation, enuresis and generalized anxiety disorder.

Discuss the use of herbal antidepressants, such as St. John's wort.

Contrast acute treatment of a manic episode and treatment designed to prevent bipolar cycling.

Discuss the use of antiseizure drugs for treatment of bipolar disorder, their advantages and disadvantages compared to lithium.

**Adverse effects, drug interactions and contraindications**

Describe and compare the most common adverse effects of the major classes of antidepressants, and where known, explain the mechanism for these effects.

Identify significant drug and dietary interactions.

Describe the signs and symptoms of overdose with each of the major classes of antidepressants and the appropriate treatment (tricyclic antidepressant toxicity, serotonin syndrome, tyramine effect).

Differentiate adverse side effects of lithium from signs and symptoms of lithium overdose. Explain why there is a contraindication to the use of lithium in patients with impaired renal function or cardiovascular disease.

<b><u>Antipsychotics</u></b>	
<b>Recommended Curriculum Equivalent: 1.5 hr</b>	
<b>Drugs to consider</b>	
Primary	Secondary
CHLORPROMAZINE ARIPIPRAZOLE CLOZAPINE FLUPHENAZINE HALOPERIDOL OLANZAPINE RISPERIDONE	paliperidone quetiapine thiothixene ziprasidone
<b>Learning Objectives</b>	
<b>Physiology, pathophysiology and therapeutic actions</b> Describe schizophrenia and discuss the theories regarding the underlying neurochemical basis. Contrast the actions of phenothiazines and haloperidol with those of atypical antipsychotics, and the implications for theories of the mechanisms of antipsychotic actions.	
<b>Mechanism of action</b> Discuss current theories regarding the therapeutic mechanism of action of antipsychotic drugs, including acute and chronic effects on major dopaminergic and serotonergic systems in the CNS.	
<b>Therapeutic uses</b> Compare the effectiveness of classical and atypical antipsychotics in the treatment of both positive and negative signs of schizophrenia. List uses of antipsychotic drugs for indications other than schizophrenia. Discuss the use of dopamine antagonists in Tourette's syndrome.	
<b>Adverse effects, drug interactions and contraindications</b> Contrast the adverse effect profile of low potency classical antipsychotics, high potency classical antipsychotics, and atypical antipsychotics. Describe the time course, signs and symptoms of antipsychotic drug-induced dyskinesias (dystonia, akathisia, parkinsonism, tardive dyskinesia), and their management and treatment. Describe neuroleptic malignant syndrome and its management and treatment.	

<b><u>Sedative, hypnotics, and anxiolytics</u></b>	
<b>Recommended Curriculum Equivalent: 2 hr</b>	
<b>Drugs to consider for sedation</b>	
Primary	Secondary
ALPRAZOLAM ESZOPICLONE FLUMAZENIL (antagonist) FLURAZEPAM MIDAZOLAM RAMELTEON ZOLPIDEM	chloral hydrate diphenhydramine gamma-hydroxybutyrate hydroxyzine lorazepam oxazepam pentobarbital phenobarbital temazepam triazolam zaleplon
<b>Learning Objectives</b>	
<b>Physiology, pathophysiology and therapeutic actions</b> Briefly describe the concepts of sedation, hypnosis, anesthesia, coma. List and describe the stages of sleep. Define anxiety, its relationship to the amygdala and differentiate the major anxiety disorders. Discuss the GABA <sub>A</sub> receptor channel complex, the heterogeneity of its subunits and the physiological and therapeutic implications.	
<b>Mechanism of action</b> Describe the effects of various sedative/hypnotic/anxiolytic drugs on GABA <sub>A</sub> function, their selectivity for different receptors with different subunit subtypes, and differences in their sites of action on the GABA <sub>A</sub> receptor channel complex. Define inverse agonist at the GABA <sub>A</sub> receptor channel complex.	
<b>Adverse effects, drug interactions and contraindications</b> List the signs and symptoms of barbiturate and benzodiazepine overdose and its treatment. Explain how flumazenil might be used, and the rationale for its use. Describe the interactions of the various classes of drugs used as hypnotics, sedative and anxiolytics with other CNS depressants. Compare the dependence liability, and withdrawal syndromes of the various classes of drugs used as hypnotics, sedative and anxiolytics.	

### **Therapeutic uses**

Compare and contrast the effects of barbiturates, benzodiazepines, and non-benzodiazepine agonists at the benzodiazepine site on induction and maintenance of sleep (including effects on sleep stages), and the adverse effects of these classes of drugs. Explain why drugs acting at the benzodiazepine receptor have virtually totally replaced barbiturates as hypnotics.

List the therapeutic uses of benzodiazepines, and prototypes for each use. Explain how pharmacokinetics of various benzodiazepines relates to their therapeutic utility.

Discuss other groups of drugs with sedative/hypnotic and anxiolytic actions. Compare and contrast the hypnotic action of ramelteon, the anxiolytic action of buspirone, and the sedative effects of chloral hydrate and hydroxyzine with that of drugs acting at the benzodiazepine site. How do the mechanisms of action and the adverse effects of these drugs differ from barbiturates, and drugs acting at the benzodiazepine site?

List drugs that are used for treating anxiety disorders other than generalized anxiety: panic disorder, obsessive-compulsive disorder, specific phobias. Can these drugs be used for generalized anxiety disorder as well?

<b><u>Substance Abuse</u></b>	
<b>Recommended Curriculum Equivalent: 4.5 hr</b>	
<b>Substance dependence, general principles</b>	
<b>Learning Objectives</b>	
<p><b>Physiology, pathophysiology and therapeutic actions</b></p> <p>Define and differentiate tolerance to, physical dependence on and substance dependence (DSM-IVR) on drugs.</p> <p>Discuss the roles of drug craving and reward vs avoidance of withdrawal in initiation and maintenance of substance dependence.</p> <p>Describe major CNS pathways involved in substance dependence</p> <p>Discuss how pharmacokinetics influences abuse liability and withdrawal syndromes.</p> <p>Compare patterns and effects of substance abuse for stimulants, opioids, sedative-hypnotics and anxiolytics.</p> <p>Compare morbidity and mortality for substance dependence on various classes of abused drugs, including the dangers of unregulated withdrawal.</p> <p>Describe tolerance and contrast the withdrawal syndrome for those classes of drugs of abuse that produce physical dependence, and discuss available techniques for detoxifying users. Define conditioned withdrawal and precipitated withdrawal and indicate their relevance.</p>	
<b>Drugs to consider - Psychostimulants</b>	
Primary	Secondary
AMPHETAMINE ATOMOXETINE CAFFEINE COCAINE METHAMPHETAMINE METHYLPHENIDATE MODAFINIL NICOTINE	bupropion ephedrine gamma-hydroxybutyrate phentermine sibutramine varenicline
<b>Learning Objectives</b>	
<p><b>Mechanism of action</b></p> <p>Discuss current theories of the mechanisms of action of the stimulant and anorexigenic drugs listed above.</p>	
<p><b>Adverse effects, drug interactions and contraindications</b></p> <p>Compare the abuse potential for the list of drugs.</p> <p>Discuss the toxic effects of stimulants used therapeutically, and the adverse effects of stimulant misuse and abuse.</p> <p>Discuss the addictive properties of nicotine and the adverse effects of nicotine and other tobacco constituents.</p>	
<p><b>Therapeutic uses</b></p> <p>Discuss therapeutic uses of stimulants and related drugs as appetite suppressants, in attention deficit hyperactivity disorder, in narcolepsy and for promoting wakefulness.</p> <p>Discuss therapies to treat nicotine dependence: nicotine patches and chewing gum, nicotine receptor partial agonists (varenicline), other agents (bupropion).</p>	
<b>Drugs to Consider - Ethanol and alcoholism</b>	
Primary	Secondary

ETHANOL FOMEPIZOLE METHANOL NALTREXONE	acamprosate disulfiram ethylene glycol topiramate
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### Learning Objectives

#### **Physiology, pathophysiology and therapeutic actions**

Describe the acute CNS actions of ethanol and discuss their relationship to blood alcohol levels.

#### **Mechanism of action**

Discuss current theories about the mechanism of action of alcohol in the CNS.

#### **Pharmacokinetics**

Describe the pharmacokinetics of ethanol, its absorption, distribution, metabolism and excretion.

#### **Adverse effects, drug interactions and contraindications**

Describe the acute and chronic organ toxicities of ethanol methanol and higher alcohols (e.g, ethylene glycol).

List drugs with which ethanol shows cross-tolerance and cross-dependence.

List drugs, both prescription and over the counter, that would entail a patient refraining from the use of alcoholic beverages. Explain the nature of the potential interactions.

Discuss the management of methanol toxicity.

List the signs and symptoms of chronic alcoholism and the ethanol abstinence syndrome. Compare and contrast the latter with abstinence syndromes following chronic use of barbiturates, benzodiazepines, or opioids.

Discuss the mechanism for the synergism between chloral hydrate and ethanol.

#### **Therapeutic uses**

Summarize the therapeutic applications of ethanol.

Discuss the treatment options for acute intoxication by ethanol or other alcohols, and for the ethanol abstinence syndrome.

Discuss the use of disulfiram, naltrexone and acamprosate in the treatment of chronic alcoholics. Describe their effects and the mechanistic rationale for their use.

Summarize the therapeutic applications of ethanol.

### Drugs to Consider - Hallucinogens and Designer Drugs

Primary	Secondary
LYSERGIC ACID DIETHYLAMIDE (LSD) MDMA (methylene dioxymethamphetamine) Mescaline PHENCYCLIDINE (PCP)	atropine bufotenin ketamine psilocin scopolamine

### Learning Objectives

#### **Physiology, pathophysiology and therapeutic actions**

Describe salient differences among the behavioral and hallucinogenic effects of the various drugs and compare and contrast the drug-induced states with endogenous psychoses.

Discuss the variability in inter-individual responses to hallucinogens and the interaction between the social setting in which hallucinogens are taken and their behavioral effects.

**Mechanism of action**  
 List the hallucinogens with primary actions on 5HT<sub>2A</sub> receptors, and those that are NMDA receptor antagonists, and muscarinic receptor antagonists and describe their mechanisms of action.

**Pharmacokinetics**  
 Describe how the pharmacokinetics of different drugs may influence their duration of action and their detection by screening tests for illicit drug use.

**Adverse effects, drug interactions and contraindications**  
 Discuss tolerance to and cross-tolerance among the various hallucinogens.  
 Describe the toxidromes expected for LSD, MDMA, PCP, and belladonna alkaloids.  
 Discuss general principles of treatment for patients with known ingestion of hallucinogens.

**Drugs to Consider - Marijuana**

Primary	Secondary
DELTA-9-TETRAHYDROCANNABINOL (THC) DRONABINOL MARIJUANA/THC	nabilone rimonabant

**Learning Objectives**

**Physiology, pathophysiology and therapeutic actions**  
 Discuss the endogenous cannabinoids, how they differ from classical neurotransmitters/neuromodulators, their receptors, and the current hypotheses about their functional roles.  
 List the psychological, physiological and pharmacologic effects of smoking marijuana; of taking dronabinol.

**Therapeutic uses**  
 List the approved therapeutic indications for dronabinol. Discuss the current controversy over the use of medical marijuana vs. the use of dronabinol or nabilone, and proposed therapeutic actions aside from those currently approved for dronabinol.  
 Describe the effects of cannabinoid receptor antagonists and their potential uses.

**Drugs to Consider - Inhalants/Organic solvents and gases**

Primary	Secondary
	carbon tetrachloride fire extinguisher accelerants fluorocarbons gasoline glue nitrous oxide toluene

**Learning Objectives**

**Adverse effects, drug interactions and contraindications**  
 Discuss the epidemiology of abuse of inhalants.  
 Describe, in general terms, the effects of organic solvents and their toxicities

**Drugs to Consider - opioids, sedative-hypnotics, and antianxiety agents**

Primary	Secondary

<p>BENZODIAZEPINES HEROIN MORPHINE METHADONE OXYCODONE (and abuse of prescribed opiates)</p>	<p>barbiturates buprenorphine naltrexone</p>
<p><b>Learning Objectives</b></p>	
<p><b>Adverse effects, drug interactions and contraindications</b> Discuss opioids, sedative-hypnotics, and antianxiety agents with respect to their substance abuse aspects (see appropriate sections above). Describe the features of addiction to and dependence on these agents.</p>	
<p><b>Therapeutic uses</b> Consider therapies for opiate dependence including maintenance therapies (methadone), antagonist therapies (naltrexone) and the use of combinations of partial agonists (buprenorphine) and antagonists (naltrexone).</p>	
<p><b>Drugs and the law</b></p>	
<p><b>Therapeutic uses</b> Define the characteristics of drugs in each of the Drug Enforcement Administration classification of controlled substances into Schedules I, II, III, and IV, and give examples of some specific drugs that are included in each schedule. Discuss the ways in which this classification affects the clinical use of drugs.</p>	

<b><u>Treatment of Alzheimer's Disease</u></b>	
<b>Recommended Curriculum Equivalent: .3 hr</b>	
<b>Drugs to consider</b>	
<b>Primary</b>	<b>Secondary</b>
DONEPEZIL GALANTAMINE MEMANTINE RIVASTIGMINE	
<b>Learning Objectives</b>	
<b>Mechanism of action</b> Discuss the drugs used for the treatment of Alzheimer's disease, their mechanisms of action, their efficacy and their adverse effects.	