Al- Mustaqbal university college

DRUGS ACTING ON CARDIOVASCULAR SYSTEM

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The Circulatory System consist of

1-Cardiovascular system which involve

a)the heart b) Blood vessels.

2-Lymphatic system which involve

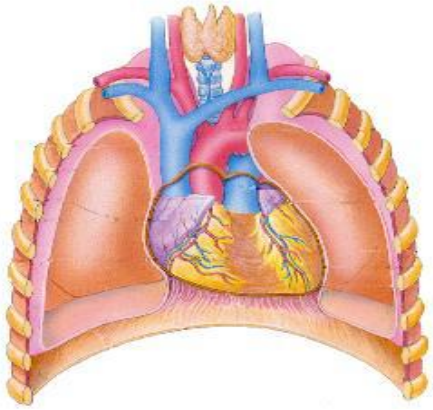
a)Lymphatic vessels

b) Lymphoid tissues (spleen, thymus, tonsils, and lymph nodes).

The Heart

The heart is situated in the mediastinum oriented more towards the left of the chest cavity.

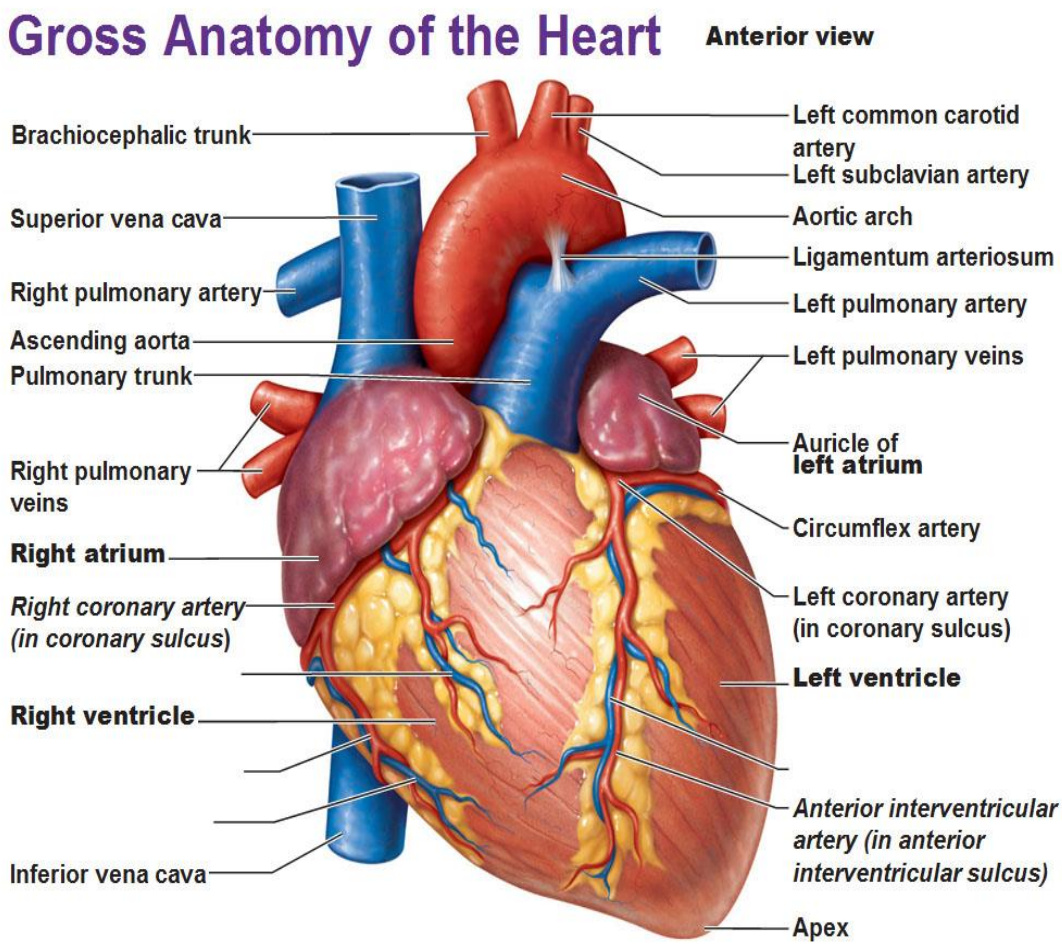
The Heart is Enclosed by Pericardium.



The wall of the heart is composed of 3 layers:
Outer-Epicardium (thin cover)
Middle-Myocardium (thick, ring-like, contractile)
Inner-Endocardium (thin sheet between chambers)

The **Epicardium** covers the outer surface of the heart
The **Myocardium** is the middle muscular layer of the heart
The **Endocardium** lines the chambers and the valves

The heart contains four chambers:
Two atria, which receive venous blood.
Two ventricles, which eject blood into arteries.
The right ventricle pumps blood to the lungs, where the blood becomes oxygenated; the left ventricle pumps oxygenated blood to the entire body.



Drugs and the cardiovascular system

The heart, arteries, veins, and lymphatics make up the cardiovascular system. These structures transport life-supporting oxygen and nutrients to cells, remove metabolic waste products, and carry hormones from one part of the body to another. Because this system performs such vital functions, a problem with the heart or blood vessels can seriously affect a person's health.

Types of drugs used to improve cardiovascular function include:

- inotropic
- antiarrhythmic
- antianginal
- antihypertensive
- diuretic
- antilipemic

Inotropics

Inotropic drugs, such as cardiac glycosides and phosphodiesterase (PDE) inhibitors, increase the force of the heart's contractions. In other words, the drugs have what's known as a *positive inotropic effect.* (Inotropic means affecting the force or energy of muscular contractions.) Cardiac glycosides also slow the heart rate (called a *negative chronotropic effect*) and slow electrical impulse conduction through the atrioventricular (AV) node (called a *negative dromotropic effect*).

Cardiac glycosides

Cardiac glycosides are a group of drugs derived from digitalis, The most frequently used cardiac glycoside is *digoxin*.

Pharmacokinetics (how drugs circulate)

The intestinal absorption of digoxin varies greatly; the capsules are absorbed most efficiently, followed by the elixir form, and then tablets. Digoxin is distributed widely throughout the body, with highest concentrations in the heart muscle, liver, and kidneys. Digoxin binds poorly to plasma proteins. In most patients, a small amount of digoxin is metabolized in
the liver and gut by bacteria. This effect varies and may be substantial in some people. Most of the drug is excreted by the kidneys as unchanged drug.

Pharmacodynamics

Digoxin is used to treat heart failure because it strengthens the contraction of the ventricles by boosting intracellular calcium at the cell membrane, enabling stronger heart contractions. Digoxin may also enhance the movement of calcium into the myocardial cells and stimulate the release, or block the reuptake, of norepinephrine at the adrenergic nerve terminal.

Drug interactions

Many drugs can interact with digoxin.

• Antacids, barbiturates, cholestyramine resin, kaolin and pectin, neomycin, metoclopramide, rifampin, and sulfasalazine reduce the therapeutic effects of digoxin.

• Calcium preparations, quinidine, verapamil, cyclosporine, tetracycline, clarithromycin, amiodarone, spironolactone, hydroxychloroquine, erythromycin, itraconazole, and omeprazole increase the risk of digoxin toxicity.

• Amphotericin B, potassium-wasting diuretics, and steroids taken with digoxin may cause hypokalemia (low potassium levels) and increase the risk of digoxin toxicity.

• Beta-adrenergic blockers and calcium channel blockers taken with digoxin may cause an excessively slow heart rate and arrhythmias.

Digoxin can also produce adverse reactions, mostly involving digoxin toxicity

Adverse reactions to cardiac glycosides

Because cardiac glycosides have a narrow therapeutic index (margin of safety), they may produce digoxin toxicity. To prevent digoxin toxicity, the dosage should be individualized based on the patient's serum digoxin concentration.

Adverse reactions to digoxin include:

• rash
• fever
• eosinophilia
• arrhythmias.

Recognizing signs and symptoms of digoxin toxicity

Digoxin toxicity usually produces cardiac, gastrointestinal, and neurologic signs and symptoms. Which include nausea , tachycardia , confusion and blured vision.

PDE inhibitors

PDE inhibitors are typically used for short-term management of heart failure or long-term management in patients awaiting heart transplant surgery. Specific PDE inhibitors are inamrinone and milrinone. *PDE inhibitors* are typically used for short-term management of heart failure or long-term management in patients awaiting heart transplant surgery. Specific PDE inhibitors are inamrinone and milrinone.

Pharmacokinetics

Administered I.V., inamrinone is distributed rapidly, metabolized by the liver, and excreted by the kidneys. It's rarely used because because secondary thrombocytopenia may occur as an adverse reaction

Adverse reactions to phosphodiesterase (PDE) inhibitors are uncommon, but the likelihood increases significantly when a patient is on prolonged therapy.

Adverse reactions may include:

• arrhythmias
• nausea and vomiting
• headache
• fever
• chest pain
• hypokalemia
• thrombocytopenia (especially with inamrinone)

Pharmacodynamics

PDE inhibitors improve cardiac output by strengthening contractions. These drugs are thought to help move calcium into the cardiac cell or to increase calcium storage in the sarcoplasmic reticulum. By directly relaxing vascular smooth muscle, they also decrease peripheral vascular resistance (afterload) and the amount of blood returning to the heart (preload).

Pharmacotherapeutics (uses)

Inamrinone and milrinone are used to manage heart failure in patients who haven't responded adequately to treatment with cardiac glycosides, diuretics, or vasodilators. Prolonged use of these drugs may increase the patient's risk of complications and death.

Drug interactions

• PDE inhibitors may interact with disopyramide, causing hypotension.

• Because PDE inhibitors reduce serum potassium levels, taking them with a potassium-wasting diuretic may lead to hypokalemia.

Antianginal drugs

Ischemic heart disease is one of the most common cardiovascular disease in developed countries, and angina pectoris is the most common condition involving tissue ischemia in which vasodilator drugs are used. angina's cardinal symptom is chest pain, the drugs used
to treat angina aren't typically analgesics. *antianginal drugs* treat angina by reducing myocardial oxygen demand (reducing the amount of oxygen the heart needs to do its work), by increasing the supply of oxygen to the heart, or both.

The three classes of antianginal drugs discussed in this section include:

- nitrates (for treating acute angina)
- beta-adrenergic blockers (for long-term prevention of angina).
- Ca channel blockers. (used when other drugs fail to prevent angina).

Angina occurs when the coronary arteries (the heartrimary source of oxygen) supply insufficient oxygen to the myocardium. This increases the heart's workload, increasing heart rate.

preload (blood vol-ume in the ventricle at the end of diastole). afterload (pres-sure in the arteries leading from the ventricle), and force of myocardial contractility.

Antianginal drugs (nitrates, beta-adreneric blockers, and calcium channel blockers) relieve angina by *decreasing* one or more of these four factors.

Nitrates

Nitrates are the drugs of choice for relieving acute angina. Nitrates commonly prescribed to treat angina include:

• amyl nitrite
• isosorbide dinitrate
• isosorbide mononitrate
• nitroglycerin.

Pharmacokinetics

Nitrates can be administered in a variety of ways.

Nitrates given sublingually (under the tongue), buccally (in the pocket of the cheek), as chewable tablets, as lingual aerosols (sprayed onto or under the tongue), or by inhalation (amyl nitrite) are absorbed almost completely because the mucous membranes of the mouth have a rich blood supply. Swallowed nitrate capsules are absorbed through the mucous

membranes of the GI tract, and only about one-half of the dose enters circulation. Transdermal nitrates (a patch or ointment placed on the skin) are absorbed slowly and in varying amounts, depending on the quantity of drug applied, the location of its application, the surface area of skin used, and circulation to the skin. I.V. nitroglycerin, which doesn't need to be absorbed, goes directly into circulation.

Pharmacodynamics

Nitrates cause the smooth muscle of the veins and, to a lesser extent, the arteries to relax and dilate. This is what happens:

• When the veins dilate, less blood returns to the heart. This, in turn, reduces the amount of blood in the ventricles at

the end of diastole, when the ventricles are full. (The volume of blood in the ventricles just before contraction is called preload.) By reducing preload, nitrates reduce ventricular size and ventricular wall tension (the left ventricle doesn't have to stretch as much to pump blood). This, in turn, reduces the oxygen requirements of the heart.

Advers reactions to nitrates

Headache is the most common adverse reaction. Hypotension may also occur, accompanied by dizziness and increased heart rate.

Beta-adrenergic antagonists

Beta-adrenergic antagonists (also called *beta blockers*) are used for long-term prevention of angina and are one of the main types of drugs used to treat hypertension. Beta-adrenergic blockers include:

• atenolol
• metoprolol
• nadolol • propranolol.

Pharmacokinetics

Metoprolol and propranolol are absorbed almost entirely from the GI tract, whereas less than one-half the dose of atenolol or nadolol is absorbed. These beta-adrenergic blockers are distributed widely. Propranolol is highly protein-bound; the other beta adrenergic blockers are poorly protein-bound.

Pharmacodynamics

Beta-adrenergic blockers decrease blood pressure and block beta adrenergic receptor sites in the heart muscle and the conduction system. This decreases the heart rate and reduces the force of the heart's contractions, resulting in a lower demand for oxygen.

Pharmacotherapeutics

Beta-adrenergic blockers are indicated for long-term prevention of angina. In acute coronary syndrome, metoprolol may be given initially I.V., and then orally. Metoprolol may also be used for heart failure.

Because of their ability to reduce blood pressure, beta-adrenergic blockers are also first-line therapy for treating hypertension.

Drug interactions

A number of drugs interact with beta-adrenergic blockers.

• Antacids reduce absorption of beta-adrenergic blockers.

• Nonsteroidal anti-inflammatory drugs (NSAIDs) can decrease the hypotensive effects of beta-adrenergic blockers

Cardiac glycosides and calcium channel blockers can have negative addictive effects on SA or AV node conduction when administered with a beta-adrenergic blocker.

• Diuretics or other hypotensive agents can potentiate the hypotensive effects of beta-adrenergic blockers.

• Lidocaine toxicity may occur when lidocaine is taken with beta adrenergic blockers.

• The requirements for insulin and oral antidiabetics can be altered by beta-adrenergic blockers.

• The ability of theophylline to produce bronchodilation is impairedby nonselective beta-adrenergic blockers.

Adverse reactions to beta adrenergic blockers

Beta-adrenergic blockers may cause:

• bradycardia
• hypotension
• dizziness
• nausea and vomiting
• diarrhea
• significant constriction of the bronchioles

Calcium channel blockers

Calcium channel blockers are commonly used to prevent angina that doesn't respond to drugs in either of the other antianginal classes. They're the drug of choice to treat Prinzmetal's angina. As mentioned earlier, several of the calcium channel blockers are also used as antiarrhythmics and to treat hypertension. Calcium channel blockers used to treat angina include:

- amlodipine
- diltiazem
- nicardipine
- nifedipine
- verapamil.

How calcium channel blockers work

Calcium channel blockers increase the myocardial oxygen supply and slow the heart rate. Apparently, the drugs
produce these effects by blocking the slow calcium channel. This action inhibits the influx of extracellular calcium
ions across both myocardial and vascular smooth muscle cell membranes. Calcium channel blockers
achieve this blockade without hanging serum calcium concentrations.

No calcium = dilation

This calcium blockade causes the coronary arteries (and, to a lesser extent, the peripheral arteries and arterioles) to dilate, decreasing afterload and increasing myocardial oxygen supply.

Pharmacokinetics

When administered orally, calcium channel blockers are absorbed quickly and almost completely. Because of the first-pass effect, however, the bioavailability of these drugs is much lower. The calcium channel blockers are highly bound to plasma proteins.

Pharmacodynamics

Calcium channel blockers prevent the passage of calcium ions across the myocardial cell membrane and vascular smooth-muscle cells. This causes dilation of the coronary and peripheral arteries, which decreases the force of the heart's contractions and reduces the workload of the heart Also, by preventing arterioles from constricting, calcium channel
blockers reduce afterload. Decreasing afterload further decreases the oxygen demands of the heart.

Some calcium channel blockers (diltiazem and verapamil) also reduce the heart rate by slowing conduction through the SA and AV nodes. A slower heart rate reduces the heart's need for additional oxygen.

Pharmacotherapeutics (uses)

Calcium channel blockers are used for long-term prevention of angina only, not short-term relief of chest pain. Calcium channel blockers are particularly effective for preventing Prinzmetal's angina.

Drug interactions

• Calcium salts and vitamin D reduce the effectiveness of calcium channel blockers.

• Verapamil and diltiazem increase the risk of digoxin toxicity, enhance the action of carbamazepine, and may cause myocardial depression.