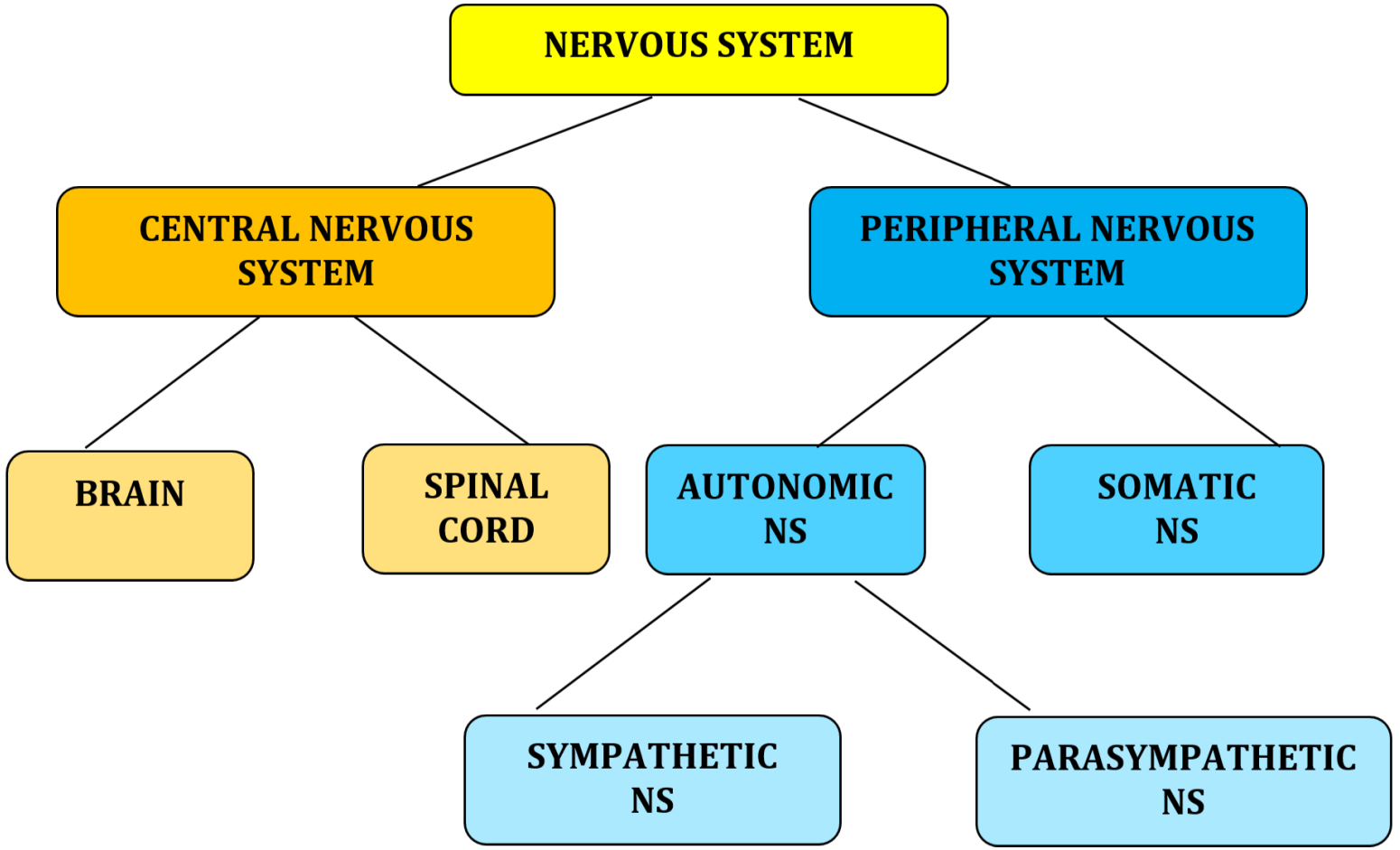
Nervous system Pharmacology

Dr. Zena Sattam



Autonomic Nervous System
(ANS)

This system is divided into two separate systems, called:

- **The parasympathetic nervous system. PNS**
- **The sympathetic nervous system. SNS**

These systems often produce opposite effects.

Drugs in this group are designed to either: enhance or mimic the autonomic nervous system or to block the effects of the neurotransmitters at their receptor sites.

Parasympathetic Nervous System (PNS)

- This system is concerned with the conservation of the body processes.
- **Its main neurotransmitter is acetylcholine.**
- Its **receptors are muscarinic, nicotinic, and the somatic skeletal muscles.**

Sympathetic Nervous System (SNS)

- This nervous system is designed to cope with emergency situations.
- This is commonly known as the “fright or flight” response.
- **Its neurotransmitters are epinephrine and norepinephrine.**
- **Its receptors are the α and β receptors.**

Autonomic Nervous System drugs

1. **Cholinergic Drugs:**

- Cholinergic agonist
- Anticholinesterase.
- Cholinergic antagonist

2. **Adrenergic Drugs:**

- Adrenergic agonist
- Adrenergic antagonist:

➢Beta Blocker

➢Alpha blocker

Cholinergic Drugs:

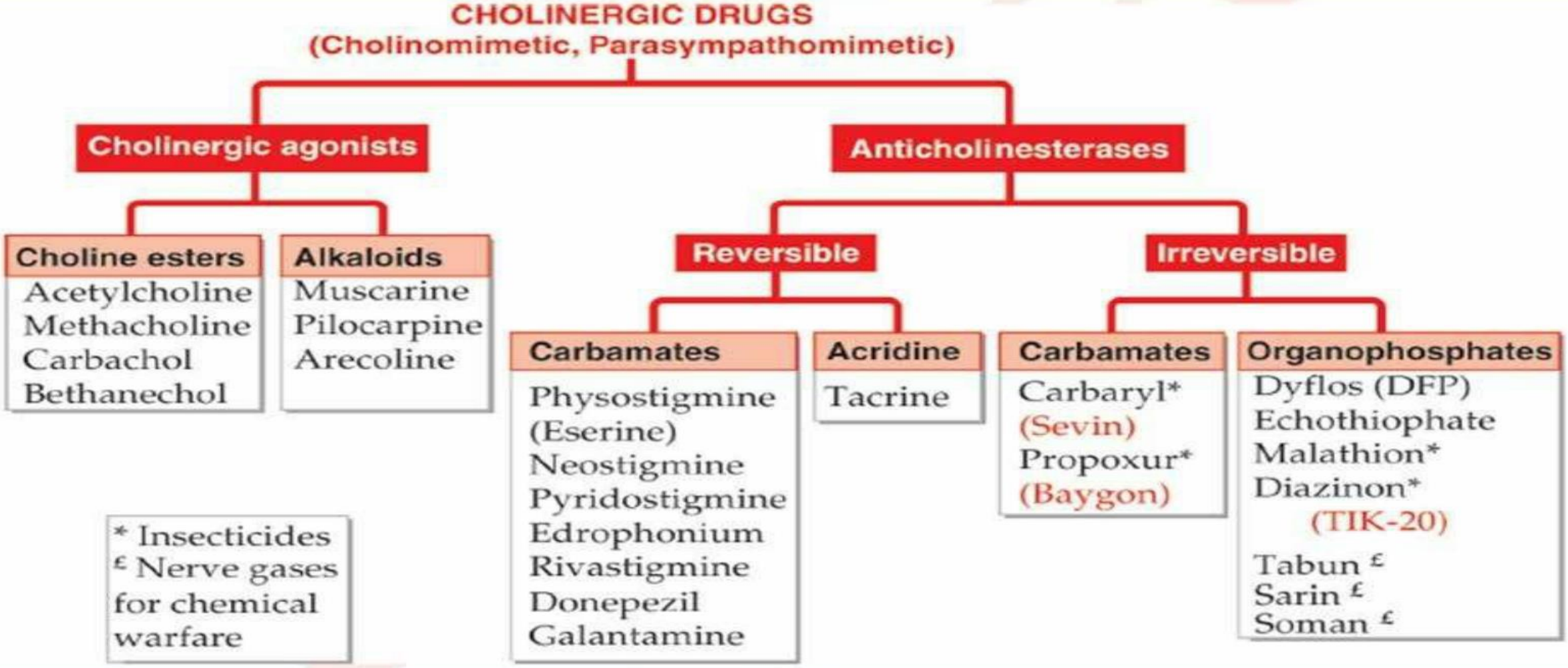
- **Cholinergic Agonist Drugs:**

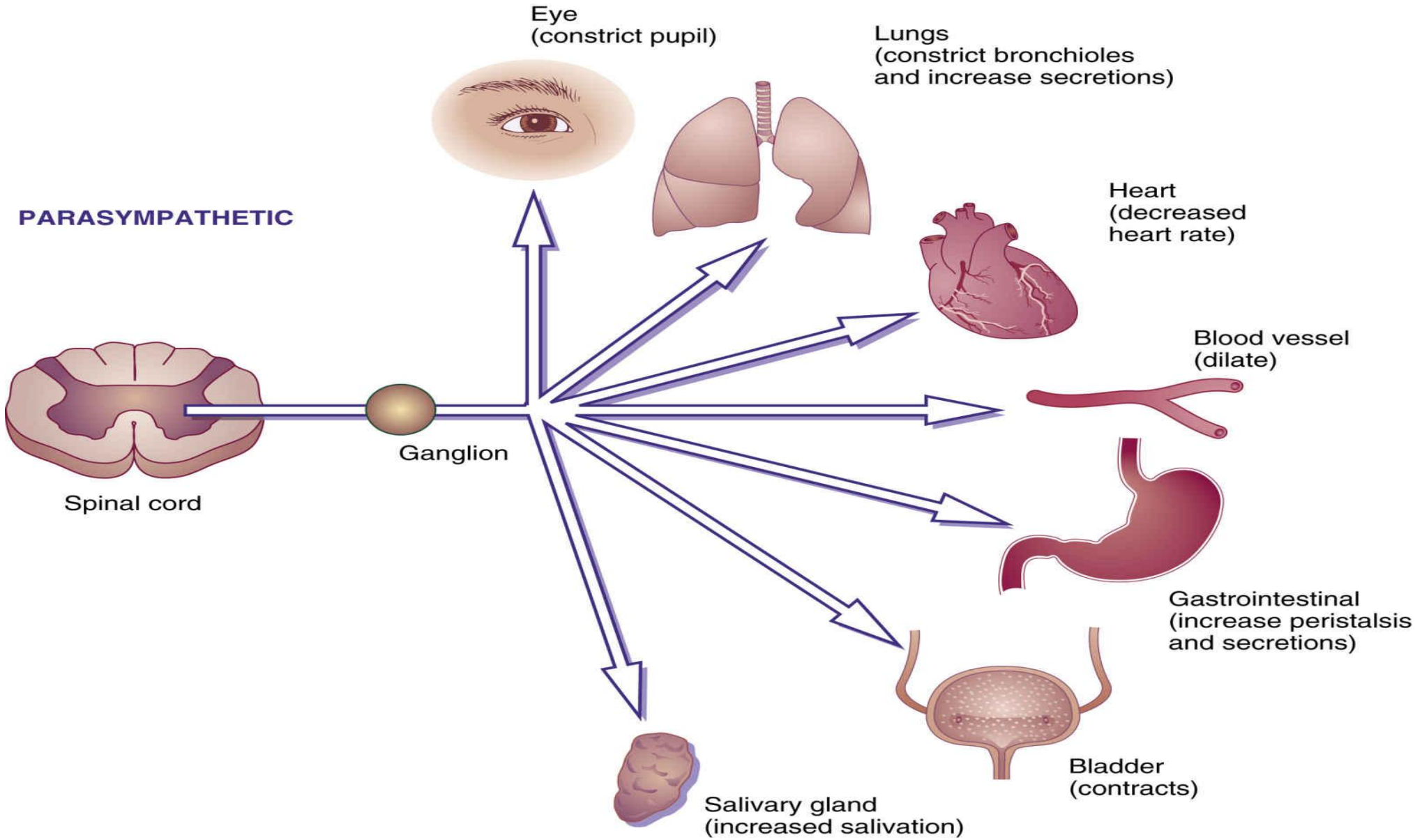
  The name given to a **group of medicines that mimic the actions of acetylcholine.** Acetylcholine is one of the most common neurotransmitters in our body, and it has actions in both the central and peripheral nervous systems.

- **Anticholinesterase Drugs:**

Drugs that **prevent an enzyme called acetylcholinesterase from breaking down acetylcholine.** This means there is a higher concentration of acetylcholine.

Drug Acting on Autonomic Nervous system




Eye
(constrict pupil)
Lungs
(constrict bronchioles
and increase secretions)
PARASYMPATHETIC
Heart
(decreased
heart rate)
Blood vessel
(dilate)
Ganglion
Spinal cord
Gastrointestinal
(increase peristalsis
and secretions)
Bladder
(contracts)
Salivary gland
(increased salivation)

Uses of Cholinergic Drugs

Cholinergic drugs stimulate the parasympathetic nervous system by copying the action of Ach.

- **They are given for Alzheimer's disease:**

Lead to better communication between nerve cells. This may ease some symptoms of Alzheimer's disease for a while.

- **They are given for glaucoma:**

To reduce intraocular pressure (IOP).

- **They are given for urinary retention:**

To stimulate contractions and aid in bladder emptying.

They are given for myasthenia gravis:

By provides more acetylcholine in the neuromuscular junction for a longer period of time, for mediating muscle contraction.

Adverse Reactions

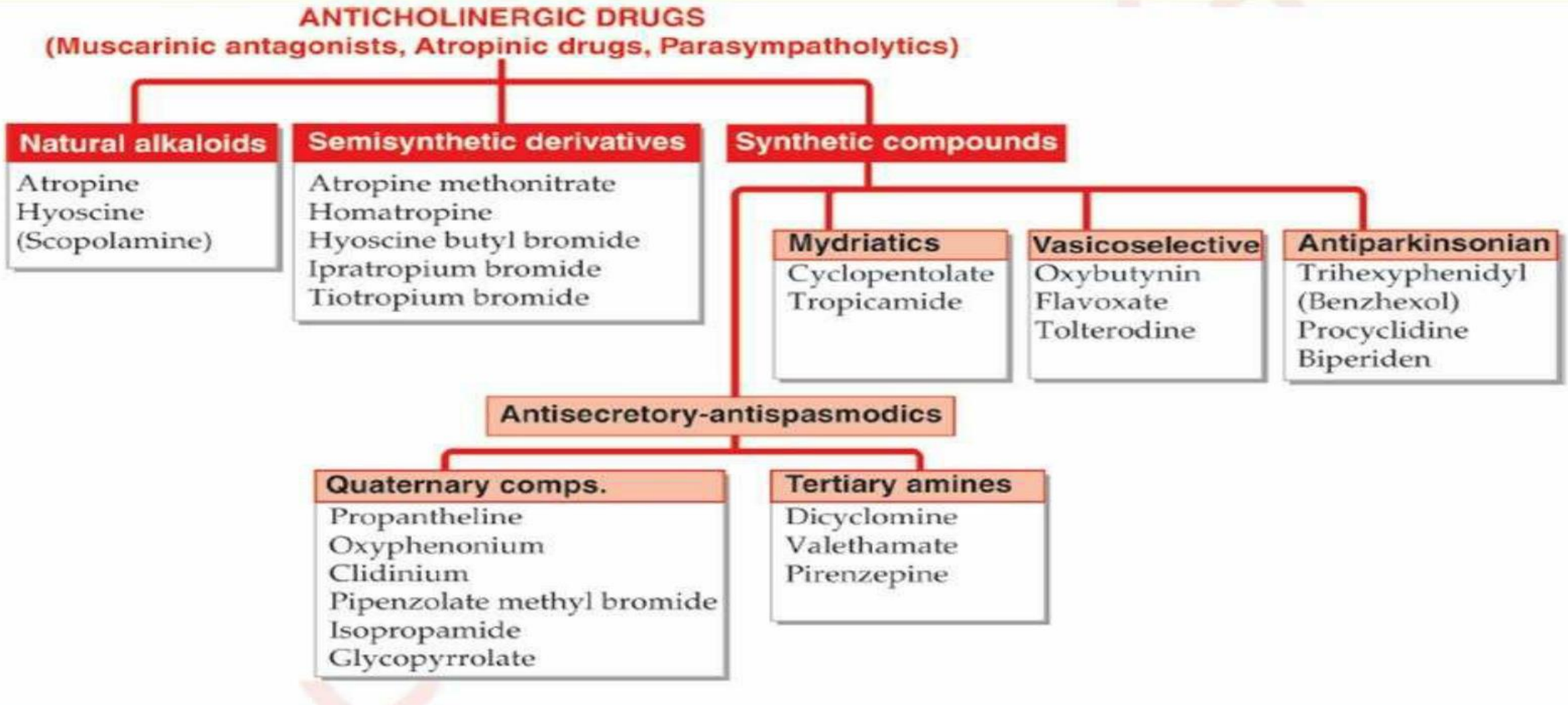
Adverse reactions are an extension of the drugs' pharmacologic effects. They include:

- Salivation
- Lacrimation
- Urination
- Defecation
- Paralysis
- Overdose

Contraindications

- The contraindications and relative cautions are a result of the drug’s pharmacologic and adverse effects. They include:
- Bronchial asthma
- Hyperthyroidism
- Gastrointestinal or urinary tract obstruction
- Peptic ulcer disease
- Severe cardiac disease

Anticholinergic Drugs



Uses of Anticholinergic Drugs

- **Preoperative Medication**

➢ They inhibit salivary and bronchial secretions.

➢ They block the vagal slowing of the heart that can Occur with general anesthesia.

- **Gastrointestinal Disorders**

➢ They decrease gastrointestinal motility and can be used to treat ulcers, diarrhea, and hypermotility.

- **Ophthalmologic Examinations**

➢ Topical use can cause mydriasis which causes a full visualization of the retina.

➢ Cycloplegia relaxes the lens so that proper prescriptions for glasses can be determined.

- **Parkinson Disease**

➢ They reduce the tremors and rigidity associated with Parkinson and drug induced Parkinson disease.

- **Motion Sickness**

➢ These drugs are used to treat or prevent motion sickness because of their central nervous system depressant action.

- **Dentistry**

➢ These drugs are used to create a dry, oral field.

Adverse Reactions

The adverse reactions are an extension of the drugs' pharmacologic effects. They include:

- Xerostomia
- Constipation
- Urinary retention
- Blurred vision
- Hyperpyrexia
- Hallucinations
- Photophobia
- Tachycardia

Contraindications

Contraindications are usually due to the drugs' pharmacologic and adverse effects. They include:

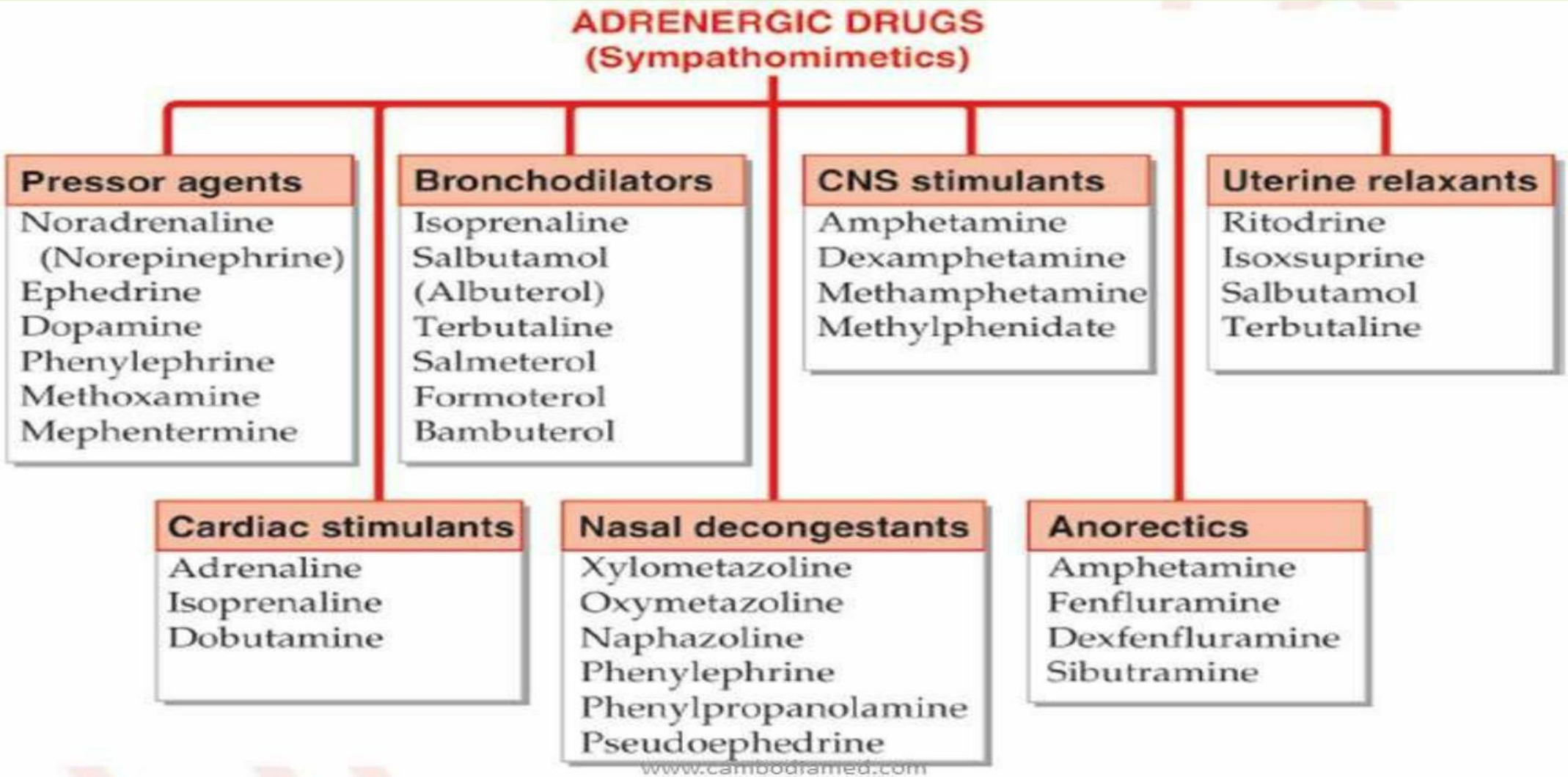
•Glaucoma

•Prostatic hypertrophy

•Intestinal or urinary obstruction or retention

•Cardiovascular disease

Adrenergic Drugs



Uses of Adrenergic Agonist Drugs

- **Vasoconstriction**

These drugs are used in dentistry because of their vasoconstrictive actions on blood vessels. They are added to local anesthetics because they prolong the action of the local anesthetic, reduce the risk for systemic toxicity, and help to create a dry field.

- **Cardiac Effects**

These drugs are used to raise blood pressure and to treat cardiac arrest.

- **Bronchodilation**

These drugs are used to treat asthma, emphysema, and allergic reaction.

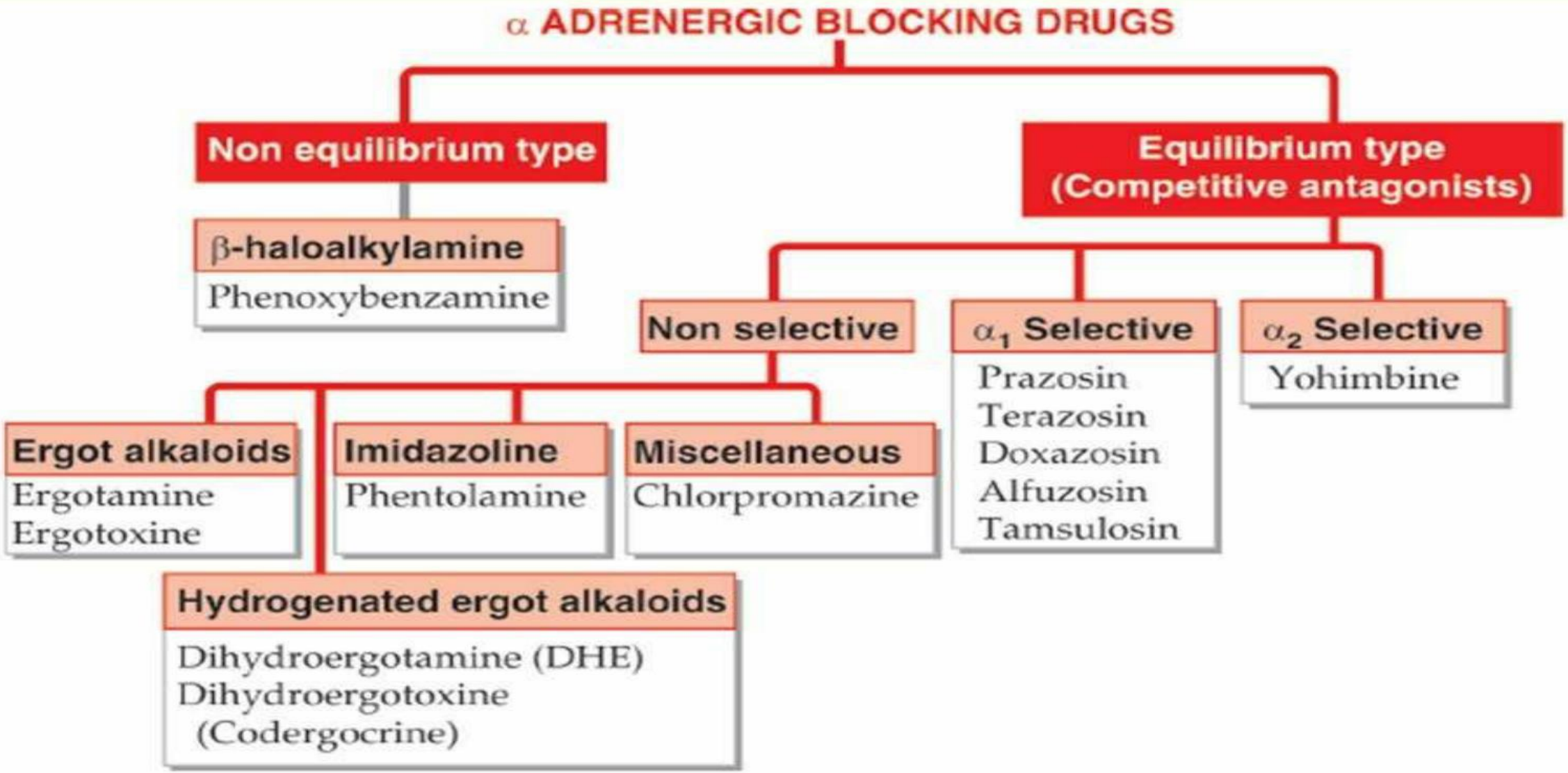
- **Central Nervous System Stimulation**

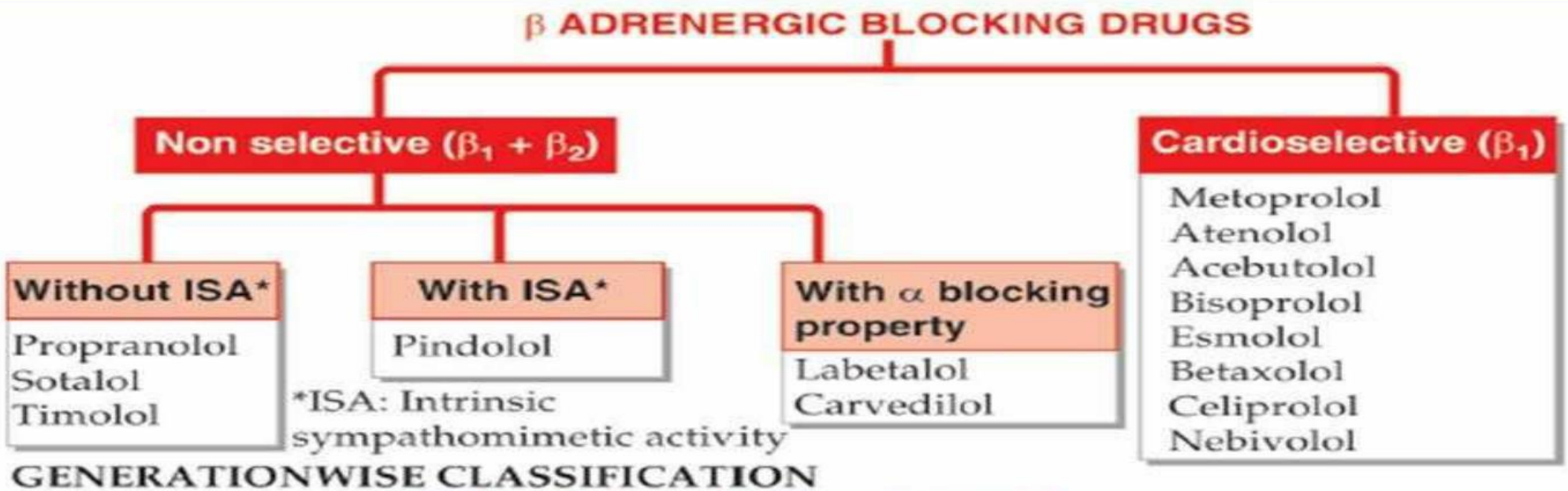
These medications are used for the treatment of attention deficit hyperactivity disorder, narcolepsy, and as diet aids.

Adverse Reactions

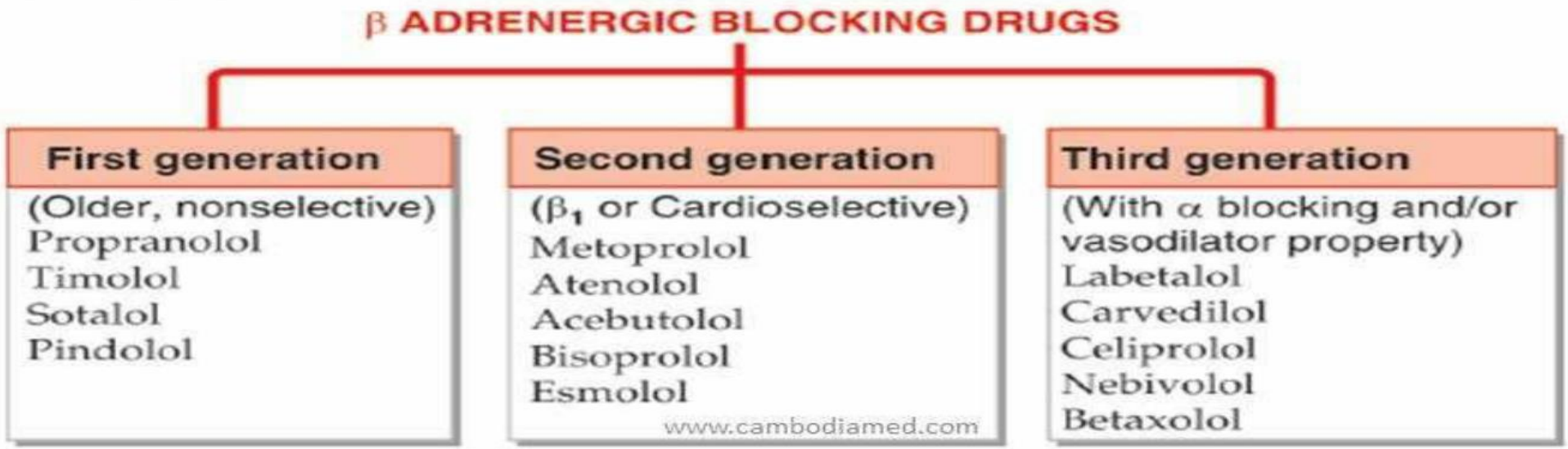
The adverse reactions associated with these drugs are an extension of the drugs' pharmacologic effects. They include:

- Anxiety
- Tremors
- Tachycardia
- Increased blood pressure
- Arrhythmias


α ADRENERGIC BLOCKING DRUGS
Non equilibrium type
β-haloalkylamine
Phenoxybenzamine
Equilibrium type (Competitive antagonists)
Non selective
α1 Selective
Prazosin
Terazosin
Doxazosin
Alfuzosin
Tamsulosin
α2 Selective
Yohimbine
Ergot alkaloids
Ergotamine
Ergotoxine
Imidazoline
Phentolamine
Miscellaneous
Chlorpromazine
Hydrogenated ergot alkaloids
Dihydroergotamine (DHE)
Dihydroergotoxine
(Codergocrine)
www.cambodiamed.com



GENERATIONWISE CLASSIFICATION



- **Pharmacology**

✓These drugs reduce sympathetic tone in the blood vessels and decrease total peripheral resistance.

✓This results in a reduction in blood pressure.

- **Uses**

✓These drugs are used to treat hypertension, and benign prostatic hypertrophy.

Nursing Implementation

• Adrenergic agents like Epinephrine can trigger cardiac arrhythmias, particularly if the patient is receiving digoxin.

• Anticholinergics like atropine may induce urine retention and constipation in elderly. It may increase intraocular pressure. Avoid them in glaucoma.

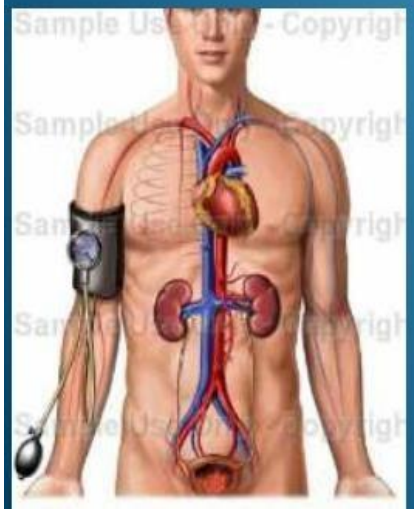
• α-Blockers like prazosin and doxazosin may cause orthostatic hypotension especially the first dose.

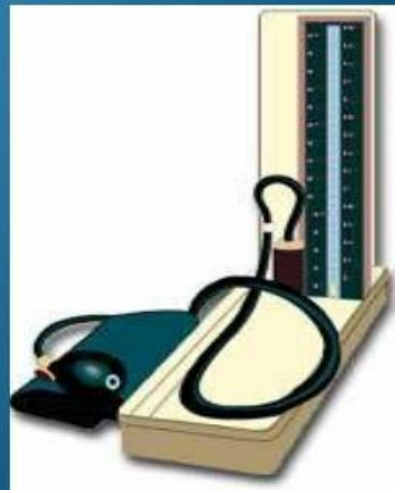
• β-blockers like Propranolol has the potential to cause significant bronchoconstriction due to blockade of β-2 receptors. Avoid in asthmatic patients, death by asphyxiation has been reported for patients with asthma.

• Treatment with β-blockers must never be stopped abruptly because of the risk of precipitating cardiac arrhythmias.

• Blockade of β-leads with Propranolol lead to decreased glycogenolysis and decreased glucagon secretion. Fasting hypoglycemia may occur avoid in diabetic patients.

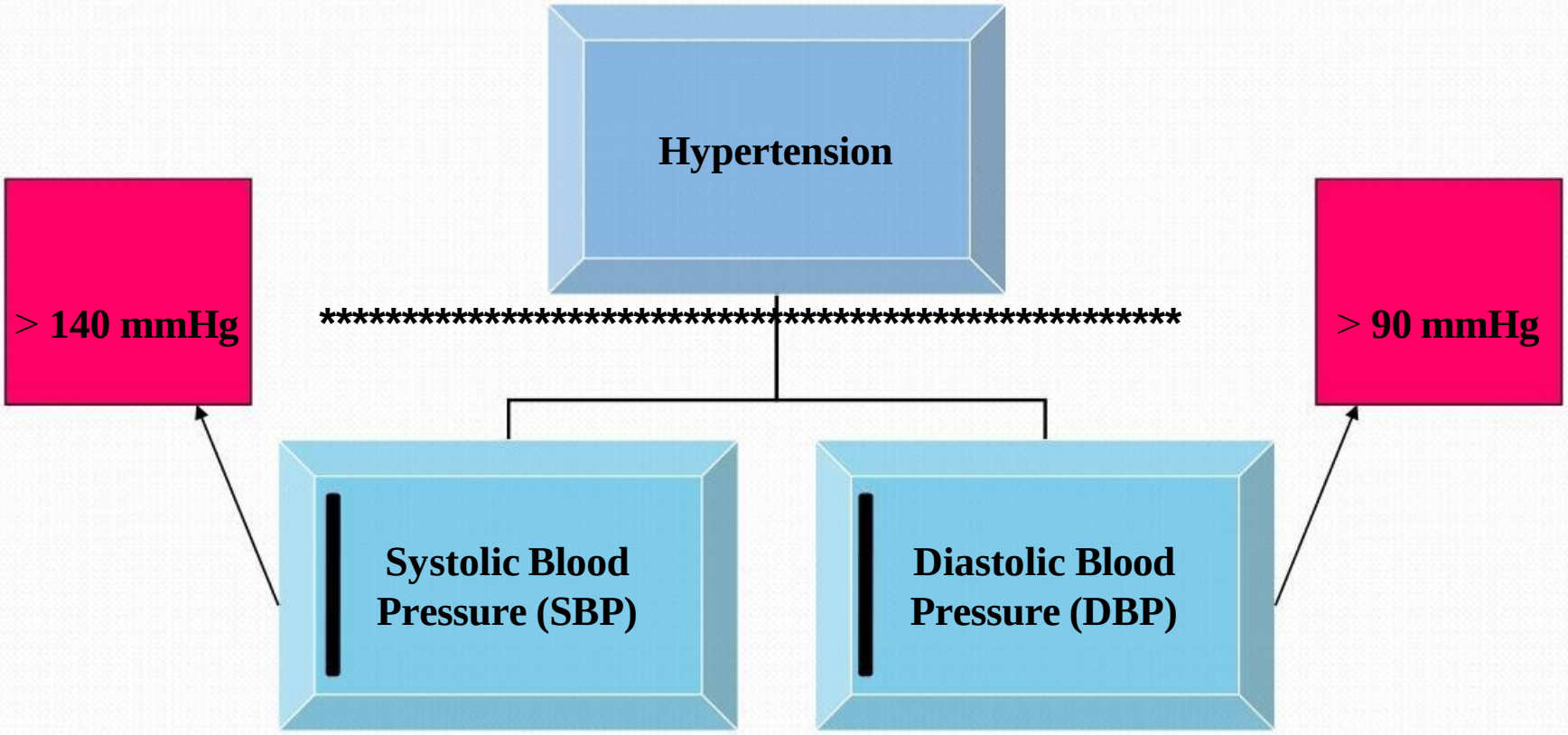
Antihypertensive Drugs

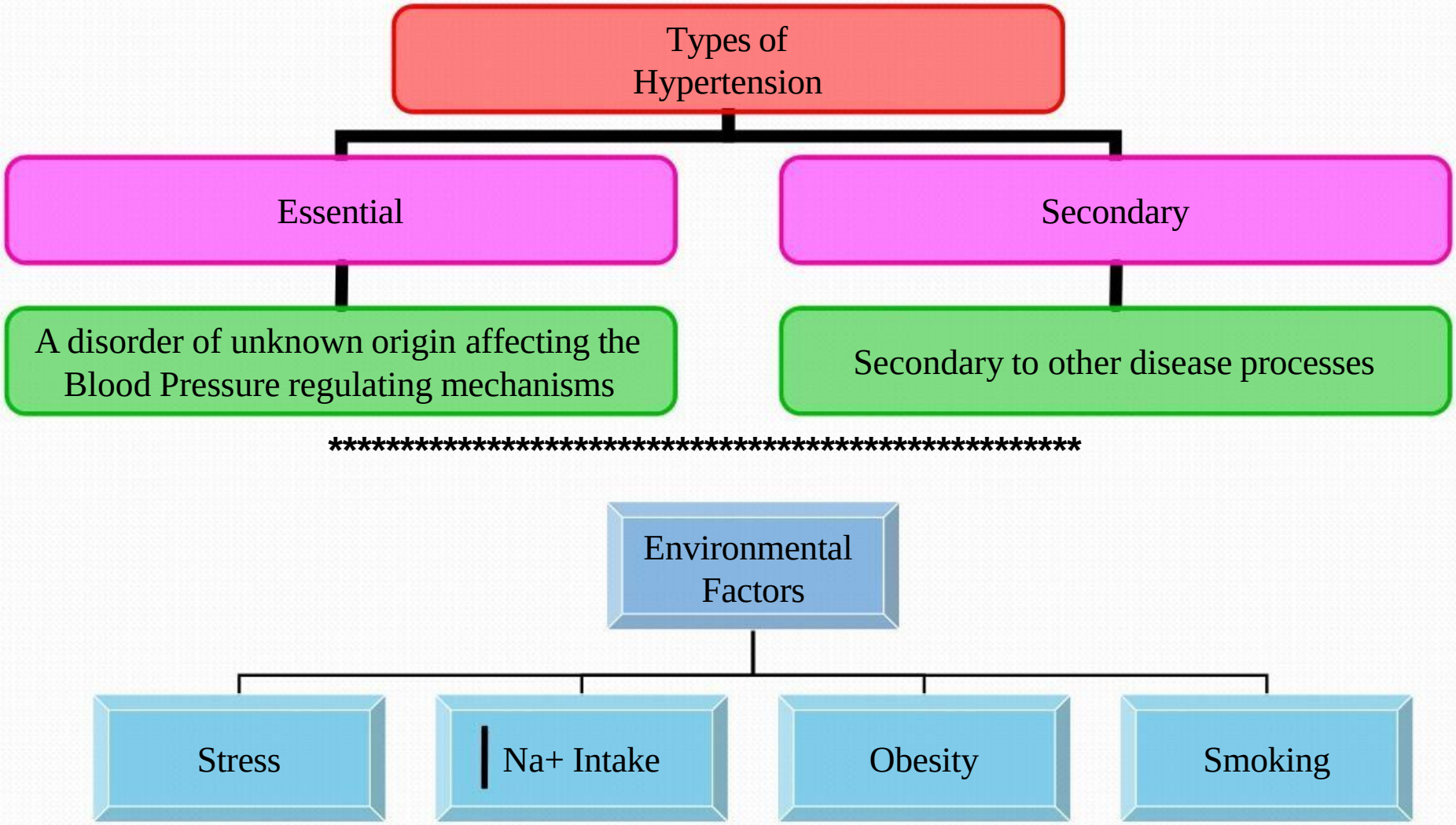




Dr. Zena Sattam

Introduction




Types of Hypertension
Essential
Secondary
A disorder of unknown origin affecting the Blood Pressure regulating mechanisms
Secondary to other disease processes
****
Environmental Factors
Stress
Na+ Intake
Obesity
Smoking

Antihypertensive Drugs

- Diuretics:
  - Thiazides: Hydrochlorothiazide, chlorthalidone
  - Loop Diuretics: Furosemide
  - K+ sparing: amiloride and Spironolactone

Mechanism of action : Acts on Kidneys to increase excretion of Na and H_2O – decrease in blood volume and decrease in BPP

- Angiotensin-converting Enzyme (ACE) inhibitors:
  - Captopril, lisinopril., enalapril, ramipril

Mechanism of action: Inhibit synthesis of Angiotensin II – decrease in peripheral resistance and blood volume

- Angiotensin (AT_1) blockers:
  - Losartan, candesartan, valsartan and telmisartan

Mechanism of action: Blocks binding of Angiotensin II to its receptors

Antihypertensive Drugs

- Centrally acting:
  - methyldopa

Mechanism: Act on central α_2 receptors to decrease sympathetic outflow

- ß-adrenergic blockers:
  - **Non selective:** Propranolol (others: nadolol, timolol, pindolol, labetolol)
  - **Cardioselective: Metoprolol** (others: atenolol, esmolol, betaxolol)

Mechanism: Bind and blocks the activity of beta adrenergic receptors

- ß and α – adrenergic blockers:
  - Labetolol and carvedilol
- α – adrenergic blockers:
  - Prazosin, terazosin, doxazosin.

Mechanism : Blocking of alpha adrenergic receptors in smooth muscles - vasodilatation

Antihypertensive Drugs

- Calcium Channel Blockers (CCB):
  - Verapamil, diltiazem, nifedipine, amlodipine, nimodipine etc.

Mechanism : Blocks influx of Ca++ in smooth muscle cells caused relaxation of Smooth muscle cell in blood vessel and decreased BP.

- K+ Channel activators:
  - Diazoxide, minoxidil, and nicorandil

Mechanism : Opening of K+ caused relaxation of SMCs

- Vasodilators:
  - Hydralazine and Sodium Nitroprusside

Thiazide diuretics (adverse effects)

Hypokalemia
Hyperglycemia
Hyperlipidemia
Hyperuricemia

Losartan

- Adverse effects:
- Fetopathy like ACEIs

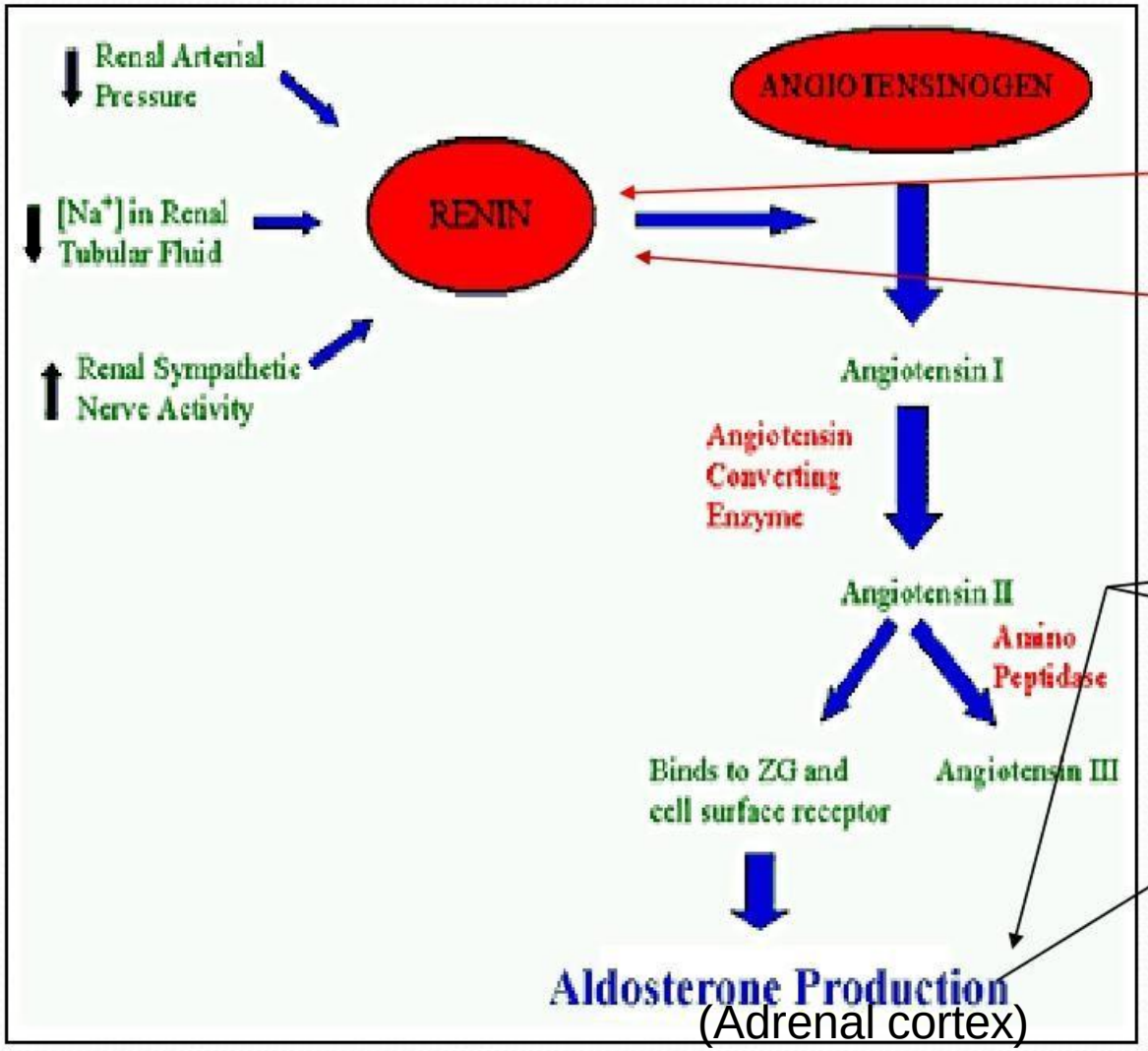
(not to be administered in pregnancy)

- Rare 1st dose effect hypotension
- No dry cough
- Lower incidence of angioedema
- Available as 25 and 50 mg tablets

Captopril (Adverse effects)

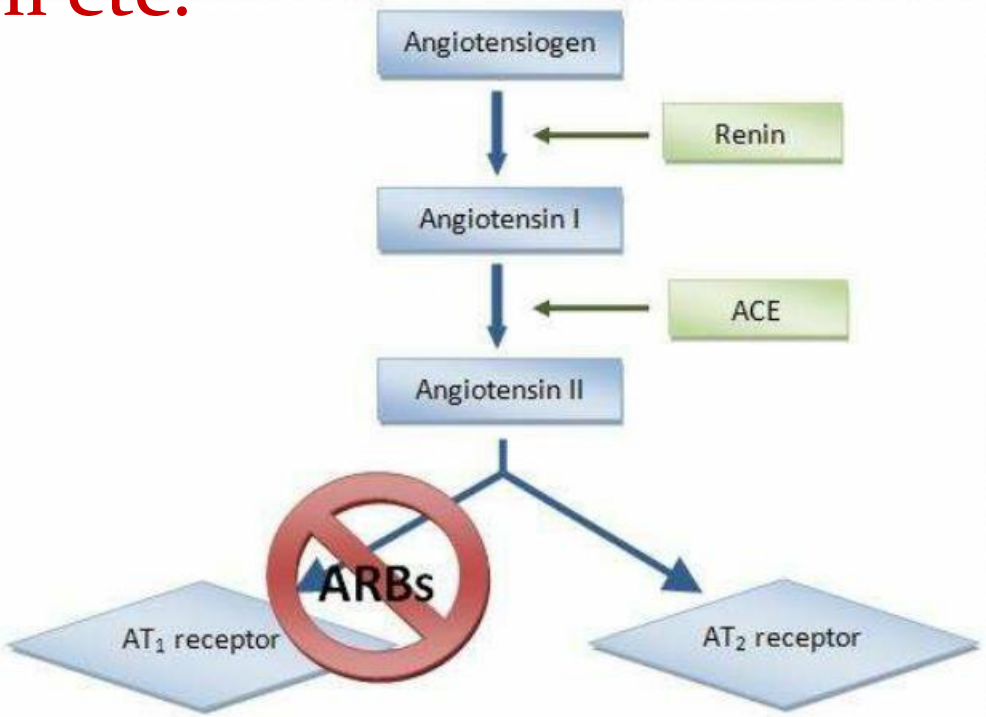
- Cough
- Hyperkalemia
- Hypotension
- Acute renal failure
- Angioedema
- Rashes, urticaria etc

RAS - Physiology



ACE inhibitors

- Captopril, lisinopril., enalapril, ramipril and fosinopril etc.

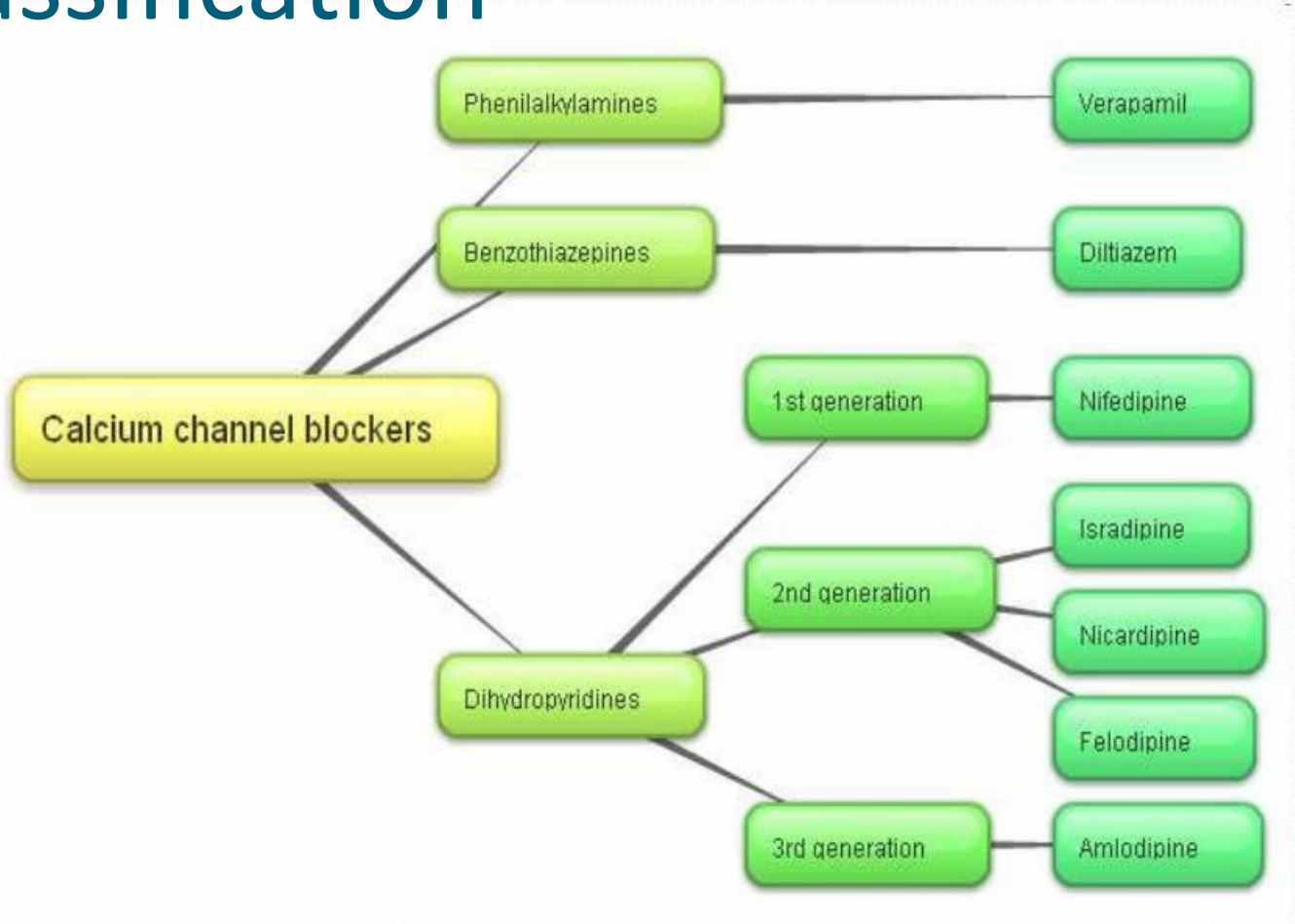


Beta-adrenergic blockers

- **Non selective: Propranolol**
  (others: nadolol, timolol, *pindolol*, labetolol)
- **Cardioselective: Metoprolol**

(others: atenolol, esmolol, betaxolol)

Calcium Channel Blockers - Classification



Calcium Channel Blockers

- Advantages:
  - Unlike diuretics no adverse metabolic effects but mild fatigue etc.
  - Do not compromise haemodynamics – no impairment of work capacity
  - No sedation
  - Can be given to asthma, angina and PVD patients
  - No renal and male sexual function impairment
  - No adverse fetal effects and can be given in pregnancy

Calcium Channel Blockers

- Contraindications:
  - Unstableangina
  - Heartfailure
  - Hypotension
  - Post infarct cases
  - Severe aortic stenosis

Hypertension in pregnancy.

- Avoid diuretics, propranolol, ACE inhibitors
- Safer drugs: Hydralazine in emergency, Methyldopa can be used.

Nursing considerations

- Teach them how to take pulse and blood pressure. Hold the medication in case of hypotension or bradycardia and consult the treating Dr.
- Monitor blood pressure frequently during initiation of therapy. Because drug-induced vasodilation has a gradual onset.
- Tell woman of childbearing age to notify doctor if pregnancy occurs. Drug will need to be stopped.
- Diabetic patient should be very careful about symptoms of hypoglycemia.
- Report any asthma-like symptoms.
- With Ca channel blockers, notify doctor if signs of heart failure occur, such as swelling of hands and feet or shortness of breath.
- Teach patient to continue taking drug, even when feeling better.
- Grapefruit juice may increase drug level and adverse reactions. Discourage use together.
- Instruct the client to report any untoward sings as dizziness. In case of postural hypotension, advise the client to change position slowly.
- Advise client to adhere to low sodium diet.
- Obtain baseline hematological studies, liver & renal functions tests prior to beginning the treatment.

Nursing considerations

- Observe client closely for hypotension 3 hours after the initial dose, especially With captopril and alpha blocker group due to first dose effect.
- With Captopril group, stop potassium sparing diuretics (hyperkalemia may occur).and consult with physician
- Take captopril 1 hour before meal or on an empty stomach.
- Report skin rash, heartburn, and chest pain to physician.
- Explain to patient that he may develop loss of taste for 2-3 months, if it persist, notify the physician.
- Diabetic patients, those with impaired renal function or heart failure, and those receiving drugs that can increase potassium level may develop hyperkalemia. Monitor potassium intake and potassium level.
- Instruct patient to report breathing difficulty or swelling of face, eyes, lips, or tongue. Swelling of the face and throat (including swelling of the larynx) may occur, especially after first dose.
- Advise patient to report signs of infection, such as fever and sore throat.
- Inform patient that light-headedness can occur, especially during first few days of therapy. Tell him to rise slowly to minimize this effect and to notify doctor if symptoms develop. If he faints, he should stop taking drug and call prescriber immediately.
- Tell patient to use caution in hot weather and during exercise. Inadequate fluid intake, vomiting, diarrhea, and excessive perspiration can lead to light-headedness and fainting.

Cardiovascular system

Drugs of Congestive heart failure

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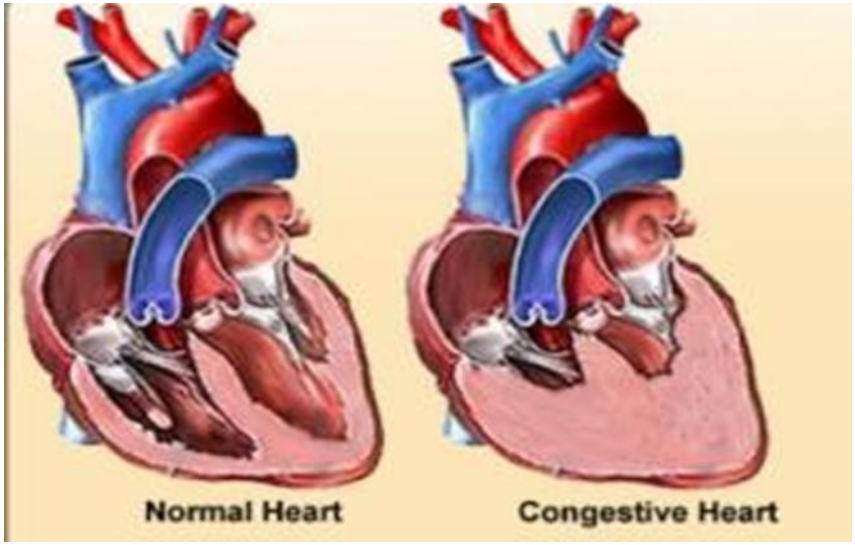
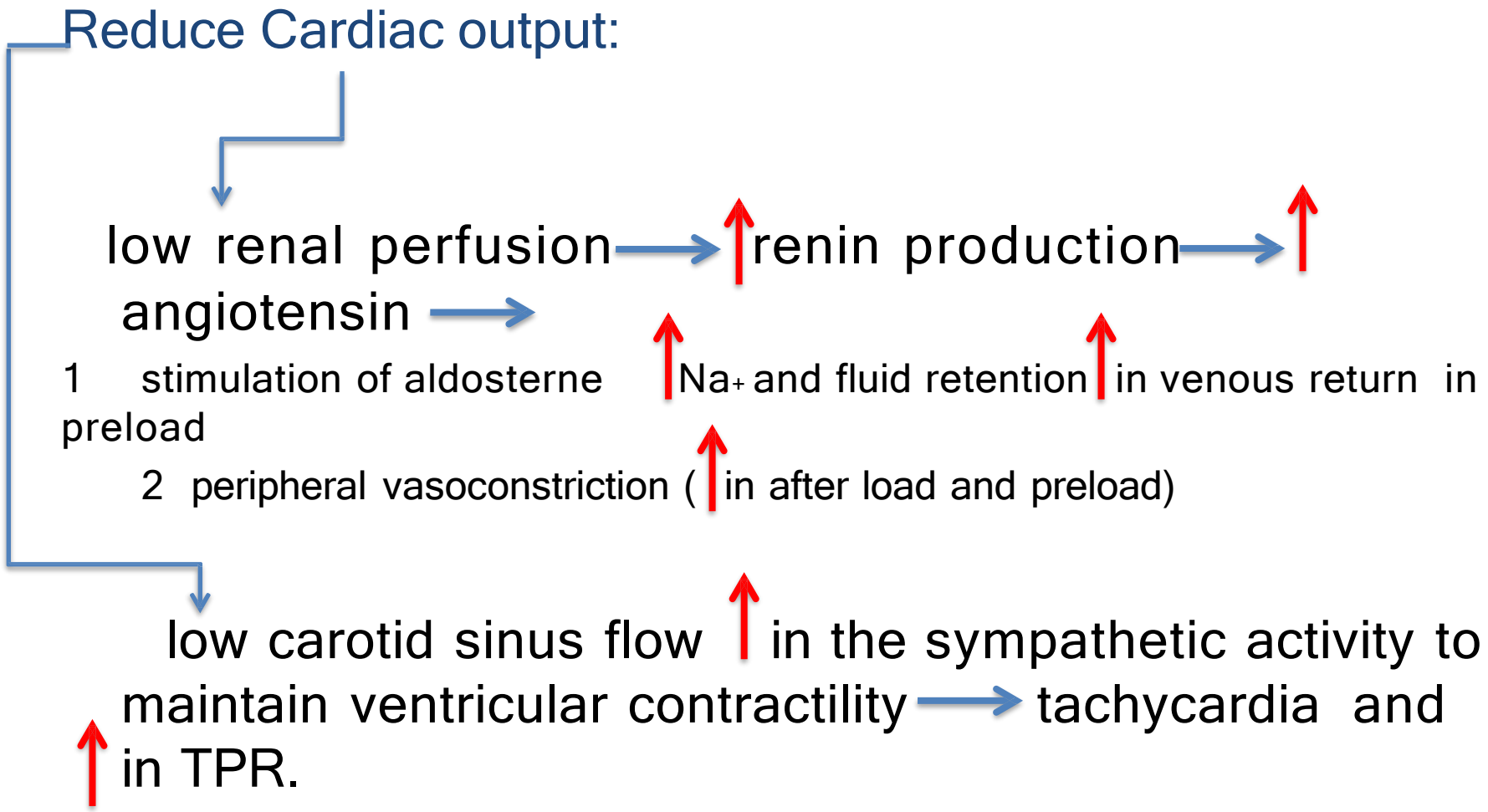
Drugs of Congestive heart failure (CHF)



- A normal individual expels about 55 to 65% of the blood from the left ventricle per heart- beat (EF 55–65%).
- Chronic CHF: the clinical condition in which an individual expels less than 40% of the blood from the left ventricle per heartbeat (ejection fraction [EF] 40%).

The pathophysiology



Therapeutic strategies in HF

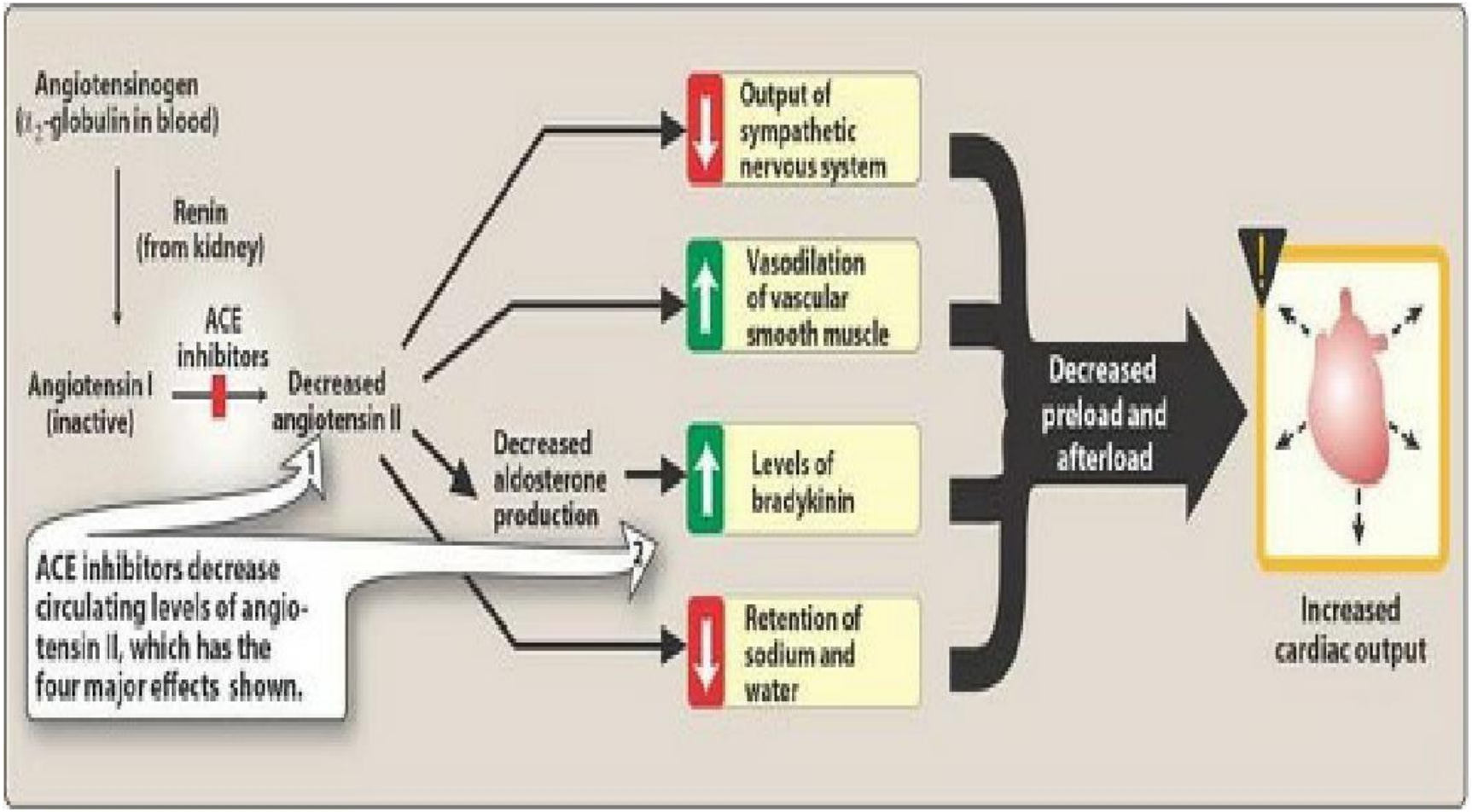
Chronic HF is typically managed by:

- a reduction in physical activity,
- fluid limitations (less than 1.5 to 2 L daily);
- low dietary intake of sodium (<1500 mg/day),
- treatment of comorbid conditions, and judicious use of:
  - diuretics,
  - inhibitors of the renin-angiotensin system,
  - and inotropic agents.

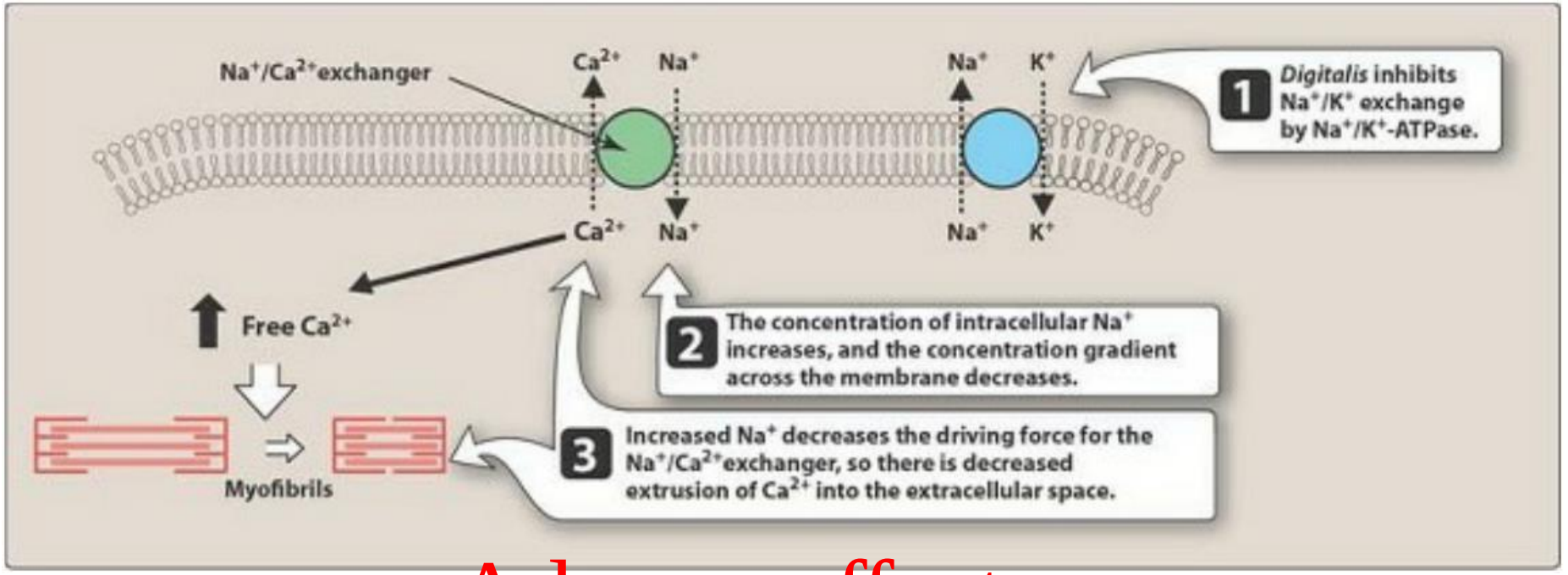
Avoid Drugs that may precipitate or exacerbate HF, such as:

- NSAIDs (nonsteroidal anti-inflammatory drugs),
- alcohol,
- Nondihydropyridine calcium-channel blockers,
- some antiarrhythmic drugs, should be avoided if possible.

Effects of (ACE) inhibitors.



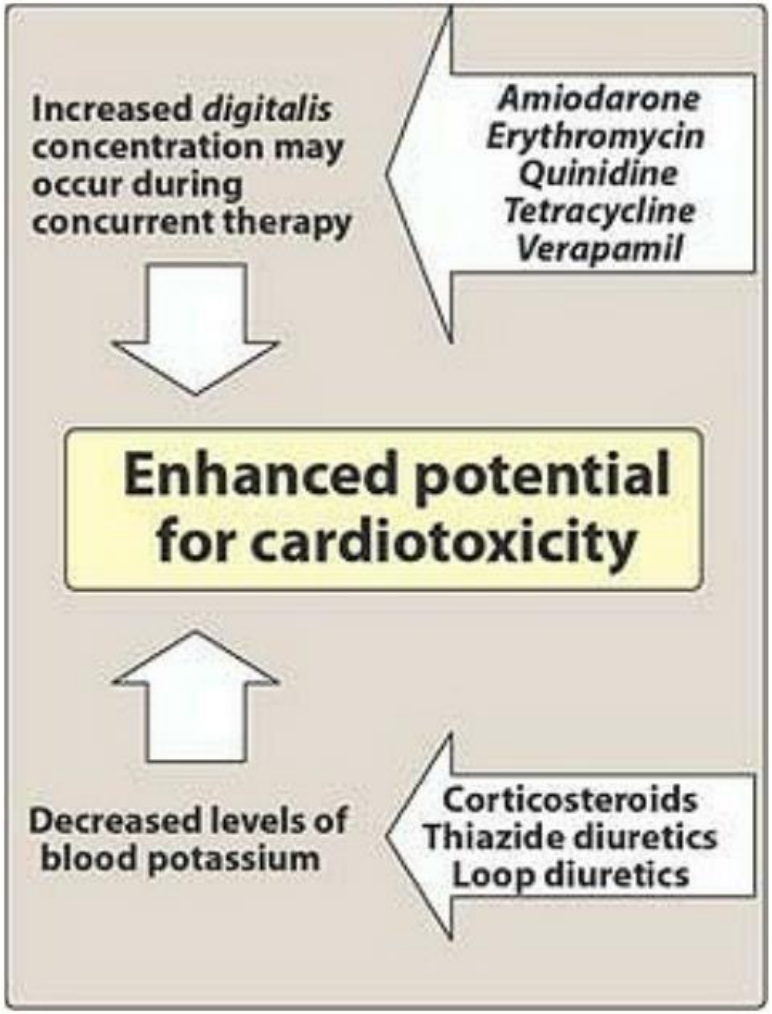
Cardiac glycosides
(Digitalis: foxglove) digoxin & digitoxin



Adverse effects

- Cardiac effects: is arrhythmia
- GIT effects: Anorexia, nausea, and vomiting.
- CNS effects: headache, fatigue, confusion, blurred vision, alteration of color perception, and halos on dark objects.

Factors predisposing to digitalis toxicity



Another inotropic agent: β_1-AGONISTS

- ex : dobutamine
- improves cardiac performance by both positive inotropic effects and vasodilation
- must be given by I.V. infusion and is primarily used in the treatment of acute heart failure in hospital setting

Antianginal drugs-Pharmacology

Angina

- Is a characteristic sudden, severe, pressing-like substernal chest pain radiating to the neck, jaw, back, and arms. Patients may also present with dyspnea or atypical symptoms such as indigestion, nausea, vomiting, or diaphoresis.
- is caused by inadequate blood flow through the coronary blood vessels, is a consequence of myocardial O_2 demand exceeding supply.

Angina-precipitating factors:

exercise, emotional stress, sex →

↑sympathetic activity → ↑HR, Contraction force, wall tension, TPR → ↑ work of the heart →

↑ myocardial O_2 demand ≠ myocardial O_2 supply

↓

Ischemia

Therapeutic strategies

1. Increase blood flow to ischemic heart muscle and/or
2. Decrease myocardial oxygen demand

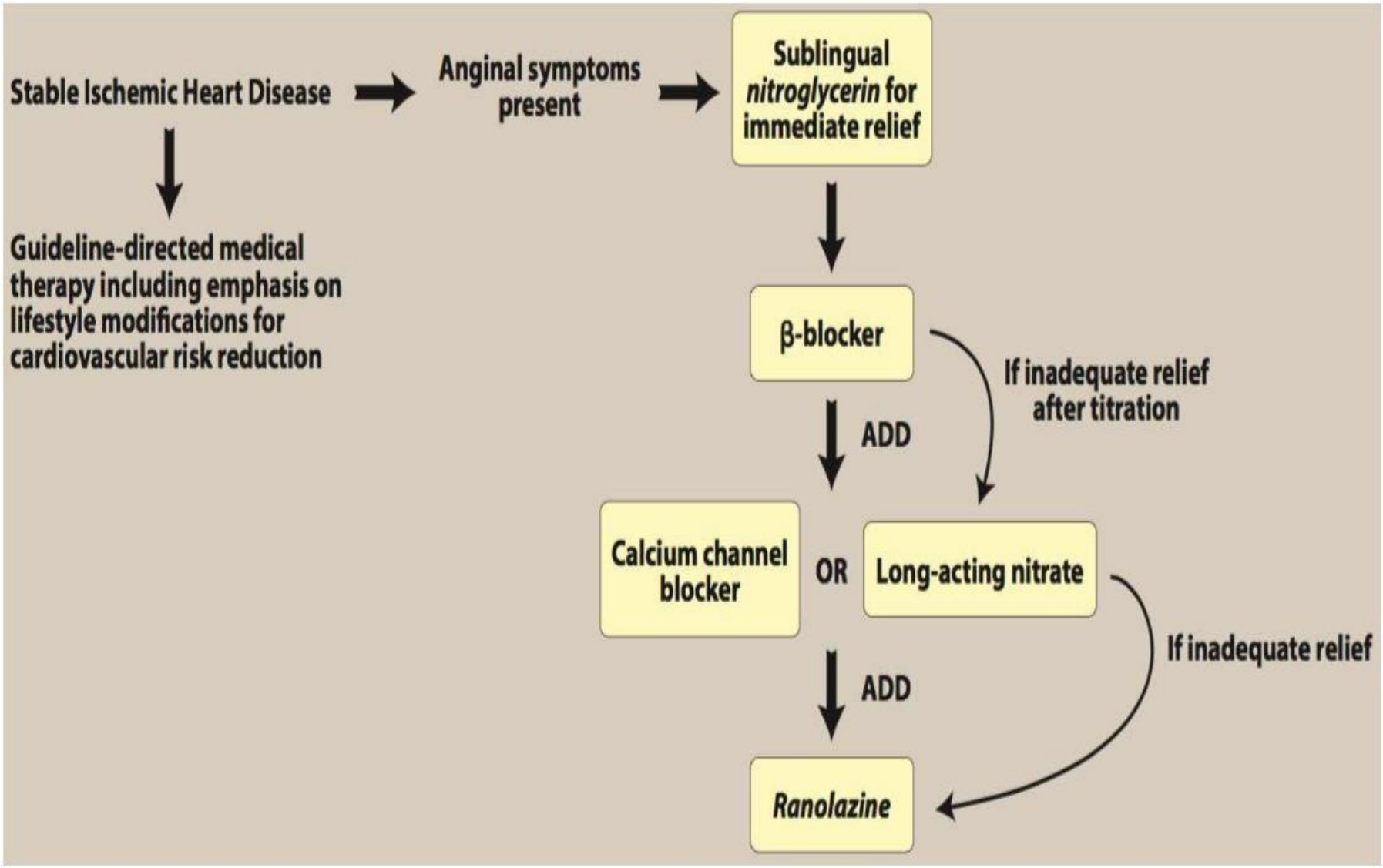
Four types of drugs, used either alone or in combination, are commonly used to manage patients with stable angina: β-blockers, CCBs, organic nitrates, and the sodium channel blocking drug, *ranolazine*. These agents help to balance the cardiac oxygen supply and demand equation by affecting blood pressure, venous return, heart rate, and contractility.

Lipid lowering drugs, particularly **statins**, can be given if elevated plasma cholesterol levels are detected

Antiplatelet drugs, especially low-dose (75mg) **aspirin** to **reduce the possibility of thrombosis**.

Fibrinolytic drugs (e.g. **heparin**) are used in **unstable angina**

Treatment algorithm for improving symptoms in patients with stable angina.



Organic nitrates

Nitroglyserin, Isosorbid dinitrat, Isosorbid mononitrate

The total effect is a decrease in myocardial oxygen consumption because of decreased cardiac work

Common nitrate preparations

Glyceryl trinitrate can be taken by sublingual tablet or spray

The effects start within minutes and last ~30 min

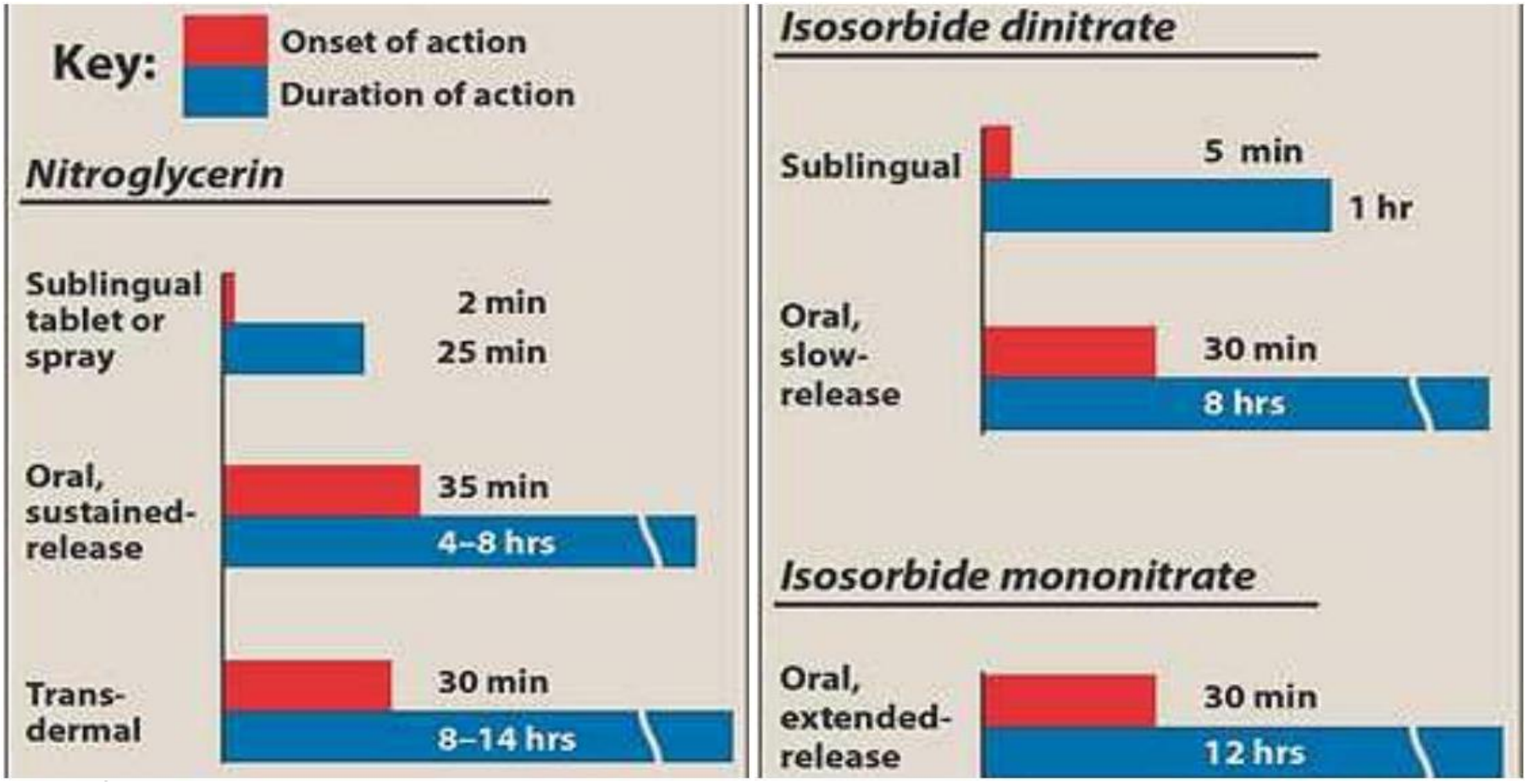
Transdermal patches and **I.V preparations** are also available

Isosorbide mononitrate is a longer acting preparation which is given orally (half-life 4hrs), and slow release preparations are available.

Side effects: nitrates can cause

Headache in about 30% - 60% of patients because of the pronounced vasodilation.

Time to peak effect and duration of action



Nitrate Tolerance

- **Tolerance** develops rapidly. The blood vessels become desensitized to vasodilation. providing a daily **"nitrate-free interval"** to restore sensitivity to the drug.
- This interval is typically 10 to 12 hours, usually at night, because demand on the heart is decreased at that time.
- Nitroglycerin patches are worn for 12 hours then removed for 12 hours.

Drugs used for Hyperlipidemia

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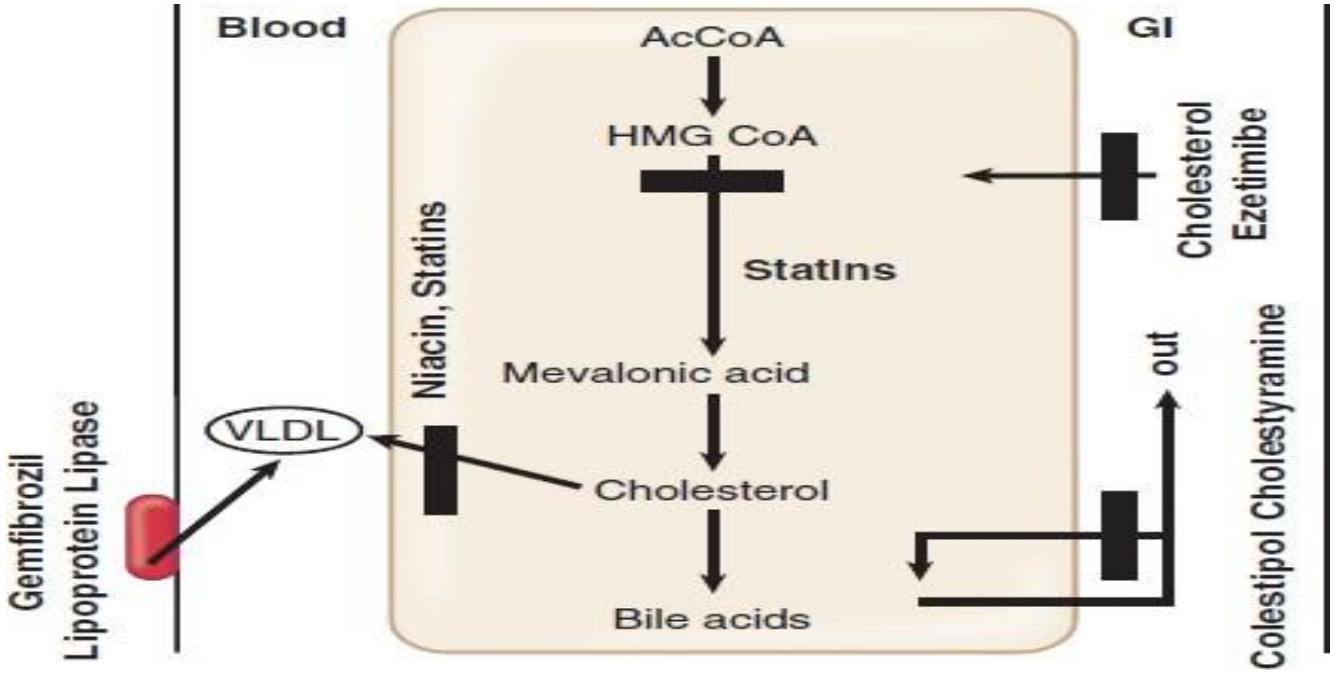


Site of action of Statins, Niacin and Gemfibrozil on the synthesis of Lipids

1- HMG-CoA REDUCTASE INHIBITORS

Atorvastatin, Rosuvastatin, Lovastatin

– Mechanisms: HMG-CoA reductase inhibition

–, results in:

↓ liver cholesterol

↓ plasma LDL ≥ 50%

↓ triglyceride

Side effects:

– Myalgia, Myopathy (check creatine kinase)

– Hepatotoxicity (check liver function tests)

Drug interaction:

– Gemfibrozil (↑ myopathy)

2- BILE ACID SEQUESTRANTS

Cholestyramine and **colestipol**

Mechanism:

- ↓ bile salts
- ↓ liver cholesterol

Side effects:

- **↑ triglycerides !!!**
- Gastrointestinal disturbances
- Malabsorption of lipid-soluble vitamins
- Hyperglycemia

3- EZETIMIBE

Mechanism: prevents intestinal absorption of cholesterol, results in↓ LDL

Side effect: gastrointestinal distress

4- NIACIN :

Mechanism: Inhibition of VLDL synthesis,

Side effects:

– Flushing, and Hyperglycemia

5- GEMFIBROZIL, FENOFIBRATE (FIBRATES)

– ↓ VLDL

– ↑ HDL

Side effects:

– Gallstones and Myositis

Drugs used for Blood disorders: A- Anticoagulants

Heparins

- Given parenterally (IV, SC), Rapid effect.
- Heparin activate antithrombin III.
- Side effects: Bleeding, osteoporosis, heparin induced thrombocytopenia (HIT).
- Antagonist in toxicity: Protamine sulfate
- Low-molecular-weight (LMW) heparins (e.g., **enoxaparin**) longer half-lives, less thrombocytopenia.

Warfarin

- Given orally, Longer-term effect
- Inhibit Hepatic synthesis of vitamin K–dependent factors II, VII, IX, X—
- Drug interactions:

–decrease oral absorption by cholestyramine

–increase metabolism by rifampin, while decreased by macrolides (erythromycin).

- Antidot : Vitamin K

Direct Activated Clotting Factor Inhibitors:

- Argatroban
- Rivaroxaban
- Dabigatran, Used orally as an alternative to warfarin.
- Bivalirudin by injection as an alternative in case of thrombocytopenia.

Thrombolytics:

They are used intravenously for short term emergency management of coronary thromboses in myocardial infarction (MI), deep venous thrombosis, pulmonary embolism, and ischemic stroke.

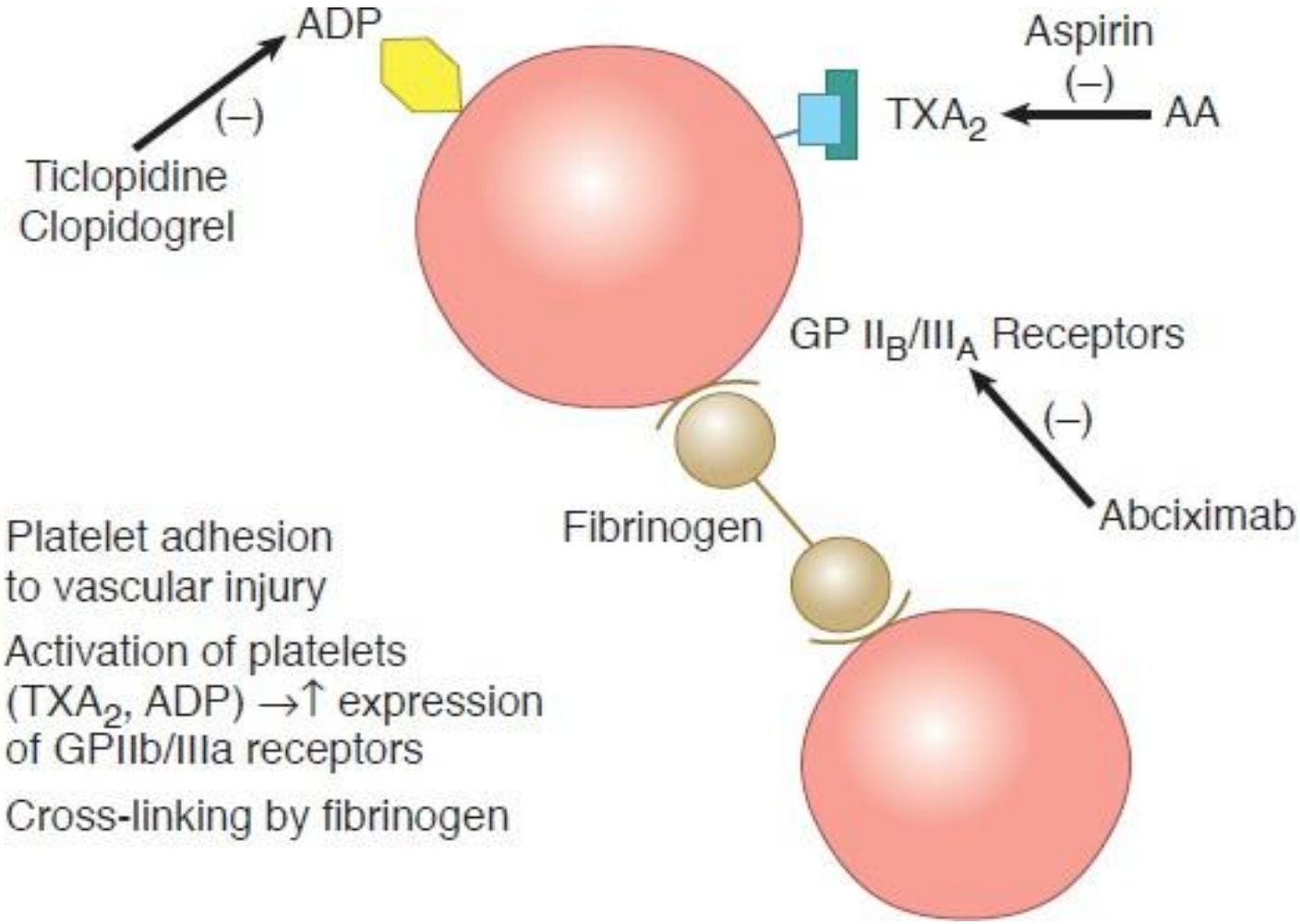
–Alteplase (tPA) Clot specific, acting mainly on fibrin-bound plasminogen, so no allergy problems

B- Antiplatelet Drugs:

Thrombus formation involves:

- Platelet adhesion to site of vascular injury
- Activation of platelets by factors that include TxA_2, ADP.
- Aggregation of platelets glycoprotein IIb by a cross-linking reaction due to fibrinogen binding to glycoprotein IIb/IIIa receptors

Platelet Activation



1. Platelet adhesion to vascular injury
2. Activation of platelets (TXA_2, ADP) $\rightarrow\uparrow$ expression of GPIIb/IIIa receptors
3. Cross-linking by fibrinogen

Antiplatelet Drugs:

١. Aspirin

– Irreversibly inhibits COX in platelets →↓ activation

– Low doses prevent MI and recurrence.

– Adverse effects: GIT problems

2. Clopidogrel

– Block ADP receptors on platelets →↓ activation

٣. Abciximab

– Antagonists that bind to glycoprotein IIb/IIIa receptors →↓ aggregation.

– Used mainly in acute coronary syndromes.

DIURETICS

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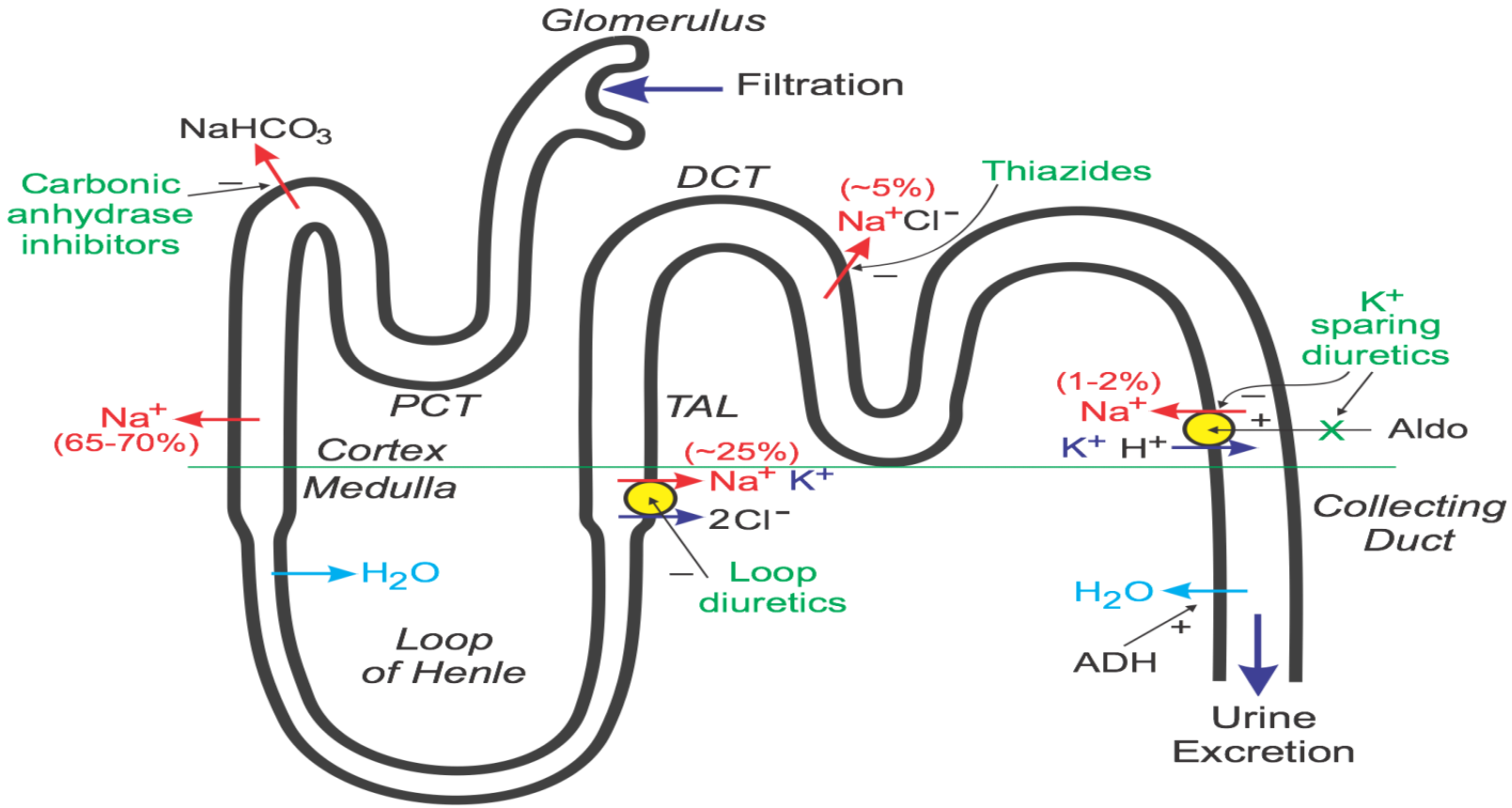
they increase urinary excretion of Na+ with water.



Renal diuretics:

1. Loop diuretics: they are high efficacy diuretics, they inhibit Na+ transport in the loop of Henle
2. Thiazide diuretics: they are moderate efficacy ,they inhibit Na+ transport in distal convoluted tubules (DCT).
3. K+-sparing diuretics: they are low efficacy diuretics:they are either aldosterone antagonists as spironolactone, or non-aldosterone antagonists as amiloride and

Thiazide diuretics: Well absorbed orally. Pass placental barrier and may cause teratogenicity. Urine will also contain excess Na+ and K+ and lesser amounts of Ca+. may reduce the risk of bone fractures.

Therapeutic uses

1. Treatment of mild and moderate hyperternsion.
2. Treatment of edema.

Adverse effects:

1. Hypokalemia.
2. Hypersensitivity.
3. Hyperlipidemia.
4. Hyperglycemia.
5. Hyperuricemia.
6. Teratogenicity.

How to Avoid Hypokalemia?

- Addition of a K+-sparing diuretic (amiloride or ACE inhibitors.
- Dietary potassium (in fruits and vegetables).
- K+ supplements:

Preparations:

1. Hydrochlorothiazide.
2. Thiazide analogues: Indapamide, Metolazone.

Loop Diuretics (High efficacy = High Ceiling Diuretics)

Frusemide, ethacrynic acid.

Pharmacokinetics: Well absorbed orally, and can be given by I.V. and I.M. injection (useful in emergencies). Pass placental barrier and may cause teratogenicity (fetotoxicity).

Actions: rapid onset, Duration, short duration.

Urine will contain excess of K+, Na+ and excess Ca+.

Therapeutic uses:

1. Edema:
2. Loop diuretics are given I.V. in acute left ventricular.
3. Hypertension: Emergency hypertension and Resistant hypertension.
4. Acute renal failure.

Adverse *effects*

1. Hypokalemia: K^+-Losing (depleting) diuretics are commonly used in treatment of heart failure with digitalis but never allow hypokalemia in these patients because it is the most important factor precipitating digitalis toxicity.
2. Hypovolemia and dehydration.
3. Hyperuricemia.
4. Hyperlipidemia.
5. Teratogenicity.
6. Ototoxicity: damage of the 8th cranial nerve which may cause deafness, especially if given concomitantly with other ototoxic drugs as aminoglycosides (streptomycin) or in renal impairment.

Potassium Sparing Diuretics

1. they are given orally only, Onset of action, not useful in emergencies, they are weak diuretic action.
2. Site of action: distal segment of DCT.
3. Diuretic action: inhibit Na+/K+ exchange. This causes excretion of Na+ and retention of K+ (hyperkalemia).
4. They are contraindicated in renal impairment to avoid severe hyperkalemia.

they are classified into:

A. Aldosterone antagonists: e.g. *Spironolactone.* They are competitive antagonists with aldosterone.

B. Non-Aldosterone antagonists: e.g. Amiloride block Na+-channels.

Uses and Adverse effects:

Uses : they are usually combined with thiazide diuretics or loop diuretics in treatment of edema and hypertension; to achieve synergism and maintain normal blood potassium.

Adverse effects:

a) Hyperkalemia especially in renal failure.
b) Feminization (Gynecomastia) and impotence in males, and irregular menstruation and masculanization in females (deepening of voice and hirsutism) due to steroid structure.

Drugs acting on gastrointestinal tract (GIT)

١ Drugs used for peptic ulcer disease
٢ Drugs used for to control emesis
٣ Antidiarrheals
٤ Laxatives
٥ Obesity

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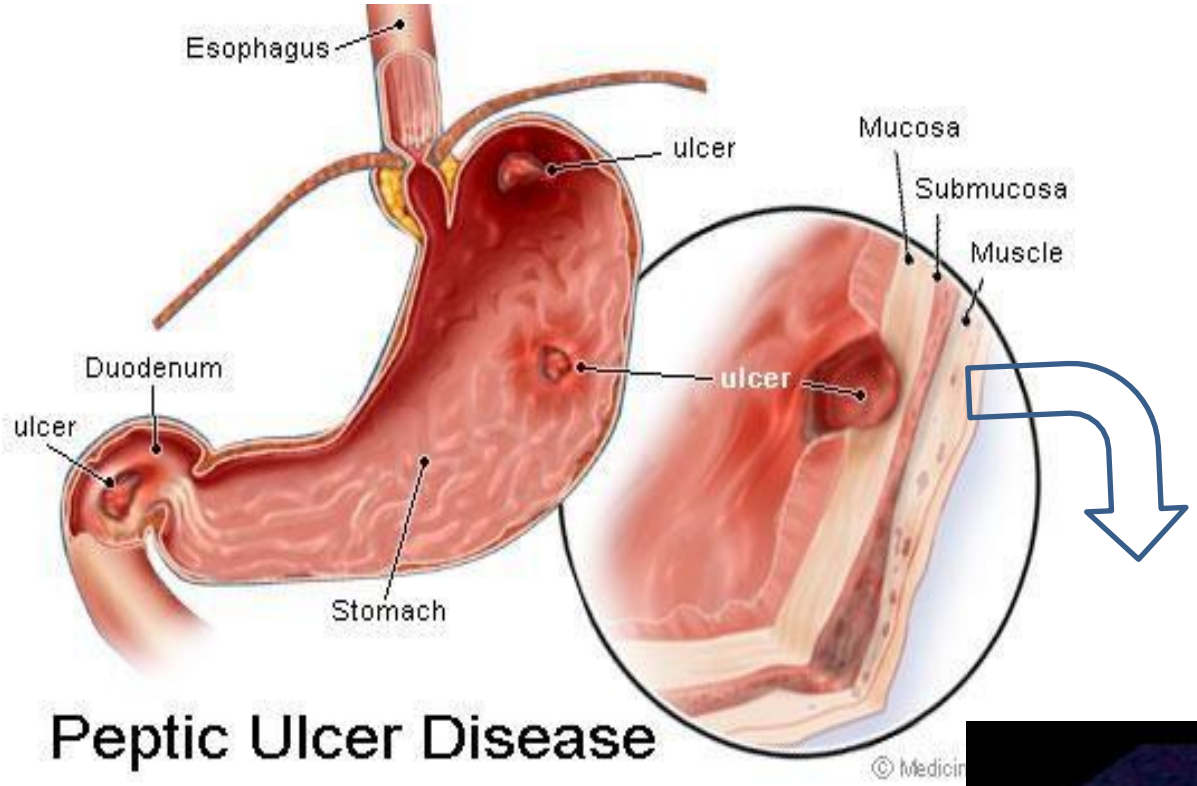
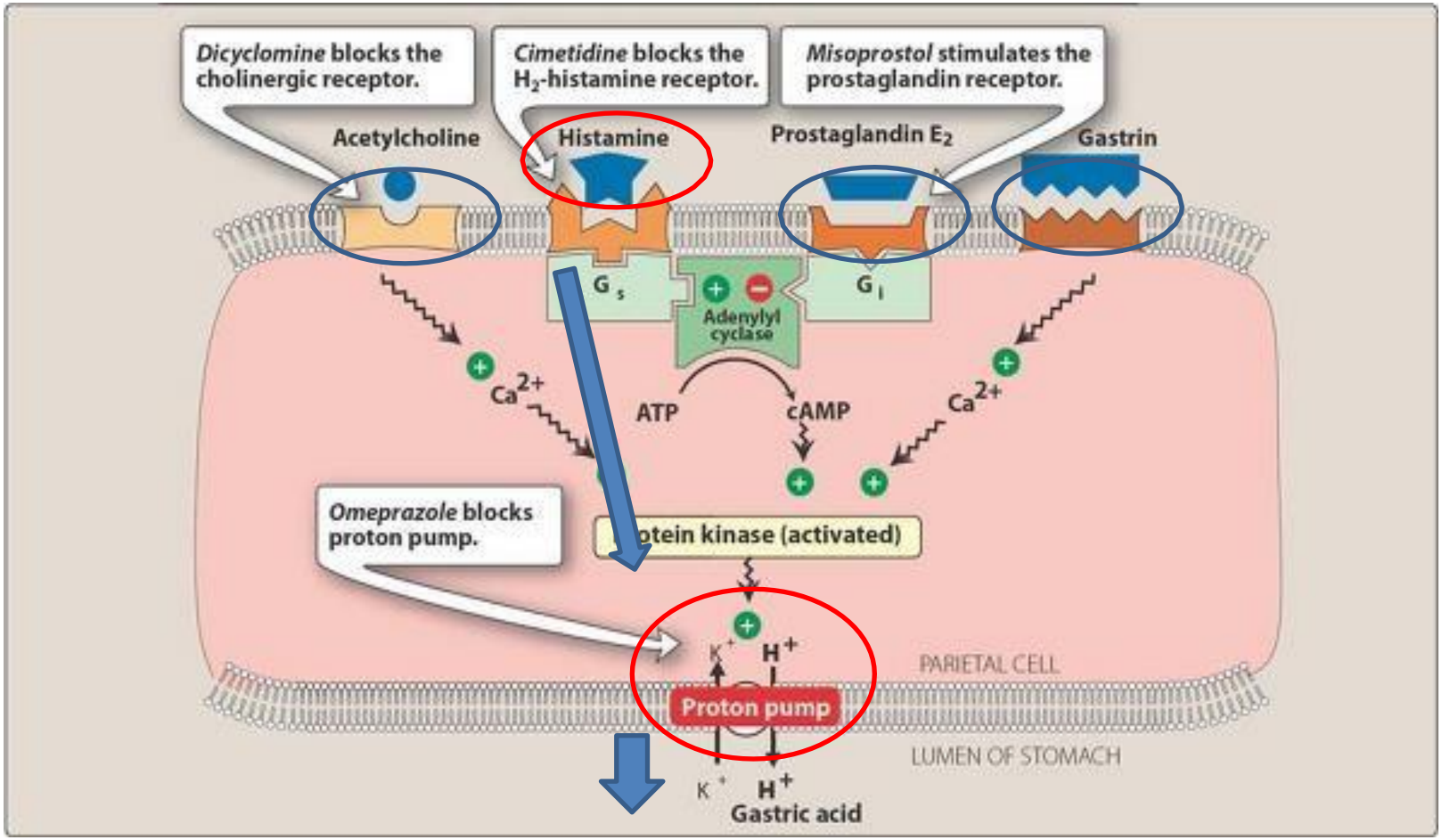


Peptic Ulcer Disease

Regulation of gastric acid secretion



Drugs used for peptic ulcer disease

A- H_2 -receptor antagonist

B- Inhibition of the H/K- ATPase proton pump

C- Antacids

H_2 -receptor antagonist (Cimetidine, Ranitidine, Famotidine)

Side effects : Headache, diarrhea, dizziness, and muscle pain.

Inhibitors of the H^+/K^--ATPase proton pump (PPIs)

Omeprazole, Lansoprazole, Rabeprazole

- are given in the form of "enteric-coated tablets" to prevent degradation by HCl.
- reduction of HCl secretion up to 100%.
- Side effects of PPIs: headache, diarrhoea, GIT infection with chronic use.

Uses of H2 antagonists and PPIs include:

1- Duodenal ulcer and stress ulcer (e.g burn)

3- In the treatment of GERD (gastroesophageal reflux disease)

4- Reduce risk of bleeding from an ulcer by NSAIDs (e.g. Ibuprofen)

Antacid

They are weak bases that react with gastric acid to form water and salt and gas.

- Aluminum hydroxide- causes constipation
- Magnesium trisilicate- causes diarrhea
- Antacid containing sodium such as sodium bicarbonate should be avoided in patients with hypertension or congestive heart failure.

Uses: They only relieve ulcer pain with rapid onset.

Nursing Implementation

- Administer H2 Blocker with meals and 1 hour apart from antacids.
- Monitor cardiovascular status when H2 blocker administered IV.
- Administer antacid drugs 2 hour after or 1 hour before other drugs.
- Tell the patients to chew the tablet thoroughly before swallowing.
- Administer PPIs before meals, don’t chew the capsule. Should be swallowed intact.

Drugs used to control emesis

A. **Phenothiazine:** e.g. Prochlorperazine

B. **5-HT3 serotonin-receptor blockers:** e.g. Ondansetron

Headache is the common side effect.

C. Substituted benzamides: e.g. Metoclpramide, Domperidone

is highly effective at high doses against the highly emetogenic cisplatin.

D. Antihistaminic with anticholinergic effects:

e.g Dimenhydrinate useful in motion sickness like sea sickness.

E. Corticosteroids: Dexamethazone They usually used in combination with other agents, are effective against mildly to moderately emetogenic chemotherapy.

Uses of Anti-emetics mainly include:

١. GIT diseases.

٢. Pregnancy.

٣. Motion sickness.

٤. Severe pain as acute myocardial infarction and renal colic.

٥. patients using drugs like morphine.

Side effects: dystonia, tremors, Hyperprolactinemia

Nursing Implementation of antiemetic drugs

- Administer only to conscious patients
- Administer with large amount of water
- Emesis is not expected to occur after repeated doses of antiemetic drugs
- Ensure that the drugs are taken on short term basis
- Avoid metoclopramide use in very young children and elderly patients with parkinsonism.
  Domperidone less CNS side effects

Antidiarrheals

A. Antimotility drugs (Diphenoxylate, loperamide)

Side effects

- Drowsiness, abdominal cramp, dizziness, toxic megacolon.
- They should not be used in young children

B. Adsorbents (Kaolin, pectin)

- suitable for young children

C. Direct smooth muscle relaxant:

e.g. Mebeverin used also in irritable bowel syndrome (IBS).

Nursing Implementation

- Monitor patients response to antidiarrheal drug and discontinue if there is no response.
- Treat the underlying cause of diarrhoea like infection.

Laxatives

Stimulants laxative (Senna and Bisacodyl)

Bisacodyl is a potent stimulant of the colon.

Side effects: Abdominal cramps and the potential of atonic colon with prolonged use.

Glycerin suppository: causes mild irritation of the colon and rectum, and softens the stools. It is used in children mainly.

Nursing Implementation

- Encourage high fluid intake, fiber diet, and daily exercise.
- Don't administer in acute abdominal condition like acute appendicitis.
- Advice the patients that chronic use may promote dependence of intestinal movements on laxative use.
- Avoid using stimulant laxatives in pregnancy.

Management of obesity

Note: Treatment mainly by regular physical exercise and low calorie diet rich in Bran and undigested fiber as methylcellulose

Drugs used in obesity:

Orlistat: reduces fat digestion and absorption. Adverse effects include fatty diarrhea impaired absorption of fat-soluble vitamins.

Metformin: may be used in certain cases which decreases appetite.

Drugs Acting on Respiratory System

- Drug liquefying sputum
- Drugs used for cough
- Drugs used for asthma

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Expectorants

- They are drugs that **loosen the sputum** and thus aid it's ejection from the bronchial tree.

Examples : **Ammonium chloride**, **Guaifenesin**, as syrups preparation given orally.

Mucolytics agents

- Mucolytic drugs are those which used to **liquefy mucus.**
- Examples :
- **1. Bromhexin (Bisolvon®)**
- **2. Ambroxol (Mucosolvan®)**

- ***Steam*** a very good expectorant as it liquifies the sputum and thus enables it to be coughed.

Cough suppressants:

- **A) Demulcents:**
- simple **linctus** which comes as syrup and should not be given to diabetic patients because it contains sugar. E.g. honey syrup
- **B) Opioids:**
- 1. **Codeine**: which is the most popular of this group, it was included in linctus codiene.
- side effects: Sleep disturbances, constipations.
- 2. **Dextromethorphan**.
- Related to codeine and it depresses cough centers.
- It is more active than codeine and it's action lasts 4- 6 hours.

C) Antihistamines: (e.g. Diphenhydramine, Loratadine).

Asthma

Drug classes used in asthma:

A- Corticosteriods

B- Bronchodilators

A. 1. Corticosteroids

- **Reduce** the inflammatory and allergic aspects of asthma and decrease bronchospasm.

Examples (inhalation):

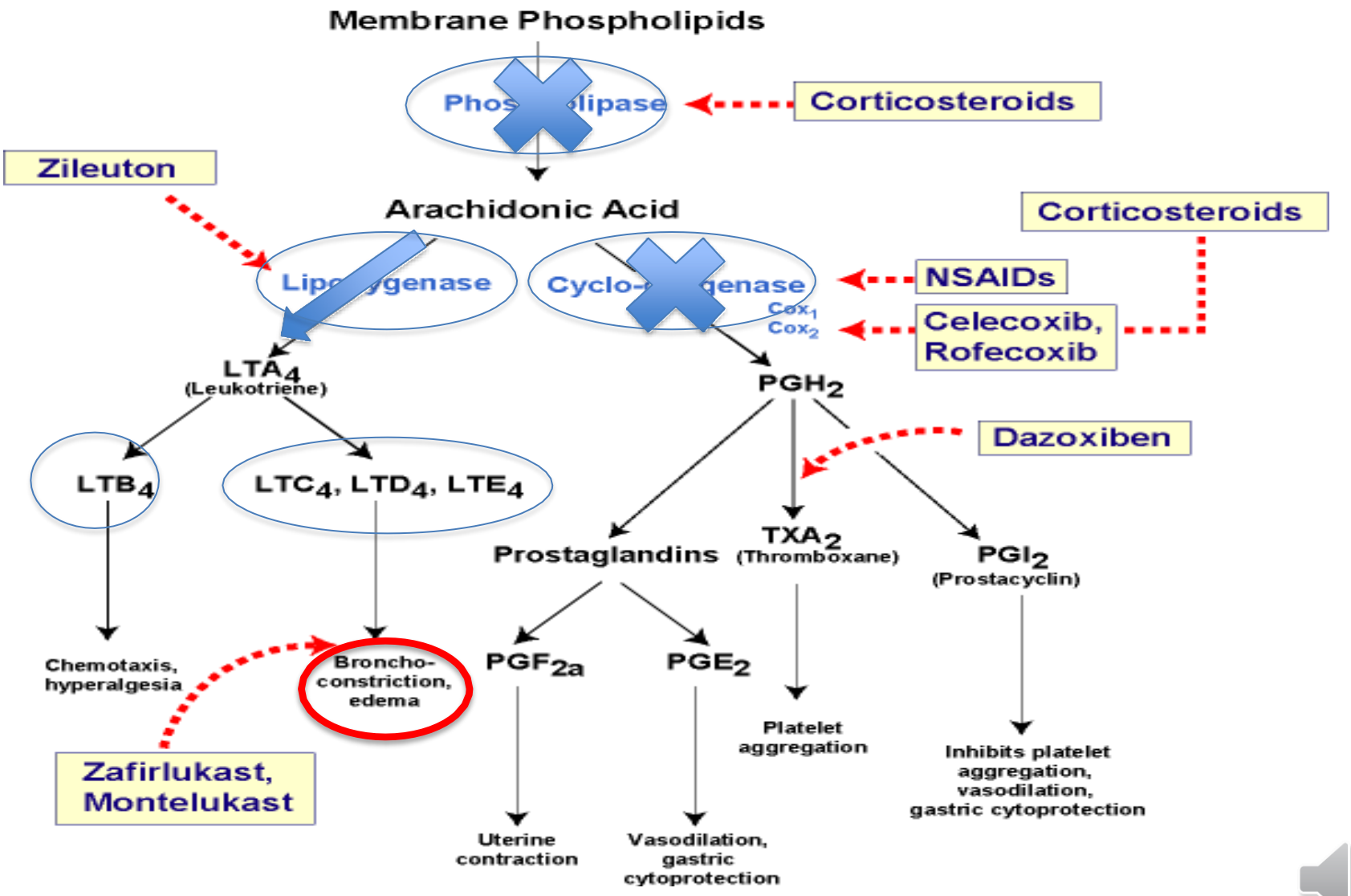
-Beclomethasone (Becotide®)

- Fluticasone (Flixotide®)

Side effects of corticosteroids

- **Oro-pharyngeal candidiasis**
- **Dysphonia (voice abnormality**
- **Growth retardation in children and osteoporosis in females**

Arachidonic Acid Metabolism



A- 2- Leukotriene receptor antagonists (LTRAs)

-Competitive antagonists of leukotriene receptors e.g. ***Montelukast*** and ***Zafirlukast.***

-They are given for prophylaxis against bronchial asthma.

They have the following advantages:

- Montelukast is safely used in children (as young as 6 months)

- easy administration as they are given orally.

B. Bronchodilators

1. β2-agonists: (inhalation, S.C, oral)

- When given by inhalation they treat a developing attack or to prevent an attack, but they do **not** control the inflammatory component of the asthma. e.g. Salbutamol (Ventolin®)

2. Methylxanthines:

- **Aminophylline (Oral or IV)** treat acute attacks by I.V infusion.

3. Anticholinergic drugs:

- Ipratropium Bromide (Atrovent®):
- Given by inhaler or nebulizer.
- Given to patients not responded to beta2-agonists.

Nursing implementation

Status asthmaticus

Management:

1. Ensure adequate hydration of the patient.
2. Give bronchodilators.
3. Give I.V hydrocortsione
4. Never use sedatives because of the respiratory distress risk
5. Treat chest infections if present
6. Give oxygen if required.
7. Aminophylline carefully administered because there is a small difference between therapeutic and toxic dose.
8. Avoid B-blockers in hypertensin, and NSAIDs as analgesics.

Antihistamine Drugs

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Histamine and antihistamine:

Storage: Histamine is stored in mast cells in skin, lungs and GIT.

Release:

1-Antigen-antibody reactions (allergy) or immunological reactions.
2-Insect bites and snake venom.
3-Drugs: some basic drugs as morphine, succinylcholine, and atropine (large and toxic doses) may induce histamine release.

Action of Histamine on different Organs

- Skin and sensory nerve endings. **Itching, urticaria**
- Smooth muscle fibers as bronchi, GIT, uterus. **Spasmogenic effect.**
- Endothelium of Blood vessels. **Vasodilatation**
- Stomach: histamine stimulates **HCl-secretion** by actingon H2-receptors.
- CNS (post-synaptic). **Alertness.**

Histamine

Histamine has no therapeutic uses nowadays .

Inhibitors of Histamine release: Glucocorticoids: inhibit antibody formation and antigen-antibody reaction, and accordingly inhibit histamine release.

Mast Cell Stabilizers act as degranulation inhibitors e.g:

disodium cromoglycate (cromolyn) and nedocromil.

Histamine Antagonists: Pharmacological Antagonists:

H_1-Antagonists : Antihistaminics used as Antiallergic drugs.

H_2-Antagonists: Cimetidine-Famotidine-Ranitidine-Nizatidine. used in the treatment of peptic ulcer.

Physiological Antagonist: "Adrenaline is the physiological antagonist of histamine" (2 different agents acting on 2 different receptors causing 2 opposing actions).

H1-Antagonists (Antihistaminics-Antiallergics)

Antihistaminics are used in treatment of allergic conditions such as: skin rash urticaria- edema-anaphylactic shock (remember: adrenaline is life-saving in anaphylactic shock).

Notes:

1. Antihistaminics are not essential in treatment of bronchial asthma because the role of histamine is insignificant.
2. Treatment of anaphylactic shock: Adrenaline (Life saving) + Corticosteroid + Antihistaminic.

First Generation=Sedating Antihistaminics.

Diphenhydramine, Chlorpheniramine maleate (in common cold medications)- Cyproheptadine

Second Generation= Non-sedating Antihistaminics

Astemizole.

Cetrizine.

Loratadine.

Adverse effects:

1. Sedation and drowsiness.
2. Atropine-like adverse effects as dry mouth, constipation, urine retention, tachycardia, and elevation of IOP.

Nursing Implementation

- Antihistamines are contraindicated in acute asthma attacks and lower respiratory diseases
- Avoid driving heavy machinery, and don’t consume alcohol or other CNS depressant drugs.
- Don’t take these medication with other OTC medication without checking.
- If dry mouth occurs, advice the patient to increase fluid intake and use chewing gum.
- Use with caution in patients with glaucoma or benign prostate hypertrophy.

Analgesics

- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
- Opioid Analgesics

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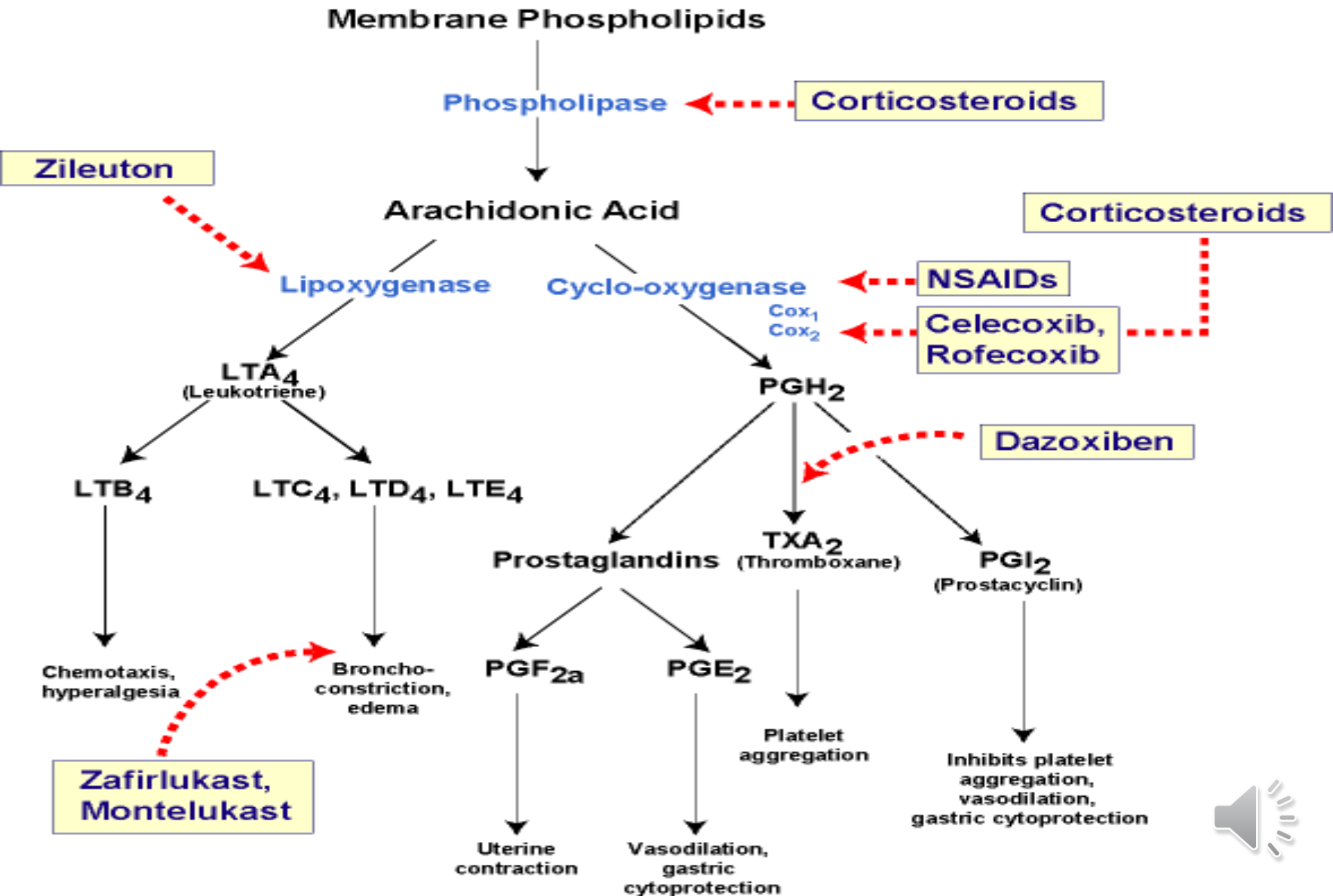
Arachidonic Acid Metabolism



Analgesics

- **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**

NSAIDs and Prostaglandin (PG) synthesis inhibition

- NSAIDs blocked PG generation.
- Prostaglandins, prostacyclin (PGI2), and thromboxane A2(TXA2) are produced from arachidonic acid by the enzyme cyclooxygenase.

NSAIDs have following actions

- Analgesic
- Antipyretic
- Antiinflammatory

Classification of NSAIDs

A. Nonselective COX inhibitors (traditional NSAIDs)

1. Salicylates: Aspirin
2. Propionic acid derivatives: Ibuprofen, Naproxen,
٣. Anthranilic acid derivative: Mephenamic acid
٤. Aryl-acetic acid derivatives: Diclofenac.
٥. Oxicam derivatives: Piroxicam.
٦. Indole derivative: Indomethacin.

B. Preferential COX-2 inhibitors Meloxicam.

C. Selective COX-2 inhibitors , Rofecoxib.

D.Analgesic-antipyratics with poor antiinflammatory action

Paracetamol (act on COX type 3).

Mechanism of action of NSAIDs

Antiinflammatory effect: due to the inhibition of the enzymes that produce prostaglandin H synthase (cyclooxygenase, or COX).

Analgesic effect: The analgesic effect of NSAIDs is due to inhibition of PG in the subcortical site.

Antipyretic effect: The antipyretic effect of NSAIDs is believed to be related to: inhibition of production of prostaglandins in the hypothalamus.

Nursing Implementation

- Take NSAIDs with food because they are GIT irritant and might lead to peptic ulcer
- Avoid aspirin in children <12 years because it might induce Reye's syndrome
- Enteric coated tablets should never be chewed or crushed
- Long term use: educate the patients to watch out their stool closely and regularly to check for any bleeding
- Avoid use of NSAIDs in asthmatic patients.
- May cause Salt and water retention, avoid in hypertension and heart failure.
- Long term use may cause Renal impairment.
- Avoid use in pregnancy, may cause teratogenicity. In pregnancy use paracetamol as analgesic

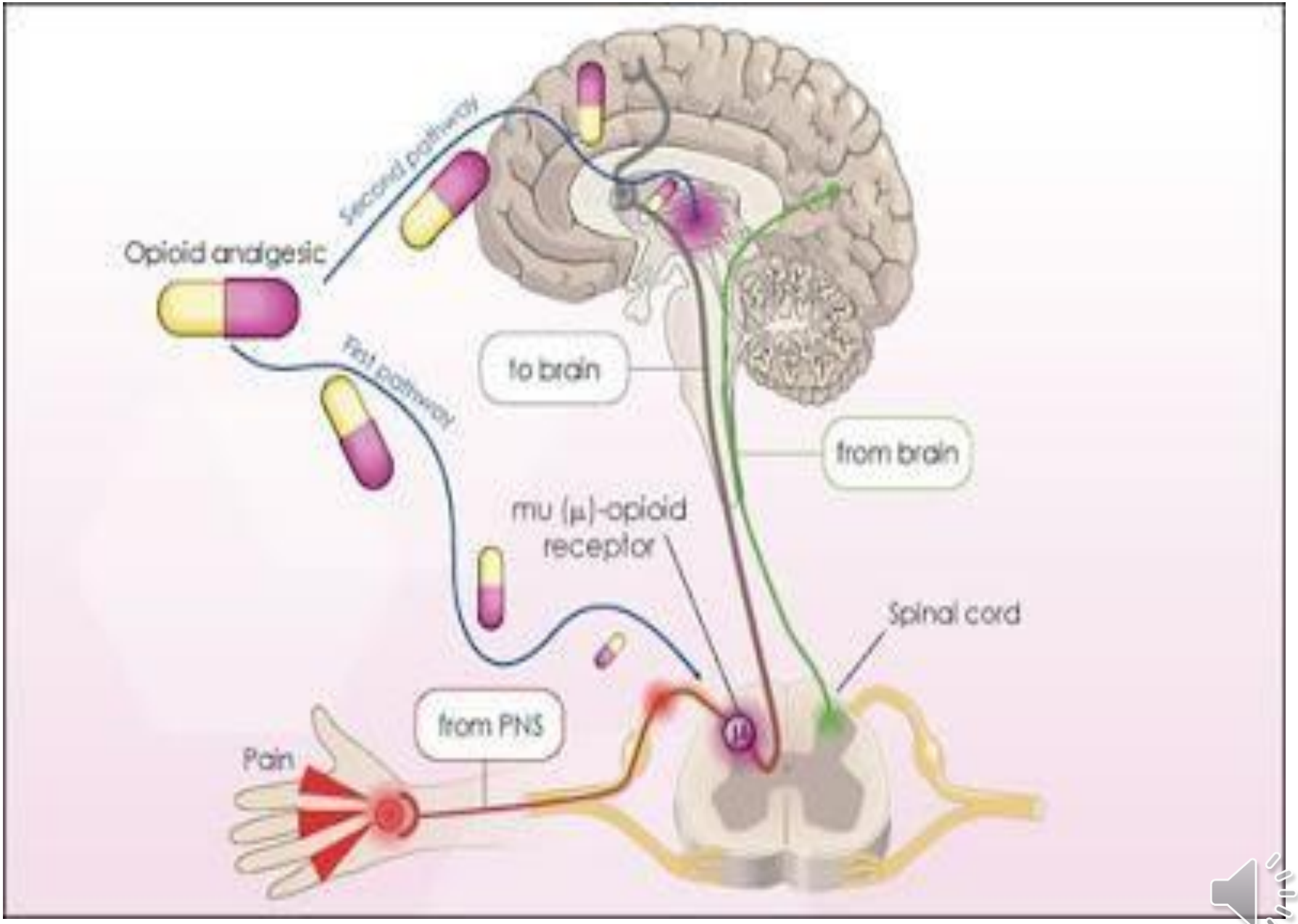
Terminology

Pain: is a protective reflex for self preservation due to presence of tissue damage. There are 2 components of pain : Perception and Reaction.

- **Perception** is the physical component of pain that carried pain through the nerve to the cortex.
- **Reaction** is psychological component of pain and involve the patients emotional response to the pain.

Analgesics: Medications that relieve pain without causing loss of consciousness.

Opioids analgesics or Opium: the dried juice of the seed-head of the opium poppy


Second pathway
Opioid analgesic
First pathway
to brain
from brain
mu (μ)-opioid
receptor
Spinal cord
from PNS
Pain

Mechanism of action: Opioids act to reduce intensity and unpleasant of pain. They produce their effects by working as endogenous **opioid peptide*** through binding to opioid receptors. There are three major classes of opioid receptor μ-opioid, κ-opioid, and δ-opioid

***Opioid peptides**
- **β-endorphin, (**μ,receptors)
- **Enkephalins (**δreceptors**)**
- **Dynorphins (** κreceptors)

Classification
- **Strong (e.g.** Morphine)
- **Moderate (e.g.** Codeine, Oxycodone)
- **Weak (e.g.** Propoxyphene)

Systemic effects of opioid analgesics

١ Central nervous system (Sedation, Respiratory depression, Cough is inhibited, Miosis)

٢ Cardiovascular system: Peripheral vasodilatation leading to Hypotension- Benefit in acute myocardial infarction and left ventricular failure (reduce pain and anxiety, and preload on the heart).

٣ Gastointestinal tract: Reduced peristalsis and delayed gastric emptying (cause constipation). opioids constrict the sphincter of oddi and thereby increase pressure within the biliary tree (biliary spasm)

٤ Urogenital tract: urinary retention

٥ Others: Cutaneous vasodilatation (flushing of face, neck and thorax)

٦ morphine release histamine in the bronchi and may cause bronchoconstriction.

Clinical Uses

- **Analgesia** (Fentanyl, morphine)
- **Cough Suppression** (Codeine, Dextromethorphan)
- **Antidiarrheal** (Diphenoxylate, Loperamide)
- **Acute Pulmonary edema** (Morphine)
- **Anesthesia** (Fentanyl)
- **Opioid Dependence** (Methadone)

Adverse effects

-CNS: Sedation, euphoria, dysphasia, respiratory depression, pruritis, and.

-GIT: Nausea and vomiting, Constipation and dry mouth

(Many of these effects diminish as tolerance develops).

Nursing Implementation

- Oral opioid should be taken with food to minimise GIT upset
- Stop Opioid administration if respiratory rate decreased to less than 12 breath/minutes.
- Advice the patient to increase fluid and fibre intake to avoid constipation
- Advice the patients to change position slowly to avoid postural hypotension