Disorders of blood pressure regulation
(arterial hypertension)

V. Rotaru

Blood pressure regulation

- **Cardiac output (CO)**=total systemic blood flow
- **Total peripheral resistance** (TPR)=resistance offered by the blood vessels to forward flow

The arterial blood pressure

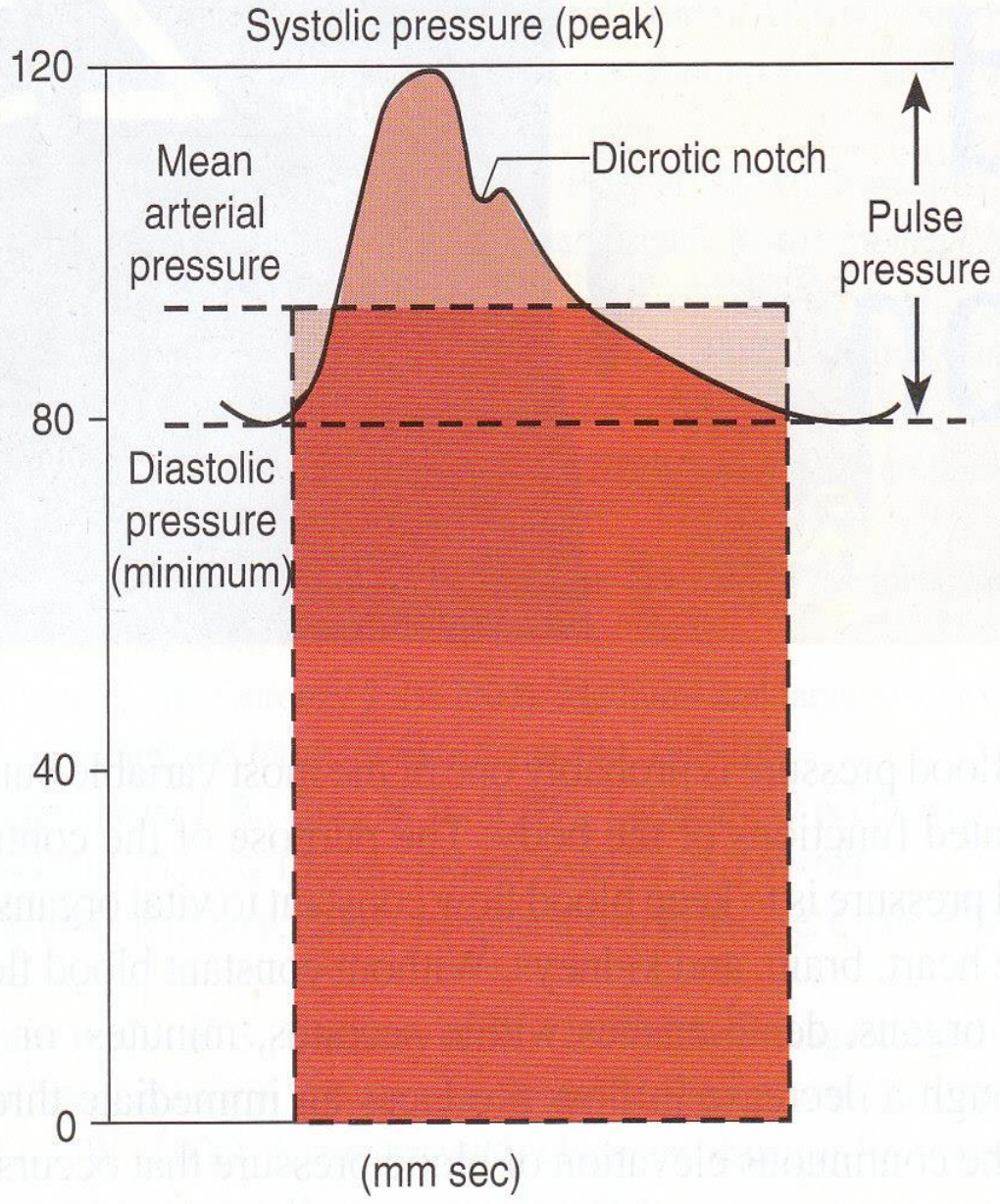
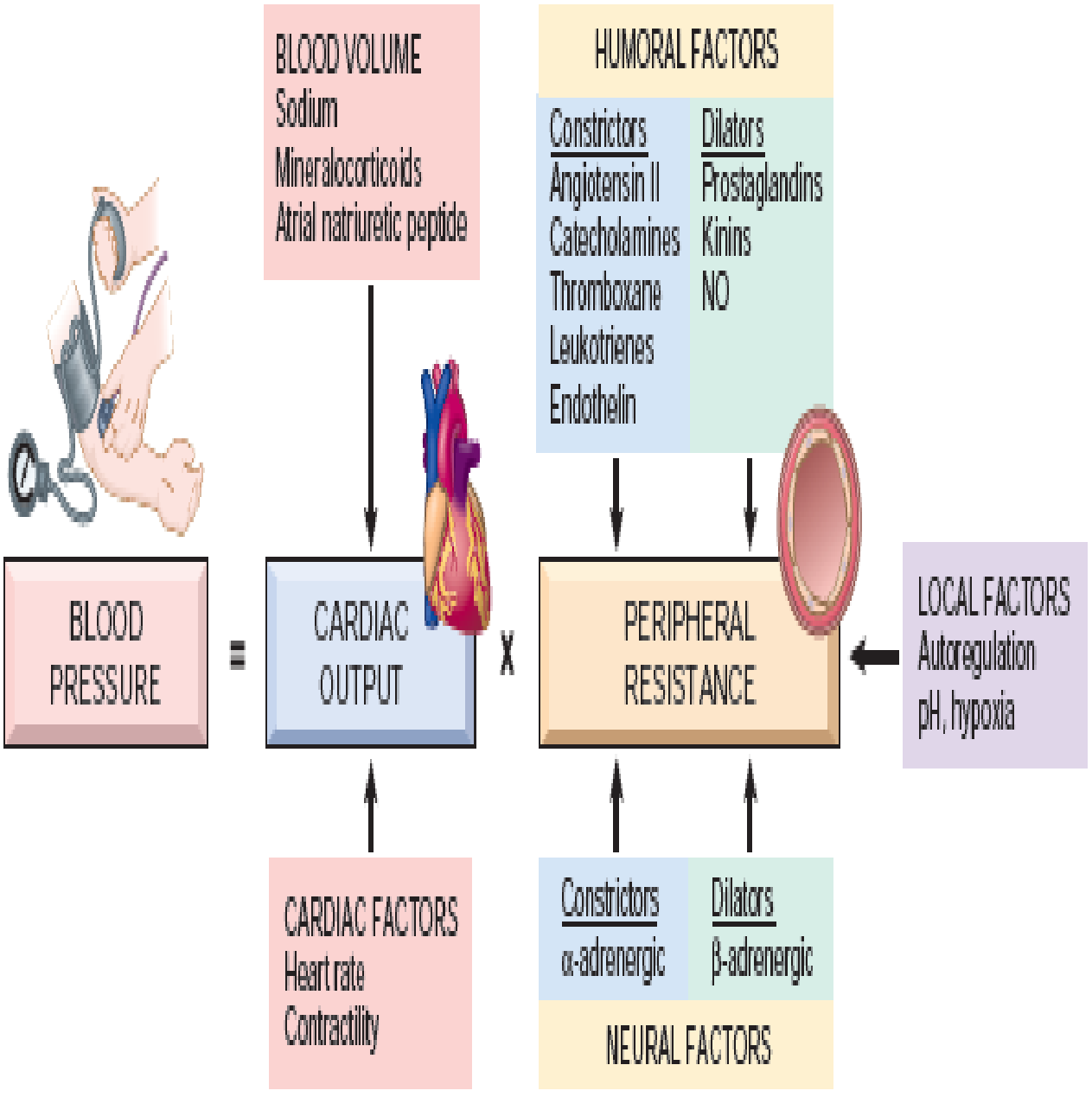
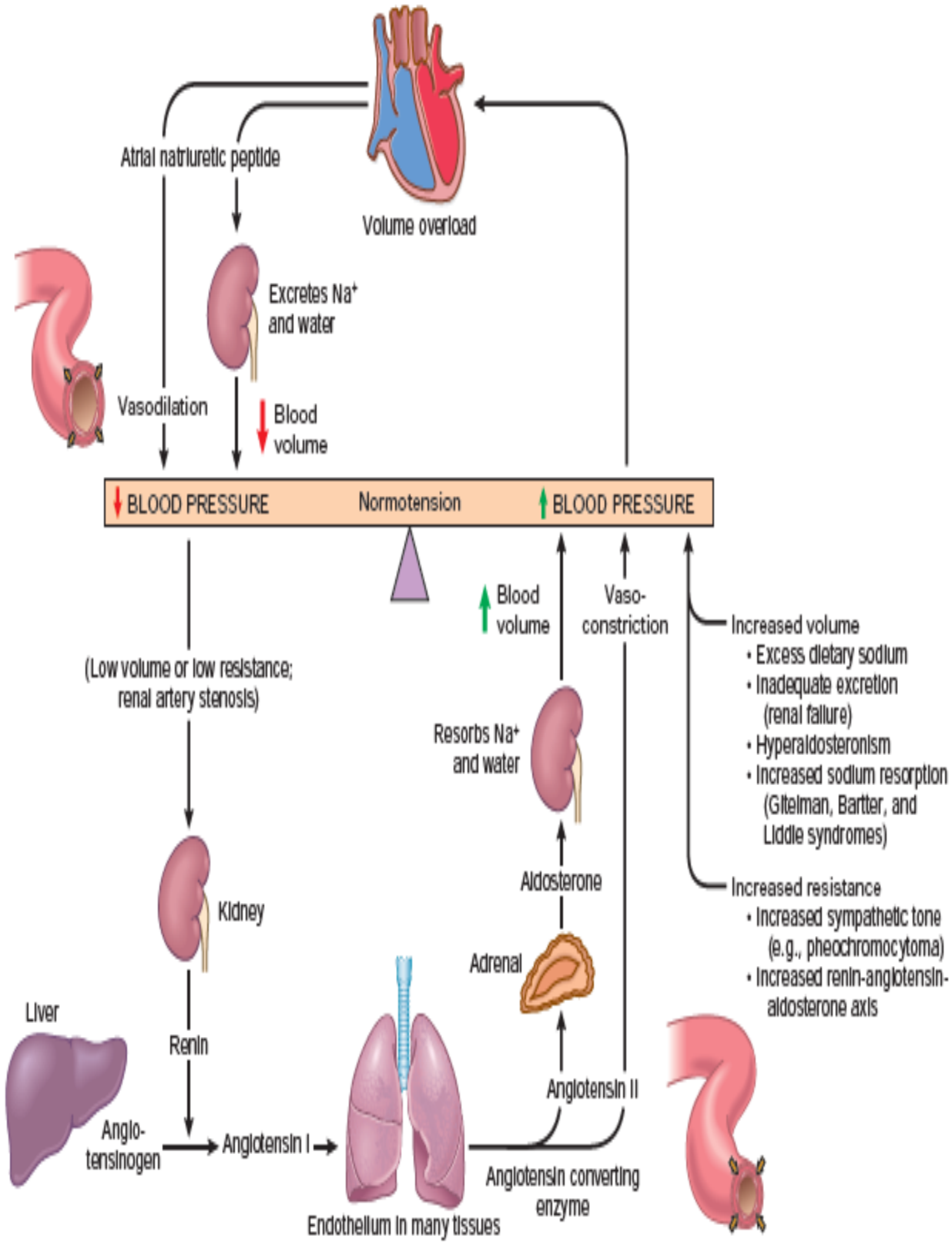


FIGURE 23-1 • Intra-arterial pressure tracing made from the brachial artery. Pulse pressure is the difference between systolic and diastolic pressures. The darker area represents the mean arterial pressure, which can be calculated by using the formula of mean arterial pressure = diastolic pressure + pulse pressure/3.

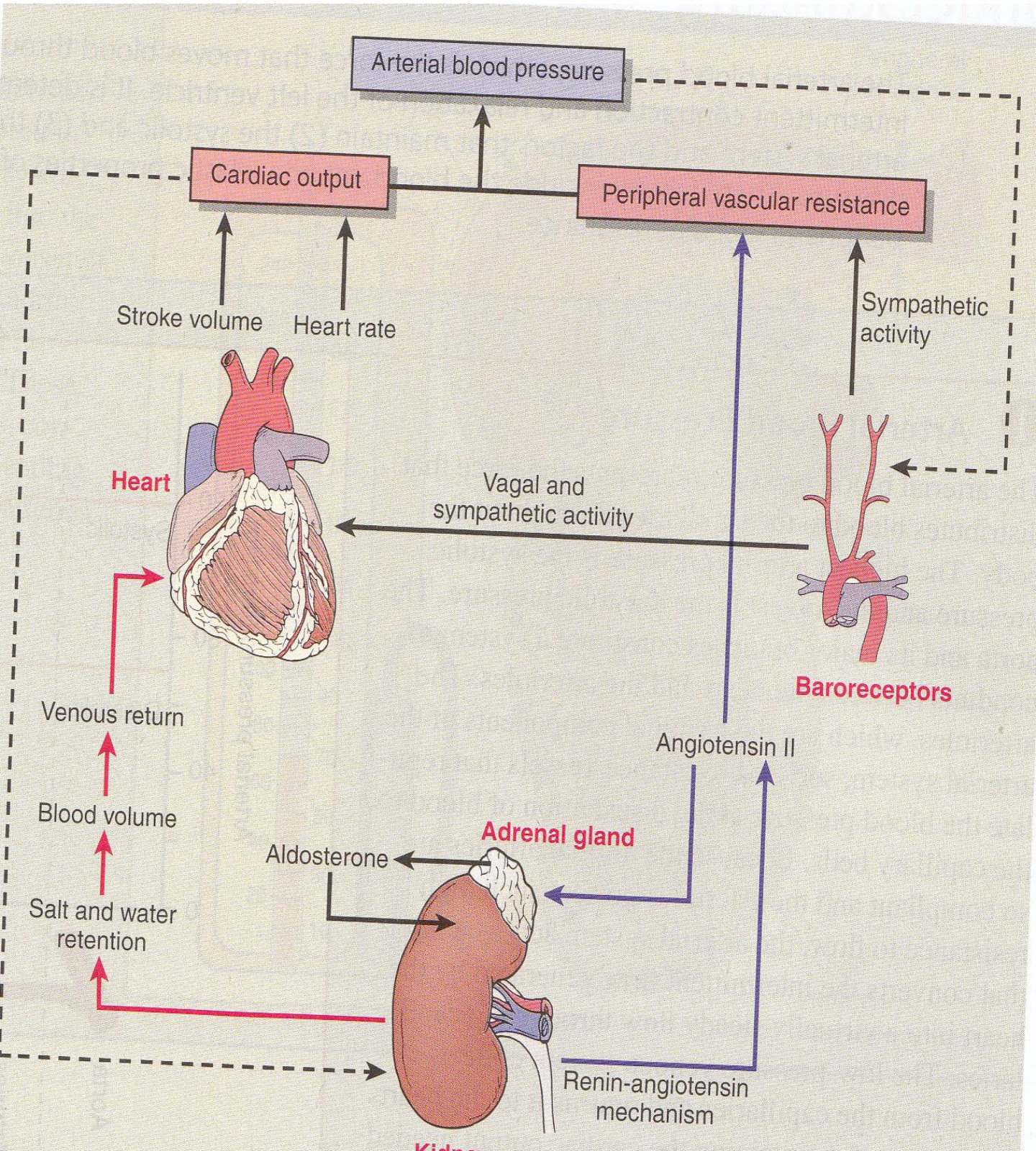
Blood Pressure Regulation



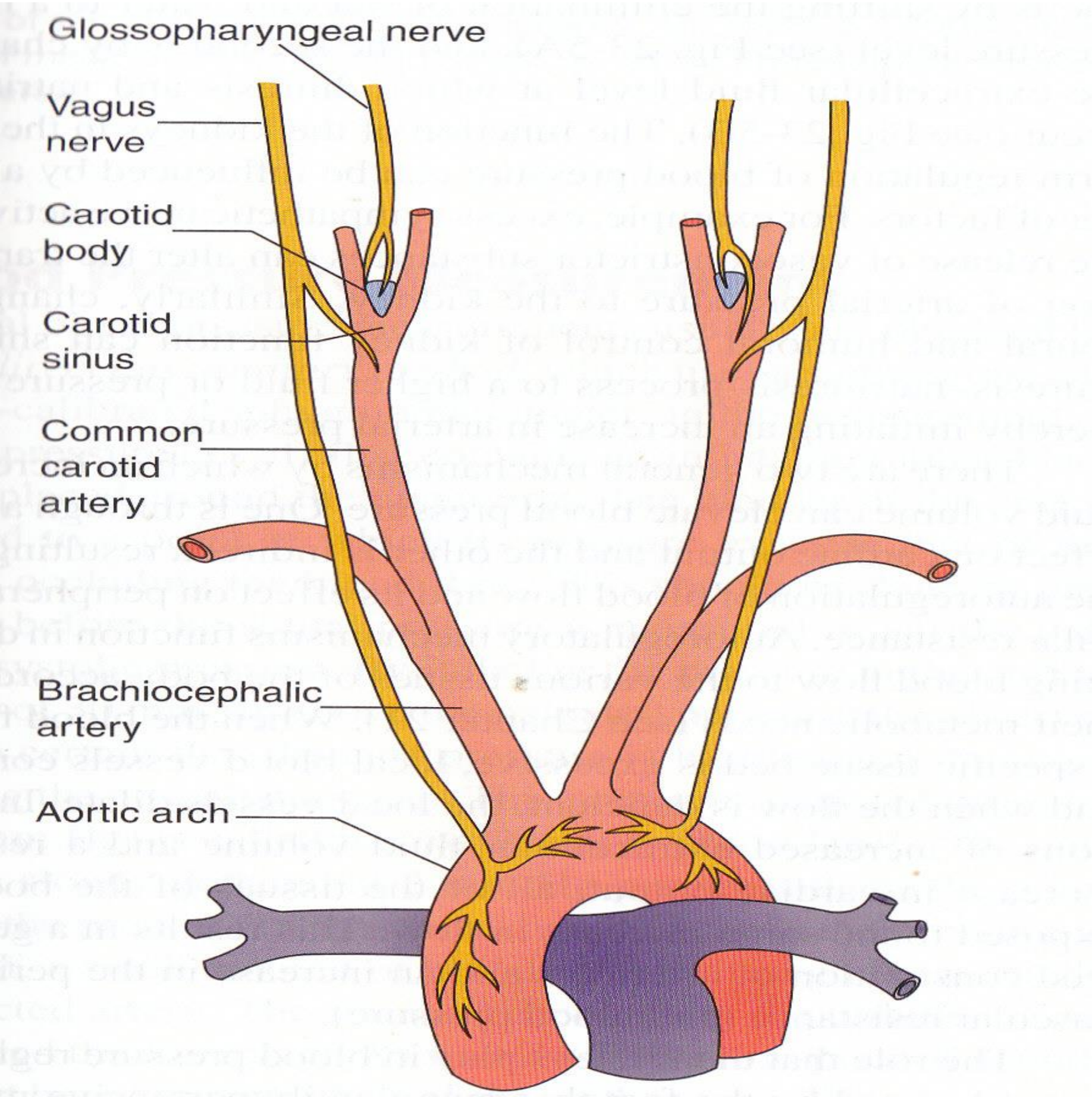

Atrial natriuretic peptide
Volume overload
Excretes Na+ and water
Vasodilation
Blood volume
BLOOD PRESSURE
Normotension
BLOOD PRESSURE
Blood volume
Vaso-constriction
Increased volume
• Excess dietary sodium
• Inadequate excretion (renal failure)
• Hyperaldosteronism
• Increased sodium resorption (Gitelman, Bartter, and Liddle syndromes)
Increased resistance
• Increased sympathetic tone (e.g., pheochromocytoma)
• Increased renin-angiotensin-aldosterone axis
(Low volume or low resistance; renal artery stenosis)
Resorbs Na+ and water
Aldosterone
Adrenal
Kidney
Liver
Renin
Angio-tensinogen
Angiotensin I
Angiotensin II
Angiotensin converting enzyme
Endothelium in many tissues

Mechanisms of Blood Pressure Regulation

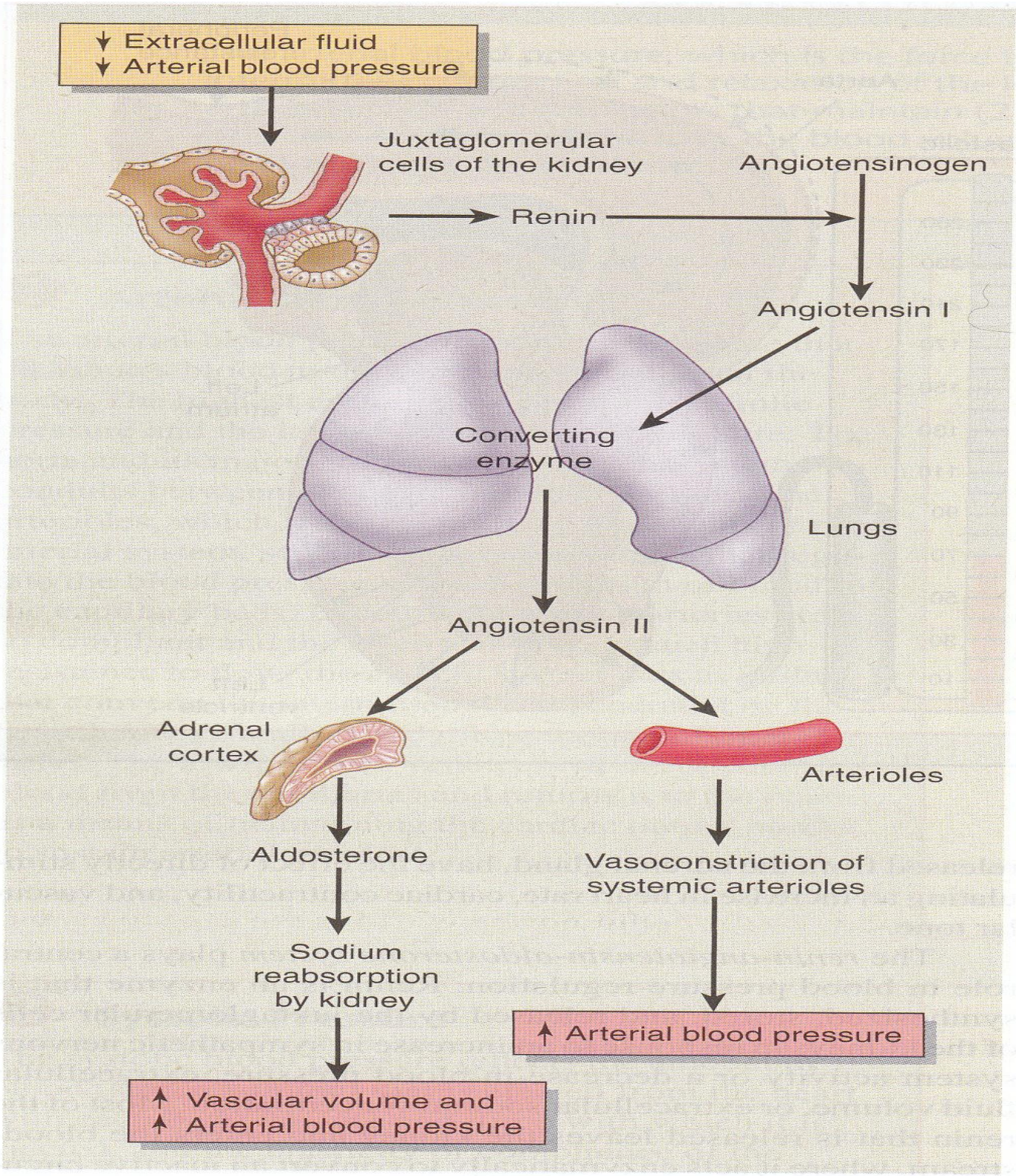
(short-term Regulation)



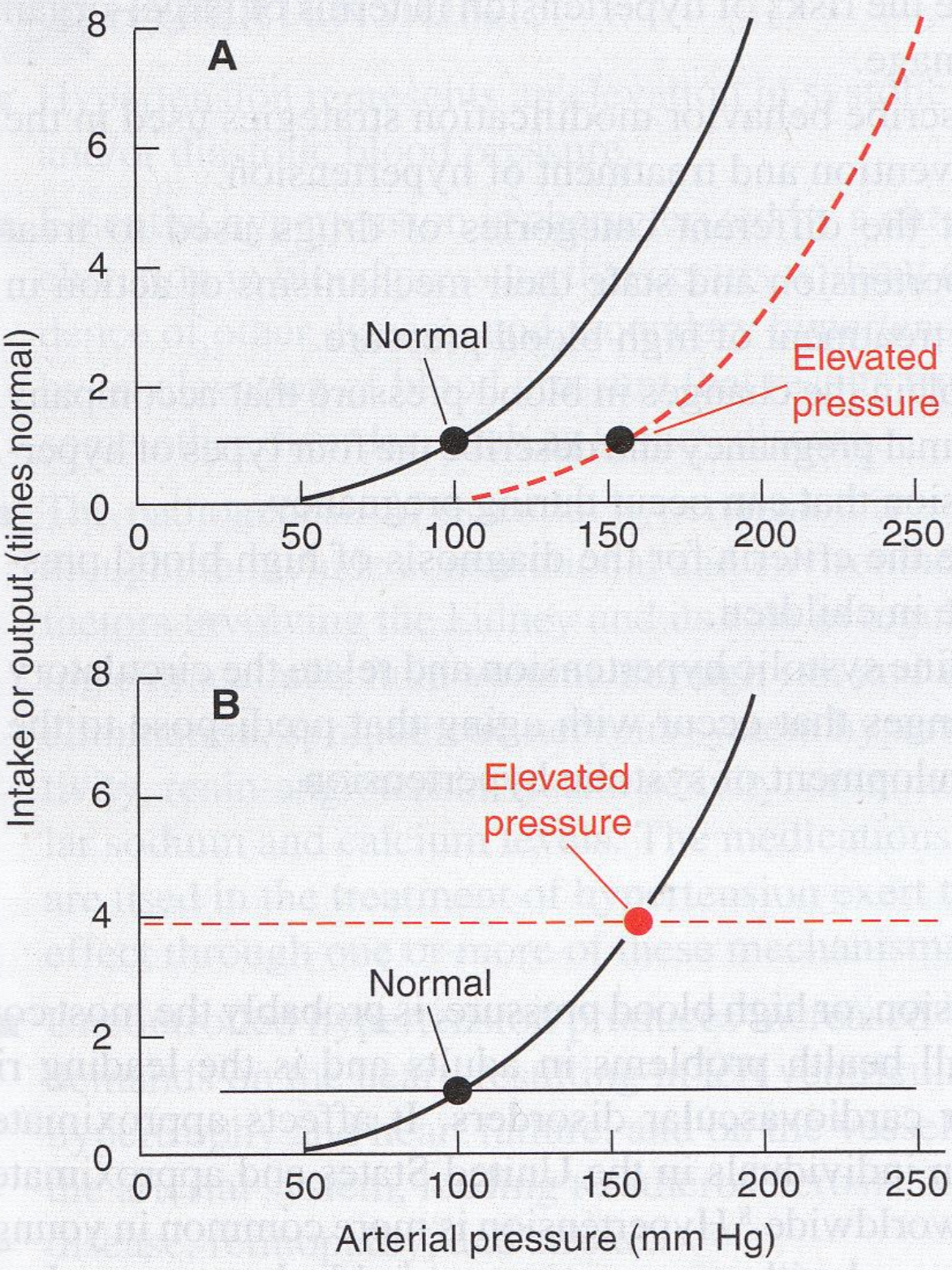
The carotid and aortic baroreceptors



Renin-angiotensin-aldosterone system



Long-Term Regulation



Hypertension is an elevation in a systolic and/or diastolic blood pressure

BP (≥ 140 mm Hg), diastolic BP (≥ 90 mm Hg), or both.

Hypertension

It affects about 50 million individuals in the US, about 1 billion worldwide; is more common in younger men compared with younger women

Contributing factors of Essential hypertension

- ***Constitutional Risk Factors***
- Family History
- Age-Related Changes in Blood Pressure
- Race
- Insulin Resistence and Metabolic Abnormalities
- ***Lifestyle Risk Factors***
- High Salt Intake
- Obesity
- Excess Alcohol Consumption
- Dietary Intake of K, Ca, Mg
- Low intake of K

- Excessive alcohol intake and use of oral contraceptives are common causes of curable hypertension. Use of sympathomimetics, NSAIDs, corticosteroids, cocaine, or licorice commonly contributes to hypertension.

- In afferent systemic arterioles, malfunction of ion pumps on sarcolemmal membranes of smooth muscle cells may lead to chronically increased vascular tone. Heredity is a predisposing factor, but the exact mechanism is unclear. Environmental factors (age, dietary Na, obesity, stress) seem to affect only genetically susceptible people.

Hypertension classification:

- Primary (essential) –applied to 95% of cases, no known cause (primary; essential hypertension) is most common.
- Secondary (endocrine, kidneys diseases)

TABLE 23-1 Classification of Blood Pressure for Adults and Recommendations for Follow-up

BLOOD PRESSURE CLASSIFICATION	SYSTOLIC BLOOD PRESSURE (mm Hg)	DIASTOLIC BLOOD PRESSURE (mm Hg)	FOLLOW-UP RECOMMENDATIONS FOR INITIAL BLOOD PRESSURE*†
Normal	<120	And <80	Recheck in 2 years
Prehypertensive	120–139	or 80–89	Recheck in 1 year‡
Stage 1 hypertension	140–159	or 90–99	Confirm within 2 months‡
Stage 2 hypertension	≥160	or ≥100	Evaluate or refer to source of care within 1 month. For those with higher pressure (*e.g.*, >180/110 mm Hg), evaluate and treat immediately or within 1 week, depending on clinical situation and complications.

Types and Causes of Hypertension (Systolic and Diastolic)

Essential hypertension
Accounts for 90% to 95% of all cases
Secondary hypertension
Renal
Acute glomerulonephritis Chronic renal disease Polycystic disease Renal artery stenosis Renal vasculitis Renin-producing tumors
Endocrine
Adrenocortical hyperfunction (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, licorice ingestion) Exogenous hormones (glucocorticoids, estrogen [including pregnancy-induced and oral contraceptives], sympathomimetics and tyramine-containing foods, monoamine oxidase inhibitors) Pheochromocytoma Acromegaly Hypothyroidism (myxedema) Hyperthyroidism (thyrotoxicosis) Pregnancy-induced
Cardiovascular
Coarctation of aorta Polyarteritis nodosa Increased intravascular volume Increased cardiac output Rigidity of the aorta
Neurologic
Psychogenic Increased intracranial pressure Sleep apnea Acute stress, including surgery

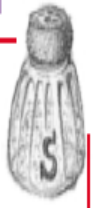
B. Causes of Hypertension

1. Primary hypertension

Genetic factors

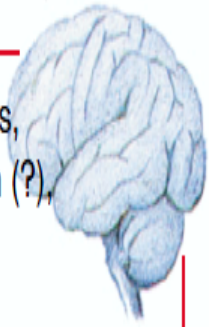
?

Na+ uptake too high,
K+ uptake too low



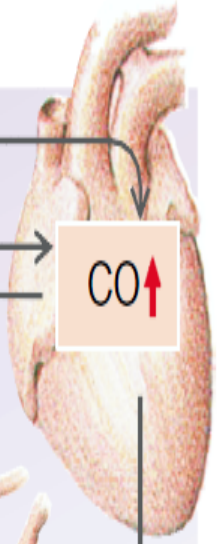
?

Psychological stress,
abnormal regulation (?),
norepinephrine,
hypersensitivity



?

Cardiac stimulation ↑



?

ECV ↑

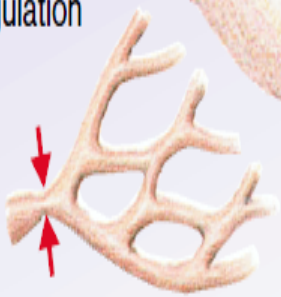
CO ↑

?

Ca^{2+} content of the muscle cells of blood vessels ↑

Autoregulation

Vasoconstriction



Hypertrophy of vascular musculature

TPR ↑

2. Renal hypertension

Renal artery stenosis etc.

Renal ischemia

Kidney

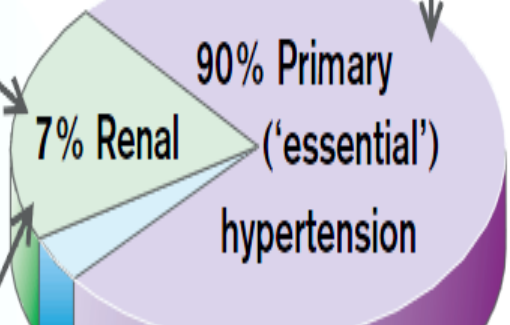
Renin

Angiotensin II

TPR ↑

Various renal diseases

Aldosterone



Aldosterone

Na^+ retention → ECV↑ → CO↑

Functioning renal mass ↓

3% Hormonal and other causes

CO↑ TPR↑

ECV↑

4. Other forms of hypertension:

cardiovascular, neurogenic, drugs

3. Hormonal hypertension

Mineralo-corticoid effect

Increased catecholamine effect

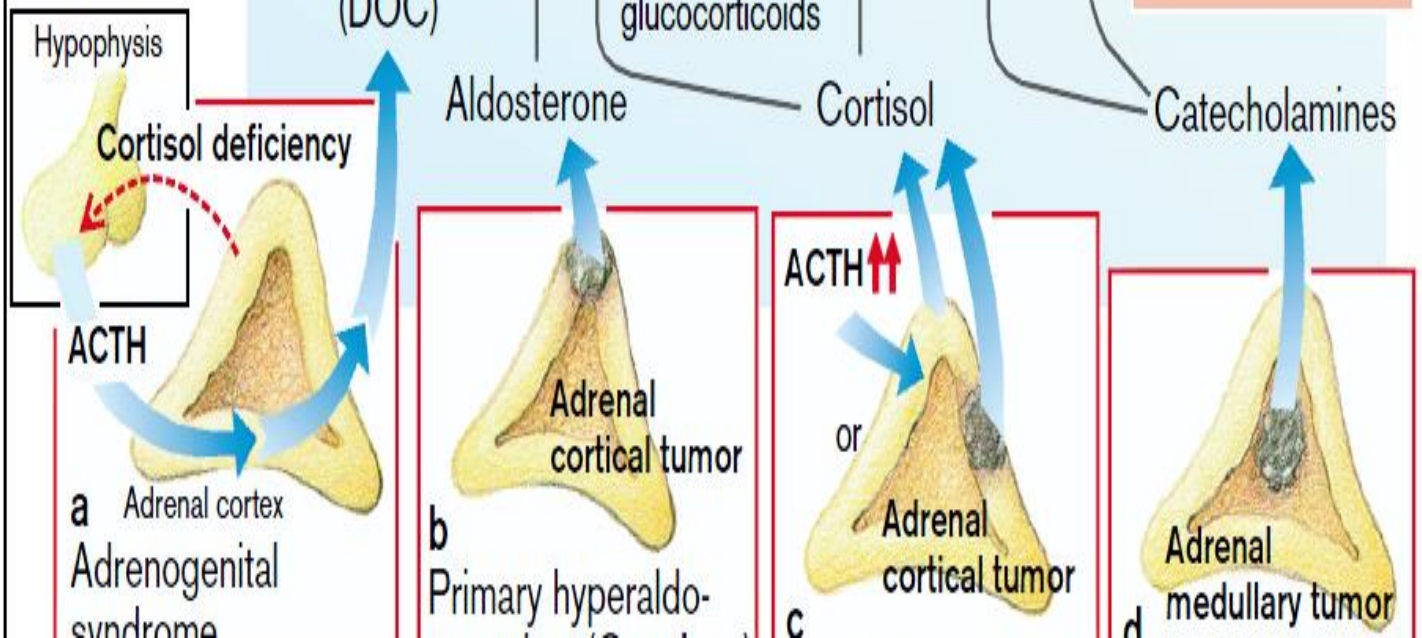
11-desoxy-corticosterone (DOC)

Therapeutic glucocorticoids

Aldosterone

Cortisol

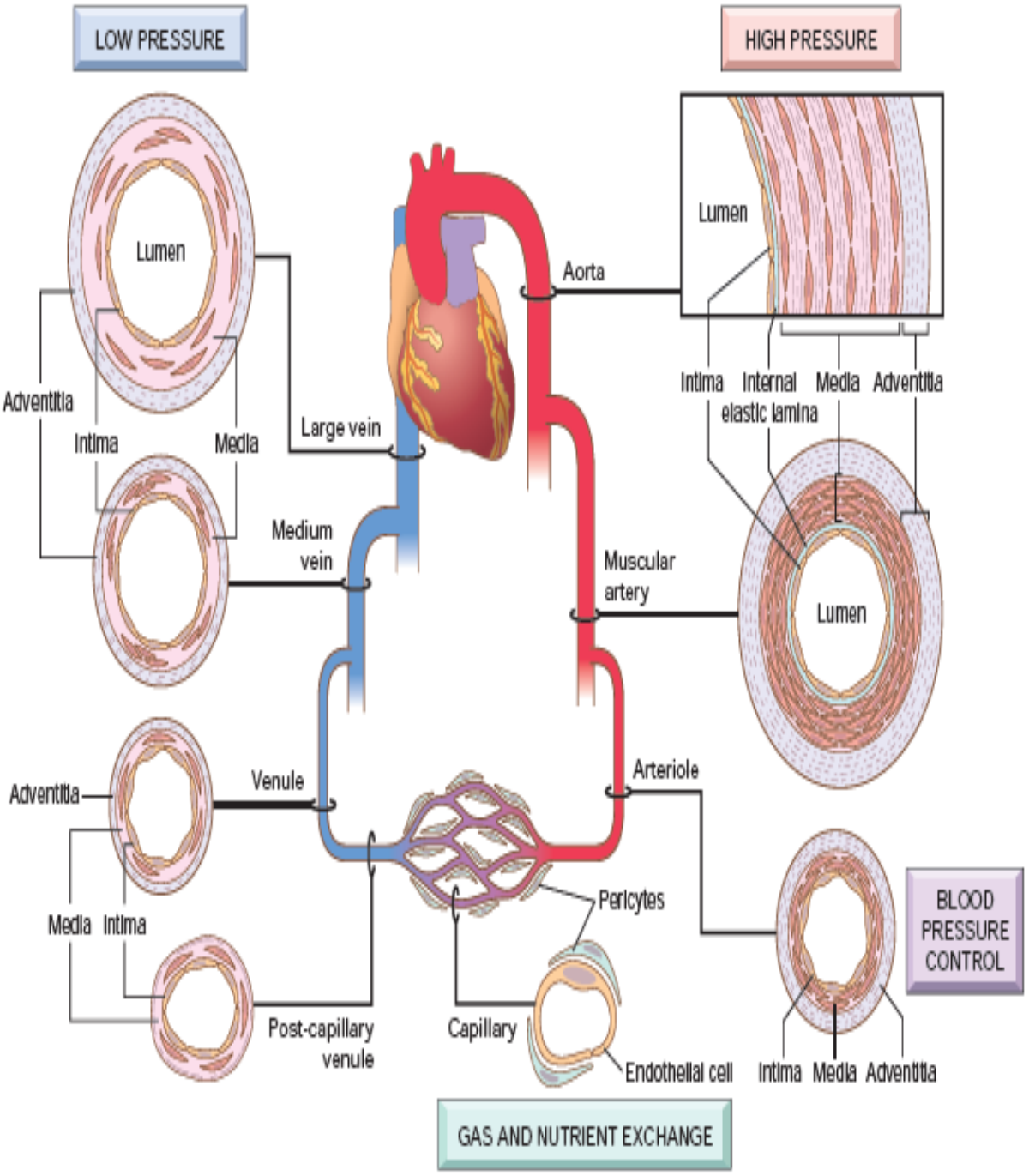
Catecholamines



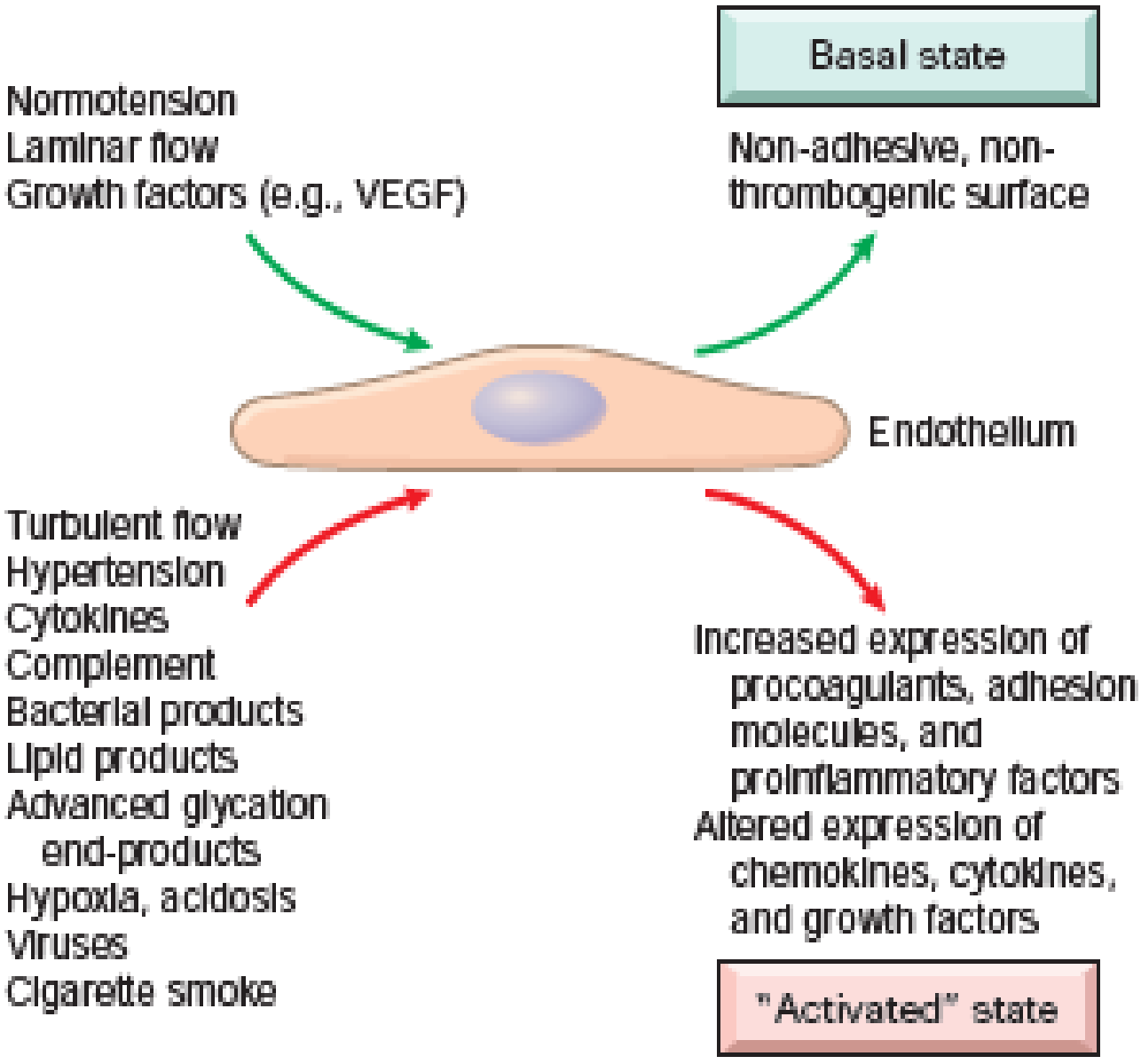
Pathogenesis of Hypertension

- *Genetic factors;*
- *Reduced renal sodium excretion;*
- *Vasoconstrictive influences;*
- *Environmental factors*

Vascular Structure and Function



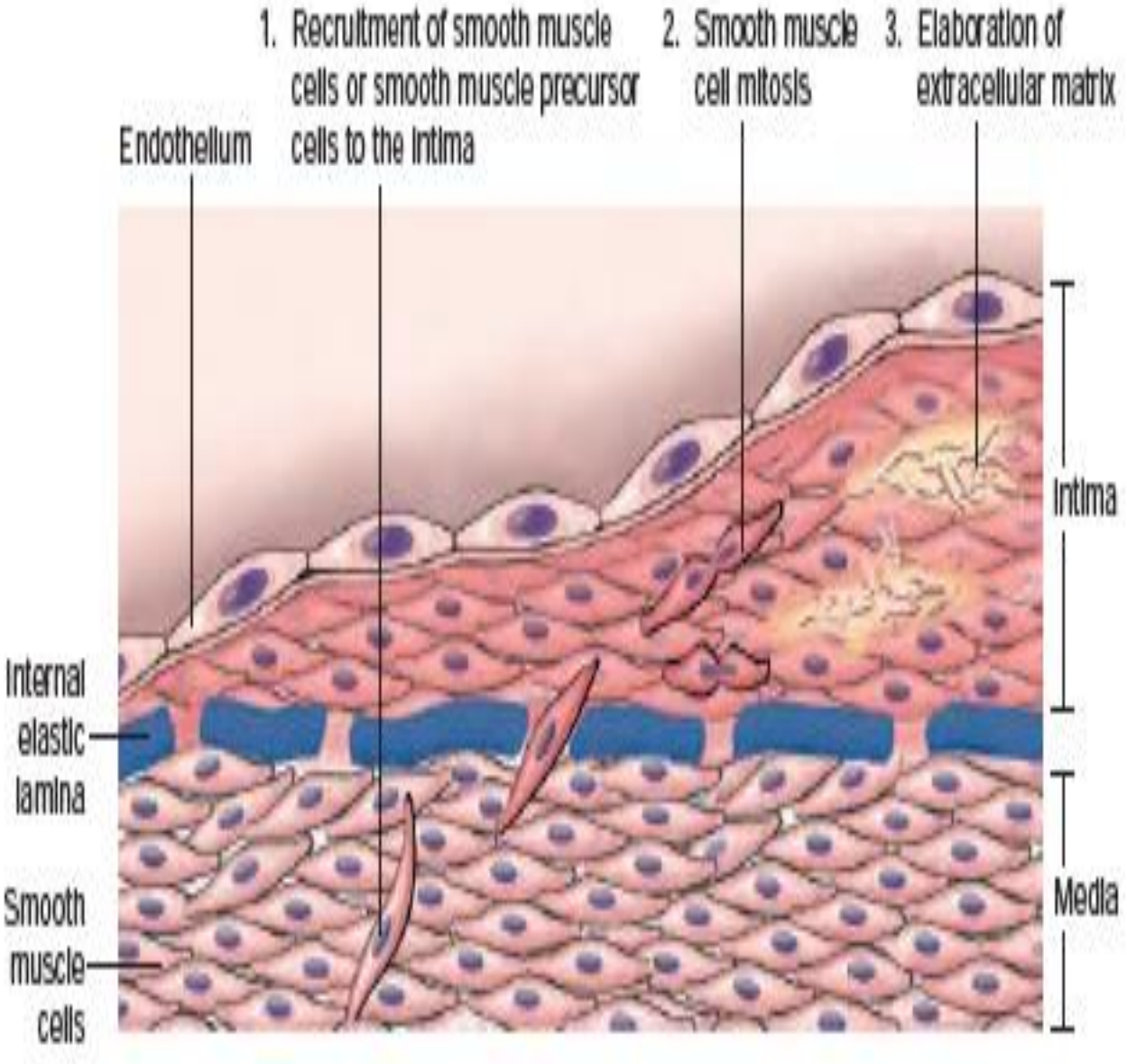
Vascular Wall Response to Injury



Vascular Wall Response to Injury

- *Endothelial dysfunction*
- *Vascular smooth muscle cells*

Intimal Thickening: A Stereotyped Response to Vascular Injury



Target-Organ Damage

CHART 23-1 TARGET ORGAN DAMAGE

Heart

- Left ventricular hypertrophy
- Angina or prior myocardial infarction
- Prior coronary revascularization
- Heart failure

Brain

- Stroke or transient ischemic attack

Chronic kidney disease

Peripheral vascular disease

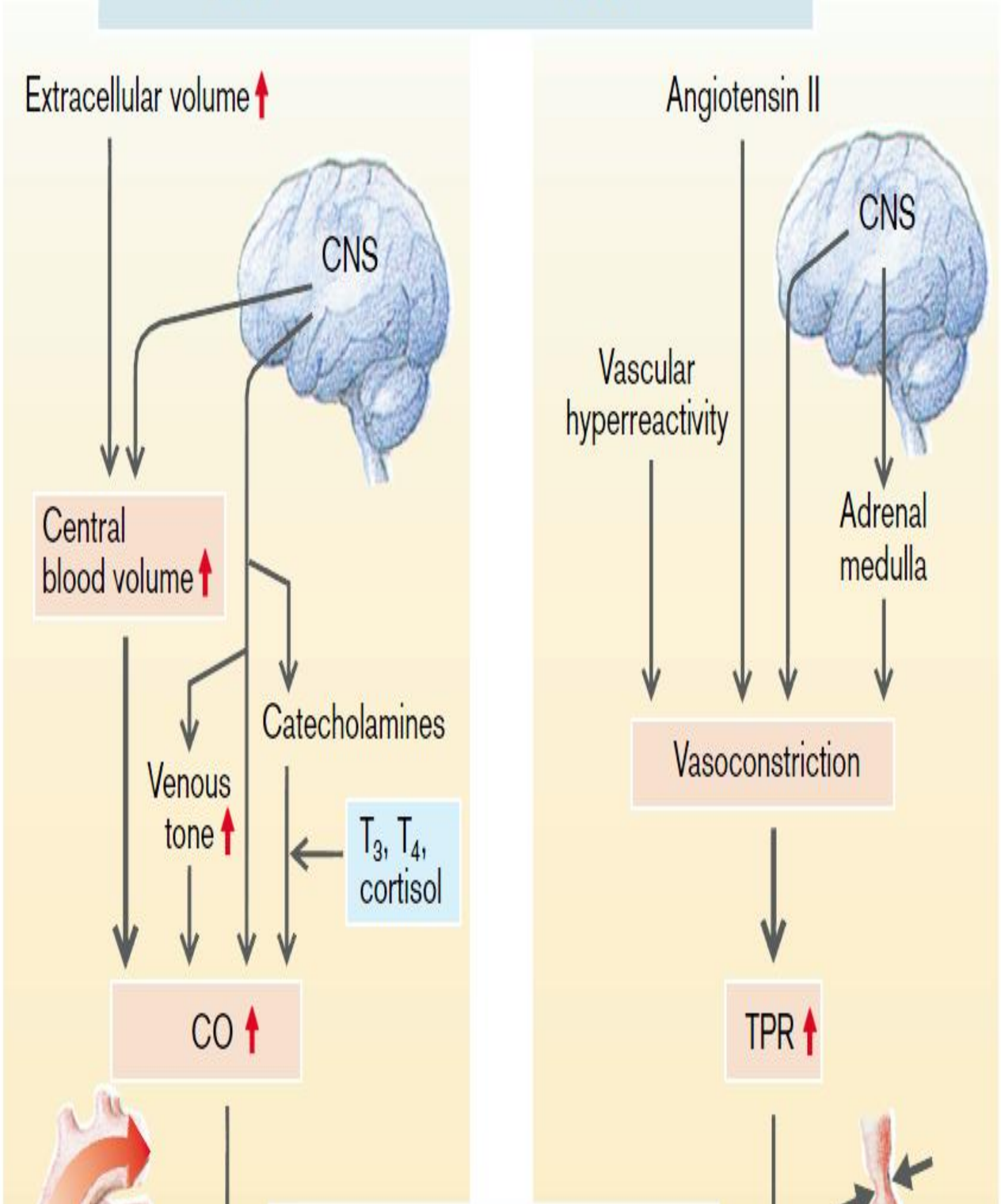
Retinopathy

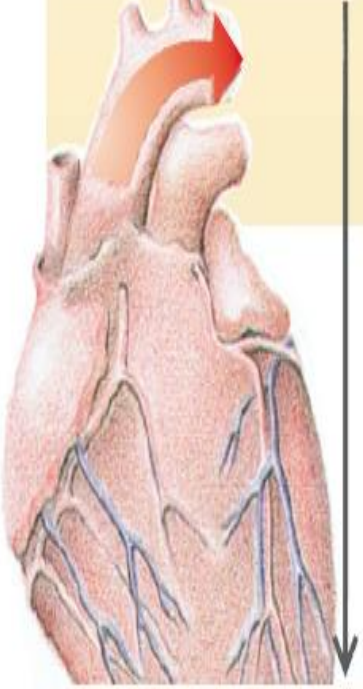
From the National Heart, Lung, and Blood Institute. (2003). *The seventh report of the National Committee on Detection, Evaluation, and Treatment of High Blood Pressure*. Publication no. 03–5233. Bethesda, MD: National Institutes of Health.

A. Principles of the Development of Hypertension

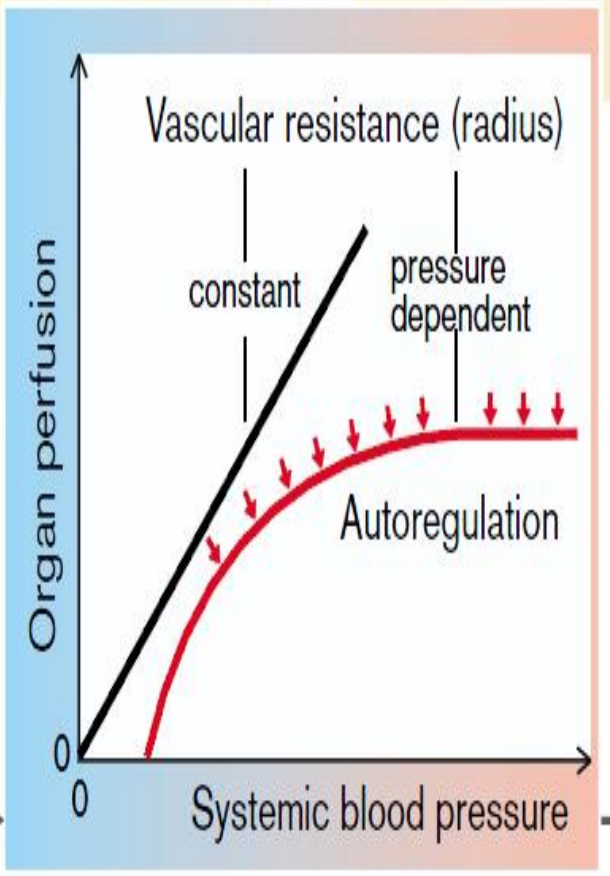
Arterial blood pressure =

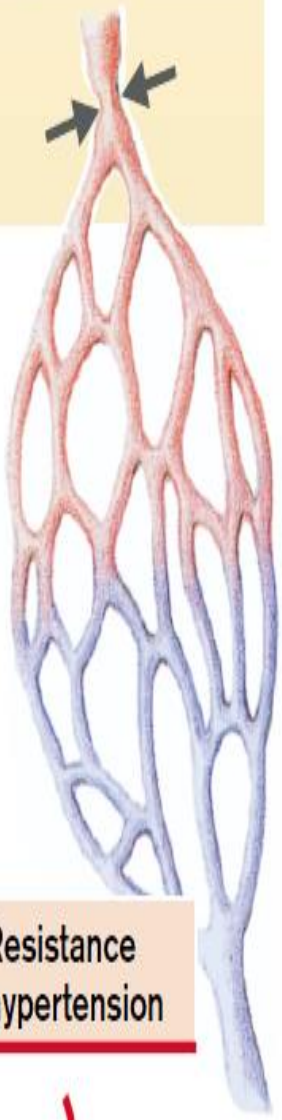
Cardiac output (CO) x Total peripheral resistance (TPR)





Hyperdynamic hypertension





Resistance hypertension

Vicious circle

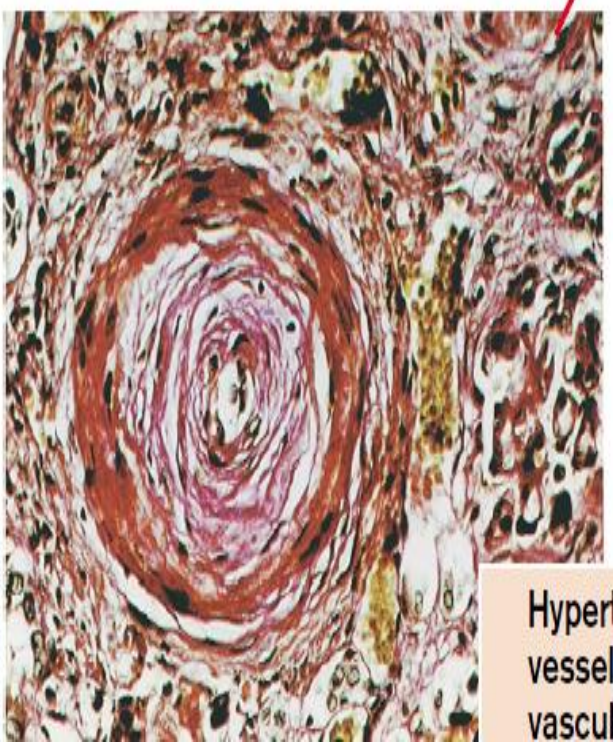


Photo: U. Pfeifer

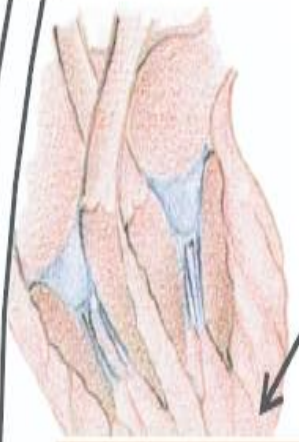
Hypertrophy of vessel musculature and vascular damage:

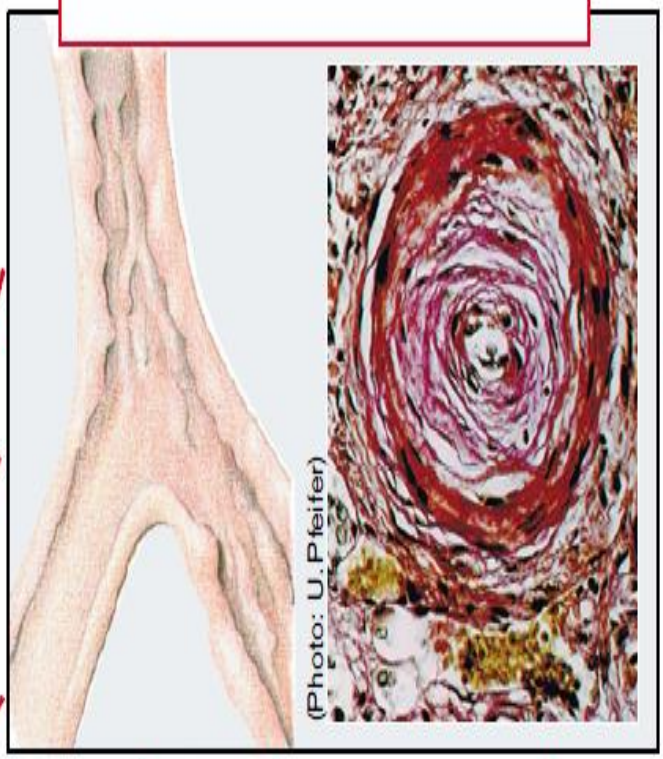
Arterial hypertension

TPR ↑

Na^+ excretion ↓

Hypertensive encephalopathy





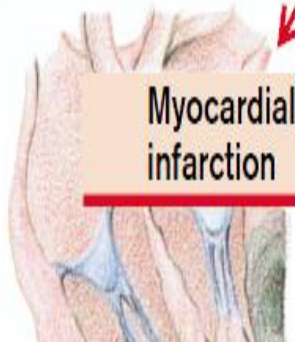
Left ventricular hypertrophie, heart failure

Bleeding

Renal ischemia

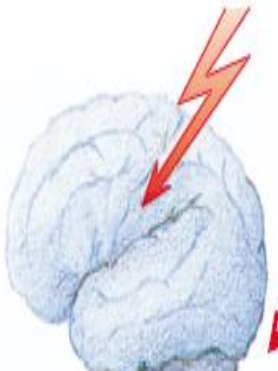
Renal failure

Malacia



Myocardial infarction

Peripheral vascular disease



Secondary hypertension

- Causes include renal parenchymal disease (eg, chronic glomerulonephritis or pyelonephritis, polycystic renal disease, connective tissue disorders, obstructive uropathy), renovascular disease, pheochromocytoma, Cushing's syndrome, primary aldosteronism, congenital adrenal hyperplasia, hyperthyroidism, myxedema, and coarctation of the aorta.

Pathogenesis of hypertention

Constitutional factors

Environmental factors (kidney)

Sympathetic nervous system hyperreactivity

Renin/angiotensin system activity

Intra cellular Na and Ca

1. Abnormal Na transport

- In many cases of hypertension, Na transport across the cell wall is abnormal, because the Na-K pump (Na+, K+-ATPase) is defective or inhibited or because permeability to Na+ is increased. The result is increased intracellular Na, which makes the cell more sensitive to sympathetic stimulation. Ca++ follows Na, so accumulation of intracellular Ca++ may be responsible for the increased sensitivity.

- Because Na+, K+-ATPase may pump norepinephrine back into sympathetic neurons (thus inactivating this neurotransmitter), inhibition of this mechanism could also enhance the effect of norepinephrine, increasing BP. Defects in Na transport may occur in normotensive children of hypertensive parents.

2.Activation Of Sympathetic Nervous System

- Sympathetic stimulation increases BP, usually more in patients with prehypertension (systolic BP 120 to 139 mm Hg, diastolic BP 80 to 89 mm Hg) or hypertension (systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or both) than in normotensive patients. Whether this hyperresponsiveness resides in the sympathetic nervous system or in the myocardium and vascular smooth muscle is unknown.

- However activation of the SNS raises blood pressure by several mechanisms, including increased cardiac output, vasoconstriction of the large veins, which leads to increased cardiopulmonary blood volume, vasoconstriction of resistance vessels, and increased renal sodium reabsorption, which expands intravascular volume.

3.Renin-angiotensin-aldosterone system

- This system helps regulate blood volume and therefore BP. Renin, an enzyme formed in the juxtaglomerular apparatus, catalyzes conversion of angiotensinogen to angiotensin I. This inactive product is cleaved by ACE, mainly in the lungs but also in the kidneys and brain, to angiotensin II, a potent vasoconstrictor that also stimulates autonomic centers in the brain to increase sympathetic discharge and stimulates release of aldosterone and ADH.

- Aldosterone and ADH cause Na and water retention, elevating BP. Aldosterone also enhances K excretion; low plasma K (< 3.5 mEq/L) increases vasoconstriction through closure of K channels. Angiotensin III, present in the circulation, stimulates aldosterone release as actively as angiotensin II but has much less pressor activity. Because chymase enzymes also convert angiotensin I to angiotensin II, drugs that inhibit ACE do not fully suppress angiotensin II production.

Renin secretion is controlled by at least 4 mechanisms:

1. A renal vascular receptor responds to changes in tension in the afferent arteriolar wall;
2. a macula densa receptor detects changes in the delivery rate or concentration of NaCl in the distal tubule;
3. circulating angiotensin has a negative feedback effect on renin secretion;
4. via the renal nerve, the sympathetic nervous system stimulates renin secretion mediated by β-receptors.

- Angiotensin is generally acknowledged to be responsible for renovascular hypertension, at least in the early phase, but the role of the renin-angiotensin-aldosterone system in primary hypertension is not established. However, in black and elderly patients with hypertension, renin levels tend to be low. The elderly also tend to have low angiotensin II levels.

- Hypertension due to chronic renal parenchymal disease (renoprival hypertension) results from the combination of a renin-dependent mechanism and a volume-dependent mechanism. In most cases, increased renin activity is not evident in peripheral blood. Hypertension is typically moderate and sensitive to Na and water balance.

4.Vasodilator deficiency

- Deficiency of a vasodilator (eg, bradykinin, nitric oxide) rather than excess of a vasoconstrictor (eg, angiotensin, norepinephrine) may cause hypertension. If the kidneys do not produce adequate amounts of vasodilators (because of renal parenchymal disease or bilateral nephrectomy), BP can increase. Vasodilators and vasoconstrictors (mainly endothelin) are also produced in endothelial cells. Therefore, endothelial dysfunction greatly affects BP.

6. Renal Sodium Retention & salt sensitivity

- The presence of salt sensitivity, defined as an increase in mean arterial pressure (MAP) of 10 mm Hg in response to high-salt dietary challenge or saline infusion, has important clinical implications, especially in terms of the choice of antihypertensive therapy.

Symptoms and Signs

- Hypertension is usually asymptomatic until complications develop in target organs. Dizziness, flushed facies, headache, fatigue, epistaxis, and nervousness are not caused by uncomplicated hypertension.

- Severe hypertension can cause severe cardiovascular, neurologic, renal, and retinal symptoms (eg, symptomatic coronary atherosclerosis, HF, hypertensive encephalopathy, renal failure).