Hypertesion

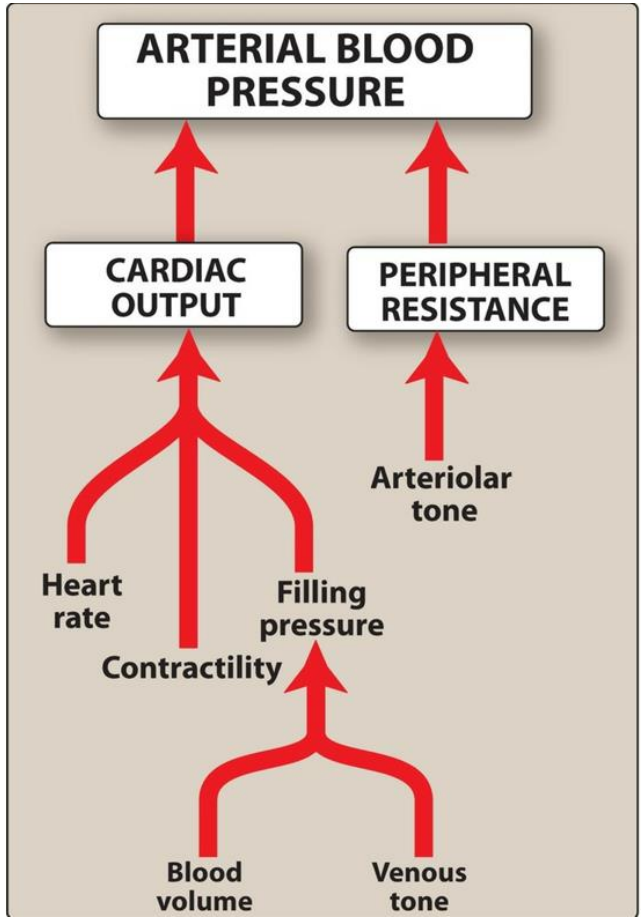
Dr. hasan falah

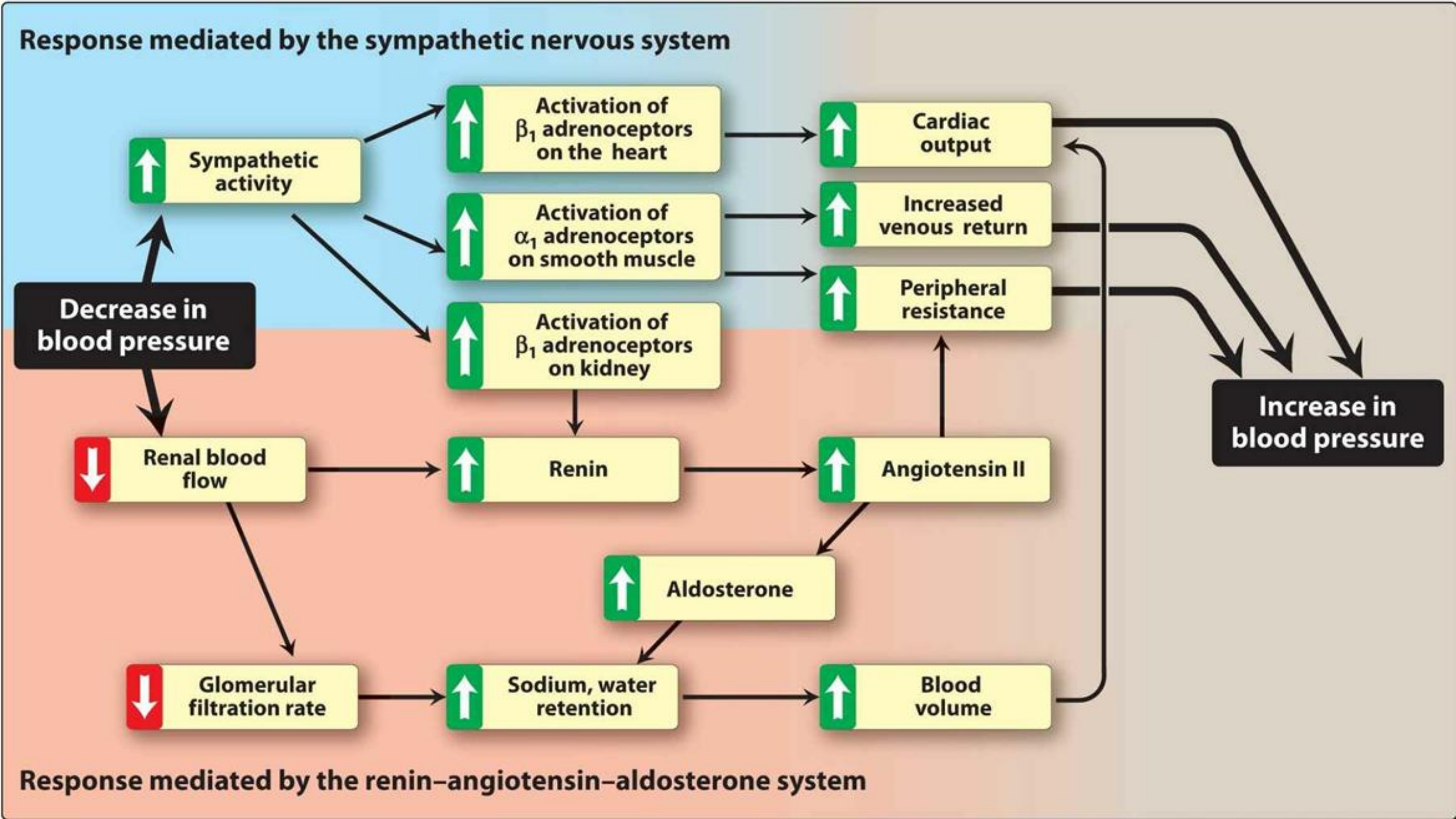
	Systolic mm Hg		Diastolic mm Hg
Normal	<120	and	<80
Elevated	120–129	or	<80
Stage 1 hypertension	130–139	or	80–89
Stage 2 hypertension	≥140	or	≥90

Etiology of Hypertension

Although hypertension may occur secondary to other disease processes, more than 90% of patients have essential hypertension (hypertension with no identifiable cause). A family history of hypertension increases the likelihood that an individual will develop hypertension. The prevalence of hypertension increases with age but decreases with education and income level. Non-Hispanic blacks have a higher incidence of hypertension than do both non Hispanic whites and Hispanic whites. Persons with diabetes, obesity, or disability status are all more likely to have hypertension than those without these conditions. In addition, environmental factors, such as a stressful lifestyle, high dietary intake of sodium, and smoking, may further predispose an individual to hypertension.

Mechanisms for Controlling Blood Pressure




Response mediated by the sympathetic nervous system
Sympathetic activity
Activation of β_1 adrenoceptors on the heart
Activation of α_1 adrenoceptors on smooth muscle
Activation of β_1 adrenoceptors on kidney
Cardiac output
Increased venous return
Peripheral resistance
Decrease in blood pressure
Increase in blood pressure
Renal blood flow
Renin
Angiotensin II
Aldosterone
Glomerular filtration rate
Sodium, water retention
Blood volume
Response mediated by the renin–angiotensin–aldosterone system

A. Baroreceptors and the sympathetic nervous system

A fall in blood pressure causes pressure-sensitive neurons (baroreceptors in the aortic arch and carotid sinuses) to send fewer impulses to cardiovascular centers in the spinal cord. This prompts a reflex response of increased sympathetic and decreased parasympathetic output to the heart and vasculature, resulting in vasoconstriction and increased cardiac output. These changes result in a compensatory rise in blood pressure

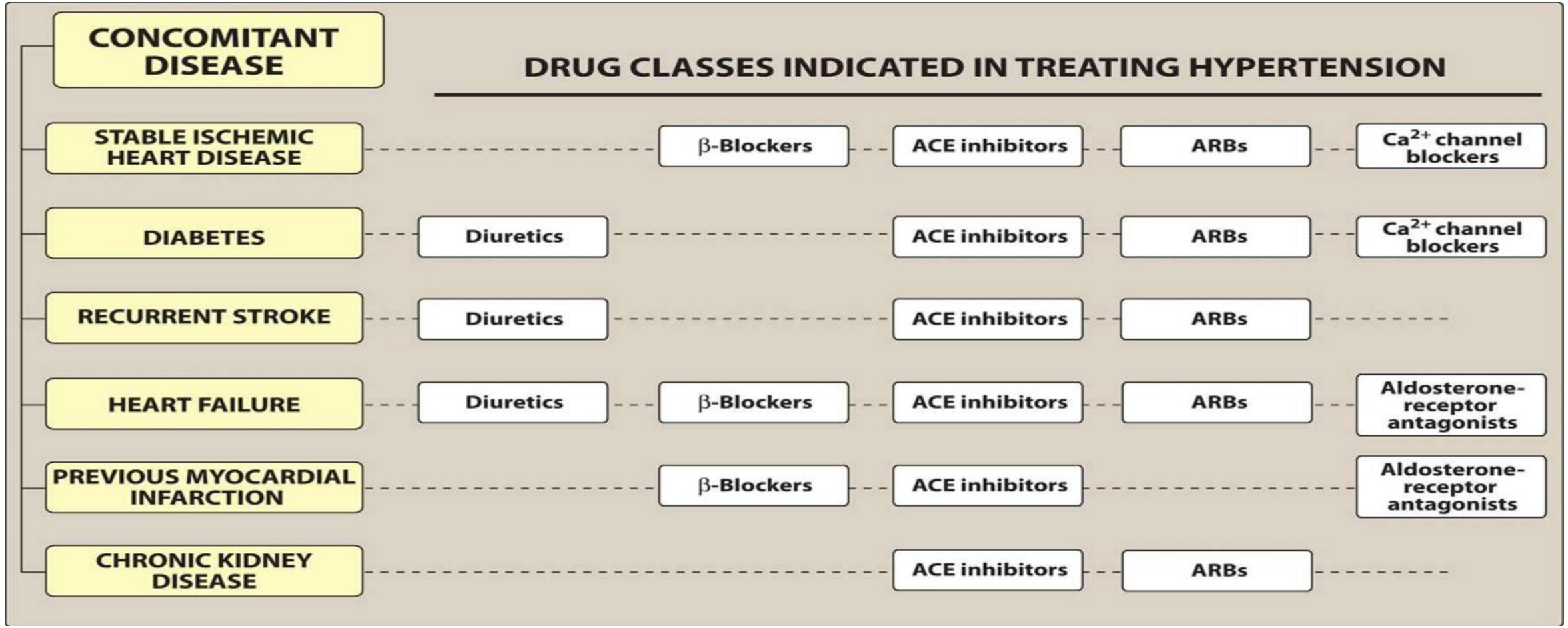
B. Renin–angiotensin–aldosterone system

The kidney provides long-term control of blood pressure by altering the blood volume. Baroreceptors in the kidney respond to reduced arterial pressure (and to sympathetic stimulation of β1-adrenoceptors) by releasing the enzyme renin . Low-sodium intake and greater sodium loss also increase renin release. Renin converts angiotensinogen to angiotensin I, which is converted in turn to angiotensin II, in the presence of angiotensin converting enzyme (ACE). Angiotensin II is a potent circulating vasoconstrictor, constricting both arterioles and veins, resulting in an increase in blood pressure. Angiotensin II exerts a preferential vasoconstrictor action on the efferent arterioles of the renal glomerulus, increasing glomerular filtration. Furthermore, angiotensin II stimulates aldosterone secretion, leading to increased renal sodium reabsorption and increased blood volume, which contribute to a further increase in blood pressure

IV. Treatment Strategies

The goal of antihypertensive therapy is to reduce cardiovascular and renal morbidity and mortality. For most patients, the blood pressure goal when treating hypertension is a systolic blood pressure of less than 130 mm Hg and a diastolic blood pressure of less than 80 mm Hg

A. Individualized care



V. Diuretics

For all classes of diuretics, the initial mechanism of action is based upon decreasing blood volume, which ultimately leads to decreased blood pressure.

A. Thiazide diuretics

*Thiazide diuretics, such as hydrochlorothiazide [hye-droe-klor-oh-THYE-a-zide] and chlorthalidone [klor-THAL ih-done], lower blood pressure initially by increasing sodium and water excretion.

*Thiazides are useful in combination therapy with a variety of other antihypertensive agents, including β-blockers, ACE inhibitors, ARBs, and potassium-sparing diuretics.

Thiazide diuretics can induce hypokalemia, hyperuricemia, and, to a lesser extent, hyperglycemia in some patients

B. Loop diuretics

*The loop diuretics (furosemide, torsemide, bumetanide, and ethacrynic acid) act promptly by blocking sodium and chloride reabsorption in the kidneys

*These agents are rarely used alone to treat hypertension, but they are commonly used to manage symptoms of heart failure and edema.

C. Potassium-sparing diuretics

*Amiloride [a-MIL-oh-ride] and triamterene [tri-AM-ter-een] are inhibitors of epithelial sodium transport at the late distal and collecting ducts, and spironolactone [speer-on-oh-LAK-tone] and eplerenone [eh-PLEH-reh-none] are aldosterone receptor antagonists. All of these agents reduce potassium loss in the urine

*Potassium-sparing diuretics are sometimes used in combination with loop diuretics and thiazides to reduce the amount of potassium loss induced by these diuretics.

VI. β-Adrenoceptor–Blocking Agents

*β-Blockers are a treatment option for hypertensive patients with concomitant heart disease or heart failure

A. Actions

The β-blockers reduce blood pressure primarily by decreasing cardiac output (Figure 16.8). They may also decrease sympathetic outflow from the central nervous system (CNS) and inhibit the release of renin from the kidneys, thus decreasing the formation of angiotensin II and the secretion of aldosterone. The prototype β-blocker is propranolol [proe-PRAN-oh-lol], which acts at both β1 and β2 receptors. Selective blockers of β1 receptors, such as metoprolol [met-OH-pro-lol] and atenolol [ah-TEN-oh-lol], are among the most commonly prescribed β-blockers. Nebivolol [ne-BIV-oh-lole] is a selective blocker of β1 receptors, which also increases the production of nitric oxide, leading to vasodilation. The selective β-blockers may be administered cautiously to hypertensive patients who also have asthma. The nonselective β-blockers are contraindicated in patients with asthma due to their blockade of β2 mediated bronchodilation.

B. Therapeutic uses

The primary therapeutic benefits of β-blockers are seen in hypertensive patients with concomitant heart disease, such as supraventricular tachyarrhythmia (for example, atrial fibrillation), previous myocardial infarction, stable ischemic heart disease, and chronic heart failure. Conditions that discourage the use of β-blockers include reversible bronchospastic disease such as asthma, second- and third-degree heart block, and severe peripheral vascular disease.

C. Pharmacokinetics

The β-blockers are orally active for the treatment of hypertension. Propranolol undergoes extensive and highly variable first-pass metabolism. Oral β-blockers may take several weeks to develop their full effects. Esmolol, metoprolol, and propranolol are available in intravenous formulations.

D. Adverse effects

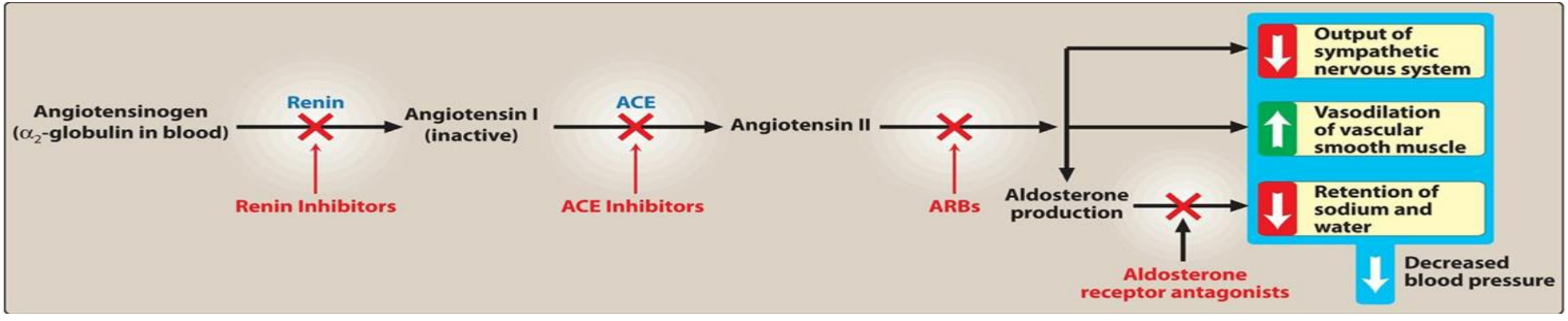
1. Common effects Hypotension ,bradycardia , fatigue , insomnia and dizzines

The β-blockers may decrease libido and cause erectile dysfunction, which can severely reduce patient compliance.

VII. ACE Inhibitors

ACE inhibitors such as captopril [KAP-toe-pril], enalapril [e-NAL-ah-pril], and lisinopril [lye-SIN-oh-pril] are recommended as first-line treatment of hypertension in patients with a variety of compelling indications, including high coronary disease risk or history of diabetes, stroke, heart failure, myocardial infarction, or chronic kidney disease

A. Actions



B. Therapeutic uses

ACE inhibitors are first-line drugs for treating heart failure, hypertensive patients with chronic kidney disease, and patients at increased risk of coronary artery disease.

C. Pharmacokinetics

All but captopril and lisinopril undergo hepatic conversion to active metabolites, so these agents may be preferred in patients with severe hepatic impairment. Fosinopril [foe-SIN-oh-pril] is the only ACE inhibitor that is not eliminated primarily by the kidneys. Therefore, it does not require dose adjustment in patients with renal impairment. Enalaprilat [en-AL-a-pril-AT] is the only drug in this class available intravenously.

ACE INHIBITORS

Benazepril LOTENSIN
Captopril GENERIC ONLY
Enalapril VASOTEC
Fosinopril GENERIC ONLY
Lisinopril PRINIVIL, ZESTRIL
Moexipril GENERIC ONLY
Quinapril ACCUPRIL
Perindopril GENERIC ONLY
Ramipril ALTACE
Trandolapril GENERIC ONLY

D. Adverse effects

- Dry cough
- Angioedema
- Hyperkalemia
- Skin rash
- Hypotension
- Altered test

VIII. Angiotensin II Receptor Blockers

The ARBs, such as losartan [LOW-sar-tan] and irbesartan [ir-be-SAR-tan], block the AT1 receptors, decreasing the activation of AT1 receptors by angiotensin II.

ARBs do not increase bradykinin levels. They may be used as first-line agents for the treatment of hypertension, especially in patients with a compelling indication of diabetes, heart failure, or chronic kidney disease

Adverse effects are similar to those of ACE inhibitors, although the risks of cough and angioedema are significantly decreased. ARBs should not be combined with an ACE inhibitor for the treatment of hypertension due to similar mechanisms and adverse effects. These agents are also teratogenic and should not be used by pregnant women.

IX. Renin Inhibitor

A selective renin inhibitor, aliskiren [a-LIS-ke-rin], is available for the treatment of hypertension.

Aliskiren should not be combined with an ACE inhibitor or ARB in the treatment of hypertension.

Aliskiren can cause diarrhea, especially at higher doses. It also causes cough and angioedema but less often than ACE inhibitors. As with ACE inhibitors and ARBs, aliskiren is contraindicated during pregnancy.

X. Classes of calcium channel blockers

1. Diphenylalkylamines

Verapamil [ver-AP-a-mil] is the only member of this class that is available in the United States. Verapamil has significant effects on both cardiac and vascular smooth muscle cells. It is also used to treat angina and supraventricular tachyarrhythmias and to prevent migraine and cluster headaches.

2. Benzothiazepines

Diltiazem [dil-TYE-a-zem] is the only member of this class that is currently approved in the United States. Like verapamil, diltiazem affects both cardiac and vascular smooth muscle cells, but it has a less pronounced negative inotropic effect on the heart compared to that of verapamil.

3. Dihydropyridines

This class of calcium channel blockers includes nifedipine [nye-FED-i-peen] (the prototype), amlodipine [am-LOE di-peen], felodipine [fe-LOE-di-peen], isradipine [is-RAD-i-peen], nicardipine [nye-KAR-di-peen], and nisoldipine [nye-ZOL-di-peen]. All dihydropyridines have a much greater affinity for vascular calcium channels than for calcium channels in the heart. They are, therefore, particularly beneficial in treating hypertension.

C. Therapeutic uses

They are useful in the treatment of hypertensive patients who also have asthma, diabetes, and/or peripheral vascular disease

All CCBs are useful in the treatment of angina.

D. Pharmacokinetics

Most of these agents have short half-lives (3 to 8 hours) following an oral dose. Sustained-release preparations are available and permit once-daily dosing. Amlodipine has a very long half-life and does not require a sustained-release formulation.

E. Adverse effects

Dizziness, headache, and a feeling of fatigue caused by a decrease in blood pressure are more frequent with dihydropyridines (. Peripheral edema is another commonly reported side effect of this class. Nifedipine and other dihydropyridines may cause gingival hyperplasia

CALCIUM CHANNEL BLOCKERS

Amlodipine NORVASC

Clevidipine CLEVIPREX

Diltiazem CARDIZEM, CARTIA, TIAZAC

Felodipine GENERIC ONLY

Isradipine GENERIC ONLY

Nicardipine CARDENE

Nifedipine ADALAT, PROCARDIA

Nisoldipine SULAR

Verapamil CALAN, VERELAN

XI. α-ADRENOCEPTOR–BLOCKING AGENTS

Action :These agents produce a competitive block of α1-adrenoceptors. They decrease peripheral vascular resistance and lower arterial blood pressure by causing relaxation of both arterial and venous smooth muscle.

Therapeutic uses :α-blockers are no longer recommended as initial treatment for hypertension but may be used for refractory cases .Other α1-blockers with greater selectivity for the prostate are used in the treatment of benign prostatic hyperplasia

****Reflex tachycardia and postural hypotension often occur at the onset of treatment and with dose increases, requiring slow titration of the drug in divided doses. Due to weaker outcome data and their side effect profile

XII. a-/b-Adrenoceptor–blocking Agents block α1, β1, and β2 receptors

Carvedilol is indicated in the treatment of heart failure and hypertension. It has been shown to reduce morbidity and mortality

Labetalol is used in the management of gestational hypertension and hypertensive emergencies.

XIII. Centrally Acting Adrenergic Drugs

A. Clonidine

Clonidine [KLON-i-deen] acts centrally as an α2 agonist to produce inhibition of sympathetic vasomotor centers, decreasing sympathetic outflow to the periphery. This leads to reduced total peripheral resistance and decreased blood pressure. Clonidine is used primarily for the treatment of hypertension that has not responded adequately to treatment with two or more drugs.

Adverse effects include sedation, dry mouth, and constipation

B. Methyldopa

Methyldopa [meth-ill-DOE-pa] is an α2 agonist that is converted to methylnorepinephrine centrally to diminish adrenergic outflow from the CNS. The most common side effects of methyldopa are sedation and drowsiness. Its use is limited due to adverse effects and the need for multiple daily doses. It is mainly used for management of hypertension in pregnancy, where it has a record of safety.

XIV. Vasodilators

The direct-acting smooth muscle relaxants, such as hydralazine [hye-DRAL-a-zeen] and minoxidil [min-OX-i-dill], are not used as primary drugs to treat hypertension. These vasodilators act by producing relaxation of vascular smooth muscle, primarily in arteries and arterioles. This results in decreased peripheral resistance and, therefore, blood pressure.

Minoxidil treatment causes hypertrichosis (the growth of body hair). This drug is used topically to treat male pattern baldness

XV. Hypertensive Emergency

Hypertensive emergency is a rare but life-threatening situation characterized by severe elevations in blood pressure (systolic greater than 180 mm Hg or diastolic greater than 120 mm Hg) with evidence of impending or progressive target organ damage

Hypertensive emergencies require timely blood pressure reduction with treatment administered intravenously to prevent or limit target organ damage. A variety of medications are used, including calcium channel blockers (nicardipine and clevidipine), nitric oxide vasodilators (nitroprusside and nitroglycerin), adrenergic receptor antagonists (phentolamine, esmolol, and labetalol), the vasodilator hydralazine, and the dopamine agonist fenoldopam. Treatment is directed by the type of target organ damage and/or comorbidities present

thank you