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USMLE Step 1 Visually in 24 Hours




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 **Pharmacology**

Rapid Learning Medical Series

Wayne Huang, PhD
Tobi Limke, PhD
Robert Maietta, MD
Susan Miller, RN
& The USMLE MD/PhD Team

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Learning Objectives

By completing this tutorial, you will learn about:

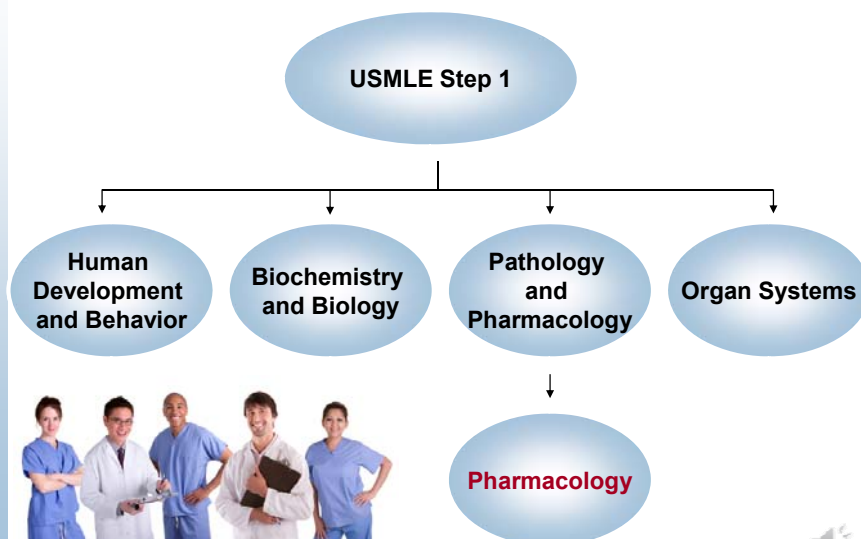


- Basic principles of pharmacology
- Drug naming conventions
- Overview of select drug classes
- Autonomic nervous system pharmacology

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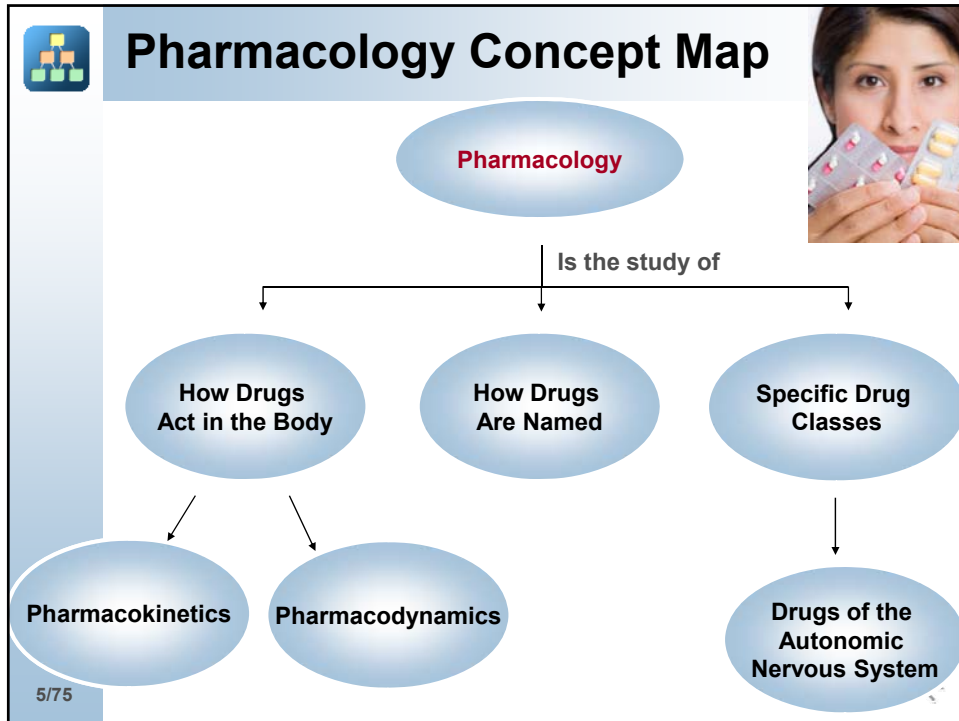


USMLE Step 1 Concept Map



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Pharmacodynamics

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What is Pharmacodynamics?

Pharmacodynamics: the study of the relationship between drug concentration in the body, and the physiological response to that concentration of drug

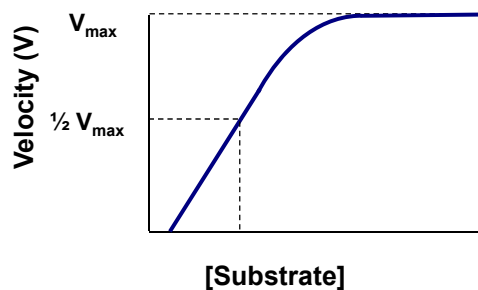
Two key principles:

- The dose of the drug is directly linked to the magnitude of the body's response to that drug
- Drugs act through receptors

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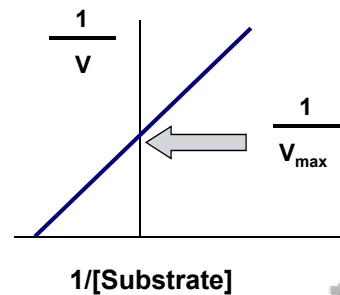


Review of Enzyme Kinetics



$$K_m = [S] \text{ at } \frac{1}{2} V_{\max}$$

$$\text{Slope} = K_m / V_{\max}$$



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> Types of Enzyme Inhibition

Competitive	Noncompetitive
Similar to natural substrate	Not similar to natural substrate
Displaced by increasing substrate	Not displaced by increasing substrate
Bind active site	Do not bind active site
No effect on V_{max}	Decrease V_{max}
Increase K_m	No effect on K_m

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> Receptors

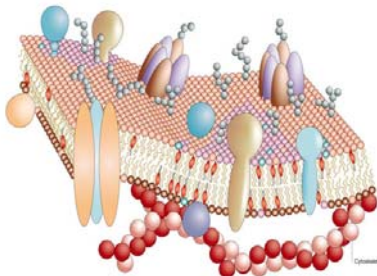
Receptors: components of a cells or organisms that interact with a drug

Initiate the chain of events that lead to the drug's observed effect

Coupling: links the drug occupancy of receptors to the pharmacological response

Efficacy of coupling determined by:

- Initial conformational change of receptor – influenced by **SAR**
- Biochemical events that transduce receptor occupancy into cellular response

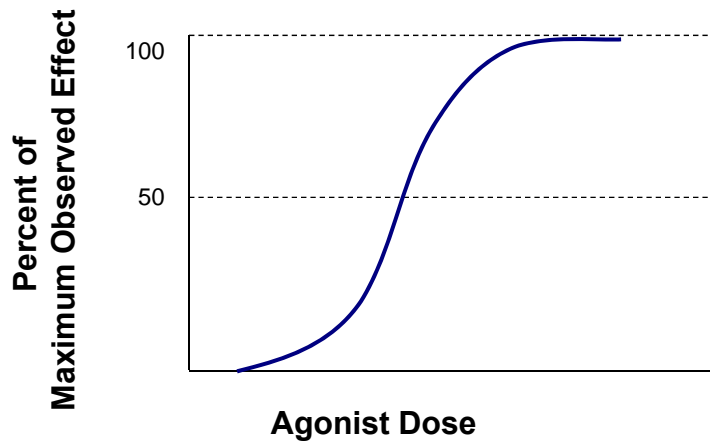


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Dose-Response Curves

Dose-response: the relationship between the given dose and the observed response is linked by the interaction of the drug with a specific receptor



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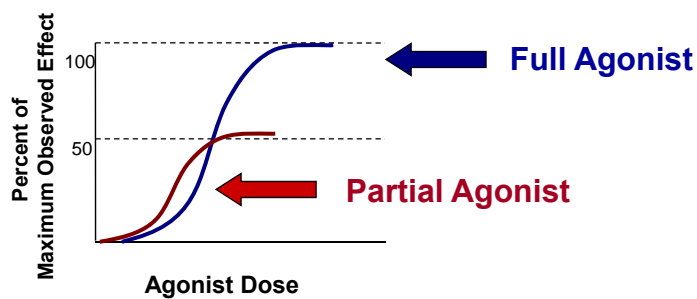


Agonists

Agonists: initiate changes in cell function through their actions at receptors

Potency: range of doses over which a chemical produces increasing responses

- **Affinity:** tendency to bind to receptors
- **Efficacy:** ability to initiate changes once bound



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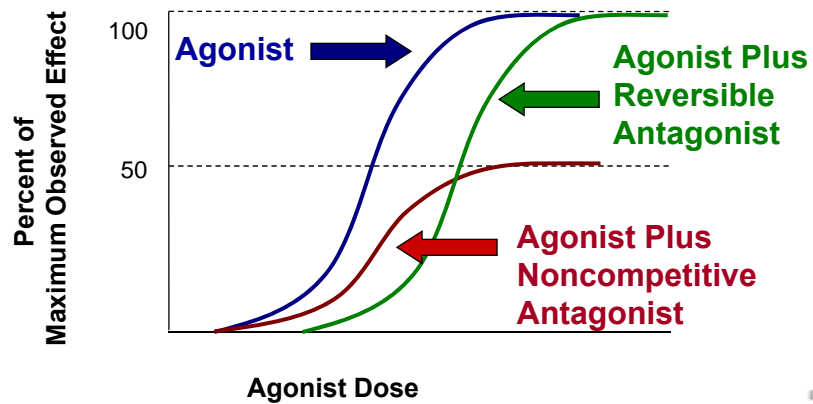




Antagonists

Antagonists: prevent agonists from activating receptors

Reversible or **noncompetitive**



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Therapeutic Index (TI)

Therapeutic index: relative measure of how safe a drug is
Safer drugs have higher TI values

TILE: $TI = LD50 / ED50$

$$TI = \frac{LD50}{ED50}$$



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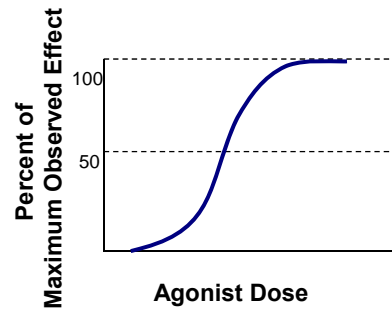


Summary: Pharmacodynamics

Pharmacodynamics:
the study of what the drug does to the body

Two key principles:

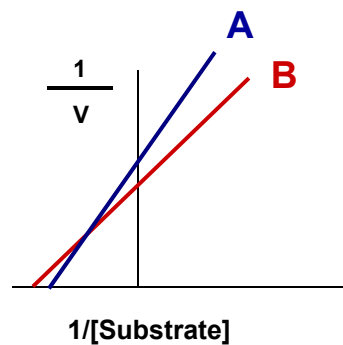
- The dose of the drug is directly linked to the magnitude of the body's response to that drug (Dose-Response)
- Drugs act through receptors



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Clinical Challenge: Exam Question



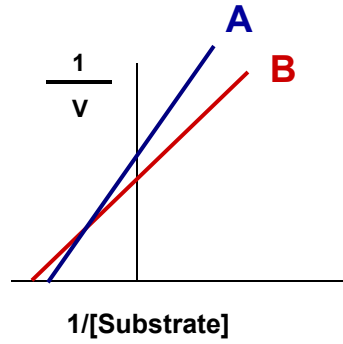
- A) The drugs are not competing
- B) The drugs are competing for the same enzyme
- C) Drug A has a higher V_{max} than Drug B
- D) Drug B has a lower V_{max} than Drug A
- E) Neither drug is causing inhibition of the enzyme

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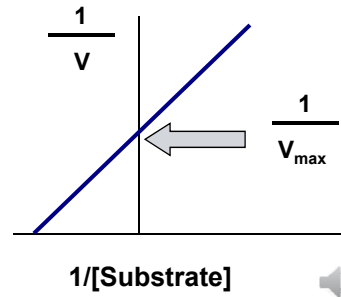




Clinical Challenge: Exam Answer




B) The drugs are competing for the same enzyme

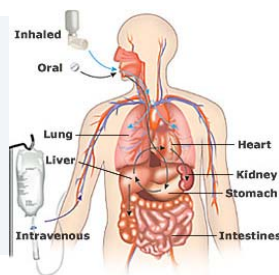



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Pharmacokinetics



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What Is Pharmacokinetics?

Pharmacokinetics: the study of the movement of drugs in the body

- How fast the drug works
- How well the drug works
- How long the drug works

■ **ADME:**

- **A**bsorption
- **D**istribution
- **M**etabolism
- **E**xcretion



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Volume of Distribution (V_d)

$$V_d = \frac{\text{Amount of drug in body}}{\text{Plasma drug concentration}}$$

V_d : relates the total amount of drug in the body to the concentration of drug in plasma

Assumes:

- Body is a single unit
- Changes that occur in the plasma concentration reflect proportional changes in tissue chemical concentrations

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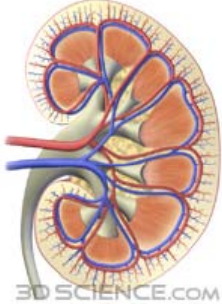


> Clearance (CL)

CL: rate of chemical elimination from the body

- Volume of fluid containing chemical cleared per unit time
- Units of flow (milliliters per minute)

Relates the rate of elimination to the plasma concentration

$$CL = V_d \times K_e$$


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> Half-Life

Half-life: time required for the blood or plasma chemical concentration to decrease to one-half its original value due to elimination

$$T_{1/2} = 0.7 \times V_d / CL$$

A drug infused at a constant rate will reach the following plasma concentrations per half-life:

Number of Half Lives	1	2	3	4
Concentration	50%	75%	87.5%	93.75%

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➤ Calculating Dose

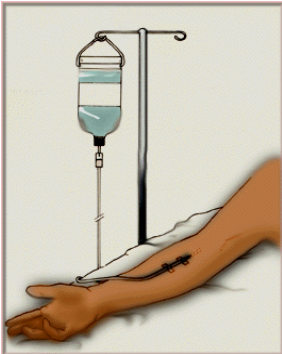
Loading dose:

$$C_p \times V_d / F$$

Maintenance dose:

$$C_p \times CL / F$$

- **C_p** = target plasma concentration
- **F** = bioavailability
 - F has a maximum value of 1
 - Impaired kidney or liver function will affect dosages



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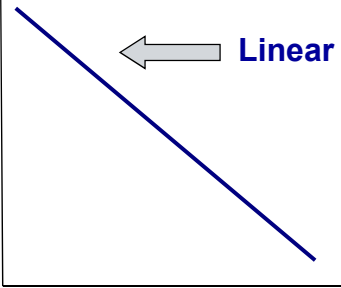
➤ Zero-Order Elimination

Zero-order elimination: elimination remains at a **constant rate** irrespective of the amount of drug in the body (C) in a linear fashion

Examples of zero-order kinetics: **PEA**

- **P**henytoin
- **E**thanol
- **A**spirin (at toxic concentrations)

Plasma Concentration (C_p)



Time

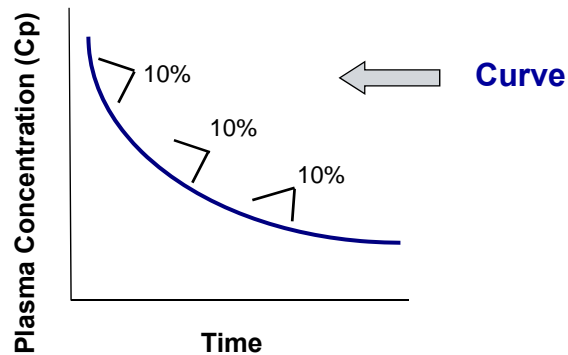
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First-Order Elimination

First-order elimination: rate of elimination is proportional to the drug concentration

A **constant fraction** of a drug (such as 20% of the amount in the body) is eliminated per unit time



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How Urine pH Affects Elimination



Non-ionized –
Reabsorbed

Ionized –
Eliminated

- **Weak acid:** made non-ionized with **bicarbonate**
- **Weak base:** made non-ionized by **ammonium chloride**

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Biotransformation

Biotransformation:
metabolic conversion
of endogenous and
xenobiotic chemicals
to more polar, water-
soluble compounds

Catalyzed by specific
enzymes



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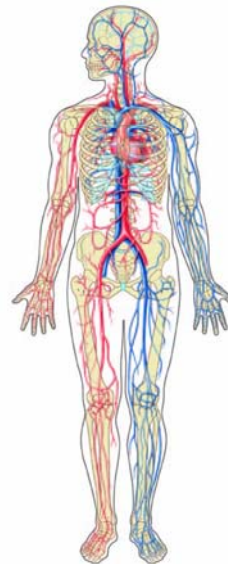
Divided into two stages:

- **Phase I:** enzymatic alteration of the parent compound into a more polar compound through oxidation (**CYP450**), reduction or hydrolysis
- **Phase II:** adds a large, highly polar functional group in a process called **conjugation** that further aids in excretion from the body



Summary: Pharmacokinetics

- **Pharmacokinetics:**
the study of the
movement of drugs
in the body
- Volume of
distribution,
clearance and half-
life
- Zero-order
elimination
- First-order kinetics
- Biotransformation



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Drug Naming Conventions




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 **Antimicrobials, Antifungals and Antivirals**

Suffix	Type of Drug (examples)
-azole	Antifungals (ketacon azole)
-cillin	Penicillins (methi cillin)
-cycline	Class of antibiotics (tetracy cline)
-navir	Protease inhibitors (saqui navir)

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> Cardiovascular System



Suffix	Type of Drug (examples)
-olol	β Antagonists (aten olol , propran olol)
-oxin	Cardiac glycosides (dig oxin , digit oxin)
-pril	ACE inhibitors (capt opril , enal opril)


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> Anesthetics and Sedatives

Suffix	Type of Drug (examples)
-ane	Inhaled general anesthetics (haloth ane)
-azepam	Benzodiazepine sedatives (diaz epam)
-caine	Local anesthetics (lidoc aine , proc aine)
-barbital	Barbiturates (phenob arbital)

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➤ Autonomic Drugs



Suffix	Type of Drug (examples)
-terol	β 2 agonists (albuterol)
-zosin	α 1 antagonists (prazosin)


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➤ Other Nervous System Drugs

Suffix	Type of Drug (examples)
-azine	Phenothiazines (chlorpromazine)
-operidol	Butyrophenones (haloperidol)
-ipramine	TCAs (imipramine)
-triptyline	TCAs (amitriptyline)

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Other Drugs



Suffix	Type of Drug (examples)
-afil	Erectile dysfunction (sildenafil)
-tidine	H2 antagonists (cimetidine)
-tropin	Pituitary hormones (somatotropin)


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Summary: Drug Naming Conventions


Drug naming conventions help **identify the class of drug**, by providing a **common ending (suffix) to the drug name** as an identifier





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Overview of Select Drug Classes




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Autacoids

- **Autacoids:** Group of biological factors produced by the body that act locally
- Includes:
 - Peptides
 - Biogenic amines
 - Prostanoids and their inhibitors
 - Small molecules
 - NO (nitric oxide)



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> Antimicrobials

Bacteriostatics: prevent further spread of bacterial infection


Mnemonic: We're **ECSTaTiC** about bacteriostatics


- Erythromycin
- Clindamycin
- Sulfamethoxazole
- Trimethoprim
- Tetracyclines
- Chloramphenicol

Bactericidals: kill bacteria

Mnemonic: Very **F**inely **P**roficient **A**t **C**ell **M**urder

- Vancomycin
- Fluoroquinolones
- Penicillin
- Aminoglycosides
- Cephalosporins
- Metronidazole

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> Antineoplastics

Work on the cell cycle, specifically by lowering or stopping cell division

ABCDEF:

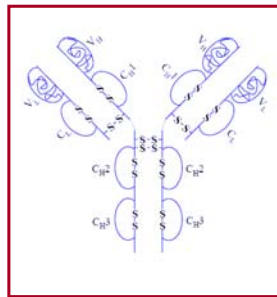
- Alkylating agents
- Bleomycin
- Cisplatin
- Dactinomycin
- Doxorubicin
- Etoposide
- Flutamide

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Immunosuppressants



Specifically target the immune system, to prevent graft rejection and treat autoimmune disorders

- Small molecules
- Antibody-based therapeutics
- Recombinant cytokines

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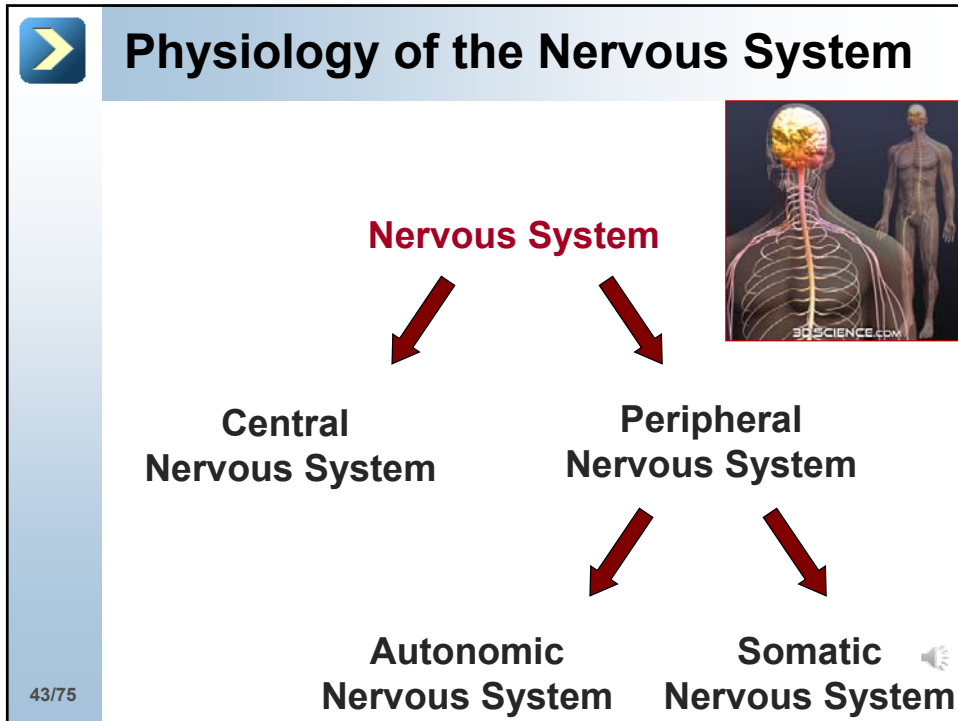


Pharmacology of the Autonomic Nervous System



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▶ Autonomic Nervous System

Cholinergic: release acetylcholine (ACh)

- Preganglionic
- Postganglionic parasympathetic

CC(=O)OCC[N+](C)(C)C

Acetylcholine

Adrenergic: release norepinephrine

- Postganglionic sympathetic

NCC(O)C1=CC=C(O)C=C1O

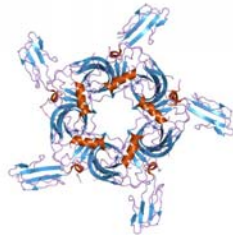
Norepinephrine

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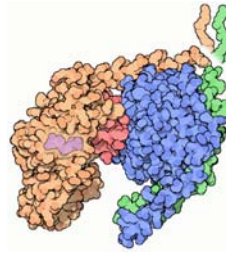


Cholinergic Receptors

Nicotinic



Muscarinic



Two types of receptors:

- **Nicotinic receptors:** these are ligand-gated, Na^+/K^+ channels
- **Muscarinic receptors:** which are G-protein coupled receptors that act through second messengers

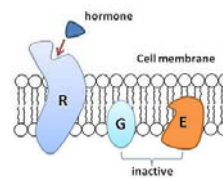
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G-Protein Coupled Receptors

Types of GPCRs:

- G_q - acts on phospholipase C
- G_s - stimulates adenylate cyclase
- G_i - inhibits adenylate cyclase



R = Receptor
G = G protein
E = cell Enzyme

**KISS and KICK till you're SICK of SEX
(QISS and QIQ till you're SIQ of SQS)**

- alpha1 = Q, alpha2 = I, beta1 = S, beta3 = S
- M1 = Q, M2 = I, M3 = Q
- D1 = S, D2 = I, H1 = Q
- H2 = S, V1 = Q, V2 = S



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Cholinergic Drugs - Overview

Direct agonists: agents that bind to and activate muscarinic or nicotinic receptors

Indirect agonists: work primarily through the inhibition of acetylcholinesterase



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Cholinergic Drugs – Direct Agonists

Bethanechol:
postoperative and neurogenic ileus and urinary retention

- **Beth Anne, call (bethanechol) me** to activate your bladder and bowels

Carbachol: applied ocularly

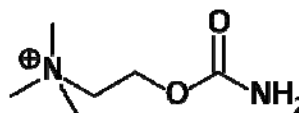
- Glaucoma

Pilocarpine: stimulates sweat tears and saliva

- **PILE** on the sweat and tears

Methacholine: inhaled muscarinic agonist

- Airway smooth muscle




Carbachol




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Cholinergic Drugs – Indirect Agonists

<p>Physostigmine: glaucoma & atropine overdose</p> <ul style="list-style-type: none"> ■ PHY is for the EYES ■ Crosses the blood-brain barrier 	<p>Edrophonium: very short acting</p> <ul style="list-style-type: none"> ■ Myasthenia gravis <p>Pyridostigmine: long-acting</p> <ul style="list-style-type: none"> ■ Myasthenia gravis ■ Does not cross the blood brain barrier
<p>Neostigmine: postoperative and neurogenic ileus and urinary retention</p> <ul style="list-style-type: none"> ■ Does not cross the blood-brain barrier - NEO CNS means NO CNS 	

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Cholinesterase Inhibitor Poisoning


<p>Poisoning symptoms - LESS DUMBB</p> <ul style="list-style-type: none"> ■ Lacrimation ■ Excitation of skeletal muscle and CNS ■ Sweating ■ Salivation ■ Diarrhea ■ Urination ■ Miosis ■ Bronchospasm ■ Bradycardia 	<p>Treatment:</p> <ul style="list-style-type: none"> ■ Atropine - muscarinic antagonist ■ Pralidoxime - chemical antagonist that will regenerate active cholinesterase
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➤ Muscarinic Antagonists

Muscarinic antagonist drugs and their primary actions:

- Inhibits **P**arasymphathetic
And **S**weat =
- I**pratropium, **P**irenzepine,
Atropine, **S**copolamine





Benztropine: CNS - used to treat Parkinson's disease


- **PARK** my **BENZ**

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📝 Clinical Note: Drugs to Treat Glaucoma

Decrease aqueous humour synthesis:

- **α agonists** – epinephrine (mydriasis) & brimonidine (no mydriasis)
- **β blockers** – timolol, betaxlol, cartelol
- **Diuretics** – acetazolamide



Increase outflow of aqueous humour:

- **Cholinomimetics** – pilocarpine, carbachol, physostigmine and echothiophate (miosis)
- **Prostaglandin** – latanoprost

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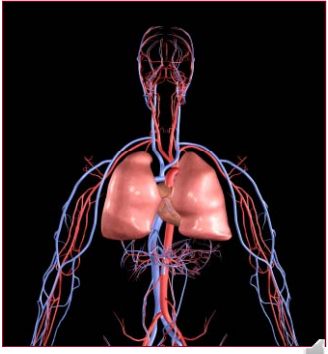
➤ Direct Sympathomimetics

Selective drugs exist for the four main- receptor subtypes of adrenoceptors: α_1 , α_2 , β_1 and β_2

- **α_1** : phenylephrine and oxymetazoline
- **α_2** : clonidine and methylnoradrenaline
- **β_1** : dobutamine
- **β_2** : albuterol, terbutaline

Primary applications:

- **Cardiovascular**
- **Lungs**



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➤ Indirect Sympathomimetics

Indirect acting sympathomimetics cause release of catecholamines

Amphetamine:

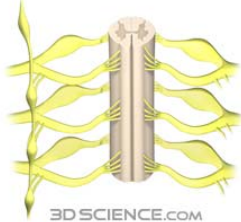
- Similar effects to **ephedrine**
- Enters the central nervous system more readily
- Alertness and appetite suppressant effects

■ **Cocaine**





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> Sympathoplegics



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- Act in the sympathetic nervous system
- Anti-hypertensive therapeutics
- **Clonidine** and **α -methyldopa**
- Centrally acting α 2 agonists
- Decrease central adrenergic outflow

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> Alpha Blockers

Nonselective α blockers: treat pheochromocytoma


- Reversible: phentolamine
- Non-reversible: phenoxybenzamine

α 1 selective blockers:

- Prazosin, terazosin and doxazosin
- Treat hypertension

α 2 selective blockers:

- Mirtazapine
- Treat depression



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Beta Blockers


Two types of β receptors: β_1 , β_2

Location:

- Cardiovascular system
- Eye

β blockers may be:

- Non-selective between β subtypes
- Non-selective between α and β receptors
- Selective for subtype of β receptor



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Summary: Pharmacology of the Nervous System

Two types of cholinergic receptors:

- Nicotinic receptors
- Muscarinic receptors

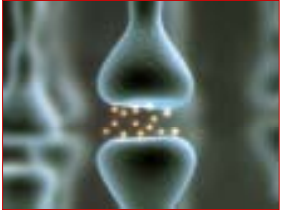

Cholinergic agonists

- Direct
- Indirect

Sympathomimetics

Sympathetic antagonists

- α blockers
- β blockers

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Clinical Challenge: Exam Question

A 25 year old man who is a farm worker develops severe diarrhea; excessive urination, lacrimation, sweating and salivation; bronchospasm and bradycardia. Which of the following is he most likely to have been exposed to?

- A) Atropine
- B) Pralidoxime
- C) Bethanechol
- D) Parathion
- E) Physostigmine



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Clinical Challenge: Exam Answer

■ Poisoning symptoms - LESS DUMBB

- **L**acrimation
- **E**xcitation of skeletal muscle and CNS
- **S**weating
- **S**alivation
- **D**iarrrhea
- **U**rination
- **M**iosis
- **B**ronchospasm
- **B**radycardia

D) Parathion



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Toxicity and Drug Reactions




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▶ Lead Poisoning


Symptoms of lead poisoning: **LEAAAD**:


- **LL**: Lead Lines on gingivae and epiphyses of long bones
- **EE**: Encephalopathy and Erythrocyte basophilic stippling
- **AA**: Abdominal colic and sideroblastic anemia
- **D**: wrist and foot drop



First line of treatment:

- Children: **succimer**
 - “it sucks to be a kid who eats lead” (suc = succimer, ks = kids)
- Adults: **EDTA** and **dimercaprol**



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Iron Poisoning


Over-consumption of iron

- Food and dietary supplements

A leading cause of fatality due to toxicity in children

Symptoms distinguished based on the length of exposure:

- Acute: gastric bleeding
- Chronic: metabolic acidosis, scarring leading to GI obstruction



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Alcohol Toxicity


Ethylene → **Oxalic Acid**

Methanol → **Formaldehyde & Formic Acid**

Ethanol → **Acetaldehyde** → **Acetic Acid**

Acidosis
Nephrotoxicity

Acidosis
Retinal Damage



Nausea
Vomiting
Hypotension
Headache

⊥

Disulfiram


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🔊

➤ Drug Interactions

Inducers


- Quinidine
- Barbiturates
- Phenytoin
- Rifamin
- Griseosulvin
- Carbamezapine
- St. John's wort

Queen Betsy takes Phen-phen and Refuses Gross Cow Steaks



Inhibitors: Isoniazid, Sulfonamides, Cimetidine, Keotoconazole, Erythromycin, Grapefruit juice

Inhibitors Stop Cool Kids from Eating Grapefruit





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➤ Sulfa Drugs

Allergies to sulfa-containing drugs:

- Celecoxib, Furosemide, Thiazides
- Sulfonylureas, Sulfasalazine, TMP-SMX





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Herbal Agents

Echinacea: GI distress, drowsiness and headache

Melatonin: sedation, hypoprolactemia and suppression of midcycle LH

St. John's Wort: GI distress, P450 induction, and serotonin syndrome when used in conjunction with SSRIs

Kava: hepatotoxicity, phototoxicity and dermatotoxicity



Ephedra: actions similar to epinephrine; side effects include CNS and cardiovascular stimulation, arrhythmia, stroke and seizure at high doses



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Summary: Toxicity & Drug Reactions

Toxicity can be caused by:

- Metals
 - Lead and iron
- Alcohol and drugs
- Herbal agents



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Clinical Challenge: Exam Question

A 30 year old man who is an active body builder exhibits metabolic acidosis and GI obstruction. Which of the following is a potential cause of these symptoms?

- A) Echinacea
- B) Pralidoxime
- C) Lead-containing supplements
- D) Iron-containing supplements
- E) Melatonin



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Clinical Challenge: Exam Answer

D) Iron-containing supplements

Poisoning symptoms distinguished based on the length of exposure:

- Acute: gastric bleeding
- Chronic: metabolic acidosis, scarring leading to GI obstruction



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Clinical Terms: Pharmacology - 1

Pharmacodynamics: the study of the relationship between drug concentration in the body, and the physiological response to that concentration of drug

Dose-response: the relationship between the given dose and the observed response is linked by the interaction of the drug with a specific receptor

Receptors: components of a cells or organisms that interact with a drug

Coupling: links the drug occupancy of receptors to the pharmacological response



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Clinical Terms: Pharmacology - 2

Agonists: initiate changes in cell function through their actions at receptors

Potency: range of doses over which a chemical produces increasing responses

Antagonists: prevent agonists from activating receptors

Pharmacokinetics: the study of the movement of drugs in the body

Half-life: time required for the blood or plasma chemical concentration to decrease to one-half its original value due to elimination



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Learning Summary

Pharmacodynamics is the study of what the drug does to the body.

Pharmacokinetics is the study of the movement of drugs in the body.


Drug naming conventions help identify the class of drug, by providing a common ending to the drug name as an identifier.

Drugs that act within the **autonomic nervous system** primarily target **cholinergic or sympathetic receptors**.

Toxicity is caused by a number of agents, including heavy metals, therapeutic drugs and herbal remedies.

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Congratulations

You have successfully completed
the core tutorial

Pharmacology

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What's Next ...

Step 1: Concepts – Core Tutorial (Just Completed)
→ Step 2: Practice – Interactive Problem Drill
Step 3: Recap – Super Review Cheat Sheet

Go for it!



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