



Drugs acting on the GIT (Gastrointestinal Tract) System

Antacids

Anti- Cholinergics

1. OverView:

A- Target Population:

To student of Institute of Pharmacy Department\NTU\ 2nd Class.

B. Rationale:

It is very important for the student to study the drugs that affect the GIT system because it is widely popularly used as OTC drugs , although lots of people suffer from GI disturbances , and the use these drugs even without medical reports from the doctor , with all the adverse effect associated with these drugs which include antacids and anti-cholinergics .

C. Central Idea:

1. Define antacids , anti-cholinergics .
2. Indicate the mechanism of action of both .
3. Notify the uses .
4. List the common adverse effects, contraindications, precautions, and drugs interaction of both .
- 5- Give the common trade name, scientific name, with the doses and the dosage forms.

D. Instructions:

1. Study the overview of the module carefully.
2. Recognize the performance objectives of this lecture.
3. Do the Pre – test & if you get:
 - a. 9 or more, so you do not need to study this lecture and review with your teacher or master.
 - b. Less than 9, so you need to continue studying this lecture precisely.
4. After studying the first lecture, do the post – test, so if you get:
 - a. 9 or more move to study the second lecture.
 - b. Less than 9, so go over the study of the first lecture or any part of it, than do the post – test again.



2. Performance objectives

When the student Finished this lecture he will be able to:

1. Define antacids , anti-cholinergics .
 2. Indicate the mechanism of action of both .
 3. Notify the uses .
 4. List the common adverse effects , contraindications , precautions , and drugs interaction of both .
 - 5- Give the common trade name, scientific name, with the doses and the dosage forms.
-

3. Pre-Test:

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Some drugs of GIT disorders are available as :
a. prescriptive b. non-prescriptive
c. none d. all
2. Cells of the stomach creates :
a. H₂SO₄ b. H₂PO₄
c. HCl d. HCO₃
3. Milk of Magnesia composed of :
a. Aluminum hydroxide b. Calcium hydroxide
c. Potassium hydroxide d. Magnesium hydroxide
4. Antacids is used in the treatment of :
a. asthma b. hypertension
c. peptic ulcer d. diarrhea
5. Antacids have :
a. Low margin of safety b. medium margin of safety
c. wide margin of safety d .no- safety
6. Anti-cholinergic drugs acts by :
a. reducing gastric motility b. increase gastric motility
c. not affect gastric motility d. all
7. Example of anti-cholinergic drug is :
a. milk of magnesia b. atenolol
c. profenal d. librax



8. Anti-cholinergic drugs is used nowadays :
- a. widely
 - b. often
 - c. not used
 - d. recommended
9. Anti-cholinergic drugs usually :
- a. increase gastric HCl
 - b. increase gastric carbonate
 - c. decrease gastric HCl
 - d. none
10. Antacids affect other drugs by coating the stomach and :
- a. decrease absorption
 - b. increase absorption
 - c. not affect absorption
 - d. non

Note: Check your answer on key answer page No.8

4. Indication of action of antacids & anticholinergic

1. Antacids

Some of the cells of the stomach secrete hydrochloric acid, a substance that aids in the initial digestive process. Antacids (against acids) are drugs that neutralize or reduce the acidity of stomach and duodenal contents by combining with hydrochloric acid and producing salt and water. Examples of antacids include aluminum hydroxide gel , and magnesia or magnesium hydroxide (Milk of Magnesia).

2. Anticholinergics

Anticholinergics (cholinergic blocking drugs) reduce gastric motility and decrease the amount of acid secreted by the stomach. Examples of anticholinergics used for GI disorders include propantheline (Pro-Banthine) and glycopyrrolate (Robinul).

The Medical Uses of Antacids & Anticholinergic drugs

1-Antacids

Antacids are used in the treatment of hyperacidity, such as heartburn, gastroesophageal reflux, sour stomach, acid indigestion, and in the medical treatment of peptic ulcer. Many antacid preparations contain more than one ingredient. An additional use for aluminum carbonate is in the treatment of hyperphosphatemia or for use with a low phosphate diet to prevent formation of phosphate urinary stones. Calcium carbonate may be used in treating calcium deficiency states such as menopausal osteoporosis.

Magnesium oxide may be used in the treatment of magnesium deficiencies or magnesium depletion from malnutrition, restricted diet, or alcoholism.

2- Anticholinergic

Specific anticholinergic drugs are occasionally used in the medical treatment of peptic ulcer. These drugs have been largely replaced by histamine H₂ antagonists, which appear to be more effective and have fewer adverse drug reactions.



common adverse effects , contraindications , precautions , and drugs interaction of antacids & anticholinergic.

1-Antacids

The magnesium- and sodium-containing antacids may have a laxative effect and produce diarrhea. Aluminum and calcium-containing products tend to produce constipation. Some of the less common but more serious

adverse reactions include:

- Aluminum-containing antacids—constipation, intestinal impaction, anorexia, weakness, tremors, and bone pain
- Magnesium-containing antacids—severe diarrhea, dehydration, and hypermagnesemia (nausea, vomiting, hypotension, decreased respirations)
- Calcium-containing antacids—rebound hyperacidity, metabolic alkalosis, hypercalcemia, vomiting, confusion, headache, renal calculi, and neurologic impairment

• Sodium bicarbonate—systemic alkalosis and rebound hypersecretion
Although the antacids have the potential for serious adverse reactions, they have a wide margin of safety, especially when used as prescribed.

The antacids are contraindicated in patients with severe abdominal pain of unknown cause and during lactation.

Sodium-containing antacids are contraindicated in patients with cardiovascular problems, such as hypertension or congestive heart failure, and those on sodium-restricted diets. Calcium-containing antacids are contraindicated in patients with renal calculi or hypercalcemia.

Aluminum-containing antacids are used cautiously in patients with gastric outlet obstruction. Magnesium- and aluminum-containing antacids are used cautiously in patients with decreased kidney function. The calcium containing antacids are used cautiously in patients with respiratory insufficiency, renal impairment, or cardiac disease. Antacids are classified as Pregnancy Category C drugs and should be used with caution during pregnancy.

Antacids may interfere with other drugs in three ways:

1. Increasing the gastric pH, which causes a decrease in absorption of weakly acidic drugs and results in a decreased drug effect (eg, digoxin, phenytoin, chlorpromazine, and isoniazid)
2. Absorbing or binding drugs to their surface, resulting in decreased bioavailability (eg, tetracycline)
3. Affecting the rate of drug elimination by increasing urinary pH (eg, the excretion of salicylates is increased, whereas excretion of quinidine and amphetamines is decreased)

The following drugs have a decreased pharmacologic effect when administered with an antacid: corticosteroids, digoxin, chlorpromazine, oral iron products, isoniazid, phenothiazine, ranitidine, phenytoin, valproic acid, and the tetracycline.



2-Anticholinergics

Dry mouth, blurred vision, urinary hesitancy, urinary retention, nausea, vomiting, palpitations, and headache are some of the adverse reactions that may be seen with the use of anticholinergic drugs .

common trade name , scientific name , with the doses and the dosage forms.

1-Antacids

GENERIC NAME	TRADE NAME	DOSAGE RANGES
aluminum hydroxide gel	Alu-Tab, Amphojel, Dialume, generic	Tablets or capsules: 500–1500 mg 3–6 times daily PO between meals and HS; suspension: 5–15 mL as needed between meals and HS PO
calcium carbonate	Chooz, Tums, generic	0.5–12 g PO as needed
magaldrate	Riopan, generic	980–1080 mg PO 1 and (hydroxymagnesium 3 hours after meals aluminate) and HS
Magnesia (magnesium)	Milk of Magnesia, Phillips' Chewable	Liquid: 5–15 mL PO QID with water; tablets: 650 mg–1.3 g QID PO; laxative: 15–60 mL PO taken with liquid
magnesium oxide	Mag-Ox 400, Maox 420, Uro-mag,	Capsules: 280 mg–1.5 g QID PO; tablets: generic 400–820 mg/d PO
aluminum carbonate gel	Basaljel	2 tablets or capsules or 10 mL of regular suspension (in water or fruit juice) or 5 mL of extra strength suspension as often as every 2 h, up to 12 times daily



2-Anticholinergics

GENERIC NAME	TRADE NAME	DOSAGE RANGES
Belladonna	Generic	Tincture: 0.6–1 mL TID–QID
clidinium bromide	Quarzan	2.5–5 mg PO TID–QID AC and HS
dicyclomine HCl	Dentyl, Di-Spaz, generic	Oral: 80–160 mg/d in 4 doses PO; parenteral: 80 mg/d IM
glycopyrrolate	Robinul, Robinul Forte, generic	Oral: 1 mg TID or 2 mg BID–TID PO; parenteral: 0.1–0.2 mg IM or IV TID–QID
hyoscyamine sulfate	Anaspaz, Donnamar, Levbid, Levsin	Oral: 0.125–0.25 mg PO TID–QID PO or sublingually ; sustained release: 0.375–0.75 mg q12h PO; parenteral: 0.25–0.5 mg SC, IM, IV BID–QID



4. Post -Test:

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Antacids are used for :

- a . hyperacidity alone
- b. peptic ulcer alone.
- c. duodenal ulcer
- d. all

2. Antacid preparations are :

- a. aluminum salt only
- b. magnesium salt
- c. aluminum & magnesium salts
- d. non of these

3. Diarrhea may be caused by :

- a. magnesium salts
- b. aluminum salt
- c. calcium salt
- d. magnesium & sodium salt

4. Constipation may be caused by :

- a. aluminum & calcium salts
- b. magnesium salt
- c. calcium salt only
- d. all

5. Sodium salt antacid is contraindicated in :

- a. asthmatic patient
- b .rheumatic patient
- c. CVS patient
- d. skin infected patient

6. Antacids affect the rate of elimination of other drugs by :

- a. decrease urinary PH
- b. neutralize urinary PH
- c. increase urinary PH
- d. non

7. The dose of aluminum gel tablet is :

- a. 0.5-1.5 g once daily
- b. 0.5-1.5g twice daily
- c. 0.5-1.5g 3 times daily
- d. 0.5-1.5g 3-6 times daily

8. Anti-cholinergic drugs adverse effect is :

- a. blurred vision
- b. dry mouth
- c. urinary hesitancy
- d. all

9. The dose of clindium bromide is :

- a. 10 mg 3-4 times daily
- b. 1 mg 3-4 times daily
- c. 5-10 mg 3-4 times daily
- d. 2.5-5 mg 3-4 times daily

10. Mepenzolate is :

- a. antacid
- b. anti-hypertensive
- c. anti-cholinergic
- d. anti- asthmatic

Note: Check your answer on key answer page No.8



Key Answer Page

Question number	Right Answer
1	b
2	c
3	d
4	c
5	c
6	a
7	d
8	b
9	c
10	a

After doing the Pre - test:

1-If you got 9 or more, so congratulation to your effort and need to transition to the second lecture.

2-If you got less than 9, so you need to continue studying this lecture carefully.

Post – test:

Question number	Right Answer
1	d
2	c
3	d
4	a
5	c
6	c
7	d
8	d
9	d
10	c

After studying the first lecture and doing the post – test, so if you got:

1- 9 or more transit to study the second lecture.

2- Less than 9, so go over the study of the first lecture or any part of it, than do the post – test again.

Drugs acting on the GIT (Gastrointestinal Tract) System

Anti - Diarrheal Drugs

Laxative Drugs

Pre-Test

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Diarrhia is :

- a.inc. in parastalasis b. dec. in parastalasis
c . no changes d. non

2. Anti-diarrheal drugs is used in the treatment of :

- a.asthma b. pain
c.diarrhea d. hypertension

3. Example of anti-diarrheal drug is :

- a. milk of magnesia b. cimitidine
c.lanszprazole d. loperamide

4 . Anti-diarrheal drug is :

- a.used in pregnancy only b. used cautiously in pregnancy
c. not used d. used cautiously in pregnancy & lactation

5. Anti-diarrheal drug cause :

- a. CNS stimulation b. CNS depression
c. don't affect CNS d. anxiety



6 . Laxatives are used to :

- a. inc. gastric motility
- b. dec. gastric motility
- c. inc. gastric secretion
- d. non

7. Example of laxative drug is :

- a. magnisium salt
- b. cimitidine
- c. biscodyle
- d. non

8. Laxative drugs cause :

- a. irreversible laxative habit
- b. no- dependence
- c. reversible laxative habit
- d. all

9 . Prolong uses of laxatives causes :

- a. no changes in electrolyte
- b. dec. electrolyte level
- c. inc. electrolyte level
- d. non

10. Example of emollient laxative is :

- a. psyllium
- b. cascara
- c. magnesium salt
- d. mineral oil

Note: Check your answer on key answer page No.12

- Diagnosed by stool consistency, NOT frequency of bowel movements.
- Seedy, pasty, formed, soft, hard.

Types of Laxative

A- Bulk Forming Laxatives

- Ex:** - Psyllium (Metamucil)
- methylcellulose (Citrucel)

Pharmacodynamics action:

- keep water in the stool to mechanically distend the colon & promote evacuation
- Also used in treatment of diarrhea, absorbs free fecal water
- Prolonged onset of action

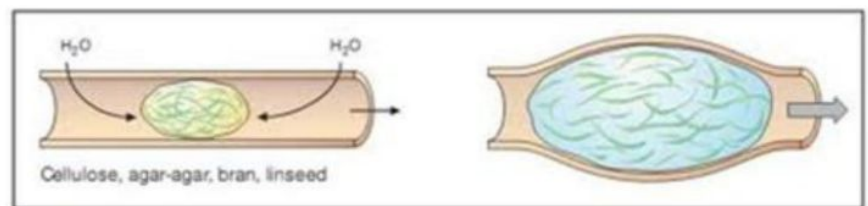
Adverse effects:

- Esophageal obstruction
- Intestinal obstruction or impaction

Unlabeled use: cholesterol lowering agent

Bulk Forming Laxative

Draws water to the stool to bulk it up and soften it and expands walls of the intestine so it can move forward more easily and be excreted - makes it softer, larger and easier to pass



B. Bulk laxatives

B- Surfactant Laxatives

- Softens stool, but does not MAKE person have a bowel movement, eases stool passing
- Ex:** Docusate (Colace)
- Pharmacodynamics action: facilitates addition of fat & water to soften stool over a few days
 - Prophylactic agent - pt. on narcotics or pt. you don't want straining (heart patients, head trauma pts.)
 - Give with a full glass of water

C- Stimulant and Irritant Laxatives

- Stimulates peristalsis

Pharmacodynamics action: 2 effects

- stimulate intestinal motility
- increases water & electrolytes within intestinal lumen - doesn't expand it/cause bulk
- Results in 6-12 hours with oral preparations
- Widely used and abused
- Direct effect on the intestinal mucosa & stimulates peristalsis.
- Works in the colon.

Ex: Bisacodyl (Dulcolax)

- Suppositories work in 15-60 min

Ex: Anthraquinones (Senna)- herbal source

- Patient teaching point: change in urine color
- Works in 6-12 hours

Ex: Castor Oil

- Works in small intestine
- 2-6 hours

D- Osmotic Laxatives

Onset of action depends on dosages

Pharmacodynamics:

- poorly absorbed salts whose osmotic action draws water into the intestinal lumen

Adverse effect:

- substantial loss of water - can result in dehydration
- Use cautiously in renal dysfunction
- Also be careful with patients with heart failure - salt will increase intravascular volume

Ex: 1-Lactulose

2-Magnesium hydroxide - Milk of Magnesia (MOM)

- Use in caution with patients with renal failure, HF
- Increases effect of sulfonylureas (diabetes), quinidine and others

E- Miscellaneous Laxatives

Ex: Mineral Oil

- Pharmacodynamics action: emollient or lubricant
- Excessive oral administration decreases absorption of fat soluble vitamins

Ex: Glycerin suppositories

- Gentle laxative, safe in infants, children
- Re-establish bowel patterns after laxative abuse

Ex: Polyethylene Glycol- Electrolyte Solutions (GoLYTELY, Miralax)

- Pulls water in and clears all fecal matter out
- Isosmotic with body fluids. Water is not lost & electrolyte balance is preserved
- Used primarily prior to diagnostic procedures for bowel cleansing - can be mixed with any drink

Abuse of Laxatives

Most frequently abused over the counter drug

Normal bowel pattern

- One stool for every 2-3 days of normal fluid and food intake

Misconception:

- daily bowel movement needed for good health
- Patients misdiagnose a normal bowel pattern for constipation and self-medicate
- A lot of bowel problems can be solved by adjusting diet

The Medical uses of Anti-diarrheal & Laxatives drugs

1- Anti-diarrheal

Antidiarrheal are used in the treatment of diarrhea.

2- Laxatives

A laxative is most often prescribed for the short-term relief or prevention of constipation. Certain stimulant, emollient, and saline laxatives are used to evacuate the colon for rectal and bowel examinations.

Psyllium may be used in patients with irritable bowel syndrome. Polycarbophil may be prescribed for constipation or diarrhea associated with irritable bowel syndrome and diverticulosis. Mineral oil is useful for the relief of fecal impaction.

Constipation may occur as an adverse drug reaction. When the patient has constipation as an adverse reaction to another drug, the primary care provider may prescribe a stool softener or another laxative to prevent constipation during the drug therapy.

Laxative use, especially high doses or use over a long time, can cause diarrhea and a loss of water and electrolytes. For some patients, this may be a serious adverse effect.

Laxatives may also cause abdominal pain or discomfort, nausea, vomiting, fainting, cramps, and weakness.

Prolonged use of a laxative can result in serious electrolyte imbalances, as well as the "laxative habit" that is, a dependency on a laxative to have a bowel movement.

Obstruction of the esophagus, stomach, small intestine, and colon has occurred when bulk-forming laxatives are administered without adequate fluid intake or in patients with intestinal stenosis.

Side Effect, Contraindication and Drug Interaction

1- Anti-diarrheal

Diphenoxylate use may result in anorexia, nausea, vomiting, constipation, rash, dizziness, drowsiness, sedation, euphoria, and headache.

This drug is a narcotic-related drug that has no analgesic activity but has sedative and euphoric effects and drug dependence potential. To discourage abuse, it is combined with **atropine** (an anticholinergic or cholinergic blocking drug), which causes dry mouth and other mild adverse effects.

Loperamide is not a narcotic-related drug, and minimal adverse reactions are associated with its use.

Occasionally, abdominal discomfort, pain, and distention have been seen, but these symptoms also occur with severe diarrhea and are difficult to distinguish from an adverse drug reaction.

These drugs are contraindicated in patients whose diarrhea is associated with **organisms that can harm the intestinal mucosa (Escherichia coli, Salmonella, Shigella)** and in **patients with:**

- **pseudomembranous colitis**
- **abdominal pain of unknown origin**
- **obstructive jaundice.**

The antidiarrheal drugs are contraindicated in **children younger than 2 years.**

The antidiarrheal drugs are used cautiously in patients with **severe hepatic impairment or inflammatory bowel disease.** Antidiarrheals should be used cautiously during **pregnancy and lactation.**

The antidiarrheal drugs cause an additive CNS depression when administered with alcohol, antihistamines, narcotics, and sedatives or hypnotics. There are additive cholinergic effects when administered with other drugs having anticholinergic activity, such as antidepressants or antihistamines.

2- Laxatives

Laxatives are contraindicated in patients with known hypersensitivity and those with persistent abdominal pain, nausea, or vomiting of unknown cause or signs of acute appendicitis, fecal impaction, intestinal obstruction,

These drugs are used only as directed because excessive or prolonged use may cause dependence. Magnesium hydroxide is used cautiously in patients with any degree of renal impairment.

Laxatives are used cautiously in pregnant women, and during lactation.

Mineral oil may impair the GI absorption of fat-soluble vitamins (A, D, E, and K). Laxatives may reduce absorption of other drugs present in the GI tract, by combining with them chemically or hastening their passage through the intestinal tract.

DO NOT USE LAXATIVES...

Don't assume it's constipation: could be gallstones, appendicitis, etc.

Do not use in the presence of undiagnosed abdominal pain

Common trade name , Scientific name , with the Doses and the Dosage forms.

1- Anti-diarrheal

Summary Drug Table		
SCIENTIFIC NAME	TRADE NAME	DOSAGE RANGES
Loperamide HCl	Imodium, Vacontil (generic)	Initial dose 4 mg PO then 2 mg after each loose stool (no more than 16 mg/d)
diphenoxylate HCl with atropine	Lomotil, Enterostop, Lonox, (generic)	Initial dose 5 mg PO TID–QID as needed
difenoxin HCl with atropine	Motofen	Initial dose 2 tablets PO, then 1 tablet after each loose stool (no more than 8 mg/d for no more than 2 days)



2- Laxatives

Summary Drug Table		
Scientific NAME	TRADE NAME	DOSAGE RANGES
Irritant or Stimulant Laxative		
Bisacodyl	Bisca-Evac, Dulcolax, Modane	Tablets: 10–15 mg daily PO Suppositories: 10 mg once daily
Senosides	Senade, Agoral, Ex-Lax, Senexon, Senna-Gel, Senokot	Follow directions given on the container
Castor oil	Castor oil	Follow directions given on the container
Cascara Sagrada	Auromatic Cascara, generic	Follow directions given on the container

Bulk Laxative		
Psyllium	Metamucil, Fiberall, Psyllium	Follow directions given on the container
Polycarbophil	Equalactin, FiberCon, Mitrolan	1250 mg one to four times daily or as needed (do not exceed 5 g in 24 h)
methylcellulose	Citrucel	Follow directions given on the container
Osmotic Laxative		
Lactulose	Duphalac	Follow directions given on the container
Magnesium hydroxide - Milk of Magnesia (MOM)	Magnesium hydroxide - Milk of Magnesia (MOM)	Follow directions given on the container
Fecal Softeners/Surfactants		
Docusate Sodium	Colace	Follow directions given on the container
Miscellaneous Laxatives		
Mineral Oil(Lubricating)	Liquid Paraffin	Follow directions given on the container



Post-Test

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Lomotil composed of :
a . loperamide
b. diphenoxine +atropine
c. diphynoxilate
d. diphynoxilate + atropine
2. Diphynoxilate is ant-diarrheal drug with :
a. narcotic effect
b. non-narcotic effect
c. analgesic effect
d. non
3. Lomotil dose is :
a. 20 mg
b. 1 mg
c.5 mg
d. 2.5 mg
4. The dose of loperamide is :
a. 2 mg
b. 10 mg
c. 5 mg
d. non
5. Anti-diarrheal + sedative drugs = :
a. dec. CNS activity
b .inc. CNS activity
c. CNS stimulation
d. non
6. Example of saline laxative is :
a. cascara
b. psyllium
c. milk of magnisia
d. miniral oil
7. Example of bulk forming laxative is :
a. biscodyle
b. glycerin
c. sennaside
d. psyllium
8. Example of irritant laxative is :
a. glycerin
b. biscodyle
c. psyllium
d. miniral oil
9. Miniral oil dose is :
a. 15-45 ml
b. 50-75 ml
c. 100 ml
d. 75-100 ml
10. Biscodyle is present in a form of :
a. tablet only
b. tablet & suppository
c. suppository only
d. solution

Note: Check your answer on key answer page No.12

Key Answer Page

Pre-test:

Question number	Right Answer
1	a
2	c
3	d
4	d
5	b
6	a
7	c
8	a
9	b
10	d

After doing the Pre - test:

1-If you got 9 or more, so congratulation to your effort and need to easily read the lecture.

2-If you got less than 9, so you need to deeply studying this lecture carefully.

Post-test:

Question number	Right Answer
1	d
2	a
3	c
4	a
5	a
6	c
7	d
8	b
9	a
10	b

After studying the third lecture and doing the post - test, so if you got:

1- 9 or more transit to study the forth lecture.

2- Less than 9, so go over the study of the third lecture or any part of it, than do the post - test again.



References:

- 1-Goodman LS , & Gilman A. The pharmacological basis of therapeutics, 11th edition, 2006 .
- 2-Drug Therapy; by Katzung BG and others, 2nd edition, Hall International Inc, 1995.
- 3-Basic And clinical pharmacology by Katzung G. Bertram, 10th edition, Lange Medical Publication, 2007 .
- 4-Michael J Neal, Medical Pharmacology at Glance. 4 the edition, Blackwell Science Ltd, UK, 2002 .
- 5-Lecture Notes on Clinical Pharmacology, by John Reid and other, Blackwell Science Publications, 1995.

Drug act on the Respiratory System (Bronchodilator)



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Bronchodilator is the drug that relieve :

- a. vasospasm*
- b. muscle spasm*
- c. bronchospasm*
- d. non*

2. Bronchospasm is associated with :

- a. bronchial asthma*
- b. chronic bronchitis*
- c. emphysema*
- d. all*

3. Example of sympathomimetic drug is :

- a. salbutamol*
- b. atenolol*
- c. acebutol*
- d. propranolol*



4. Sympathomimetic drug is :

- a. B1 antagonist*
- b. B1 agonist*
- c. B 2agonist*
- d. B2 antagonist*

5. Example of xanthine derivative is :

- a. theophylline*
- b . terbutaline*
- c. clibinclamide*
- d .propranolol*

6. Xanthine derivative used to :

- a. block CNS*
- b. stimulate CNS*
- c. block CVS*
- d. non*



7. Xanthine derivative have a direct effect on :

- a. smooth muscle of heart*
- b. smooth muscle of stomach*
- c. smooth muscle of bronchi*
- d. smooth muscle of esophagus*

8. Aminophylline is given :

- a. IV bolus*
- b. oral*
- c. SC*
- d. IV inj.*

9. Xanthin derivatives stimulate CNS and :

- a. hepatic function*
- b. CVS*
- c. renal function*
- d. digestive system*

10. Xanthin derivatives stimulates CNS and causes :

- a. vasodilatation*
- b. bronchospasm*
- c. non*
- d. bronchodilator*

Note: Check your answer on key answer page No.11

Bronchodilator

A bronchodilator is a drug used to relieve bronchospasm associated with respiratory disorders, such as **bronchial asthma**, **chronic bronchitis**, and **emphysema**. These conditions are progressive disorders characterized by a **decrease in the inspiratory and expiratory capacity of the lung**. Collectively, they are often referred to as **COPD**.

1-Bronchodilators: Sympathomimetic

Examples of sympathomimetic bronchodilators include

- **albuterol (Ventolin)**
- **epinephrine (Adrenalin)**
- **salmeterol (Serevent)**
- **terbutaline (Brethine)**



Many of the sympathomimetic used as bronchodilators have the subclassification of beta-2 (B₂) receptor agonists (eg, albuterol, salmeterol, and terbutaline). allows more air to enter the lungs, which in turn, completely or partially relieves respiratory distress.

2- Bronchodilators: Xanthine Derivatives

Examples of the xanthine derivatives (drugs that stimulate the central nervous system [CNS] resulting in bronchodilation, also called methylxanthines) Such as:

- theophylline
- aminophylline.

The uses of Bronchodilator Drugs

Sympathomimetic (drugs that mimic the sympathetic nervous system) are used primarily to treat reversible airway obstruction caused by bronchospasm associated with acute and chronic bronchial asthma, exercise-induced bronchospasm, bronchitis, emphysema.

The xanthine derivatives are used for symptomatic relief or prevention of bronchial asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

1-Bronchodilators: Sympathomimetic

Administration of a sympathomimetic bronchodilator may result in:

- restlessness
- anxiety
- increase in blood pressure
- palpitations
- cardiac arrhythmias
- insomnia



When these drugs are used by inhalation, excessive use (e.g. over the recommended times) may result in **paradoxical bronchospasm**.

The sympathomimetic bronchodilators are contraindicated in patients with:

- known hypersensitivity to the drug
- cardiac arrhythmias associated with tachycardia
- organic brain damage
- cerebral arteriosclerosis
- angle glaucoma

The sympathomimetic are used cautiously in patients with:

- hypertension
- cardiac dysfunction
- hyperthyroidism
- glaucoma
- diabetes
- prostatic hypertrophy
- history of seizures.

The sympathomimetic drugs are used cautiously during pregnancy, and lactation.

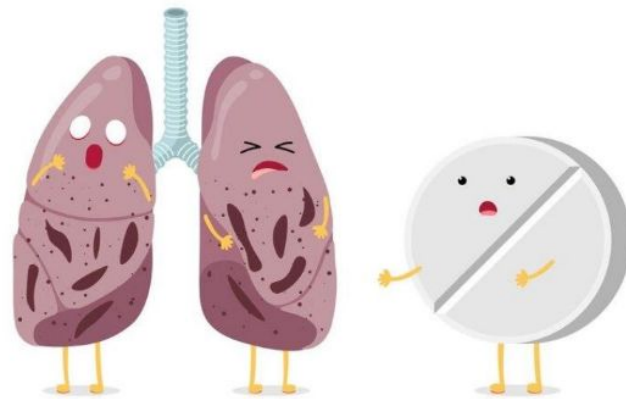
When the sympathomimetic are used concurrently with other sympathomimetic drugs, additive adrenergic effects can occur. When used with the monoamine.

When the sympathomimetic are administered with a B-adrenergic blocker, the drugs may inhibit the cardiac, bronchodilating, and vasodilating effects of the sympathomimetic .

2- Bronchodilators: Xanthine Derivatives

Adverse reactions associated with administration of the xanthine derivatives include -

- nausea\vomiting
- restlessness
- nervousness
- tachycardia
- tremors
- headache
- palpitations
- increased respirations
- fever
- hyperglycemia
- electrocardiographic changes



The xanthine derivatives are contraindicated in those with:

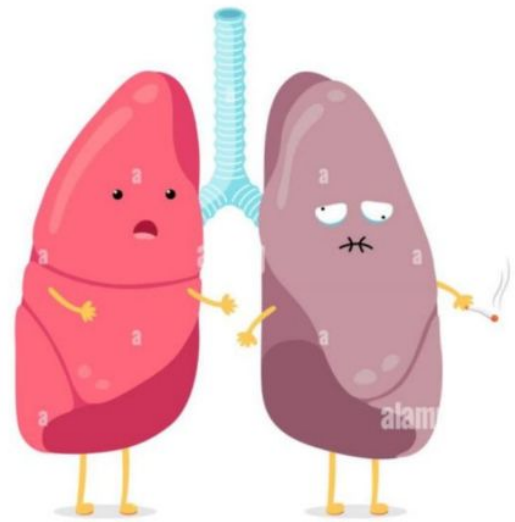
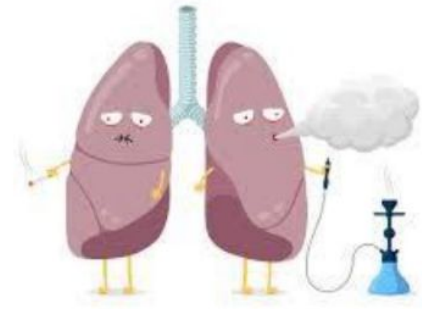
- known hypersensitivity
- peptic ulcers
- seizure disorders
- serious uncontrolled arrhythmias
- hyperthyroidism.

The xanthine derivatives are used cautiously in patients older than 60 years, those with cardiac disease, hypoxemia, hypertension, congestive heart failure, or liver disease. Aminophylline, used cautiously during pregnancy and lactation.

When xanthine bronchodilators are administered with sympathomimetic drugs , additive CNS and cardiovascular effects may occur. Certain foods contain xanthine (e.g.

coffee, colas, or chocolate) and may increase the risk of cardiac and CNS adverse reactions.

Cigarettes, nicotine gum and patches, barbiturates, phenytoin, loop diuretics, isoniazid, and rifampin may decrease the effectiveness of the xanthine. There is an increased risk of xanthine toxicity when the drugs are administered with **oral contraceptives, glucocorticoids, B-adrenergic blockers, cimetidine, macrolides, thyroid hormones, or allopurinol.**



Scientific name , Common trade name, with the Doses and the Dosage forms.

Summary Drug Table		
Bronchodilators: Sympathomimetic		
SCIENTIFIC NAME	TRADE NAME	DOSAGE RANGES
albuterol sulfate	Ventolin, Bronchospasm	2—4 mg TID, QID PO; 1—2 inhalations q4—6h; 2 inhalations before exercise; may also be given by nebulization, up to 32 mg/d
ephedrine sulfate	generic Asthma, bronchospasm	25—50 mg PO q3—4h PRN; 25—50 mg IM, SC, IV
epinephrine	Adrenalin, Asthma, bronchospasm Epinephrine	Inhalation aerosol: individualize dose; injection: solution 1:1000, 0.3—0.5 mL SC, IM Suspension (1:200): 0.1—0.3 mL SC only
salmeterol	Serevent	2 inhalations BID morning and evening
terbutaline sulfate		2.5—5 mg q6h PO TID during waking hours; 0.25 mg SC (may repeat one time if needed)
Bronchodilators: Xanthine Derivatives		
SCIENTIFIC NAME	TRADE NAME	DOSAGE RANGES
aminophylline	Phyllocontin, Truphylline	10—20 mcg/mL
theophylline	Theo-24 , Theo-dur , Theolair	Long-term therapy: 16 mg/kg/24h or 400 mg/24h in divided doses



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1- Sympathomimetic drug is used cautiously in patient with :

- a .hypertension** **b. glaucoma**
- c . cardiac dysfunction** **d. all**

2- When sympathomimetic drug is used excessively by inhalation it causes :

- a. bronchodilatation** **b. broncho-spasm**
- c. paradoxical relaxation** **d. non**

3- Xanthine derivatives is cautiously used in patient with :

- a. younger than 60 y** **b. younger than 20 y**
- c. older than 60 y** **d. older than 20 y**

4- Certain foods with xanthine derivatives may :

- a. only CNS effect** **b. inc. risk of CNS & CVS**
- c. dec. risk of CNS effect** **d. dec. risk of CNS & CVS**

5- The dose of albuterol is :

- a. 2-4 mg** **b . 10-20 mg**
- c. 50-100 mg** **d. 20-50 mg**

6- The dose of epinephrine is :

- a. 1-2 ml** **b. 0.3-0.5 ml**
- c. 10-20 ml** **d. 5-10 ml**



7- Aminophylline dose is :

- a. 5-100 mcg/ml b. 10-20 mg/ml
c. 10-20 mcg/ml d. 10-20 g / ml

8- The dose of theophylline is :

- a. 10 mg/d b. 400 mg/d
c. 100 mg /d d. 250 mg/d

9- The dose of ephedrine sulphate is :

- a. 25-50 mg b. 100-200 mg
c. 200-300 mg d. 1-5 mg

10- The dose of terbutaline is :

- a. 100-200 mg b. 2.5-5 mg
c. 50-75 mg d. 20-50 mg



(Diuretics)
osmotic
Carbonic anhydrase inhibitor
loop

Pre-Test

**Q: Choose the correct answer by encircle on the right letter:
(1 degree to each branch)**

1. Diuretics is used to :

- a. inc. urine secretion b. dec. urine secretion
c .not affect urine secretion d. non

2. Diuretics is used in :

- a. heart failure b. endocrine disturbances
c. kidney & liver failure d. all

3. Diuretic types are :

- a. carbonic anhydrase inhibitors b. loop
c. potassium sparing d. all

4 . Diuretics is used in the treatment of :

- a. hypertension b. asthma
c. pain d. non

5 . Example of diuretics are used in combination therapy in hypertension :

- a. thiazide & atenolol b .mannitol & atenolol
c. diamox & atenolol d . aldactone & atenolol

6. Diamox is used in :

- a. hypertension
- b. pain
- c. open angle glaucoma
- d. hyper-acidity

7. Furosemide is used in :

- a. edema
- b. pulmonary edema
- c. hypertension
- d. all

8. Mannitol diuretic is used in :

- a. cerebral edema
- b. hypertension
- c. pulmonary edema
- d. all

9. Glycerol diuretic is used in :

- a. heart failure
- b. hypertension
- c. glaucoma
- d. non

10. Bumetanide diuretic is :

- a. thiazide diuretic
- b. loop diuretic
- c. osmotic diuretic
- d. carbonic anhydrase inhibitor diuretic

Note: Check your answer on key answer page No.16

Diuretics

are the class of drugs which acts on **kidney** and used to increase urine volume or urine output by increasing the water and sodium secretion in urine.

Or may be defined as the drugs which cause a net loss of Na^+ and water in urine.



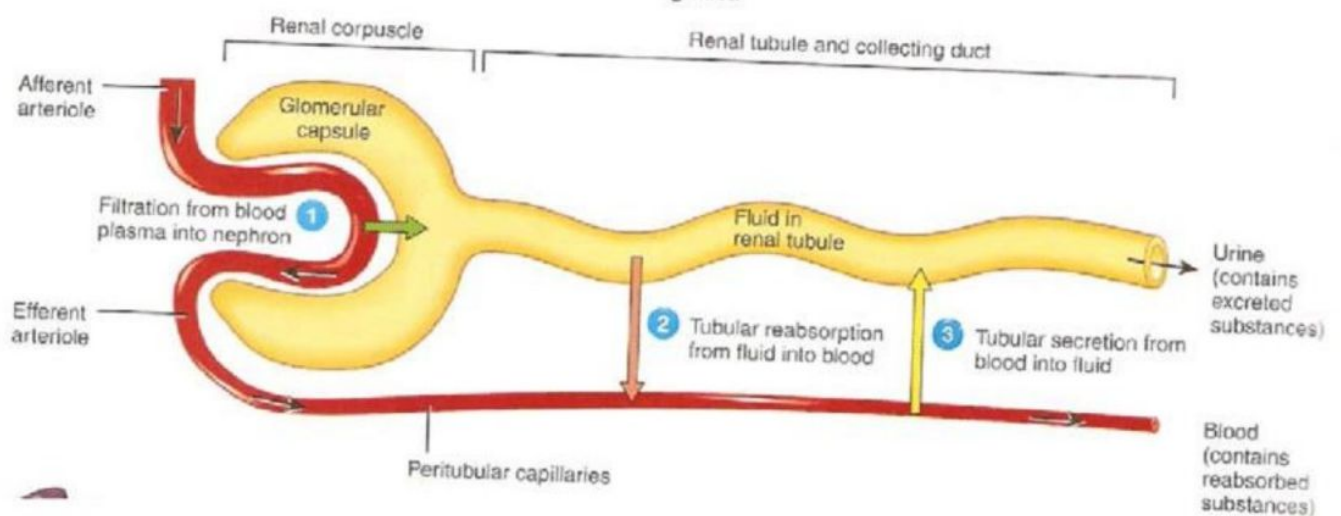
- Application of diuretics to the management of hypertension & in Edema

- There are several categories of diuretics. All diuretics increases the excretion of water from body.

- **Mechanism of urine formation**

The formation of urine occurs in three separate steps

Nephron - The Functional unit



1- FILTRATION

The movement of fluids from the blood into the Bowman's capsule of the nephron. Blood moves from the afferent arteriole into the glomerulus (a high-powered filter, acting at 65 mm of Hg, ~1.5 times the normal pressure of a capillary).

Dissolved solutes pass from the blood into the Bowman's capsule along the pressure gradient. Not all solutes make it through.

DO:

- Water
- Plasma proteins
- Sodium chloride
- Glucose
- Amino acids
- protons

DON'T (too large)

- Red blood cells
- Platelets

2- REABSORPTION

- The transfer of essential solutes and most water back into the surrounding cells and the blood stream.
- For every 120 mL of fluid (amount filtered by kidneys each minute), 1 mL of urine is formed, 119 mL of fluid and solutes is reabsorbed.
- Occurs throughout the nephron, mainly in the proximal tubule and loop of Henle.

Water Reabsorption

Water is automatically reabsorbed back into the cells and bloodstream for 2 reasons:

- A- The blood that left the glomerulus by the efferent arteriole travels through the peritubular capillaries.
- B- It has a very high concentration in plasma.

3- SECRETION

The release of substances into the filtrate from the blood and cells surrounding the nephron.

Occurs mainly in the distal tubules and in the collecting duct, but some also occurs in the proximal tubule.

Purpose:

to release any toxins and drugs that have not been filtered Maintain the electrolyte balance of the body (if positive sodium ions are reabsorbed then positive ions like potassium must be secreted to keep the balance - even though reabsorbed initially).

Acid-base balance (usually it is an acid being secreted, essentially a proton plus whatever it is attached to).

CLASSIFICATION

Diuretics are Classified as:

1- Osmotic diuretics:

Ex: Mannitol, Glycerol, Urea, Isosorbide

2- Carbonic anhydrase inhibitors.

Ex: Acetazolamide,

3- Thiazides and Thiazides like diuretics

Ex:

Hydrochlorothiazide(HCTZ),Chlorthaizide, Indapamide, Chlorthalidone, Hydroflumethiazide, Clopamide

4- Loop diuretics

Ex. A- Sulfamoyl Derivatives: e.g. Furosemide, Bumetanide, Torsemide

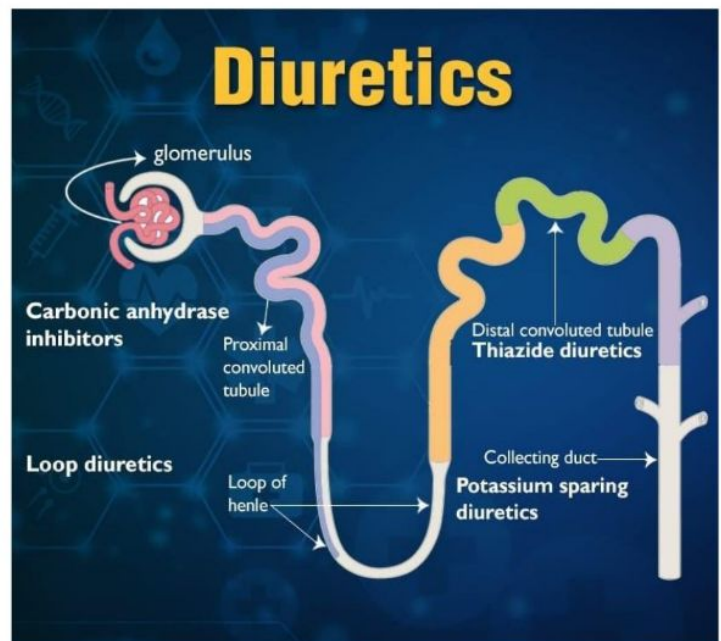
B- Phenoxy acetic acid Derivatives: e.g. Ethacrynic acid

5- Potassium - sparing diuretics

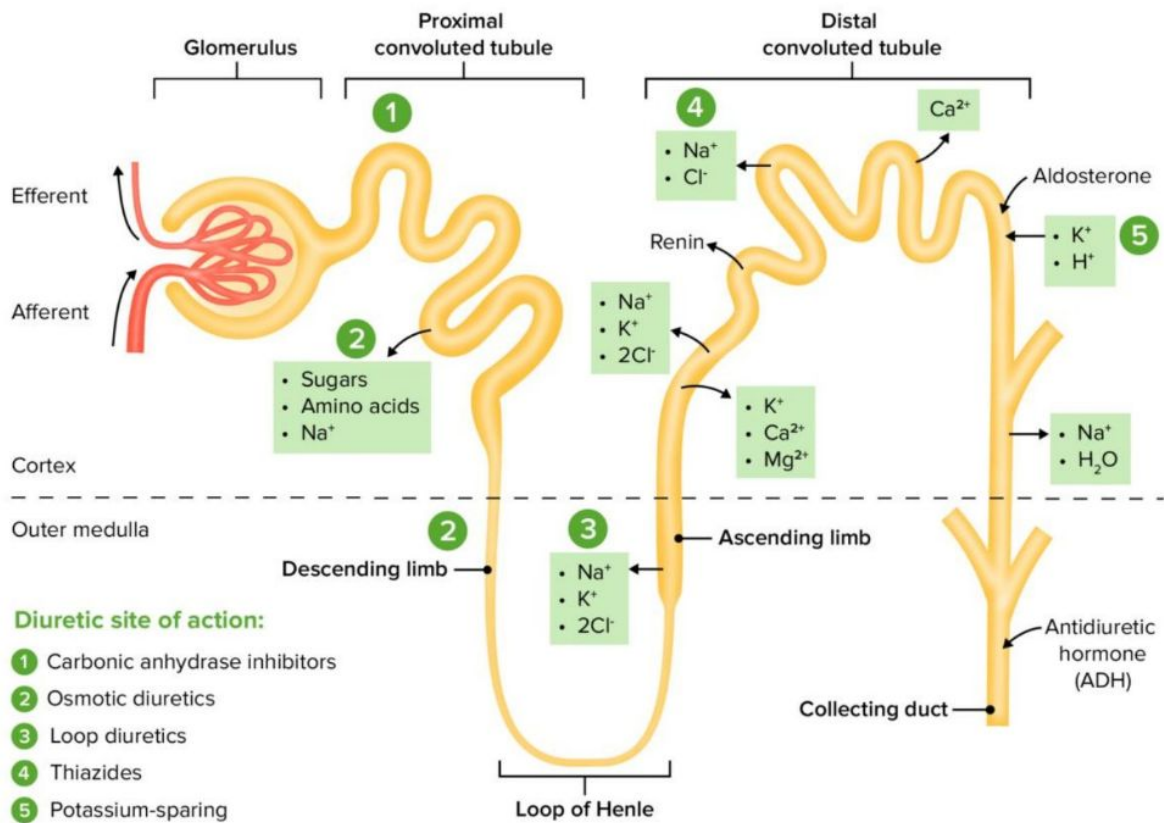
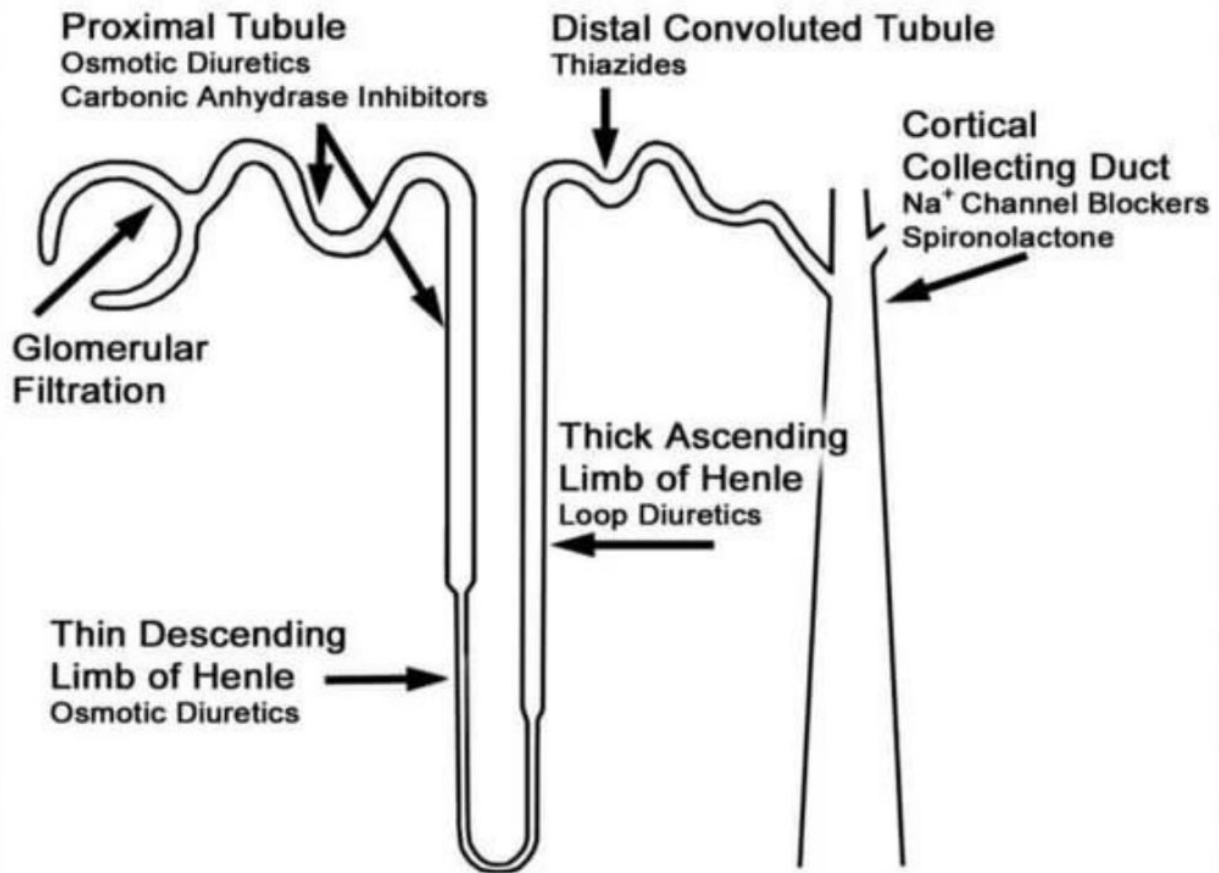
Ex. A- Aldosterone antagonist: e.g. Spironolactone

B- Pteridine derivatives: e.g. Trimeterene

C- Sod. Channel antagonist: e.g. Amiloride



Site of Action

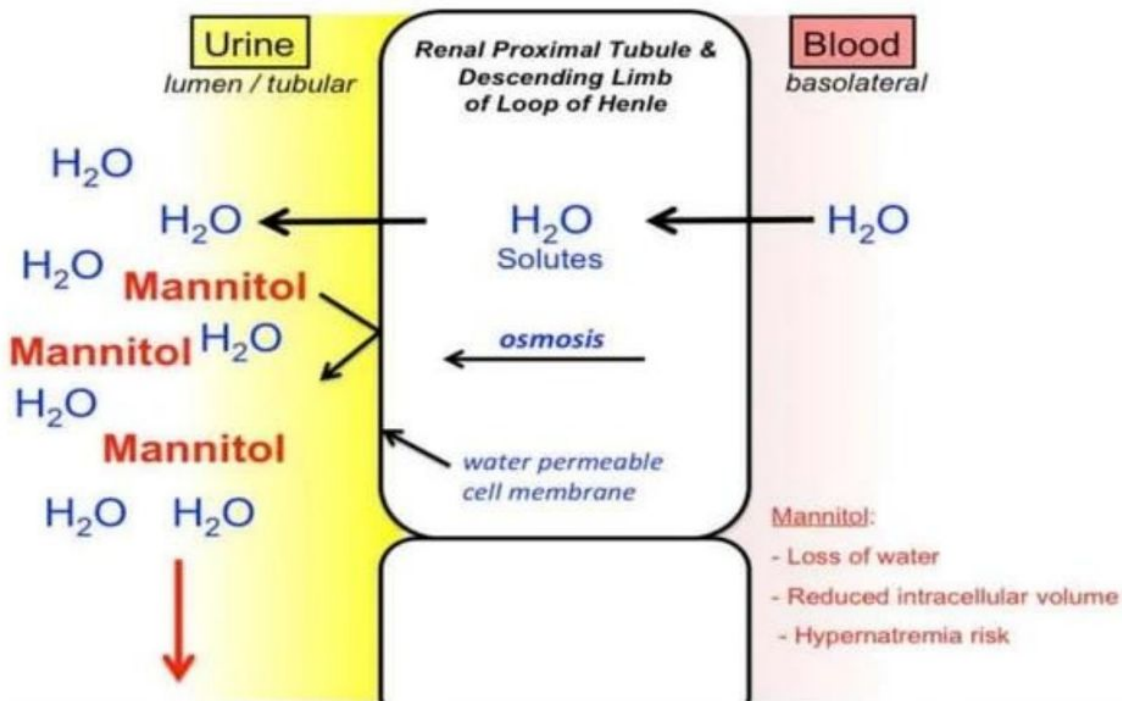


Osmotic diuretics

Osmotic diuretics increase the density of the filtrate in the glomerulus. This prevents selective reabsorption of water, which allows the water to be excreted. Sodium and chloride excretion is also increased.

MOA: - Retains water isoosmotically in PT- dilutes luminal fluid which opposes NaCl reabsorption.

- inhibits transport processes in the thick AscLH by an unknown mechanism. Quantitatively this appears to be the most important cause of diuresis
- Expands extracellular fluid volume (because it does not enter cells, draws water from the intracellular compartment)
- increases GFR and inhibit renin release.



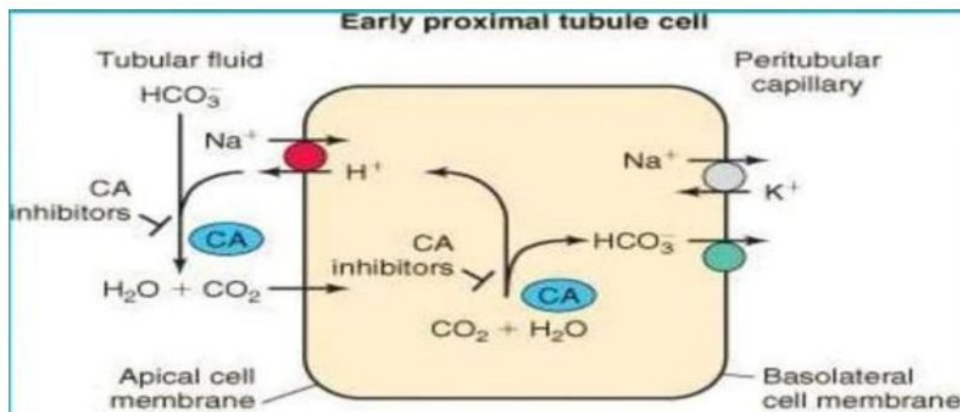
Carbonic anhydrase inhibitors.

Carbonic anhydrase is an enzyme that produces free hydrogen ions, which are then exchanged for sodium ions in the kidney tubules. Carbonic anhydrase inhibitors inhibit the action of the enzyme carbonic anhydrase. This effect results in the excretion of sodium, potassium, bicarbonate, and water. Carbonic anhydrase inhibitors also decrease the production of

aqueous humor in the eye, which in turn decreases intraocular pressure (IOP) (i.e., the pressure within the eye).

MOA: Carbonic anhydrase catalyzes formation of HCO_3^- and H^+ from H_2O and CO_2 .

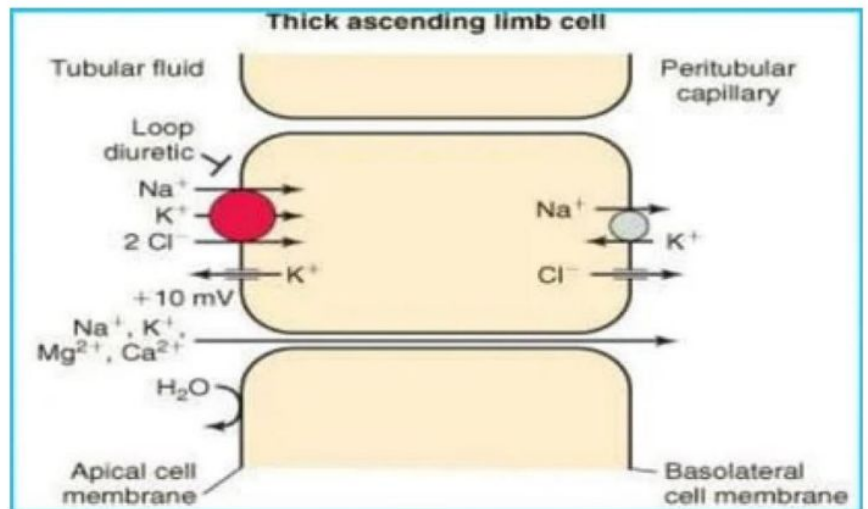
- inhibition of carbonic anhydrase decreases $[\text{H}^+]$ in tubule lumen
- less H^+ for Na^+/H^+ exchange increased lumen Na^+ , increased H_2O retention.



Loop diuretics

The loop diuretics, furosemide (Lasix) and ethacrynic acid (Edecrin),

MOA: increase the excretion of sodium and chloride by inhibiting reabsorption of these ions in the distal and proximal tubules and in the loop of Henle.



This mechanism of action at these three sites appears to increase their effectiveness as diuretics..

Bumetanide (Bumex) primarily increases the excretion of chloride but also has some sodium-excreting ability.

The Medical uses of Diuretics drugs

Osmotic diuretics

Mannitol (Osmitrol) is used for

- promotion of diuresis in the prevention and treatment of the oliguric phase of acute renal failure,
- reduction of IOP: short term treatment of acute glaucoma
- cerebral edema: infused to lower intracranial pressure

Carbonic anhydrase inhibitor diuretics

Glaucoma is an increase in the IOP that, if left untreated, can result in blindness . Acetazolamide (Diamox) is used in the treatment of simple glaucoma,

- treatment of edema caused by congestive heart failure (CHF), drug-induced edema, and control of epilepsy
- used in combination with other diuretics in resistant patients.

Loop diuretics

- Edema: Cardiac, Pulmonary or renal
- Chronic renal failure
- Hypertension & hypercalcemia
- Acute and chronic hyperkalemia

Side Effect, Contraindication and Drug Interaction

Osmotic Diuretics

The osmotic diuretics urea and mannitol are administered intravenously (IV), whereas glycerin and isosorbide are administered orally. Administration by the IV route may result in a rapid fluid and electrolyte imbalance, especially when these drugs are administered before surgery with the patient in a fasting state.

The osmotic diuretics are contraindicated in patients with known hypersensitivity to the drugs, electrolyte imbalances. Osmotic diuretics are used cautiously in patients with renal or kidney impairment or electrolyte imbalances.

Additive hypotensive effects occur when the osmotic diuretics are given with other antihypertensive drugs or nitrates.

Carbonic anhydrase inhibitor diuretics

Adverse reactions associated with short-term therapy with carbonic anhydrase inhibitors are rare. Long-term use of these drugs may result in fever, rash, paresthesia numbness, tingling), photosensitivity reactions, anorexia, and crystalluria (crystals in the urine)..

The carbonic anhydrase inhibitors are contraindicated in patients with known hypersensitivity to the drugs, electrolyte imbalances, severe kidney or liver dysfunction, There is an increased risk of cyclosporine toxicity when the drug is administered with acetazolamide.

Loop Diuretics

- Hypokalemia
- Hyeruricemia
- Metabolic alkalosis



- Hyponatremia
- Ototoxicity
- Mg^{2+} depletion
- postural hypotension (dizziness and light-headedness , when rising suddenly from a sitting or lying position),
- orthostatic hypotension (hypotension after standing in one place for a long time)
- photosensitivity reactions
- glycosuria (glucose in the urine).

Loop diuretics are contraindicated in patients with known hypersensitivity to the loop diuretics or to the sulfonamides, severe electrolyte imbalances, hepatic coma, Loop diuretics are used cautiously in patients with renal dysfunction.. Furosemide is used in children but should be used cautiously. Loop diuretics may increase the effectiveness of the anticoagulants or the thrombolytic.

There is an increased risk of glycoside toxicity and digitalis-induced arrhythmias if the patient experiences hypokalemia while taking the loop diuretics.



Applications of Diuretics:

Diuretics are very effective in the treatment of conditions like:

- Chronic heart failure
- Nephrotic syndrome
- Chronic hepatic diseases
- HT
- Pregnancy associated edema
- Cirrhosis of the liver
- Edema



Common trade name , Scientific name , with the Doses and the Dosage forms

Summary Drug Table		
Scientific NAME	TRADE NAME	DOSAGE RANGES
Osmotic Diuretics		
glycerin (glycerol)	Osmoglyn	1 to 2 grams per kg
isosorbide	Ismotic	1.5 gm per kg
mannitol	Osmitrol	50-200 g/d IV
urea	Ureaphil	
Carbonic anhydrase inhibitor diuretics		
acetazolamide	Diamox	125-250 mg q4 hr
Loop Diuretics		
furosemide	Lasix	20 to 80 mg PO
bumetanide	Bumex	0.5 mg to 2 mg
ethacrynic acid	Edecrin	50 to 200 mg daily

Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Example of carbonic anhydrase inhibitor enzyme is diamox which inhibits:

- a . CA enzyme
- b. ATPase
- c. oxidase enzyme
- d. non

2. Lasix acts by inhibiting sodium and water re absorption in :

- a. distal tubules
- b. proximal tubule
- c. loop of Henle
- d. all

3. Osmotic diuretics acts by :

- a. dec. density of filterate
- b. inc. density
- c. not affect the density
- d. non

4. The common side effect of loope diuretics is

- a. hypertension
- b. orthostatic hypotension
- c. postural hypotension
- d. non

5. Mannitol diuretic when given IV causes :

- a. rapid fluid imbalance
- b . slow fluid imbalance
- c. not affect fluids
- d. non

6. Lasix is cautiously used in patient with :

- a. severe hypertension
- b. asthma
- c. electrolyte imbalance
- d. jaundice



7. The dose of furosemide is :

- a. 600mg/d single dose
- b. 40 mg BID
- c. 200mg/d single dose
- d. 30 mg IM

8. The dose of diamox in glaucoma is :

- a. 10-20 mg q4 hr.
- b. 5-10 mg q 4 hr
- c. 125-250 mg q4 hr.
- d. 50-75 mg q4hr

9. The dose of mannitol is :

- a. 50-200 g/d IM
- b. 50-200 g/d orally
- c. 50-200 g/d SC
- d. 50-200 g/d IV

10. Diamox is used in :

- a. asthma
- b. hypertension
- c. epilepsy
- d. pain

Note: Check your answer on key answer page No.16



Key Answer Page

Pre-test:

Question number	Right Answer
1	a
2	d
3	d
4	a
5	a
6	c
7	d
8	a
9	c
10	b

After doing the Pre - test:

1-If you got 9 or more, so congratulation to your effort and need to easily read the lecture.

2-If you got less than 9, so you need to deeply studying this lecture carefully.

Post-test:

Question number	Right Answer
1	a
2	d
3	b
4	c
5	a
6	c
7	b
8	c
9	d
10	c

After studying the third lecture and doing the post - test, so if you got:

1- 9 or more transit to study the fifth lecture.

2- Less than 9, so go over the study of the third lecture or any part of it, than do the post - test again.



References:

- 1-Goodman LS , & Gilman A. The pharmacological basis of therapeutics, 11th edition, 2006 .
- 2-Drug Therapy; by Katzung BG and others, 2nd edition, Hall International Inc, 1995.
- 3-Basic And clinical pharmacology by Katzung G. Bertram, 10th edition, Lange Medical Publication, 2007 .
- 4-Michael J Neal, Medical Pharmacology at Glance. 4 the edition, Blackwell Science Ltd, UK, 2002 .
- 5-Lecture Notes on Clinical Pharmacology, by John Reid and other, Blackwell Science Publications, 1995.

Antiseptics

And Disinfectants



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *Antiseptics are a chemical compounds which applied to :*
 - a. *skin*
 - b. *living tissues*
 - c. *both*
 - d. *non*
2. *Antiseptics is used to :*
 - a. *reduce infection*
 - b. *inc. infection*
 - c. *not affect infection*
 - d. *non*
3. *Antiseptics is used to reduce :*
 - a. *infection*
 - b. *sepsis*
 - c. *putrifaction*
 - d. *all*
4. *Antiseptics ia applied to :*
 - a. *surgical apparatus*
 - b. *non living tissue*
 - c. *living tissues*
 - d. *non*
5. *Ethanol concentration is :*
 - a. *10-20 %*
 - b. *60-90 %*
 - c. *100 %*
 - d. *20-40 %*
6. *Surgical alcohol is a mixture of :*
 - a. *ethanol*
 - b. *1- propanol*
 - c. *2-propanol+ isopropanol*
 - d. *all*
7. *Hydrogen peroxide is used as :*
 - a. *50% sol*
 - b. *25 % sol*
 - c. *6 % sol*
 - d. *100 %*
8. *Iodine is used as :*
 - a. *tr. of iodine*
 - b. *solution of iodine*
 - c. *both*
 - d. *non*

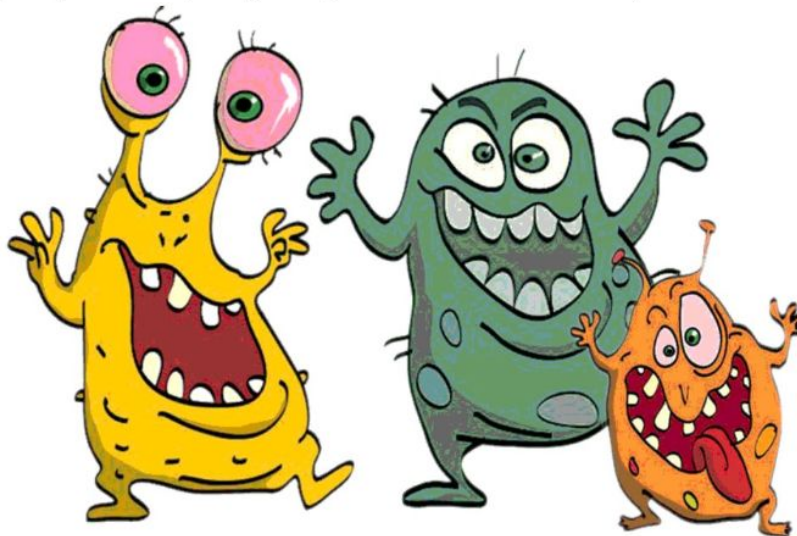
9. Sodium chloride is used as :
- a. 0.9% mouth wash
 - b. alcohol solution
 - c. mouth wash above 9%
 - d. non
10. Antiseptic should be distinguished from :
- a. antibiotic
 - b. disinfectant
 - c. non
 - d. both
11. Disinfectant is a _____ applied to non-living tissues :
- a. anti-bacterial
 - b. chemical
 - c. anti-microbial
 - d. non
12. Disinfectant is used to :
- a. destroy bacteria
 - b. stimulate bacterial growth
 - c. stop bacterial growth
 - d. non
13. Most disinfectant is harmful to :
- a. human
 - b. bacteria
 - c. both
 - d. non
14. Disinfectant is used in :
- a. hospitals
 - b. bathrooms
 - c. kitchens
 - d. all
15. The ideal disinfectant is :
- a. non-corrosive
 - b. non-toxic
 - c. inexpensive
 - d. all
16. Disinfectant should be :
- a. wide spectrum
 - b. narrow spectrum
 - c. both
 - d. non

introduction to antiseptics:

Antiseptic are antimicrobial substances that are applied to living tissues / skin , to reduce the possibility of infection, sepsis, or putrefaction. They should generally be distinguished from antibiotics that destroy bacteria within the body, and from disinfectants, which destroy microorganisms found on non-living objects.

introduction to Disinfectants

Disinfectants are antimicrobial agents that are applied to non-living objects to destroy microorganisms, the process of which is known as disinfection . A perfect disinfectant would offer complete sterilization, without harming other forms of life .Unfortunately ideal disinfectants do not exist. Most disinfectants are also, by their very nature, potentially harmful (even toxic) to humans or animals. They are frequently used in hospitals, dental surgeries, kitchens and bathrooms to kill infectious organisms. The choice of the disinfectant to be used depends on the particular situation. Some disinfectants have a wide spectrum (kill nearly all microorganisms), whilst others kill a smaller range of disease-causing organisms but are preferred for other properties (they may be non-corrosive, non-toxic, or inexpensive).



The Types of antiseptics

Some common antiseptics

- Alcohols

Most commonly used are ethanol (60-90%), 1-propanol (60-70%) and 2-propanol/isopropanol (70-80%) or mixtures of these alcohols. They are commonly referred to as "surgical alcohol". Used to disinfect the skin before injections are given, often along with iodine (tincture of iodine)

Quaternary ammonium compounds

include the chemicals benzalkonium chloride , cetyl trimethylammonium bromide , cetylpyridinium chloride and benzethonium chloride .

Benzalkonium chloride is used in some pre-operative skin disinfectants (conc. 0.05 - 0.5%) and antiseptic towels.

Boric acid

Used in suppositories to treat yeast infections of the vagina, in eyewashes, and as an antiviral to shorten the duration of cold sore attacks.

Chlorhexidine Gluconate

A biguanidine derivative, used in concentrations of 0.5 - 4.0% alone or in lower concentrations in combination with other compounds, such as alcohols. Used as a skin antiseptic and to treat inflammation of the gums (gingivitis).

Hydrogen peroxide

Used as a 6% (20Vols) solution to clean and deodorize wounds and ulcers. with mild soap More common 1% or 2% solutions of hydrogen peroxide have been used in household first aid for scrapes .

- Iodine

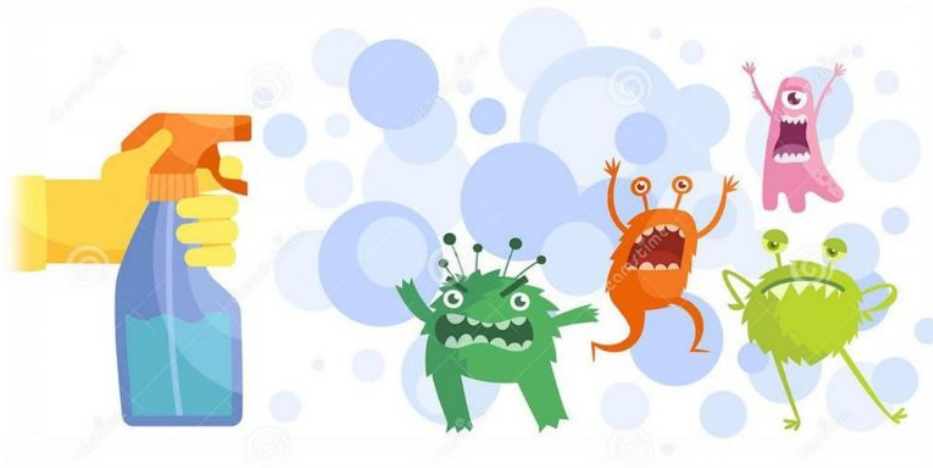
Usually used in an alcoholic solution (called tincture of iodine) or as Lugol's iodine solution as a pre and post-operative antiseptic. No longer recommended to disinfect minor wounds because it induces scar tissue formation and increases healing time.

- Mercurochrome

Not recognized as safe and effective by the U.S. Food and Drug Administration (FDA) due to concerns about its mercury content.

- Sodium chloride

Used as a general cleanser. Also used as an antiseptic mouthwash. Only a weak antiseptic effect, due to hyper osmolality of the solution above 0.9%.



The Types of disinfectant

Types of disinfectants

1- Alcohols

usually ethanol or isopropanol, are wiped over skin and allowed to evaporate for quick disinfection. They have wide microbicidal activity, are non corrosive, but can be a fire hazard .

Alcohols are more effective combined with purified water.

2- Aldehydes

Aldehydes, such as Glutaraldehyde, have a wide microbicidal activity and are sporicidal and fungicidal.

3- Halogens

Chloramine is used in drinking water treatment instead of chlorine

Hypochlorite Sodium hypochlorite often in the form of common bleach are used in the home to disinfect drains, and Other

4- Oxidizing agents

Oxidizing agents act by oxidizing the cell membrane of microorganisms, which results in a loss of structure and leads to cell lysis and death.

Chlorine dioxide

Hydrogen peroxide

Ozone is a gas that can be added to water for sanitation.

Acidic Electrolyzed Water

Potassium permanganate ($KMnO_4$) is a red crystalline powder that colors everything .

5- Phenolic

Phenolic are active ingredients in some household disinfectants. They are also found in some mouthwashes and in disinfectant soap and hand washes. Like Dettol .

6- Quaternary ammonium compounds

such as benzalkonium chloride, are a large group of related compounds. Some have been used as low level disinfectants .

7- Other

The biguanide polymer polyaminopropyl biguanide is specifically bactericidal at very low concentrations .

High-intensity shortwave ultraviolet light can be used for disinfecting smooth surfaces such as dental tools, but not porous materials that are opaque to the light such as wood or foam



Post-Test

Q: Choose the correct answer by encircle on the right letter:

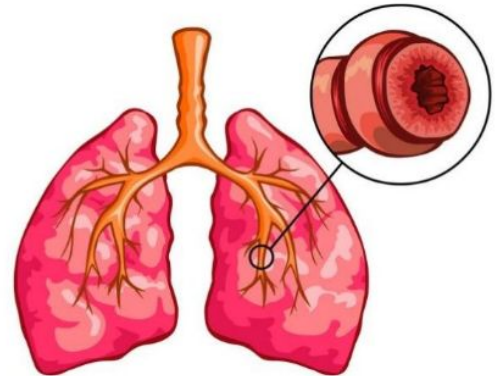
(1 degree to each branch)

- Surgical alcohol is used as antiseptic :*
 - before injection*
 - after injection*
 - with injection*
 - non*
- The concentration of benzelkinium bromide is :*
 - 5-10 %*
 - 1-5 %*
 - 0.05-0.5 %*
 - 10-20 %*
- Boric acid is used for treatment of vaginal yeast in the form of :*
 - solution*
 - suppositories*
 - tr. of iodine*
 - non*
- Boric acid is used as :*
 - vaginal wash*
 - eye wash*
 - anti-viral*
 - all*
- 1-2 % solution of hydrogen peroxide is used in :*
 - cleaning wounds*
 - clean ulcer*
 - house holds*
 - all*
- Chlorohexidine is used in :*
 - skin antiseptic*
 - gingivitis*
 - both*
 - non*
- The concentration of biguanides derivatives is :*
 - 10-20 %*
 - 0.5-4 %*
 - 15-25 %*
 - 25-50 %*



8. Iodine solution is no longer used because :
- a. induce scar tissue b. dec. scar tissue
c. not affect scaring d. all
9. Mercurchorome is not used because of presence of :
- a. copper b. iodine
c. mercury d. guanides
10. Luglos solution is used as :
- a. preoperative b. post operative
c. both d. non
11. Example of aldehyde disinfectant is :
- a. boric acid b. biguanide
c. glutaraldehyde d. all
12. Aldehyde is used as :
- a. sporicidal b. fungicidal
c. both d. non
13. Chloramine is used :
- a. normal water b. drinking water
c. washing water d. non
14. Hypocholite is used as :
- a. antibiotic b. sporacidal
c. bleach d. non
15. Oxidizing agent acts by :
- a. oxidizing cell membrane b. cell protein
c. oxidizing cell wall d. all

Drug act on the Respiratory System (Anti Asthmatic drug)



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *Asthma is an obstructive disease of the lower airway which :*

- a. *irreversible*
- b. *reversible*
- c. *constant*
- d. *non*

2. *Extrinsic asthma is called :*

- a. *non-allergic asthma*
- b. *allergic asthma*
- c. *mixed asthma*
- d. *non*

3. *Internist asthma is caused by :*

- a. *respiratory inflammation*
- b. *emotional upset*
- c. *exercise*
- d. *all*

4. *Extrinsic asthma is caused by :*

- a. *exercise*
- b. *allergy*
- c. *emotional factor*
- d. *thick mucous*

5. *In asthma , the respiratory airway is :*

- a. *wide*
- b. *relaxed*
- c. *narrow*
- d. *non*

6. *The anti-asthmatic drugs is always :*

- a. *single dose*
- b. *two drugs*
- c. *multi-therapy*
- d. *non*



7. Multi-drug regime allows :

- a. higher dose
- b. same dose
- c. smaller dose
- d. non

8. Multi-drug regime allows :

- a. dec. severity of side effect
- b. inc. severity of side effect
- c. same side effect
- d. non .

9. Various combination is used depending on :

- a. drug response
- b. patient response
- c. drug & patient response
- d. non

10. Anti-asthmatic drugs include :

- a. corticosteroids
- b. leukotriene receptor inhibitor
- c. mast cell stabilizers
- d. all

A- Corticosteroids

Corticosteroids, such as beclomethasone (Beclovent), flunisolide (AeroBid), and triamcinolone (Azmacort), are given by inhalation and act to decrease the inflammatory process in the airways of the patient with asthma. In addition, the corticosteroids increase the sensitivity of the B₂-receptors. With increased sensitivity of the B₂-receptors, the B₂-receptor agonist drugs are more effective.

B- Antiasthma Drugs: Leukotriene Receptor Antagonists and Leukotriene Formation Inhibitors

Leukotrienes are Broncho constrictive substances released by the body during the inflammatory process. When leukotriene production is inhibited, bronchodilation is facilitated. Zileuton acts by decreasing the formation of leukotrienes.

C-Antiasthma Drugs: Mast Cell Stabilizers

Mast cell stabilizers include cromolyn sodium (Intal) and nedocromil sodium (Tilade).

These drugs inhibit the release of substances that cause bronchoconstriction and inflammation from the mast cells in the respiratory



Uses of Anti Asthmatic Drugs

A- Corticosteroids

The corticosteroids are used in the management and prophylactic treatment of the inflammation associated with chronic asthma or allergic rhinitis.

B- Antiasthma Drugs: Leukotriene Receptor Antagonists and Leukotriene Formation Inhibitors

Zafirlukast and zileuton are used in the prophylaxis and treatment of chronic asthma in adults and children older than 12 years. **Montelukast** is used in the prophylaxis and treatment of chronic asthma in adults and in children older than 2 years.

C-Antiasthma Drugs: Mast Cell Stabilizers

The mast cell stabilizers are used in combination with other drugs in the treatment of asthma and other allergic disorders, including allergic rhinitis (nasal solution), and in the prevention of exercise-induced bronchospasm.

When the mast cell stabilizers are used in conjunction with other antiasthma drugs, a reduction in dosage of the drugs may be possible after using the

mast cell stabilizer for 3 or 4 weeks. These drugs may be given by nebulization, aerosol spray, or as an oral concentrate.

Side Effect, Contraindication and interaction of Anti Asthmatic Drug

A- Corticosteroids

When used to manage chronic asthma, the corticosteroids are most often given by inhalation. Adverse reactions to the corticosteroids are less likely to occur when the drugs are given by inhalation rather than taken orally.

Occasionally, patients may experience throat irritation causing hoarseness, cough, or fungal infection of the mouth and throat. Vertigo or headache also may occur.

The corticosteroids are contraindicated in patients with hypersensitivity to the corticosteroids, acute bronchospasm, status asthmatics, or other acute episodes of asthma. The corticosteroids are used cautiously in patients with compromised immune systems, glaucoma, kidney or liver



disease, convulsive disorders, or diabetes, those taking systemic corticosteroids, and during pregnancy and lactation. Ketoconazole may increase plasma levels of budesonide and fluticasone.

B- Antiasthma Drugs: Leukotriene Receptor Antagonists and Leukotriene Formation Inhibitors

Adverse reactions include headache, dizziness, myalgia, pain, nausea, diarrhea, abdominal pain, vomiting, and fever.

These drugs are contraindicated in patients with a known hypersensitivity to the drugs. And are not used in the reversal of bronchospasm in acute asthma attacks.

Administration of zafirlukast and aspirin increases plasma levels of zafirlukast, When zafirlukast is administered with warfarin, there is an increased effect of the anticoagulant. Administration of zafirlukast and theophylline or erythromycin may result in a decreased level of zafirlukast. Administration of montelukast with other drugs has not revealed any adverse responses.

Administration of montelukast with aspirin and NSAIDs is avoided in patients with known aspirin sensitivity. Administration of zileuton with propranolol increases the activity of the propranolol; with theophylline increases serum theophylline levels; and with warfarin may increase prothrombin time (PT). A prothrombin blood test should be done regularly in the event dosages of warfarin need to be decreased.

C-Antiasthma Drugs: Mast Cell Stabilizers

The more common adverse reactions associated with the mast cell stabilizers include headache, dizziness, nausea, fatigue, hypotension, or unpleasant taste in the mouth. These drugs may cause nasal or throat irritation when given intranasally or by inhalation. The mast cell stabilizers

are contraindicated in patients with known hypersensitivity to the drugs. The mast cell stabilizers are contraindicated in patients during attacks of acute asthma because they may worsen bronchospasm during the acute asthma attack.

It is important to use the mast cell stabilizers cautiously in patients with impaired renal or hepatic function and during pregnancy (Pregnancy Category B) and lactation. No significant drug interactions have been reported.



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Example of corticosteroid is :

- a . aminophylline
- b. salbutamol
- c. buclamethasone
- d. atenolol

2. Corticosteroids is used to :

- a. not affect inflammation
- b. dec. inflammatory process
- c. normal inflammation
- d. non

3. Corticosteroids increase the sensitivity of :

- a. B2 receptor to agonist
- b. B2 receptor to antagonist
- c. B1 receptor to agonist
- d. B1 receptor to antagonist

4. When corticosteroids is given by inhalation , its side effect is :

- a. normal occurring
- b. more likely to occur
- c. less likely to occur
- d. all

5. Example of leukotriene antagonist is :

- a. cromlyne sod.
- b. buclomethasone
- c. Montelukast
- d. salbutamol

6. Corticosteroids is cautiously used in patient with :

- a. glaucoma
- b. compromised immune sys.
- c. liver disease
- d. all

7. Leukotriene inhibitor drugs usually cause:

- a. bronchodilator
- b. Broncho spasm
- c. vasodilator
- d. vasospasm

8. Example of mast cell stabilizer drug is :

- a. Montelukast
- b. turbutaline
- c. zileuton
- d. neodocromil



9. Mast cell stabilizer is used with other anti-asthmatic drugs and lead to :

- a. inc. doses
- b. dec. the dose
- c. not affect the dose
- d. non

10. Mast cell stabilizers is used with other anti-asthmatic drugs for :

- a. one week
- b. 1-2 weeks
- c. 3-4 weeks
- d. 5-6 weeks

Drug act on the Cardiovascular System (Anti Hypertensive drug)

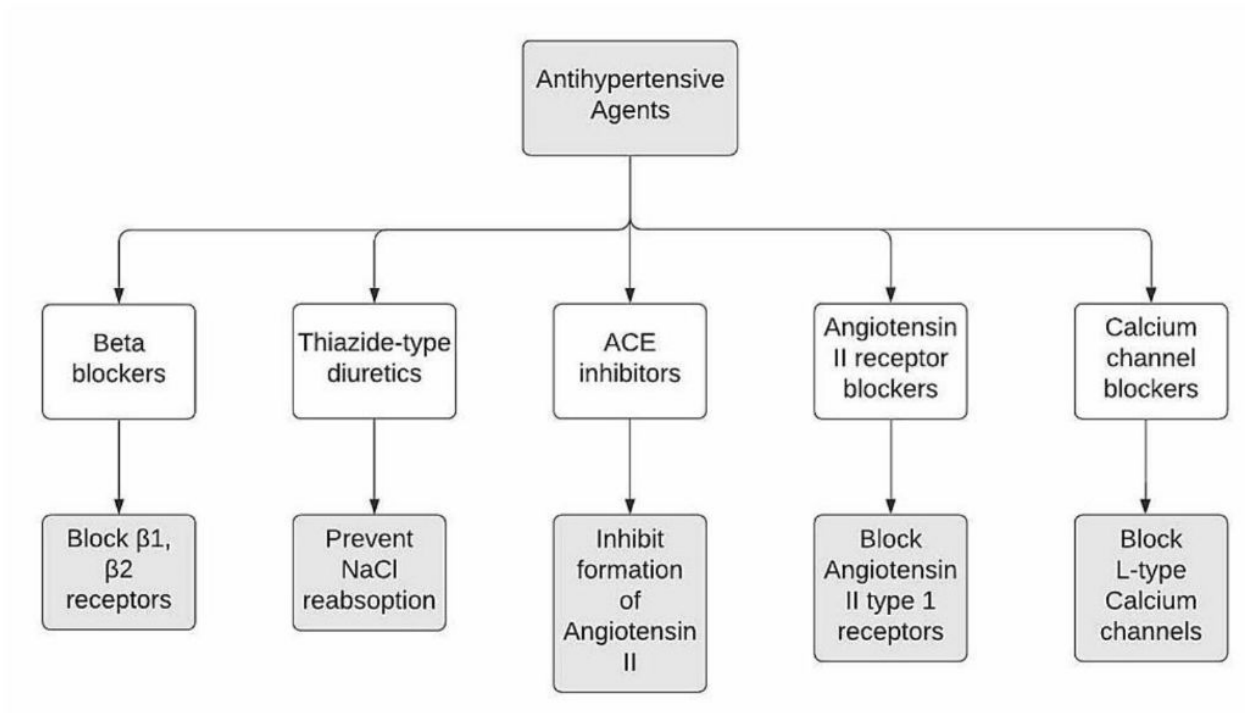


Introduction

It is very important for the student to study the drugs that affect the cardiovascular system, cause its an controlling system in the body, it have a great effect on the blood pressure, which is a rolling factor in all body activity, and the passage of blood to the body tissues, and consequently rolling oxygen supply to the body.

Hypertension is an elevation in the blood pressure, and serious disease and should be controlled and reach to the normal values.

Anti-hypertensive drugs are of different groups and different mechanisms of action.



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *Hypertension is defined as :*

- a. *systolic BP above 80*
- b. *systolic BP above 90*
- c. *systolic BP above 140*
- d. *systolic BP above 150*

2. *Essential hypertension is linked to :*

- a. *life style & diet*
- b. *kidney disease*
- c. *abn. In adrenal gland*
- d. *non*

3. *Examples of vaso-dilating drugs is :*

- a. *atenolol*
- b. *hydralazine*
- c. *doxazosine*
- d. *methyl dopa*

4. *Examples of selective B- adrenergic blocking drugs is :*

- a. *amilodipine*
- b. *propranolol*
- c. *atenolol*
- d. *captopril*

5. *Example of angiotensin converting enzyme inhibitor drugs :*

- a. *valsartan*
- b. *enalpril*
- c. *atenolol*
- d. *metaprolol*

6. *Example of cal. Channel blocking agent is :*

- a. *prazosin*
- b. *lisnopril*
- c. *chlorothiazide*
- d. *nifidipine*

7. Anti-hypertensive drug that acts as vaso-dilator is :

- a. adrenergic blocking b. cal. channel blockers
c. anti-adrenergic blocking d. all

8. Angiotensin converting enzyme inhibitor drug acts by inhibiting :

- a. ATPase b. aldosterone
c. ACE d. cyclo-oxygenase

9. In severe cases of hypertension , treatment is achieved by :

- a. single hypertensive agent b. diuretics only
c. combined hypertensive agents d. all

10. Diazoxide & nitropruside is given :

- a. orally b. IM
c. S C d. IV



Indicate the mechanism of action for Anti-hypertensive drugs:

Many antihypertensive drugs lower the blood pressure by dilating or increasing the size of the arterial blood vessels (vasodilatation). Vasodilatation creates an increase in the lumen (the space or opening within an artery) of the arterial blood vessels, which in turn increases the amount of space available for the blood to circulate. Because blood volume (the amount of blood) remains relatively constant, an increase in the space in which the blood circulates (i.e. the blood vessels) lowers the pressure of the fluid (measured as blood pressure) in the blood vessels

Antihypertensive drugs that have vasodilating activity include:

- Adrenergic blocking drugs
- Anti adrenergic blocking drugs
- Calcium channel blocking drugs
- Vasodilating drugs



Another type of antihypertensive drug is the diuretic, The mechanism by which the diuretics reduce elevated blood pressure is to their ability to increase the excretion of sodium from the body.

The mechanism of action of the ACE inhibitors is not fully understood. It is believed that these drugs may prevent (or inhibit) the activity of angiotensin-converting enzyme, which converts angiotensin I to angiotensin II, a powerful vasoconstrictor.

The uses of anti-hypertensive drugs

Antihypertensive are used in the treatment of hypertension. Some antihypertensive drugs are used only in severe cases of hypertension and when other less potent drugs have failed to lower the blood pressure. At times, two antihypertensive drugs may be given together to achieve a better response.

Diazoxide (Hyperstate IV) and nitroprusside (Nitropress) are examples of intravenous (IV) drugs that may be used to treat hypertensive emergencies.

Indicate the side effect , contraindication and drug interaction

When any antihypertensive drug is given, postural or orthostatic hypotension may be seen in some patients, especially early in therapy. Postural hypotension is the occurrence of dizziness and light-headedness when the individual rises suddenly from a lying or sitting position. Orthostatic hypotension occurs when the individual has been standing in one place for a long time. These reactions can be avoided or minimized by having the patient rise slowly from a lying or sitting position and by avoiding standing in one place for a prolonged period.

Antihypertensive drugs are contraindicated in patients with known hypersensitivity to the individual drugs.

When an antihypertensive is administered by a transdermal system (eg, clonidine), the system is contraindicated if the patient is allergic to any component of the adhesive layer of the transdermal system. Use of the angiotensin II receptor antagonists during the second and third trimester of pregnancy is contraindicated because use may cause fetal and neonatal injury or death.

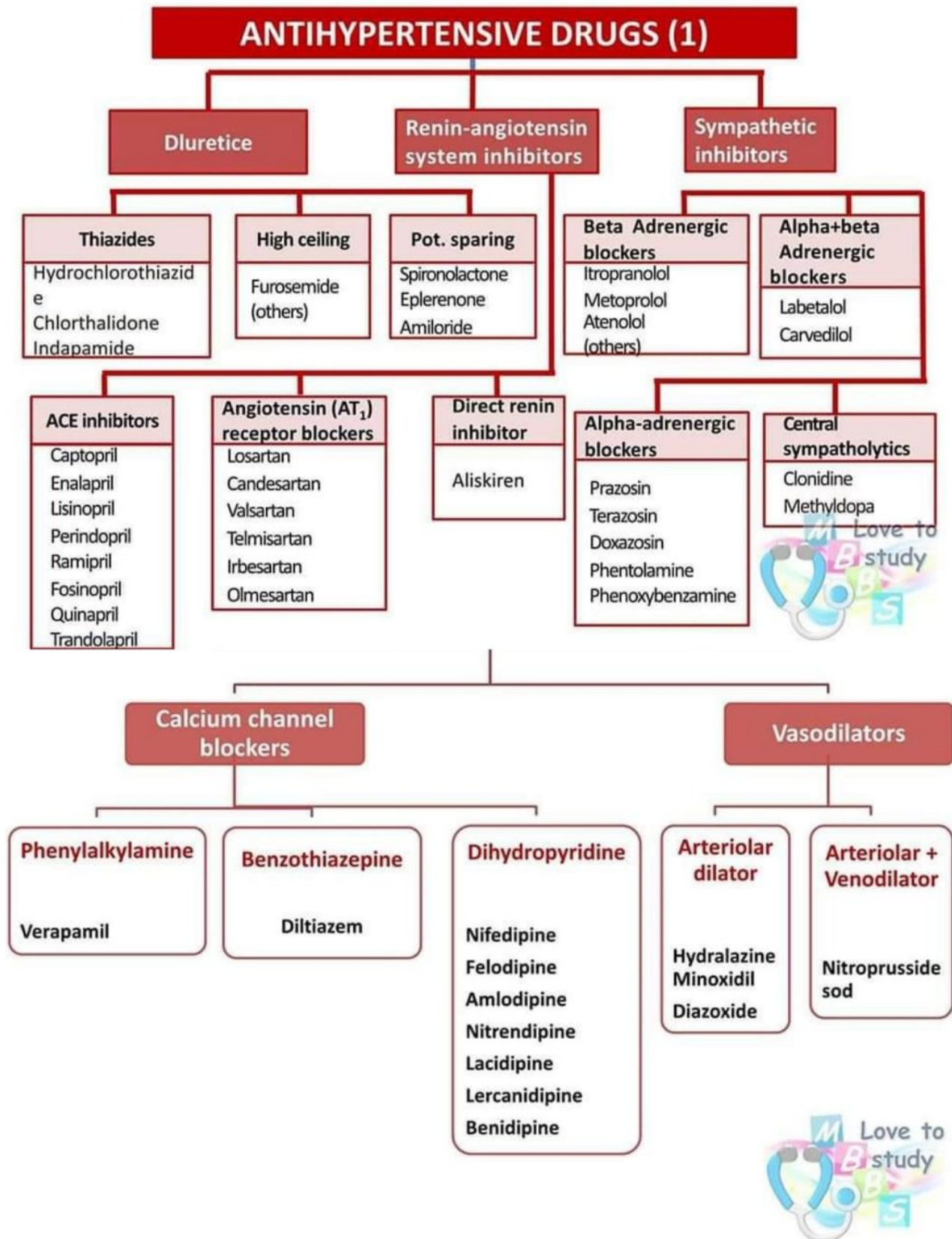
Antihypertensive drugs are used cautiously in patients with renal or hepatic impairment or electrolyte imbalances, during lactation and pregnancy, and in older patients. ACE inhibitors are used cautiously in patients with sodium depletion, hypovolemia, or coronary or cerebrovascular insufficiency and those receiving diuretic therapy or dialysis. The angiotensin II receptor agonists are used cautiously in patients with renal or hepatic dysfunction, hypovolemia, or volume or salt depletion, and patients receiving high doses of diuretics.

The hypotensive effects of most antihypertensive drugs are increased when administered with diuretics and other antihypertensive. Many drugs can interact with the antihypertensive drugs and decrease their effectiveness (e.g. antidepressants, monoamine oxidase inhibitors, antihistamines, and sympathomimetic bronchodilators). When the ACE inhibitors are administered with the NSAIDs, their antihypertensive effect may be decreased. Absorption of the ACE inhibitors may be decreased when administered with the antacids.

Administration of potassium-sparing diuretics or potassium supplements concurrently with the ACE inhibitors may cause hyperkalemia. When the angiotensin II receptor agonists are administered with NSAIDs or phenobarbital, their antihypertensive effects may be decreased



Cardiovascular Drugs



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *The common side effect of anti-hypertensive drug is :*
 - a . *postural hypotension*
 - b. *orthostatic hypotension*
 - c. *light headedness*
 - d. *all*

2. *Anti-hypertensive drugs is cautiously used in :*
 - a. *renal& hepatic failure*
 - b. *electrolyte imbalance*
 - c. *pregnancy & lactation*
 - d. *all*

3. *Anti-hypertensive effect is increased when given :*
 - a. *thiazide & pot. sparing*
 - b. *antihypertensive + NSAID*
 - c. *antihypertensive + diuretic*
 - d. *non*

4. *When using ACE inhibitor with NSAID s , the hypertension effect is :*
 - a. *increased*
 - b. *decreased*
 - c. *not affected*
 - d. *non*

5. *The dose of propranolol is :*
 - a. *80-240 mg/d*
 - b. *50-100 mg/d*
 - c. *20-40 mg/d*
 - d. *5-20 mg/d*

6. *The dose of clonidine is :*
 - a. *2-5 mg/d*
 - b. *10-20 mg/ d*
 - c. *0.1-0.8 mg/d*
 - d. *25-50 mg/d*

7. *The dose of captopril is :*
 - a. *5-10 mg/d*
 - b. *50-450 mg/d*
 - c. *10-20 mg/d*
 - d. *1-5 mg/ d*

8. The dose of enapril is :

- a. 20-50 mg/d b. 5-10 mg/d
c. 5-40 mg /d d. 50-100 mg/d

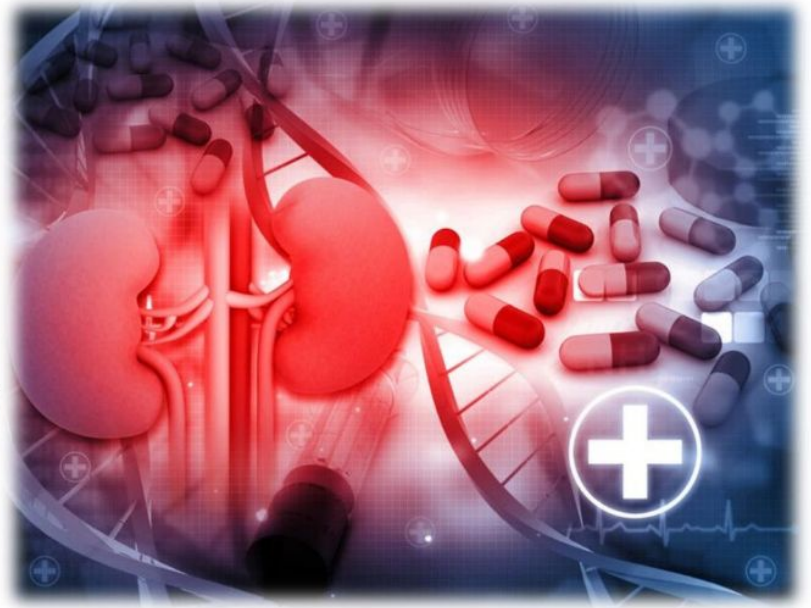
9. The dose of valsartan is :

- a. 50-100 mg/d b. 5-20 mg/d
c. 25-75 mg/d d. 80-160 mg/d

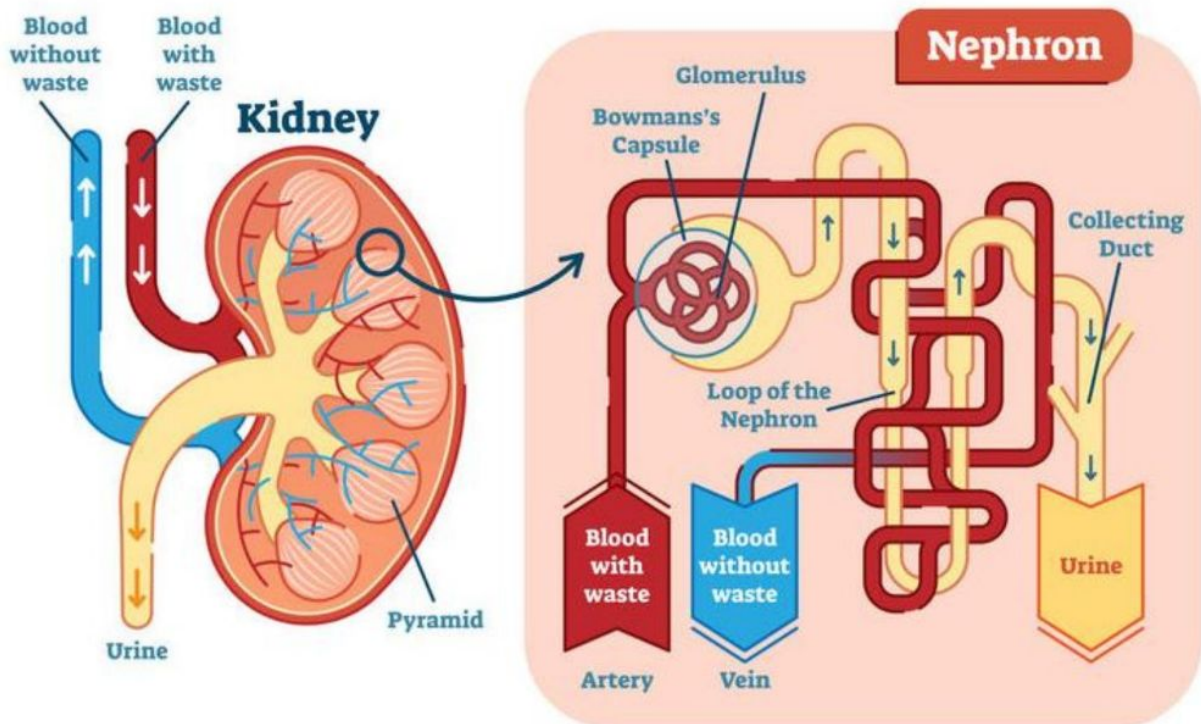
10. The dose of zestril is :

- a. 2-5 mg/d b. 50-100 mg/d
c. 10-40 mg/d d. 50-450 mg/d

(Diuretics) Part 2 Thiazide Potassium Sparing



Nephron Anatomy



6. Blocking the activity of aldosterone lead to :

- a. sod.& pot. reabsorption
- b. sod. & water excreted
- c. sod. only is excreted
- d. sod. ,pot . & water excreted

7. Amiloride is used in treatment of :

- a. CHF
- b. hypertension
- c. edema
- d. all

8. Triameterne is :

- a. weak diuretic
- b. strong diuretic
- c. medium diuretic
- d. non

9. Chlorothiazide is used for :

- a. hypertension
- b. heart failure
- c. epiplipsy
- d. asthma

10. Pot. Sparing diuretic cause :

- a. hypokalemia
- b. hyponiteremia
- c. hyperkalemia
- d. hypernitremia

Note: Check your answer on key answer page No.11

Diuretics

1- Thiazide diuretics

Thiazides and related diuretics inhibit the reabsorption of sodium and chloride ions in the ascending portion of the loop of Henle and the early distal tubule of the nephron. This action results in the excretion of sodium, chloride, and water.

Thiazide Diuretics

DRUGS THAT INCREASE URINE FLOW



2- Potassium sparing diuretics

Potassium-sparing diuretics work in either of two ways. Triamterene (Dyrenium) and amiloride (Midamor) depress the reabsorption of sodium in the kidney tubules, therefore increasing sodium and water excretion. Both drugs additionally depress the excretion of potassium and therefore are called potassium-sparing (or potassiumsaving) diuretics. Spironolactone (Aldactone), also a potassium-sparing diuretic, antagonizes the action of aldosterone. Aldosterone, a hormone produced by the adrenal cortex, enhances the reabsorption of sodium in the distal convoluted tubules of the kidney. When this activity of aldosterone is blocked, sodium (but not potassium) and water are excreted

MOA:

1- Thiazide diuretics

Acts in the distal convoluted tubule • Inhibit tubular resorption of sodium, chloride, and potassium ions •

Result: water, sodium, and chloride are excreted •

Potassium is also excreted to a lesser extent •

Diuretics

Mechanism of Action



Dilate the arterioles by direct relaxation •

Results:

Lowered peripheral vascular resistance •

Sodium, water, chloride and potassium are excreted

2- Potassium sparing diuretics

Interfere with sodium-potassium exchange in collecting ducts and convoluted tubules •

Competitively bind to aldosterone receptors •

Block the resorption of sodium and water •

Prevent potassium from being pumped into the tubule, thus preventing its secretion •

Competitively block the aldosterone receptors and inhibit its action •
Sodium and water are excreted

amiloride (Midamor) •

spironolactone (Aldactone) •

triamterene (Dyrenium)

Also known as aldosterone-inhibiting diuretics

The Medical uses of Diuretics drugs

1- Thiazide diuretics

Thiazides and related diuretics are used in the treatment of hypertension, edema caused by CHF, hepatic cirrhosis, corticosteroid and estrogen therapy, and renal dysfunction.

2- Potassium-Sparing Diuretics

spironolactone and triamterene:

Hyperaldosteronism •

Hypertension •

Reversing the potassium loss caused by potassium-losing drugs •

Certain cases of heart failure •

Liver failure •

Amiloride:(Midamor)

is used in the treatment of CHF and hypertension and is often used with a thiazide diuretic. Spironolactone and triamterene are also used in the treatment of hypertension and edema caused by CHF, cirrhosis, and the nephrotic syndrome. Amiloride, spironolactone, and triamterene are also available with hydrochlorothiazide, a thiazide diuretic that enhances the antihypertensive and diuretic effects of the drug

combination while still conserving potassium

Side Effect, Contraindication and Drug Interaction

1- Thiazide And Thiazide-like diuretics

S.E. For Hydrochlorothiazide (HCTZ), Indapamide and Chlorthalidone are:

- Hyponatremia
- Hypokalemia
- Hypotension
- Hyperglycemia
- Hyperlipidemia
- Hypercalcemia

Increase risk of acute gout.

Effectiveness reduced by NSAIDs.

Act at distal convoluted tubule.

2- Potassium sparing diuretics

S.E. For Amiloride :

- GI upset
- Hypotension
- Dizziness
- Hyperkalemia

Side effects uncommon at low doses.

Avoid with K-elevating drugs.

Increase digoxin/lithium toxicity.

Avoid in severe renal impairment.

Blocks epithelial sodium channels, inhibiting sodium reabsorption in the late distal convoluted tubules and collecting ducts.

Aldosterone antagonists

S.E. of Spironolactone and Eplerenone

- Hyperkalemia
- Gynecomastia
- Liver impairment
- Muscle weakness
- Electrolyte imbalance
- Nausea / vomiting
- Dry skin / rash
- Decreased libido
- Dehydration
- Menstrual disturbance

Competitively bind to aldosterone receptors to increase sodium and water excretion and promote potassium retention.

Can cause Stevens-Johnson syndrome.

Avoid with K-elevating drugs.(The potassium-sparing diuretics are contraindicated in patients with hyperkalemia and)

Avoid in Addison's disease, severe renal impairment and hyperkalemia.

The potassium-sparing diuretics are contraindicated in patients with known hypersensitivity to the drugs, serious electrolyte imbalances, significant renal impairment, and those receiving another potassium-sparing diuretic.

not recommended for children.



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Pot. Sparing diuretics is CI in :

- a. serious electrolyte imbalance b. medium
- c. mild d. non

2. The dose of spirenelactone is :

- a. 200 mg / d b. 10-20 mg / d
- c. up to 400 mg/ d d. 50-75 mg / d

3. Spirenelactone is used in :

- a. hypokalemia b. hyponitremia
- c. hypochloremia d. hypomagnesemia

4. The dose of triametrene is :

- a. 100-200 mg single dose b. 300 mg single dose
- c.100-200 mg divided dose d. 300 mg divided dose



5. Chlorothiazide dose in hypertension is :

- a. 25-100 mg/d b . 100-200 mg/d
- c. 5-10 mg/d d. 200-400 mg/d

6. Chlorothiazide is used in edema caused by :

- a. CHF b. liver cerrhosis
- c. corticostteroids therapy d. all

7. Spirinolactone antagonized aldosterone excreted by :

- a. adrenal medulla b. thyroid gland
- c. adrenal cortex d. pituitary gland

8. Pot. Sparing diuretics is CI in patient having :

- a. another pot. Spring diuretic b. acetazolamide
- c. thiazide diuretics d. non

9. Pot. Spring diuretics is :

- a. used in child b. safe in child
- c. not used in child d. non

10. The dose of amiloride is :

- a. 50-200 mg orally b. 50-200 mg SC
- c. 50-200 mg IM d. 50-200 mg IV

Note: Check your answer on key answer page No.11



Key Answer Page

Pre-test:

Question number	Right Answer
1	b
2	a
3	c
4	b
5	a
6	b
7	d
8	a
9	c
10	a

After doing the Pre - test:

1-If you got 9 or more, so congratulation to your effort and need to easily read the lecture.

2-If you got less than 9, so you need to deeply studying this lecture carefully.

Post-test:

Question number	Right Answer
1	a
2	c
3	a
4	d
5	a
6	d
7	c
8	a
9	c
10	a

After studying the third lecture and doing the post - test, so if you got:

1- 9 or more transit to study the fifth lecture.

2- Less than 9, so go over the study of the third lecture or any part of it, than do the post - test again.

Antiemetic

Nausea and Vomiting

Nausea And Vomiting

Nausea: is an uneasiness of the stomach that often comes before vomiting.

Vomiting: is the forcible voluntary or involuntary emptying ("throwing up") of stomach contents through the mouth.

Causes

Nausea and vomiting are not diseases, but they are symptoms of many conditions such as:

- 1) Motion sickness or seasickness
- 2) Early stages of pregnancy (nausea occurs in approximately 50%-90% of all pregnancies; vomiting in 25%-55%)
- 3) Medication-induced vomiting
- 4) Intense pain
- 5) Emotional stress (such as fear)
- 6) Gallbladder Diseases
- 7) Food Poisoning
- 8) Infections (such as the "stomach flu")
- 9) Overeating
- 10) A reaction to certain smells or odours
- 11) Heart Attack
- 12) Concussion or Brain injury
- 13) Brain Tumor
- 14) Ulcers
- 15) Some forms of cancer
- 16) Bulimia or other psychological illnesses

The causes of vomiting differ according to age. For children, it is common for vomiting to occur from a viral infections, food poisoning, milk allergy, motion sickness, overeating or feeding, coughing, or blocked intestines and illnesses in which the child has a high fever.

The timing of the nausea or vomiting can indicate the cause. When appearing shortly after a meal, nausea or vomiting may be caused by food poisoning, gastritis (inflammation of the stomach lining), an ulcer, or bulimia. Nausea or vomiting one to eight hours after a meal may also indicate food poisoning. However, certain food- borne bacteria, such as salmonella, can take longer to produce symptoms.

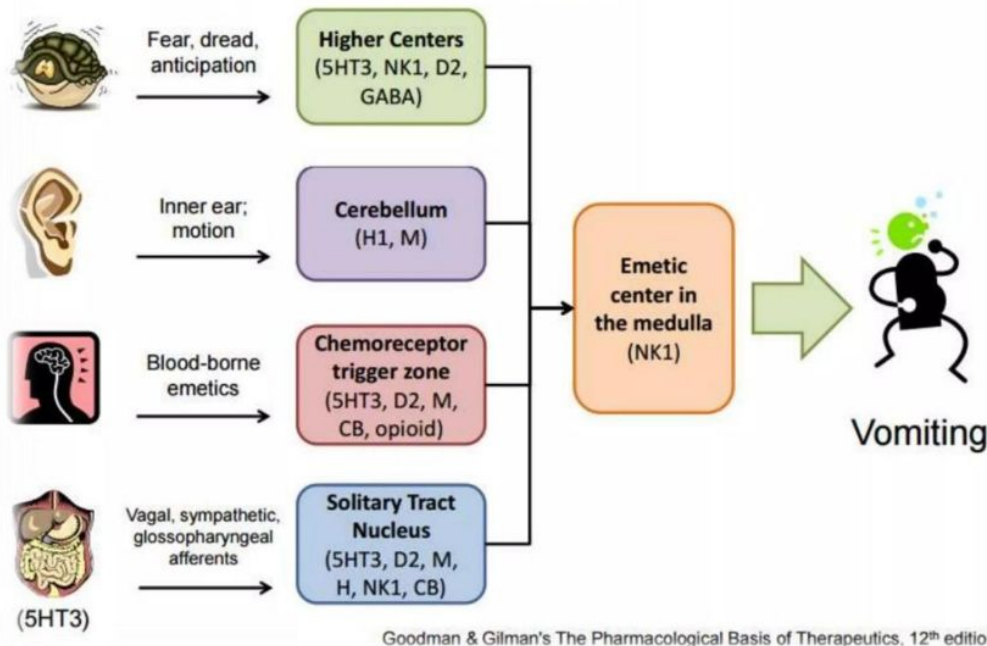
Pathophysiology

- There are four general pathways that are activated by specific triggers in the human body that go on to create the sensation of nausea and vomiting.
- Central Nervous System(CNS): Stimuli can affect areas of the CNS including the cerebral cortex and the limbic system. These areas are activated by elevated intracranial pressure, irritation of the meninges (i.e. blood or infection), and extreme emotional triggers such as anxiety. •

Chemoreceptor trigger zone (CTZ): The CTZ is located in the area postrema in the floor of the fourth ventricle within the brain. This area is outside the blood brain barrier, and is therefore readily exposed to substances circulating through the blood and cerebral spinal fluid. Common triggers of the CTZ include metabolic abnormalities, toxins, and medications. Activation of the CTZ is mediated by dopamine (D2) receptors, serotonin (5HT3) receptors, and neurokinin receptors (NK1).

- Vestibular System: This system is activated by disturbances to the vestibular apparatus in the inner ear. These include movements that cause motion sickness and dizziness. This pathway is triggered via histamine (H1) receptors and acetylcholine (ACh) receptors.

Pathophysiology Review



- **Peripheral Pathways:** These pathways are triggered via chemoreceptors and mechanoreceptors in the gastrointestinal tract, as well as other organs such as the heart and kidneys. Common activators of these pathways include toxins present in the gastrointestinal lumen and distension of the gastrointestinal lumen from blockage or dysmotility of the bowels. Signals from these pathways travel via multiple neural tracts including the vagus, glossopharyngeal, splanchnic, and sympathetic nerves.
- Signals from any of these pathways then travel to the brainstem, activating several structures including the nucleus of the solitary tract, the dorsal motor nucleus of the vagus, and central pattern generator. These structures go on to signal various downstream effects of nausea and vomiting.
- Autonomic effects involve increased salivation and the sensation of feeling faint that often occurs with nausea and vomiting.

Treatment

• If dehydration is present due to loss of fluids from severe vomiting, rehydration with oral electrolyte solutions is preferred. If this is not effective or possible, intravenous rehydration may be required. Medical care is recommended if: a person cannot keep any liquids down, has symptoms more than 2 days, is weak, has a fever, has stomach pain, vomits more two times in a day or does not urinate for more than 8 hours.

Medications

1- Benzamides

- Metoclopramide (Plasil)

It is a prokinetic drug that promotes GI. transit & gastric emptying.

MOA: on the GIT & CNS through Blocks dopamine receptors (D2) and serotonin receptors (5-HT antagonism & 5-HT4 agonism) in chemoreceptor trigger zone (CTZ) of CNS; and enhance sensitizes tissues to acetylcholine; increases peristalsis and emptying upper gut and accelerate evacuation; increases lower esophageal sphincter tone.



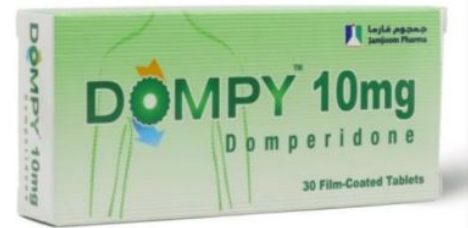
Adverse Effects: Sedation, Dizziness, Loose stool, Muscle dystonia, Galactorrhoea & Gynecomastia. □ **Uses:** Antiemetic, Gastrokinetic, Dyspepsia & Gastroesophageal reflux disease.

USES OF Metoclopramide :

- 1.G.E.R.D
- 2.Before endoscopy.
- 3.Before emergency surgery.
- 4.Anti emetic

2- Domperidone (Motillium)

MOA: It is a D2 antagonist, related chemically to Haloperidol & pharmacologically to Metoclopramide. Unlike other dopamine antagonists It crosses BBB very poorly, hence does not affect the CTZ. which minimizes central nervous system (CNS) side effects. Its prokinetic action is based on D2 antagonism in the upper GIT that works by blocking dopamine receptors in the gut. It increases the movement or contractions of the muscles in your stomach and intestines, increasing how quickly and easily food moves through your digestive tract. It also acts on the chemoreceptor trigger zone in your brain, which is involved in nausea and vomiting. This area of your brain is outside the blood-brain barrier.



Side Effects: Dry mouth, Rashes, Disorientation, Dizziness, fainting, irregular heartbeat, light-headedness

Drug & Dose: Motillium tab, 10mg, liq. 1mg/ml

3- Phenothiazine (Stemetil)

Phenothiazine derivatives, which include prochlorperazine (stemetil) ,

MOA: act at the CTZ by inhibiting dopaminergic transmission (antidopaminergic effect) Blocking dopamine receptor in the brain, blocking vegus nerve in GI tract that decrease vomiting caused by gastric irritants, suggesting that they inhibit stimulation of peripheral afferents. .

Side effect: Extra pyramidal, weakness, sedative, weight gain



4- Serotonin (5-HT₃) antagonists:

- Ondansetron (Zoferan)

MOA: selective 5-HT₃ receptor antagonist; binds to 5-HT₃ receptors both in periphery and in CNS, with primary effects in GI tract.

Has no effect on dopamine receptors and therefore does not cause extrapyramidal symptoms.

Side effect:

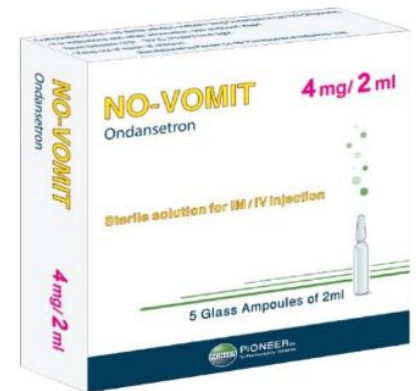
1-headache

2-fatigue

3-constipation

Clinical Use: CIV, Parkinson's disease, Alcoholism

Dosage: No-Vomit, tab. 4mg, 8mg, inj. 2mg/ml



5. Antihistamine

Most effective in motion sickness and inner ear dysfunction. Diphenhydramine, and meclizine hydrochloride are the antihistamines primarily used in the prevention of nausea .

Cinnarizine

It is an Anti vertigo or Antihistaminic drug, & also protective for motion sickness causing nausea & vomiting.

MOA: Probably by inhibiting influx of Ca²⁺ from endolymph into the vestibular sensory cells which mediates labyrinthine reflexes.

Contraindications: acute & chronic parkinsonism, drowsiness & blurred vision.

Side effect: include drowsiness, sweating, dry mouth, headache, skin problems, lethargy, gastrointestinal irritation



6-Corticosteroids as antiemetic drugs

by unknown mechanism of action (with respect to antiemetic effects) glucocorticoid receptors are widespread in the brain including, the hypothalamus and the cortex, which are all regions with inputs to the vomiting center. commonly used in combination with antagonists of serotonin(5-HT₃)for prevention of vomiting due to cancer chemotherapy.



7-Vitamin B-6 (Pyridoxine)

for morning sickness 10mg-25mg three times daily
And it is the best for vomiting in pregnancy.

The choice of antiemetic medication may be based on the situation during which the person experiences nausea.

- For people with motion sickness and vertigo, antihistamines and anticholinergics such as meclizine and scopolamine are particularly effective.
- Nausea and vomiting associated with migraine headaches respond best to dopamine antagonists such as metoclopramide, prochlorperazine and chlorpromazine.



- In cases of gastroenteritis, serotonin antagonists such as ondansetron were found to suppress nausea and vomiting, as well as reduce the need for IV fluid resuscitation.
- The combination of pyridoxine and doxylamine is the first line treatment for pregnancy-related nausea and vomiting.
- Dimenhydrinate is an inexpensive and effective over the counter medication for preventing postoperative nausea and vomiting. Other factors to consider when choosing an antiemetic medication include the person's preference, side-effect profile, and cost

Alternative medicine

- Cannabinoids may be effective for nausea and vomiting in the advanced stages of illnesses such as cancer (chemotherapy) and AIDS.

- Ginger has also been shown to be potentially effective in treating several types of nausea.



References:

- 1-Goodman LS , & Gilman A. The pharmacological basis of therapeutics, 11th edition, 2006 .
- 2-Drug Therapy; by Katzung BG and others, 2nd edition, Hall International Inc, 1995.
- 3-Basic And clinical pharmacology by Katzung G. Bertram, 10th edition, Lange Medical Publication, 2007 .



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- 5-Lecture Notes on Clinical Pharmacology, by John Reid and other, Blackwell Science Publications, 1995.



Drugs acting on the GIT (Gastrointestinal Tract) System

H2 Antagonist

Proton-Pump Inhibitors

Pre-Test:

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

- H2 antagonist drugs are blockers for :
 - delta receptor
 - beta receptor
 - .alpha receptor
 - histamine receptor
- H2 antagonist drugs acts by :
 - reduce HCl
 - reduce HCl & pepsin
 - increase HCl
 - non
- H2 antagonist drugs is used in the treatment of :
 - asthma
 - hypertension
 - peptic ulcer only
 - peptic & duodenal ulcer
- Examples of H2 antagonist drug is :
 - omeprazole
 - milk of magnesia
 - cimetidine
 - lansoprazole
- H2 antagonist drugs are used in :
 - erosive esophagitis only
 - .erosive esophagitis & GERD
 - H. pylori
 - non
- Proton pump inhibitor drugs acts by :
 - block acid production
 - increase acid secretion
 - not affect acid secretion
 - all
- Proton pump inhibitor drugs examples is :
 - cimetidine
 - famotidine
 - lansoprazole
 - lansoprazole & omeprazole
- Proton pump inhibitor drugs uses in :
 - duodenal ulcer
 - peptic & duodenal ulcer
 - peptic & duodenal ulcer with H. pylori
 - non
- Lansoprazole affect acid secretion in :
 - epithelial cells
 - fibrous cells
 - parietal cells
 - all
- Proton pump inhibitor drugs affect the enzyme :
 - carbonic anhydrase
 - ATPase
 - cyclo-oxygenase
 - non

Note: Check your answer on key answer page No.6



1-H₂ antagonists

These drugs inhibit the action of histamine at histamine H₂ receptor cells of the stomach, which then reduces the secretion of gastric acid and reduces total pepsin output. The decrease in acid allows the ulcerated areas to heal. Examples of histamine H₂ antagonists include cimetidine (Tagamet), famotidine (Pepcid), ranitidine (Zantac).

2-Proton pump inhibitors

The proton pump inhibitors suppress gastric acid secretion by blocking the final step in the production of gastric acid by the gastric mucosa.

The Medical uses of H₂ antagonist & proton pump inhibitor drugs

1-H₂ antagonists

These drugs are used for the medical treatment of a gastric or duodenal ulcer, gastric hypersecretory (excessive gastric secretion of hydrochloric acid) conditions, and GERD. These drugs may also be used as prophylaxis of stress-related ulcers and acute upper GI bleeding in critically ill patients.

2- Proton pump inhibitors

The proton pump inhibitors are used for treatment or symptomatic relief of various gastric disorders, including gastric and duodenal ulcers, GERD, or pathological hypersecretory conditions. Painful, persistent heartburn 2 or more days a week may indicate acid reflux disease, which can erode the delicate lining of the esophagus, causing erosive esophagitis. Esomeprazole (Nexium) or Omeprazole (Prilosec) may provide 24-hour relief from the heartburn associated with GERD or erosive esophagitis while healing occurs.

An important use of these drugs is combination therapy for the treatment of H. pylori in patients with duodenal ulcers. One treatment regimen used to treat infection with H. pylori is a triple-drug treatment regimen, such as one of the proton pump inhibitors (e.g., omeprazole or lansoprazole) and two anti-infective (e.g., amoxicillin and clarithromycin). Another treatment regimen includes bismuth subsalicylate plus two anti-infective drugs. Helidac, a treatment regimen of three drugs (bismuth subsalicylate, metronidazole, and tetracycline) may be given along with a histamine H₂ antagonist to treat disorders of the GI tract infected with H. pylori.



Indicate the side effect , contraindication and drug interaction

1-H₂ antagonist

Adverse reactions of the histamine H₂ antagonists include dizziness, somnolence, headache, confusion, hallucinations, diarrhea, and impotence (that is reversible when the drug is discontinued). Adverse reactions are

The histamine H₂ antagonists are contraindicated in patients with a known hypersensitivity to the drugs. These drugs are used cautiously in patients with renal or hepatic impairment and in the severely ill or debilitated patient. Cimetidine is used cautiously in patients with diabetes. The histamine H₂ antagonists are used cautiously in the older adult (causes confusion). A dosage reduction may be required. Histamine antagonists are Pregnancy Category B (cimetidine, famotidine, and ranitidine) drugs and should be used with caution during pregnancy and lactation.

There are many drug–drug interactions with the histamine H₂ antagonists. The following discussion does not cover all drugs that may interact with the H₂ antagonists but represents some of the more common interactions.

Antacids and metoclopramide may decrease absorption of the H₂ antagonists if administered concurrently.

Concurrent use of cimetidine and digoxin may decrease serum digoxin levels. There may be a decrease in white blood cell count when the H₂ antagonists are administered with the alkylating drugs or the antimetabolites. There is an increased risk of toxicity of oral anticoagulants, phenytoin, quinidine, lidocaine, or theophylline when administered with H₂ antagonists. Concurrent use of cimetidine and morphine increases the risk of respiratory

2-Proton pump inhibitors

The most common adverse reactions seen with the proton pump inhibitors include headache, diarrhea, and abdominal pain. Other less common adverse reactions include nausea, flatulence, constipation, and dry mouth.

The proton pump inhibitors are contraindicated in patients who have hypersensitivity to any of the drugs.

Omeprazole (Pregnancy Category C) and lansoprazole, rabeprazole, and pantoprazole (Pregnancy Category B) are contraindicated during pregnancy and lactation. The proton pump inhibitors are used cautiously in older adults and in patients with hepatic impairment. There is a decreased absorption of lansoprazole when it is administered with sucralfate. Lansoprazole may decrease the effects of ketoconazole, iron salts, and digoxin. When lansoprazole is administered with theophylline, there is an increase in theophylline clearance requiring dosage changes of the theophylline.



**Common trade name , Scientific name , with the Doses and the Dosage forms.
1-H₂ antagonist**

GENERIC NAME	TRADE NAME	DOSAGE RANGES
Cimetidine	Tagamet, Ulceran generic	300–2400 mg/d PO; 300 mg q6h IM, IV; 50 mg/h continuous IV infusion
Famotidine	Pepcid, Pepcid IV, generic	20–40 mg PO, IV as one dose or BID
Ranitidine	Zantac	150 mg PO BID or 300 mg PO HS; 50 mg q6–8h IM, IV (do not exceed 400 mg/d)

2-Proton pump inhibitors

GENERIC NAME	TRADE NAME	Uses	DOSAGE RANGES
Omeprazole	Prilosec	Duodenal ulcer, H.pylori eradication, hypersecretory conditions, gastric ulcer, erosive esophagitis, GERD,	20–40 mg/d PO; 60 mg/d up to 120 mg TID
Lansoprazole	Prevacid	=	15–30 mg/d PO
Pantoprazole sodium	Protonix	=	20-40 mg PO daily to BID up to 120 mg/d; IV, 80 mg; maximum dosage 240 mg/d
Esomeprazole	Nexium	=	20–40 mg/d PO
Rabeprazole sodium	Aciphex	=	20–60 mg/d



Post -Test:

Q1: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. H₂ antagonist drugs include :
 - a. cimetidine
 - b. ranitidine
 - c. famotidine
 - d. all

2. H₂ antagonist drugs is cautiously used in :
 - a. pregnancy
 - b. hepatic & renal failure
 - c. peptic ulcer
 - d. duodenal ulcer

3. Concurrent administration of cimetidine & digoxin :
 - a. inc. serum digoxin
 - b. not affect digoxin level
 - c. dec. serum digoxin
 - d. non

4. Concurrent administration of cimetidine & morphine :
 - a. inc. respiration
 - b. not affect respiration
 - c. dec. respiration
 - d. non

5. Dose of famotidine is :
 - a. 5-10 mg
 - b. 20-40 mg
 - c. 80-100 mg
 - d. 200-300 mg

6. The dose of cimetidine is :
 - a. 300-2400 mg
 - b. 1-3 g
 - c. 100-300 mg
 - d. 5-10 g

7. Proton pump inhibitors is used in combination in H. pylori with :
 - a. amoxicillin
 - b. clarithromycin
 - c. tetracycline
 - d. all

8. Lansoprazole affect theophylline clearance and need to :
 - a. dec. the dose
 - b. no need to change the dose
 - c. non
 - d. inc. the dose

9. The dose of lansoprazole is :
 - a. 15-30 mg /d
 - b. 50-100 mg/d
 - c. 70-150 mg / d
 - d. 2.5-5 mg/d

10. The dose of omeprazole is :
 - a. 100-200 mg/d
 - b. 50-100 mg/d
 - c. 20-40 mg/d
 - d. 200-400 mg/d

Note: Check your answer on key answer page No.6



Key Answer Page

Question number	Right Answer
1	d
2	b
3	d
4	c
5	b
6	a
7	d
8	c
9	c
10	b

After doing the Pre - test:

1-If you got 9 or more, so congratulation to your effort and need to transition to the second lecture.

2-If you got less than 9, so you need to continue studying this lecture carefully.

Post – test:

Question number	Right Answer
1	d
2	b
3	c
4	a
5	b
6	a
7	d
8	d
9	a
10	c

After studying the first lecture and doing the post – test, so if you got:

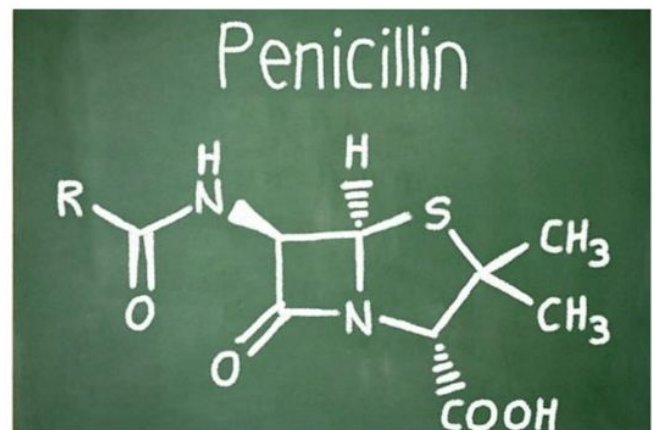
1- 9 or more transit to study the second lecture.

2- Less than 9, so go over the study of the first lecture or any part of it, than do the post – test again.

References:

- 1-Goodman LS , & Gilman A. The pharmacological basis of therapeutics, 11th edition, 2006 .
- 2-Drug Therapy; by Katzung BG and others, 2nd edition, Hall International Inc, 1995.
- 3-Basic And clinical pharmacology by Katzung G. Bertram, 10th edition, Lange Medical Publication, 2007 .
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- 5-Lecture Notes on Clinical Pharmacology, by John Reid and other, Blackwell Science Publications, 1995.

Antibiotics (Penicillin)



Introduction

It is very important for the student to study the drugs that affect bacterial growth in the body . The development of the sulfonamide antibiotics was a breakthrough in the treatment of bacterial infections. Since that time. The antibacterial properties of natural penicillin's were discovered in 1928 by Alexander Fleming while he was performing research on influenza.

There are two groups of penicillin:

1- natural penicillin

2- semisynthetic penicillin include:

A- penicillinase-resistant penicillin (Antistaphylococcal penicillin)

B - amino penicillin

C - and the extended-spectrum penicillin.





Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Penicillin is discover in :

- a. 1910
- b. 1900
- c. 1928
- d. 1945

2. The groups of penicillin's are :

- a. natural
- b. amino-penicillin
- c. extended -spectrum
- d. all

3. Penicillinase resistant is the ability of the bacteria to :

- a. synthesis of pen.
- b. destroy pen.
- c. multiply
- d. non

4. The enzyme that idistroyed by the bacteria in resistance is

- a. cyclo-oxygenase
- b. oxidase
- c. penicillinase
- d. ATPase

5. Penicillin is :

- a. bacteriocidal
- b. bacteriostatic
- c. both
- d . non

6. Penicillin affect :

- a. cell-wall synthesis
- b. RNA synthesis
- c. DNA synthesis
- d. non

7. Bactericidal means :

- a. retard multiplication
- b. destroy bacteria
- c. fast multiplication
- d. all

8. Example of natural penicillin is :

- a. pen . G
- b. ampicillin
- c. amoxicillin
- d. cloxacillin

9. Example of aminopenicillin is :

- a. ampicillin
- b. cloxacillin
- c. amoxicillin
- d. pen.G

10. Procaine penicillin is composed of :

- a. amp.+procaine
- b. amo.+procain
- c. clo.+ procaine
- d. pen.G + procaine

Action of antibiotics " penicillin "

Penicillin is an antibiotic used to treat certain types of bacterial infections, such as pneumonia, meningitis, or strep throat.

Penicillin are antibiotics that belong to a larger family of drugs known as beta-lactam antibiotics.

Penicillin have the same type of action against bacteria. Penicillin prevent bacteria from using a substance that is necessary for the maintenance of the bacteria's outer cell wall. Unable to use this substance for cell wall maintenance, the bacteria swell, rupture, assume unusual shapes, and finally die. penicillin may be bactericidal



(destroy bacteria) or bacteriostatic (slow or retard the multiplication of bacteria). They are bactericidal against sensitive microorganisms (i.e., those microorganisms that will be affected by penicillin) provided there is an adequate concentration of penicillin in the body. An adequate concentration of any drug in the body is referred to as the blood level. An inadequate concentration or inadequate blood level) of penicillin may produce bacteriostatic activity, which may or may not control the infection.

Penicillin may be administered by mouth or by injection. When given by injection, it may be administered intravenously (IV, into a vein), or intramuscularly (IM, in a large muscle).

MOA

Penicillin work by binding to molecules on the walls of bacteria called peptidoglycan. When the bacteria divide, penicillin prevents proteins in the cell wall from reassembling properly, causing the bacterial cell to rupture and quickly die.

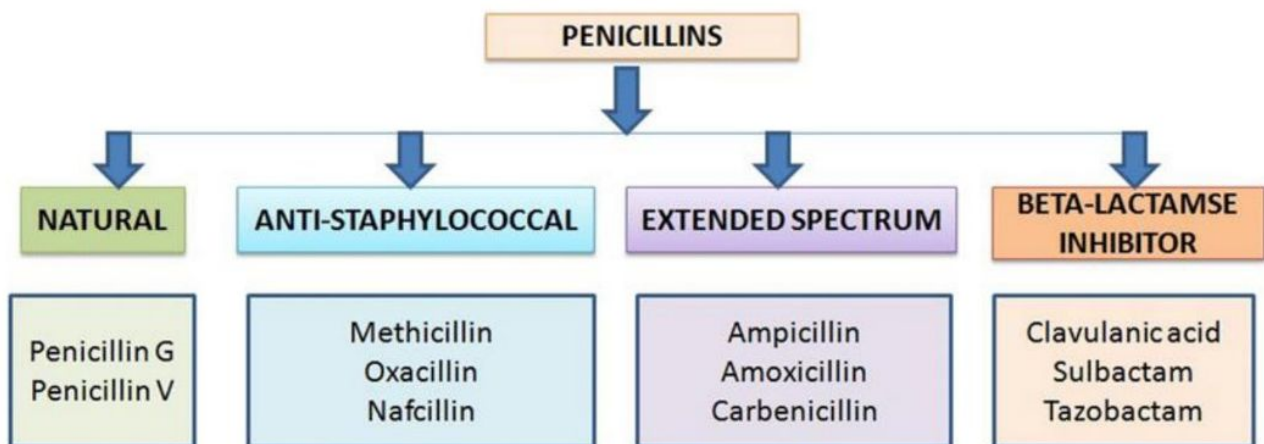
Natural penicillin

There are two natural penicillin.

Semisynthetic penicillin

There are four classes of semisynthetic penicillin, including commonly prescribed antibiotics like amoxicillin

Natural	Semisynthetic
Penicillin G (benzylpenicillin)	Aminopenicillins (ampicillin, amoxicillin, and hetacillin)
Penicillin V (phenoxymethylpenicillin)	Antistaphylococcal penicillin (cloxacillin, dicloxacillin, nafcillin, and oxacillin)
	Broad-spectrum penicillins (carbenicillin, mezlocillin, piperacillin, ticarcillin)
	Beta-lactamase inhibitor (clavulanic acid)



The uses of penicillin

Infectious Disease

The natural and semi synthetic penicillin are used in the treatment of bacterial infections due to susceptible microorganisms. Penicillin may be used to treat infections such as **urinary tract infections, septicemia, meningitis, intra-abdominal infection, gonorrhea, syphilis, pneumonia, and other respiratory infections.**

Examples of infectious microorganisms (bacteria) that may respond to penicillin therapy include **gonococci, staphylococci, streptococci, and pneumococci.**

Culture and sensitivity tests are performed whenever possible to determine which penicillin will best control an infection caused by a specific strain of bacteria. A penicillinase-resistant penicillin is used as initial therapy for any suspected staphylococcal infection until culture and sensitivity results are known.

Prophylaxis

Penicillin is of no value in the treatment of viral or fungal infections. However, the primary health care provider occasionally will prescribe penicillin as prophylaxis (prevention) against a potential secondary bacterial infection that can occur in a patient with a viral infection. In these situations the viral infection has weakened the body's defenses and the person is susceptible to other infections, particularly a bacterial infection.

Penicillin also may be prescribed as prophylaxis for a potential infection in high-risk individuals, such as those with a history of rheumatic fever. Penicillin is taken several hours or, in some instances days, before and after an operative procedure, such as dental, oral, or upper respiratory tract procedures that can result in bacteria entering the bloodstream. Taking penicillin before and after the procedure will usually prevent a bacterial



infection in these high-risk patients. Penicillin also may be given prophylactically on a continuing basis to those with rheumatic fever and chronic ear infections.

Possible uses	Amoxicillin	Penicillin
mild to moderate upper respiratory tract infections*	x	x
mild skin infections	x	x
scarlet fever		x
tooth infections	x	x
urinary tract infections	x	
ulcers	x	

Indicate the side effect, contraindication and drug interaction

Common adverse reactions include **mild nausea, vomiting, diarrhea, sore tongue or mouth, fever, and pain at injection site**. Penicillin can stimulate a hypersensitivity (allergic) reaction within the body. Another adverse reaction that may be seen with penicillin, as well as with almost all antibiotics, is a **superinfection** (a secondary infection that occurs during antibiotic treatment).

Hypersensitivity Reactions

A hypersensitivity (or allergic) reaction to a drug occurs in some individuals, especially those with a history of allergy to many substances. Signs and symptoms of a hypersensitivity to penicillin are highlighted in Display 7-3.

Anaphylactic shock, which is a severe form of hypersensitivity reaction, also can occur. Anaphylactic shock occurs more frequently after parenteral administration but can occur with oral use. This reaction is likely to be immediate and severe in susceptible individuals. Signs of anaphylactic shock include severe hypotension, loss of consciousness, and acute respiratory distress. If not immediately treated, anaphylactic shock can be fatal. Once an individual is allergic to one penicillin, he or she is most likely allergic to all of the penicillin. Those allergic to penicillin also have a higher incidence of allergy to the cephalosporin. Allergy to drugs in the same or related groups is called cross-sensitivity or cross-allergenicity.



Superinfections

Antibiotics can disrupt the normal flora (nonpathogenic microorganisms within the body) causing a superinfection. The destruction of large numbers of nonpathogenic bacteria (normal flora) by the antibiotic alters the chemical environment. This allows uncontrolled growth of bacteria or fungal microorganisms, which are not affected by the antibiotic being administered.

CANDIDIASIS OR MONILIASIS

Another type of superinfection may occur due to an overgrowth of the yeast like fungi that usually exist in small numbers in the vagina. The multiplication rate of these microorganisms is normally slowed and kept under control because of the presence of a strain of bacteria bacillus in the vagina. If penicillin therapy destroys these normal microorganisms of the vagina bacillus, the fungi are now uncontrolled, multiply at a rapid rate, and cause symptoms of a fungal infection called candidiasis (or moniliasis). Symptoms include vaginal itching and discharge.

Other Adverse Reactions

Other adverse reactions associated with penicillin are hematopoietic changes such as anemia, thrombocytopenia (low platelet count), leukopenia (low white blood cell count), and bone marrow depression. When penicillin is given orally, glossitis (inflammation of the tongue), stomatitis (inflammation of the mouth), dry mouth, gastritis, nausea, vomiting, and abdominal pain occur. When penicillin is given intramuscularly (IM),

there may be pain at the injection site. Irritation of the vein and phlebitis (inflammation of a vein) may occur with intravenous (IV) administration.

Penicillin are contraindicated in patients with a history of hypersensitivity to penicillin or the cephalosporin.

Penicillin should be used cautiously in patients with renal disease, pregnancy, lactation (may cause diarrhea or candidiasis in the infant), and in those with a history of allergies. Any indication of sensitivity is reason for



caution. The drug is also used with caution in patients with asthma, renal disease, bleeding disorders, and gastrointestinal disease.

Some penicillin (ampicillin, bacampicillin, penicillin V) may interfere with the effectiveness of birth control pills that contain estrogen. There is a decreased effectiveness of the penicillin when it is administered with the tetracycline. Large doses of penicillin can increase bleeding risks of patients taking anticoagulant agents. Some reports indicate that when oral penicillin are administered with beta-adrenergic blocking drugs, the patient may be at increased risk for an anaphylactic reaction. Absorption of most penicillin is affected by food. In general, penicillin should be given 1 hour before or 2 hours after meals.

Common side effects	Amoxicillin	Penicillin
mild skin rash	x	x
stomach upset	x	x
nausea		x
vomiting	x	x
diarrhea	x	x
black, hairy tongue	x	x

Drugs that may cause interactions	Amoxicillin	Penicillin
methotrexate	x	x
allopurinol	x	
probenecid	x	x
warfarin	x	x
birth control pills	x	x
mycophenolate	x	x
other antibiotics	x	x



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Penicillin is used in :

- a. UTI
- b. septicemia
- c. syphilis
- d. all

2. The common side effect of penicillin is :

- a. CVS effect
- b. CNS effect
- c. hypersensitivity
- d. asthma

3. Anaphylactic shock occurs in :

- a. oral use
- b. parenteral use
- c. SC use
- d. non

4. The penicillin allergic patient also shows allergy to :

- a. cephalosporin
- b. ciprofloxacin
- c. tetracycline
- d. aminoglycosides

5. Pen. Is used cautiously in :

- a. renal & hepatic failure
- b. pregnancy & lactation
- c. allergy
- d. all

6. The dose of pen . G is :

- a. 250-500 mg
- b. 50-100 mg
- c. 20-30 mg IV
- d. 200-250 mg

7. The dose of ampicillin is :

- a. 250-500 mg/4 times
- b. 20-50 mg/4 times
- c. 100-200 mg/4 times
- d. 400-800 mg / 4 times

8. Example of extended -spectrum pen. Is :

- a. ampicillin
- b. mezlocillin
- c. pen.G
- d. cloxacillin

9. The dose oxacillin is :

- a. 200-250mg/4 times
- b. 10-30 mg/4 times
- c. 0.5-1 gm/ 4 times
- d. 100-150 mg/4 times

10. The dose of piperacillin is :

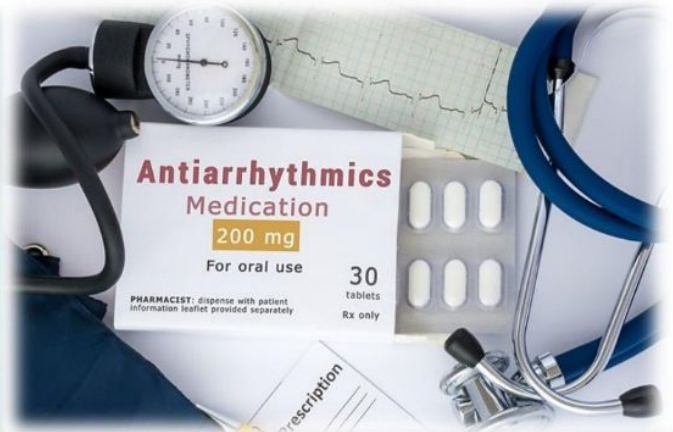
- a. 80-120 mg
- b. 3-4 gm
- c. 200-300 mg
- d. 10-15 mg



Drug acting on the Cardiovascular System



(Anti-arrhythmic Drugs)
(Cardio tonic Drugs)



Introduction

It is very important for the student to study the drugs that affect the cardiovascular system , A cardiac arrhythmia is a disturbance or irregularity in the heart rate, rhythm, or both, which requires administration of one of the antiarrhythmic drugs. An arrhythmia may occur as a result of heart disease or from a disorder that affects cardiovascular function.

Conditions such as emotional stress, hypoxia, and electrolyte imbalance also may trigger an arrhythmia.

The cardio tonics are drugs used to increase the efficiency and improve the contraction of the heart muscle, which leads to improved blood flow to all tissues of the body. The drugs have long been used to treat congestive heart failure (CHF), a condition in which the heart cannot pump enough blood to meet the tissue needs of the body.



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Cardiac arrhythmias is a disturbances in :
a. heart rate
b. heart rhythm
c. heart rate & rhythm
d. non
2. arrhythmias may be resulted from :
a. disorder in heart
b. disorder in the vessels
c. disorder in CVS
d. non
3. Factors that may trigger arrhythmias are :
a. emotional stress
b. hypoxia
c. electrolyte imbalance
d. all
4. Cardiac arrhythmias may be caused by the generation of :
a. normal no. of stimuli
b. abnormal no. of impulses
c. abnormal beat
d. non
5. Example of class I A anti-arrhythmic drug is :
a. propafenone
b. lidocaine
c. propranolol
d. procainamide
6. Example of class II anti-arrhythmic drug is :
a. amlodipine
b. acebutolol
c. lidocaine
d. rythmol
7. Example of class IV anti-arrhythmic drug is :
a. lidocaine
b. propranolol
c. amiodarone
d. verapamil
8. Heart failure may be caused by :
a. ischemic heart disease
b. hypertension
c. hyperthyroidism
d. all
9. Orthopnea is :
a. normal breathing
b. difficulty in breathing
c. stop breathing
d. non
10. The condition that lead to heart failure is :
a. stimulation of ventricles
b. impairment of ventricles
c. impairment of auricular
d. non



Mechanism of action of anti-arrhythmic & cardio tonics drugs:

1 - Anti-arrhythmic drugs

The cardiac muscle (myocardium) has attributes of both nerve and muscle and therefore has the properties of both.

Some cardiac arrhythmias are caused by the generation of an abnormal number of electrical impulses (stimuli).

These abnormal impulses may come from the sinoatrial node or may be generated in other areas of the myocardium.

Class I Antiarrhythmic Drugs

Class I anti arrhythmic drugs, such as moricizine, have a membrane-stabilizing or anesthetic effect on the cells of the myocardium, making them valuable in treating cardiac arrhythmias. Class I antiarrhythmic drugs contain the largest number of drugs of the four classifications. Because the actions differ slightly, they are subdivided into classes Ia, Ib, and Ic.

Class Ia

The drugs **disopyramide**, **procainamide**, and **quinidine** are examples of class Ia drugs.

Class Ib Drugs

Lidocaine (Xylocaine), the representative class Ib drug.

Class Ic Drugs

Flecainide (Tambocor) and **propafenone** (Rythmol) are examples of class Ic drugs.

Class II Antiarrhythmic Drugs

Class II antiarrhythmic drugs include beta (B)-adrenergic blocking drugs, such as **acebutolol** (Sectral), **esmolol** (Brevibloc), and **propranolol** (Inderal). These drugs also decrease myocardial response to epinephrine and norepinephrine (adrenergic neurohormones) because of their ability to block stimulation of B receptors of the heart.

Class III Antiarrhythmic Drugs

Bretylium (Bretylol) , **Amiodarone** (Cordarone)

Class IV Antiarrhythmic Drugs

Class IV antiarrhythmic drugs include **verapamil** (Calan) and the other calcium channel blockers. Calcium channel blockers produce their antiarrhythmic action by inhibiting the movement of calcium through channels across the myocardial cell membranes and vascular smooth muscle.

2-Cardiotonic drugs

Digitalis acts in two ways:

1. Increases cardiac output through positive inotropic activity
2. Decreases the conduction velocity through the atrioventricular (AV) and sinoatrial (SA) nodes in the heart



The uses of anti- arrhythmic & cardio tonics drugs:

1 - Anti-arrythmic drugs

The goal of anti arrhythmic drug therapy is to restore normal cardiac function and to prevent life-threatening arrhythmias.

2-Cardiotonic drugs

Digoxin (Lanoxin) is the most commonly used cardio tonic drug. Other terms used to identify the cardio tonics are cardiac glycosides or digitalis glycosides.

The digitalis or cardiac glycosides are obtained from the leaves of the purple foxglove plant or the *Digitalis purpurea* and the *Digitalis lanata*.

Miscellaneous drugs with positive inotropic action such as **inamrinone** and **milrinone** (Primacor) are **nonglycosides** used



Indicate the side effect , contraindication and drug interaction

1- Anti-arrhythmic drugs

The antiarrhythmic drugs are reserved for emergency situations and are contraindicated in patients with known hypersensitivity to the antiarrhythmic drugs and during pregnancy and lactation. Antiarrhythmic drugs are contraindicated in patients with second- or third-degree AV block (if the patient has no artificial pacemaker), severe congestive heart failure (CHF), aortic stenosis, hypotension, and cardiogenic

shock. Quinidine and procainamide are contraindicated in patients with myasthenia gravis .All antiarrhythmic drugs are used cautiously in patients with renal or hepatic disease. When renal or hepatic dysfunction is present, a dosage reduction may be necessary. All patients should be observed for renal and hepatic dysfunction. Quinidine and procainamide are used cautiously in patients with CHF. Disopyramide is used cautiously in patients with CHF, myasthenia gravis, or glaucoma, and in men with prostate enlargement. When two antiarrhythmic drugs are administered concurrently the patient may experience additive effects and is at increased risk for drug toxicity. When quinidine and procainamide are administered with digitalis, the risk of digitalis toxicity is increased.



2-Cardiotonic drugs

The cardio tonics are contraindicated in patients with **known hypersensitivity, ventricular failure, ventricular tachycardia, or AV block.**

The cardio tonics are given cautiously in patients with electrolyte imbalance (especially hypokalemia, hypocalcemia, and hypomagnesemia), severe carditis, heart block, myocardial infarction, severe pulmonary disease, acute glomerulonephritis, and impaired renal or hepatic function.

The cardio tonics react with many different drugs. Drugs that may increase plasma digitalis levels leading to toxicity include amiodarone, benzodiazepines, cyclosporine, diphenoxylate, indomethacin, itraconazole, macrolides (erythromycin, clarithromycin), propafenone, quinidine, quinine, spironolactone, tetracyclines, and verapamil. Drugs that may decrease plasma digitalis levels include the oral aminoglycosides, antacids, antineoplastics (bleomycin, carmustine, cyclophosphamide, methotrexate, and vincristine), activated charcoal, cholestyramine, colestipol, kaolin/pectin, neomycin, penicillamine, rifampin and sulfasalazine.

The thyroid hormones may decrease the effectiveness of digitalis glycosides, requiring a larger dosage of digoxin. Thiazide and loop diuretics may increase diuretic induced electrolyte disturbances, predisposing the patient to digitalis-induced arrhythmias.



Class	Known as	Examples	Mechanism	Medical uses ¹
Ia	Fast Na channel blockers	<ul style="list-style-type: none"> • <u>Aimaline</u> • <u>Disopyramide</u> • <u>Procainamide</u> • <u>Quinidine</u> • <u>Sparteine</u> 	<p><u>Na⁺ channel</u> block (intermediate association/dissociation) and K⁺ channel blocking effect.</p> <p>Class 1a prolongs the action potential and has an intermediate effect on the 0 phase of depolarization</p>	<ul style="list-style-type: none"> • Increase QT interval • Prevent paroxysmal recurrent <u>atrial fibrillation</u> triggered by <u>vagal</u> overactivity • Treat ventricular <u>arrhythmia</u> • Treat <u>Wolff-Parkinson-White syndrome</u> (procainamide)
Ib		<ul style="list-style-type: none"> • <u>Lidocaine</u> • <u>Mexiletine</u> • <u>Phenytoin</u> • <u>Tocainide</u> 	<p><u>Na⁺ channel</u> block (fast association/dissociation).</p> <p>Class 1b shorten the action potential of myocardial cell and has a weak effect on the initiation of phase 0 of depolarization</p>	<ul style="list-style-type: none"> • Treat and prevent ventricular <u>arrhythmia</u> during and immediately after <u>myocardial infarction</u>, though this is now discouraged given the increased risk of <u>asystole</u>
Ic		<ul style="list-style-type: none"> • <u>Encainide</u> • <u>Flecainide</u> • <u>Moricizine</u> • <u>Propafenone</u> 	<p><u>Na⁺ channel</u> block (slow association/dissociation).</p> <p>Class 1c do not affect action potential duration and has the strongest effect on the initiation phase 0 of depolarization</p>	<ul style="list-style-type: none"> • Contraindicated immediately after myocardial infarction • Prevent paroxysmal <u>atrial fibrillation</u> • Treat recurrent <u>tachycardia</u> associated with abnormal <u>conduction pathways</u>, such as <u>Wolff-Parkinson-White syndrome</u>
II	Beta-blockers	<ul style="list-style-type: none"> • <u>Atenolol</u> • <u>Bisoprolol</u> • <u>Carvedilol</u> • <u>Esmolol</u> • <u>Metoprolol</u> • <u>Nebivolol</u> • <u>Propranolol</u> • <u>Timolol</u> 	<p><u>Beta blocker</u></p> <p>Propranolol also has some sodium channel-blocking effects.</p>	<ul style="list-style-type: none"> • Decrease mortality in patients with <u>myocardial infarction</u> • Prevent recurrence of <u>tachycardia</u>
III	Potassium channel blockers	<ul style="list-style-type: none"> • <u>Amiodarone</u> • <u>Dofetilide</u> • <u>Dronedarone</u> • <u>E-4031</u> • <u>Ibutilide</u> • <u>Sotalol</u> • <u>Vernakalant</u> 	<p><u>K⁺ channel</u> blocker</p> <p><u>Sotalol</u> is also a <u>beta blocker</u>⁶¹ <u>Amiodarone</u> has Class III mostly, but also I, II, & IV activity</p>	<ul style="list-style-type: none"> • Prevent paroxysmal atrial fibrillation⁷² and haemodynamically stable ventricular tachycardia⁸¹ (amiodarone) • Treat <u>atrial flutter</u> and atrial fibrillation (ibutilide) • Treat <u>ventricular tachycardia</u> and <u>atrial fibrillation</u> (sotalol) • Treat <u>Wolff-Parkinson-White syndrome</u>

IV	Calcium channel blockers	<ul style="list-style-type: none"> • <u>Diltiazem</u> • <u>Verapamil</u> 	<u>Ca²⁺ channel blocker</u>	<ul style="list-style-type: none"> • Prevent recurrence of <u>paroxysmal supraventricular tachycardia</u> • Reduce <u>ventricular rate</u> in patients with <u>atrial fibrillation</u>
V		<ul style="list-style-type: none"> • <u>Adenosine</u> • <u>Digoxin</u> • <u>Magnesium sulfate</u> 	Work by other or unknown mechanisms (direct nodal inhibition)	<ul style="list-style-type: none"> • Contraindicated in ventricular arrhythmias • Diagnose and treat Supraventricular Tachycardias (Adenosine)³¹ • Treat supraventricular arrhythmias, especially in heart failure with atrial fibrillation • Treat <u>torsades de pointes</u> (magnesium sulfate)



Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Digitalis acts by :

- a .+ve inotropic effect
- b. dec. conducting velocity
- c .all
- d. non

2. Digitalis is contraindicated in :

- a. articular failure
- b. ventricular failure
- c. hypotension
- d. non

3. Cardio tonics is cautiously used in :

- a. electrolyte imbalance
- b. electrolyte low level
- c. electrolyte high level
- d. non

4. The thyroid hormone affect digitalis level by :

- a. inc. digitalis level
- b. not affect the level
- c. dec. digitalis level
- d. non

5. The dose of digitalis is :

- a. 50-70 mg/d
- b .0 .125-0.250 mg /d
- c. 1-2 mg/d
- d. 5-10 mg/d

6. The dose of lidocaine is :

- a.50-100 mg IM
- b. 50-100 mg IV
- c.50-100 mg SC
- d. 50-100 mg oral

7. The dose of diasopyramide is :

- a. 5-10 mg/d
- b. 20-50 mg/d
- c. 100-200 mg/d
- d. 400-800 mg / d

8. The dose of propafenone is :

- a. 10-20 mg
- b. 2-5 mg
- c. 150-300 mg
- d. 20-50 mg

9. The dose of propranolol is :

- a. 1-2 mg
- b. 10-30 mg
- c. 5-10 mg
- d. 100-150 mg

10. The initial dose of verapamil is :

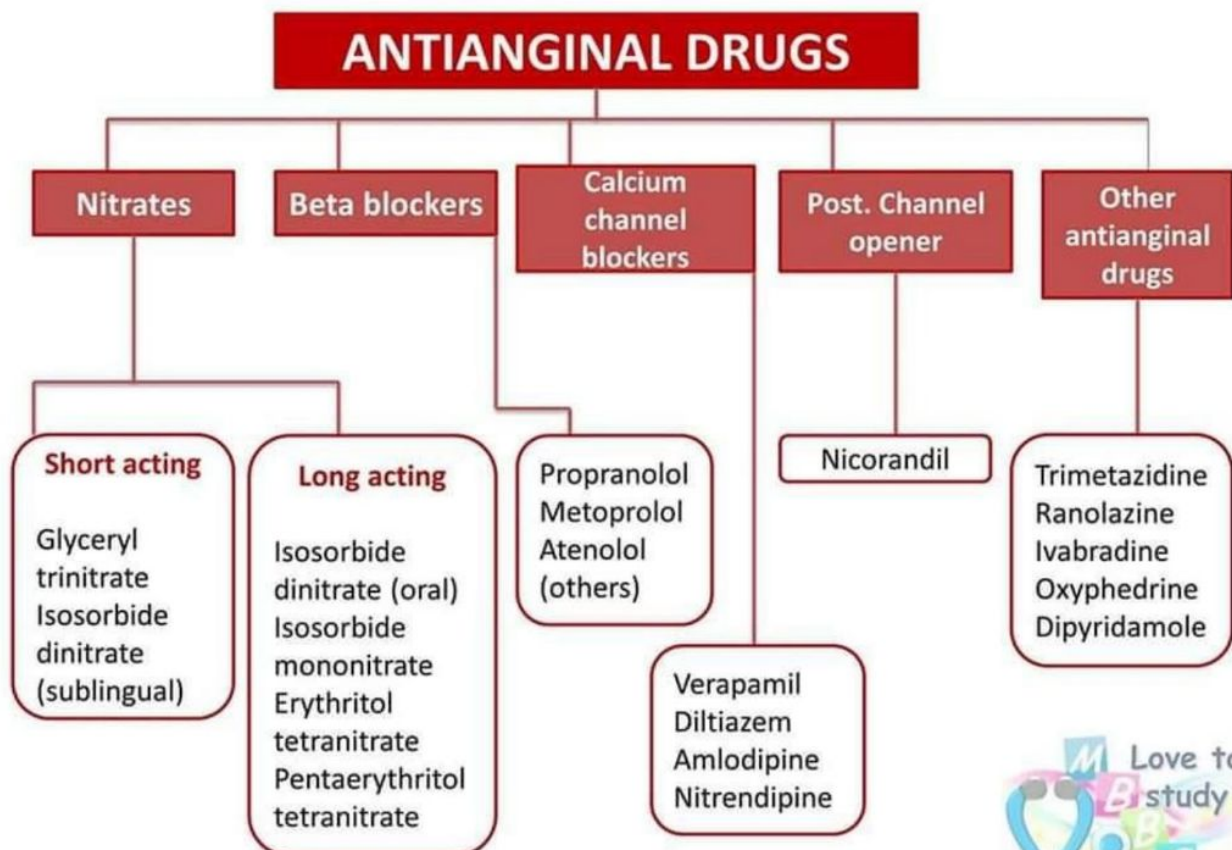
- a. 80-120 mg
- b. 2-5 mg
- c. 200-300 mg
- d. 10-15 mg

Drug act on the Cardiovascular System (Anti Anginal drug)



Introduction

It is very important for the student to study the drugs that affect the cardiovascular system, Diseases of the arteries can cause serious problems, namely coronary artery disease, cerebral vascular disease, and peripheral vascular disease. Drug therapy for vascular diseases may include drugs that dilate blood vessels and thereby increase blood supply to an area. Angina is a disorder characterized by atherosclerotic plaque formation in the coronary arteries, which causes decreased oxygen supply to the heart muscle and results in chest pain or pressure. Any activity that increases the workload of the heart, such as exercise or simply climbing stairs, can precipitate an angina attack. Antianginal drugs relieve chest pain or pressure by dilating coronary arteries, increasing the blood supply to the myocardium.



9. Isordil is used in angina for :

- a. short term
- b. long term
- c. medium term
- d. non

10. Prinzmetal angina is treated by :

- a. nitrate
- b. diltiazem
- c. nitroglycerine
- d. non



Mechanism of action of anti-anginal drugs:

1- Nitrates

The nitrates, such as isosorbide (Isordil) and nitroglycerin, have a direct relaxing effect on the smooth muscle layer of blood vessels. The result of this effect is an increase in the lumen of the artery or arteriole and an increase in the amount of blood flowing through these vessels. An increased blood flow results in an increase in the oxygen supply to surrounding tissues.

2- Calcium Channel Blockers

Systemic and coronary arteries are influenced by movement of calcium across cell membranes of vascular smooth muscle. The contractions of cardiac and vascular smooth muscle depend on movement of extracellular calcium ions into these walls through specific ion channels. Calcium channel blockers, such as amlodipine (Norvasc), diltiazem (Cardizem), nifedipine (Procardia), and verapamil (Calan), inhibit the movement of calcium ions across cell membranes. This results in less calcium available for the transmission of nerve impulses. This drug action of the calcium channel blockers (also known as slow channel blockers) has several effects on the heart, including an effect on the smooth muscle of arteries and arterioles. These drugs dilate coronary arteries and arterioles, which in turn deliver more oxygen to cardiac muscle. Dilation of peripheral arteries reduces the workload of the heart. The end effect of these drugs is the same as that of the nitrates.

The uses of anti-anginal drugs

1-Nitrates

The nitrates are used to treat angina pectoris. Some of these drugs, such as isosorbide dinitrate (Isordil), are used for prophylaxis (prevention) and long-term treatment of angina, whereas others, such as sublingual nitroglycerin (Nitrostat), are used to relieve the pain of acute angina attacks when they occur. See the Summary Drug Table: Antianginal Drugs for additional uses of the nitrates. Intravenous nitroglycerin is used to control perioperative hypertension associated with surgical procedures.

2-Calcium Channel Blockers

Calcium channel blockers are primarily used to prevent anginal pain associated with certain forms of angina, such as vasospastic (Prinzmetal's variant) angina and chronic stable angina. They are not used to abort (stop) anginal pain once it has occurred. When angina is caused by coronary artery spasm, these drugs are recommended when the patient cannot tolerate therapy with the beta -adrenergic blocking drugs or the nitrates. Verapamil affects the conduction system of the heart and may be used to treat cardiac arrhythmias. Diltiazem, nifedipine, and verapamil also are used in the treatment of essential hypertension.



Indicate the side effect , contraindication and drug interaction

- Nitrates

The nitrate antianginal drugs all have the same adverse reactions, although the intensity of some reactions may vary with the drug and the dose. A common adverse reaction seen with these drugs is headache, especially early in therapy. Hypotension, dizziness, vertigo, and weakness may also be associated with headache. Flushing caused by dilatation of small capillaries near the surface of the skin may also be seen.

The nitrates are available in various forms (eg, sublingual, transmucosal, translingual spray, and inhalation). Some adverse reactions are a result of the method of administration. For example, sublingual nitroglycerin may cause a local burning or tingling in the oral cavity. However, the patient must be aware that an absence of this effect does not indicate a decrease in the drug's potency. Contact dermatitis may occur from use of the transdermal delivery system.

The nitrates are contraindicated in patients with known hypersensitivity to the drugs, severe anemia, closed angle glaucoma, postural hypertension, head trauma, cerebral hemorrhage (may increase intracranial hemorrhage), allergy to adhesive (transdermal system), or constrictive pericarditis. The nitrates are used cautiously in patients with severe hepatic or renal disease, severe head trauma, acute myocardial infarction (MI), and during pregnancy or lactation. If the nitrates are administered with the antihypertensives, alcohol, calcium channel blockers, there may be an increased hypotensive effect. Increased nitrate serum concentrations may occur when the nitrates are administered with aspirin.



- Calcium Channel Blockers

Adverse reactions to the calcium channel blocking drugs usually are not serious and rarely require discontinuation of the drug therapy. The more common adverse reactions include dizziness, light-headedness, nausea, diarrhea, constipation, peripheral edema, headache, bradycardia, flushing, dermatitis, skin rash, and nervousness. See the Summary Drug Table: Antianginal Drugs for a more specific listing of the adverse reactions of the calcium channel blockers.

Calcium channel blockers are contraindicated in patients who are hypersensitive to the drugs and those with sick sinus syndrome, second- or third-degree AV block (except with a functioning pacemaker), hypotension (systolic less than 90 mm Hg), ventricular dysfunction, or cardiogenic shock. The calcium channel blockers are used cautiously during pregnancy (Pregnancy Category C) and lactation and in patients with congestive heart failure (CHF), hypotension, or renal or hepatic impairment. The effects of the calcium channel blockers are increased when administered with cimetidine or ranitidine. A decrease in effectiveness of the calcium channel blockers may occur when the agents are administered with phenobarbital or phenytoin. The calcium channel blockers have an antiplatelet effect (inhibition of platelet function) when administered with aspirin, causing easy bruising, petechiae (pinpoint purplish red spot caused by intradermal hemorrhage), and bleeding. There is an additive depressive effect on the myocardium when the calcium channel blockers are administered with the alpha adrenergic blocking drugs. When the calcium channel blockers are administered with digoxin, there is an increased risk for digitalis toxicity.

Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *The common side effect of anti-angina drug is :*

- a . headache
- b. hypotension
- c . flushing
- d. all

2. *Isosorbide mononitrate dose is :*

- a. 50-100 mg/d
- b. 30-60 mg/d
- c. 5-10 mg/d
- d. 100-200 mg/d

3. *Isosorbide mononitrate is given :*

- a. SL
- b. IV
- c. oral
- d. IM

4. *The dose of isosorbide dinitrate is :*

- a. 2.5-5 mg on need
- b. 50-100 mg on need
- c. 10-20 mg on need
- d. 100-200 mg on need

5. *Isosorbide dinitrate is used :*

- a. IM
- b . SC
- c. oral
- d. SL

6. *The dose of nitroglycerine is :*

- a. 1-2 mg / hr
- b. 10-20 mg/ d
- c. 0.2-0.8 mg/ hr
- d. 25-50 mg/d



7. The dose of diltiazem is :

- a. 30-260 mg/d
- b. 30-50 mg/d
- c. 50-100 mg/d
- d. 100-200 mg / d

8. The dose of amlodipine is :

- a. 20-50 mg/d
- b. 5-10 mg/d
- c. 5-40 mg /d
- d. 50-100 mg/d

9. Nitrate is contraindicated in :

- a. glaucoma
- b. hypotension
- c. severe anemia
- d. all

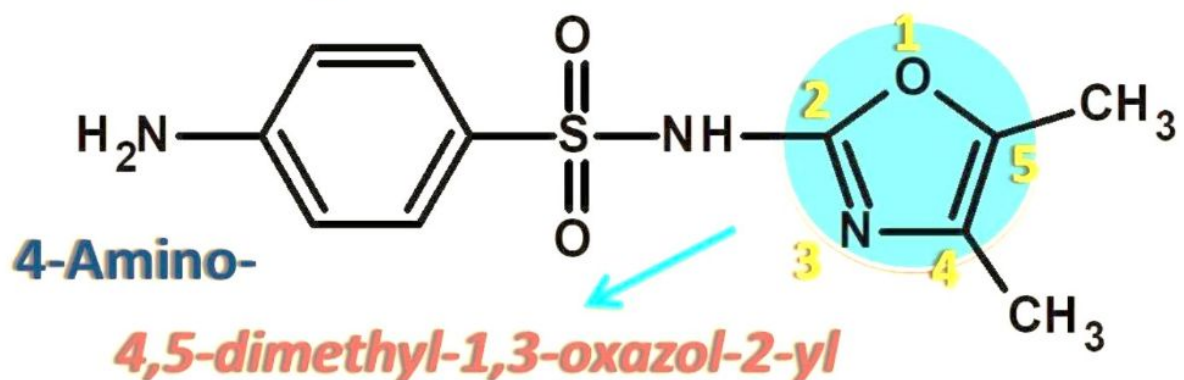
10. The calcium channel blockers is contraindicated in :

- a. CNS disturbances
- b. respiratory failure
- c. CVS disturbances
- d. all



Anti-bacterial Drugs
Sulphonamides + Cotrimoxazole

Sulfonamides





Introduction

It is very important for the student to study the drugs that affect bacterial growth in the body . The sulfonamides (sulfa) drugs were the first antibiotic drugs developed that effectively treated infections. Although the use of sulfonamides began to decline after the introduction of more effective anti-infectives, such as the penicillins and other antibiotics, these drugs still remain important for the treatment of certain types of infections. **NAMIDES**

Sulfonamides are antibacterial agents, meaning they are active against bacteria. Sulfadiazine, sulfisoxazole, and sulfamethizole are examples of sulfonamide preparations.



Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. Sulpha is effectively used in the treatment of :

- a. infection
- b. pain
- c. asthma
- d. hypertension

2. Sulpha drug is :

- a. anti-anginal
- b. antibiotic
- c. anti-bacterial
- d. anti-hypertensive

3. Example for sulpha drug is :

- a. sulfadiazine
- b. sulfamethaxazole
- c. sulfasuxizole
- d. all

4. Sulpha is primarily :

- a. bacteriocidal
- b. bacteriostatic
- c. both
- d. non

5. Sulpha is usually affect the bacterial multiplication by :

- a. faster multiplication
- b. no effect
- c. slow multiplication
- d. all

6. Sulpha usually affect PABA by :

- a. agonist
- b. antagonist
- c. partial agonist
- d. non

7. UTI is caused by :

- a. E. coli
- b. St. aureous
- c. K. enterobac.
- d. all

8. +Sulfadiazine is used in the treatment of :

- a. UTI
- b. burns
- c. skin infection
- d. bowel syndrome

9. PABA is important for the bacteria to :

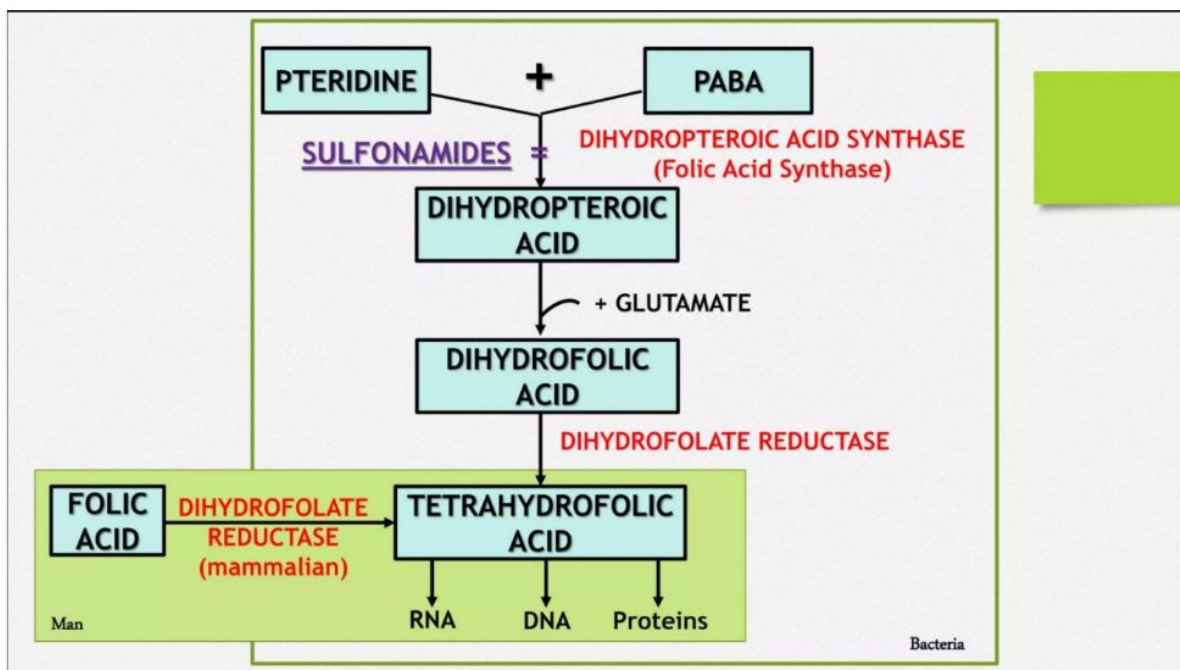
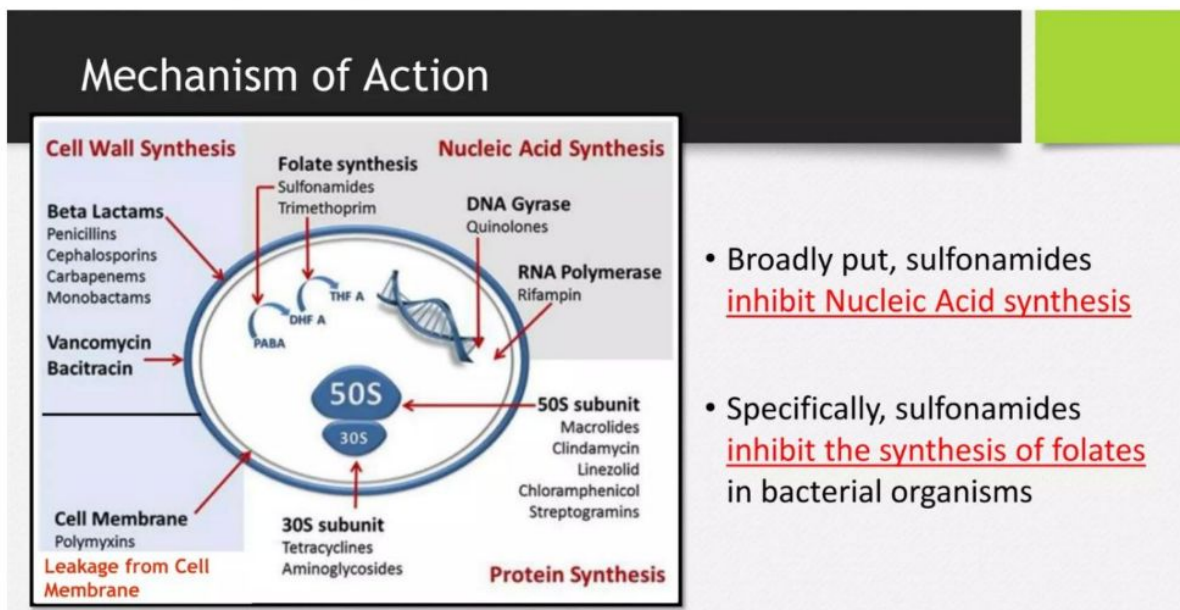
- a. stop growth
- b. both
- c. multiplication
- d. non

10. The main side effect of sulpha drug is :

- a. CVS effect
- b. haematological
- c. CNS effect
- d. all

Indicate the action of anti-bacterial "sulpha drugs"

The sulfonamides are primarily bacteriostatic, which means they slow or retard the multiplication of bacteria. This bacteriostatic activity is due to sulfonamide antagonism to para-amino benzoic acid (PABA), a substance that some, but not all, bacteria need to multiply. Once the rate of bacterial multiplication is slowed, the body's own defense mechanisms (white blood cells) are able to rid the body of the invading microorganisms and therefore control the infection.



Mechanism of Action

- **Folic Acid** is very essential for the growth of bacteria as it is **crucial for nucleic acid synthesis**.
- Many **bacteria synthesize their own folic acid** from **PABA**
- Sulfonamides are **structural analogues of PABA** → enters the sequence in place of PABA
- Sulfonamides **compete for enzyme dihydropteroic acid synthase** to create a **non-functional analogue of folic acid**
- This is of **no use to bacteria** hence → → → **GROWTH CEASES**
(BACTERIOSTATIC ACTION)

Mechanism of Action

* Humans absorb folic acid directly from diet, hence **sulfonamides are SELECTIVELY TOXIC TO THE BACTERIA ONLY** and not to the host cells!



Classification The sulfonamides still of clinical interest			
A	Short Acting	(4-8 hrs)	Sulfadiazine
B	Intermediate Acting	(8-12 hrs)	Sulfamethoxazole
C	Long Acting	(~7 days)	Sulfadoxine Sulfamethopyrazine
D	SPECIAL PURPOSE		Sulfacetamide sodium Silver sulfadiazine Sulfasalazine Mafenide

Classification :The sulfonamides still of clinical interest			
Orally Absorbable			
A	1.	Short Acting	(4-8 hrs) Sulfadiazine Sulfacytine Sulfamethizole Sulfisoxazole
	2.	Intermediate Acting	(8-12 hrs) Sulfamethoxazole Sulfamoxole
	3.	Long Acting	(~7 days) Sulfadoxine Sulfamethopyrazine
B	Orally Non- Absorbable		Sulfasalazine Olsalazine Balsalazine
C	Topical Agents		Silver sulfadiazine Mafenide Sulfacetamide sodium

The uses of Sulpha drug

The sulfonamides are often used to control **urinary tract infections** caused by certain bacteria such as **Escherichia coli, Staphylococcus aureus, and Klebsiella-Enterobacter.**

Mafenide (Sulfamylon) and silver sulfadiazine (Silvadene) are topical sulfonamides used in the treatment of second- and third-degree burns.

Indicate the side effect, contraindication and drug interaction

The sulfonamides are capable of causing a variety of adverse reactions. Some of these are serious or potentially serious; others are mild.

The following hematologic changes may occur during sulfonamide therapy:

- **Agranulocytosis**—decrease in or lack of granulocytes, a type of white blood cell
- Thrombocytopenia—decrease in the number of platelets
- Aplastic anemia—**anemia** due to deficient red blood cell production in the bone marrow
- Leukopenia—decrease in the number of white blood cells

- The sulfonamides are **contraindicated** in patients with hypersensitivity to the sulfonamides, during lactation, and in children less than 2 years old.

The sulfonamides are used with caution in patients with renal or hepatic impairment and bronchial asthma. These drugs are given with caution to patients with allergies.

When a sulfonamide is administered with an oral anticoagulant, the action of the anticoagulant may be enhanced.

Sulfonamides may inhibit the (hepatic) metabolism of the oral hypoglycemic drugs tolbutamide (Orinase) and chlorpropamide (Diabinese). This would increase the possibility of a hypoglycemic reaction.

Cotrimoxazole

Introduction (Cotrimoxazole)

- Introduced in 1969
- It is a **RATIONAL** fixed drug dose combination
- **Sulfamethoxazole + Trimethoprim**
- This combination is **BACTERICIDAL**
(Both drugs are bacteriostatic when given alone)



Trimethoprim vs. Sulfamethoxazole (Cotrimoxazole)

<u>TRIMETHOPRIM</u>	<u>SULFAMETHOXAZOLE</u>
<ul style="list-style-type: none"> • Diaminopyrimidine related to antimalarial drug PYRIMETHAMINE • MOA: Inhibits bacterial dihydrofolate reductase (DHFRase) 	<ul style="list-style-type: none"> • Intermediate acting PABA structural analogue • MOA: Inhibits folate synthase
HUMAN FOLATE METABOLISM IS NOT INTERFERED WITH	
<ul style="list-style-type: none"> • Bacteriostatic 	<ul style="list-style-type: none"> • Bacteriostatic
Combination is <u>BACTERICIDAL</u> against many organisms	
<ul style="list-style-type: none"> • Pharmacokinetics: A - More rapidly absorbed D - 40% plasma protein bound M - Partly metabolized in Liver E - Excreted in urine 	<ul style="list-style-type: none"> • Pharmacokinetics: A - Rapidly absorbed D - 65% plasma protein bound M - Acetylation in Liver E - Renal excretion by glomerular filtration



Rationale (Cotrimoxazole)

- Both compounds have a **similar half life** (~10 hours)
- Two bacteriostatic drugs produces **bactericidal action** when combined
- The combination has a **wider antibacterial spectrum**
- The combination **delays the development of bacterial resistance**
- The MIC of each component can be **reduced 3-6 times**
- Trimethoprim **enters many tissues** and has a **larger volume of distribution**

Mechanism of Action (Cotrimoxazole)

- Cotrimoxazole **inhibits Nucleic Acid Synthesis** by...
- causing **SEQUENTIAL BLOCKADE** of **Folic Acid Synthesis** in bacterial organisms

Spectrum of Action (Cotrimoxazole)

- All organisms sensitive for sulfonamides
 - Additional organisms: S. typhi, Klebsiella, P. jiroveci
Sulfonamide resistant strains
 - **Mechanism of Resistance:** Resistance to Trimethoprim is mostly through **plasmid mediated acquisition** of DHFRase
- *Resistance to the combination is **slow to develop** compared to the drugs alone!

Uses (Cotrimoxazole)

* Cotrimoxazole is **still used now...** however, its **popularity has decreased** in the treatment of systemic infections

1. Urinary Tract Infections

- Acute uncomplicated infections respond rapidly
 - 1 tablet twice daily X 3-10 days
- **Acute Cystitis** → Single dose therapy with 4 tablets
- **Prostatitis**
 - Acute → 1 tablet twice daily X 3 weeks
 - Chronic → 1 tablet twice daily X 6-12 weeks

2. Respiratory Tract Infections

- URTI + LRTI
 - Chronic Bronchitis
 - Sinusitis
 - Otitis Media
- } Especially infections caused by Gram positive cocci and Hemophilus species
- One DS tablet twice a day

3. Bacterial Diarrheas + Dysentery

- Acute gastroenteritis
 - Traveller's Diarrhea
 - Cholera
- } E. coli, Shigella, non-typhoid Salmonella, Yersinia
- One DS tablet twice a day X 7 days

* **Fluourquinolones are the drugs of choice, however Cotrimoxazole is a valuable alternative**

4. Pneumocystis jiroveci (Pneumonia in Neutropenic/AIDS patient)

- High doses Cotrimoxazole is prophylactic as well as therapeutic
- **Drug of choice for pneumonia due to P. jiroveci**

Treatment → One DS tablet four times a day X 2-3 weeks
Prophylaxis → One DS tablet daily

* **Adverse effects necessitates discontinuation in 20% cases**

5. Sexually transmitted Diseases

- Chancroid –

Cotrimoxazole is the 3rd choice drug

→ One DS tablet twice daily X 14 days

- Non-specific urethritis
- Lymphogranuloma
- Gonorrhoea

6. Nocardiosis

- Drug of choice for pulmonary lesions/brain abscesses due to Nocardia

7. Typhoid

- Was initially effective and an alternate drug for typhoid. Now it is unreliable and seldomly used

8. Melioidosis

Adverse Effects

(Cotrimoxazole)

- All the adverse effects seen with Sulfonamides can be seen with Cotrimoxazole

- Nausea, Vomiting, Headache, Stomatitis
- Rashes
- **Folate deficiency ONLY in patients with marginal folate levels**
- Blood dyscrasias (RARE)

Contraindications

(Cotrimoxazole)

- **AVOID IN PREGNANCY**

- Trimethoprim is an antifolate → Theoretical teratogenic risk
- Given near term → methemoglobinemia and neonatal hemolysis

- **Uremia in renal disease**

- Greater risk of **bone marrow toxicity** in the **elderly**

- **Fever, Rash and bone marrow hypoplasia among AIDS patients with P. jiroveci infection**



Interactions

(Cotrimoxazole)

- **Diuretics** + Cotrimoxazole → Higher incidence of **THROMBOCYTOPENIA**



Trade & Scientific names with the dose

Single Agents		Clinical use	Side effect	Dosage range
1	Sulfadiazine	Urinary tract infections due to susceptible microorganisms, acute otitis media, Hemophilus influenzae and meningococcal meningitis, rheumatic fever	Hematologic changes, Stevens-Johnson syndrome, nausea, vomiting, headache, diarrhea, chills, fever, anorexia, crystalluria, stomatitis, urticaria, pruritus	Loading dose: 2-4 g PO; maintenance dose: 2-4 g/d PO in 4-6 divided doses
2	Sulfamethoxazole	Urinary tract infections due to susceptible microorganisms, meningococcal meningitis, acute otitis media	Same as sulfadiazine	Initial dose: 2 g PO, maintenance dose: 1 g PO bid, tid
3	Sulfasalazine	Ulcerative colitis, rheumatoid arthritis	Same as sulfadiazine; may cause skin and urine to turn orange-yellow	Initial therapy: 1-4 g/d PO in divided doses; maintenance dose: 2 g/d in evenly spaced doses 500 mg qid
4	Sulfisoxazole	Same as sulfadiazine	Same as sulfadiazine	Loading dose: 2-4 g PO; maintenance dose: 4-8 g/d PO in 4-6 divided doses
Multiple Preparations				
1	trimethoprim (TMP) sulfamethoxazole (SMZ)	Urinary tract infections due to susceptible microorganisms, acute otitis media, traveler's diarrhea due to Escherichia coli	Gastrointestinal disturbances, allergic skin reactions, hematologic changes, Stevens-Johnson syndrome, headache	160 mg TMP/800 mg SMZ PO q12h; 8-10 mg/kg/d (based on TMP) IV in 2-4 divided doses



Miscellaneous Sulfonamide Preparations

1	Mafenide	Second- and third-degree burns	Pain or burning sensation, rash, itching, facial edema	Apply to burned area 1-2 times/d
2	Silver sulfadiazine	Same as mafenide	Leukopenia, skin necrosis, skin discoloration, burning sensation	Same as mafenide



Antibiotics (Cephalosporin)



CEPHALOSPORINS





Introduction

It is very important for the student to study the drugs that affect bacterial growth in the body . The effectiveness of penicillin in the treatment of infections prompted research directed toward finding new antibiotics with a wider range of antibacterial activity. The cephalosporin are a valuable group of drugs that are effective in the treatment of almost all of the strains of bacteria affected by the penicillin , as well as some strains of bacteria that have become resistant to penicillin. The cephalosporin are structurally and chemically related to penicillin. The cephalosporin are divided into first-, second-, and third-generation drugs. Particular cephalosporin also may be differentiated within each group according to the microorganisms that are sensitive to them. Generally, progression from the first-generation to the second-generation and then to the third-generation drugs shows an increase in the sensitivity of gram-negative microorganisms and a decrease in the sensitivity of gram-positive microorganisms. For example, a first-generation cephalosporin would have more use against gram-positive microorganisms than would a third-generation cephalosporin. This scheme of classification is becoming less clearly defined as newer drugs are introduced.

Pre-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. *Cephalosporin is used in :*
 - a. almost all bacteria
 - b. all bacteria
 - c. few bacteria
 - d. non
2. *Cephalosporin is related to penicillin :*
 - a. chemically
 - b. structurally
 - c. both
 - d. non
3. *First generation is used in the treatment of :*
 - a. gm(-)ve
 - b. gm(+ve)
 - c. non
 - d. both
4. *Example of first generation cephalosporin is :*
 - a. cephataxime
 - b. cepharidine
 - c. cephalozone
 - d. cephalixin
5. *Third generation of cephalosporin is used against :*
 - a. gm(-) ve
 - b. gm(+ve)
 - c. anti-bacterial
 - d. non
6. *Third generation of cephalosporin is :*
 - a. cephalozone
 - b. cephataxime
 - c. cepharidine
 - d. cephalixin
7. *Cephalosporin acts as :*
 - a. bacteriostatic
 - b. both
 - c. bactericidal
 - d. non
8. *Cephalosporin is used in :*
 - a. septicemia
 - b. otitis media
 - c. gonorrhea
 - d. all
9. *Example of cephalosporin is :*
 - a. amoxicillin
 - b. gentamicin
 - c. Keflex
 - d. tetracycline
10. *The common side effect of cephalosporin is :*
 - a. hypersensitivity
 - b. CVS effect
 - c. CNS effect
 - d. non

Action of cephalosporin

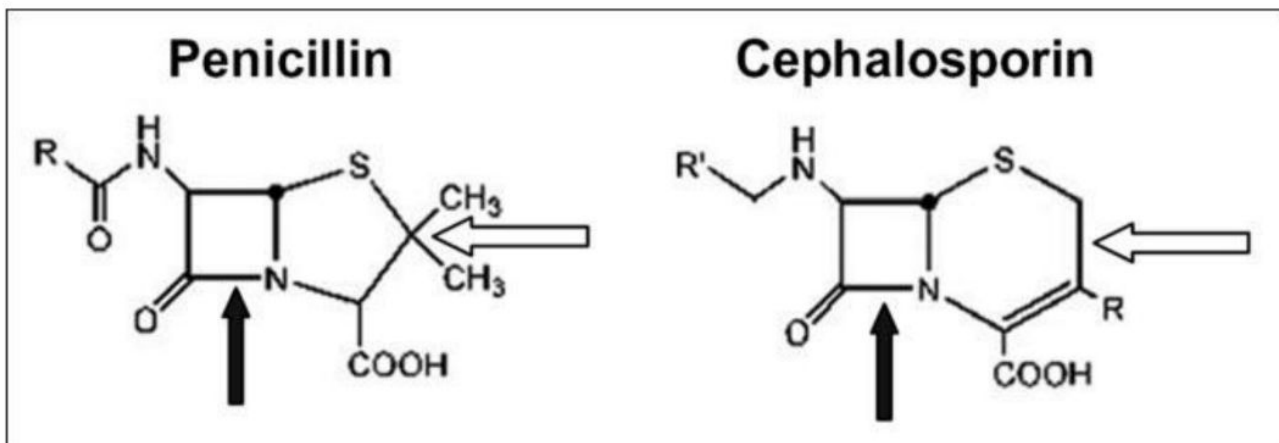
Cephalosporin affect the bacterial cell wall, making it defective and unstable. This action is similar to the action of penicillin. The cephalosporin are usually bactericidal (capable of destroying bacteria).

Cephalosporin are beta-lactam antimicrobials that share mechanisms of action and a similar structure with penicillin (Figure). Penicillin and cephalosporin have the same four-member "core" beta-lactam ring, but cephalosporin have an additional atom in the side ring. Modified side chains on either ring alter antimicrobial activity, resistance to beta-lactamases, or pharmacokinetics. Penicillin-susceptible pathogens usually are cephalosporin-susceptible. Exceptions are *Listeria* and *Pasteurella* spp. Cephalosporin have activity against common gram-negative organisms such as *Escherichia coli*, nontypeable *Haemophilus influenzae* (nHfi), and methicillin-susceptible *Staphylococcus aureus* (MSSA).

Penicillin Vs Cephalosporin

Cephalosporin versus penicillin ring structures. The solid arrows indicate the core four-member beta-lactam ring within both penicillin and cephalosporin. Open arrows indicate the five- and six-member side rings for penicillin and cephalosporin, respectively.

R indicates additional side chain sites where substitutions of various chemical groups produce different antimicrobial spectra, pharmacokinetics, or stability to beta lactamase.





Cephalosporin are classified by "generation" In general, lower-generation cephalosporin have more gram-positive activity and higher-generation cephalosporin more gram-negative activity. The fourth generation drug cefepime is the exception, with gram positive activity equivalent to first-generation and gram-negative activity equivalent to third-generation cephalosporin. However, individual cephalosporin in the higher generations have differentiating properties that may mark them for specific indications ,Dose and dosing intervals vary with each drug.

The uses of cephalosporin

The cephalosporin are used in the treatment of infections caused by susceptible microorganisms. Examples of microorganisms that may be susceptible to the cephalosporin include **streptococci, staphylococci, citrobacters, gonococci, shigella, and clostridia.**

Culture and sensitivity tests are performed whenever possible to determine which antibiotic, including a cephalosporin, will best control an infection caused by a specific strain of bacteria. **Pharyngitis, tonsillitis, otitis media, lower respiratory infections, urinary tract infections, septicemia, and gonorrhea** are examples of the types of infections that may be treated with the cephalosporin.

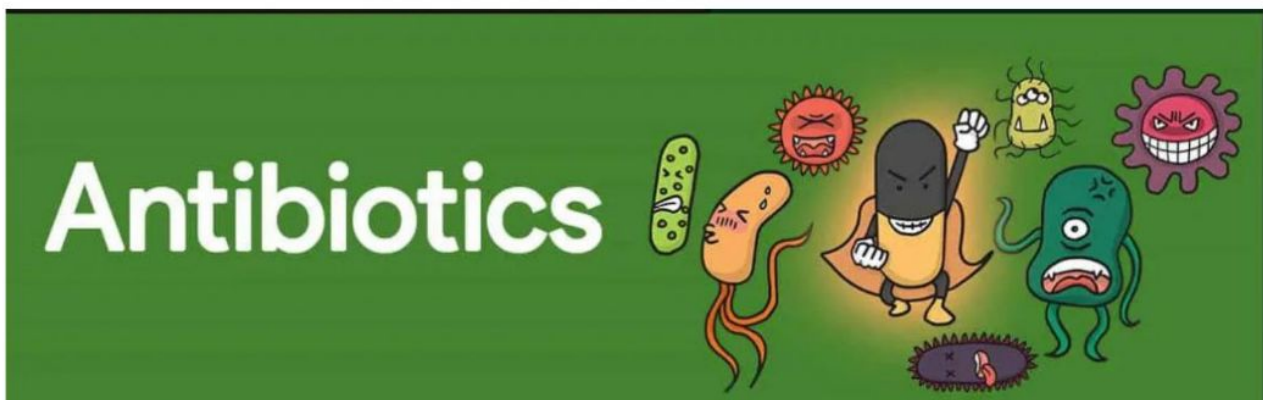
The cephalosporin also may be used preoperatively during the **preoperative, intraoperative, and postoperative periods**, to prevent infection in patients having surgery on a contaminated or potentially contaminated area, such as the **gastrointestinal tract or vagina**. In some instances, a specific drug may be recommended for postoperative **prophylactic use only**.

Indicate the side effect, contraindication and drug interaction

The most common adverse reactions seen with administration of the cephalosporin are **gastrointestinal disturbances**, such as :

- Nausea & vomiting (N\V)
- Diarrhea

Hypersensitivity (allergic) reactions may occur with administration of the cephalosporin and range from mild to life threatening. Mild hypersensitivity reactions include **pruritus, urticaria, and skin rashes**. More serious hypersensitivity reactions include **Stevens-Johnson syndrome (fever, cough, muscular aches and pains, headache, and the appearance of lesions on the skin, mucous membranes, and eyes), hepatic and renal dysfunction, aplastic anemia** (anemia due to deficient red blood cell production), and **epidermal necrolysis** (death of the epidermal layer of the skin). **Because of the close relation of the cephalosporin to penicillin, a patient allergic to penicillin also may be allergic to the cephalosporin.**



Other adverse reactions that may be seen with administration of the cephalosporin are **headache, dizziness, nephrotoxicity** (damage to the kidneys by a toxic substance), **malaise, heartburn, and fever**. **Intramuscular (IM) administration often results in pain, tenderness, and inflammation at the injection site. Intravenous (IV) administration has resulted in thrombophlebitis and phlebitis.**

Therapy with cephalosporin may result in a bacterial or fungal superinfection. Diarrhea may be an indication of pseudomembranous colitis, which is one type of bacterial superinfection.

cephalosporin should not administer if the patient has a history of allergies to cephalosporin or penicillin.

cephalosporin should use cautiously in patients with renal or hepatic impairment and in patients with bleeding disorders.

Safety of cephalosporin administration has not been established in pregnancy or lactation; these drugs are assigned to **Pregnancy Category B**.

The risk of nephrotoxicity increases when the cephalosporin are administered with the aminoglycosides. The risk for bleeding increases when the cephalosporin are taken with oral anticoagulants.

A **disulfiram-like** reaction may occur if alcohol is consumed within 72 hours after cephalosporin administration. Symptoms of a disulfiram-like reactions include **flushing, throbbing in the head and neck, respiratory difficulty, vomiting, sweating, chest pain, and hypotension**. Severe reactions may cause **arrhythmias and unconsciousness**. When the cephalosporin are administered with the aminoglycosides, the risk for nephrotoxicity increases



Table 1. **Classification of Cephalosporins**

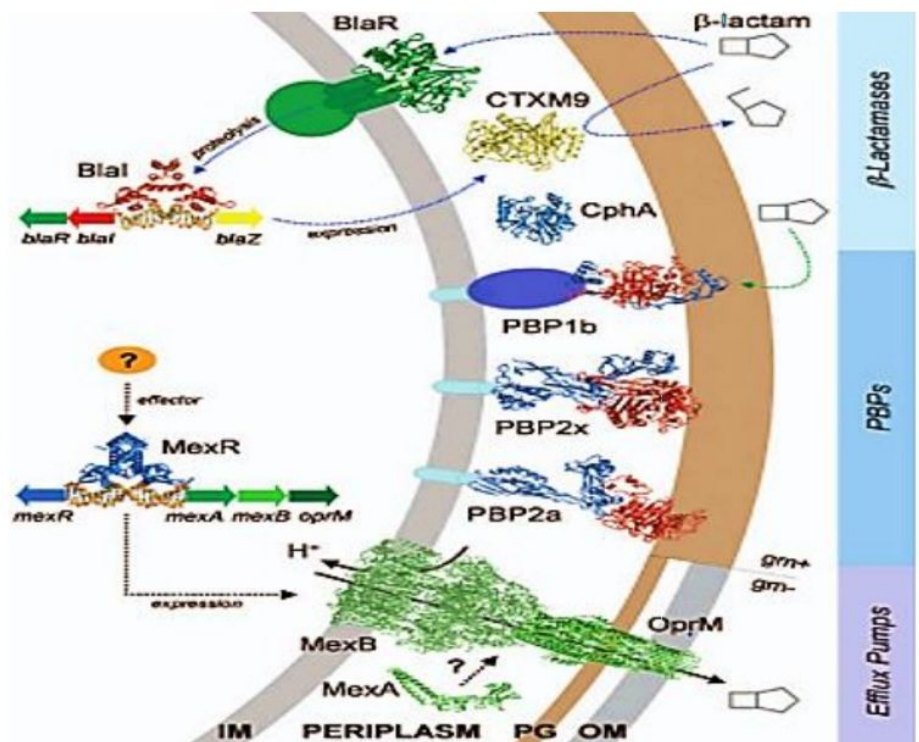
Generic Name	Trade Name	Trade Manufacturer*	Route
First-generation			
Cefadroxil	Duricef [®]	Bristol Myers Squibb, Princeton, NJ	PO
Cephalexin	Keflex [®]	Advancis Middle Brook, Germantown, MD	PO
Cephradine	Velosef [®]	Bristol Myers Squibb, Princeton, NJ	PO, IM, IV
Cefazolin	Ancef [®]	GlaxoSmith Kline, Research Triangle Park, NC	IM, IV
Second-generation			
Cefaclor	Ceclor [®]	Eli Lilly and Company, Indianapolis, IN	PO
Cefprozil	Cefzil [®]	Bristol Myers Squibb, Princeton, NJ	PO
Cefuroxime axetil	Ceftin [®]	GlaxoSmith Kline, Research Triangle Park, NC	PO
Cefuroxime	Zinacef [®]	GlaxoSmith Kline, Research Triangle Park, NC	IM, IV
Cephameycins			
Cefoxitin	Mefoxin [®]	Merck and Company, Whitehouse Station, NJ	IM, IV
Third-generation			
[†] Cefdinir	Omnicef [®]	Abbott, Abbott Park, IL	PO
Cefixime	Suprax [®]	Lupin, Baltimore, MD	PO
Cefpodoxime proxetil	Vantin [®]	Pfizer, New York, NY	PO
Ceftibuten	Cedax [®]	Shinogi, Florham Park, NJ	PO
Cefotaxime	Claforan [®]	Hospira, Lake Forest, IL	IM, IV
Ceftazidime	Fortaz [®]	GlaxoSmith Kline, Research Triangle Park, NC	IM, IV
[†] Ceftriaxone	Rocephin [®]	Roche, Nutley, NJ	IM, IV
Fourth-generation			
[†] Cefepime	Maxipime [®]	Elan, Gainesville, GA; ER Squibb and Sons, Inc, New Brunswick, NJ	IV

IM=intramuscular, IV=intravenous, PO=oral
*See *Lexi-Comp Online* for generic manufacturers, Lexi-Corp, Inc, Hudson, Ohio.
[†]Not manufactured as a generic medication at this time.

B-LACTAM ANTIBIOTIC RESISTANCE

As with most antimicrobial agents, b-lactams are rendered inactive against bacteria by way of three primary mechanisms of resistance

1. The most common mechanism is the production of enzymes that degrade or modify the antibiotic before it can reach the appropriate target site. In this case, the b-lactamase family of enzymes degrade b-lactam antibiotics and are found widely disseminated amongst Gram-positive and Gram-negative bacteria.
2. The second mechanism is alteration of the antibiotic target site. In this case, the b-lactam-resistant cell-wall transpeptidases perform this role; this is now a major cause of resistance in several pathogens including the problematic Gram-positive Staphylococcal and Streptococcal species.
3. The final mechanism is prevention of access of the antibiotic to the target by way of altered permeability or forced efflux.

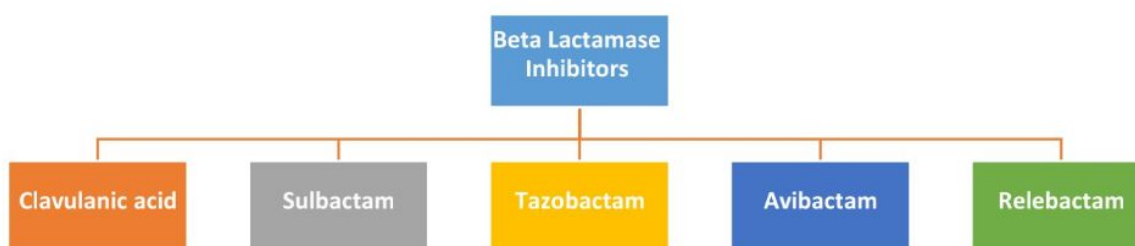


B-LACTAMASE INHIBITORS

Beta-lactamase inhibitors (BLIS) are a class of antibiotics that work by inhibiting the enzyme responsible for the breakdown of beta-lactam antibiotics.

BLIs are used in combination with beta-lactam antibiotics to combat antibiotic resistance. The antibacterial activities of BLIS are due to their ability to inhibit the production of the antibiotic's degrading enzyme, beta-lactamase. This is important because resistance to beta-lactam antibiotics arises when bacteria acquire a mutation that enables them to produce beta-lactamases. These enzymes break down the drug before it can kill the bacteria. The use of beta-lactamase inhibitors has been shown to prevent the spread of this type of resistance, as it prevents the degradation of antibiotics before they have a chance to kill bacteria.

The most commonly used BLIS are clavulanic acid and sulbactam.

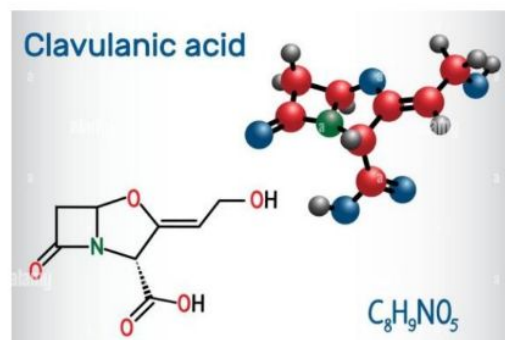


Classification of beta lactamase inhibitores

Clavulanic acid

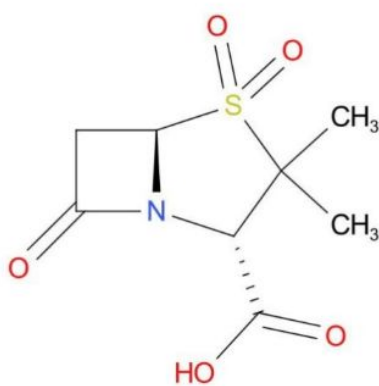
Is a potent inhibitor of many bacterial beta-lactamases. A naturally occurring, low molecular weight substance isolated as a metabolite of *Streptomyces clavuligerus*, clavulanic acid inhibits beta-lactamases through a time-dependent irreversible reaction. Because the compound binds initially at the enzyme active site and is converted into an inactivator by action of the beta lactamase, it is known as a "suicide inhibitor".

Clavulanic acid is itself a beta-lactam antibiotic which possesses weak intrinsic antibacterial activity against some Enterobacteriaceae, gram-positive bacteria, and anaerobes. It has moderate activity against *H. influenzae* and good activity against *N.gonorrhoeae*. Because of its overall weak antibacterial activity and limited spectrum, clavulanic acid has no role as a single agent for treating infections. In combination with many penicillin and cephalosporin, however, clavulanic acid acts synergistically to improve their activity. Improvement is marked against bacteria that owe their resistance to beta-lactamases that can be inhibited by clavulanic acid.



Sulbactam

It is a potent irreversible inhibitor of beta-lactamases. Although sulbactam possesses weak intrinsic antibacterial activity The profile of beta-lactamases inhibited by sulbactam is similar to that of clavulanic acid. Sulbactam has been shown to be slightly more active than clavulanic acid in inhibiting certain cephalosporinases , but less active against the broad range beta-lactamase of Enterobacteriaceae. Sulbactam, unlike clavulanic acid, has not been shown to induce chromosomal beta-lactamases in susceptible bacteria.





Post-Test

Q: Choose the correct answer by encircle on the right letter:

(1 degree to each branch)

1. The common side effect of cephalosporin is :
a. haematological b. hypersensitivity
c. GIT disorder d. all
2. Cephalosporin is cautiously used in :
a. pregnancy& lactation b. bleeding disorder
c. hepatic & renal failure d. all
3. Cephalosporin + anticoagulants =..... :
a. dec. bleeding b. inc. bleeding
c. not affect d. non
4. The dose of cefazolin is :
a. 10-20 mg/12 hr b. 100-200 mg/12 hr
c. 250-1 gm/12 hr d. 50-100 mg / 12 hr
5. The dose of cephalixin is :
a. 1-4 gm/d oral b. 1-4 gm/d IV
c. 1-4 gm/d IM d. 1-4 gm/d SC
6. The dose of cefixime is :
a. 100-200 mg /d b. 10-20 mg /d
c. 400 mg/d d. 1-4 g/d
7. The dose of cephtriaxone is :
a. 1-2 g/ d b. 20-50 mg/ d
c. 100 mg/ d. 400-800 mg / d
8. Ceftriaxone is given :
a. oral b. IM
c. IV d. IM & IV
9. Cephalosporin is used in the treatment of :
a. St. coccus b. Str.coccus
c. Clostridium d. all
10. cephalosporin is used :
a. preoperative b. post operative
c. both d. non