Chapter 22
Drugs Affecting Circulation: Antihypertensives, Antianginals, Antithrombotics

Antihypertensives

1. Read this article in its entirety
   “Clinical Practice Guidelines for the Management of Hypertension in the Community”

2. Angiotensin-Converting Enzyme Inhibitors (ACE Inhibitors)
3. Angiotensin Receptor Blockers (ARB)
4. Thiazide Diuretics

Thiazide diuretics block the reabsorption of sodium (and therefore water) by the kidneys. Sodium and water are excreted as urine.

**Mechanism of Action of Thiazide**
5. Calcium Channel Blockers (CCB)

Calcium ions increase the peripheral vessel tone and contractility of the cardiac muscles. Calcium constricts the peripheral blood vessels and strengthen the cardiac muscles.

Calcium channel blockers reduce the peripheral vessel tone and reduce the contractility of the heart. These two events reduce the overall blood pressure.

**CALCIUM CHANNEL BLOCKERS**

**Mode of action:**

- Interference with Ca^{++} uptake in smooth muscles & cardiac muscle
- Dilation of peripheral arterioles
  - Reduction in PVR
  - Reduction in Afterload
  - No effect on preload
  - Negative inotropic effect
6. Beta-Blockers

Beta-blockers (beta-adrenergic blocking agents) are used to reduce blood pressure. Among other actions, beta blockers work by blocking the effects of the hormone epinephrine. This results in a slower heart rate, a slower electrical conduction, and a lower cardiac contractility. These changes help to lower the overall blood pressure.

Note: Some beta-blockers also block beta-2 receptors and produce mild airflow obstruction. Cardioselective β blockers such as atenolol and metoprolol are at least 20 times more potent at blocking β-1 receptors than β-2 receptors. At therapeutic doses of atenolol and metoprolol, the β-2 blocking effect, and therefore the risk of bronchoconstriction, is negligible.

Chronotropic: related to the heart rate
Dromotropic: related to the electrical conduction of the heart
Inotropic: related to contractile force of the heart

![Actions of Beta Blockers](image)
7. Alpha Blockers

Alpha blockers (alpha adrenergic antagonists) relax certain muscles and dilate peripheral small blood vessels. Among other effects of alpha blockers, they keep the hormone norepinephrine (noradrenaline) from tightening the muscles in the walls of smaller arteries and veins. Blocking that effect causes the vessels to remain open and relaxed. This improves blood flow and lowers blood pressure.
8. Central Acting Agents

Clonidine (Catapres) is a centrally acting α2 adrenergic agonist and imidazoline receptor agonist. Catapres is used to treat high blood pressure. It is also used to treat attention deficit hyperactivity disorder, anxiety disorders, withdrawal (from either alcohol, opioids, or smoking), migraine, menopausal flushing, diarrhea, and certain pain conditions.
9. Direct Vasodilators

Direct vasodilators reduce blood pressure by dilating the blood vessels (e.g., arteries). Hydralazine (Apresoline) is a direct-acting smooth muscle relaxant and vasodilator. As a vasodilator, it decreases peripheral vascular resistance, thereby lowering blood pressure and decreasing afterload. [Afterload is the blood volume (or blood pressure) downstream from the ventricles that the ventricles must pump against in order to deliver a stroke volume]

Direct vasodilators often cause fluid retention and tachycardia. For these reasons, diuretics, beta blockers or sympathoytics are often used together. Minoxidil is another direct vasodilator. One of its side effects is hair growth. Minoxidil (Rogaine) comes in a foam preparation and it can be used to treat thinning hair or baldness. But the "hair growth" effect is short lived and this drug must be used on a regular basis.

10. Mineralocorticoid Receptor Antagonists (Aldosterone Blockers)

Spironolactone (Aldactone) is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule. Aldactone causes increased amounts of sodium and water to be excreted, while potassium is retained. Aldactone acts both as a diuretic and as an antihypertensive drug by this mechanism. It may be given alone or with other diuretic agents that act more proximally in the renal tubule.

Additional resources for management of hypertension

Pharmacology of Antihypertensive Agents
Antianginals

11. Myocardial ischemia refers to a reduction of blood flow in the coronary arteries. This condition is called angina pectoris (or angina). Angina is not life threatening and symptoms may include sensation of intermittent chest pain, pressure, or squeezing. On the other extreme, myocardial infarction (MI) is life threatening because the heart muscles are damaged (or dead) due to prolonged lack of blood flow and oxygen supply. Besides severe chest pain (and radiating pain), other signs of an MI include shortness of breath, dizziness, faintness, or nausea. The pain of a severe MI has been described as a giant fist enclosing and squeezing the heart.

![Diagram of Most Common Drugs Used in Treating Angina Pectoris]

Antianginal drugs are used to manage angina by either improving perfusion of the myocardium (e.g., vasodilators), reducing the metabolic demand of the heart (e.g., beta blockers), or both. Antianginal drugs cannot undo the damages of the heart muscles following an MI.

12. Vasodilators Two of the main groups of antianginal drugs are organic nitrates and calcium antagonists. Nitrates and calcium blockers are vasodilators. When the coronary arteries are dilated, the heart receives blood flow and oxygen. The work of heart is generally reduced due to a lower afterload (downstream resistance).

Figure 22-3 outlines the mechanism of action of nitrates. (p.382)

Review Table 22-11 and describe the different available dosage forms of nitroglycerin.

13. Beta Blockers Beta blockers are also called beta-adrenoreceptor antagonists. These drugs slow the heart rate, electrical conduction, and contractile force of the heart. These actions reduce the metabolic demand of the heart.
Antithrombotics

14. Antithrombotics include anticoagulants (e.g., heparin), antiplatelet agents (e.g., aspirin), and thrombolytic agents (e.g., streptokinase).

15. Anticoagulants

*Heparin* is a natural compound (sulfur-containing polysaccharide) occurring in the liver and other tissues such as the mast cells. It inhibits blood coagulation by binding to Antithrombin III—a substance needed to convert thrombin to fibrinogen. Fibrinogen is needed for fibrin clot (blood clotting). (See figure below)

![Image of platelet aggregation](image)

*Warfarin* Warfarin decreases blood clots by blocking the formation of vitamin K–dependent clotting factors. (See figure below)
16. Antiplatelet agents

The enzymes that produce prostaglandins are called cyclooxygenase (COX). There are two types of COX enzymes, COX-1 and COX-2. Both enzymes produce prostaglandins that promote inflammation, pain, and fever; however, only COX-1 produces prostaglandins that activate platelets and protect the stomach and intestinal lining. **Aspirin blocks COX-1**, thus reducing the blood clotting action of the platelets.

Figure below shows the pathway of how antiplatelets (e.g., aspirin) work to decrease blood clotting mechanism.
Thrombolysis is often used as an emergency treatment to dissolve blood clots that form in arteries feeding the heart and brain -- the main cause of heart attacks and ischemic strokes -- and in the arteries of the lungs (acute pulmonary embolism).