A study guide to aid students preparing for the general and ocular pharmacology areas of the basic sciences test administered by the National Board of Examiners in optometry

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A study guide to aid students preparing for the general and ocular pharmacology areas of the basic sciences test administered by the National Board of Examiners in optometry

Abstract
For many optometry students across the nation, much systemic and ocular pharmacology is not presented in their school’s curriculum until after they have taken the Basic Sciences Test of the National Board Exam. The Pharmacology sections of the popular study guides in use today have been described by most students as overwhelming and confusing. This guide follows the outline of the Candidate Guide to provide a clear, concise study aid of drug groupings, drug uses, mechanisms of action, possible adverse reactions, contraindications and precautions, and the primary drug of treatment for specific conditions and alternate drugs for use when the primary drug is contraindicated.

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Thesis

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A STUDY GUIDE TO AID STUDENTS PREPARING FOR THE GENERAL AND OCULAR PHARMACOLOGY AREAS OF THE BASIC SCIENCES TEST ADMINISTERED BY THE NATIONAL BOARD OF EXAMINERS IN OPTOMETRY

BY

GARY W. ABEL
JOHN H. STADICK

A thesis submitted to the faculty of the College of Optometry Pacific University Forest Grove, Oregon in partial fulfillment for the degree of Doctor of Optometry May, 1994

Advisers:
Robert P. Rosenow, O.D.
Salisa K. Williams, O.D.
AUTHOR BIOGRAPHIES

JOHN H. STADICK

John Stadick is a resident of Sheridan, Wyoming. He attended Sheridan College and the University of Wyoming. John earned a bachelor's degree in Zoology from the University of Wyoming in May, 1990. In college John was active as a member of the U.W. Cycling Team, the U.W. Honors Program, and the Phi Theta Kappa National Honor Fraternity. Awards received include the Outstanding Pre-Optometry Student from the Wyoming Optometric Association, the WICHE Scholarship for Optometry, and the President's Honor Scholarship from Sheridan College. At Pacific, John was Treasurer of the Amigos Volunteer Optometric Organization and participated in missions to Merida, Mexico; Santiago, Chile; and Colombia.

John's career goal is to practice full scope, primary care optometry with an emphasis on pathology.

GARY W. ABEL

Gary W. Abel attended the University of Nevada, Reno where he graduated with a Bachelor of Science degree in Electrical Engineering. After taking additional classes in the biological sciences, Gary entered Pacific University and will graduate with a Doctor of Optometry degree in May of 1994. He plans to practice in Nevada after graduation.
ABSTRACT

For many optometry students across the nation, much systemic and ocular pharmacology is not presented in their school's curriculum until after they have taken the Basic Sciences Test of the National Board Exam. The Pharmacology sections of the popular study guides in use today have been described by most students as overwhelming and confusing. This guide follows the outline of the Candidate Guide to provide a clear, concise study aid of drug groupings, drug uses, mechanisms of action, possible adverse reactions, contraindications and precautions, and the primary drug of treatment for specific conditions and alternate drugs for use when the primary drug is contraindicated.
Acknowledgments

We would like to thank Salisa K. Williams, O.D., and Robert P. Rosenow, O.D. for their time, suggestions, and wisdom as advisors. It was greatly appreciated.
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ADRENERGIC AGONISTS

Adrenergic Agonists

Catecholamines
- dobutamine
- dopamine (Intropin)
- epinephrine (Parenteral: Adrenalin) (Inhalation: Primatene Mist)
- isoproterenol (Oral: Isuprel) (Inhalation: Vaso-Iso)
- norepinephrine (Levophed, Noradrenaline)

Noncatecholamines
- albuterol (Proventil, Ventolin) #21 & #24 drugs in 1991
- ephedrine (Efedron)
- isoetharine
- mephentermine
- metaproterenol (Alupent)
- metaraminol
- methoxamine
- nylidrin
- phenylephrine (Neo-Synephrine)
- ritodrine
- terbutaline (Brethine)

"\(\Delta\)\" indicates a top 200 drug in 1991 -- note ranking after trade name
"\(\Delta\)\" indicates major drugs -- see table

Indications for Use:
- Catecholamines-- the therapeutic uses of catecholamines are related to both their systemic effects and to their local effects
  a) local vasoconstrictive actions of the drugs make them useful as:
      - nasal decongestants to treat inflammatory and allergic conditions
      - ophthalmic decongestants to treat conjunctivitis and ocular congestion
      - intraocular hypotensive agents to treat open-angle glaucoma
      - topical hemostatics to control superficial bleeding
      - antiallergists to treat hypersensitivity and anaphylaxis
      - local application of various drugs dilate pupils without concurrent cycloplegia or increased IOP to provide beneficial effects in ophthalmic examinations
  b) beta\(_1\)-active drugs are used:
      - to treat bradycardia and heart block and insufficient cardiac output
      - to terminate paroxysmal atrial or nodal tachycardia
      - in cases of ventricular fibrillation, asystole, or cardiac arrest
c) beta₂-active catecholamines are used to:
- treat acute and chronic bronchial asthma, emphysema, bronchitis, and acute hypersensitivity reactions to drugs
- Non catecholamines -- have a wide variety of therapeutic uses related to the many physiologic effects of the drugs including:
  - local or systemic vasoconstriction
  - nasal and ophthalmic decongestion
  - bronchodilation
  - smooth muscle relaxation

---

**CATECHOLAMINES**

**Mechanism of Action:**
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

**Adverse Reactions:**
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

**Ocular Adverse Reactions:**
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

**Contraindications and Precautions:**
- note signs of overdose such as headache, vomiting, hypotension, hypertension, blurred vision, cardiac dysrhythmias, or chest pains

use cautiously in the following conditions:
- elderly patients due to possible reduced cardiac reserve and likelihood of dysrhythmias, confusion, or cerebrovascular accident
- pregnant patients due to possible adverse effects on the fetus
- hypertensive patients since drugs may cause further increase in blood pressure, cardiac output, or vasoconstriction
- diabetes mellitus since may have an anti-insulin effect with unpredictable effects on diabetes control
- circulatory or cardiovascular disease since may cause vasoconstriction, dysrhythmias, tachycardia or bradycardia, hypertension or hypotension
- glaucoma since may cause increased intraocular pressure

**Drug Interactions:**
- drug interactions involving catecholamines can be among the most serious
- knowledge of the interactions between catecholamines and other agents is essential because of the potential for additive effects which might lead to a hypertensive crisis or cardiac dysrhythmias
- drugs that must not be used with catecholamines or that should be used concurrently only with extreme caution include MAO inhibitors, tricyclic antidepressants, oxytocics, furazolidone, ergot alkaloids, antihistamines, some general anesthetics, digitalis, or other sympathomimetic agents.

- catecholamines can produce similar and significant reactions throughout the body including hypotension, hypertension, cardiac dysrhythmias, seizures, and hyperglycemia in diabetics.

- beta-blockers such as propranolol reduce the effects of the catecholamines and increase total peripheral resistance by allowing uncompensated alpha stimulation with beta blockade, which may result in hypertension and reflex bradycardia.

### NONCATECHOLAMINES

#### Mechanism of Action:
- mechanism of action for all classes of drugs are listed in the tables for each of the specific major drugs

#### Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

#### Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

#### Contraindications and Precautions:
- use noncatecholamines cautiously in diabetic patients because of the possibility of hyperglycemia.
- don't use mephentermine with epinephrine or hydralazine because they are incompatible.

#### Drug Interactions:
- drugs known to interact with various noncatecholamines encompass many of the drugs also contraindicated with catecholamines including MAO inhibitors, furazolidone, beta blockers, other sympathomimetics, acetazolamide, ascorbic acid, and many others.

- can produce significant reactions throughout the body, including hypotension, hypertension, cardiac dysrhythmias, seizures, and hyperglycemia in diabetics.
## ADRENERGIC AGONISTS

### b2a  Catecholamines

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indication for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>dopamine (Intropin)</td>
<td>stimulates dopaminergic, alpha, and beta receptors to increase force of myocardial contractions and increase cardiac output</td>
<td>used to treat cardiogenic or bacteremic shock with related renal shutdown and chronic congestive heart failure</td>
<td>ectopic heart beats, nausea, vomiting, tachycardia, anginal pain, headache, hypotension</td>
<td>high doses may cause dilated pupils</td>
</tr>
<tr>
<td>epinephrine (Adrenalin)</td>
<td>stimulates alpha, beta, beta2 receptors to increase cardiac output and to relieve respiratory distress due to bronchospasm</td>
<td>used to treat bronchospasm, asthma, open-angle glaucoma, allergic conditions, hypotension, cardiac arrest</td>
<td>transient anxiety, headache, fear and heart palpitations</td>
<td>mydriasis-may precipitate narrow-angle glaucoma red-green color vision defect hemianopsia</td>
</tr>
<tr>
<td>isoproterenol (Isuprel)</td>
<td>stimulates beta and beta2 receptors of the heart and smooth muscle of bronchi to produce cardiac stimulation and bronchodilation</td>
<td>used to treat asthma, bronchospasm, shock cardiac arrest, cardiac dysrhythmias</td>
<td>nervousness, headache, dizziness, tachycardia, palpitations, angina, flushing of the skin, sweating</td>
<td></td>
</tr>
<tr>
<td>norepinephrine (Levophed)</td>
<td>stimulates alpha and beta receptors to produce peripheral vasoconstriction and to increase cardiac output due to increased myocardial contractions</td>
<td>used to treat acute hypotension, shock, cardiac arrest, myocardial infarctions, anaphylactic shock</td>
<td>bradycardia as a reflex result of a rise in blood pressure, headache may indicate overdosage</td>
<td>none listed</td>
</tr>
<tr>
<td>DRUGS</td>
<td>Generic Name (Brand)</td>
<td>Mechanism of Action</td>
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</tr>
<tr>
<td>albuterol (Proventil, Ventolin)</td>
<td>#21 &amp; #24 drugs in 1991</td>
<td>Stimulates beta2 adrenergic receptors of the lung's smooth muscle causing relaxation</td>
<td>used to relieve acute bronchial asthma and to reduce frequency and severity of chronic, recurrent asthmatic attacks</td>
<td>nervousness, heart palpitations, hand tremor, headache, leg cramps, dizziness</td>
</tr>
<tr>
<td>ephedrine (Efedron)</td>
<td></td>
<td>Dual acting drug that stimulates alpha, beta, and CNS receptors to cause bronchodilation and vasoconstriction</td>
<td>used to treat nasal congestion, hypotension, and narcolepsy</td>
<td>heart palpitation, tachycardia, headache, insomnia, sweating, nervousness, nausea, vomiting,</td>
</tr>
<tr>
<td>metaproterenol (Alupent)</td>
<td></td>
<td>Direct acting beta2-selective agent with stimulation of beta2 adrenergic receptors of lung smooth muscle causes relaxation resulting in bronchodilatory effects</td>
<td>used to treat asthma, bronchitis, and emphysema</td>
<td>tachycardia, hypertension, heart palpitations, nervousness, tremor, nausea, and vomiting</td>
</tr>
<tr>
<td>phenylephrine (Neo-Synephrine)</td>
<td></td>
<td>Potent direct-acting agent with strong alpha-receptor and weak beta-receptor actions to produce vasoconstriction</td>
<td>used for its systemic and topical vasopressor effects with anesthesia and for treating shock, tachycardia, rhinitis, allergies, uveitis, and to produce mydriasis</td>
<td>headache, reflex bradycardia, excitability, restlessness, drowsiness, lassitude, nausea, and rarely arrhythmias</td>
</tr>
<tr>
<td>terbutaline (Brethine)</td>
<td></td>
<td>Direct-acting agent which exerts selective beta2 activity to produce bronchodilation effects</td>
<td>used to treat bronchial asthma, bronchitis, and emphysema</td>
<td>nervousness, tremor, headache, increased heart rate, palpitations, drowsiness, nausea, vomiting, sweating, and muscle cramps</td>
</tr>
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</table>
**ADRENERGIC ANTAGONISTS**

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**Adrenergic Antagonists**

**Alpha-Adrenergic Blockers**
- ergoloid
- △ ergotamine (Ergostat, Cafergot suppositories)
- phenoxybenzamine
- △ phentolamine (Regitine)

**Beta-Adrenergic Blockers**
- acebutolol
- △ atenolol (Tenormin)
- labetalol
- △△ metoprolol (Lopressor) #23 drug in 1991
- △△ nadolol (Corgard) #90 drug in 1991
- pindolol
- △△ propranolol (Inderal) #41 drug in 1991
- △△ timolol (Timoptic) #60 drug in 1991

**Autonomic Ganglionic Blockers**
- mecamylamine
- trimethaphan (Arfonad)

"△△" indicates a top 200 drug in 1991 -- note ranking after trade name
"△" indicates major drugs -- see table

---

**Indications for Use:**

- **Alpha-Adrenergic Blockers**
  - Use is based on their smooth muscle relaxation and vasodilation and the resultant increased local blood flow to skin and other organs and decreased blood pressure from decreased peripheral vascular resistance.
  - Hypertension and peripheral vascular disorders are conditions in which these effects prove beneficial.
  - Peripheral vascular disorder with a vasospastic component causing poor local blood flow such as Raynaud's disease, acrocyanosis, and aftereffects of frostbite respond well to alpha-adrenergic therapy.
  - Migraine headaches are treated with ergotamine because it causes vasoconstriction of the dilated carotid artery.

- **Beta-Adrenergic Blockers**
  - Used extensively to treat hypertension, cardiac dysrhythmias, angina pectoris, hyperthyroidism, and other related disorders of sympathetic nervous system overstimulation.
  - Other uses include treatment of migraine headaches, anxiety, wide-angle glaucoma, and cardiovascular symptoms associated with thyrotoxicosis.
- Autonomic Ganglionic Blockers
  - used in the management of moderate to severe hypertension and are used to produce controlled hypotension for the reduction of surgical hemorrhage

**ALPHA-ADRENERGIC BLOCKERS**

**Mechanism of Action:**
- mechanisms of action for the specific drugs are listed in the tables

**Adverse Reactions:**
- adverse reactions for the specific drugs are listed in the table

**Ocular Adverse Reactions:**
- ocular adverse reactions for the specific drugs are listed in the table

**Contraindications and Precautions:**
- do not use in patients with congestive heart failure, angina, MI, or cerebrovascular insufficiency
- use cautiously in pregnant patients, patients with renal insufficiency, or marked cerebral or coronary arteriosclerosis, or respiratory infection
- alcohol consumption should be avoided because alcohol used in combination with alpha-adrenergic blocking agents may cause tachycardia and hypotension

**Drug Interactions:**
- many agents interact synergistically with alpha-adrenergic blocking agents and can potentiate or cause mutually additive effects
  - the interactions primarily affect the cardiovascular system and may include profound hypotension or vascular collapse, hypertension, and cardiac dysrhythmias
- interactions with:
  - alcohol may cause hypotension
  - caffeine increases ergotamine effects
  - dopamine increases pressor effects
  - nitroglycerin may cause potential hypotension by excessive vasodilation
  - sympathomimetics enhance cardiac stimulation and may cause hypotension rebound hypertension
BETA-ADRENERGIC BLOCKERS

Mechanism of Action:
- mechanisms of action for the specific drugs are listed in the table

Adverse Reactions:
- adverse reactions for the specific drugs are listed in the table

Ocular Adverse Reactions:
- ocular adverse reactions for the specific drugs are listed in the table

Contraindications and Precautions:
- contraindications include a history of congestive heart failure, bradycardia, heart block, liver or kidney disease, thyroid disease, myasthenia gravis, current pregnancy, use of psychotropic drugs, or use of MAO inhibitors
- use of beta-adrenergic blockers can potentiate hypoglycemia in diabetes and mask its signs and symptoms
- use beta-blockers with extreme caution in cases of respiratory conditions such as asthma, hayfever, bronchitis, emphysema, or allergic rhinitis since severe bronchospasm may occur

Drug Interactions:
- many agents interact synergistically with beta-adrenergic blockers to primarily affect the cardiovascular and respiratory systems
- some of the most serious potential effects include cardiac depression, dysrhythmias, respiratory depression, severe bronchospasm, and severe hypotension that could lead to vascular collapse

AUTONOMIC GANGLIONIC BLOCKERS

Mechanism of Action:
- by inhibiting the action of acetylcholine, ganglionic blocking agents reduce or prevent the transmission of impulses in the autonomic nervous system
- mecamylamine and trimethaphan belong to the nondepolarizing category of autonomic ganglionic blockers which function as competitive antagonists of acetylcholine at postganglionic receptor sites and exert no initial stimulatory action
- they cause primarily sympatholytic effects: vasodilation and decreased blood pressure

Adverse Reactions:
- possible cardiovascular manifestations include either tachycardia or bradycardia and orthostatic hypotension
- CNS effects may include restlessness, weakness, fatigue, sedation, cycloplegia, or mydriasis
- GI and genitourinary signs and symptoms may include nausea, vomiting, or anorexia as well as parasympathetic manifestations—dry mouth, constipation
- Dose-related severe adverse reactions can include extreme hypotension, rapid pulse, angina-like pain, vascular collapse, abdominal distention, dizziness, syncope, tremors, mental disturbance, and impaired sexual function

**Ocular Adverse Reactions:**
- With systemic administration
  - Decreased vision
  - Mydriasis—May precipitate narrow-angle glaucoma
  - Paralysis of accommodation
  - Conjunctival edema
  - Decreased IOP

**Contraindications and Precautions:**
- Trimethaphan should be used with extreme caution in patients with histories of allergy because it can cause histamine release
- Mecamylamine should be used with caution in patients with renal, cerebral, or coronary hypertrophy; bladder neck or urethral obstruction; prostatic hypertrophy; or elevated serum blood urea nitrogen levels

**Drug Interactions:**
- Combining certain drugs with ganglionic blocking agents can cause significant adverse reactions, including tachycardia, orthostatic hypotension, congestive heart failure, and stroke
  - Alcohol, anesthetics, anticholinergics, reserpine, MAO inhibitors, thiazide diuretics, and vasodilators all increase hypotensive effects
  - Depolarizing muscle relaxants and nondepolarizing muscle relaxants increase neuromuscular blocking effects with prolonged respiratory depression
  - Sympathomimetics increase sympathomimetic effects
### ADRENERGIC ANTAGONISTS

#### b3a  Alpha-Adrenergic Blockers

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indication for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
</table>
| ergotamine (Ergostat, Cafergot suppositories) | -- has partial antagonist activity against alpha-adrenergic receptors  
-- constricts peripheral and cranial blood vessels and depresses central vasomotor centers  
-- is a highly active uterine stimulant | -- used in treatment of vascular headaches, especially migraine and "cluster" headaches  
-- often effective in terminating the headache if taken within the first hour following onset of pain | -- nausea and vomiting occur in up to 10% of patients  
-- numbness and tingling of fingers and toes, muscle pain in the extremities, weakness in the legs, transient tachycardia or bradycardia | none listed |
| phentolamine (Regitine) | -- blocks presynaptic (alpha2)and postsynaptic (alpha1) alpha-adrenergic receptors  
-- acts on both the arterial tree and venous bed so total peripheral resistance is lowered and venous return to the heart is diminished | used to diagnose pheochromocytoma (a chromaffin cell tumor of the sympatho-adrenal system that produces catecholamines) and to control hypertension during surgical excision of the tumor | -- acute and prolonged hypotensive episodes, tachycardia and cardiac arrhythmias  
-- weakness, dizziness, flushing, orthostatic hypotension | none reported |
<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
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<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
</table>
| atenolol (Tenormin)       | -- competes with epinephrine for beta-receptor sites  
-- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow  
-- reduces rate and contraction force of the heart to decrease the oxygen requirement for heart function and reduce the degree of contraction of blood vessel walls, resulting in lowered blood pressure | used for treatment of angina pectoris and hypertension | Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension  
Unusual: headache, dizziness, drowsiness, nausea,  
Serious unusual: mental depression, anxiety, chest pain, shortness of breath | rare and transient and may include ocular irritation, dry eyes, decreased tear production, and blurred vision |
| metoprolol (Lopressor) #23 drug in 1991 | - competes with epinephrine for beta-receptor sites  
- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow | used to treat hypertension and myocardial infarction | same adverse reactions as for atenolol | effects are rare but may include decreased vision, conjunctival irritation, ocular pain, dry eyes and decreased tear production |
| nadolol (Corgard) #90 drug in 1991 | -- competitive blockade of beta adrenergic receptors  
-- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow  
-- actions in angina to decrease cardiac work | used to treat angina pectoris and hypertension | Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension  
Unusual: headache, dizziness, drowsiness, nausea,  
Serious unusual: facial swelling, chest pain, shortness of breath, precipitation of congestive heart failure | rare and transient and may include diplopia, decreased vision, allergic reactions of conjunctiva and lids, decreased IOP, and visual hallucinations |
<table>
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<tr>
<th>DRUGS</th>
<th>Generic Name (Brand)</th>
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<th>Ocular Adverse Reactions</th>
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</thead>
<tbody>
<tr>
<td>propranolol (Inderal)</td>
<td>#41 drug in 1991</td>
<td>-- non-selective competitive blocker of beta receptors -- decreased cardiac output, and/or decreased central sympathetic outflow -- actions in angina to decrease heart rate and cardiac work -- has a membrane stabilizing or local anesthetic effect to decrease action potential conduction and prolong the conduction time of nerve impulses through the heart</td>
<td>used to treat hypertension, angina pectoris, cardiac arrhythmias, and migraine headaches</td>
<td>Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension Unusual: skin rash, temporary loss of hair, headache, dizziness, drowsiness, nausea Serious unusual: acute behavioral disturbances, disorientation, confusion, amnesia, mental depression, anxiety, chest pain, shortness of breath, precipitation of congestive heart failure</td>
<td>rare and transient and may include diplopia, decreased vision, allergic reactions of conjunctiva and lids, decreased IOP, and visual hallucinations</td>
</tr>
<tr>
<td>timolol (Timoptic)</td>
<td>#60 drug in 1991</td>
<td>-- non-selective beta adrenergic blocking agent -- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow -- has a membrane stabilizing or local anesthetic effect to decrease action potential conduction and prolong the conduction time of nerve impulses through the heart -- decreases aqueous formation in the anterior chamber to lower IOP</td>
<td>used to treat angina pectoris, glaucoma, hypertension, to prevent the recurrence of myocardial infarction, and to reduce the frequency and severity of migraine headaches</td>
<td>Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension Unusual: skin rash, temporary loss of hair, headache, dizziness, drowsiness, nausea Serious unusual: laryngospasm, severe dermatitis, acute behavioral disturbances, mental depression, chest pain, shortness of breath, precipitation of congestive heart failure</td>
<td>mild ocular irritation including conjunctivitis, blepharitis, and keratitis -- has infrequently caused refractive changes, corneal hypoesthesia, and blepharoptosis</td>
</tr>
</tbody>
</table>
CHOLINERGIC AGONISTS

Cholinergic Agonists

Δ bethanechol (Duvoid)
Δ carbachol (Carbacel)
ΔΔ metoclopramide (Reglan) #176 drug in 1991
Δ pilocarpine (Pilocar)

"ΔΔ" indicates a top 200 drug in 1991 -- note ranking after trade name
"Δ" indicates major drugs -- see table

Indications for Use:
- used to treat atonic conditions of the GI tract or bladder
- used to reduce intraocular pressure in the anterior chamber of the eye
  (useful in patients with glaucoma and those undergoing ophthalmologic surgery)

Mechanism of Action:
- mechanisms of action for the specific drugs are listed in the table

Adverse Reactions:
- adverse reactions for the specific drugs are listed in the table

Ocular Adverse Reactions:
- ocular adverse reactions for the specific drugs are listed in the table

Contraindications and Precautions:
- cholinergic overstimulation can result from patient hypersensitivity or drug overdose which may cause circulatory collapse resulting in hypotension, shock, and cardiac arrest
- note the patient's cardiovascular function to detect adverse reactions

Drug Interactions:
- drug interactions involving the cholinergic agonists usually occur with drugs that also act at the autonomic effector cells
- other cholinergic agents, particularly anticholinesterase agents increase potential for cholinergic toxicity
- cholinergic blocking agents antagonize the effect of acetylcholine at the muscarinic receptors
- ganglionic blocking agents antagonize the effect of cholinergic agonists at autonomic ganglia
- neuromuscular blocking agents antagonize the effect of acetylcholine at neuromuscular junction
- sympathomimetics antagonize effects of cholinergic agonists
- procainamide and quinidine diminish vagal transmission
### CHOLINERGIC AGONISTS (Parasympathomimetics)

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>bethanachol</strong> (Urecholine)</td>
<td>combines with cholinergic receptors at organs innervated by the parasympathetic nervous system to produce stimulation of the PNS and release of acetylcholine at the nerve endings -- produces a contraction strong enough to initiate emptying of the bladder and stimulates gastric motility</td>
<td>-- urination retention -- postoperative abdominal distention</td>
<td>-- malaise, abdominal discomfort, salivation, flushing of the skin, sweating, nausea, vomiting, urinary urgency, and headaches</td>
<td>-- w/systemic use: hyperemia, lacrimation, decreased accommodation, and miosis</td>
</tr>
<tr>
<td><strong>carbachol</strong> (Carbacel)</td>
<td>combines with cholinergic receptors at organs innervated by the parasympathetic nervous system to produce stimulation of the PNS and release of acetylcholine at the nerve endings -- direct acting stimulation of muscarinic receptor</td>
<td>-- used in open-angle glaucoma -- effective in the management of postoperative lack of intestinal muscle tone and urinary retention</td>
<td>-- fever, syncope, nausea, diarrhea</td>
<td>-- w/systemic use: decreased accommodation -- w/local ocular use: miosis, decreased vision, decreased intraocular pressure, accommodative spasm</td>
</tr>
<tr>
<td><strong>metoclopramide</strong> (Reglan) #176 drug in 1991</td>
<td>combines with cholinergic receptors at organs innervated by the parasympathetic nervous system to produce stimulation of the PNS and release of acetylcholine at the nerve endings -- stimulates motility of the upper GI tract without stimulating gastric, biliary or pancreatic secretions</td>
<td>used to stimulate contractions of the stomach and facilitate emptying of the stomach in disorders such as: 1) diabetic gastric stasis 2) acid reflux from the stomach into the esophagus 3) nausea and vomiting of migraine headaches 4) nausea and vomiting induced by anticancer drugs</td>
<td>-- skin rash -- headache, dizziness, restlessness, depression -- dry mouth, nausea, diarrhea</td>
<td>-- inability to close the eyes, nystagmus, diplopia, strabismus, -- decreased vision -- edema and urticaria of eyelids or conjunctiva</td>
</tr>
<tr>
<td><strong>pilocarpine</strong> (Piloc)</td>
<td>combines with cholinergic receptors at organs innervated by the parasympathetic nervous system to produce stimulation of the PNS and release of acetylcholine at the nerve endings -- direct stimulation of muscarinic receptor -- directly stimulates constriction of the pupil to enlarge outflow canal in the anterior chamber and promote drainage of aqueous to lower IOP</td>
<td>-- used for management of all types of glaucoma -- combined with epinephrine (dilation) to utilize actions of both drugs in lowering IOP -- (pilocarpine constricts, epinephrine dilates) to provide a balance that prevents excessive constriction or dilation</td>
<td>headache, perspiration, nausea and vomiting, heart palpitations, tremors</td>
<td>miosis, decreased vision, paralysis or spasm of accommodation, decreased anterior chamber depth, itching or swelling of the eyelids</td>
</tr>
</tbody>
</table>
CHOLINERGIC ANTAGONISTS

Cholinergic Antagonists

Anticholinesterase Agents
- ambenonium
- demecarium (Humorsol)
- echothiophate (Phospholine Iodine)
- edrophonium (Tensilon)
- neostigmine (Prostigmin)
- physostigmine (Antilirium)
- pyridostigmine

Cholinergic Blockers
- atropine (Atropine Sulfate Injection)
- belladonna
- benztpine (Cogentin)
- clidinium
- dicyclomine (Bentyl)
- ethopropazine
- glycopyrrolate
- homatropine (Homatropel Ophthalmic)
- hyoscyamine
- oxybutynin
- propantheline (Banthine)
- scopolamine (Transderm Scop)
- trihexyphenidyl

"△△" indicates a top 200 drug in 1991 -- note ranking after trade name
* △ " indicates major drugs -- see table

Indications for Use:
Anticholinesterase Agents
- anticholinesterase agents inhibit the enzyme acetylcholinesterase, thereby slowing the destruction of acetylcholine
- with reversible anticholinesterase agents, the blocking effect lasts for minutes to hours
- reversible (short-term) agents are used therapeutically
- used to promote muscle contraction in patients with myasthenia gravis
- ability to reduce intraocular pressure makes them useful in ophthalmologic surgery and in treating glaucoma
- used to stimulate tone and peristalsis in the GI tract in patients with gastroparesis
- with irreversible anticholinesterase agents, the effects are sustained for days or even weeks
- irreversible (long-term) agents, the organophosphates, are used primarily as toxic insecticides and pesticides and have also been used as nerve gases in chemical warfare
Indications for Use: (continued)

**Cholinergic Blockers**
- Cholinergic blocking agents interrupt parasympathetic nerve impulses in the central and autonomic nervous systems.
- Primary indications include spastic conditions of the GI and urinary tracts, cardiac dysrhythmias, motion sickness, parkinsonism, and chronic asthma.
- Used as preanesthesia medications and as relaxants for the GI tract during diagnostic procedures and for the eye and pupil during ophthalmologic surgery.
- Serve as antidotes to cholinergic agents, certain organophosphate pesticides, and neuromuscular blocking agents.

---

**ANTICHOLINESTERASE AGENTS**

Mechanism of Action:
- Inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm.
- May be one of three types (specifics indicated in table):
  - **a)** Long-acting, irreversible anticholinesterase
    - I.e., demecarium, echothiophate
  - **b)** Short-acting anticholinesterase
    - I.e., physostigmine
  - **c)** A reversible anticholinesterase
    - I.e., edrophonium, neostigmine

Adverse Reactions:
- Adverse reactions for the specific drugs are listed in the table.

Ocular Adverse Reactions:
- Ocular adverse reactions for the specific drugs are listed in the table.

Contraindications and Precautions:
- Reaction to the anticholinesterase agents is difficult to predict in patients with myasthenia gravis.
- When the agents are used for parasympathomimetic effects, contraindications and precautions are the same as for the cholinergic agonists.
  1) Overstimulation can result from patient hypersensitivity or drug overdose which may cause circulatory collapse resulting in hypotension, shock, and cardiac arrest.
  2) Note the patient's cardiovascular function to detect adverse reactions.
Anticholinesterase Agents (continued)

Drug Interactions:
- drug interactions involving anticholinesterase agents usually occur at either nicotinic or muscarinic receptor sites
- anesthetics and antibiotics antagonize neuromuscular blockade effect
- other cholinergic agents, particularly cholinergic agonists increase potential for toxicity
- cholinergic blocking agents antagonize effect of acetylcholine at muscarinic receptors
- ganglionic blocking agents antagonize effect of anticholinesterase agents at autonomic ganglia, producing both an anticholinergic and a cholinergic effect
- neuromuscular blocking agents antagonize the effect of acetylcholine at the neuromuscular junction
- procainamide and quinidine diminish vagal transmission and produce neuromuscular blockade
- quinine increases the refractory period of skeletal muscle, reducing its response to acetylcholine

CHOLINERGIC BLOCKERS

Mechanism of Action:
- all compete with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle
- some block cholinergic stimulation of the iris sphincter muscle and ciliary body producing pupillary dilation and paralysis of accommodation i.e. atropine, belladonna, homatropine
- others are tertiary amines with little antimuscarinic activity; exhibit a selective CNS activity i.e. benztropine, dicyclomine

Adverse Reactions:
- adverse reactions for the specific drugs are listed in the tables

Ocular Adverse Reactions:
- ocular adverse reactions for the specific drugs are listed in the tables
Cholinergic Blockers (continued)

Contraindications and Precautions:
- drugs should be administered cautiously to patients over age 40 because of the chance of undiagnosed glaucoma
- tachycardia secondary to administration of cholinergic blocking agents in coronary artery disease patients can lead to congestive heart failure
- may produce urinary obstruction in patients with benign prostatic hypertrophy
- since these drugs inhibit such heat-regulating mechanisms as sweating, heatstroke is a potential complication
- should not be administered concurrently with antacids or antidiarrheals
- order analgesics for patients in pain when they are receiving cholinergic blocking agents; otherwise, the likelihood of CNS excitation increases

Drug Interactions:
- carbonic anhydrase inhibitors enhance antimuscarinic effect from alkalization of the urine
- antacids and antidiarrheals reduce absorption of cholinergic blockers
- antiarhythmics, tricyclic and tetracyclic antidepressants, antidyskinetics, antiemetids and antivertigo agents, and diphenhydramine antipsychotics enhance antimuscarinic effects
- cholinergic agonists reverse antimuscarinic action
- interact with digoxin to increase serum concentration levels of digoxin by decreasing gastrointestinal motility
- ganglionic blocking agents decrease anticholinergic effect in the eye and the GI tract
- opiate-like analgesics decrease gastrointestinal motility
## CHOLINERGIC ANTAGONISTS

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
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<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>demecarium</td>
<td>(Humorsol)</td>
<td>-- inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm -- long acting, irreversible anticholinesterase</td>
<td>used to treat glaucoma and accommodative esotropia in children</td>
<td>-- nausea, vomiting, diarrhea -- urinary incontinence (loss of bladder control) -- dyspnea (labored or difficult breathing) -- bradycardia, cardiac arrhythmia</td>
<td>-- miosis -- decreased vision -- accommodative spasm -- hyperemia, photophobia, edema -- cataracts (anterior or PSC)</td>
</tr>
<tr>
<td>echothiopate</td>
<td>(Phospholine Iodine)</td>
<td>-- inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm -- long acting, irreversible anticholinesterase</td>
<td>used to treat: -- open-angle glaucoma -- conditions obstructing aqueous outflow -- accommodative esotropia</td>
<td>-- nausea, vomiting, diarrhea -- urinary incontinence (loss of bladder control) -- dyspnea (labored or difficult breathing) -- bradycardia, cardiac arrhythmia</td>
<td>-- miosis -- decreased vision -- accommodative spasm -- hyperemia, photophobia, edema -- cataracts (anterior or PSC)</td>
</tr>
<tr>
<td>edrophonium</td>
<td>(Tensilon)</td>
<td>-- inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm -- a reversible anticholinesterase</td>
<td>-- drug of choice for the diagnosis of myasthenia gravis -- also used to differentiate myasthenia gravis from cholinergic toxicity -- used to terminate attacks of paroxysmal supraventricular tachycardia and tachydysrhythmia unresponsive to digitalis</td>
<td>-- perspiration -- asthma -- apnea -- bradycardia, cardiac arrest, hypotension</td>
<td>-- miosis -- decreased vision -- diplopia -- blepharoclonus (sustained contraction of muscles closing the eyes)</td>
</tr>
</tbody>
</table>
### Anticholinesterase Agents (continued)

<table>
<thead>
<tr>
<th>DRUGS</th>
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<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>neostigmine (Prostigmin)</strong></td>
<td>-- inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm -- a reversible anticholinesterase</td>
<td>-- diagnosis and treatment of myasthenia gravis -- prevention and treatment of postoperative distention and urine retention -- used as an antidote to neuromuscular blocking agents</td>
<td>-- allergic reactions and anaphylaxis -- dizziness, convulsions, loss of consciousness, drowsiness, headache -- cardiac arrhythmias (bradycardias, tachycardias) -- dyspnea, respiratory depression -- nausea, vomiting</td>
<td>w/systemic use: -- miosis -- decreased vision -- urticaria and allergic reactions to eyelids or conjunctiva</td>
</tr>
<tr>
<td><strong>physostigmine (Antilirium)</strong></td>
<td>-- inactivate the enzyme cholinesterase, allowing acetylcholine to exert its cholinergic effects which include pupil constriction and accommodative spasm -- short-acting anticholinesterase</td>
<td>- used to treat open-angle glaucoma - used to reverse the CNS effects caused by clinical or toxic dosages of drugs capable of producing an anticholinergic syndrome - used to treat tricyclic antidepressant and diazepam overdose (its ability to cross the blood-brain barrier makes it the drug of choice for this purpose)</td>
<td>-- nausea, vomiting -- salivation -- bradycardia -- convulsions</td>
<td>w/systemic use: -- miosis -- decreased vision -- urticaria and allergic reactions to eyelids or conjunctiva</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>w/ocular use: -- miosis -- decreased intraocular pressure -- hyperemia, photophobia -- accommodative spasm -- decreased vision</td>
</tr>
<tr>
<td><strong>DRUGS</strong></td>
<td><strong>Mechanism of Action</strong></td>
<td><strong>Indications for Use</strong></td>
<td><strong>Adverse Reactions</strong></td>
<td><strong>Ocular Adverse Reactions</strong></td>
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<tr>
<td><strong>atropine (Atropine Sulfate Injection)</strong></td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle</td>
<td>-- used to treat bradycardia, spastic conditions of the GI tract, and asthma</td>
<td>-- adverse reactions increase in severity as the dosage increases</td>
<td>w/systemic use: -- decreased vision - mydriasis may precipitate narrow-angle glaucoma -- absence of reaction to light -- paralysis of accommodation -- photophobia -- decreased lacrimation</td>
</tr>
<tr>
<td></td>
<td>-- blocks cholinergic stimulation of the iris sphincter muscle and ciliary body producing pupillary dilation and paralysis of accommodation</td>
<td>-- used to decrease secretions of the respiratory tract</td>
<td>-- agitation, confusion, psychosis, delirium, hallucinations, ataxia, hostility, fever, dry mouth, vasodilation, tachycardia, and convulsions</td>
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<tr>
<td></td>
<td>-- also used in treatment of hyperactive carotid sinus reflex and Parkinson's disease</td>
<td>-- topically used for mydriatic and cycloplegic effects in refractions, semiocclusive therapy, and treatment of accommodative spasms and uveitis</td>
<td>larger doses produce: -- psychotic reactions, hypotension, and progressive respiratory depression</td>
<td>w/ocular use: -- decreased vision -- paralysis of accommodation -- mydriasis may precipitate narrow-angle glaucoma -- irritation including hyperemia, photophobia, ocular pain, edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-- topically used for mydriatic and cycloplegic effects in refractions, semiocclusive therapy, and treatment of accommodative spasms and uveitis</td>
<td></td>
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</tr>
<tr>
<td><strong>belladonna (combinations of belladonna alkaloids)</strong></td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle</td>
<td>-- primarily used to decrease GI motility and inhibit gastric secretions in peptic ulcer, irritable bowel syndrome, and other GI disorders</td>
<td>-- adverse reactions increase in severity as the dosage increases</td>
<td>w/systemic use: -- decreased vision - mydriasis may precipitate narrow-angle glaucoma -- absence of reaction to light -- paralysis of accommodation -- photophobia -- decreased lacrimation</td>
</tr>
<tr>
<td></td>
<td>-- blocks cholinergic stimulation of the iris sphincter muscle and ciliary body producing pupillary dilation and paralysis of accommodation</td>
<td>-- topically used for mydriatic and cycloplegic effects in refractions, semiocclusive therapy, and treatment of accommodative spasms and uveitis</td>
<td>-- agitation, confusion, psychosis, delirium, hallucinations, ataxia, hostility, fever, dry mouth, vasodilation</td>
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<td>larger doses produce: -- psychotic reactions, hypotension, and progressive respiratory depression</td>
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</table>
### b5b Cholinergic Blockers (continued)

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>benztropine (Cogentin)</td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle</td>
<td>-- primarily used as an antidyskinetic in treating parkinsonism</td>
<td>-- adverse reactions increase in severity as the dosage increases</td>
<td>adverse ocular reactions are common with benztropine</td>
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<tr>
<td></td>
<td>-- a tertiary amine with little antimuscarinic activity; exhibits a selective CNS activity</td>
<td>-- also used in the control of extrapyramidal disorders due to central nervous system drugs, such as reserpine or the phenothiazines</td>
<td>-- decreased salivation, bronchial secretions, and sweating with small doses</td>
<td>w/systemic administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-- used to treat irritable bowel syndrome (irritable colon, spastic colon, mucous colitis)</td>
<td>-- pupil dilation, decreased visual accommodation, and increased heart rate with increased doses</td>
<td>- pupils</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-- larger doses inhibit urination and intestinal motility</td>
<td>a. mydriasis</td>
</tr>
<tr>
<td>dicyclomine (Bentyl)</td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle</td>
<td></td>
<td>-- decreased salivation, bronchial secretions, and sweating with small doses</td>
<td>b. decreased reaction to light</td>
</tr>
<tr>
<td></td>
<td>-- a tertiary amine with little antimuscarinic activity; exhibits a nonspecific direct relaxant effect on smooth muscle</td>
<td></td>
<td>-- pupil dilation, decreased visual accommodation, and increased heart rate with increased doses</td>
<td>-- decreased vision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-- larger doses inhibit urination and intestinal motility</td>
<td>-- mydriasis (may precipitate narrow-angle glaucoma)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-- paralysis of accommodation</td>
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<td></td>
<td></td>
<td></td>
<td>-- photophobia</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>-- diplopia</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-- problems with color vision</td>
</tr>
<tr>
<td>DRUGS Generic Name (Brand)</td>
<td>Mechanism of Action</td>
<td>Indications for Use</td>
<td>Adverse Reactions</td>
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</tr>
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</tr>
<tr>
<td>homatropine (Homatrocel Ophthalmic)</td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle. -- blocks cholinergic stimulation of the iris sphincter muscle and ciliary body producing pupillary dilation and paralysis of accommodation.</td>
<td>-- a moderately long-acting mydriatic and cycloplegic for refraction and in the treatment of inflammatory conditions of the uveal tract. -- for preoperative and postoperative states when mydriasis is required. -- used as an optical aid in some cases of axial lens opacities. -- also used in treatment of painful menstruation.</td>
<td>-- adverse reactions increase in severity as the dosage increases. -- agitation, confusion, psychosis, delirium, hallucinations, ataxia, hostility, fever, dry mouth, vasodilation, tachycardia, and convulsions. larger doses produce: -- psychotic reactions, hypotension, and progressive respiratory depression.</td>
<td>w/systemic use: -- decreased vision. -- mydriasis may precipitate narrow-angle glaucoma. -- absence of reaction to light. -- paralysis of accommodation. -- photophobia. -- decreased lacrimation.</td>
</tr>
<tr>
<td>propantheline (Banthine)</td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle.</td>
<td>-- used in the treatment of peptic ulcer. -- has been used for its antisecretory and antispasmodic effects.</td>
<td>-- adverse reactions increase in severity as the dosage increases. -- decreased salivation, bronchial secretions, and sweating with small doses. -- pupil dilation, decreased visual accommodation, and increased heart rate with increased doses. -- larger doses inhibit urination and intestinal motility.</td>
<td>w/systemic administration: -- decreased vision. -- mydriasis (may precipitate narrow-angle glaucoma). -- paralysis of accommodation. -- photophobia. -- diplopia. -- problems with color vision. w/inadvertent ocular exposure: -- mydriasis. -- absence of reaction to light.</td>
</tr>
</tbody>
</table>
### b5b Cholinergic Blockers (continued)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>scopolamine (Transderm Scop)</td>
<td>-- competes with acetylcholine and cholinergic agonists at muscarinic receptor sites in the CNS and at the neuromuscular junction between the postganglionic parasympathetic nerve and the smooth muscle</td>
<td>-- drug of choice for motion sickness (administered topically via a skin patch behind the ear) -- useful as a preanesthesia medication (reduces excessive salivation and respiratory tract secretions in anesthesia, and produces a sense of euphoria and amnesia) larger doses produce: -- psychotic reactions, hypotension, and progressive respiratory depression</td>
<td>-- adverse reactions increase in severity as the dosage increases -- agitation, confusion, psychosis, delirium, hallucinations, ataxia, hostility, fever, dry mouth, vasodilation w/systemic administration - mydriasis (may precipitate narrow-angle glaucoma) - paralysis of accommodation - decreased vision - decreased lacrimation - decreased tear lysozymes w/ocular use - decreased vision - mydriasis - paralysis of accommodation - follicular conjunctivitis - hyperemia, photophobia w/systemic absorption from topical application - mydriasis, anisocoria of pupils, absent reaction to light - paralysis of accommodation - decreased vision - decreased lacrimation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
GANGLIONIC AGONISTS AND ANTAGONISTS

Ganglionic Agonists

Catecholamines
- dobutamine
- Δ dopamine (Intropin)
- Δ epinephrine (Parenteral: Adrenalin)
- Δ isoproterenol (Oral: Isuprel)
- Δ norepinephrine (Levophed, Noradrenaline)

Noncatecholamines
- ΔΔ albuterol (Proventil, Ventolin) #21 & #24 drugs in 1991
- Δ ephedrine (Efedron)
- Δ isoetharine
- Δ mephenetermine
- Δ metaproterenol (Alupent)
- Δ metaraminol
- Δ methoxamine
- Δ nylidrin
- Δ phenylephrine (Neo-Synephrine)
- Δ ritodrine
- Δ terbutaline (Brethine)

Ganglionic Antagonists

Sympatholytic Agents
- ΔΔ clonidine (Catapres) #152 drug in 1991
- Δ guanabenz
- Δ guanfacine
- Δ methyldopa (Aldomet)
- Δ mecamylamine
- Δ trimethaphan
- ΔΔ atenolol (Tenormin) #12 drug in 1991
- ΔΔ metoprolol (Lopressor) #23 drug in 1991
- ΔΔ nadolol (Corgard) #90 drug in 1991
- Δ pindolol
- ΔΔ propranolol (Inderal) #41 drug in 1991
- ΔΔ timolol (Timoptic) #60 drug in 1991
- Δ phentolamine
- Δ prazosin
- Δ terazosin
- Δ labetalol
- Δ guanadrel
- Δ guanethidine
- Δ reserpine (Serpasil)

" ΔΔ " indicates a top 200 drug in 1991 -- note ranking after trade name
" Δ " indicates major drugs -- see table
Indications for Use:
- **adrenergic agents** are compounds that cause biological responses similar to those produced by activation of the sympathetic nervous system (SNS).
- **adrenergics** are divided into two groups: catecholamines (including endogenous and synthetic agents) and noncatecholamines and are further divided by their method of action:
  - **direct-acting** (acting directly on the sympathetically innervated organ or tissue)
  - **indirect-acting** (triggering the release of a neurotransmitter, usually norepinephrine)
  - **dual-acting** (combining both direct and indirect action)

**Catecholamines**
- The particular receptor activity that exists alone or predominates if more than one receptor type is activated determines how the drug is used therapeutically.
- Local vasoconstrictive actions of the drugs make them useful as:
  - nasal decongestants to treat inflammatory and allergic conditions
  - ophthalmic decongestants to treat conjunctivitis and ocular congestion
  - intraocular hypotensive agents to treat simple, open-angle glaucoma
  - antiallergens to treat hypersensitivity and anaphylaxis
- **alpha stimulators** can be used systemically to relieve hypotension.
- **beta1-active drugs** are used to treat bradycardia and heart block and to terminate paroxysmal atrial or nodal tachycardia.
  - also used in cases of ventricular fibrillation, asystole, or cardiac arrest
- **beta2-active drugs** are used to treat acute and chronic bronchial asthma, emphysema, bronchitis, and acute hypersensitivity reactions to drugs.
- The specific mechanisms of action and uses of the individual drugs are listed in the tables to follow.

**Noncatecholamines**
- Noncatecholamine adrenergic drugs have a wide variety of therapeutic uses related to the many physiologic effects of these drugs.
- The effects include:
  - local or systemic vasoconstriction
  - nasal and ophthalmic decongestion
  - bronchodilation
  - smooth muscle relaxation
  - CNS stimulation and appetite suppression
- Bronchodilator effects of the drugs are used to treat acute and chronic bronchial asthma, emphysema, pulmonary fibrosis, and chronic bronchitis.
Indications for Use (continued)

**Noncatecholamines** (continued)
- the pressor effects of the drugs are useful with spinal anesthesia; for hypotension and nosebleeds; and vasoconstriction during regional anesthesia
- ephedrine is used to treat nasal congestion, hypotension, and narcolepsy
- the specific mechanisms of action and uses of the individual drugs are listed in the tables to follow

**Sympatholytic Agents**
- used to lower the blood pressure of patients with mild-to-severe essential hypertension
- the type of drug used can be changed and the dosage altered to achieve effective therapeutic effects with the fewest adverse reactions

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**CATECHOLAMINES**

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- use cautiously in elderly patients because of possible reduced cardiac reserve and the likelihood of dysrhythmias, confusion, or cerebrovascular accident
- use cautiously in pregnant patients because of possible adverse effects on the fetus
- use cautiously in hypertensive patients since catecholamines may cause further increase in blood pressure, cardiac output, or vasoconstriction
- use cautiously in patients with hyperthyroidism since may cause increase in hypermetabolic state
- use cautiously in patients with diabetes mellitus since may produce an anti-insulin effect with unpredictable effects on diabetes control
- use cautiously in patients with glaucoma since may cause increased intracocular pressure
- also use cautiously in patients with parkinsonism, circulatory or cardiovascular disease, and prostate hypertrophy
- note signs of overdose, such as headache, vomiting, hypotension, hypertension, blurred vision, cardiac dysrhythmias, or chest pains
- be alert for the possibility of edema, oliguria, anuria, or hemorrhage with prolonged use
Catecholamines (continued)

Drug Interactions:
- drug interactions involving catecholamines can be among the most serious
- knowledge of the interactions between catecholamines and other agents is essential because of the potential for additive effects which might lead to a hypertensive crisis or cardiac dysrhythmias
- drugs that must not be used with catecholamines or that should be used concurrently only with extreme caution include MAO inhibitors, tricyclic antidepressants, oxytocics, furazolidone, ergot alkaloids, antihistamines, some general anesthetics, digitalis, or other sympathomimetic agents
- catecholamines can produce similar and significant reactions throughout the body including hypotension, hypertension, cardiac dysrhythmia, seizures, and hyperglycemia in diabetics
- beta-blockers such as propranolol reduce the effects of the catecholamines and increase total peripheral resistance by allowing uncompensated alpha stimulation with beta blockade, which may result in hypertension and reflex bradycardia

NONCATECHOLAMINES

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- use cautiously in diabetic patients because of the possibility of hyperglycemia
- although rare, overdose of nasal decongestants can cause marked somnolence, sedation, hypotension, bradycardia, and even coma
- confusion, delirium, or even hallucinations, as well as tremors, may follow large doses of ephedrine
- ephedrine may also produce paradoxical bronchospasm or aggravation of ketoacidosis
Noncatecholamines (continued)

Drug Interactions:
- drugs known to interact with various noncatecholamines encompass many of the drugs also contraindicated with catecholamines including MAO inhibitors, furazolidone, beta blockers, other sympathomimetics, acetazolamide, ascorbic acid, and many others
- can produce significant reactions throughout the body, including hypotension, hypertension, cardiac dysrhythmias, seizures, and hyperglycemia in diabetics

SYMPATHOLYTIC AGENTS

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- use central-acting nervous system inhibitors cautiously in patients with coronary insufficiency, recent MI, cerebrovascular disease, or severe hepatic or renal impairment because of the risks of adverse reactions
- to prevent severe first-dose orthostatic hypotension, have the patient take the first dose of prazosin or terazosin at bedtime or remain lying down for at least 3 hours after taking it
- use reserpine cautiously in a patient with epilepsy because this agent may lower the threshold for seizures
- beta-adrenergic blocking agents may mask signs of hypoglycemia
  - gradually discontinue a beta-adrenergic blocking agent over 3 to 14 days during this time, the patient should avoid vigorous physical activity

Drug Interactions:
- sympatholytic agents can interact with many drugs to produce blood pressure changes as well as other severe reactions
### Catecholamines

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>dopamine (Intropin)</td>
<td>stimulates dopaminergic, alpha, and beta&lt;sub&gt;1&lt;/sub&gt; receptors to increase force of myocardial contractions and increase cardiac output</td>
<td>used to treat cardiogenic or bacteremic shock with related renal shutdown and chronic congestive heart failure</td>
<td>ectopic heart beats, nausea, vomiting, tachycardia, anginal pain, headache, hypotension</td>
<td>high doses may cause dilated pupils</td>
</tr>
<tr>
<td>epinephrine (Adrenalin)</td>
<td>stimulates alpha, beta&lt;sub&gt;1&lt;/sub&gt;, beta&lt;sub&gt;2&lt;/sub&gt; receptors to increase cardiac output and to relieve respiratory distress due to bronchospasm</td>
<td>used to treat bronchospasm, asthma, open-angle glaucoma, allergic conditions, hypotension, cardiac arrest</td>
<td>transient anxiety, headache, fear and heart palpitations</td>
<td>mydriasis-may precipitate narrow-angle glaucoma - red-green color vision defect - hemianopsia</td>
</tr>
<tr>
<td>isoproterenol (Isuprel)</td>
<td>stimulates beta&lt;sub&gt;1&lt;/sub&gt; and beta&lt;sub&gt;2&lt;/sub&gt; receptors of the heart and smooth muscle of bronchi to produce cardiac stimulation and bronchodilation</td>
<td>used to treat asthma, bronchospasm, shock cardiac arrest, cardiac dysrhythmias</td>
<td>nervousness, headache, dizziness, tachycardia, palpitations, angina, flushing of the skin, sweating</td>
<td></td>
</tr>
<tr>
<td>norepinephrine (Levophed)</td>
<td>stimulates alpha and beta&lt;sub&gt;1&lt;/sub&gt; receptors to produce peripheral vasoconstriction and to increase cardiac output due to increased myocardial contractions</td>
<td>used to treat acute hypotension, shock, cardiac arrest, myocardial infarctions, anaphylactic shock</td>
<td>- bradycardia as a reflex result of a rise in blood pressure. - headache may indicate overdosage</td>
<td>none listed</td>
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<tr>
<td>albuterol</td>
<td>Stimulates beta2 adrenergic receptors of the lung's smooth muscle causing relaxation</td>
<td>used to relieve acute bronchial asthma and to reduce frequency and severity of chronic, recurrent asthmatic attacks</td>
<td>nervousness, heart palpitations, hand tremor, headache, leg cramps, dizziness</td>
<td>decreased vision, edema of eyelids and conjunctiva, blepharoconjunctivitis, decreased lacrimation, and decreased intraocular pressure</td>
</tr>
<tr>
<td>ephedrine</td>
<td>dual acting drug that stimulates alpha, beta, and CNS receptors to cause bronchodilation and vasoconstriction</td>
<td>used to treat nasal congestion, hypotension, and narcolepsy</td>
<td>heart palpitation, tachycardia, headache, insomnia, sweating, nervousness, nausea, vomiting.</td>
<td>w/systemic use: mydriasis, decreased intraocular pressure, w/local ocular use: conjunctival vasoconstriction, decreased vision</td>
</tr>
<tr>
<td>metaproterenol</td>
<td>direct acting beta2 selective agent -- stimulation of beta2 adrenergic receptors of lung smooth muscle causes relaxation resulting in bronchodilatory effects</td>
<td>used to treat asthma, bronchitis, and emphysema</td>
<td>tachycardia, hypertension, heart palpitations, nervousness, tremor, nausea, and vomiting</td>
<td>no ocular effects reported after systemic administration</td>
</tr>
<tr>
<td>phenylephrine</td>
<td>potent direct-acting agent with strong alpha-receptor and weak beta-receptor actions to produce vasoconstriction</td>
<td>used for its systemic and topical vasopressor effects with anesthesia and for treating shock, tachycardia, rhinitis, allergies, uveitis, and to produce mydriasis</td>
<td>headache, reflex bradycardia, excitability, restlessness, drowsiness, lassitude, nausea, and rarely arrhythmias</td>
<td>w/systemic use: visual hallucinations, w/local ocular use: mydriasis, decreased vision, conjunctival vasoconstriction, lacrimal irritation, punctate keratitis</td>
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<tr>
<td>terbutaline</td>
<td>direct-acting agent which exerts selective beta2 activity to produce bronchodilation effects</td>
<td>-- used to treat bronchial asthma, bronchitis, and emphysema -- may also be used to delay delivery in preterm labor</td>
<td>nervousness, tremor, headache, increased heart rate, palpitations, drowsiness, nausea, vomiting, sweating, and muscle cramps</td>
<td>no ocular effects have been reported</td>
</tr>
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<tr>
<td>clonidine (Catapres)</td>
<td>-- a central-acting nervous system inhibitor</td>
<td>-- used as a step-2 drug in the treatment of mild to moderate hypertension</td>
<td>-- most common: dry mouth, drowsiness, dizziness, sedation and constipation</td>
<td>w/systemic administration:</td>
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<td></td>
<td>-- acts in the CNS to reduce sympathetic activity and thus decrease arteriolar vasoconstriction</td>
<td>-- lowers the supine and standing blood pressures and is frequently given with a diuretic or another antihypertensive agent to achieve the maximum blood pressure reduction</td>
<td>-- CNS effects: depression, forgetfulness, inability to concentrate, vivid dreams</td>
<td>-- decreased IOP</td>
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<td>-- additional reactions include: water retention, edema, nasal congestion, weakness, may decrease libido and produce impotence</td>
<td>-- urticaria of eyelids or conjunctiva</td>
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<td></td>
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<td>-- visual hallucinations</td>
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<td>w/ocular administration:</td>
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<td>-- decreased IOP</td>
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<td>-- miosis</td>
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<tr>
<td>methyldopa (Aldomet)</td>
<td>-- a central-acting nervous system inhibitor</td>
<td>-- used to control mild to moderate hypertension (produces water and sodium retention, so frequently combined with a diuretic)</td>
<td>-- CNS effects: sedation, drowsiness, dizziness, depression, forgetfulness, inability to concentrate, vivid dreams</td>
<td>w/systemic administration:</td>
</tr>
<tr>
<td></td>
<td>-- acts in the CNS to reduce sympathetic activity and thus decrease arteriolar vasoconstriction</td>
<td>-- useful for treating patients with impaired renal function -- used to treat hypertensive crisis</td>
<td>-- additional reactions include: water retention, edema, nasal congestion, weakness, may decrease libido and produce impotence</td>
<td>-- decreased IOP</td>
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<td>-- eyelids or conjunctiva:</td>
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<td></td>
<td></td>
<td>allergic reactions, hyperemia, conjunctivitis, edema, urticaria</td>
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<td></td>
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<td>-- subconjunctival or retinal hemorrhages secondary to drug-induced anemia</td>
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<td></td>
<td></td>
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<td>-- paralysis of extraocular muscles</td>
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<tr>
<td>atenolol (Tenormin)</td>
<td>-- competes with epinephrine for beta-receptor sites</td>
<td>used for treatment of angina pectoris and hypertension</td>
<td>Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension</td>
<td>rare and transient and may include ocular irritation, dry eyes, decreased tear production, and blurred vision</td>
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<tr>
<td></td>
<td>-- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow</td>
<td></td>
<td>Unusual: headache, dizziness, drowsiness, nausea,</td>
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<td></td>
<td>-- reduces rate and contraction force of the heart to decrease the oxygen requirement for heart function and reduce the degree of contraction of blood vessel walls, resulting in lowered blood pressure</td>
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<td>Serious unusual: mental depression, anxiety, chest pain, shortness of breath</td>
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</table>
### Sympatholytic Agents (continued)

<table>
<thead>
<tr>
<th>Drug</th>
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</table>
| metoprolol (Lopressor) #23 drug in 1991 | - competes with epinephrine for beta-receptor sites  
- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow  
-- actions in angina to decrease cardiac work | used to treat hypertension and myocardial infarction | same adverse reactions as for atenolol | rare and transient and may include decreased vision, conjunctival irritation, ocular pain, dry eyes and decreased tear production |
| nadolol (Corgard) #90 drug in 1991 | -- competitive blockade of beta adrenergic receptors  
-- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow  
-- actions in angina to decrease cardiac work | used to treat angina pectoris and hypertension | Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension  
Unusual: headache, dizziness, drowsiness, nausea,  
Serious unusual: facial swelling, chest pain, shortness of breath, precipitation of congestive heart failure | rare and transient and may include diplopia, decreased vision, allergic reactions of conjunctiva and lids, decreased IOP, and visual hallucinations |
| propranolol (Inderal) #41 drug in 1991 | -- non-selective competitive blocker of beta receptors  
-- decreased cardiac output, and/or decreased central sympathetic outflow  
-- actions in angina to decrease heart rate and cardiac work  
-- has a membrane stabilizing or local anesthetic effect to decrease action potential conduction and prolong the conduction time of nerve impulses through the heart | used to treat hypertension, angina pectoris, cardiac arrhythmias, and migraine headaches | Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension  
Unusual: skin rash, temporary loss of hair, headache, dizziness, drowsiness, nausea  
Serious unusual: acute behavioral disturbances, disorientation, confusion, amnesia, mental depression, anxiety, chest pain, shortness of breath, precipitation of congestive heart failure | rare and transient and may include diplopia, decreased vision, allergic reactions of conjunctiva and lids, decreased IOP, and visual hallucinations |
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<tr>
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| timolol (Timoptic)        | -- non-selective beta adrenergic blocking agent  
-- antagonizes the effect of epinephrine and blocks sympathetic stimulation, resulting in decreased cardiac output, and/or decreased central sympathetic outflow  
-- has a membrane stabilizing or local anesthetic effect to decrease action potential conduction and prolong the conduction time of nerve impulses through the heart  
-- decreases aqueous formation in the anterior chamber to lower IOP | used to treat angina pectoris, glaucoma, hypertension, to prevent the recurrence of myocardial infarction, and to reduce the frequency and severity of migraine headaches | Expected: lethargy, fatigability, cold extremities, slow heart rate, orthostatic hypotension  
Unusual: skin rash, temporary loss of hair, headache, dizziness, drowsiness, nausea | -- mild ocular irritation including conjunctivitis, blepharitis, and keratitis  
-- has infrequently caused refractive changes, corneal hypoesthesia, and blepharoptosis |
| reserpine (Serpasil)      | -- a norepinephrine depletor  
-- interferes with the synthesis, storage, and release of norepinephrine from the nerve terminals leading to loss of peripheral sympathetic tone, decreased peripheral resistance and a reduction in blood pressure  
-- (sometimes referred to as peripheral-acting sympatholytic agents) | used to treat mild essential hypertension  
-- also useful as adjunctive therapy with other antihypertensive agents in the more severe forms of hypertension | -- frequent adverse reactions: drowsiness, sleep altertations, weight gain, and nasal congestion  
-- also may produce: increased Gi motility, abdominal cramps, diarrhea, nightmares, depression, uterine contractions, and bronchoconstriction | w/ systemic administration:  
-- conjunctival hyperemia  
-- Horner's syndrome (miosis, ptosis, increased sensitivity to epinephrine)  
-- nonspecific ocular irritation (lacrimation, hyperemia)  
-- extraocular muscles: (decreased spontaneous movements, jerky pursuit movements)  
-- decreased vision  
-- retinal hemorrhages |
NEUROMUSCULAR TRANSMISSION AGONISTS AND ANTAGONISTS

Neuromuscular Transmission Agonists

acetylcholine

Neuromuscular Transmission Antagonists

Nondepolarizing Blocking Agents

- atracurium
- gallamine
- metocurine
- pancuronium (Pavulon)
- tubocurarine (Tubarine)
- vecuronium

Depolarizing Blocking Agents

- succinylcholine (Quelicin)

"ΔΔ" indicates a top 200 drug in 1991 -- note ranking after trade name
"Δ" indicates major drugs -- see table

Indications for Use:

Neuromuscular Transmission Agonists

- to produce complete miosis in seconds by irrigating the iris after delivery of the lens in cataract surgery
- in penetrating keratoplasty, iridectomy and other anterior segment surgery where rapid, complete miosis may be required

Neuromuscular Transmission Antagonists

Nondepolarizing Blocking Agents

- used as an adjunct to induce skeletal muscle relaxation; to reduce the intensity of muscle contractions in pharmacologically or electrically induced convulsions; to facilitate management of patients undergoing mechanical ventilation
- produce intermediate to prolonged muscle relaxation, such as that required during surgery for intubation and ventilation
- tubocurarine is used as a diagnostic agent for myasthenia gravis when the results of tests with neostigmine or edrophonium are inconclusive

Depolarizing Blocking Agents

- succinylcholine is the drug of choice for short-term muscle relaxation, such as during intubation and electroshock therapy
- used as an adjunct to general anesthesia to facilitate endotracheal intubation, and to induce skeletal muscle relaxation during surgery or mechanical ventilation
- used to reduce the intensity of muscle contractions of pharmacologically-induced or electrically-induced convulsions
NEUROMUSCULAR TRANSMISSION AGENTS

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
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Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- hypersensitivity to any component of the product

Drug Interactions:
- anticholinergics decrease the activity of acetylcholine
- sympathomimetics decrease the activity of acetylcholine

NONDEPOLARIZING BLOCKING AGENTS

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- use nondepolarizing blocking agents cautiously in patients with renal, hepatic, cardiac, or pulmonary impairment; fluid and electrolyte imbalances; or myasthenia gravis
- order pain medication because neuromuscular blocking agents do not relieve pain
- contraindicated in patients who have shown an allergic reaction or hypersensitivity to these drugs
- use with caution in patients in whom a sudden increase of histamine release is a definite hazard
Nondepolarizing Blocking Agents (continued)

Drug Interactions:
- most interacting drugs enhance the blocking action of the neuromuscular blocking agents and require that the patient be closely observed to prevent fatal complications
- the following interacting drugs potentiate neuromuscular blockade
  - local or parenteral anesthetics, inhalation anesthetics, aminoglycosides, clindamycin, polymyxin, calcium channel blockers, magnesium salts, potassium-depleting medications (including amphotericin B, furosemide, and thiazide diuretics)
- the anticholinesterases (neostigmine, pyridostigmine, and edrophonium) are antagonistic to nondepolarizing blocking agents and are used as antidotes to the neuromuscular blocking agents

DEPOLARIZING BLOCKING AGENTS

Mechanism of Action:
- mechanisms of action for all classes of drugs are listed in the tables for each of the specific major drugs

Adverse Reactions:
- adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Ocular Adverse Reactions:
- ocular adverse reactions for all classes of drugs are listed in the tables for each of the specific major drugs

Contraindications and Precautions:
- the overall implications for succinylcholine are the same as those for the nondepolarizing blocking agents

Drug Interactions:
- the action of succinylcholine is potentiated by a number of anesthetics, antibiotics, and cholinesterase inhibitors
  - cholinesterase inhibitors antagonize phase II of succinylcholine's blocking action
- succinylcholine does not interact with the majority of drugs that alter serum electrolyte levels
### Neuromuscular Transmission Agents

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
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<tr>
<td>Acetylcholine</td>
<td>-- major neurotransmitter (NT) of the motorneurons, autonomic preganglionic fibers, postganglionic cholinergic (parasympathetic fibers) -- synthesized from choline and acetyl-coenzyme A by the enzyme choline acetyltransferase (CAT) -- upon release, Ach stimulates cholinergic receptors of adjacent structures -- interaction terminated by hydrolysis of Ach to choline and acetate by acetylcholinesterase (ACE) -- levels of acetylcholine regulated by the activity of choline acetyltransferase and by choline re-uptake</td>
<td>-- intraocular quaternary ammonium parasympathomimetic agent used to produce prompt, short-term miosis</td>
<td>w/local ophthalmic use-- subconjunctival or intracameral injection: -- bradycardia -- hypotension -- vasodilation -- dyspnea -- perspiration</td>
<td>w/local ophthalmic use-- subconjunctival or intracameral injection: -- miosis -- increased IOP -- conjunctival hyperemia -- accommodative spasm -- iris atrophy -- blepharoclonus</td>
</tr>
</tbody>
</table>

- Intracameral injection: miosis, increased IOP, conjunctival hyperemia, accommodative spasm, iris atrophy, blepharoclonus.
### Neuromuscular Transmission Antagonists

#### 67b1 Nondepolarizing Blocking Agents

<table>
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<tr>
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<td>Pancuronium</td>
<td>-- compete with Ach at the cholinergic receptor sites of the skeletal muscle membrane&lt;br&gt; -- blocks Ach's transmitter action, preventing the muscle membrane from depolarizing&lt;br&gt; -- initial muscle weakness produced quickly changes to a flaccid paralysis affecting muscles in a specific sequence&lt;br&gt; -- first muscles to exhibit flaccid paralysis are those innervated by the motor portions of the CN's and small rapidly moving muscles in the eyes, face, and neck&lt;br&gt; -- next, the limb, abdomen, and trunk muscles become flaccid and finally the intercostal muscles and diaphragm are paralyzed</td>
<td>-- used as adjunct to anesthesia to induce skeletal muscle relaxation&lt;br&gt; -- used as to manage patients undergoing mechanical intubation and ventilation</td>
<td>-- most serious adverse reaction is apnea&lt;br&gt; -- ganglionic blockade and histamine release may cause hypotension&lt;br&gt; -- histamine release may also produce skin reactions (rash), bronchospasm, and excessive bronchial and salivary secretions&lt;br&gt; -- selectively block the vagus nerve and may result in tachycardia, cardiac dysrhythmias, and hypertension</td>
<td>-- initial muscle weakness quickly changing to flaccid paralysis of rapidly moving muscles of the eyes</td>
</tr>
<tr>
<td>Tubocurarine</td>
<td>-- compete with Ach at the cholinergic receptor sites of the skeletal muscle membrane&lt;br&gt; -- blocks Ach's transmitter action, preventing the muscle membrane from depolarizing&lt;br&gt; -- initial muscle weakness produced quickly changes to a flaccid paralysis affecting muscles in a specific sequence&lt;br&gt; -- first muscles to exhibit flaccid paralysis are those innervated by the motor portions of the CN's and small rapidly moving muscles in the eyes, face, and neck&lt;br&gt; -- next, the limb, abdomen, and trunk muscles become flaccid and finally the intercostal muscles and diaphragm are paralyzed</td>
<td>-- used as adjunct to anesthesia to induce skeletal muscle relaxation&lt;br&gt; -- used as to manage patients undergoing mechanical intubation and ventilation&lt;br&gt; -- used as a diagnostic aid for myasthenia gravis</td>
<td>-- most serious adverse reaction is apnea&lt;br&gt; -- ganglionic blockade and histamine release may cause hypotension&lt;br&gt; -- histamine release may also produce skin reactions (rash), bronchospasm, and excessive bronchial and salivary secretions</td>
<td>-- initial muscle weakness quickly changing to flaccid paralysis of rapidly moving muscles of the eyes&lt;br&gt; w/systemic administration: -- decreased convergence -- diplopia -- nystagmus -- paralysis of extraocular muscles -- ptosis -- decreased IOP</td>
</tr>
<tr>
<td>DRUGS Generic Name (Brand)</td>
<td>Mechanism of Action</td>
<td>Indications for Use</td>
<td>Adverse Reactions</td>
<td>Ocular Adverse Reactions</td>
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</tr>
<tr>
<td>succinylcholine (Quelicin)</td>
<td>-- an ultrashort-acting depolarizing skeletal muscle relaxant -- like Ach, it combines with cholinergic receptors of the motor endplate to produce depolarization observed as fasciculations -- neuromuscular transmission is inhibited as long as an adequate concentration of drug remains at the receptor site; the neuromuscular block produces a flaccid paralysis</td>
<td>-- primarily used to induce short-term muscle relaxation -- used as adjunct to anesthesia to induce skeletal muscle relaxation -- used as to manage patients undergoing mechanical intubation and orthopedic manipulation</td>
<td>-- most serious adverse reaction is apnea -- cardiovascular: bradycardia, tachycardia, hypertension, hypotension, cardiac arrest, arrhythmias</td>
<td>w/systemic administration: -- eyelid retraction -- enophthalmos -- globe rotaes inferiorly -- paralysis of EOM's -- initial increased IOP, then decreased IOP -- ptosis -- diplopia -- edema and allergic reactions of eyelids or conjunctiva</td>
</tr>
</tbody>
</table>
AUTACOID AGONISTS AND ANTAGONISTS

Pituitary Agents

Anterior Pituitary Hormones
- corticotropin (ACTH) (Acthar)
- cosyntropin (Cortrosyn)
- somatrem (Protropin)

Posterior Pituitary Hormones
- posterior pituitary injection (Pituitrin)
- vasopressin (Pitressin)
- oxytocin (Pitocin)

Androgenic and Anabolic Steroid Agents
- fluoxymesterone (Halotestin)
- testosterone cypionate (Andro-Cyp)
- nandrolone decanoate (Deca-Durabolin)
- oxandrolone (Anavar)
- stanozolol (Winstrol)

Thyroid and Antithyroid Agents

Thyroid Agents
- thyroid USP (dessicated)
- levothyroxine (Synthroid) #6 drug in 1991
- thyrotropin TSH (Thytropar)
- protirelin TRH (Thypinone)

Antithyroid Agents
- methimazole (Tapazole)
- propylthiouracil (PTU)
- iodine (Potassium iodide Solution, USP)

Insulin and Synthetic Antidiabetics
- insulin
- chlorpropamide (Diabinese)
- tolazamide (Tolinase)
- tolbutamide (Orinase)
- glipizide (Glucotrol) #47 drug in 1991
- glyburide (Micronase, Diabeta) #28 & #46 drugs in 1991

Glucagon
- glucagon
<table>
<thead>
<tr>
<th>Estrogens, Progestins, Contraceptive Agents, and Androgens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estrogens</strong></td>
</tr>
<tr>
<td>ΔΔ estradiol (Estrace) #170 drug in 1991</td>
</tr>
<tr>
<td>ΔΔ estradiol transdermal system (Estraderm) #58 drug in 1991</td>
</tr>
<tr>
<td>ΔΔ estropipate (Ogen) #160 drug in 1991</td>
</tr>
</tbody>
</table>

| Progestins                                               |
| ΔΔ medroxyprogesterone (Provera) #26i drug in 1991        |

| Contraceptive Agents                                     |
| ΔΔ ethinyl estradiol and levonorgestrel (Triphasil)      |
| #37 drug in 1991, other brands of this drug #91, #122 in 1991 |
| ΔΔ ethinyl estradiol and norethindrone (Ortho-Novum 7/7/7) |
| #15 drug in 1991, other brands of this drug #127, #155 in 1991 |
| ΔΔ norethindrone and ethinyl estradiol (Ortho-Novum)     |
| #33 drug in 1991                                         |
| ΔΔ norgestrel and ethinyl estradiol (Lo/Ovral)            |
| #48 drug in 1991                                         |

| Androgens                                                |
| Δ fluoxymesterone (Halotestin)                           |
| Δ methyltestosterone (Metandren)                         |
| Δ testosterone cypionate (Andro-Cyp)                     |

"ΔΔ" indicates a top 200 drug in 1991 -- note ranking after trade name
"Δ" indicates major drugs -- see table

Since so many different agents among the numerous classes of autacoid (hormone) agonists and antagonists are in current usage, only the more widely used agents are listed in the tables that follow in this section.

Within the tables for the major agents will be included mechanisms of action, indications for use, adverse reactions, and ocular adverse reactions. The complete lists for all agents and drugs within the classes of hormone agents can be found in the sections which list all the drugs acting of the endocrine system and in the sections covering steroids. Within those sections are also listed drug interactions as well as contraindications and precautions. The specific sections to find any additional information are as follows:

- Adenohypophyseal hormones
- Thyroid and antithyroid drugs
- Insulin and synthetic antidiabetics
- Estrogens, progestins and androgens
### AUTACOID AGONISTS AND ANTAGONISTS

#### c1 Pituitary Agents

<table>
<thead>
<tr>
<th>Drugs and Brand Names</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
</table>
| **corticotropin (ACTH)** (Acthar)** | secreted by the anterior pituitary and stimulates the adrenal cortex to produce and secrete adrenocortical hormones  
- ACTH secretion is regulated by a negative feedback mechanism, whereby elevated plasma corticosteroid levels suppress ACTH secretion  
- in the absence of ACTH stimulation, the adrenal cortex may atrophy | used for diagnostic testing of adrenocortical function  
- treatment of adrenal insufficiency from long-term use of corticosteroids  
- also used like corticosteroids for many anti-inflammatory and immunosuppressive purposes  
- used to treat symptoms of acute episodes of multiple sclerosis  
- used to increase muscle strength in patients with myasthenia gravis | sodium and water retention  
- impaired wound healing  
- dizziness, convulsions, and euphoria  
- may mask signs of infection  
- long-term ACTH use can cause iatrogenic Cushing's syndrome indistinguishable from the naturally occurring condition | posterior subcapsular cataracts  
- increased IOP  
- glaucoma with possible damage to optic nerve  
- exophthalmos |
| **cosyntrpin (Cortrosyn)** | synthetic peptide corresponding to the amino acid residues 1 to 24 of human ACTH  
- more potent and less allergenic than the exogenous ACTH preparations  
- stimulates the adrenal cortex to produce and secrete adrenocortical hormones | because it is unavailable in a repository form, it is not used therapeutically, only diagnostically  
- diagnostically used to differentiate between primary (adrenal) and secondary (pituitary) adrenal insufficiency | more potent and less allergenic than the exogenous ACTH preparations  
- can cause pruritus and flushing | none reported with diagnostic testing |
| **somatrem (Protropin)** | regulate growth by stimulating the actions of other endocrine glands  
- the pharmacokinetic equivalent of the natural pituitary growth hormone  
- when administered parenterally, somatrem is well absorbed, distributed, metabolized in the liver, and excreted in the urine | used to treat linear growth failure from hormonal deficiency  
- may be used as replacement therapy before epiphyseal closure in patients with GH deficiency  
- produces an increase in the size and number of muscle cells, affecting organ growth and tissue metabolism | pain at injection site  
- glucose intolerance  
- transient hypothyroidism during treatment  
- development of antibodies that interfere with treatment (rare) | none listed |
<table>
<thead>
<tr>
<th>DRUGS</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
</table>
| posterior pituitary injection (pitiutr-rrin) | -- includes all forms of antidiuretic hormone (ADH)  
-- an increase in cyclic AMP in the target cells mediates the effects of ADH  
-- normally synthesized by the nerve bodies of the hypothalamus and stored in the posterior pituitary  
-- must be given by injection or topical intranasal spray  
-- have a pressor effect from arteriole and capillary vasoconstriction, an antidiuretic action from increased reabsoption of water in the renal tubular and collecting duct, and a stimulation effect on smooth muscles in the body | -- natural extract with oxytocic, vasopressor, and antidiuretic properties has a rapid pressor effect that makes its use hazardous  
-- can be used to treat postoperative intestinal obstruction  
-- can be used to treat diabetes insipidus  
-- can be used to stimulate the uterus after incomplete expulsion of the placenta | -- tremors, diaphoresis, vertigo, circumoral and facial pallor, increased GI motility, abdominal and uterine cramps, tinnitus, anxiety, | -- mydriasis  
-- blindness |
| vasopressin (Pitressin) | -- possesses vasopressor and antidiuretic hormone (ADH) activity  
-- an increase in cyclic AMP in the target cells mediates the effects of ADH  
-- normally synthesized by the nerve bodies of the hypothalamus and stored in the posterior pituitary  
-- must be given by injection or topical intranasal spray  
-- have a pressor effect from arteriole and capillary vasoconstriction, an antidiuretic action from increased reabsoption of water in the renal tubular and collecting duct, and a stimulation effect on smooth muscles in the body | -- used to treat neurogenic diabetes insipidus  
-- used in treatment of postoperative abdominal distention, and in abdominal roentgenography to dispel interfering gas shadows | -- tremor, sweating, vertigo, cardiac arrest, circumoral pallor, "pounding" in head, abdominal cramps, passage of gas, nausea, vomiting, urticaria, and bronchial constriction | -- none listed |
<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
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<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluoxymesterone (Halotestin)</td>
<td>-- has uterine stimulant properties, as well as vasopressive and antidiuretic effects -- exact role in labor is not fully understood, but may act primarily on uterine myofibril activity to augment the number of contractile myofibrils -- has a weak antidiuretic effects -- has transient relaxing effect on vascular smooth muscle</td>
<td>-- used to initiate or improve uterine contractions to achieve early vaginal delivery -- used to treat preeclampsia, eclampsia, and the premature rupture of membranes -- used to control postpartum hemorrhage, hasten uterine involution, and complete inevitable abortions after the 20th week of pregnancy</td>
<td>-- anaphylactic reaction -- postpartum hemorrhage -- cardiac arrhythmia -- nausea -- vomiting -- premature ventricular contractions</td>
<td>-- decreased vision -- paralysis of accommodation -- mydriasis -- acute -- miiosis -- decreased reaction to light -- toxic amblyopia</td>
</tr>
</tbody>
</table>

### c2 Androgenic and Anabolic Steroid Agents

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
<th>Adverse Reactions</th>
<th>Ocular Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluoxymesterone (Halotestin)</td>
<td>-- synthetic derivative of testosterone -- produces androgenic and anabolic effects by binding to androgen receptors in target organs, such as skeletal muscle, the prostate gland, and bone marrow -- receptor binding stimulates development in these organs and also increases protein synthesis -- may promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms) -- by blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass</td>
<td>-- has a predominant androgenic activity -- used to treat hypogonadism and impotence caused by a testicular deficiency -- can also be used to prevent hereditary angioedema -- inoperable breast carcinoma in females</td>
<td>-- GI: nausea, vomiting, diarrhea, abdominal fullness -- CNS: excitation, insomnia, chills -- Endocrine adverse effects: a) virilization, acne, in all age groups b) in prepubertal males: first signs of virilization are phallic enlargement and increase in frequency of erections c) in postpubertal males: inhibition of testicular function with oligospermia, gynecostasia, testicular atrophy, male-pattern baldness d) in females: hisutism, hoarseness or deepening of the voice, clitoral enlargement, change in libido, male-pattern baldness</td>
<td>-- none listed</td>
</tr>
<tr>
<td>DRUGS</td>
<td>Mechanism of Action</td>
<td>Indications for Use</td>
<td>Adverse Reactions</td>
<td>Ocular Adverse Reactions</td>
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<tr>
<td>-------</td>
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</tr>
<tr>
<td>Testosterone cypionate (Andro-Cyp)</td>
<td>-- used primarily as an androgen</td>
<td>used to treat:</td>
<td>1) in females:</td>
<td>-- none listed</td>
</tr>
<tr>
<td></td>
<td>-- produces anabolic and</td>
<td>-- eunuchism,</td>
<td>- produces masculinizing</td>
<td></td>
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<tr>
<td></td>
<td>anabolic effects by binding</td>
<td>-- male hormone deficiency</td>
<td>- hoarseness or deepening of</td>
<td></td>
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<tr>
<td></td>
<td>to androgen receptors in</td>
<td>-- male climacteric symptoms</td>
<td>the voice and clitoral</td>
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<tr>
<td></td>
<td>target organs such as skeletal</td>
<td>-- also used to treat metastatic</td>
<td>enlargement</td>
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<tr>
<td></td>
<td>muscle, the prostate gland,</td>
<td>breast cancer in women</td>
<td>- male-pattern hair distribution</td>
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<tr>
<td></td>
<td>and bone marrow</td>
<td></td>
<td>- menstrual irregularities</td>
<td></td>
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<tr>
<td></td>
<td>-- receptor binding stimulates</td>
<td></td>
<td>- acne</td>
<td></td>
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<td></td>
<td>development in these organs and</td>
<td></td>
<td>- increased libido</td>
<td></td>
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<td></td>
<td>also increases protein synthesis</td>
<td></td>
<td>2) in males:</td>
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<tr>
<td></td>
<td>-- may promote anabolic effects</td>
<td>-- management of anemia of</td>
<td>- gynecomastia</td>
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<td></td>
<td>by blocking cortisol uptake in</td>
<td>renal insufficiency (this drug</td>
<td>- testicular atrophy</td>
<td></td>
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<tr>
<td></td>
<td>muscle and liver cells (cortisol normally</td>
<td>increases hemoglobin and red</td>
<td>- decreased levels of pituitary</td>
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<tr>
<td></td>
<td>acts as a catabolic agent increasing</td>
<td>cell mass)</td>
<td>reproductive hormones</td>
<td></td>
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<tr>
<td></td>
<td>muscle breakdown and body</td>
<td>-- indicated to build tissue</td>
<td>- prostatic hypertrophy</td>
<td></td>
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<tr>
<td></td>
<td>stress mechanisms)</td>
<td></td>
<td>3) GI: nausea, jaundice</td>
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<td></td>
<td>-- by blocking cortisol uptake</td>
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<td>4) CNS: increased or</td>
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<td></td>
<td>in muscle cells, steroid agents</td>
<td></td>
<td>decreased libido, headache,</td>
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<tr>
<td></td>
<td>reduce muscle breakdown and</td>
<td></td>
<td>anxiety, depression</td>
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<td></td>
<td>increase muscle mass</td>
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<td>5) retention of sodium,</td>
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<td></td>
<td></td>
<td></td>
<td>chloride, water, potassium</td>
<td></td>
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<tr>
<td>Nandrolone decanoate (Deca-Durabolin)</td>
<td>-- predominantly used as an</td>
<td>-- management of anemia of</td>
<td>1) in females:</td>
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<tr>
<td></td>
<td>anabolic agent</td>
<td>renal insufficiency (this drug</td>
<td>- hoarseness or deepening of</td>
<td></td>
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<td></td>
<td>-- may promote anabolic effects</td>
<td>increases hemoglobin and red</td>
<td>the voice</td>
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<td></td>
<td>by blocking cortisol uptake in</td>
<td>cell mass)</td>
<td>- male-pattern hair distribution</td>
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<td></td>
<td>muscle and liver cells (cortisol normally</td>
<td>-- indicated to build tissue</td>
<td>- menstrual irregularities</td>
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<tr>
<td></td>
<td>acts as a catabolic agent increasing</td>
<td></td>
<td>- acne</td>
<td></td>
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<tr>
<td></td>
<td>muscle breakdown and body</td>
<td></td>
<td>- increased libido</td>
<td></td>
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<td></td>
<td>stress mechanisms)</td>
<td></td>
<td>2) in males:</td>
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<tr>
<td></td>
<td>-- by blocking cortisol uptake</td>
<td>-- gynecomastia</td>
<td>- gynecomastia</td>
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<td></td>
<td>in muscle cells, steroid agents</td>
<td>- testicular atrophy</td>
<td>- testicular atrophy</td>
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<td></td>
<td>reduce muscle breakdown and</td>
<td>- decreased levels of pituitary</td>
<td>- decreased levels of pituitary</td>
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<td></td>
<td>increase muscle mass</td>
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<td>reproductive hormones</td>
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<td>- prostatic hypertrophy</td>
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<td>3) GI: nausea, jaundice</td>
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<td>4) CNS: increased or</td>
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<td>decreased libido, headache,</td>
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<td></td>
<td>anxiety, depression</td>
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<td>5) retention of sodium,</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>chloride, water, potassium</td>
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</tbody>
</table>

1) in females: - produces masculinizing effects - hoarseness or deepening of the voice - male-pattern hair distribution - menstrual irregularities - acne - increased libido 2) in males: - gynecomastia - testicular atrophy - decreased levels of pituitary reproductive hormones - prostatic hypertrophy 3) GI: nausea, jaundice 4) CNS: increased or decreased libido, headache, anxiety, depression 5) retention of sodium, chloride, water, potassium
<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
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</tr>
</thead>
</table>
| oxandrolone (Anavar)      | - used primarily for its anabolic effects  
- may promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms)  
-- by blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass | - adjunct treatment to promote weight gain after extensive surgery, chronic infection, trauma, or other medically related weight loss  
- may also be used to relieve bone pain in osteoporosis or to offset catabolism from long-term corticosteroid use | 1) in females:  
- hoarseness or deepening of the voice  
- male-pattern hair distribution  
- menstrual irregularities  
- acne  
- increased libido  
2) in males:  
- gynecomastia  
- testicular atrophy  
- decreased levels of pituitary reproductive hormones  
- prostatic hypertrophy  
3) GI: nausea, jaundice  
4) CNS: increased or decreased libido, headache, anxiety, depression  
5) retention of sodium, chloride, water, potassium | - none listed |
| stanozolol (Winstrol)     | - primarily used for its anabolic activity  
- may promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms)  
-- by blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass | - can be used to treat hereditary angioedema | 1) in females:  
- hoarseness or deepening of the voice  
- male-pattern hair distribution  
- menstrual irregularities  
- acne  
- increased libido  
2) in males:  
- gynecomastia  
- testicular atrophy  
- decreased levels of pituitary reproductive hormones  
- prostatic hypertrophy  
3) GI: nausea, jaundice  
4) CNS: increased or decreased libido, headache, anxiety, depression  
5) retention of sodium, chloride, water, potassium | - none listed |
### c3 Thyroid and Antithyroid Agents

#### c3a Thyroid Agents

<table>
<thead>
<tr>
<th>DRUGS Generic Name (Brand)</th>
<th>Mechanism of Action</th>
<th>Indications for Use</th>
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</tr>
</thead>
<tbody>
<tr>
<td>thyroid USP (dessicated)</td>
<td>mechanisms are not well understood - the principal effect of thyroid hormones is an increased metabolic rate in body tissues - affect protein and carbohydrate metabolism and stimulate protein synthesis - promote gluconeogenesis and increase the use of glycogen stores - by decreasing hepatic and serum cholesterol concentrations, thyroid hormones affect lipid metabolism - stimulate heart and increase cardiac output</td>
<td>act as replacement or substitute hormones when the body's hormone level cannot meet its need - thyroid hormone replacement in hypothyroidism - for suppression of thyrotropin secretion in patients with goiters or chronic lymphocytic thyroiditis</td>
<td>GI reactions: diarrhea, cramps, weight loss, increased appetite - cardiovascular: palpitations, sweating, tachycardia, increased blood pressure - CNS: headache, tremors, nervousness, insomnia</td>
<td>decreased vision, eyelid edema and hyperemia, blepharospasm, photophobia, visual hallucinations, exophthalmos, and paralysis of extraocular muscles resulting in ptosis and diplopia</td>
</tr>
<tr>
<td>levothyroxine (Synthroid) #6 drug in 1991</td>
<td>mechanisms are not well understood - the principal effect of thyroid hormones is an increased metabolic rate in body tissues - affect protein and carbohydrate metabolism and stimulate protein synthesis - promote gluconeogenesis and increase the use of glycogen stores - by decreasing hepatic and serum cholesterol concentrations, thyroid hormones affect lipid metabolism - stimulate heart and increase cardiac output</td>
<td>act as replacement or substitute hormones when the body's hormone level cannot meet its need - drug of choice for thyroid hormone replacement in hypothyroidism - drug of choice for thyroid stimulating hormone suppression therapy</td>
<td>GI reactions: diarrhea, cramps, weight loss, increased appetite - cardiovascular: palpitations, sweating, tachycardia, increased blood pressure - CNS: headache, tremors, nervousness, insomnia</td>
<td>decreased vision, eyelid edema and hyperemia, blepharospasm, photophobia, visual hallucinations, exophthalmos, and paralysis of extraocular muscles resulting in ptosis and diplopia</td>
</tr>
<tr>
<td>DRUGS Generic Name (Brand)</td>
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</tr>
<tr>
<td>thyrotropin TSH (Thytropar)</td>
<td>- mechanisms are not well understood - the principal effect of thyroid hormones is an increased metabolic rate in body tissues - affect protein and carbohydrate metabolism and stimulate protein synthesis - promote gluconeogenesis and increase the use of glycogen stores - by decreasing hepatic and serum cholesterol concentrations, thyroid hormones affect lipid metabolism - stimulate heart and increase cardiac output</td>
<td>- for differential diagnosis between primary and secondary hypothyroidism</td>
<td>- GI reactions: diarrhea, cramps, weight loss, increased appetite - cardiovascular: palpitations, sweating, tachycardia, increased blood pressure - CNS: headache, tremors, nervousness, insomnia</td>
<td>- decreased vision, eyelid edema and hyperemia, blepharospasm, photophobia, visual hallucinations, exophthalmos, and paralysis of extraocular muscles resulting in ptosis and diplopia</td>
</tr>
<tr>
<td>protirelin TRH (Thypinone)</td>
<td>- mechanisms are not well understood - the principal effect of thyroid hormones is an increased metabolic rate in body tissues - affect protein and carbohydrate metabolism and stimulate protein synthesis - promote gluconeogenesis and increase the use of glycogen stores - by decreasing hepatic and serum cholesterol concentrations, thyroid hormones affect lipid metabolism - stimulate heart and increase cardiac output</td>
<td>- for differential diagnosis of secondary and tertiary hypothyroidism</td>
<td>- GI reactions: diarrhea, cramps, weight loss, increased appetite - cardiovascular: palpitations, sweating, tachycardia, increased blood pressure - CNS: headache, tremors, nervousness, insomnia</td>
<td>- decreased vision, eyelid edema and hyperemia, blepharospasm, photophobia, visual hallucinations, exophthalmos, and paralysis of extraocular muscles resulting in ptosis and diplopia</td>
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<tr>
<td>DRUGS Generic Name (Brand)</td>
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</tr>
</tbody>
</table>
| methimazole (Tapazole)    | prevents thyroid hormone synthesis by blocking the combination of iodine and tyrosine | - used to treat hyperthyroidism by decreasing concentrations of thyroid hormones in circulation  
- can also serve as an adjunct before thyroid surgery and with radioactive iodine therapy  
- 10 times as potent as propylthiouracil | - adverse reactions occur in less than 3% of patients  
- can produce toxic reactions such as hypersensitivity reactions and granulocytopenia  
- paresthesias, neuritis, headache, nausea and vomiting, skin rash, urticaria, jaundice, hepatitis | - nystagmus  
- keratitis  
- eyelids or conjunctiva: a) allergic reactions  
  b) conjunctivitis  
  c) depigmentation  
  d) decreased lacrimation  
  e) exophthalmos  
  f) subconjunctival or retinal hemorrhages secondary to drug-induced anemia |
| propylthiouracil (PTU)    | prevents thyroid hormone synthesis by blocking the combination of iodine and tyrosine | - used to treat severe hyperthyroidism because it takes effect faster than methimazole  
- used to treat thyroid crisis because it inhibits the conversion of T4 to T3  
- drug of choice during pregnancy because it is safer for the fetus | - adverse reactions occur in less than 3% of patients  
- can produce toxic reactions such as hypersensitivity reactions and granulocytopenia  
- paresthesias, neuritis, headache, nausea and vomiting, skin rash, urticaria, jaundice, hepatitis | - keratitis  
- eyelids or conjunctiva: a) allergic reactions  
  b) conjunctivitis  
  c) depigmentation  
  d) exophthalmos  
  e) subconjunctival or retinal hemorrhages secondary to drug-induced anemia |
| iodine (Potassium Iodide Solution, USP) | inhibits thyroid hormone synthesis through the Wolff-Chaikoff effect, in which above-critical concentrations of intracellular iodide seem to deter hormone synthesis  
- can limit the release of thyroid hormones by inhibiting thyroglobulin endocytosis, which results in colloid accumulation in the follicles | - used for rapid treatment of hyperthyroidism (produces visible effects in three days)  
- used to prepare thyroid for surgery by firming the gland and reducing vascularity | - iodism, chronic toxicity related to iodine therapy is dose dependent  
- can produce unpleasant brassy taste, burning sensation in the mouth, increased salivation, and swelling of the parotid and submaxillary glands  
- other signs and symptoms may include headache, rhinitis, conjunctivitis, gastric irritation, bloody diarrhea, anorexia, and depression | - decreased vision  
- decreased accommodation  
- exophthalmos  
- lacrimation, ocular pain, burning sensation  
- eyelids or conjunctiva: allergic reactions, hyperemia, conjunctivitis, edema  
- punctate keratitis |
### Insulin and Synthetic Antidiabetics

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<thead>
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<th>DRUGS Generic Name (Brand)</th>
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<tr>
<td>insulin</td>
<td>decreases blood glucose by facilitating the uptake and metabolism of glucose by insulin-dependent target cells located in striated muscle and adipose tissue</td>
<td>primary use is for patients with Type I diabetes mellitus (characterized by insufficient insulin production ability of pancreatic beta cells) who require exogenous insulin to control blood glucose</td>
<td>hypoglycemia from too much insulin, too little food or too much exercise</td>
<td>decreased vision</td>
</tr>
<tr>
<td></td>
<td>also inhibits hepatic glucose production and the breakdown of glycogen, protein, and fat</td>
<td>also used for Type II and other types of diabetes mellitus when other methods are ineffective or contraindicated</td>
<td>signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision</td>
<td>nystagmus</td>
</tr>
<tr>
<td></td>
<td>increases the active transport of amino acids in muscle, thereby increasing protein synthesis</td>
<td>sometimes used for hyperkalemia because it lowers potassium levels</td>
<td>if hypoglycemia is untreated, it may progress to unconsciousness, convulsions, coma, or death</td>
<td>paresis of extraocular muscles</td>
</tr>
<tr>
<td>chloropropamide (Diabinese)</td>
<td>mechanism of action remains unknown but the pancreas must already be functioning at a minimal level</td>
<td>indicated for patients with Type II diabetes mellitus if diet and exercise do not maintain blood glucose at normal or near-normal levels</td>
<td>hypoglycemia typically resulting from too little food or too much medication</td>
<td>diplopia</td>
</tr>
<tr>
<td></td>
<td>probably stimulate pancreatic beta cells to release insulin</td>
<td>not indicated for patients with Type I diabetes mellitus, because pancreatic beta cells are not functioning at a sufficient level</td>
<td>signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision</td>
<td>red-green defect</td>
</tr>
<tr>
<td></td>
<td>decrease glucose production by the liver</td>
<td>a first-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone</td>
<td>other rare reactions may include nausea, vomiting, skin rashes, pruritis, headache, numbness and tingling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>may increase the number and sensitivity of cellular insulin receptors</td>
<td>- a first-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>may partially reverse the post-receptor deficit in insulin action enabling the completion of intracellular glucose metabolism</td>
<td></td>
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</tr>
</tbody>
</table>

**Signs of Hypoglycemia:**
- Nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision

**Other Rare Reactions:**
- Nausea, vomiting, skin rashes, pruritis, headache, numbness and tingling
- Diplopia
- Red-green defect
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<th>Generic Name (Brand)</th>
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</thead>
</table>
| tolazamide (Tolinase) | - mechanism of action remains unknown but the pancreas must already be functioning at a minimal level  
- probably stimulate pancreatic beta cells to release insulin  
- decrease glucose production by the liver  
- may increase the number and sensitivity of cellular insulin receptors  
- may partially reverse the post-receptor deficit in insulin action enabling the completion of intracellular glucose metabolism | - indicated for patients with Type II diabetes mellitus if diet and exercise do not maintain blood glucose at normal or near-normal levels  
- not indicated for patients with Type I diabetes mellitus, because pancreatic beta cells are not functioning at a sufficient level  
- a first-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone | - hypoglycemia typically resulting from too little food or too much medication  
- signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision  
- other rare reactions may include nausea, vomiting, skin rashes, pruritis, headache, numbness and tingling | - decreased vision  
- paresis of extraocular muscles  
- diplopia  
- eyelids or conjunctiva: a) allergic reactions b) hyperemia c) conjunctivitis  
- photophobia  
- red-green defect |
| tolvaptamida (Orinase) | - mechanism of action remains unknown but the pancreas must already be functioning at a minimal level  
- probably stimulate pancreatic beta cells to release insulin  
- decrease glucose production by the liver  
- may increase the number and sensitivity of cellular insulin receptors  
- may partially reverse the post-receptor deficit in insulin action enabling the completion of intracellular glucose metabolism | - indicated for patients with Type II diabetes mellitus if diet and exercise do not maintain blood glucose at normal or near-normal levels  
- not indicated for patients with Type I diabetes mellitus, because pancreatic beta cells are not functioning at a sufficient level  
- a first-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone | - hypoglycemia typically resulting from too little food or too much medication  
- signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision  
- other rare reactions may include nausea, vomiting, skin rashes, pruritis, headache, numbness and tingling | - decreased vision  
- paresis of extraocular muscles  
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- eyelids or conjunctiva: a) allergic reactions b) hyperemia c) conjunctivitis  
- photophobia  
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</tr>
</thead>
</table>
| glipizide (Glucotrol) | #47 drug in 1991 | - mechanism of action remains unknown but the pancreas must already be functioning at a minimal level  
- probably stimulate pancreatic beta cells to release insulin  
- decrease glucose production by the liver  
- may increase the number and sensitivity of cellular insulin receptors  
- may partially reverse the post-receptor deficit in insulin action enabling the completion of intracellular glucose metabolism | - indicated for patients with Type II diabetes mellitus if diet and exercise do not maintain blood glucose at normal or near-normal levels  
- not indicated for patients with Type I diabetes mellitus, because pancreatic beta cells are not functioning at a sufficient level  
- a second-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone | - hypoglycemia typically resulting from too little food or too much medication  
- signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision  
- other rare reactions may include nausea, vomiting, skin rashes, pruritis, headache, dizziness, fatigue, drowsiness | - decreased vision  
- paresis of extraocular muscles  
- diplopia  
- eyelids or conjunctiva: a) allergic reactions  
   b) hyperemia  
   c) conjunctivitis  
- photophobia  
- red-green defect |
| glyburide (Micronase, Diabeta) | #28 & #46 drugs in 1991 | - mechanism of action remains unknown but the pancreas must already be functioning at a minimal level  
- probably stimulate pancreatic beta cells to release insulin  
- decrease glucose production by the liver  
- may increase the number and sensitivity of cellular insulin receptors  
- may partially reverse the post-receptor deficit in insulin action enabling the completion of intracellular glucose metabolism | - indicated for patients with Type II diabetes mellitus if diet and exercise do not maintain blood glucose at normal or near-normal levels  
- not indicated for patients with Type I diabetes mellitus, because pancreatic beta cells are not functioning at a sufficient level  
- a second-generation sulfonylurea used to assist in the control of mild to moderately severe type II diabetes mellitus (adult, maturity-onset) that doesn't require insulin but can't be controlled by diet alone | - hypoglycemia typically resulting from too little food or too much medication  
- signs of hypoglycemia are nervousness, shakiness, sweating, weakness, irritability, hunger, tachycardia, changes in speech, hearing or vision  
- other rare reactions may include nausea, vomiting, skin rashes, pruritis, headache, dizziness, fatigue, drowsiness | - decreased vision  
- paresis of extraocular muscles  
- diplopia  
- eyelids or conjunctiva: a) allergic reactions  
   b) hyperemia  
   c) conjunctivitis  
- photophobia  
- red-green defect |
<table>
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<tr>
<th>c5  Glucagon</th>
<th>Mechanism of Action</th>
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<th>Adverse Reactions</th>
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</tr>
</thead>
</table>
| glucagon    | - opposes the actions of insulin  
|           | - regulates the rate of glucose production through glycogenolysis, gluconeogenesis, and lipolysis  
|           | - stimulates the conversion of glycogen to glucose through the process of glycogenolysis  
|           | - also stimulates the production of glucose from plasma amino acids resulting from gluconeogenesis  
|           | - increases lipolysis and inhibits the storage of triglycerides | - indicated for the emergency treatment of severe hypoglycemia  
|           | - also used during radiologic examination of the GI tract to produce a hypokinetic state | - adverse reactions are rare  
|           | - nausea and vomiting may occur occasionally  
|           | - with large doses or prolonged treatment with glucagon, hypokalemia can result  
|           | - since glucagon is a protein a patient can develop an allergy to it (this reaction is rare) | - none listed |

<table>
<thead>
<tr>
<th>c6 Estrogens, Progestins, Contraceptive Agents, and Androgens</th>
</tr>
</thead>
<tbody>
<tr>
<td>c6a Estrogens</td>
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<td>----------------</td>
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</table>
| estradiol (Estrace) #170 drug in 1991 | - believed to involve cytoplasmic receptor proteins found in estrogen-responsive tissues in the female breast and genitourinary tract  
|           | - estrogen binds to these cytoplasmic receptors and the resulting estrogen-receptor complex is transported into the nucleus  
|           | - this action stimulates the synthesis of mRNA and DNA which promotes the synthesis of specific proteins responsible for the actions of the estrogens | primary use is supplemental ("replacement" therapy) of the hormone in the following conditions:  
|           | - ovarian failure or removal in the young woman  
|           | - menopausal syndrome  
|           | - postmenopausal atrophy of genital tissues  
|           | - postmenopausal osteoporosis  
|           | - also used in selected cases of breast cancer and prostate cancer | - GU: breakthrough bleeding, change in menstrual flow, dysmenorrhea  
|           | - GI: nausea, vomiting, abdominal cramps, bloating  
|           | - Dermatologic: chloasma or melasma, erythema nodosum/multiforme, scalp hair loss  
|           | - CNS: headache, migraine, dizziness, mental depression  
|           | - increased risk of endometrial cancer  
|           | - increased incidence of gall bladder disease  
|           | - thromboembolisms  
|           | - hypertension | - steepening of corneal curvature  
|           | - contact lens intolerance  
<p>|           | - increased risk of retinal thrombosis and optic neuritis | |</p>
<table>
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<tr>
<th>DRUGS</th>
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</tr>
</thead>
</table>
| estradiol transdermal system (Estraderm) #58 drug in 1991 | - believed to involve cytoplasmic receptor proteins found in estrogen-responsive tissues in the female breast and genitourinary tract  
- estrogen binds to these cytoplasmic receptors and the resulting estrogen-receptor complex is transported into the nucleus  
- this action stimulates the synthesis of mRNA and DNA which promotes the synthesis of specific proteins responsible for the actions of the estrogens | primary use is supplemental ("replacement" therapy) of the hormone in the following conditions:  
- ovarian failure or removal in the young woman  
- menopausal syndrome  
- postmenopausal atrophy of genital tissues  
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- also used in selected cases of breast cancer and prostate cancer | - GU: breakthrough bleeding, change in menstrual flow, dysmenorrhea  
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- Dermatologic: chloasma or melasma, erythema nodosum/multiforme, scalp hair loss  
- CNS: headache, migraine, dizziness, mental depression  
- increased risk of endometrial cancer  
- increased incidence of gall bladder disease  
- thromboembolisms  
- hypertension | - steepening of corneal curvature  
- contact lens intolerance  
- increased risk of retinal thrombosis and optic neuritis |
| estropipate (Ogen) #160 drug in 1991 | - believed to involve cytoplasmic receptor proteins found in estrogen-responsive tissues in the female breast and genitourinary tract  
- estrogen binds to these cytoplasmic receptors and the resulting estrogen-receptor complex is transported into the nucleus  
- this action stimulates the synthesis of mRNA and DNA which promotes the synthesis of specific proteins responsible for the actions of the estrogens | primary use is supplemental ("replacement" therapy) of the hormone in the following conditions:  
- ovarian failure or removal in the young woman  
- menopausal syndrome  
- postmenopausal atrophy of genital tissues  
- postmenopausal osteoporosis  
- also used in selected cases of breast cancer and prostate cancer | - GU: breakthrough bleeding, change in menstrual flow, dysmenorrhea  
- GI: nausea, vomiting, abdominal cramps, bloating  
- Dermatologic: chloasma or melasma, erythema nodosum/multiforme, scalp hair loss  
- CNS: headache, migraine, dizziness, mental depression  
- increased risk of endometrial cancer  
- increased incidence of gall bladder disease  
- thromboembolisms  
- hypertension | - steepening of corneal curvature  
- contact lens intolerance  
- increased risk of retinal thrombosis and optic neuritis |
### Progestins

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</table>
| medroxyprogesterone (Provera) #26 drug in 1991 | - act at the cellular level on receptor proteins in cellular cytoplasm  
- resulting progesterone-receptor complex is transported into the cell nucleus where the synthesis of mRNA is stimulated and the cell is directed to produce various proteins responsible for the pharmacologic effects of the progestins  
- by inducing and maintaining a lining in the uterus that resembles pregnancy, uterine bleeding can be prevented  
- by suppressing the release of the pituitary gland hormone that induces ovulation and by stimulating the secretion of mucus by the uterine cervix, pregnancy can be prevented | - used in a cyclic manner with estrogens to regulate or restore the menstrual cycle and treat uterine bleeding due to hormonal imbalance and endometriosis  
- used to treat endometrial or renal cancer, endometriosis and premenstrual syndrome (PMS)  
- used for oral contraception in combination with estrogens | - breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, breast changes (tenderness)  
- edema, changes in weight  
- less common: cervical erosions, abnormal secretions, uterine fibrosis, vaginal candidiasis, mental depression, melasma (skin discoloration)  
- CNS reactions sometimes occur: migraines, dizziness, nervousness, insomnia, fatigue  
- thrombophlebitis, pain or tenderness in thigh or leg | - rare except when used in higher concentrations: retinal thrombosis (sudden impairment or loss of vision) |
<table>
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</tr>
</thead>
<tbody>
<tr>
<td>ethinyl estradiol and levonorgestrel (Triphasil) #37 drug in 1991 other brands of this drug #91, #122 in 1991</td>
<td>- act as contraceptives by suppressing ovulation and inhibiting implantation of the fertilized ovum - create negative feedback upon the hypothalamus and pituitary gland, reducing follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentration levels - the diminished FSH concentration level prevents follicle development, and the absence of the midcycle surge of LH prevents ovulation - alters the cervical mucus so that it resists the passage of sperm - alters the lining of the uterus so that it resists implantation of the egg (if ovulation occurs)</td>
<td>- used primarily to prevent pregnancy and are the most effective form of reversible contraception available - sometimes used to treat menstrual irregularity, excessively heavy menstrual flow, and endometriosis</td>
<td>- most are related to dose and estrogen content - GI reactions: nausea is #1 reaction, vomiting, abdominal cramping, diarrhea, constipation - hypertension and increased risk of myocardial infarction - increased risk of thromboembolism - can affect levels of several serum proteins produced by the liver - increased risk of liver tumors and gall bladder disease</td>
<td>- decreased vision - retinal vascular disorders 1) occlusion 2) thrombosis 3) hemorrhage 4) retinal or macular edema - visual field scotomas, constriction, quadrantanopsia or hemianopsia - retrobulbar or optic neuritis - diplopia - papilledema secondary to pseudotumor cerebri</td>
</tr>
<tr>
<td>ethinyl estradiol and norethindrone (Ortho-Novum 7/7/7) #15 drug in 1991 other brands of this drug #127, #155 in 1991</td>
<td>- act as contraceptives by suppressing ovulation and inhibiting implantation of the fertilized ovum - create negative feedback upon the hypothalamus and pituitary gland, reducing follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentration levels - the diminished FSH concentration level prevents follicle development, and the absence of the midcycle surge of LH prevents ovulation - alters the cervical mucus so that it resists the passage of sperm - alters the lining of the uterus so that it resists implantation of the egg (if ovulation occurs)</td>
<td>- used primarily to prevent pregnancy and are the most effective form of reversible contraception available - sometimes used to treat menstrual irregularity, excessively heavy menstrual flow, and endometriosis</td>
<td>- most are related to dose and estrogen content - GI reactions: nausea is #1 reaction, vomiting, abdominal cramping, diarrhea, constipation - hypertension and increased risk of myocardial infarction - increased risk of thromboembolism - can affect levels of several serum proteins produced by the liver - increased risk of liver tumors and gall bladder disease</td>
<td>- decreased vision - retinal vascular disorders 1) occlusion 2) thrombosis 3) hemorrhage 4) retinal or macular edema - visual field scotomas, constriction, quadrantanopsia or hemianopsia - retrobulbar or optic neuritis - diplopia - papilledema secondary to pseudotumor cerebri</td>
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</tr>
</tbody>
</table>
|       | norethindrone and ethinyl estradiol (Ortho-Novum) | - act as contraceptives by suppressing ovulation and inhibiting implantation of the fertilized ovum  
- create negative feedback upon the hypothalamus and pituitary gland, reducing follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentration levels  
- the diminished FSH concentration level prevents follicle development, and the absence of the midcycle surge of LH prevents ovulation  
- alters the cervical mucus so that it resists the passage of sperm  
- alters the lining of the uterus so that it resists implantation of the egg (if ovulation occurs) | - used primarily to prevent pregnancy and are the most effective form of reversible contraception available  
- sometimes used to treat menstrual irregularity, excessively heavy menstrual flow, and endometriosis | - most are related to dose and estrogen content  
- GI reactions: nausea is #1 reaction, vomiting, abdominal cramping, diarrhea, constipation  
- hypertension and increased risk of myocardial infarction  
- increased risk of thromboembolism  
- can affect levels of several serum proteins produced by the liver  
- increased risk of liver tumors and gall bladder disease | - decreased vision  
- retinal vascular disorders  
1) occlusion  
2) thrombosis  
3) hemorrhage  
4) retinal or macular edema  
- visual field scotomas, constriction, quadrantanopia or hemianopia  
- retrobulbar or optic neuritis  
- diplopia  
- papilledema secondary to pseudotumor cerebri |
|       | norgestrel and ethinyl estradiol (Lo/Ovral) | - act as contraceptives by suppressing ovulation and inhibiting implantation of the fertilized ovum  
- create negative feedback upon the hypothalamus and pituitary gland, reducing follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentration levels  
- the diminished FSH concentration level prevents follicle development, and the absence of the midcycle surge of LH prevents ovulation  
- alters the cervical mucus so that it resists the passage of sperm  
- alters the lining of the uterus so that it resists implantation of the egg (if ovulation occurs) | - used primarily to prevent pregnancy and are the most effective form of reversible contraception available  
- sometimes used to treat menstrual irregularity, excessively heavy menstrual flow, and endometriosis | - most are related to dose and estrogen content  
- GI reactions: nausea is #1 reaction, vomiting, abdominal cramping, diarrhea, constipation  
- hypertension and increased risk of myocardial infarction  
- increased risk of thromboembolism  
- can affect levels of several serum proteins produced by the liver  
- increased risk of liver tumors and gall bladder disease | - decreased vision  
- retinal vascular disorders  
1) occlusion  
2) thrombosis  
3) hemorrhage  
4) retinal or macular edema  
- visual field scotomas, constriction, quadrantanopia or hemianopia  
- retrobulbar or optic neuritis  
- diplopia  
- papilledema secondary to pseudotumor cerebri |
fluoxymesterone (Halotestin)

**Mechanism of Action**
- Synthetic derivative of testosterone
- Produces androgenic and anabolic effects by binding to androgen receptors in target organs, such as skeletal muscle, the prostate gland, and bone marrow
- Receptor binding stimulates development in these organs and also increases protein synthesis
- May promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms)
- By blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass

**Indications for Use**
- Has a predominant androgenic activity
- Used to treat hypogonadism and impotence caused by a testicular deficiency
- Can also be used to prevent hereditary angioedema
- Inoperable breast carcinoma in females

**Adverse Reactions**
- GI: nausea, vomiting, diarrhea, abdominal fullness
- CNS: excitation, insomnia, chills
- Endocrine adverse effects:
  a) Virilization, acne, in all age groups
  b) In prepubertal males: first signs of virilization are phallic enlargement and increase in frequency of erections
  c) In postpubertal males: inhibition of testicular function with oligospermia, gynecomastia, testicular atrophy, male-pattern baldness
  d) In females: hisutism, hoarseness or deepening of the voice, clitoral enlargement, change in libido, male-pattern baldness

**Ocular Adverse Reactions**
- None listed
<table>
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</table>
| methyltestosterone (Metandren) | -- synthetic derivative of testosterone  
-- produces androgenic and anabolic effects by binding to androgen receptors in target organs, such as skeletal muscle, the prostate gland, and bone marrow  
-- receptor binding stimulates development in these organs and also increases protein synthesis  
-- may promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms)  
-- by blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass | - used to treat eunuchism, eunuchoidism, and hypogonadism  
- also used to treat male climacteric syndrome  
- also used to treat breast cancer 1 to 5 years after menopause and postpartum breast engorgement in women | -- GI: nausea, vomiting, diarrhea, abdominal fullness  
-- CNS: excitation, insomnia, chills  
-- Endocrine adverse effects:  
a) virilization, acne, in all age groups  
b) in prepubertal males: first signs of virilization are phallic enlargement and increase in frequency of erections  
c) in postpubertal males: inhibition of testicular function with oligospermia, gynecomastia, testicular atrophy, male-pattern baldness  
d) in females: hisutism, hoarseness or deepening of the voice, clitoral enlargement, change in libido, male-pattern baldness | -- none listed |
| testosterone cypionate (Andro-Cyp) | -- used primarily as an androgen  
-- produces androgenic and anabolic effects by binding to androgen receptors in target organs such as skeletal muscle, the prostate gland, and bone marrow  
-- receptor binding stimulates development in these organs and also increases protein synthesis  
-- may promote anabolic effects by blocking cortisol uptake in muscle and liver cells (cortisol normally acts as a catabolic agent increasing muscle breakdown and body stress mechanisms)  
-- by blocking cortisol uptake in muscle cells, steroid agents reduce muscle breakdown and increase muscle mass | used to treat:  
-- eunuchism,  
-- male hormone deficiency after castration  
-- male climacteric symptoms  
-- also used to treat metastatic breast cancer in women | 1) in females:  
- produces masculinizing effects  
- hoarseness or deepening of the voice and clitoral enlargement  
- male-pattern hair distribution  
- menstrual irregularities  
- acne  
- increased libido  
2) in males:  
- gynecomastia  
- testicular atrophy  
- decreased levels of pituitary reproductive hormones  
- prostatic hypertrophy  
3) GI: nausea, jaundice  
4) CNS: increased or decreased libido, headache, anxiety, depression  
5) retention of sodium, chloride, water, potassium | -- none listed |
**Bronchodilators**

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Remember</th>
</tr>
</thead>
</table>
| Albuterol         | - Available as metered dose inhaler  
                   | - For bronchospasm associated with reversible obstructive airway disease and exercise-induced bronchospasm |
| Ephedrine         | - In oral or injectable forms  
                   | - For acute and chronic asthma, hay fever, allergic rhinitis, and sinusitis |
| Metapranolol      | - In oral or inhaler forms  
                   | - For asthma, bronchitis and emphysema |
| Pirbuterol        | - In inhaler form  
                   | - Prevention and reversal of bronchospasm in patients with asthma |
| Terbutaline       | - In oral injectable and inhaler forms  
                   | - For asthma, bronchitis and emphysema |

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name

**Indications for Use:**
These noncatecholamine adrenergic agents are used to treat acute and chronic asthma, emphysema, pulmonary fibrosis, and chronic bronchitis. Additionally, some are used for systemic and local vasoconstriction, nasal and ophthalmic decongestion, smooth muscle relaxation, CNS stimulation and appetite suppression.

**Mechanism of Action:**
Direct-acting agents, such as albuterol, metaproteranol, pirbuterol and terbutaline, act by stimulating beta receptor sites (beta_2 more so than beta_1). The indirect-acting agents work by stimulating the release of norepinephrine. Dual-acting agents, like epinephrine, combine both actions.
Adverse Reactions:
- often causes headache, anxiety or euphoria, irritability, trembling, drowsiness or insomnia, lethargy, dizziness, light-headedness, incoherence, and convulsions.
- occasional hypotension or hypertension, palpitations, bradycardia or tachycardia, dysrhythmias, cardiac arrest, cerebral hemorrhage, weakness, muscle cramps, sweating, increased urination, incontinence, vomiting.

Ocular Adverse Reactions:
- stinging, blurred vision

Contraindications and Precautions:
- use caution in cases of pregnancy or diabetes

Drug Interactions:
- with general anesthetics: cardiac dysrhythmias, increased hypertension
- with beta blockers: increases effects of agents with beta activity
- with MAO inhibitors and tricyclic antidepressants: increased hypertension
MAST CELL STABILIZERS

△△ cromolyn sodium (Intal #119, Nasalcrom)

"△△" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
Mast cell stabilizers are used prophylactically to prevent topical allergic reactions from occurring on the lung mucosa, nasal mucosa, and ocular tissue. Intal is also approved as an antiasthmatic.

Mechanism of Action:
Mast cell stabilizers inhibit the degranulation of sensitized mast cells which occurs after exposure to specific antigens. Mast cells contain the chemical mediators which trigger the allergic response.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>cromolyn sodium (Nasalcrom)</td>
<td>a metered dose inhaler for the prevention and treatment of the symptoms of allergic rhinitis</td>
</tr>
<tr>
<td>cromolyn sodium (Intal)</td>
<td>a metered dose inhaler</td>
</tr>
<tr>
<td></td>
<td>a prophylactic for patients with asthma</td>
</tr>
</tbody>
</table>

Adverse Reactions:
with Nasalcrom:
- commonly: stinging, burning, sneezing upon application.
- rarely: headaches, rash, post-nasal drip, epistaxis occur
with Intal:
- commonly: throat irritation and dryness, bad taste, cough, wheeze, nausea
- rarely: anaphylaxis, angioedema, dizziness, headache, rash, urticaria

Ocular Adverse Reactions:
- Transient burning and stinging upon instillation were reported with Opticrom, a cromolyn sodium approved for ocular use, but now no longer available.
- Intal rarely causes increased lacrimation

Contraindications and Precautions:
- contraindicated in patients with known hypersensitivity
- caution advised in patients with renal or hepatic impairment, pregnancy, breast feeding mothers

Drug Interactions:
no known drug interactions
Indications for Use:
- Acetylcysteine is used as an adjunct therapy (with the bronchodilator isoproterenol) to treat patients with obstructive mucus secretions. Patients with bronchitis, emphysema, or cystic fibrosis may benefit from mucolytic therapy.
- Acetylcysteine is the antidote for acetaminophen overdosage.

Mechanism of Action:
Acetylcysteine reduces the viscosity of respiratory tract secretions by splitting disulfide bonds on glycoprotein molecules.

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetylcysteine</td>
<td>- available as an inhaler</td>
</tr>
<tr>
<td></td>
<td>- used for lung disorders in which overproduction of</td>
</tr>
<tr>
<td></td>
<td>mucus causes an accumulation of secretions.</td>
</tr>
<tr>
<td></td>
<td>- available in combination with isoproterenol</td>
</tr>
</tbody>
</table>

Adverse Reactions:
With prolonged use, acetylcysteine may produce stomatitis, nausea, vomiting, drowsiness, and severe rhinorrhea. Asthmatic patients may have difficulty breathing due to severe bronchospasm.

Contraindications and Precautions:
Use caution in patients with asthma or respiratory insufficiency due to increased airway obstruction.

Drug Interactions:
- Acetylcysteine is incompatible with: amphotericin B, chlortetracycline, erythromycin, oxytetracycline, ampicillin, tetracycline, iodized oil, hydrogen peroxide, chymotrypsin and trypsin.
- Activated charcoal decreases acetylcysteine's effectiveness, so when using as a remedy for acetaminophen overdose, any activated charcoal administered prior to acetylcysteine therapy should be removed by gastric lavage.
### Gastrointestinal Agents

**Adsorbent Agents**
- Activated charcoal

**Antiflatulant Agents**
- Simethicone (Mylicon)

**Digestive Agents**
- Glutamic acid hydrochloride (Acidulin)
- Dehydrocholic acid (Decholin)
- Pancreatin (Dizymes)
- Pancrelipase (Cotazym)

**Antidiarrheal Agents**
- Opium tincture
- Paregoric or camphorated opium tincture
- Loperamide (Imodium)
- Diphenoxylate hydrochloride (Lomotil)
- Diphenoxin with atropine (Motofen)
- Kaolin and pectin mixtures (Kaopectate, Pecto kay)

**Laxative Agents**
- Lactulose (Cephalac, Chronulac)
- Magnesium salts (Milk of Magnesia)
- Sodium phosphate, sodium biphosphate
- Glycerin
dietary fiber
- Psyllium hydrophilic mucilloid (Metamucil)
- Methylcellulose (Cologel)
- Docusate sodium (Dolace, Doxinate, Regutol)
- Bisacodyl
cascara sagrada
castor oil
phenolphthalein
senna
mineral oil

**Emetic Agents**
- Ipecac syrup
- Apomorphine
**antiemetic agents**

- buclizine
- cyclizine
- Δ dimenhydrinate
- diphenhydramine
- ΔΔ hydroxyzine
- Δ meclizine
- Δ trimethobenzamide
- chlorpromazine
- ΔΔ promethazine
- ΔΔ prochlorperazine
- thiethylperazine
- perphenazine
- trifluromazine
- trimeprazine tartrate

**peptic ulcer agents**

- Δ magnesium hydroxide, aluminum hydroxide with simethicone
  (Maalox TC, Mylanta-II)
- Δ magaldrate or aluminum magnesium complex
  (Riopan, Riopan Plus)
- ΔΔ cimetidine
- ΔΔ ranitidine
- ΔΔ famotidine
- ΔΔ nizatidine
- ΔΔ sucralfate
  (Tums)
  (Tagamet #19)
  (Zantac #3)
  (Pepcid #54)
  (Axid #125)
  (Carafate #75)

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name
Indications for Use:
- used in acute oral poisoning to prevent the absorption of drugs or toxins from the GI tract

Mechanism of Action:
- attracts and binds molecules of liquid, gas, or dissolved substance in the GI tract
- No adsorbent is effective for all toxins, but activated charcoal is indicated for most cases of acute oral poisoning (see exceptions).

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>activated charcoal</td>
<td>- the most common adsorbant agent</td>
</tr>
<tr>
<td></td>
<td>- indicated for most toxins except: cyanide, ethanol, methanol, iron, sodium chloride, alkalis, inorganic acids, organic solvents</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- black stools and constipation

Contraindications and Precautions:
- ineffective in cases of poisoning by: cyanide, ethanol, methanol, iron, sodium chloride, alkalis, inorganic acids, organic solvents

Drug Interactions:
- emetics (vomit inducers), are adsorbed by activated charcoal
- use emetics before adsorbents and allow emesis (vomiting) to occur prior to administration of the adsorbents (enhances the effectiveness of the adsorbent by decreasing the amount of toxin in the GI tract)
ANTIFLATULANTS

Indications for Use:
- used to treat conditions in which gas retention is a problem

Mechanism of Action:
- defoaming and water-repellent properties prevents and disperses gas pockets in the GI tract

<table>
<thead>
<tr>
<th><strong>major drugs</strong></th>
<th><strong>things to remember</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>simethicone</td>
<td>often a component of over-the-counter antacids</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- expulsion of gas via belching or flatus (passing of gas from rectum)

Contraindications and Precautions:
- contraindicated in cases of pathological abdominal conditions

Drug Interactions:
- no significant drug interactions
**DIGESTIVE AGENTS**

**Indications for Use:**
- aid digestion in patients who lack one or more of the specific enzymes and substances that naturally digest food

**Mechanism of Action:**
- replace the normal digestive substances
- glutamic acids act by converting pepsinogen in the stomach to pepsin, the activated form of the enzyme
- pancreatin and pancrelipase replace the normal pancreatic enzymes that aid in the digestion of protein, carbohydrates and fats

<table>
<thead>
<tr>
<th>major drugs</th>
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</tr>
</thead>
<tbody>
<tr>
<td>glutamic acid hydrochloride and hydrochloric acid</td>
<td>- to treat: hypochlorhydria (decreased secretion of hydrochloric acid) and achlorhydria (absence of free hydrochloric acid in the stomach)</td>
</tr>
<tr>
<td>dehydrochloric acid</td>
<td>- to stimulate bile flow from the liver</td>
</tr>
</tbody>
</table>
| pancreatin | - from fresh porcine (pig) or bovine (cattle) pancreas  
- combination of amylase, trypsin, lipase  
- aids digestion of starch, fats, proteins |
| pancrelipase | - from porcine pancreas  
- longer lasting than pancreatin  
- indicated for pancreatic insufficiency associated with cystic fibrosis |

**Adverse Reactions:**
- pancreatic enzymes often cause nausea and diarrhea

**Contraindications and Precautions:**
- hydrochloric acid aggravates peptic ulcers
- pancreatic enzymes derived from pigs or cattle are contraindicated in patients sensitive to porcine or bovine products

**Drug Interactions:**
- no significant drug interactions
ANTIDIARRHEAL AGENTS

Indications for Use:
for treatment of diarrhea

Mechanism of Action:
act systemically or locally to reduce the fluidity of the stool and the frequency of defecation
- diphenoxin with atropine:
diphenoxin has a local effect on the gastrointestinal wall to slow intestinal motility, while atropine decreases intestinal spasticity
- opium tincture and camphorated opium tincture:
act on the brain to inhibit intestinal peristalsis and enhance anal sphincter tone; also decreases HCL secretion and stomach motility
- loperamide and diphenoxylate:
decrease peristalsis in the large and small intestines
- kaolin and pectin:
kaolin and pectin bind bacteria, toxins and other irritants on intestinal mucosa while pectin also reduces the pH in the intestine and soothes the irritated mucosa

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>opium tincture &amp; camphorated opium tincture</td>
<td>for acute nonspecific diarrhea</td>
</tr>
<tr>
<td>loperamide &amp; diphenoxylate</td>
<td>for acute nonspecific diarrhea and chronic diarrhea</td>
</tr>
<tr>
<td>diphenoxin with atropine</td>
<td>a modification of phenoxylate</td>
</tr>
<tr>
<td>kaolin and pectin mixtures</td>
<td>for acute nonspecific diarrhea and chronic diarrhea</td>
</tr>
<tr>
<td></td>
<td>for acute diarrhea from various causes</td>
</tr>
</tbody>
</table>
Adverse Reactions:
- opium preparations: nausea, vomiting, dizziness
- loperamide and diphenoxylate: nausea, vomiting, abdominal pain and distension, drowsiness, CNS depression, tachycardia
- diphenoxin with atropine: anticholinergic effect of atropine occurs if recommended dose is exceeded (esp. in patients with Down's Syndrome) resulting in dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia, urinary retention
- kaolin and pectin mixtures may cause constipation in elderly or debilitated patients

Ocular Adverse Reactions:
- atropine-containing agents such as diphenoxin rarely cause mydriasis, cycloplegia and decreased lacrimation

Contraindications and Precautions:
- diarrhea caused by an infection
- use opium preparations cautiously in cases of decreased respiratory rate, asthma, narcotic dependence, liver dysfunction
- hypersensitivity to any of the active ingredients
- do not take kaolin and pectin concurrently with other medications as their binding effects may interfere with their absorption

Drug Interactions:
- opium preparations, loperamide and diphenoxylate interact with CNS depressants to increase the depressant effect
- kaolin and pectin mixtures interfere with absorption of many drugs
LAXATIVE AGENTS

Indications for Use:
for relief of constipation

Mechanism of Action:
act by increasing water content of the feces and/or increasing peristalsis
- hyperosmolar laxatives:
  produce an osmotic effect in the intestinal lumen that
causes fluid accumulation by the feces
- dietary fiber and related bulk forming laxatives:
  hydrophilic properties increase water content of the stool
- emollient laxatives:
  detergent action allows water to penetrate fecal material
  and increase fluid accumulation
- stimulant laxatives:
  simulate peristalsis and defecation by irritating the intestinal
  mucosa
- lubricant laxatives:
  lubricates the feces and intestinal mucosa by preventing
  water reabsorption from the lumen of the bowel

<table>
<thead>
<tr>
<th>major drugs</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>hyperosmolar laxatives</strong></td>
<td></td>
</tr>
<tr>
<td>lactulose</td>
<td>- for chronic constipation</td>
</tr>
<tr>
<td>magnesium salts</td>
<td>- to induce prompt and complete bowel evacuation</td>
</tr>
<tr>
<td>glycerin</td>
<td>- available as suppository or rectal liquid</td>
</tr>
<tr>
<td></td>
<td>- to establish proper bowel patterns in laxative-</td>
</tr>
<tr>
<td></td>
<td>dependent adults</td>
</tr>
<tr>
<td><strong>dietary fiber and related bulk-forming laxatives</strong></td>
<td></td>
</tr>
<tr>
<td>psyllium hydrophilic mucilloid</td>
<td>- for prevention of constipation</td>
</tr>
<tr>
<td>methylcellulose</td>
<td>- for prevention of constipation</td>
</tr>
<tr>
<td><strong>emollient laxatives</strong></td>
<td></td>
</tr>
<tr>
<td>docusate sodium</td>
<td>- a stool softener for patients at risk for chronic constipation</td>
</tr>
</tbody>
</table>
Adverse Reactions:
- hyperosmolar laxatives:
  - abdominal distention, cramps, flatulence (gas), nausea, vomiting, diarrhea, fluid and electrolyte imbalances
- dietary fiber and related bulk-forming laxatives:
  - flatulence, intestinal obstruction, diarrhea
- stimulant laxatives:
  - weakness, nausea, abdominal cramps, reddish colored urine
- lubricant laxatives:
  - nausea, vomiting, diarrhea, abdominal cramping, fat soluble vitamin deficiency

Contraindications and Precautions:
- all laxatives contraindicated with intestinal obstruction, ulceration and symptoms of appendicitis
- hyperosmotic laxatives:
  - hyperosmolars, because they increase water retention, are contraindicated in cases of edema and congestive heart failure
  - use lactulose with caution in diabetics, pregnant or lactating women
- emollient laxatives:
  - potassium salts contraindicated in renal dysfunction
  - use sodium salts with caution in cases of edema, congestive heart failure, or renal dysfunction
- stimulant laxatives:
  - castor oil contraindicated in pregnant or menstruating women
  - use with caution in cases of rectal bleeding
- lubricant laxatives:
  - contraindicated in children under 6 years of age, elderly patients, debilitated patients, pregnant patients

Drug Interactions:
- emolient laxatives increase intestinal mucosal damage with aspirin
- emolient laxatives should not be used with oral mineral oil as they increase the systemic absorption of mineral oil
- emolients enhance absorption of oral drugs
- mineral oil impairs absorption of many oral medications and impairs antibacterial activity of sulfonamides
- Lactulose contraindicated in patients taking oral anti-infectives
EMETIC AGENTS

Indications for Use:
- to induce vomiting after ingestion of toxic substances

Mechanism of Action:
- induces vomiting via a local affect on the gastric mucosa and a central effect on the chemoreceptor trigger zones (CTZ) located on the carotid body and aortic body in the carotid and aortic arteries

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipecac syrup</td>
<td>- drug of choice for emptying the stomach</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- ipecac syrup contains a cardiotoxin that may cause cardiac reactions such as arrhythmia, or fatal myocarditis (inflammation of the heart muscle)

Contraindications and Precautions:
- use with caution in pregnant or lactating women
- emetics are contraindicated in poisoning by petroleum distillates or caustic substances because vomiting may cause the aspiration of toxic gases into the lungs resulting in aspiration pneumonitis

Drug Interactions:
- no significant interactions
ANTIEMETIC AGENTS

Indications for Use:
- to decrease nausea and hence, the urge to vomit
- to prevent and treat motion sickness

Mechanism of Action:
- antihistamine antiemetics:
  block histamine (H$_1$) receptors and decrease nausea, vomiting, and vertigo
- phenothiazine antiemetics:
  block dopaminergic receptors in the chemoreceptor trigger zone (CTZ) located on the carotid body and aortic body in the carotid and aortic arteries

<table>
<thead>
<tr>
<th>major drugs</th>
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</tr>
</thead>
<tbody>
<tr>
<td>antihistamine antiemetics</td>
<td></td>
</tr>
<tr>
<td>dimenhydrinate</td>
<td>- to prevent motion sickness</td>
</tr>
<tr>
<td>hydroxyzine</td>
<td>- taken with narcotic analgesics for its synergistic analgesic effect and because it decreases the nausea associated with narcotic administration</td>
</tr>
<tr>
<td>meclizine</td>
<td>- to prevent motion sickness</td>
</tr>
<tr>
<td>trimethobenzamide</td>
<td>- to prevent and treat mild nausea and vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>phenothiazine antiemetics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>prochlorperazine and promethazine</td>
<td>- to prevent and treat severe nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td>- not effective for motion sickness</td>
</tr>
<tr>
<td></td>
<td>- prochlorperazine indicated prior to administering oral hyperosmotics in patients with angle closure glaucoma experiencing nausea or vomiting</td>
</tr>
</tbody>
</table>

Adverse Reactions:
antihistamine antiemetics
- drowsiness, mild nausea, anorexia, anticholinergic effects (dry mouth, dry throat, painful or difficult urination, urine retention and impotence), rarely hypersensitivity reactions
phenothiazine antiemetics:
- sedation, hypotension, anxiety, euphoria, depression, headache
Ocular Adverse Reactions:
effects are rare, reversible and usually of little clinical significance
- decreased vision, mydriasis, decreased contact lens tolerance,
diplopia, hallucinations

Contraindications and Precautions:
antihistamine antiemetics:
- use caution in narrow angle glaucoma, urine retention, asthma
phenothiazine antiemetics:
- contraindicated in coma, CNS depression, bone marrow
  depression, subcortical brain damage
- use with caution in encephalitis, tetanus, hepatic disease,
cardiovascular disease, respiratory disorders, convulsive
  disorders, patients undergoing electroshock therapy, brain tumor,
glaucoma, elderly or debilitated patients, children with acute
  illnesses

Drug Interactions:
antihistamine antiemetics:
- additive effects with other agents that have anticholinergic and
  sedative properties
phenothiazine antiemetics:
- CNS depressants: CNS depressant effects increased
- anticholinergic agents: anticholinergic effects increased
- antacids decrease phenothiazine absorption
- barbiturates decrease phenothiazine's effect
PEPTIC ULCER AGENTS

Indications for Use:
- **antacids:** over the counter drugs used alone or in conjunction with others for treatment of peptic ulcer disease
- **histamine$_2$-receptor antagonists:** for duodenal and gastric ulcers
- **sucralfate:** for short term treatment of duodenal ulcers

Mechanism of Action:
- **antacids:** increase the pH of the stomach, neutralizing gastric acid and decreasing pepsin's proteolytic activity
- **histamine$_2$-receptor antagonists:** block histamine-receptor sites on the parietal cells of the stomach, inhibiting acid secretion
- **sucralfate:** by binding to the ulcer site, it protects the ulcer from acid & pepsin

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>antacids</strong></td>
<td></td>
</tr>
</tbody>
</table>
| magnesium hydroxide, aluminum hydroxide with simethicone | - over the counter drugs  
  - used alone or in conjunction with others for treatment of peptic ulcer disease |
| magaldrate or aluminum magnesium complex |                   |
| **histamine$_2$-receptor antagonists** |                   |
| cimetidine | - for duodenal and gastric ulcers |
| ranitidine |                       |
| famotidine |                       |
| nizatidine |                       |
| **sucralfate** |                   |
| sucralfate | - for short term treatment of duodenal ulcers |
Adverse Reactions:
antacids:
    diarrhea and constipation
histamine₂-receptor antagonists:
    headache, dizziness, malaise, nausea, diarrhea, constipation
sucralfate:
    constipation, nausea, metallic taste

Ocular Adverse Reactions:
histamine H₂ receptor antagonists: ocular reactions uncommon unless taken in large doses
    - decreased vision secondary to cycloplegic effect
    - hallucinations
    - photophobia secondary to mydriasis
    - lid and conjunctiva irritation

Contraindications and Precautions:
antacids:
    - those containing magnesium are contraindicated in patients with severe renal disease due to risk of hypermagnesemia
    - calcium carbonate contraindicated for long term use: hypercalcemia can result
    - use with caution in patients with decreased bowel motility: constipation can result
histamine₂-receptor antagonists:
    - use with caution in cases of impaired renal or hepatic function because the drug's metabolism and elimination will be delayed

Drug Interactions:
    - antacids: impairs absorption of many oral drugs
    - histamine₂-receptor antagonists: inhibited by antacids
    - sucralfate: impairs absorption of many oral drugs and is inhibited by antacids
Antiseptics & Disinfectants

Δ benzalkonium chloride (Zephiran)
Δ boric acid
Δ chlorobutanol
Δ chlorhexidine (Hibiclens)
Δ EDTA
Δ ethyl alcohol
Δ hexachlorophene
Δ hydrogen peroxide
Δ iodine (Betadine)
Δ isopropyl alcohol
Δ potassium permanganate
Δ sorbic acid
Δ thimerosal (Thimerosal)

"Δ" indicates major agents -- see tables

Indications for Use:
- antiseptics prevent and control infection by killing or inhibiting the growth of microorganisms on living tissue
- disinfectants act by destroying microorganisms on instruments and in solutions
- some disinfectants can be used as antiseptics in appropriate concentrations

Mechanism of Action:
- highly variable among agents

<table>
<thead>
<tr>
<th>major agents</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzalkonium chloride</td>
<td>- active against bacteria and some viruses, fungi and protozoa</td>
</tr>
<tr>
<td></td>
<td>- preoperative skin antiseptic and wound treatment</td>
</tr>
<tr>
<td></td>
<td>- surgical equipment disinfectant</td>
</tr>
<tr>
<td></td>
<td>- in RGP contact lens solutions</td>
</tr>
<tr>
<td>boric acid</td>
<td>- a preservative in eye washes</td>
</tr>
<tr>
<td>chlorobutanol</td>
<td>- combined with EDTA in RGP contact lens solutions</td>
</tr>
<tr>
<td></td>
<td>- seldom used</td>
</tr>
<tr>
<td>chlorhexidine</td>
<td>- effective against gram + &amp; -, including pseudomonas</td>
</tr>
<tr>
<td></td>
<td>- surgical scrub and pre-operative skin antiseptic</td>
</tr>
<tr>
<td></td>
<td>- antibacterial wound cleanser</td>
</tr>
<tr>
<td></td>
<td>- in soft contact lens solutions</td>
</tr>
<tr>
<td></td>
<td>- causes buildup on lenses</td>
</tr>
<tr>
<td>EDTA</td>
<td>- a chelating agent, it binds divalent ions needed for bacterial growth</td>
</tr>
<tr>
<td></td>
<td>- used in combination with other preservatives</td>
</tr>
</tbody>
</table>

79
table continued

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<thead>
<tr>
<th>Compound</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethyl alcohol and</td>
<td>- pre-injection skin antiseptic</td>
</tr>
<tr>
<td>isopropyl alcohol</td>
<td></td>
</tr>
<tr>
<td>hexachlorophene</td>
<td>- a phenol antiseptic</td>
</tr>
<tr>
<td></td>
<td>- bacteriostatic against gram + bacteria</td>
</tr>
<tr>
<td></td>
<td>- used as a surgical scrub and to control outbreaks of gram + infections</td>
</tr>
<tr>
<td></td>
<td>when other procedures are unsuccessful</td>
</tr>
<tr>
<td>hydrogen peroxide</td>
<td>- superficial wound cleanser</td>
</tr>
<tr>
<td>iodine</td>
<td>- superficial wound cleanser, pre-op antiseptic</td>
</tr>
<tr>
<td></td>
<td>- affective against bacteria, fungi, viruses, protozoa</td>
</tr>
<tr>
<td></td>
<td>- often combined with povidone to decrease irritation</td>
</tr>
<tr>
<td>potassium permanganate</td>
<td>- an oxidative antiseptic like hydrogen peroxide</td>
</tr>
<tr>
<td></td>
<td>- may be used for athlete’s foot and intertriginous candidiasis</td>
</tr>
<tr>
<td>silver nitrate</td>
<td>- drops given at birth to prevent gonorrheal ophthalmia neonatorium</td>
</tr>
<tr>
<td>sorbic acid</td>
<td>- in soft contact lens solutions</td>
</tr>
<tr>
<td>thimerosal</td>
<td>- contains mercury</td>
</tr>
<tr>
<td></td>
<td>- 30% of people are allergic</td>
</tr>
<tr>
<td></td>
<td>- bacteriostatic and fungistatic against common pathogens</td>
</tr>
<tr>
<td></td>
<td>- used in combination with EDTA and chlorhexidine</td>
</tr>
<tr>
<td></td>
<td>- found in soft and RGP contact lens disinfecting solutions</td>
</tr>
</tbody>
</table>

**Adverse Reactions:**
- most antiseptic agents are known to cause hypersensitivity reactions
- hexachlorophene may cause brain lesions in newborns

**Contraindications and Precautions:**
- all agents are contraindicated in cases of hypersensitivity
- thimerosal: hypersensitivity to the thio or mercuri radicals may cause erythematous, papular and vesicular eruptions
- hexachlorophene contraindicated for use on burned or denuded skin or any mucous membrane. contraindicated for infants

**Drug Interactions:**
- thimerosal is incompatible with strong acids, salts, heavy metal, potassium permanganate, iodine, and aluminum
Contact Lens Solution Interactions:

<table>
<thead>
<tr>
<th>concurrent use of these disinfectants</th>
<th>cause these complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>polyvinyl alcohol and borate</td>
<td>produces a gummy residue</td>
</tr>
<tr>
<td>storage in solutions containing sorbic acid</td>
<td>causes yellow-brown lens discoloration</td>
</tr>
<tr>
<td>chlorhexidine and anionic detergents</td>
<td>causes lens to become opaque</td>
</tr>
<tr>
<td>thimerosal and benzalkonium chloride</td>
<td>forms a precipitate</td>
</tr>
<tr>
<td>thimerosal and hydrogen peroxide</td>
<td>thimerosal is degraded by hydrogen peroxide</td>
</tr>
<tr>
<td>chlorhexidine and: bicarbonates, borates, phosphates, sulfates</td>
<td>form a precipitate</td>
</tr>
<tr>
<td>quaternary ammonium compound and: isorbate, chlorhexidine</td>
<td>can cause red eye</td>
</tr>
<tr>
<td>chemical disinfectants &amp; oxidative disinfectants</td>
<td>form black, brown, yellow, pink or purple precipitates</td>
</tr>
</tbody>
</table>
THE ANTIBACTERIALS

aminoglycosides
- amikacin
- gentamicin (Garamycin)
- kanamycin
- neomycin (Mycifradin, Neobiotic, Neosporin)
- netilmicin
- paromomycin
- streptomycin
- tobramycin (Tobrex #173, Neobiotic)

bacitracin (Baciguent)
- used with polymixin B in Polysporin
- used with polymixin B and neomycin in Neosporin
- used with polymixin B, neomycin, hydrocortisone in Cortisporin

cephalosporins
1ST GENERATION
- cephadine
- cephadroxil (Duricef, Ultracet #53)
- cephalexin (Keflex #159)
- cephalothin (Keflin)
- cephradin
- cephalizin (Ancef, Kefzol)

2ND GENERATION
- cefaclor (Cefclor #7)
- cefamandole nafate (Mandole)
- cefonicid
- ceforanide
- cefoxitin (Mefoxin)
- cefuroxime (Ceftin #63)

3RD GENERATION
- cefixime (Suprax #118)
- cefotetan
- ceftizoxime (Cefizox)
- ceftriaxone (Rocephin)
- cefazidime
- cephoperazone (Cefobid)
- cephapaxime sodium ( Claforan)
- moxa lactam disodium

chloramphenicol (Chloromycetin)
- clindamycin (Cleocin T #142)
**erythromycin**

(PCE #56, E-Mycin #64, E.E.S. #87, Eryc #104, Erythromycin Base #110, Ery-Tab #121, Erythrocin Stearate #141)

**penicillins**

**NATURAL PENICILLINS**

- Δ penicillin G
- ΔΔ penicillin V

(Penicillin V #72, Veetids #79, Pen-Vee K #85, Penicillin VK #174, Beepen VK #188, V-Cillin K)

**PENICILLINASE-RESISTANT PENICILLINS**

- cloxacillin
- Δ dicloxacillin
- methicillin
- nafcillin
- Δ oxacillin

(Dynapen)

**AMINOPENICILLINS**

- Δ amoxicillin
- ampicillin
- bacampicillin
- cyclacillin

(Amoxil #1, Trimox #27, generic Amoxicillin #30, Polymox #36, Wymox #136)

**EXTENDED-SPECTRUM PENICILLINS**

- ΔΔ amoxicillin / clavulanate (Augmentin #20)
- azlocillin
- carbenicillin
- mezlocillin
- piperacillin
- Δ ticarcillin

(Ticar)

**quinolones**

- cinoxacin
- ΔΔ ciprofloxacin
- nalidixic acid
- ΔΔ norfloxacin

(Cipro #25)

(Noroxacin #150)

**sulfonamides**

- Δ sulfacetamide and Prednisolone (Blephamide)
- sulfacytine
- sulfadiazine
- Δ sulfamethoxazole (Gantanol)
- ΔΔ sulfamethoxazole and Trimethoprim (SMZ-TMP #73)
- sulfapyridine
- sulfasalazine
- Δ sulfisoxazole (Gantrisin)
tetracyclines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlortetracycline</td>
<td>(Aureomycin)</td>
</tr>
<tr>
<td>demeclocycline</td>
<td></td>
</tr>
<tr>
<td>doxycycline</td>
<td>(Vibramycin)</td>
</tr>
<tr>
<td>methacycline</td>
<td></td>
</tr>
<tr>
<td>minocycline</td>
<td>(Minocin #179)</td>
</tr>
<tr>
<td>oxytetracycline</td>
<td>(Sumycin #156, Achromycin-V #181)</td>
</tr>
<tr>
<td>tetracycline</td>
<td>(Vancocin)</td>
</tr>
</tbody>
</table>

vancomycin

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Vancocin)</td>
</tr>
</tbody>
</table>

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name
THE AMINOGLYCOSIDES

- Δ streptomycin (Mycifradin, Neobiotic, Neosporin)
- Δ neomycin (Garamycin)
- Δ paromomycin (Tobrex #173, Nebcin)
- Δ kanamycin
- Δ gentamicin
- ΔΔ tobramycin
- netilmicin
- amikacin

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
- aerobic gram negative bacilli
- some aerobic gram + (many strains of staph), but resistance is common
- mycobacteria
- some protozoa

Mechanism of Action:
- inhibit protein synthesis in pathogens by binding to 30S subunit of ribosome

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to know</th>
</tr>
</thead>
<tbody>
<tr>
<td>streptomycin</td>
<td>- for treatment of tuberculosis, bacterial endocarditis</td>
</tr>
<tr>
<td>neomycin</td>
<td>- surgical prophylactic</td>
</tr>
<tr>
<td></td>
<td>- found with bacitracin &amp; polymixin B in Neosporin</td>
</tr>
<tr>
<td></td>
<td>- effective against gram negatives only</td>
</tr>
<tr>
<td>gentamycin</td>
<td>- drug of choice for many gram - and gram +</td>
</tr>
<tr>
<td></td>
<td>- P. aeruginosa, E. coli, Staph., mycobacteria</td>
</tr>
<tr>
<td></td>
<td>- available in ophthalmic preparations</td>
</tr>
<tr>
<td>tobramycin</td>
<td>- spectrum of activity similar to gentamycin but more</td>
</tr>
<tr>
<td></td>
<td>- effective against Pseudomonas aeruginosa</td>
</tr>
<tr>
<td></td>
<td>- available in ophthalmic preparations</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- nausea, vomiting, diarrhea when used systemically
- toxicity with systemic use: damages auditory (8th nerve), vestibular, renal and neuromuscular functions (especially neomycin)
- allergic reactions
Ocular Adverse Reactions
with systemic administration: (reactions are rare)
- double vision and ptosis due to muscle paresis
- decreased pupillary light reflex
- gentamycin: papilledema secondary to pseudotumor cerebri

with ocular administration:
- neomycin: contact allergic reactions in lids and conjunctiva in 4% of patients
- overgrowth of nonsusceptible organisms

Contraindications and Precautions:
- known allergies to aminoglycosides

Drug Interactions:
- extended spectrum penicillins can inactivate aminoglycosides when administered simultaneously
bacitracin (Baciguent)
used with polymixin B in Polysporin
used with polymixin B and neomycin in Neosporin
used with polymixin B, neomycin, hydrocortisone in Cortisporin

Indications for Use:
- a topical ointment for gram + skin and ocular infections such as impetigo, staph. blepharitis and corneal ulcers caused by Neisseria gonorrhea
- narrow spectrum includes gram positives and Neiseria gonorrhea

Mechanism of Action:
- inhibits cell wall synthesis

Adverse Reactions:
- contact dermatitis
- delayed wound healing

Ocular Adverse Reactions:
with systemic application: (reactions are rare)
- muscle paralysis leading to ptosis, blurred vision and diplopia
with ocular application: (reactions are rare)
- irritation upon application
- allergic reactions of lids and conjunctiva
- keratitis
- overgrowth of nonsusceptible organisms

Contraindications and Precautions:
- known sensitivity to bacitracin

Drug Interactions:
- inactivated by silver nitrate
THE CEPHALOSPORINS

1st generation
Δ cephalizin (Ancef, Kefzol)
Δ cephalothin (Keflin)
cephaprim
cephadine
ΔΔ cephalaxin (Keflex #159)
ΔΔ cephadroxil (Duricef, Ultracel #53)

2nd generation
ΔΔ cefaclor (Ceclor #7)
Δ cefoxitin (Mefoxin)
Δ cefamandole nafate (Mandole)
ΔΔ cefuroxime (Ceftin #63)
cefonicid
ceforanide

3rd generation
ΔΔ ceftixime (Suprax #118)
cefotetan
Δ cepheperazone (Cefobid)
Δ cephotaxime sodium (Clkfuran)
moxalactam disodium
Δ ceftizoxime (Cefzox)
Δ ceftriaxone (Rocephin)
ceftazidime

“Δ” indicates major drug -- see table
“ΔΔ” indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
1st generation
- most gram + (staph and strep)
- some gram -, including E. Coli, Klebsiella, Proteus, H. influenza

2nd generation
same spectrum as 1st generation, plus:
- gram negatives including N. gonorrhoeae
- anaerobes

3rd generation
same spectrum as 1st and 2nd generations, plus:
- most gram -, including Pseudomonas Auruginosa
- less affective on gram +

Mechanism of Action:
- similar to penicillins, they block the terminal step in the synthesis of peptidoglycan, thus inhibiting cell wall synthesis.
### Major Drugs

<table>
<thead>
<tr>
<th><strong>1st generation</strong></th>
<th><strong>Things to Know</strong></th>
</tr>
</thead>
</table>
| **Cephalothin (Keflin)** | - for severe Staph infections  
- administered I.V. or I.M.  
- the 1st cephalosporin developed |
| **Cephazolin (Ancef, Kefzol)** | - similar to cephalothin, except better for *E. Coli* and *Klebsiella* |
| **Cephalexin (Keflex)** | - administered orally  
- for urinary tract infections |
| **Cephadroxil (Duricef)** | - only oral cephalosporin that can be taken with food |

<table>
<thead>
<tr>
<th><strong>2nd generation</strong></th>
<th><strong>Things to Know</strong></th>
</tr>
</thead>
</table>
| **Cefaclor (Ceclor)** | - administered orally  
- for respiratory infections, otitis media (ear infections) |
| **Cefoxitin (Mefoxin)** | - administered I.V.  
- for diabetic foot ulcers, pelvic inflammatory disease, lung abscess, aspiration pneumonia  
- penicillinase producing *N. Gonorrhoea, Proteus* |
| **Cefamandole nafate (Mandol)** | - administered I.V or I.M.  
- for *H. Influenza, Enterobacter, Proteus* |

<table>
<thead>
<tr>
<th><strong>3rd generation</strong></th>
<th><strong>Things to Know</strong></th>
</tr>
</thead>
</table>
| **Cefixime (Suprax)** | - only oral 3rd gen. cephalosporin, also in I.V and I.M  
- for urinary tract infections, ear infections due to *H. influenza*, pharyngitis and tonsillitis, bronchitis |
| **Cephoperazone (Cefobid)** | - administered I.V. or I.M.  
- used topically for corneal ulcers  
- effective against *Pseudomonas Auruginosa* |
| **Cephotaxime sodium (Claloran)** | - administered I.V. or I.M.  
- for gram -, except *P. Auruginosa*  
- for gram +, except enterococci |
| **Ceftiraxone (Rocephin)** | - for ophthalmic neonatorum due to *N. gonorrhea* |

**Adverse Reactions:**
- Cephalosporins are relatively safe but second generation drugs are more toxic than first, and third generation more toxic than second.
- Cross-sensitivity occurs with penicillins
- Pain at injection site
- Seizures in high doses of cefazolin
- Coagulation disorders in elderly and poorly nourished
- Nausea, vomiting and diarrhea upon oral administration
- Pseudomembranous colitis
- Nephrotoxicity in patients with renal dysfunction

89
Ocular Adverse Reactions:
  with systemic application: (reactions are rare)
    - nystagmus
    - allergic reactions in lids and conjunctiva
  with ocular application: (reactions are rare)
    - irritation upon application
    - allergic reaction to lids and conjunctiva

Contraindications and Precautions:
  - cases of renal dysfunction
  - patients with a known allergy to penicillins or cephalosporins

Drug Interactions:
  - alcohol intolerance
  - probenicid is used to increase and prolong cephalosporin concentrations
  - nephrotoxicity may occur when cephalothin is administered with an aminoglycoside
CHLORAMPHENICOL

chloramphenicol (Chloromycetin)

**Indications for Use:**
- most gram + and gram -
- reserved for severe infections due to risk of fatal aplastic anemia
- drug of choice for ampicillin resistant typhoid fever and other Salmonella infections
- for *H. influenza* meningitis

**Mechanism of Action:**
- inhibits protein synthesis by binding to the 50S subunit (same as erythromycin and clindamycin)

**Adverse Reactions:**
- bone marrow suppression
- GI reactions: nausea, vomiting, glossitis, unpleasant taste, stomatitis, diarrhea, perineal irritation
- gray syndrome in neonates causing fatalities in 40% of cases
- hypersensitivity reactions: fever, rash, anaphylaxis
- fatal aplastic anemia

**Contraindications and Precautions:**
- hepatic or renal dysfunction
- use caution in pregnant women and young children

**Drug Interactions:**
- inhibits metabolism of hypoglycemic agents, phenytoin, oral anticoagulants and cyclophosphamide
- interferes with the action of penicillins
CLINDAMYCIN


\[ \Delta\Delta \text{ clindamycin} \]

(Cleocin T #142)

"\(\Delta\Delta\)" indicates Top 200 Drug in 1991 -- note ranking after trade name

**Indications for use:**
- Effective against most gram + and anaerobes, but used only when safer drugs are contraindicated or not available.
- Used primarily to treat anaerobic intraabdominal or pleuropulmonary infections caused by *B. fragilis*.

**Mechanism of Action:**
- Inhibits protein synthesis by binding with the 50S subunit of ribosomes (same as erythromycin and chloramphenicol).

**Adverse Reactions:**
- GI reaction with diarrhea in 80% of patients.
- Pseudomembranous colitis caused by overgrowth of *Clostridium difficile*.
- Hypersensitivity reactions.

**Ocular Adverse Reactions:**
- (Reactions are rare)
  - Allergic reactions of lids and conjunctiva.
  - Ptosis and diplopia due to muscle paresis.

**Contraindications and Precautions:**
- Intestinal disorders.

**Drug Interactions:**
- Erythromycin may block their site of action (the 50S subunit).
- Effects of muscle relaxants are enhanced by clindamycin.
ERYTHROMYCIN

ΔΔ erythromycin (PCE #56, E-Mycin #64, E.E.S. #87, Eryc #104, Erythromycin Base #110, Ery-Tab #121, Erythrocin Stearate #141)

"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
- gram + and some gram -
- drug of choice for *Mycoplasma pneumonia* and *Legionella pneumonia*
- for syphilis and gonorrhea when penicillin and tetracyclines are contraindicated
- for minor staph infections including blepharitis

Mechanism of Action:
- inhibits protein synthesis by binding to the 50S subunit of the ribosome (similar to chloramphenicol and clindamycin)

Adverse Reactions:
- one of the safest antibiotics
- GI reactions: stomatitis (inflammation of mucous membranes, heartburn, anorexia, melena black {tarry feces due to action of intestinal secretions on free blood})
- allergic reactions: rashes, fever, anaphylaxis
- cholestatic hepatitis: nausea, vomiting, and abdominal pain followed by jaundice, fever and abnormal liver function

Ocular Adverse Reactions:
with systemic administration: (reactions are rare)
- blue yellow color defect
- allergic reactions
- photosensitivity
- extracocular muscle paresis
with ocular administration: (reactions are rare)
- irritation: hyperemia, pain, edema
- allergic reactions
- overgrowth of nonsusceptible organisms

Contraindications and Precautions:
- known allergy to erythromycin
- hepatic dysfunction

Drug Interactions:
- spectrum of activity of chloramphenicol, clindomycin and lincomycin changes when used with erythromycin due to competition for common binding sites (the 50S subunit)
- inhibits metabolism of theophylline and carbamazepine
THE PENICILLINS

natural penicillins
- Δ penicillin G (Wycillin, Pentids, Bicillin, Bicillin L-A)
- ΔΔ penicillin V (generic Penicillin V # 72, Veetids # 79)

penicillinase-resistant penicillins
- cloxacillin
- Δ dicloxacillin (Dynapen)
- methicillin
- nafcillin
- Δ oxacillin (Prostaphilin)

aminopenicillins
- ΔΔ amoxicillin (Amoxil #1, Trimox #27)
- Δ ampicillin (Omnipen)
- bacampicillin
- cyclacillin

extended-spectrum penicillins
- azlocillin
- carbenicillin
- mezlocillin
- piperacillin
- Δ ticarcillin (Ticar)
- ΔΔ amoxicillin / clavulanate (Augmentin #20)

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
Used to treat a variety of bacterial infections, this class has the widest spectrum of antimicrobial activity.

Mechanism of Action:
inhibits cell wall synthesis by preventing synthesis of peptidoglycan
### natural penicillins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
</tr>
</thead>
</table>
| penicillin G | - available in oral, IV, and IM forms  
|            | - ineffective against Staph. due to resistance  
|            | - drug of choice for syphilis                                         |
| penicillin V | - in oral form  
|            | - for infections of throat, respiratory tract, soft tissues          |

### penicillinase-resistant penicillins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>oxacillin</td>
<td>- for <em>Staph. aureus, Staph. epidermis</em> and some streptococci infections</td>
</tr>
<tr>
<td>dicloxacillin</td>
<td>- oral drug of choice for Staph infections</td>
</tr>
</tbody>
</table>

### aminopenicillins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ampicillin</td>
<td>- spectrum same as amoxicillin but many ampicillin resistant strains have emerged</td>
</tr>
</tbody>
</table>
| amoxicillin | - #1 prescribed drug of 1991  
|            | - for *Haemophilus influenza*, urinary tract infections, gonorrhea  |

### extended spectrum penicillins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
</tr>
</thead>
</table>
| amoxicillin / clavulanate | - clavulanate inhibits beta-lactamases that can inactivate amoxicillin, which extends it's spectrum to include *Staph aureus* and *Klebsiella*.  
|            | - for skin infections, otitis media (ear infection) and urinary tract infections |
| ticarcillin | - spectrum similar to ampicillin but also effective with *P. aeruginosa*, Proteus, *Enteropacter* |

### Adverse Reactions:

- few because the peptidoglycan in cell walls is unique to bacteria
- allergic reactions may occur
- neurotoxicity, nephrotoxicity
- changes in normal GI flora may occur causing nausea, vomiting, diarrhea
- Pseudomembranous colitis due to overgrowth of *Clostridium difficile*
- potassium imbalance (hyperkalemia or hypokalemia) with ticarcillin
- hemolytic anemia
- blood platelet dysfunction

### Ocular Adverse Reactions:

*with systemic administration*: (reactions are rare)
- allergic reaction of lids and conjunctiva (esp. with ampicillin)
- ptosis and diplopia due to muscle paresis

*with ocular administration*: (reactions are rare)
- irritation upon application
- allergic reactions of lids and conjunctiva
Contraindications and Precautions:
- penicillin allergy
- use with caution in cases of cardiac dysfunction, renal dysfunction, hepatic disease, uremia

Drug Interactions:
- efficacy is increased by concurrent administration of probenicid
- high doses of penicillin G and extended spectrum penicillins inactivate the cephalosporins, aminoglycosides
- tetracyclines and chloramphenicol inactivate penicillins
- penicillins interfere with renal tubular secretion of methotrexate
- sulfonamides inhibit GI absorption of oxacillin

Other Notes:
- Many bacteria, especially Staph, produce penicillinase, which inactivates most penicillins. Only penicillinase resistant penicillins are effective in these cases.
THE SULFONAMIDES

- sulfamethoxizole (Gantanol)
- sulfamethoxizole and Trimethoprim (SMZ-TMP #73)
- sulfisoxazole (Gantrisin)
- sulfacetamide and Prednisolone (Blephamide)
- sulfadiazine
- sulfapyridine
- sulfacytine
- sulfasalazine

"Δ" indicates major drugs -- see table
"ΔΔ" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
- broad spectrum gram + and gram -, but widespread resistance limits use
- primarily for acute urinary tract infections caused by chlamydia, plasmodia, toxoplasma

Mechanism of Action:
- inhibits bacterial growth by preventing folic acid synthesis

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to know</th>
</tr>
</thead>
<tbody>
<tr>
<td>sulfisoxazole</td>
<td>- short acting</td>
</tr>
<tr>
<td></td>
<td>- urinary tract infections</td>
</tr>
<tr>
<td></td>
<td>- conjunctivitis</td>
</tr>
<tr>
<td>sulfamethoxizole</td>
<td>- intermediate acting</td>
</tr>
<tr>
<td></td>
<td>- urinary tract infections and otitis media</td>
</tr>
<tr>
<td>sulfamethoxizole and trimethoprim</td>
<td>- a combination used to treat recurrent urinary tract infections and otitis media (ear infection)</td>
</tr>
<tr>
<td>sulfacetamide</td>
<td>- combined with prednisolone in Blephamide for topical treatment of blepharitis</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- GI reactions: nausea, vomiting and diarrhea are common
- crystalluria (sulfonamide crystals in the urine) and tubular deposits of sulfonamide crystals
- hypersensitivity reactions such as Stevens-Johnson syndrome
- increases UV sensitivity of skin and eyes
- transient myopia
Ocular Adverse Reactions:

with systemic administration:
- transient myopia resulting from ciliary body edema is most common ocular reaction
- paresis of extraocular muscles
- ocular irritation, lacrimation and photophobia
- color defects

with ocular administration:
- ocular irritation
- allergic reactions to lid and conjunctiva such as anaphylaxis, and Stevens-Johnson syndrome
- follicular conjunctivitis

Contraindications and Precautions:
- known sensitivity to sulfonamides
- pregnancy or breast feeding
- because presence of pus inhibits sulfonamides, they are contraindicated in purulent infections

Drug Interactions:
- local anesthetics and PABA (para-aminobenzoic acid) decreases the activity of sulfonamides
- sulfamethoxazole decreases the hepatic metabolism of anticoagulants
THE QUINOLONES

- cinoxacin
- ciprofloxacin (Cipro #25)
- nalidixic acid
- norfloxacin (Noroxin #150)

"△△" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
- these are new drugs with broad spectrum of gram + and gram -
- primary use is for treatment of urinary tract infections
  - ciprofloxacin: also used systemically for GI infections and topically for corneal ulcers and conjunctivitis
  - norfloxacin: also used topically for conjunctivitis

Mechanism of Action:
- inhibit DNA gyrase activity, preventing the supercoiling unique to bacterial DNA

Adverse Reactions:
- usually well tolerated
- GI reactions: nausea, vomiting, diarrhea, abdominal pain
- CNS reactions: headaches, drowsiness, seizures, depression, agitation
- hypersensitivity reactions
- photosensitivity

Ocular Adverse Reactions:
with systemic administration of nalidixic acid:
- most common ocular reaction involves a color disturbance in which objects appear bright and with a tinge of green, yellow, blue or orange
- photophobia
- paresis of extraocular muscles causing diplopia
- mydriasis and cycloplegia
- papilledema secondary to increased intracranial pressure in adolescents

with ocular administration:
- discomfort, itching and foreign body sensation
- may form white precipitate
- causes bitter taste following installation

Contraindications and Precautions:
- known allergy to drug
- convulsive disorders

Drug Interactions:
- few significant drug interactions occur
THE TETRACYCLINES

Δ chlortetracycline (Aureomycin)
  demeclocycline
Δ doxycycline (Vibramycin)
  methacycline
ΔΔ minocycline (Minocin #179)
  oxytetracycline
  tetracycline (Sumycin #156, Achromycin-V #181)

“Δ” indicates major drugs -- see table
“ΔΔ” indicates a Top 200 Drug in 1991 -- note ranking after trade name

Indications for Use:
- widespread resistance (esp. by Staph and Strep) limits their use
- broad spectrum: gram +, gram -, anaerobes and aerobes
  - spirochetes (syphilis) when patient is allergic to penicillin
  - mycoplasmas (drug of choice for M. pneumonia)
  - rickettsiae (Rocky Mountain Spotted Fever)
  - some protozoa (not Pseudomonas Auruginosa)
  - for sebaceous gland disorders such as acne and acne rosacea

Mechanism of Action:
- inhibits protein synthesis by binding to the 30S subunit of ribosome

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to know</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlortetracycline</td>
<td>- in ointment form for topical use</td>
</tr>
<tr>
<td></td>
<td>- for skin infections and bacterial conjunctivitis</td>
</tr>
<tr>
<td>tetracycline</td>
<td>- in oral, I.V., and I.M. forms</td>
</tr>
<tr>
<td></td>
<td>- for chronic bronchitis, gonorrhea, syphilis</td>
</tr>
<tr>
<td>doxycycline</td>
<td>- oral form may be taken on an empty stomach</td>
</tr>
<tr>
<td></td>
<td>- a prophylaxis for traveler's diarrhea</td>
</tr>
<tr>
<td></td>
<td>- for chlamydia</td>
</tr>
<tr>
<td>minocycline</td>
<td>- oral form may be taken on an empty stomach</td>
</tr>
<tr>
<td></td>
<td>- for acne and acne rosacea</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- hepatotoxicity, nephrotoxicity, CNS toxicity
- GI reactions: nausea, vomiting, diarrhea and superinfections
- bone growth depression and discoloration of developing teeth
- increases UV sensitivity of skin and eyes
Ocular Adverse Reactions:

with systemic application: (reactions are rare)
- myopia
- papilledema secondary to pseudotumor cerebri
- photophobia
- diplopia and ptosis due to muscle paresis
- chlortetracycline: causes color defects possibly due to yellowing of cornea

with ocular application: (reactions are rare)
- irritation upon installation
- allergic reactions of lids and conjunctiva
- overgrowth of nonsusceptible organisms

Contraindications and Precautions:
- pregnant women, breast feeding mothers, and children under age 8 due to inhibition of bone growth and tooth discoloration
- cases of renal dysfunction

Drug Interactions:
- doxycycline metabolism is enhanced by alcohol, barbiturates and carbamazepine
- antacids and ferrous sulfate cause decreased absorption of tetracycline
vancomycin (Vancocin)

Indications for Use:
- for pseudomembranous colitis caused by *Clostridium difficile*
- for serious *Staph* or *Strep* infections with resistance to less toxic agents

Mechanism of Action:
- damages bacterial cell wall by inhibiting synthesis of peptidoglycan

Adverse Reactions:
- ototoxicity: tinnitus (ringing of the ears) followed by deafness due to 8th nerve damage if drug is continued
- nephrotoxicity: toxic to kidneys
- hypersensitivity may occur with rapid I.V. administration

Ocular Adverse Reactions:
- with systemic administration: (reactions are rare)
  - Allergic reactions
  - photosensitivity

Contraindications and Precautions:
- use of other nephrotoxic drugs
- cases of renal dysfunction

Drug Interactions:
- increased nephrotoxicity when used with aminoglycosides, amphotericin B, cisplatin
**ANTIFUNGAL AGENTS**

- △ amphotericin B (Fungizone)
- △△ clotrimazole (Lotrimin # 193, Gyne-Lotrimin, Mycelex)
- △△ clotrimazole and betamethasone (Lotrisone #74)
- △ flucytosine (Ancobon)
- griseofulvin
- △△ ketoconazole (Nizoral #198)
- miconazole
- △ natamycin (Natacyn)
- △ nystatin (Mycostatin, Nilstat)
- △△ terconazole (Terazol #67)

"△" indicates a major drug -- see table
"△△" indicates a Top 200 Drug in 1991-- note ranking after trade name

**Indications for Use:**

amphotericin B:
- drug of choice for serious yeast and filamentous fungal infections including histoplasmosis, blastomycosis, cryptococcosis and coccidioidomycosis

clotrimazole:
- popular for topical treatment of superficial, oral (with an oral troche which dissolves in the mouth), and vaginal dermatophyte and Candida infections

flucytosine:
- used in combination with amphotericin B to reduce the dose and toxicity of amphotericin B or by itself for treatment of urinary tract Candida infections

ketoconazole:
- effective treatment for most topical and systemic fungal infections, it is also active against some gram + bacteria

natamycin:
- only topical ophthalmic drug approved for treatment of fungal keratitis, conjunctivits, blepharitis and corneal ulcers

nystatin:
- used primarily to treat local yeast infections of the skin, vagina and oral cavity due to Candida species

terconazole:
- a new suppository agent used to treat vaginal Candida infections
Mechanism of Action:

amphotericin B, nystatin and natamycin:
they bind to sterols in the fungal cell membrane, producing channels that increase membrane permeability resulting in leakage of intracellular components leading to inhibition of cell growth or cell death

flucytosine:
penetrates fungal cell where it is converted to the metabolite, fluorouracil, and is incorporated into the cells' RNA, altering protein synthesis and causing cell death

ketoconazole, miconazole and clotrimazole:
interact with sterol synthesis to damaging the cell membrane and increase its permeability - the result is the loss of essential intracellular elements and inhibition of cell growth or cell death

terconazole:
kills fungus by disrupting fungal cell membrane permeability

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>amphotericin B</td>
<td>- the most toxic antibiotic in use today</td>
</tr>
<tr>
<td></td>
<td>- usually reserved for life-threatening infections</td>
</tr>
<tr>
<td></td>
<td>- administered IV, intrathecally, and topically</td>
</tr>
<tr>
<td>clotrimazole</td>
<td>- a popular topical agent for superficial, oral and vaginal dermatophyte and candida infections</td>
</tr>
<tr>
<td>clotrimazole and betamethasone</td>
<td>- a popular new topical combination drug, adds anti-inflammatory effect to clotrimazole</td>
</tr>
<tr>
<td>flucytosine</td>
<td>- used in combination with amphotericin B</td>
</tr>
<tr>
<td></td>
<td>- administered orally</td>
</tr>
<tr>
<td>ketoconazole</td>
<td>- oral and topical drug used for systemic and topical infections</td>
</tr>
<tr>
<td>natamycin</td>
<td>- only antifungal approved for ophthalmic use</td>
</tr>
<tr>
<td></td>
<td>- for treatment of fungal corneal ulcers</td>
</tr>
<tr>
<td>nystatin</td>
<td>- administered orally and topically</td>
</tr>
<tr>
<td></td>
<td>- few adverse reactions</td>
</tr>
<tr>
<td>terconazole</td>
<td>- topical treatment for vaginal Candidiasis</td>
</tr>
</tbody>
</table>
Adverse Reactions:

amphotericin B:
- the most toxic antibiotic in use today
- IV administration almost always causes chills, fever, nausea, vomiting, anorexia, muscle and joint pain, headache, abdominal pain, weight loss, dyspepsia (severe indigestion) and often normocytic anemia (reduction in RBC count without changes in size or functioning of RBC's). 80% develop nephrotoxicity, 25% develop hypokalemia (low blood potassium levels). Other reactions to IV administration include phlebitis (inflammation of a vein), thrombophlebitis (inflammation of a vein in conjunction with a thrombus formation), hypotension, flushing, parasthesias and seizures.
- intrathecal administration may cause headaches, leg and back pain, paresthesias, peripheral neuropathies, sensory loss, and urine retention
- topical application may result in pruritis, skin dryness, thickening and discoloration, erythema, and contact dermatitis

nystatin:
- reactions are rare and mild
- oral use may cause diarrhea, nausea, vomiting, abdominal pain and hypersensitivity reactions
- topical use may cause skin irritation and hypersensitivity reactions

natamycin:
- hypersensitivity

flucytosine:
- affects rapidly proliferating cells causing bone marrow depression leading to leukopenia, thrombocytopenia, anemia, pancytopenia, agranulocytosis
- may also cause nausea, vomiting, abdominal distension, diarrhea and anorexia
- increases photosensitivity

ketoconazole:
- GI: nausea and vomiting, diarrhea, flatulence (gas), abdominal pain
- CNS: headache, insomnia, dizziness, vivid dreams, lethargy, paresthesias
- dermatological: pruritis, rash
- endocrine effects: gynecomastia (breast enlargement), breast pain

clotrimazole:
- various skin irritations may occur with topical treatment: blistering, stinging, pruritis, erythema, urticaria, peeling
- treatment with oral troches may cause elevated liver function test results, nausea and vomiting
terconazole:
- headaches and genital pain

Ocular Adverse Reactions:

amphotericin B:
with systemic administration:
- decreased vision
- extraocular muscle paresis resulting in diplopia
- retinal exudates
- subconjunctival or retinal hemorrhages due to anemia
with topical ocular administration:
- pain and burning
- punctate keratitis
- allergic reactions
with ocular subconjunctival injection:
- nodules on conjunctiva
- permanent yellowing of conjunctiva
- uveitis

Contraindications and Precautions:

amphotericin B:
- contraindicated in cases of known hypersensitivity unless patient has a life-threatening condition that can only be treated with amphotericin B

nystatin:
- contraindicated in cases of known hypersensitivity to nystatin
- use caution with patient with allergy to penicillin because a cross-sensitivity exists

natamycin:
- contraindicated in cases of known hypersensitivity

flucytosine:
- contraindicated in cases of known hypersensitivity or bone marrow depression

ketoconazole:
- contraindicated in cases of known hypersensitivity

clotrimazole:
- contraindicated in cases of known hypersensitivity

terconazole:
- contraindicated in cases of known hypersensitivity
Drug Interactions:

amphotericin B:
- with aminoglycosides and cyclosporin - increased nephrotoxicity
- with corticosteroids, digitalis glycosides and extended-spectrum penicillins - increased hypokalemia
- with nondepolarizing skeletal muscle relaxants and flucytosine - amphotericin B increases the effects of these agents
- with miconazole - amphotericin B decreases its antimycotic affects
- with electrolyte solutions - precipitate & inactivate amphotericin B

nystatin:
- no significant drug interactions are known

natamycin:
- no significant drug interactions are known

flucytosine:
- antacids delay flucytosine absorption
- amphotericin B decreases renal excretion of flucytosine, increasing its antimycotic activity
- bone marrow depressants such as antineoplastics enhance bone marrow toxicity

ketoconazole:
- drugs that decrease gastric activity such as cimetidene, ranitidine, famotidine, antacids, and anticholinergics may decrease the absorption of topical ketoconazole

clotrimazole:
- no significant drug interactions occur

terconazole:
- suppository may interact with rubber latex products such as contraceptive devices

Other Notes:

- when using two or more topical agents concurrently on an affected area, apply them 1/2 to 1 hour apart to avoid any interactions or inactivations of the agents.

- fungi should be cultured on a Saborad plate to select proper drug therapy
## ANTIPARASITIC AGENTS

### Antimalarials
- Δ chloroquine (Aralan)
- Δ primaquine
- Δ pyrimethamine (Daraprim)
- Δ quinine (Quinamm, Strema)

### Other Antiprotosozals
- Δ pentamidine (Pentam 300)
- Δ mebendazole (Flagyl, Metryl, Satric)
- iodoquinol (Moebiquin)
- emetrine
- Δ quinacrine (Atabrine)
- furazolidone (Furoxone)

### Anthelmintic Agents
- Δ mebendazole (Vermox)
- Δ piperazine (Antepar)
- Δ pyrantel (Antiminth)
- Δ thiabendazole (Mintezol)
- Δ niclosamide (Niciocide)
- Δ paromomycin
- Δ praziquantel (Biltricide)
- Δ oxamniqueine (Vansil)

"Δ" indicates a major drug -- see table
ANTIMALARIALS

Indications for Use:
- prevention and treatment of infections caused by the protozoa, malaria

<table>
<thead>
<tr>
<th>major drugs</th>
<th>facts to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>chloroquine</td>
<td>- drug of choice for prevention and treatment of all types of malaria except <em>P. falciparum</em> malaria</td>
</tr>
<tr>
<td>primaquine</td>
<td>- for <em>P. ovale and P. vivax</em> malaria</td>
</tr>
<tr>
<td></td>
<td>- also used to eliminate hepatic forms of the parasite that are not eradicated by chloroquine</td>
</tr>
<tr>
<td>pyrimethamine</td>
<td>- for chloroquine resistant malaria</td>
</tr>
<tr>
<td></td>
<td>- also used with sulfonamides for toxoplasmosis (caused by the protozoa, <em>T. gondii</em>)</td>
</tr>
<tr>
<td>quinine</td>
<td>- drug of choice for chloroquine resistant <em>P. falciparum</em> malaria</td>
</tr>
</tbody>
</table>

Mechanism of Action:
- chloroquine disrupts the parasite's mitochondria, affecting metabolism
- primaquine acts on the parasite's mitochondria, affecting metabolism
- pyrimethamine inhibits folic acid synthesis
- quinine incorporates into parasite's DNA rendering it ineffective

Adverse Reactions:
In normal doses, few serious reactions occur
- GI: anorexia, nausea, vomiting, abdominal cramps, diarrhea
- CNS reactions: hearing disturbances, excitement, delerium, confusion
- anemia
- pyrimethamine can cause folic acid deficiency
- with quinine a mild poisoning may occur called cinchonism, caused by the dried bark of the cinchona tree, the source of quinine.

Adverse Ocular Reactions:
- chloroquine: bull's eye maculopathy, corneal changes and blurred vision may occur
- primaquine: difficulty in focusing may be experienced

Contraindications and Precautions:
- chloroquine: known allergy, retinal disorders, hepatic disorders, alcoholism, concurrent use of other hepatotoxic agents, children
- primaquine: known allergy, arthritis, lupus
- pyrimethamine: anemia, folic acid deficiency
- quinine: known allergy, tinnitus, optic neuritis
Drug Interactions:
- chloroquine: antacids with magnesium trisilicate decrease absorption
- primaquine: quinacrine increases toxicity of primaquine
- pyrimethamine: folic acid inhibits action
- quinine: interactions occur with antacids with aluminum, neuromuscular blocking agents, anticoagulants, cardiac glycosides

Other Notes:
- The sulfonamides, sulfones and tetracyclines are often used in conjunction with these drugs to treat malaria
**OTHER ANTIPROTOZOAALS**

**Indications for Use:**
- for cases of *P. carinii* pneumonia, amebiasis, giardiasis, trichomoniasis, toxoplasmosis, African trypanosomiasis and leishmaniasis

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>pentamidine</td>
<td>- for <em>P. carinii</em> pneumonia, African trypanosomiasis and leishmaniasis</td>
</tr>
<tr>
<td>metronidazole</td>
<td>- drug of choice for amoebic hepatic abscess, intestinal amebiasis and vaginal trichomoniasis</td>
</tr>
<tr>
<td>quinacrine</td>
<td>- drug of choice for giardiasis</td>
</tr>
</tbody>
</table>

**Mechanism of Action:**
- pentamidine: interferes with the metabolic systems of protozoa
- metronidazole: disrupts protozoal DNA
- quinacrine: binds with DNA, preventing replication and protein synthesis

**Adverse Reactions:**
Several of these drugs can produce severe and life-threatening reactions
- all commonly cause various GI reactions
- pentamidine: nephrotoxicity, leukopenia, anorexia
- metronidazole: headache, anorexia, dry mouth, metallic taste
- quinacrine: headache, discolored urine, nervousness, aplastic anemia

**Ocular Adverse Reactions**
- quinacrine: corneal deposits

**Contraindications and Precautions:**
- pentamidine: caution in cases of hypotension, hypertension, hypoglycemia, hyperglycemia, leukopenia, anemia, hepatic or renal dysfunction
- quinacrine: caution in cases of cardiac disease, renal disease, hepatic disease, alcoholism, psychosis, over age 60

**Drug Interactions:**
- metronidazole: interacts with anticoagulants and disulfiram
- pentamidine: interacts with aminoglycosides, cisplatin, amphotericin B
- quinacrine: increases toxicity of primaquine
**ANTHELMINTIC AGENTS**

<table>
<thead>
<tr>
<th><strong>antinematode agents</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ mebendazole</td>
<td>(Vermox)</td>
</tr>
<tr>
<td>Δ piperazine citrate</td>
<td>(Vermox)</td>
</tr>
<tr>
<td>Δ pyrantel pamoate</td>
<td>(Antiminth)</td>
</tr>
<tr>
<td>Δ thiabendazole</td>
<td>(Mintezol)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>antisectode agents</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ niclosamide</td>
<td>(Niclocide)</td>
</tr>
<tr>
<td>paromomycin sulfate</td>
<td></td>
</tr>
<tr>
<td>Δ praziquantel</td>
<td>(Biltricide)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>antitrematode agents</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ oxamniquine</td>
<td>(Vansil)</td>
</tr>
<tr>
<td>Δ praziquantel</td>
<td>(Biltricide)</td>
</tr>
</tbody>
</table>

"Δ" indicates a major drug -- see table

**Indications for Use:**

anthelmintic agents destroy helminths - parasitic worms that infect humans
- antinematodes are for roundworm infections (in intestines)
- antisectodes are for tapeworm infections (in intestines)
- antitrematodes are for fluke infections (in blood, lungs or liver)

<table>
<thead>
<tr>
<th><strong>major drugs</strong></th>
<th><strong>things to remember</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>antinematodes</strong></td>
<td></td>
</tr>
<tr>
<td>mebendazole</td>
<td>- drug of choice for whipworm, pinworm, hookworm, and giant intestinal roundworm</td>
</tr>
<tr>
<td></td>
<td>- low toxicity</td>
</tr>
<tr>
<td>piperazine citrate</td>
<td>- alternative to mebendazole for severe infections</td>
</tr>
<tr>
<td></td>
<td>- greater toxicity than mebendazole</td>
</tr>
<tr>
<td>pyrantel pamoate</td>
<td>- alternative to mebendazole</td>
</tr>
<tr>
<td>thiabendazole</td>
<td>- drug of choice for threadworm infections</td>
</tr>
<tr>
<td></td>
<td>- acts as an anti-inflammatory in trichinosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>antisectode agents</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>niclosamide</td>
<td>- for all tapeworm species</td>
</tr>
<tr>
<td>praziquantel</td>
<td>- drug of choice for tapeworm infections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>antitrematode agents</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>oxamniquine</td>
<td>- for the blood fluke S. mansoni</td>
</tr>
<tr>
<td>praziquantel</td>
<td>- drug of choice for all fluke infections</td>
</tr>
</tbody>
</table>
ANTINEMATODES

Mechanism of Action:
- mebendazole interferes with the roundworm's microtubule system, blocking glucose uptake
- piperazine paralyzes worm by blocking acetylcholine
- pyrantel pamoate interferes with neuromuscular transmission causing spastic paralysis
- thiabendazole acts on microtubules, inhibiting fumerate reductase critical to anaerobic metabolism

Adverse Reactions:
- GI reactions: abdominal pain, nausea, vomiting, diarrhea
- other side effects occur, but are rare

Contraindications and Precautions:
- known hypersensitivity
- piperazine is contraindicated in cases of epilepsy

Drug Interactions:
- none

ANTISECTODE AGENTS

Mechanism of Action:
- niclosamide: inhibits tapeworm's metabolism
- paramomycin: inhibits protein synthesis

Adverse Reactions:
- side effects are uncommon
- GI reactions: nausea, abdominal pain, cramps, vomiting, diarrhea

Contraindications and Precautions:
- hypersensitivity
- paramomycin contraindicated in cases of renal dysfunction because accumulation of drug in blood may cause ototoxicity and nephrotoxicity

Drug Interactions:
- no significant drug interactions exist
ANTITREMATODE AGENTS

Mechanism of Action:
- oxamniquine: induces migration of adult flukes to the liver, where they die
- praziquantel: causes spastic paralysis and eventual disintegration of flukes

Adverse Reactions:
- 1/3 of patients experience drowsiness, dizziness, headache, nausea, diarrhea
- oxamniquine causes orange-red discoloration of urine

Contraindications and Precautions:
- pregnant women (embryocidal)
- oxamniquine may cause seizure in epileptic patients

Drug Interactions:
- studies suggest that concommittant administration of these two drugs enhances their effectiveness against S. mansoni
**THE ANTIVIRALS**

ΔΔ acyclovir (Zovirax #68)
Δ vidarabine (Vira-A)
Δ amantadine (Symmetrel)
Δ zidovudine (AZT) (Retrovir)
Δ ganciclovir (Cytovene)
Δ trifluridine (Viroptic)
Δ idoxuridine (IDU) (Stoxil, Herplex)

"Δ" indicates a major drug -- see table
"ΔΔ" indicates a Top 200 Drug in 1991-- note ranking after trade name

**Indications for Use:**
- used in the treatment and prevention of viral infections

**Mechanism of Action:**
- acyclovir, vidarabine and zidovudine: inhibits virus specific DNA polymerase, disrupting viral replication
- amantadine: works by inhibiting the uncoating of the virus - an early stage of viral replication
- ganciclovir: (1) competitive inhibition of viral DNA polymerase and (2), direct incorporation into viral DNA, terminating viral DNA elongation
- trifluridine: interferes with viral DNA synthesis in a way not yet known
- idoxuridine: prevents incorporation of thymidine into viral DNA, preventing viral replication

<table>
<thead>
<tr>
<th><strong>major drugs</strong></th>
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</tr>
</thead>
<tbody>
<tr>
<td>acyclovir</td>
<td>- effective against herpes simplex virus types I and II and the varicella-zoster virus</td>
</tr>
<tr>
<td></td>
<td>- available in oral, parental, and ointment forms</td>
</tr>
<tr>
<td>vidarabine</td>
<td>- IV form used for herpes simplex virus (HSV) encephalitis and varicella-zoster infections in immunocompromised patients</td>
</tr>
<tr>
<td></td>
<td>- ophthalmic ointment for corneal involvement of HSV I and II</td>
</tr>
<tr>
<td>amantadine</td>
<td>- treatment and prevention of influenza A infections</td>
</tr>
<tr>
<td></td>
<td>- also used to treat Parkinson's disease</td>
</tr>
<tr>
<td></td>
<td>- available in oral form</td>
</tr>
<tr>
<td>zidovudine</td>
<td>- used to reduce the incidence and severity of opportunistic infections in patients with AIDS and AIDS-related complex</td>
</tr>
<tr>
<td>ganciclovir</td>
<td>- used to treat cytomegalovirus (CMV) retinitis in immunocompromised patients</td>
</tr>
<tr>
<td>trifluridine</td>
<td>- drug of choice for corneal involvement of HSV I&amp;II</td>
</tr>
<tr>
<td></td>
<td>- available in ophthalmic solution and ointment</td>
</tr>
<tr>
<td>idoxuridine</td>
<td>- ophthalmic solution for HSV type I keratitis</td>
</tr>
</tbody>
</table>
Possible Adverse Reactions:
- minimal toxicity to host cells due to specificity for virus
- acyclovir: renal impairment, headaches, nausea, vomiting, diarrhea, vertigo, hematuria (blood in the urine) and rarely; diaphoresis (profuse sweating), fatigue, insomnia, irritability, depression, hypotension, muscle cramps and leg pain
- vidarabine: nausea, vomiting, diarrhea, anorexia, weakness, tremors hallucinations, malaise, confusion, and hypersensitivity reactions.
- amantadine: (usually well tolerated) nausea, anorexia, nervousness, fatigue, depression, irritability, insomnia, psychosis, anxiety, confusion, hallucinations, headache, dizziness, light headedness, seizures in patients already prone to seizures
- zyndovudine: anemia, granulocytopenia (low neutrophil count), headache, nausea, insomnia, myalgia (muscle pain) are the most common reactions
- ganciclovir: granulocytopenia, thrombocytopenia (low platelet count), anemia, fever, rash and liver dysfunction are the most common reactions

Ocular Adverse Reactions:
- acyclovir:
  - systemic administration reactions include decreased vision, hallucinations, subconjunctival or retinal hemorrhages, eyelid erythema and urticaria
  - ocular application may cause irritation, SPK, allergic reactions, blepharitis, follicular conjunctivitis, narrowing of puncta
- idoxuridine, trifluridine, vidarabine:
  - systemic administration reactions include visual hallucinations blepharospasm and subconjunctival and retinal hemorrhages due to drug induced anemia
  - ocular application may cause irritation, corneal reactions (SPK, edema, erosions, opacities, delayed wound healing), lid reactions (allergy, hyperemia, blepharitis, follicular conjunctivitis, edema), ptosis, and narrowing of the puncta
- amantadine: transient decrease of vision, hallucinations

Contraindications and Precautions:
- known hypersensitivity
- use caution in renally impaired, pregnant or lactating patients
- amantadine: use caution in cases of advanced age, epilepsy, hepatic disease, renal impairment, cardiovascular disease
- idoxuridine: use caution in pregnant or breast feeding women
Drug Interactions:
- acyclovir: probenicid increases plasma concentration of acyclovir, nephrotoxic agents increase the chance of renal dysfunction, and interferon and intrathecal methotrexate increase the chance of neurotoxicity
- amantadine: enhances the effects of anticholinergic agents and CNS stimulants. Triamterene and thiazide diuretics increase CNS toxicity of amantadine by slowing its renal elimination.
- zidovudine and ganciclovir: These agents increase their nephrotoxic and cytotoxic effects: dapsone, pentamidine, fluycytosine, vincristine, vinblastine, doxorubicin, interferon and amphotericin B. The following agents inhibit their metabolism and increase their toxicity: probenicid, aspirin, acetaminophen and indomethacin. (concurrent use of gancyclovir and zidovudine is not well tolerated)
- idoxuridine causes discomfort in presence of boric acid-containing solutions
### ANTINEOPLASTIC AGENTS

#### alkylating agents
- Δ mechlorethamine (Mustargen)
- Δ cyclophosphamide (Cytoxan)
- Δ melphalan (Leukeran)
- Δ chlorambucil (Leukeran)
- Δ thiotepa (Leukeran)
- Δ estramustine (Leukeran)
- Δ uracil mustard (Leukeran)
- Δ busulfan (Mylaran)
- Δ carmustine (BiCNU)
- Δ lomustine (BiCNU)
- Δ streptozocin (DTIC-Dome)
- Δ dacarbazine (DTIC-Dome)
- Δ cisplatin (Platinol)

#### antimetabolite agents
- Δ methotrexate (Folex, Mexate)
- Δ fluorouracil (Adurucil, Efudex)
- Δ cytarabine (Cytosar-U)
- Δ 5-azacytidine (Cytosar-U)
- Δ mercaptopurine (Purinethol)
- Δ thioguanine (Purinethol)
- Δ bleomycin (Blenoxane)
- Δ dactinomycin (Cerubidine)
- Δ daunorubicin (Adriamycin)
- Δ doxorubicin (Adriamycin)
- Δ mitomycin (Adriamycin)
- Δ mitoxantrone (Adriamycin)
- Δ plicamycin (Mithracin)
### Hormonal Antineoplastic Agents

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogens</td>
<td>Diethylstilbestrol</td>
<td>(Stilphostrol)</td>
</tr>
<tr>
<td>Antiestrogen</td>
<td>Tamoxifen</td>
<td>(Nolvadex #131)</td>
</tr>
<tr>
<td>Androgens</td>
<td>Fluoxymesterone</td>
<td>(Halotestin)</td>
</tr>
<tr>
<td>Adrenocortical suppressants</td>
<td>Aminogluthimide</td>
<td>(Cytadren)</td>
</tr>
<tr>
<td>Progestins</td>
<td>Medroxyprogesterone acetate</td>
<td>(Depo-Provera #26)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Hydrocortisone</td>
<td>(Cortef)</td>
</tr>
<tr>
<td></td>
<td>Prednisone</td>
<td>(Deltasone #138)</td>
</tr>
<tr>
<td></td>
<td>Prednisolone</td>
<td>(Delta-Cortef)</td>
</tr>
<tr>
<td></td>
<td>Methylprednisolone</td>
<td>(Medrol #192)</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>(Decadron)</td>
</tr>
</tbody>
</table>

### Other Antineoplastic Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinblastine sulfate</td>
<td>(Velban)</td>
</tr>
<tr>
<td>Vincristine sulfate</td>
<td>(Oncovin)</td>
</tr>
<tr>
<td>Etoposide</td>
<td>(VePesid)</td>
</tr>
<tr>
<td>Asparaginase</td>
<td>(Elspar)</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>(Matulane)</td>
</tr>
</tbody>
</table>

*Δ* indicates major drugs -- see table

*ΔΔ* indicates a Top 200 Drug in 1991 -- note ranking after trade name
ALKYLATING AGENTS

Indications for Use:
Effective against a variety of malignant neoplasms including leukemias, non-Hodgkin's lymphomas, multiple myeloma, melanoma, sarcoma, and cancers of the breast, ovaries, uterus, lung, brain, testes, bladder, prostate, and stomach.

Mechanism of Action:
It is believed that the alkylating agents enter cells and cause covalent bonding to occur (alkylation). Alkylation of the DNA inhibits its function and slows cell division. Effect is greatest in rapidly replicating cells including cancer cells, as well as hair follicles, bone marrow cells and cells lining the gastric mucosa.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>mechlorethamine</td>
<td>- for Hodgkin's and non-Hodgkin's lymphomas</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>- for Hodgkin's and non-Hodgkin's lymphomas, breast cancer, lung cancer, leukemia</td>
</tr>
<tr>
<td>busulfan</td>
<td>- primarily affects granulocytes</td>
</tr>
<tr>
<td></td>
<td>- drug of choice for chronic myelocytic leukemia</td>
</tr>
<tr>
<td>carmustine</td>
<td>- for primary and metastatic CNS tumors, myeloma, melanoma, lymphomas</td>
</tr>
<tr>
<td>dacarbazine</td>
<td>- for malignant melanomas, Hodgkin's disease, soft-tissue sarcomas</td>
</tr>
<tr>
<td>cisplatin</td>
<td>- an &quot;alkylating-like&quot; agent containing platinum</td>
</tr>
<tr>
<td></td>
<td>- for cancer of testicles, lungs, ovaries, bladder, colon, head, neck</td>
</tr>
<tr>
<td></td>
<td>- for melanomas and intraarterial sarcomas</td>
</tr>
<tr>
<td>chlorambucil</td>
<td>- for chronic lymphocytic leukemia, Hodgkins disease, and non-Hodgkins lymphomas</td>
</tr>
</tbody>
</table>
Adverse Reactions:
nitrogen mustards (mechlorethamine and cyclosphamide):
- bone marrow suppression leading to anemia and leukopenia and fatigue
- nausea and vomiting due to CNS irritation
- damage to rapidly proliferating cells produces stomatitis (inflammation of mucous membranes) and alopecia (hair loss)
- less commonly: hemorrhagic cystitis, alterations in fertility, hepatotoxicity and anaphylaxis
busulfan:
- decrease in WBC count
- nausea, vomiting and diarrhea
- hyperuricemia (elevated uric acid levels in blood)
- with long term therapy: hyperpigmentation, weight loss, interstitial pulmonary fibrosis
carmustine:
- bone marrow depression
- severe nausea and vomiting
- pain at infusion site
- renal dysfunction
- less commonly: nephrotoxicity, hepatotoxicity, blood toxicity, glucose intolerance
dacarbazine:
- leukopenia and thrombocytopenia
- nausea and vomiting
- pain at site of infusion
- phototoxicity, flu-like syndrome, alopecia
cisplatin:
- nephrotoxicity
- tinnitus and hearing loss
- rarely: neurotoxicity

Contraindications and Precautions:
- use cisplatin with caution in cases of renal impairment, myelosuppression, hearing impairment

Drug Interactions:
cyclophosphamide:
- allopurinol prolongs cyclophosphamide's half life causing greater bone marrow suppression
- corticosteroids inhibit metabolism of cyclophosphamide.
- phenobarbital induces enzymes of the hepatic oxidase system
cisplatin:
- aminoglycosides administered concurrently can lead to nephrotoxicity and ototoxicity
Indications for Use:
used in the treatment of a wide variety of neoplasms

Mechanism of Action:
- These agents closely resemble the natural metabolites sufficiently
  enough to become involved in the processes of protein synthesis, but
  differ sufficiently to interfere with this synthesis in both normal as well as
  cancer cells. However, their effect is greatest on rapidly proliferating
  cells. The antimetabolites are classified by the metabolite they
  resemble.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Know</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>follic acid analogues</strong></td>
<td></td>
</tr>
<tr>
<td>methotrexate</td>
<td>- for leukemia, choriocarcinoma, meningeal leukemia, lymphoma, sarcoma</td>
</tr>
<tr>
<td><strong>pyrimidine analogues</strong></td>
<td></td>
</tr>
<tr>
<td>fluorouracil</td>
<td>- for solid tumors of the GI tract and breast</td>
</tr>
<tr>
<td></td>
<td>- for cancers of the colon, rectum and lungs</td>
</tr>
<tr>
<td>cytarabine</td>
<td>- for inducing remission of leukemia</td>
</tr>
<tr>
<td><strong>purine analogues</strong></td>
<td></td>
</tr>
<tr>
<td>mercaptopurine</td>
<td>- for acute lymphoblastic leukemia and chronic granulocytic leukemia</td>
</tr>
<tr>
<td>thioguanine</td>
<td>- for acute leukemia, acute granulocytic leukemia</td>
</tr>
</tbody>
</table>

Adverse Reactions:
- bone marrow suppression
- stomatitis (inflammation of mucous membranes)
- fatigue
- nausea and vomiting caused by some antimetabolite agents
- mercaptopurine often causes cholestatic jaundice
- less commonly: hepatotoxicity, nephrotoxicity, photosensitivity

Contraindications and Precautions:
- fluorouracil should be used with caution in cases of post surgery, poor nutritional state, serious infection, bone marrow depression, pelvic irradiation, hepatic dysfunction or renal dysfunction.

Drug Interactions:
- methotrexate
  - oral anticoagulants are enhanced
  - phenytoin, digoxin, salicylates, and sulfonamides may increase the toxicity of methotrexate
- mercaptopurine
  - allopurinol may increase bone marrow suppression
  - warfarin’s anticoagulant effect decreases with mercaptopurine
ANTINEOPLASTIC ANTIBIOTIC AGENTS

Indications for Use:
Act against many tumors including: Hodgkin's disease; non-Hodgkin's lymphomas; testicular carcinoma; squamous cell carcinoma of the head, neck and cervix; carcinomas of the breast, ovaries and bladder.

Mechanism of Action:
These agents insert themselves into the DNA chain resulting in mutant DNA after replication. The overall effect is cell death. They are most effective on rapidly proliferating cells.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>bleomycin</td>
<td>- for Hodgkin's disease, testicular carcinoma, squamous cell carcinoma of the head, neck, uterine cervix, esophagus, skin, lungs</td>
</tr>
<tr>
<td>daunorubicin</td>
<td>- for acute leukemias</td>
</tr>
<tr>
<td>doxorubicin</td>
<td>- for sarcomas, breast carcinoma, cancer of the bronchi, lymphomas, bladder carcinoma</td>
</tr>
<tr>
<td>plicamycin</td>
<td>- hypercalcemia, testicular tumors</td>
</tr>
</tbody>
</table>

Possible Side Effects:
- With the exception of bleomycin, they cause bone marrow suppression resulting in pancytopenia (a reduction of all blood cells) and leukopenia (decrease in WBC).
- nausea and vomiting
- alopecia (hair loss)
- stomatitis (inflammation of mucous membranes)

Contraindications and Precautions:
- use caution in cases of hypersensitivity
- doxorubicin:
  - caution in cases of pre-existing myelosuppression or heart disease
- plicamycin:
  - caution in cases of thrombocytopenia, blood coagulation disorders, bone marrow suppression

Drug Interactions:
- concurrent administration of bleomycin and cisplatin can decrease creatine clearance
- barbiturates and heparin diminish the effects of doxorubicin
HORMONAL ANTINEOPLASTIC AGENTS

Indications for Use:
used to treat hormone dependent tumors such as those of the prostate, breast and endometrium of the uterus.

Mechanism of Action:
these agents exhibit a cytostatic action stopping growth of hormone dependent tumors through a process not entirely understood.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>diethylstilbestrol</td>
<td>- an estrogen</td>
</tr>
<tr>
<td></td>
<td>- for breast cancer in women at least 5 years postmenopausal</td>
</tr>
<tr>
<td>tamoxifen</td>
<td>- an antiestrogen</td>
</tr>
<tr>
<td></td>
<td>- drug of choice for advanced breast cancer involving estrogen receptor positive tumors</td>
</tr>
<tr>
<td>fluoxymesterone</td>
<td>- an androgen, a synthetic derivative of testosterone</td>
</tr>
<tr>
<td></td>
<td>- for metastatic breast cancer and prostate cancer</td>
</tr>
<tr>
<td>aminoglutethimide</td>
<td>- an adrenocortical suppressant</td>
</tr>
<tr>
<td></td>
<td>- for breast and prostate cancer</td>
</tr>
<tr>
<td></td>
<td>- also for Cushing's disease</td>
</tr>
<tr>
<td>medroxy progesterone</td>
<td>- a progestin</td>
</tr>
<tr>
<td></td>
<td>- for endometrial, breast and renal cancer</td>
</tr>
<tr>
<td>the corticosteroids</td>
<td>- lymphocytic activity is useful in treating lymphatic leukemias, myeloma, and malignant lymphomas</td>
</tr>
<tr>
<td>-- hydrocortisone</td>
<td>- used to reduce edema in metastatic cancer</td>
</tr>
<tr>
<td>prednisone</td>
<td></td>
</tr>
<tr>
<td>prednisolone</td>
<td></td>
</tr>
<tr>
<td>methylprednisolone</td>
<td></td>
</tr>
<tr>
<td>dexamethasone</td>
<td></td>
</tr>
</tbody>
</table>
Adverse Reactions:
estrogens
- nausea, abdominal cramps
- increased urination
- temporary feminization in males; decreased libido and breast
tenderness in females
antiestrogens
- nausea, vomiting, hot flashes
- rare ocular lesions, retinopathy, corneal opacities
androgens
- nausea and vomiting
- fluid retention
- masculinization of females (reversible if discontinued promptly)
- jaundice
adrenocortical suppressants
- rash
- fatigue, hypotension, drowsiness, dizziness
progestins
- one of the best tolerated antineoplastic agents
- mild fluid retention
- local allergic reaction to the oil carrier used for injection
- thromboemboli can develop
corticosteroids
- fluid and sodium retention
- hyperglycemia (high blood sugar)
- epigastric distress due to increased HCl secretion and
decreased gastric mucous secretion
- mood swings, insomnia, nervousness

Contraindications and Precautions:
- all contraindicated in cases of hypersensitivity
- estrogens
  - use with caution in cases of thromboembolic disorders
- progestins
  - use with caution in cases of pregnancy, thromboembolic
disorders, history of stroke, breast cancer

Drug Interactions:
corticosteroid action enhanced or prolonged by:
- erythromycin, troleandomycin, estrogen
corticosteroid action decreased by:
- barbiturates, phenytoin, rifampin
corticosteroids produce complications with:
- furosemide: increased incidence of hypokalemia
- salicylates: decreased salicylate activity, increased risk of ulcer
- NSAIDs: increased risk of peptic ulcer
- vaccines & toxoids: decreases patient's response to vaccines
  and toxoids; may increase replication of attenuated viruses
- warfarin: anticoagulant effect decreased by corticosteroids
OTHER ANTINEOPLASTIC AGENTS

Indications for Use:
used to treat a variety of neoplasms

Mechanism of Action:
- vinca alkaloids:
  bind to the microtubule protein tubulin, disrupting miosis in all cells, but particularly detrimental to rapidly replicating cells including cancer cells as well as hair follicles, bone marrow, gastric mucosa
- podophylotoxins:
  by mechanisms not understood, podophyllotoxins block replication of cells at the late S or G_2 phase; etoposide and teniposide may cause breaks in the DNA strand and inhibit nucleoside transport and incorporation into nucleic acids; affect all cells, but particularly the most rapidly replicating cells
- asparaginase:
  breaks down exogenous asparagine, needed by leukemia cells for survival; non-leukemic cells are less affected
- procarbazines:
  produces various cell changes resulting in damaged DNA which disrupts miosis and protein synthesis; has greatest effect on rapidly proliferating cells

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Know</th>
</tr>
</thead>
</table>
| vinblastine sulfate | - a vinca alkaloid 
|                    | - for breast carcinoma, neuroblastoma, metastatic testicular cancer, lymphomas, Kapo's sarcoma, choriocarcinoma |
| vincristine sulfate | - a vinca alkaloid 
|                    | - for Hodgkin's disease, non-Hodgkin's lymphoma |
| etoposide         | - a podophyllotoxin, similar to the vinca alkaloids 
|                    | - for testicular and lung cancer |
| asparaginase      | - for inducing remission in acute lymphocytic leukemia |
| procarbazine      | - for Hodgkin's disease, lung cancer, lymphoma, myeloma, melanoma, and CNS tumors |
Adverse Reactions:
- vinca alkaloids:
  - bone marrow suppression leading to leukopenia
  - alopecia
  - neuromuscular abnormalities
  - stomatitis
- podophyllotoxins:
  - bone marrow suppression leading to leukopenia
  - alopecia
  - nausea, vomiting, anorexia
  - stomatitis
- asparaginase:
  - anaphylaxis
  - nausea and vomiting
  - fever, headache, abdominal pain
  - hepatotoxicity manifested by elevated liver enzyme levels
  - personality changes, seizures, abnormal electroencephalogram results (EEG's)
- procarbazine:
  - bone marrow suppression
  - nausea and vomiting
  - flu-like syndrome (fever, chills, sweating)

Contraindications and Precautions:
- due to the serious nature of neoplastic disease, few circumstances warrant the contraindication of these drugs

Drug Interactions:
- procarbazine:
  - alcohol causes a "disulfiram-like" reaction: nausea, vomiting, headache, visual disturbances
  - CNS depressants: enhancement of CNS depressant action
  - sympathomimetics and antidepressants cause hypertension, tremors, excitation, tachycardia, angina
alopecia: hair loss

anaphylaxis: an allergic hypersensitivity reaction to a foreign protein or drug; reactions include: irritability, labored breathing, cyanosis (blue discoloration of skin), convulsions, unconsciousness and death

aplastic anemia: anemia caused by deficient red cell production due to disorders of bone marrow. 50% of cases are idiopathic. Many cases are caused by exposure to chemical and antineoplastic agents and ionizing radiation

cholastic jaundice: characterized by yellow bile deposits in skin, membranes and sclera due to excess bilirubin in the blood as a result of failure of bile to reach the duodenum

choriocarcinoma: a rare malignant neoplasm of the uterus

Cushing's disease: protein loss, abnormal adipose deposits, fatigue osteoporosis, etc. due to hyperssecretion of glucocorticoids from the adrenal cortex or prolonged administration of large doses of adrenocortical hormones

cystitis: inflammation of the bladder

gray syndrome: occurs in neonates as a result of decreased ability to conjugate chloramphenicol and to excrete the active form in the urine. May also occur in adults receiving high doses of chloramphenicol

Hodgkin's disease: of unknown etiology, it produces enlargement of lymphoid tissue, spleen, and liver with invasion of other tissues

Kaposi's sarcoma: multiple neoplasias of the skin which spread to other body sites; associated with AIDS

leukemia: of unknown etiology, it produces unrestrained growth of leukocytes and their precursors in the tissues

leukopenia: decrease in white blood cell count below 5000 per cubic mm

lymphoma: a general term for growth of new tissue in the lymphatic system

metastasis: movement of a body of cells (especially cancer cells) from one part of the body to another

myelocytic leukemia: overgrowth of granulocytes in the bone marrow most often caused by a chromosome abnormality

myelocythemia: an excess number of myelocytes in the blood

myeloma: a tumor originating in the bone marrow

myelosuppression: inhibition of bone marrow function

neuroblastoma: a malignant hemorrhagic tumor affecting neuroblastic cells that give rise to the sympathetic nervous system; occurs primarily in infants and children

ototoxic: detrimental to the 8th nerve or the organs of hearing

pseudotumor cerebri: benign intracranial hypertension
stomatitis: inflammation of the mucus membranes

thrombocytopenia: a decrease in the number of blood platelets

tinnitus: a subjective ringing sound in the ear

tumor: a spontaneous new growth of tissue forming an abnormal mass
carcinoma: malignant tumor of epithelial tissues which tend to metastasize (spread through out the body)
melanoma: a pigmented mole or tumor that may or may not be malignant
sarcoma: cancer of connective tissues such as muscle, bone, bladder, kidneys, liver, lungs parotids, spleen
CORTICOSTEROIDS AS IMMUNOSUPPRESSANTS

<table>
<thead>
<tr>
<th>Systemic Glucocorticoids</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>beclomethasone</td>
<td>Beconase AQ #95</td>
</tr>
<tr>
<td>betamethasone</td>
<td>Celestone</td>
</tr>
<tr>
<td>cortisone</td>
<td>Cortone</td>
</tr>
<tr>
<td>dexamethasone</td>
<td>Decadron</td>
</tr>
<tr>
<td>dexamethasone acetate</td>
<td>Decadron-LA</td>
</tr>
<tr>
<td>hydrocortisone acetate</td>
<td>Anusol-HC #195</td>
</tr>
<tr>
<td>methylprednisone</td>
<td>Medrol #192</td>
</tr>
<tr>
<td>prednisolone</td>
<td>Cortalone</td>
</tr>
<tr>
<td>prednisone</td>
<td>Deltasone #138</td>
</tr>
<tr>
<td>triamcinolone</td>
<td>Azmacort #151</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Topical Glucocorticoids</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>flucinolone</td>
<td>Fluonid</td>
</tr>
<tr>
<td>flurandrenolide</td>
<td>Cordran</td>
</tr>
<tr>
<td>triamcinolone</td>
<td>Aristocort</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mineralocorticoids</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>desoxycorticosterone</td>
<td>Doca Acetate</td>
</tr>
<tr>
<td>fludrocortisone</td>
<td>Flurinef</td>
</tr>
</tbody>
</table>

"\(\Delta\)" indicates major drugs -- see table
"\(\Delta\Delta\)" indicates a Top 200 Drug in 1991 -- note ranking after trade name

Background Information:
Natural corticosteroids are hormones produced in the adrenal cortex and are classified by their biological activities:
- glucocorticoids affect carbohydrate and protein synthesis
- mineralocorticoids regulate electrolyte and water balance
Production of the natural corticosteroids is stimulated by trauma, infection, heat, cold, and mental stress. Corticotropic releasing hormone (CRH) is released from the hypothalamus which stimulates the secretion of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland which in turn triggers the release of the corticosteroids from the adrenal cortex.
Indications for Use:

GLUCOCORTICOIDs:
- primarily used for inflammation, immunosuppression, replacement therapy in patients with adrenocortical insufficiency and suppression of adrenocortical hyperfunction in patients with adrenogenital syndrome.
- their primary immunosuppressant application is treatment of hypersensitivity reactions by reducing inflammation. Specific indications are: rheumatoid arthritis, osteoarthritis, rheumatic fever, nephrotic syndrome, collagen diseases, asthma, chronic obstructive pulmonary disease, hay fever, bee stings, systemic and topical hypersensitivity reactions, prevention and treatment of transplant rejection, leukemias, lymphomas and myelomas.

MINERALOCORTICOIDs:
- used in replacement therapy for patients with adrenocortical insufficiency and in the treatment of salt-losing congenital adrenogenital syndrome after the patient's electrolyte balance has been restored.

Mechanism of Action:

GLUCOCORTICOIDs:
- controlling inflammation primarily by inhibiting the release of the arachadonic acid metabolites (the prostoglands and platelet activating factor); thereby decreasing platelet aggregation, chemotaxis, macrophage accumulation and histamine activity.

MINERALOCORTICOIDs:
- act on the distal renal tubule to enhance the reabsorption of sodium and secretion of potassium and hydrogen -- resulting in sodium retention.

<table>
<thead>
<tr>
<th>Major Drugs</th>
<th>Things to Remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>beclomethasone</td>
<td>used in inhalents for asthma sufferers</td>
</tr>
<tr>
<td>cortisone</td>
<td>drug of choice for replacement therapy in adrenocortical insufficiency</td>
</tr>
<tr>
<td>dexamethasone</td>
<td>for self-limiting allergic disorders and exacerbation of chronic allergies</td>
</tr>
<tr>
<td>dexamethasone acetate</td>
<td>for chronic inflammations and cancer</td>
</tr>
<tr>
<td>hydrocortisone</td>
<td>the prototype systemic glucocorticoid</td>
</tr>
<tr>
<td></td>
<td>for adrenocortical insufficiency and severe inflammation</td>
</tr>
<tr>
<td>methylprednisolone</td>
<td>used for anti-inflammatory and immunosuppressive effects</td>
</tr>
<tr>
<td>prednisolone</td>
<td>used for anti-inflammatory and immunosuppressive effects</td>
</tr>
<tr>
<td>prednisone</td>
<td>oral glucocorticoid of choice for anti-inflammatory and immunosuppressive effects</td>
</tr>
<tr>
<td>triamcinolone</td>
<td>used for anti-inflammatory and immunosuppressive effects</td>
</tr>
</tbody>
</table>
TOPICAL GLUCOCORTICOIDS

- fluocinolone
- flurandrenolide
- triamcinolone

- for acute and chronic inflammatory dermatoses, psoriasis, atopic eczema, pruritis ani, neurodermatitis, exfoliative dermatitis, seborrheic dermatitis, contact dermatitis

MINERALOCORTICOIDs

- desoxycorticosterone
  - the most potent mineralocorticoid
  - to treat salt-losing adrenogenital syndrome
- fludrocortisone
  - given with cortisone to treat salt losing adrenogenital syndrome

Relative Potencies of Glucocorticoids:

The table below groups the glucocorticoids by their length of action and compares their anti-inflammatory potencies relative to hydrocortisone.

<table>
<thead>
<tr>
<th></th>
<th>half-life</th>
<th>generic name</th>
<th>oral dose equivalent</th>
<th>rel. anti-inflamm. potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>short-acting</td>
<td>8-12 hr</td>
<td>cortisone</td>
<td>25 mg</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydrocortisone</td>
<td>20 mg</td>
<td>1</td>
</tr>
<tr>
<td>intermediate-acting</td>
<td>18-36</td>
<td>prednisolone</td>
<td>5 mg</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>prednisone</td>
<td>5 mg</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>methylprednisolone</td>
<td>4 mg</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>triamcinolone</td>
<td>4 mg</td>
<td>5</td>
</tr>
<tr>
<td>long-acting</td>
<td>36-54</td>
<td>dexamethasone</td>
<td>0.75 mg</td>
<td>25-30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>betamethasone</td>
<td>0.60 mg</td>
<td>25</td>
</tr>
</tbody>
</table>

Adverse Reactions:

SYSTEMIC GLUCOCORTICOIDS:

- adrenocortical insufficiency (decreased production of corticosteroids in the adrenal cortex, temporary or permanent) may occur in response to the introduction of exogenous steroids -- this affect is minimized by tapering dosages when ending therapy
- severe muscle weakness
- immunosuppression predisposes patients to infection
- Cushing's syndrome (abnormal fat distibution -- depleting fat from extremities and depositing it in face, abdomen and between shoulder blades)
- GI reactions: abdominal distension, pancreatitis, ulcerative esophagitis, gastric irritation, increased appetite, peptic ulcers
- skin atrophy and thinning, acne, excessive diaphoresis, facial edema, etechiae, ecchymosis (easy bruising).
- CNS reactions: insomnia, headache, restlessness, seizures, severe mood swings
- may slow the growth of young children by interfering with DNA synthesis and cell division
- others: electrolyte imbalances, increased red blood cell and hemoglobin levels, increased risk of emboli formation

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TOPICAL GLUCOCORTICOIDS:
- local effects include: skin atrophy, muscle and fat wasting, rosacea eruptions
- absorption of topical glucocorticoids through the skin can cause the same adverse reactions as systemic glucocorticoids

MINERALOCORTICOIDS:
- fluid and electrolyte imbalances and these associated symptoms: edema, hypertension, congestive heart failure (CHF), hypernatremia, hypokalemia, hypocalcemia.

Ocular Adverse Reactions:
SYSTEMIC AND TOPICAL GLUCOCORTICOIDS:
- posterior subcapsular cataracts
- increased intraocular pressure
- exophthalmos
- secondary ocular infections due to immunosuppression

Contraindications and Precautions:
SYSTEMIC GLUCOCORTICOIDS:
- contraindicated in pregnant or breast feeding women
- cases of Cushing's syndrome, tuberculosis, severe infections, psychosis
- use caution in patients with diabetes mellitus, hypothyroidism, congestive heart failure, cardiac disease, hypertension, hepatic dysfunction, renal dysfunction, glaucoma, thromboembolic disorders, seizures

TOPICAL GLUCOCORTICOIDS:
- contraindicated in cases of skin infections
- use cautiously in ophthalmic applications in cases of glaucoma

MINERALOCORTICOIDS:
- contraindicated in cases of hypertension, congestive heart failure (CHF), or cardiac disease.
- use cautiously in pregnant women, diabetics, and cases of Addison's disease
- use fludrocortisone cautiously in patients with GI ulceration, renal disease, hypertension, osteoporosis, varicella, vaccinia, exanthema, cushingoid symptoms, thromboembolic disorders
Drug Interactions:

SYSTEMIC GLUCOCORTICOIDS AND MINERALOCORTICOIDS:
- steroid action increased by: erythromycin, troleandomycin, estrogen
- steroid action decreased by: barbiturates, phenytoin, rifampin
- complications with: furosemide (hypokalemia), salicylates & NSAIDs (peptic ulcers), vaccines (decrease immune response), warfarin (steroids decrease its anticoagulant effect)

TOPICAL GLUCOCORTICOIDS:
- ethylenediamine, a stabilizing agent in some topical glucocorticoid agents interacts with systemic aminophylline, antazoline, antazoline hydrochloride ophthalmic solution, and edetate disodium, a preservative common in ophthalmic solutions -- these interactions can cause allergic contact dermatitis, urticaria, and systemic eczematous contact-type dermatitis
- parabens, another additive in glucocorticoid preparations can interact with other paraben-containing formulations such as toothpaste, cosmetics, and soaps, resulting in allergic contact dermatitis and urticaria
OTHER IMMUNOSUPPRESSANTS

△ ATG (antithymocyte globulin)  (Atgam)
△ azathioprine  (Imuran)
△ cyclosporine  (Sandimmune)
△ lymphocyte immune globulin
△ muromonab-CD3  (Orthoclone OKT3)

"△" indicates major drugs -- see table

Indications for Use:
used with corticosteroids for patients undergoing allograft transplantation (such as kidney, bone marrow, heart, or skin allografts) to prevent or treat tissue rejection

Mechanism of Action:
- ATG: believed to eliminate T-cells in peripheral blood or alter T-cell function.
- azathioprine: suppresses cell-mediated hypersensitivities, alters antibody production.
- muromonab-CD3: inhibits T-cell function.
- cyclosporine: inhibits helper T cells and suppressor T cells.

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
</table>
| ATG                  | - prevention or delay of kidney, skin and heart allograft rejections  
|                      | - also for treatment of aplastic anemia                  |
| azathioprine         | - for prevention of kidney transplant rejection         |
|                      | - for severe rheumatoid arthritis unresponsive to less toxic therapy |
| cyclosporin          | - for prevention of organ allograft rejection and graft- versus-host disease after bone marrow transplantation |
| muromonab-CD3        | - used to prevent and treat allograft rejection          |

Adverse Reactions:
secondary infections are a common side effect of these drugs, as well as:
ATG:
- fever, chills
- leukopenia, thrombocytopenia
- nausea, vomiting, diarrhea
- rash, urticaria, erythema
azathioprine:
- severe bone marrow depression leading to leukopenia,
thrombo-cytopenia, hemorrhaging, anemia, nausea, vomiting,
anorexia, diarrhea

cyclosporin:
- nephrotoxicity, hyperkalemia, hyperuricemia,
- hypertension, tremors,
- diarrhea, nausea, vomiting,
- muromonab-CD3:
  - fever, chills, dyspnea, chest pain
  - vomiting, nausea

Ocular Adverse Reactions:
- azathioprine: retinopathy
- cyclosporin: rarely conjunctivitis

Contraindications and Precautions:
- hypersensitivity to the drug
- contraindicated in pregnant patients
- rheumatoid arthritis patients who have previously been treated with alkylating agents have a prohibitive risk of neoplasia if treated with azathioprine

Drug Interactions:
- ATG, cyclosporin and muromonab-CD3
  - other immunosuppressives increase risk of infection, lymphoma
- azathioprine
  - allopurinol decreases the hepatic metabolism of azathioprine
  - depolarizing muscle relaxants are inhibited by azathioprine
- cyclosporin
  - acyclovir, aminoglycosides, amphotericin B increase the potential for nephrotoxicity
  - ketoconazole and cimetidine increases blood cyclosporin levels
  - rifampin, phenytoin, sulfamethazine, trimethoprim decrease plasma cyclosporin levels
ACTIVE IMMUNITY AGENTS

- Diptheria and tetanus toxoids and pertussis vaccine [DTP] (Tri-Immunol)
  - Tetanus and diptheria, adsorbed [Td]
  - Tetanus toxoid
- Measles, mumps, and rubella virus vaccine live [MMR] (M-M-R II)
- Poliovirus vaccine, live, oral, trivalent [OPV] (Orimune)
- Rabies vaccine, human diploid cell [HDCV] (Imovax)
- Influenza virus vaccine, trivalent types A and B, split virus (Fluogen)
- Influenza virus vaccine, trivalent types A and B, whole virus (Fluzone)
- Hepatitis B vaccine (Heptavax-B)
  - Haemophilus influenza b polysaccharide vaccine [HIB] (HibImmune)
- Pneumococcal vaccine, polyvalent (Pneumovax-23)

"Δ" indicates major drugs -- see table

Indications for Use:
to prevent or eradicate commonly occurring communicable diseases.

Mechanism of Action:
Vaccines and toxoids initiate the formation of specific antibodies by stimulating the body's antigen-antibody mechanism. This action provides active, acquired immunity for the individual. Bacterial vaccines are prepared from whole bacteria or from purified capsular polysaccharides. Viral vaccines are prepared from nonliving or living viruses.

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diptheria and tetanus toxoids and pertussis vaccine [DTP]</td>
<td>Used to provide immunity to diphtheria, tetanus and pertussis in individuals aged 2 months to 7 years</td>
</tr>
<tr>
<td>Tetanus and diptheria, adsorbed [Td]</td>
<td>Used to immunize individuals over the age of 7</td>
</tr>
<tr>
<td>Tetanus toxoid</td>
<td>Given prophylactically for wound management</td>
</tr>
<tr>
<td>Measles, mumps, and rubella vaccine, live [MMR]</td>
<td>To prevent measles, mumps, and rubella</td>
</tr>
<tr>
<td>Poliovirus vaccine</td>
<td>To provide immunity to the polio virus</td>
</tr>
<tr>
<td>Rabies vaccine, human diploid cell [HDCV]</td>
<td>To provide immunity in high risk groups (such as veterinarians) and also used to treat after exposure</td>
</tr>
<tr>
<td>Influenza virus vaccine, trivalent types A and B, whole or split</td>
<td>Prevents influenza infection</td>
</tr>
<tr>
<td>Influenza virus vaccine, trivalent types A and B, whole or split</td>
<td>The split virus form causes fewer adverse reactions than the whole virus</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Provides immunity to hepatitis B</td>
</tr>
<tr>
<td>Pneumococcal vaccine, polyvalent</td>
<td>A polysaccharide vaccine used to prevent pneumococcal diseases, especially useful for the elderly and those with cardiac, pulmonary, hepatic, and renal disease</td>
</tr>
</tbody>
</table>
Adverse Reactions:
all immunizations can cause mild symptoms of the disease they prevent
- DTP: fever in 50% of children within 48 hours. Local reactions include erythema, induration, tenderness. Also, mild anorexia, fretfulness and drowsiness may occur.
- MMR: rash, lymphadenopathy, fever within 6-11 days. Arthralgia, arthritis and painful parasthesias may occur 2-8 wks after shot.
- OPV produces no predictable reactions
- HDCV: pain, swelling, erythema, itching at injection site. Also headaches, nausea, dizziness, muscle aches and abdominal pain.
- influenza virus vaccines: fever, malaise, malgia
- hepatitis B vaccine: discomfort at injection site, local inflammation, fever transient malaise, headache, dizziness, nausea, vomiting
- Hib: erythema, swelling tenderness at injection site, and fever irritability and anorexia may occur
- pneumococcal vaccine: soreness at injection site, fever, mild myalgia

Ocular Adverse Reactions:
- MMR: subacute sclerosing panencephalitis and blindness associated with optic neuritis

Contraindications and Precautions:
- children with neurologic disorders (except hydrocephalus or cerebral palsy) should not be immunized as it may aggravate the disorder
- avoid live-virus vaccines in immunosuppressed patients

Drug Interactions:
- DTP: antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids decrease the immune response.
- MMR: other live-virus vaccines may impair its immune response
- OPV: plasma, whole blood, immune serum globulin and other live-virus vaccines may impair the immune response
- HDCV: steroids may activate the injected rabies virus
- Hib: chemotherapeutic agents may impair the antibody response
PASSIVE IMMUNITY AGENTS

- immune globulin [IG] (Gamastam)
- hepatitis B immune globulin [HBIG] (H-BIG)
- rabies immune globulin [RIG] (Hyperab)
- Rh(D) immune globulin, human (Gamulin Rh)
- tetanus immune globulin [TIG] (Hyper-Tet)
- varicella-zoster immune globulin [VZIG]

"Δ" indicates major drugs -- see table

Passive immunity agents contain preformed antibodies obtained from humans or animals that have had a disease or were injected with live organisms or their toxins.

**Indications for Use:**
- temporary protection from a disease for nonimmunized individuals when time does not allow for the production of immunity by the active processes
- when a disease is present to either alleviate the disease or prevent it from becoming worse
- to prevent the formation of active antibodies, as in Rh_0-negative mothers who deliver Rh_0-positive infants

**Mechanism of Action:**
- provides passive immunity by increasing the antibody concentration

<table>
<thead>
<tr>
<th>major drugs</th>
<th>things to remember</th>
</tr>
</thead>
</table>
| immune globulin [IG] | - for patients with immunodeficiency syndroms and immunoglobulin deficiency  
- also for patients with hepatitis A |
| hepatitis B immune globulin [HBIG] | - for post exposure prophylaxis against hepatitis B  
- for adults and newborns whose mothers are hepatitis B surface antigen positive |
| rabies immune globulin [RIG] | - for patients exposed to rabies  
- always given with the rabies vaccine |
| Rh(D) immune globulin, human | - to suppress the active antibody response and formation of ant- Rh(D) in Rh(D)-negative individuals exposed to Rh(D)-positive blood |
| tetanus immune globulin [TIG] | - for nonimmunized patients with susceptible wounds  
- for post tetanus exposure prophylaxis and to treat tetanus |
| varicella-zoster immune globulin [VZIG] | - for children exposed to chicken pox |
Adverse Reactions:
IG: pain at injection site, malaise, fever, chills, headache, nausea, vomiting, chest tightness, faintness, dyspnea, chest or back pain
HBIG: tenderness at injection site, urticaria, angioedema
Rh(D) immune globulin, RIG and TIG: pain at injection site, mild fever
TIG: IV administration may cause rapid fall in blood pressure and anaphylaxis
VZIG: mild rash and mild fever

Ocular Adverse Reactions:
- ocular reaction are rare

Contraindications and Precautions:
- use IG cautiously in pregnant women
- use these agents cautiously in patients with known hypersensitivity to immunoglobins
- use RIG and TIG cautiously in patients with sensitivity to thimerosal
- Rh(D) contraindicated in Rh(D)-positive patients and those previously immunized against Rh(D) blood factor

Drug Interactions:
no known drug interactions