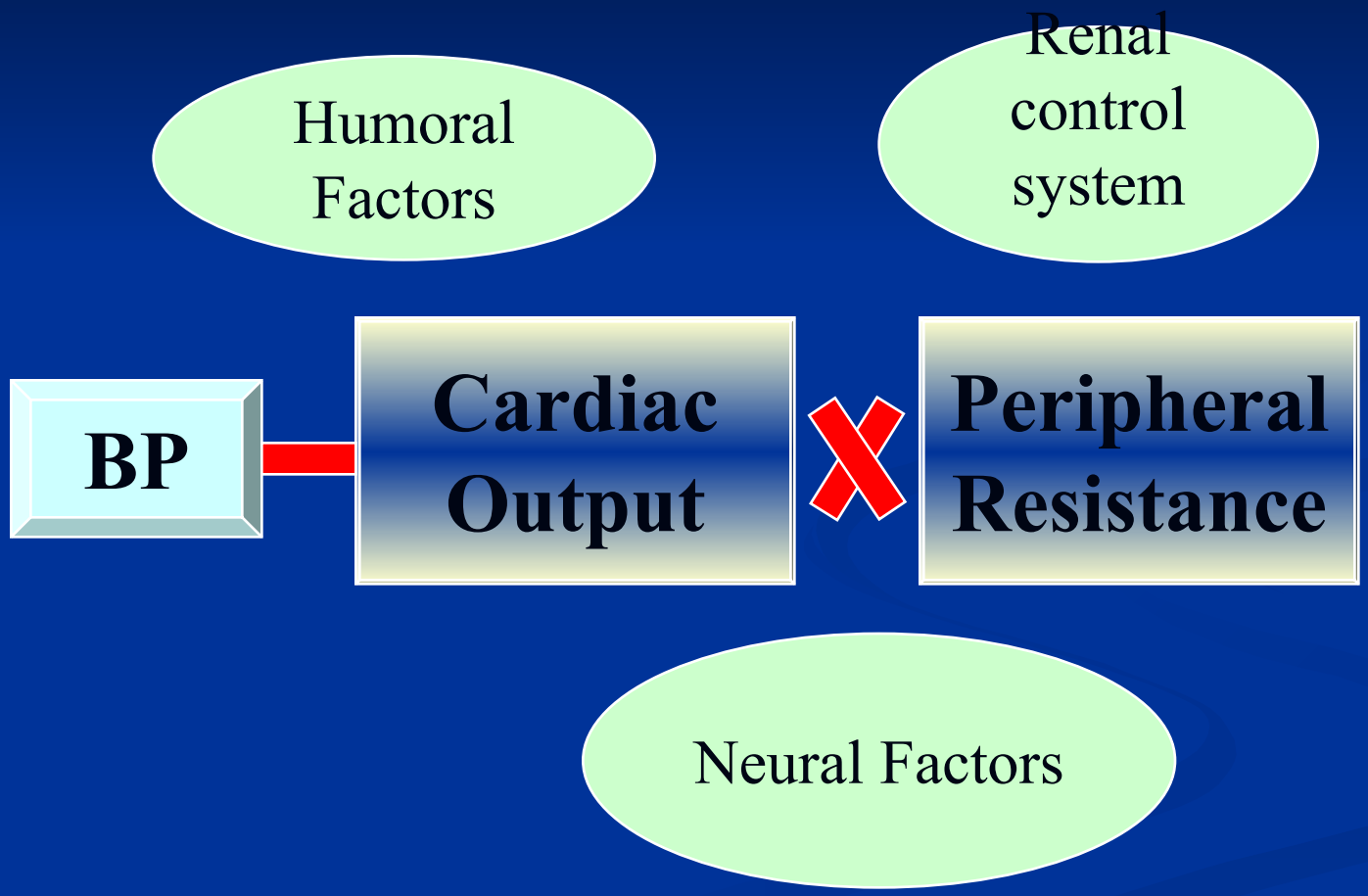
Blood vessels pathology

Lecture Plan

Blood pressure regulation



Blood pressure regulation

The **increase of BP:**

- sympathetic nervous system
- humoral factors (rennin-angiotensin-aldosterone system, vasopressine, glucocorticoids)
- kidney and fluid balance mechanisms

Blood pressure regulation

The **decrease of BP** :

- baroreceptor reflexes from aorta arch and carotid sinuses.
- prostoglandins A, E, I
- kallikrein –kinin system
- atrium natriuretic factor

Rapid pressure control

Nervous reflexes mechanisms

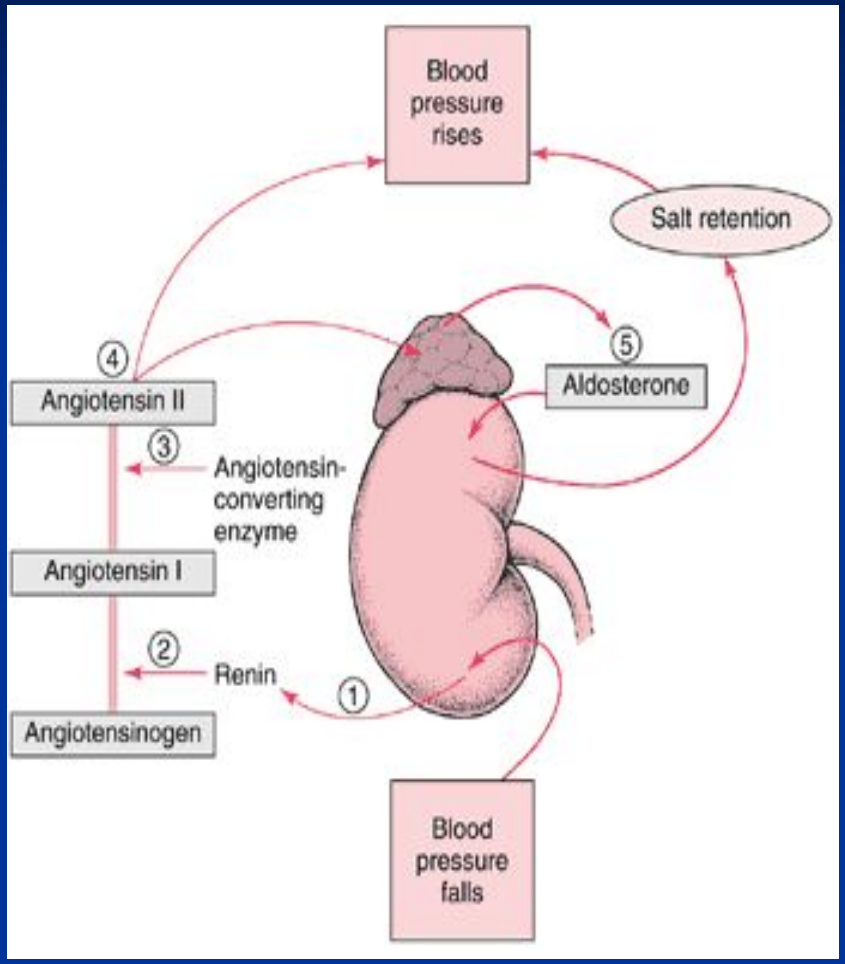
- **Baroreceptors** control BP in posture change, exercise, and moderate temperature changes
- **Sympathetic activity** - increased heart rate, and cardiac contractility, vasoconstriction, increased BP
- **Parasympathetic activity** produces the opposite motor responses.
- **Cardiopulmonary receptors** - vasoconstriction, tachycardia.
- **Chemoreceptors** (pH, blood gases, changes in plasma composition) - vasoconstriction and bradycardia.

Rapid pressure control

Hormonal mechanisms

- **Norepinephrine/epinephrine** – vasoconstriction, increased heart rate
- **Vasopressin** - vasoconstriction.
- **Renin-angiotensin-aldosterone** system

Renin-angiotensin-aldosterone system



angiotensin-converting enzyme is present in the endothelium of the lung vessels.

Angiotensin II:

- **vasoconstrictor response** increases TPVR and BP (short-term regulation)
- **stimulation of aldosterone secretion** (long term regulation)

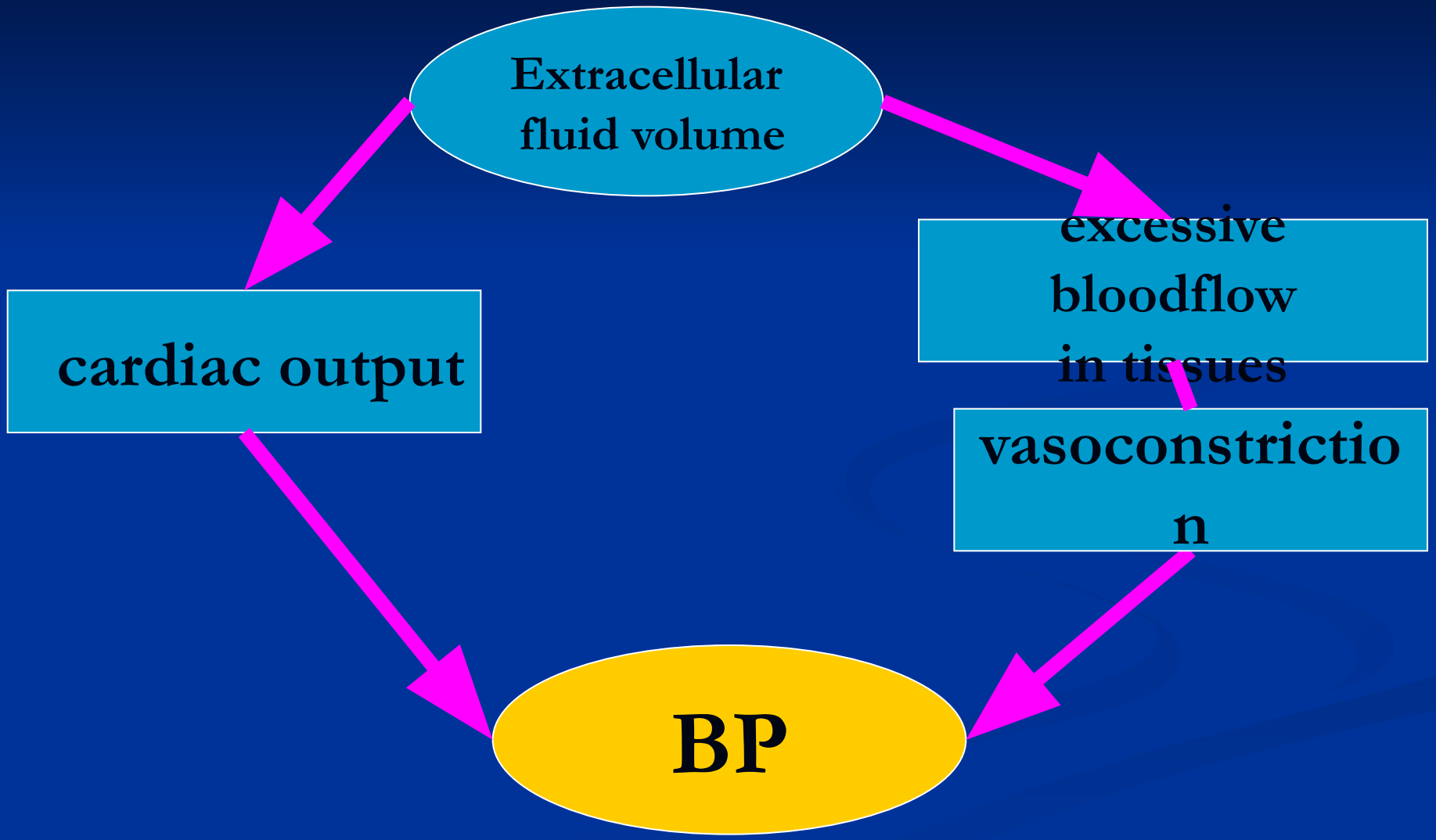
Aldosterone causes salt and water retention (increase of blood volume and BP).

Long-term regulation of BP

Renal regulation

- Water resorption - aldosterone and vasopressin
- Sodium retention - aldosterone.
- An increase in renal output - decrease in venous return and arterial pressure.
  - in extracellular volume without compensation from the kidneys - high BP.

Long-term regulation of BP



Classification of arterial hypertension

Category	Systolic BP (mm hg)	Diastolic BP (mm hg)
Normal BP	Below 130	Below 85
High-normal BP (pre-hypertension)	130-139	85-89
Stage 1 (mild) hypertension	140-159	90-99
Stage 2 (moderate) hypertension	160-179	100-109
Stage 3 (severe) hypertension	180 or higher	110 or higher

Arterial hypertension

Primary hypertension (90%) -

- without evidence of other diseases
- multifactorial syndrome
- increased TPVR

Secondary hypertension (10%)

- depends on other diseases (kidneys, endocrine etc.)

Factors contributing to primary hypertension

- Stress
  - Increased sympathetic activity
  - Stress-induced vasoconstriction
- Genetic factors
  - familiar cases of hypertension,
  - identification of gene responsible for hypertension
- Racial and environmental factors
  - Black race -higher incidence of essential hypertension
  - salt intake (due to blood volume, sensitivity of CVS to adrenergic influences)

Risk factors modifying the course of essential hypertension

- age (in younger persons more severe)
- sex (premenopausal females have better prognosis)
- atherosclerosis (impairs vessels elasticity)
- smoking, excess of alcohol intake
- diabetes mellitus and insulin-resistance

Insulin resistance and hypertension

part of **syndrome X, or the metabolic syndrome** which includes:

- central obesity,
- dyslipidemia (especially elevated triglycerides),
- insulin resistance and/or hyperinsulinemia
- high blood pressure.

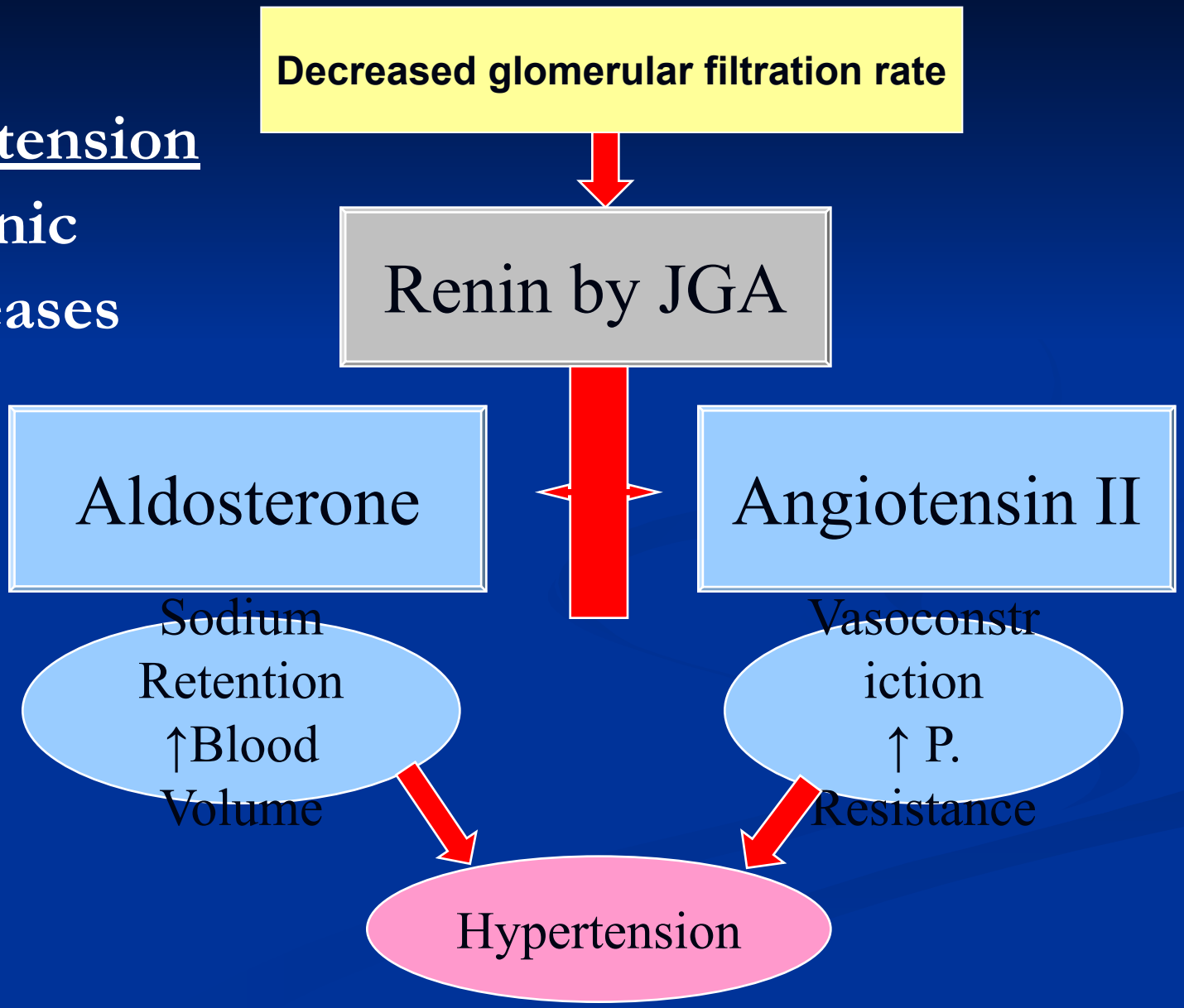
Hyperinsulinemia can increase BP:

- produces renal sodium retention (at least acutely) and increases sympathetic activity.
- mitogenic action of insulin promotes is vascular smooth-muscle hypertrophy increasing TPVR

Secondary hypertension

Renal hypertension

- from chronic kidneys diseases



Etiology of secondary hypertension

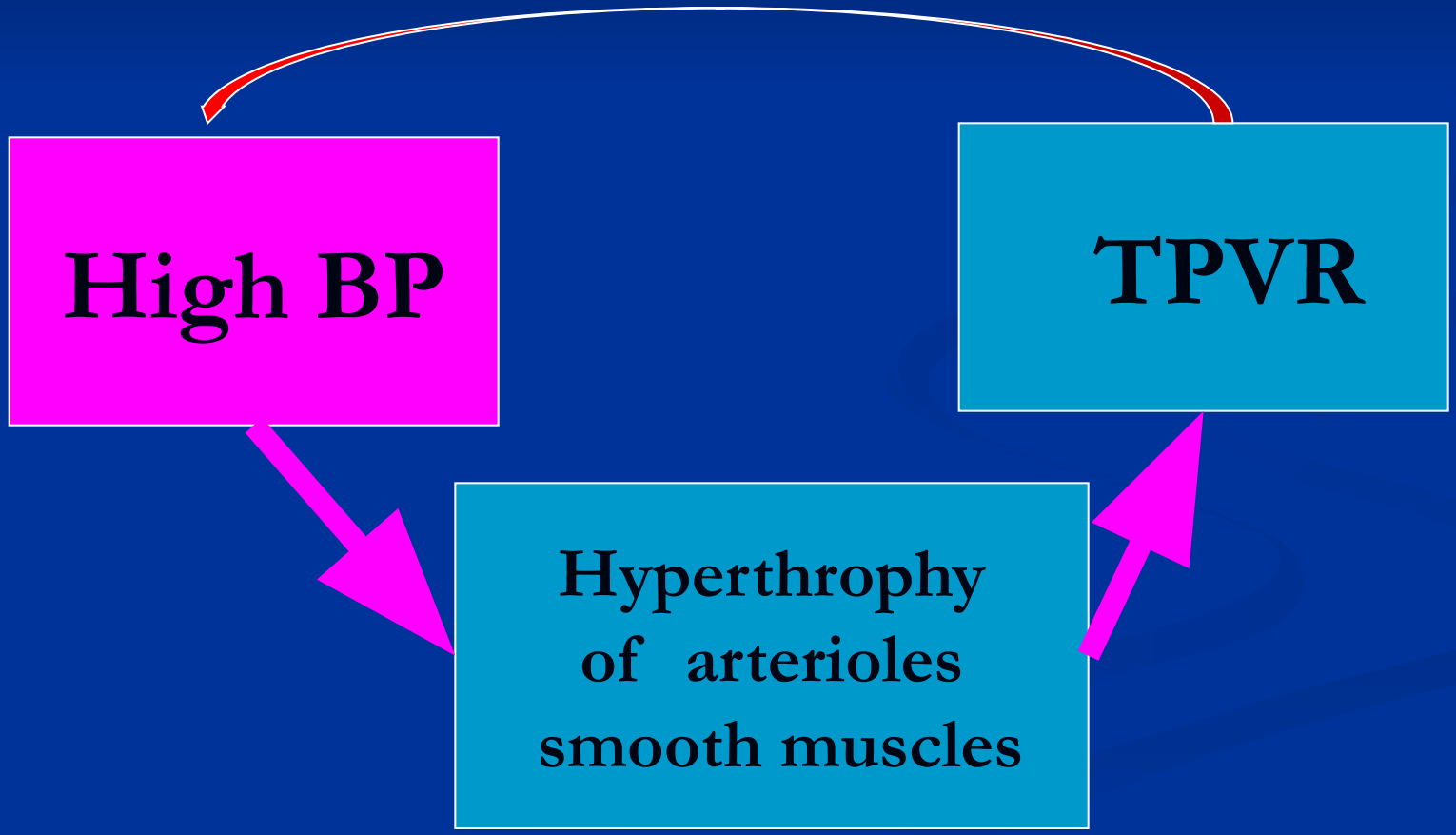
- ↑secretion of aldosterone
- Cushing's syndrome/disease - ↑ glucocorticoid secretion.
- Phaeochromocytoma - tumour releasing both noradrenaline and adrenaline.
- Pregnancy (the last 3 months)
- Drugs (steroids, oral contraceptives, sympatomimetics, aldosterone, and vasopressin).
- Cardiovascular disorder (coarctation of the aorta) - low pressure distal to the coarctation.
- Atherosclerosis

Hypertension pathogenesis

- Stress, hypodynamia sympathetic overactivity increased cardiac output.
- Episodes of high BP increase of TPVR
- increase of TPVR glomerular filtration renin-angiotensin-aldosterone cascade increased NaCl/water retention.
- increased vascular tone results in a rise in TPVR

Hypertension pathogenesis

Vicious circle of hypertension



Hypertension pathogenesis

- Deficiency of vasodilator substances
  - bradykinin from kinin-kallikrein system
  - neutral lipid and prostaglandin from renal parenchyma
    - renoprival hypertension in anephric persons
- Endothelial dysfunction
  - Imbalance between endothelin and NO, prostacyclin

Hypertension signs and symptoms

Primary hypertension is asymptomatic until complications develop in target organs.

Heart

- **left ventricule hypertrophy**
- **angina pectoris**
- **myocardial infarction**
- **heart failure**

Hypertension signs and symptoms

- **Hypertensive retinopathy** - retinal hemorrhages, exudates, vascular accidents.
- **Hypertensive encephalopathy** - dizziness, headache, fatigue, nervousness.
- **Brain stroke** – ischemic and hemmorrhagic
- **Hypertensive nephropathy** - chronic renal failure due to chronically high blood pressure.

Hypertension treatment

Primary hypertension cannot be cured, but it can be controlled to prevent complications.

- Losing weight.
- Changes in diet.
- Stop smoking.
- Reducing the intake of alcohol and sodium.
- Moderate regular aerobic exercise.
- If modification of lifestyle in 6 months was not successful, antihypertensive drugs are prescribed.

Arterial hypotension

Neurogenic causes - autonomic dysfunction or failure:

- central nervous system abnormalities (Parkinson's disease)
- secondary to systemic diseases (diabetes, vasovagal hyperactivity).

Nonneurogenic causes of hypotension

- vasodilation (alcohol, drugs, fever)
- cardiac disease (cardiomyopathy, valvular disease);
- reduced blood volume (hemorrhage, dehydration, or other causes of fluid loss.

Orthostatic or postural hypotension

- is an abnormal drop in BP on assumption of the standing position.
  - normally, it is compensated by increase in heart rate
- Weakness, dizziness, syncope (i.e., fainting),
  - common complaints of elderly persons.

Causes

- ANS dysfunction
- reduced blood volume– dehydration (diuretics, excessive diaphoresis, loss of gastrointesinal fluids through vomiting and diarrhea).

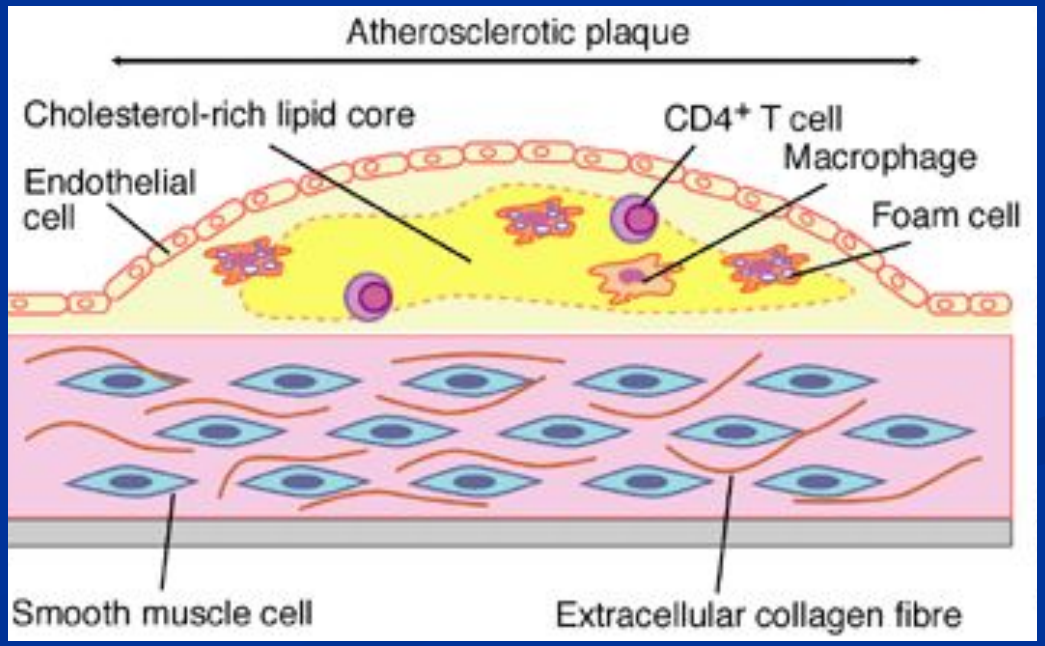
Hypotension treatment

- Avoidance of factors that can precipitate hypotension
  - sudden changes in posture,
  - hot environments,
  - alcohol,
  - certain drugs,
  - large meals.
- Volume expansion (using salt supplements and/or medications with salt-retaining properties),
- Mechanical measures (to prevent the blood from pooling in the veins of the legs upon standing).

Atherosclerosis

Atherosclerosis is a process of progressive lipid accumulation with the formation of multiple plaques within the arteries.

- Atherosclerotic plaque contains
  - lipids
  - inflammatory cells
  - smooth muscle cells,
  - connective tissue
  - thrombi,
  - Ca^{2+} deposits.



Atherosclerosis

- **Arteriosclerosis** - any hardening (and loss of elasticity) of medium or large arteries
- **Arteriolosclerosis** - affectiong of the arterioles (small arteries)
- **Atherosclerosis** is a hardening of an artery specifically due to an **atheromatous plaque** (in Greek, "athero" means "porridge").
  - Atherosclerosis is a form of arteriosclerosis.

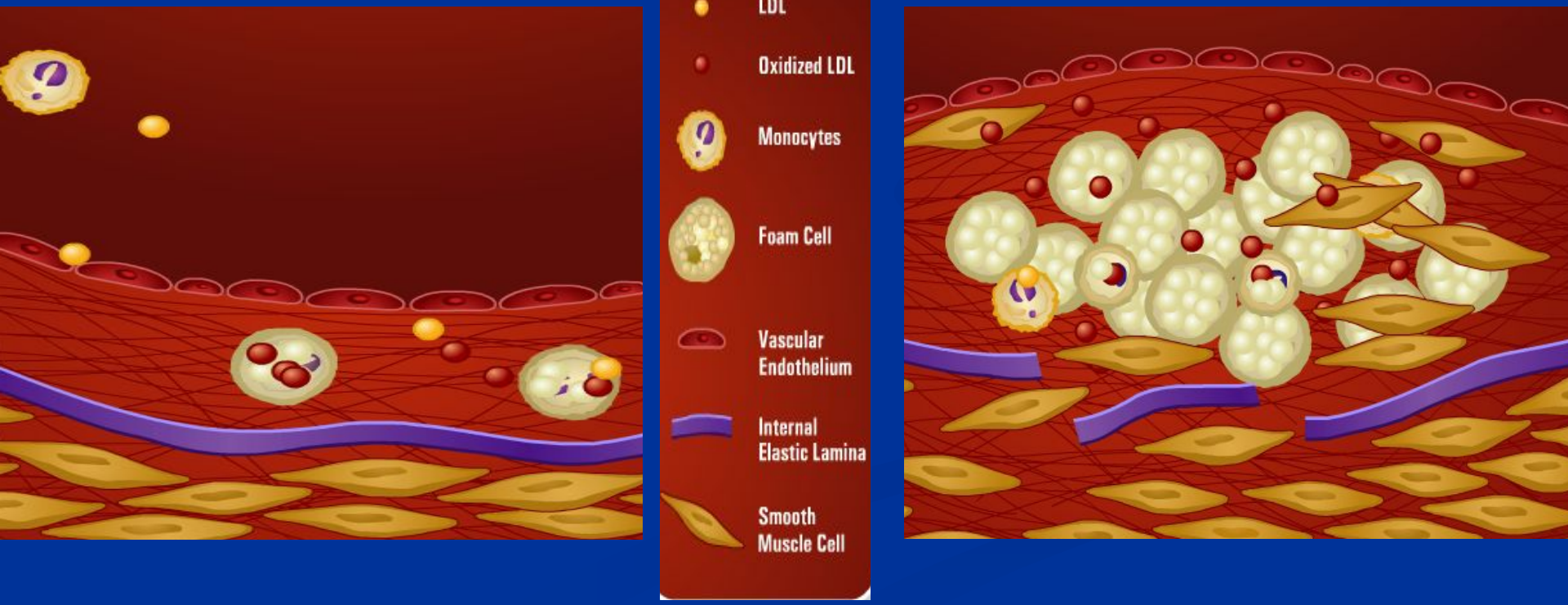
Lipoproteins classification

- **Chylomicrons** - carry triacylglycerol (fat) from the intestines to the liver and to adipose tissue.
- **Very low density lipoproteins** - carry (newly synthesised) triacylglycerol from the liver to adipose tissue.
- **Low density lipoproteins** - carry cholesterol from the liver to cells of the body ("bad cholesterol“).
- **High density lipoproteins** - collects cholesterol from the body's tissues, and brings it back to the liver ("good cholesterol“).

Atherosclerosis pathogenesis

The lipid hypothesis

plasma LDL penetration into the arterial wall lipid accumulation in smooth muscle cells and in macrophages (foam cells) smooth muscle cell hyperplasia and migration into the subintimal and intimal region



Atherosclerosis pathogenesis

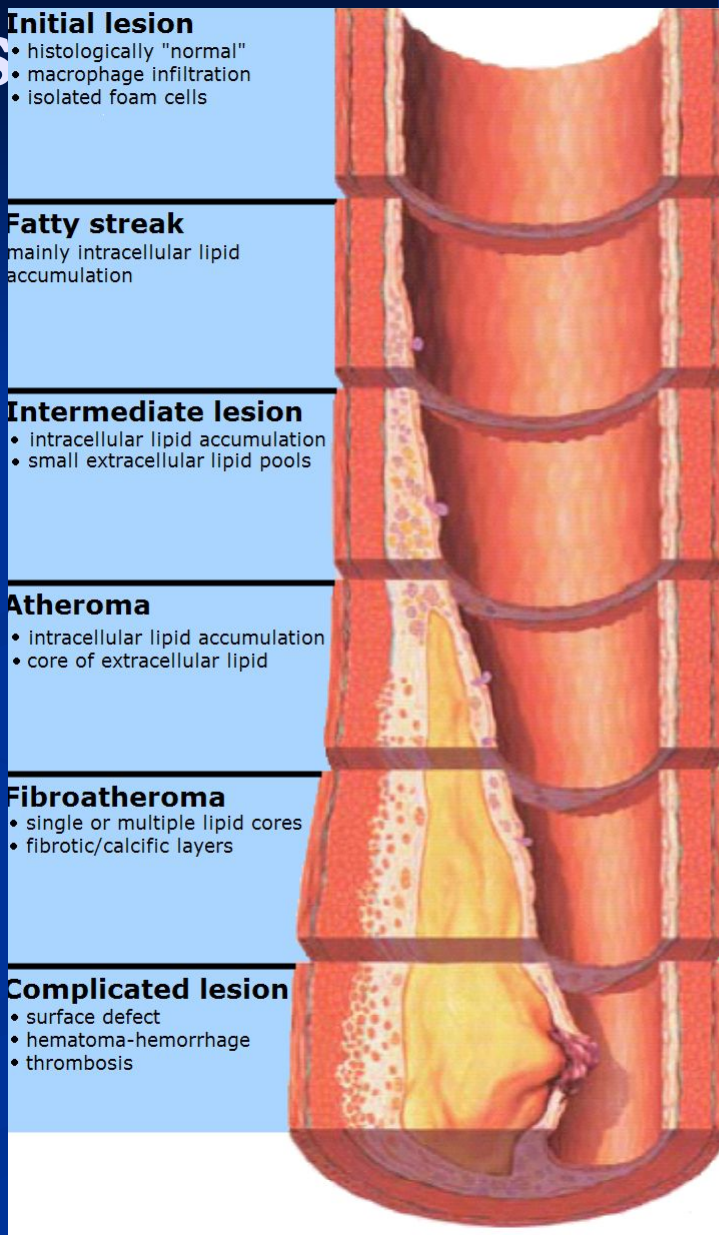
The chronic endothelial injury hypothesis

Endothelial injury

- loss of endothelium,
- adhesion of platelets to subendothelium,
- aggregation of platelets,
- chemotaxis of monocytes and T-cell lymphocytes
- release of growth factors
  - induce migration and replication
  - their synthesis of connective tissue and proteoglycans

Atherosclerosis pathogenesis

- The atherosclerotic plaque may produce a severe stenosis or may progress to total arterial occlusion.
- With time, the plaque becomes calcified.
- Some plaques are stable
- Others may undergo spontaneous fissure or rupture (unstable or vulnerable)
- The ruptured plaque stimulates thrombosis.



Atherosclerosis: positive risk factors

Non modifiable

- Age – middle to late.
- Sex – Males, complications
- Genetic – Familiar Hypercholesterolemia
- Family history.

Potentially Modifiable

- Hyperlipidemia – HDL/LDL ratio.
- Hypertension.
- Smoking.
- Diabetes
- Life style, diet, exercise

Atherosclerosis risk factors

- Negative risk factors
  - high levels of circulating high density lipoproteins
  - moderate alcohol consumption
  - cardiovascular fitness

Atherosclerosis symptoms

If the narrowing of an artery is less than 70% - asymptomatic

Symptoms occur due to the location of the narrowing

- Coronary arteries – angina pectoris, heart attack
- Carotid arteries - brain stroke.
- Arteries in the legs - leg cramps (intermittent claudication).
- Renal arteries - kidney failure or high blood pressure (malignant hypertension).

Atherosclerosis symptoms

- Symptoms occur due to deprivation of tissues blood supply
- The first symptom may be pain or cramps.
- Typically, symptoms develop gradually as the atheroma slowly narrows an artery.

Prevention and Treatment

Prevention – to modify risk factors

- smoking,
- high blood cholesterol levels,
- high blood pressure,
- obesity,
- physical inactivity.

- When atherosclerosis becomes severe the complications themselves must be treated.