**Drugs for Hypertension**

* **Hypertension (elevated blood pressure) is a common and chronic disorder that affects about 50 million Americans.**
* **Left untreated, hypertension can lead to heart disease, kidney disease, blindness, and stroke.**
* **Conversely, a treatment program of lifestyle modifications and drug therapy can reduce both blood pressure and the risk of long-term complications.**
* **Unfortunately, drug therapy does not cure hypertension, it only reduces symptoms.**
* **Accordingly, for most patients, treatment must continue lifelong.**
* **As a result, noncompliance can be a significant problem.**

**Management of Essential Hypertension I: Lifestyle Modification.**

* **Weight loss**
* **Sodium Restriction**
* **Alcohol Restriction**
* **Exercise**
* **Smoking Cessation**
* **Maintenance of Potassium and Calcium Intake**

**Antihypertensive Mechanisms: Sites of Drug Action and Effects Produced**

* **Drugs can lower blood pressure by reducing heart rate, myocardial contractility, blood volume, venous return, and the tone of arteriolar smooth muscle.**
* **In this section we survey the principle mechanisms by which drugs produce these effects.**
* **The major mechanisms for lowering blood pressure are summarized in figure 45-2. The figure depicts the 10 principle sites at which antihypertensive drugs act.**
* **Brainstem**
* **Sympathetic Ganglia**
* **Terminals of Adrenergic Nerves**
* **Beta₁- Adrenergic Receptors on the Heart**
* **Alpha₁- Adrenergic Receptors on the Blood**
* **Vascular Smooth Muscle**
* **Renal Tubules**
* **Beta₁ Receptors on Juxtaglomerular Cells**
* **Angiotension- Converting Enzyme**
* **Angiotension II Receptors**

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**The Antihypertensive Drugs**

* **Diuretics**
* **Diuretics are a mainstay of antihypertensive therapy.**
* **These drugs reduce blood pressure when used alone, and they can enhance the effects of other hypertensive drugs.**
* **Thiazide Diuretics**
* **The thiazide diuretics (e.g., hydrochlorothiazide) are among the most commonly used antihypertensive drugs.**
* **Thiazides reduce blood pressure by two mechanisms: reduction of blood volume and reduction of arterial resistance.**
* **Reduced blood volume is responsible for initial antihypertensive effects.**
* **Reduced vascular resistance develops over time and is responsible for long-term antihypertensive effects.**
* **The mechanism by which thiazides reduce vascular resistance has not been determined.**
* **The principal adverse effect of thiazides is hypokalemia.**
* **This can be minimized by consuming potassium-rich foods (e.g., bananas, citrus fruits) and using potassium supplements or a potassium-sparing diuretic.**
* **Other side effects include dehydration, hyperglycemia, and hyperuricemia.**

**High-Ceiling (loop) Diuretics**

* **High-ceiling diuretics (e.g., furosemide) produce much greater diuresis than the thiazides.**
* **For most individuals with essential hypertension, the amount of fluid loss that loop diuretics can produce is greater than needed or desirable.**

**Potassium-Sparing Diuretics**

* **The degree of diuresis induced by the potassium-sparing agents (e.g., spironolactone) is small.**
* **These drugs are not very effective as hypotensive agents.**

**Sympatholytics (Adrenergic Antagonists)**

* **Sympatholytic drugs suppress the influence of the sympathetic nervous system on the heart, blood vessels, and other structures.**
* **These drugs are used widely in the treatment of hypertension.**
* **There are five subcategories of sympatholytic drugs: (1) beta-adrenergic blockers, (2) centrally acting alpha₂ agonists, (3) adrenergic neuron blockers, (4) alpha₁- adrenergic antagonists, and (5) alpha beta blockers.**

**Beta-adrenergic Blockers.**

* **The beta blockers (e.g., propranolol, metoprolol) are among the most widely used antihypertensive drugs.**
* **The beta blockers have at least four useful actions in hypertension.**
* **First, blockade of cardiac beta₁ receptors decrease heart rate and contractility, thereby decreasing cardiac output.**
* **Second, beta blockers can suppress reflex tachycardia caused by vasodilators in the regimen.**
* **Third, blockade of beta₁ receptors on juxtaglomerular cells of the kidney reduces release of renin, thereby reducing angiotensin II-mediated vasoconstriction and aldosterone-mediated volume expansion.**
* **Fourth, recent studies indicate that longterm use of beta blockers reduces peripheral vascular resistance- by a mechanism that is unknown.**
* **This newly discovered action could readily account for most of their antihypertensive effects.**

**Centrally Acting Alpha₂ Agonists**

* **These drugs (e.g., clonidine, methyldopa) act within the brainstem to suppress sympathetic outflow to the heart and blood vessels.**
* **The result is vasodilation and reduced cardiac output, both of which help lower blood pressure.**

**Alpha/Beta-Adrenergic Blockers: Carvedilol and Labetalol**

* **Carvedilol and labetalol are unusual in that they can block alpha₁ receptors as well as beta receptors.**
* **Blood pressure reduction results from a combination of actions:**

1. **alpha ₁ blockade promotes dilation of arterioles and veins,**
2. **Blockade of cardiac beta₁ receptors reduces heart rate and contractility, and**
3. **Blockade of beta₁ receptors on juxtaglomerular cells suppressed release of renin.**

**Calcium Channel Blockers**

* **The calcium channel blockers (CCBs) fall into two group: dihydropyridines (e.G., nifedipine) and nondihydropyridines (verapamil and diltiazam).**
* **Drugs in both groups promote dilation of erterioles.**
* **In addition, verapamil and diltiazem have direct suppressant effects on the heart.**

**ACE Inhibitors**

* **The ACE Inhibitors (Angiotensin Converting Enzyme) (e.g., captopril, enalapril) lower blood pressure by preventing formation of angiotensin II-mediated vasoconstriction and aldosterone-mediated volume expansion.**

**Angiotensin II Receptor Blockers**

* **Angiotensin II Receptor Blockers (ARBs) are relatively new drugs for use in hypertension.**
* **These agents lower blood pressure in much the same was as do the ACE inhibitors.**