Anatomie

Histology and embryology

5.1 lecture

DEVELOPMENT AND PECULIARITIES OF THE STRUCTURE OF THE HEART AND BLOOD VESSELS

Department of Histology and Embriology

Assoc.prof. I. Balnytė

Structure of the heart

Three layers of the heart:
1) **Epicardium** is the outer layer of the heart (or inner visceral layer of the pericardium).
2) **Myocardium** is the middle layer of the heart, which consists of cardiac cells and interstitium. Myocardium is thickest in the left ventricle.
3) **Endocardium** is the inner layer of the heart. The thickness of endocardium varies inversely with the thickness of myocardium (it is thicker in the atria than in the ventricles, as the muscular walls are more substantial in the ventricles). The layer of connective tissue closest to the myocardium is slightly looser and is called the subendocardial layer. It contains veins and nerves, as well as the Purkinje fibres (when present). The outer layer of the endocardium is the subendocardial layer. Endocardium is the innermost lining of the heart chambers, valves, chordae tendineae, papillary muscles. It is continuous with the tunica intima of the great vessels which pass to and from the heart.

Impulse conducting system of the heart. Impulses originating in the sinoatrial node (SA node or pacemaker) pass along the cardiac myocytes of the atria and along internodal tracts of modified cardiac muscle cells to the atrioventricular node (AV node) near the tricuspid valve. The AV node provides the only bridge between atrial and ventricular muscle. From the AV node, impulses pass across the fibrous skeleton of the heart to the ventricles via the AV bundle of His. The bundle of His divides into a right and left branch (the latter with 2 fascicles) which travel
along the ventricular septum to the apex of the heart and then reverse their direction, then into subendothelial branches commonly called Purkinje fibers. Purkinje fibers are modified cardiac muscle cells with a diameter about twice that of regular cardiac myocytes. Purkinje fibers are much faster conducting than regular cardiomyocytes, with which they make contact via gap junctions.

**Blood vessels**

Blood vessels are made of three layers, called (from the luminal side outward) *tunica intima*, *tunica media* and *tunica adventitia*. The thickness of these three layers varies greatly depending upon the size and type of vessel (large, medium & small arteries and veins; capillaries). Tunics (or layers) are:

1. The *tunica intima* (is the innermost layer) consists of an endothelium (present in all vessels) and any subendothelial connective tissue that may be present (highly variable depending on vessel). The endothelium of vessels entering or leaving the heart is continuous with that of the heart.

2. The *tunica media* (the middle layer) is the layer of concentrically-arranged smooth muscle cells, the autonomic control of which can alter the diameter of the vessel and affect the blood pressure. Smooth muscle cells (in contrast to cardiac and skeletal) have secretory capabilities, and (depending on the vessel), the tunica media contains varying amounts of collagen fibres, elastic fibres, elastic lamellae, and proteoglycans secreted by the smooth muscle cells. The tunica media of arteries is larger than that of veins of similar size.

3. The *tunica adventitia* (the outer layer) is made chiefly of longitudinally arranged collagen fibers and elastic fibers. It tends to be much larger in veins than arteries. This layer gradually becomes continuous with the connective tissue of the organ through which the vessel runs.

Capillaries are the smallest diameter vessels and the site of exchange of metabolites between blood and tissues. Capillaries consist of a single layer of endothelial cells, their basement membrane and pericytes. Endothelial cells are joined together by tight junctions. Capillaries are classified according to the structure of their endothelial cells and basal lamina:

1. *Continuous*, or *somatic*, capillaries (most capillaries) have a continuous endothelial cells and basal lamina with no fenestrations (openings) in their walls.

2. *Fenestrated*, or *visceral*, capillaries have endothelial cells in which are found small openings, called fenestrae. The fenestrations are covered by a small non-membranous diaphragm (which may be the remnant of the glycocalyx enclosed by pinocytotic vesicles from which the fenestrae may be formed). The basal lamina of endothelial cells is continuous over the fenestrae.

3. *Sinusoids*, also called *discontinuous capillaries*, have a large lumen and follow a tortuous path. They have many fenestrations with no diaphragm, and a discontinuous basal lamina.

**Lymphatics**

Three types of lymphatics can be distinguished based on their size and morphology:

1) *Lymphatic capillaries* are somewhat larger than blood capillaries and very irregularly shaped. They begin as blind-ending tubes in connective tissue. The basal lamina is an incomplete and the endothelial cells do not form tight junctions, which facilitates the entry of liquids into the lymphatic capillary.
2) Lymphatic vessels are larger and form valves, have structure similar to that of veins except that they have thinner walls and lack a clear-cut separation between layers.

3) Lymphatic ducts are the largest lymphatic vessels, which contain one or two layers of smooth muscle cells in their wall.

**Peculiarities of heart development and fetal blood circulation**

The entire cardiovascular system (heart, blood vessels, blood cells) originates from the mesodermal germ layer. The cardiovascular system begins to develop during 3rd week. The primordium of the heart forms in the cardiogenic plate located at the cranial end of the embryo. Angiogenic cell clusters which lie in a horse-shoe shape configuration in the plate coalesce to form two endocardial tubes. These tubes are then forced into the thoracic region due to cephalic and lateral foldings where they fuse together forming a single endocardial tube. The tube can be subdivided into primordial heart chambers starting caudally at the inflow end: the sinus venosus, primitive atrium, primitive ventricle, and bulbus cordis. The splanchnic mesoderm proliferates and develops into the myocardial mantle which gives rise to the myocardium. The epicardium develops from cells that migrate over the myocardial mantle from areas adjacent to the developing heart.

The sinus venosus receives: the umbilical veins from the chorion, the vitelline veins from the yolk sac and the common cardinal veins from the embryo.

The primitive atrium acts as a temporary pacemaker. But the sinus venosus soon takes over.

The truncus arteriosus is continuous caudally with the bulbus cordis, and enlarges cranially to form the aortic sac from which the aortic arches arise. Three systems of paired veins drain into the primitive heart: the vitelline system will become the portal system, the cardinal veins will become the caval system and the umbilical system which degenerates after birth.

During the 4th to 7th weeks the heart divides into 4-chambered heart. The heart tube begins to grow rapidly forcing it to bend upon itself and the result of this is formation of the bulboventricular loop. Septa begin to grow in the atrium, ventricle and bulbus cordis to form right and left atria, right and left ventricles and two great vessels- the pulmonary trunk and the ascending aorta. By the end of the eighth week partitioning is completed and the fetal heart has formed.

1) The sinuatrial (SA) node develops during 5th week. It is part of the sinus venosus which becomes incorporated into the right atrium.

2) The atrioventricular (AV) node also develops from the cells in the wall of the sinus venosus together with cells from the atrioventricular canal region.

The critical period of development is from day 20 to day 50 after fertilization. Improper partitioning of the heart may result in defects of the cardiac septa, of which the ventricular septal defects are most common (25% of congenital heart disease); membranous ventricular septal defect (most common); muscular septal defect. Failure of the circulatory changes to occur at birth is the cause of two of the most common congenital anomalies of the heart and great vessels (patent oval foramen, patent ductus arteriosus).

**Fetal circulation**

Before birth oxygenated blood (about 80%) returns from the placenta to the fetus by the umbilical vein. During its course from the placenta to the organs of the fetus, blood in the
umbilical vein gradually loses its high oxygen content as it mixes with desaturated blood. Theoretically, mixing may occur in the following places:

1) in the liver (by mixture with a small amount of blood returning from the portal system);
2) in the inferior vena cava (which carries deoxygenated blood returning from the lower extremities, pelvis, kidney);
3) in the right atrium (by mixture with blood returning from the head and limbs);
4) in the left atrium (by mixture with blood returning from the lungs);
5) at the entrance of the ductus arteriosus into descending aorta.

50% of the blood passes via the umbilical arteries into the placenta for reoxygenation, the rest supplies the viscera and the inferior 1/2 of the body.

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**Biochemistry**

**5.4 lecture**

**HEART METABOLISM IN NORMAL AND ISCHEMIC CONDITIONS**

Department of Biochemistry  
Prof. R. Morkūnienė


References:

ELECTRICAL AND MECHANICAL ACTIVITY OF THE HEART

Department of Physiology

Lect. I. Korotkich

Contractile myocardium and conductive system of the heart. Ionic mechanism of cardiac automaticity. Propagation of electrical impulse in the heart. Origin of the electrocardiogram. Electromechanical coupling and mechanisms of myocardial contraction and relaxation. Pressure-volume changes during the cardiac cycle. Parameters of mechanical activity of the heart (stroke volume, cardiac output, ejection fraction, cardiac index). Intracardiac and extracardiac regulation of the heart pumping (heterometric and homeometric mechanisms, nervous and humoral regulation). Factors controlling cardiac output (preload, afterload, contractility). Pathophysiological mechanisms of the heart failure due to increased preload and afterload. Compensatory mechanisms. Functional properties of the hypertrophied myocardium.
**5.5 lecture**

**CORONARY CIRCULATION AND REGULATION OF LOCAL BLOOD FLOW. Pathophysiological mechanisms of myocardial ischemia and infarction**

Department of Physiology

Assoc. prof. A. Laukevičienė


**5.11 lecture**

**ARTERIAL BLOOD PRESSURE REGULATORY MECHANISMS AND THEIR ALTERATIONS**

Department of Physiology

Assoc. prof. A. Laukevičienė

The blood pressure – important characteristic of systemic circulation. Neural regulation of arterial blood pressure: the role of autonomic nervous system, nervous control of the heart function, the vasomotor center and its control of the vasoconstrictor

Pathological physiology

5.2 lecture

PATHOLOGICAL MECHANISMS OF THE HEART FAILURE DUE TO INCREASED PRELOAD AND AFTERLOAD. COMPENSATORY MECHANISMS. FUNCTIONAL PROPERTIES OF THE HYPERTROPIED MYOCARDIUM

Department of Physiology
Lect.D.Akramienė

Heart failure is the term which describes several types of cardiac dysfunction that result in inadequate perfusion of tissues, due to impaired pumping ability of the heart. The heart has the capacity to adjust its pumping ability to meet the varying needs of the body. The ability to increase cardiac output during increased activity is called the cardiac reserve. Heart failure occurs when pumping ability of the heart becomes impaired. Pathophysiology of heart failure: decreased pumping ability + compensatory mechanisms those serve to maintain the cardiac output but contributing to the progression of heart failure.

Heart failure may be described as high-output or low-output failure, right-sided or left-sided heart failure, and systolic dysfunction or diastolic dysfunction.

Causes of left-sided heart failure:

- **Volume overload:** Insuff. of valves (mitral or aortic, renal failure)
- **Pressure overload:** systemic hypertension, outflow obstruction (aortic stenosis, asymmetric septal hypertrophy)
- **Loss of muscle or contractibility:** Myocardial infarction, connective tissue disease, poisons, infection
• **Restricted filling**: Mitral stenosis, pericardial disease, infiltrative disease (amyloidosis)

Causes of right-sided heart failure:

• **Volume overload**: insuff. of valves (Tricuspidal or pulmonary

• **Pressure overload**: left-sided heart failure (mitral stenosis) idiopathic pulmonary hypertension, *cor pulmonale* (pulmonary embolism, COPD)

• **Loss of muscle or contractibility**: MI, connective tissue disease, poisons, infection

• **Restricted filling**: infiltrative disease (amyloidosis)

Changes in the body during heart failure:

• **Hemodynamic changes**
  Decreased output (systolic dysfunction)
  Decreased filling (diastolic dysfunction)

• **Neurohumoral changes**
  Sympathetic activation
  Renin-Aldosteron-Angiotensin system activation
  Vasopressin release
  Cytokine release (TNF-α, IL-6)

• **Cellular changes**
  Insufficient intracellular Ca²⁺ handling
  Adrenergic desensitization
  Myocyte hypertrophy
  Cell death (apoptosis), fibrosis

• **Changes in myocardium**
  Changes in myocyte myofilaments,
  Myocyte apoptosis and necrosis,
  Fibrin deposition,
  Myocardial hyperthrophy,
  Changes in the ventricular chamber geometry

### 5.5 lecture

**PATHOPHYSIOLOGICAL MECHANISMS OF MYOCARDIAL ISCHEMIA AND INFARCTION. CORONAROGENIC AND NON-CORONAROGENIC INJURY OF THE MYOCARDIUM. REVERSIBLE AND IRREVERSIBLE ALTERATIONS OF CARDIAC MYOCYTES DURING MYOCARDIAL ISCHEMIA. NECROTIC RESORPTION SYNDROME OF MYOCARDIAL INFARCTION**

Department of Physiology
Imbalance between coronary blood supply and myocardial demand can cause myocardial ischemia. Myocardial ischemia can occur when:

- **Supply of oxygen and nutrients decreased due to:**
  - ↓ coronary perfusion
  - ↓ arterial oxygen content
- **Demand of oxygen and nutrients increased due to:**
  - ↑ heart rate
  - ↑ preload
  - ↑ afterload
  - ↑ contractility of the heart
or can be combination of both.

Most common causes of myocardial ischemia related with blood flow through the coronary arteries, these are **coronarogenic factors**. If coronary arteries are healthy, myocardial ischemia can occur due to **noncoronarogenic factors**.

**Coronarogenic factors of myocardial ischemia:**
- Atherosclerosis of coronary arteries
- Thrombus
- Spasm
- Embolus
- Congenital pathology of the coronary blood vessels

**Noncoronarogenic factors of myocardial ischemia:**
- **Intracardial factors**
  - Aortic valve disease, arrhythmias, hypertrophy
- **Extracardial factors**
  - ↑O2 demand
  - ↓O2 supply
  - ↑viscosity of the blood

Myocardial cells became ischemic within 10 second of absent of coronary blood flow. After several minutes the heart cells lose the ability to contract, and cardiac output decreases. Ischemia also causes conduction abnormalities that lead to changes in electrocardiogram and may initiate dysrhythmias. Anaerobic processes take over ad lactic acid accumulates due to the anaerobic metabolism. Cardiac cells remain viable for approximately 20 minutes under ischemic conditions. If blood flow is restored, aerobic metabolism resumes and cells repair again. If coronary blood flow can’t compensate lack of oxygen, irreversible changes in the cells start and myocardial infarction develops.

Individuals with reversible myocardial ischemia present clinically in several ways. Chronic coronary obstruction results in recurrent predictable chest pain called **stable**
angina. Abnormal vasospasm of coronary artery result in unpredictable chest pain called Prinzmetal angina. Myocardial ischemia that does not cause detectable symptoms is called silent ischemia. Unstable angina and myocardial infarction represents the acute coronary syndromes.

5.11 lecture

PRIMARY AND SECONDARY ARTERIAL HYPERTENSION. ARTERIAL BLOOD PRESSURE REGULATION ALTERATIONS

Department of Physiology
Lect. D.Akramienė

Hypertension – is an elevation of systolic and/or diastolic blood pressure. Hypertension is divided into the categories of primary (or essential) and secondary hypertension. Essential hypertension is characterized by a chronic elevation in blood pressure that occurs without evidence of other disease. Secondary hypertension is characterized by an elevation of blood pressure that results from some other disorder. Primary hypertension is the result of a complicated interaction between genetics and the environment and their effects on vascular and renal function. Genetic changes interact with the environment to increase vascular tone and blood volume, and these cause sustained increase in blood pressure. Multiple pathophysiologic mechanisms influence these effects including sympathetis nervous system, rennin-angiotensin-aldosteron system, adducing, natriuretic peptide, inflammation and endothelial dysfunction, insulin resistance.

Secondary hypertension is caused by a systemic disease process that raises peripheral vascular resistance or cardiac output. If the cause is removed before permanent structural changes occur, blood pressure returns to normal. Below are the groups of disorders that can cause secondary hypertension:

- Renal hypertension: renal parenchymal disease, renovascular disease, renal failure, renin-producing tumors
- Endocrine disorders: disorders of Adrenocortical hormones, Pheochromocytoma, hyperthyroidism, hypothyroidism
- Neurologic disorders
- Vascular disorders: Coarctation of the aorta, arteriosclerosis
- Drugs: Oral contraceptive, corticosteroids

Pathoanatomy

5.7 lecture
ANTIARYTHMIC DRUGS

Departement of Pharmacology
Assoc.prof. R.Pilvinienė


DRUGS USED IN THE HEART FAILURE

Departement of Pharmacology
Assoc.prof. R.Pilvinienė

Key elements of pathophysiology of heart failure. Therapeutic strategies of treatment of heart failure. Inotropic agents. Cardiac glycosides: prototypes and pharmacokinetics; mechanism of action; cardiac effects; clinical uses; toxicity. Phosphodiesterase inhibitors: prototypes; mechanism of action; cardiac effects; clinical
uses; toxicity. Beta adrenergic agonists: prototypes and pharmacokinetics; mechanism of action; cardiac effects; clinical uses; toxicity. Other drugs used in congestive heart failure: Angiotensin antagonists: prototypes; mechanism of action; cardiac effects; clinical uses; toxicity.

5.13 lecture

**DRUGS USED IN THE TREATMENT OF ANGINA PECTORIS. DRUGS USED IN HYPERTENSION**

*Departement of Pharmacology*

Assoc.prof. R.Pilvinienė

Definition of angina. Therapeutic strategies of treatment of angina. Nitrates: prototypes and pharmacokinetics; mechanism of action; organ system effects; clinical uses; toxicity. Other drugs used for treatment of angina: calcium blockers, beta adrenergic blocking drugs: prototypes; mechanism of action; effects; clinical uses; toxicity.

Definition of hypertension. Classification of antihypertensive agents (based on clinical indication): sympathoplegics – blockers of adreceptors (acting on CNS sympathetic outflow; acting on ganglia; acting on nerve terminals; acting on alfa or beta adrenoreceptors); vasodilators (older oral vasodilators; calcium blockers; parenteral vasodilators); angiotensin antagonists (ACE inhibitors, AT receptors blockers). Prototypes, mode of action, clinical uses.
Kinds of body homeostasis disorders.
Etiology and pathogenesis of water, electrolyte, acid-base disbalance in surgical diseases, types, ways of determination, principles of correction.
Corrections of deficit, principles of replacement and maintenance therapy.
Hemocorrectors.