KHARKOV NATIONAL MEDICAL UNIVERCITY
Physiology department

WORKBOOK

FOR INDIVIDUAL STUDENTS' WORK

PHYSIOLOGY OF VISCERAL SYSTEMS

"BLOOD AND CIRCULATION"

Name_____

Faculty_____

Group_____ course_____

2018

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ УКРАИНЫ
Харьковский национальный медицинский университет

Module 2. Physiology of visceral systems.

Physiology of Visceral Systems “Blood and Circulation”

Manual for individual work of
second-year students (English-medium)

Модуль2. Физиология висцеральных систем.

«Физиология крови и кровообращения»

Методические рекомендации для индивидуальной работы
студентов 2-го курса с английской формой обучения

Харьков
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2018

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Compilers V.G. Samokhvalov
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Introduction

The blood, heart and blood vessels constitute the circulatory system and provide a link between the bodies' internal compartments and external environment. More specifically, the blood transports nutrients from gastro-intestinal tract to cells, oxygen from respiratory system to cells, wastes from cells to excretory organs; it carries hormones from endocrine glands to target cells and aids in body thermoregulation. Thus, the blood provides vital support for cellular activities and participates in maintaining a favorable cellular environment. However, all these functions of blood are possible just in case of normal physiological state of heart and closed system of vessels that move blood throughout the body.

We hope that this workbook will help you to understand physiology of blood and circulation system and to acquire good knowledge for your future medical education and practice.

Good luck!

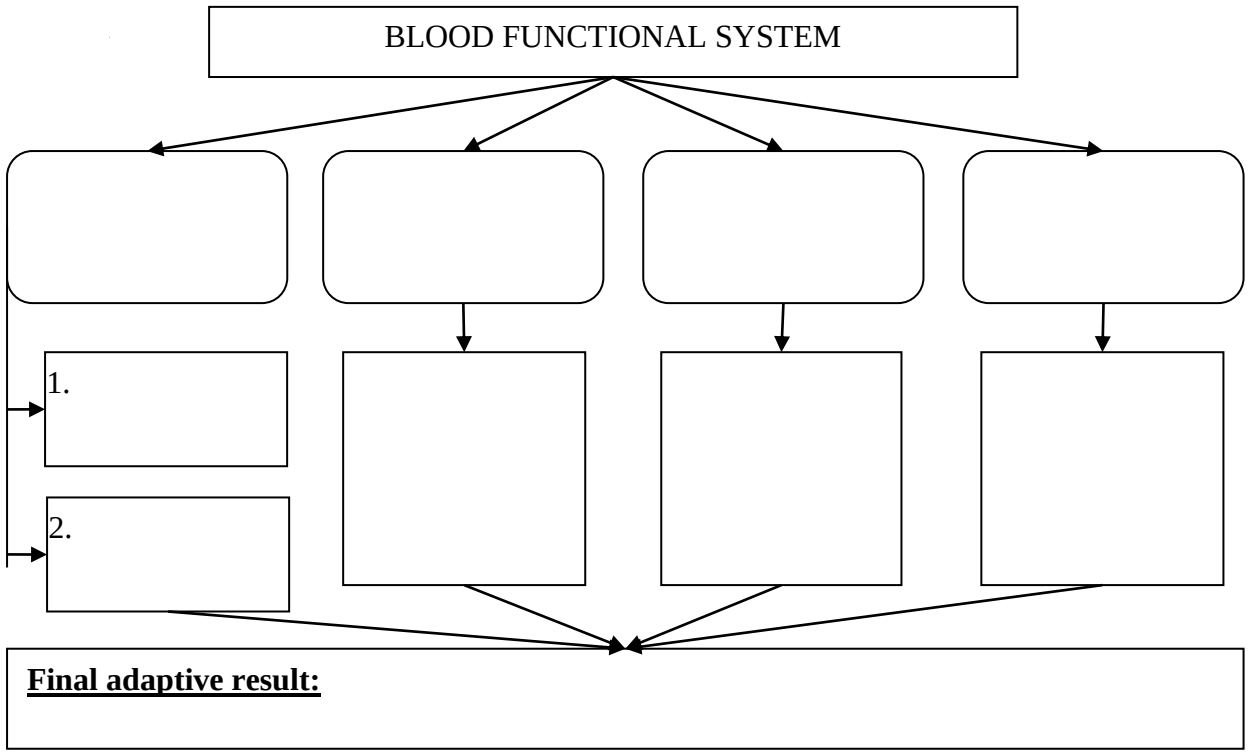
Recommended publications

1. *«Physiology of Blood Systems». Manual for second-year students of medical faculty (English-medium) / V.G. Samokhvalov, L.V. Chernobay, D.I. Marakushin, I.N. Isaeva, I.S. Karmazina, D.A. Bevzuk. – Kharkov: KhNMU, 2012. – 64 p.*
2. *«Physiology of Heart». Manual for second-year students of medical faculty (English-medium) / V.G. Samokhvalov, L.V. Chernobay, D.I. Marakushin, I.N. Isaeva, I.S. Karmazina, R.V. Alexeenko. – Kharkov: KhNMU, 2013. – 64 p.*
3. *Human physiology volume II / G.I. Kositsky.-Medicine, 1990.*
4. *Medical physiology (eleventh edition) / Arthur C. Guyton, John E. Hall. – Elseveier, 2006.*
5. *Ganong's review of medical physiology (23rd edition) / Kim E. Barrett, Susan M. Barman, Scott Boitano, Heddwen L. Brooks. – McGrawHill Lange, 2010.*
6. *Human Physiology / E. Babsky, B. Khodorov, G. Kositsky, A. Zubkov,. Moskow: Mir Publishers, 1975*
7. *Instructions for laboratory studies on normal Physiology course for students having higher medical education in English / Samokhvalov V. G., Lyubetska V.G., Kharkov, 2001.*
8. *Saladin: Anatomy & Physiology: The Unity of Form and Function (Third Edition) / Saladin K.S. - © The McGraw−Hill Companies, 2003.*

PHYSIOLOGY OF BLOOD SYSTEM

1. Functions and composition of blood. Physical and chemical properties of blood.

Task 1.1. *Complete the scheme of the blood functional system structure.*



Task 1.2. *Give definition of blood.*

_____

_____

_____

Task 1.3. *Functions of the blood are*:

1._____

_____

2._____

_____

3._____

_____

4._____

_____

5._____

_____

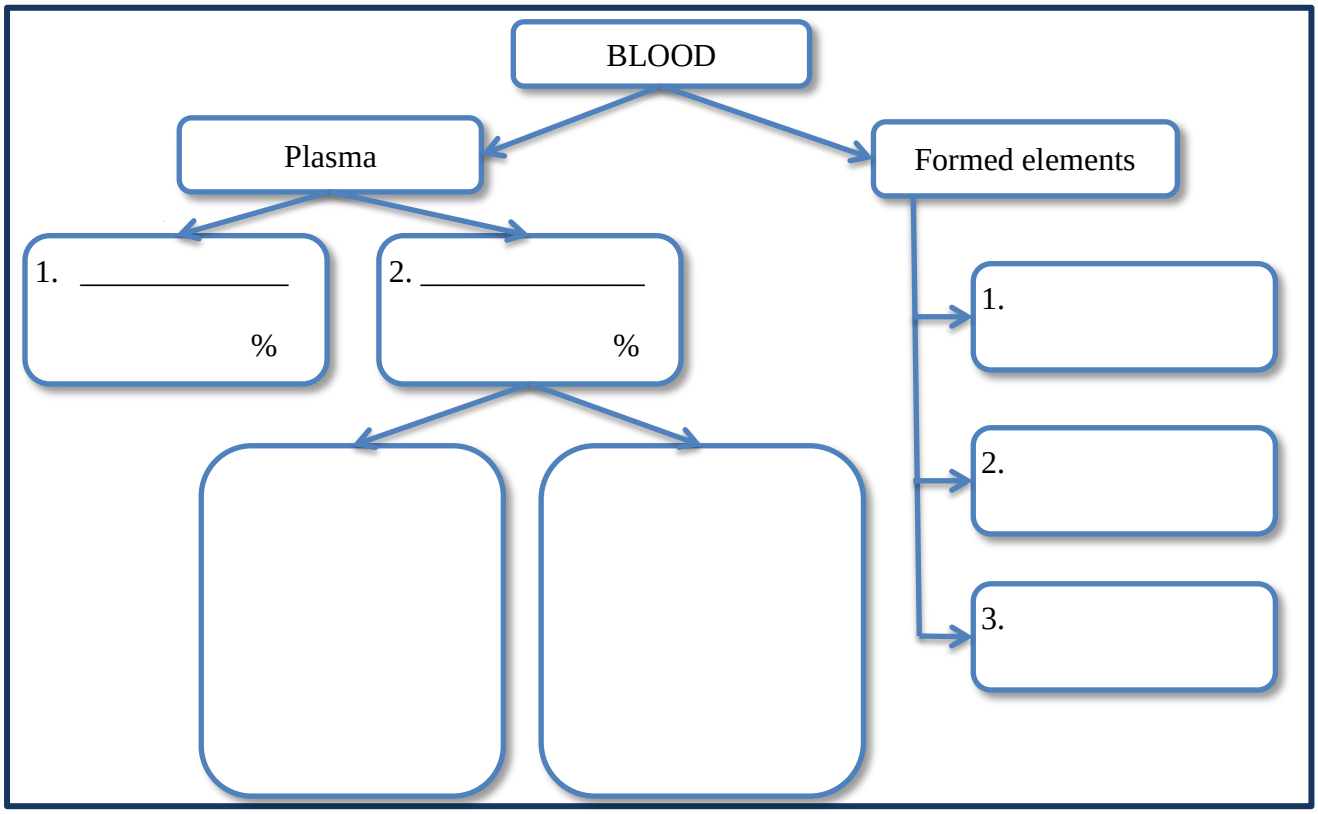
6._____

_____

7._____

_____

Task 1.4. *Define the blood composition and content of its components.*



Task 1.5. *Define the volume of blood and calculate its value in patients with different body weight.*

If body weight is 60 kg, blood volume is_____
If body weight is 80 kg, blood volume is_____
If body weight is 50 kg, blood volume is_____

Task 1.6. *List physical and chemical properties of blood:*

- _____
- _____
- _____
- _____
- _____

Task 1.7. *Give definition of osmotic pressure and osmolarity of blood and label their normal values. Use the following illustration.*

Osmotic pressure is _____
_____
_____
_____*Os*
molarity is _____
_____
_____
_____

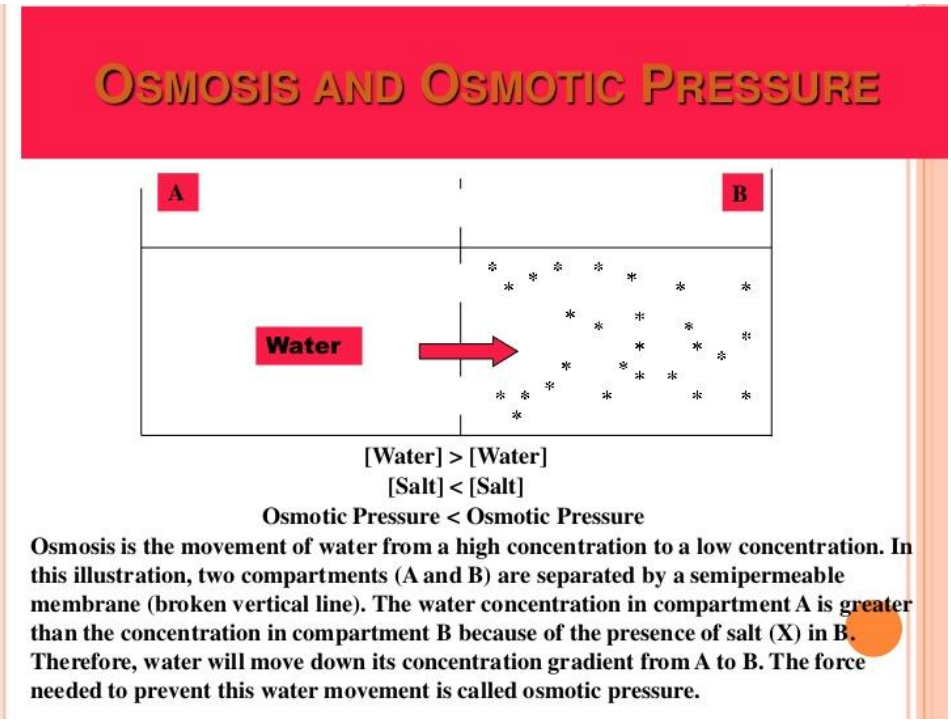


Figure 1. *Phenomenon of osmosis.*

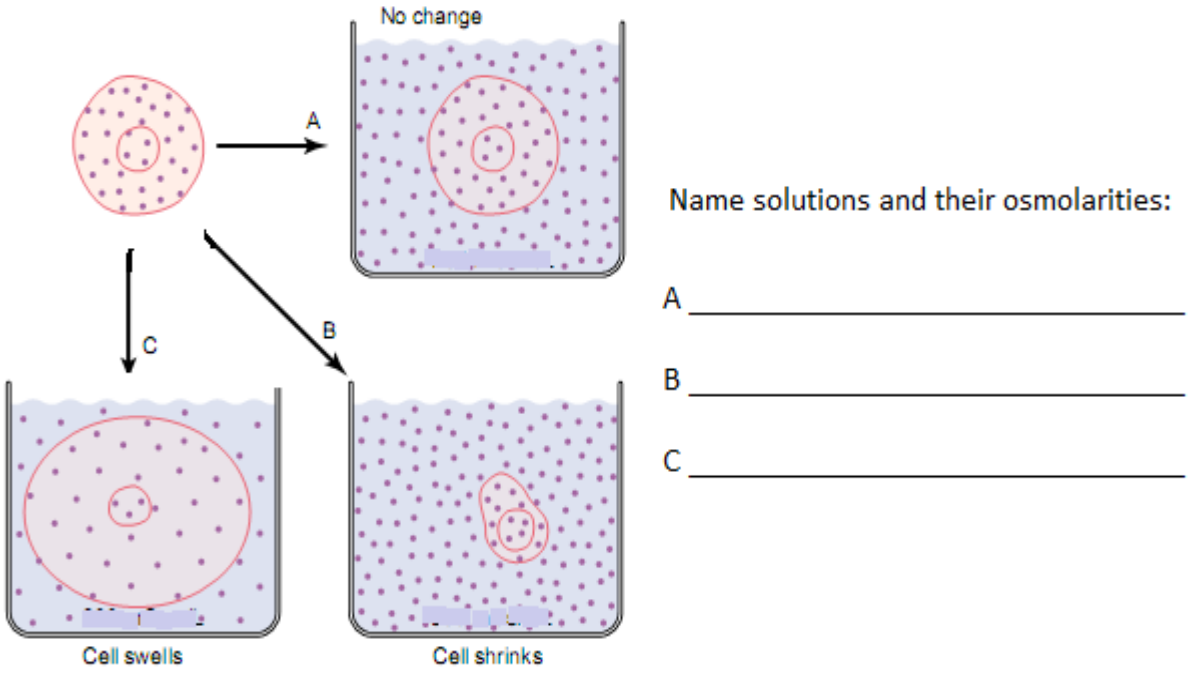
Task 1.8. *Name the types of solution according to osmotic pressure.*

The solution is called _____ if its osmotic pressure is equal to the osmotic pressure of _____.

The solution is called _____ if its osmotic pressure is less than the osmotic pressure of _____.

The solution is called _____ if its osmotic pressure is more than the osmotic pressure of _____

Task 1.9. *Define the osmotic resistance of RBC.*



Task 1.10. *Define the factors influencing the osmotic pressure of blood.*

1. _____
   _____
   _____
2. _____

Task 1.11. *It's known that osmotic pressure is regulated by humoral way. Please, explain regulation of osmotic pressure in case of dehydration and hyperhydration*

	Osmotic pressure	**Hormone**	**Response**
Dehydration			
Hyperhydration			

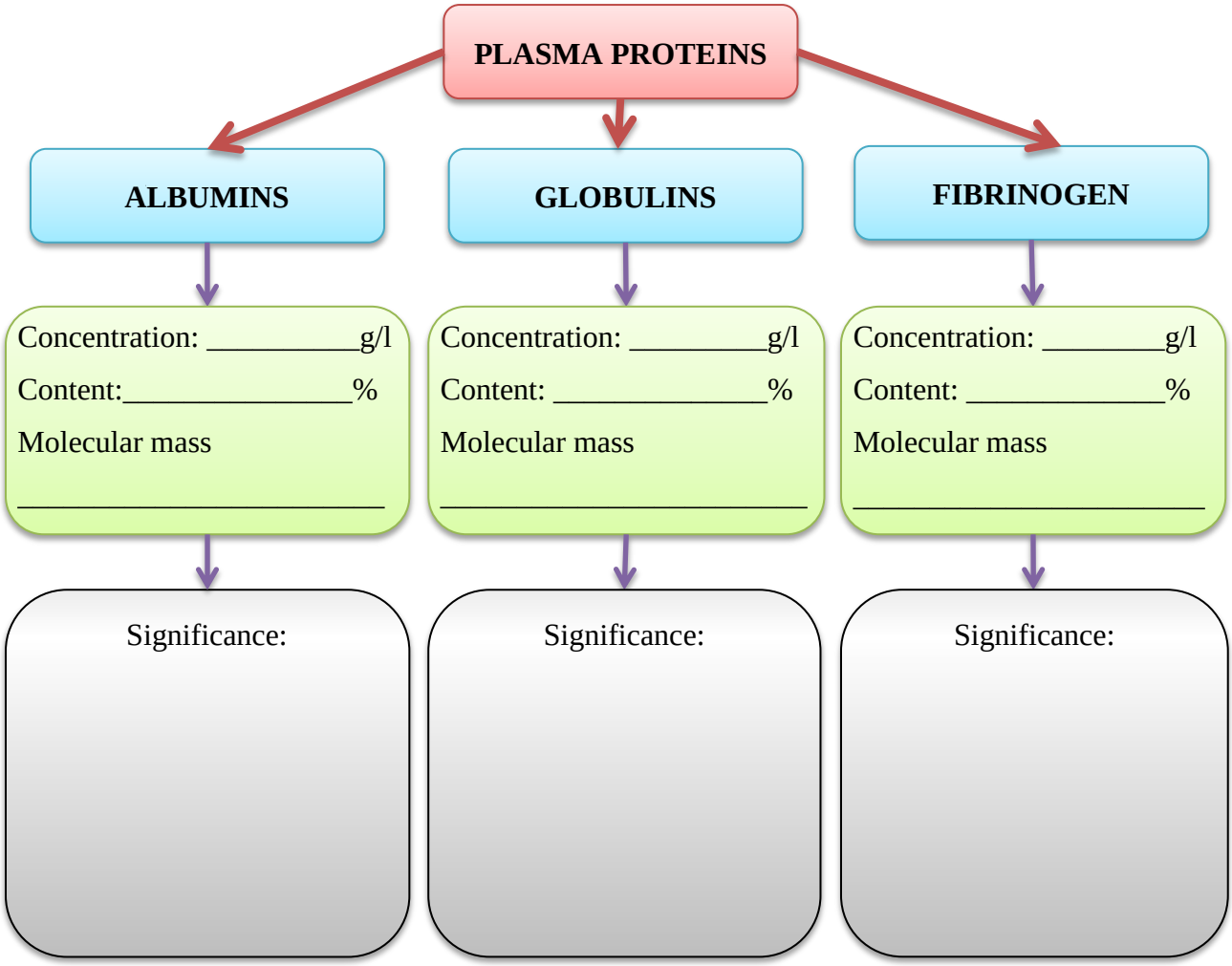
Task 1.12. *Define the oncotic pressure of blood and its value.*

_____
_____
_____

Task 1.13. *List the functions of plasma proteins:*

- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____
- _____
  _____

Task 1.14. *Define the significance of different plasma proteins:*



Task 1.15. Explain changes of water balance in case of:

1) *oncotic pressure rises* _____

_____

_____

2) *oncotic pressure drops* _____

_____

_____

Task 1.16. *Define the value of pH:*

1) in arterial blood_____

2) in venous blood _____

Explain different values of them

_____

_____

_____

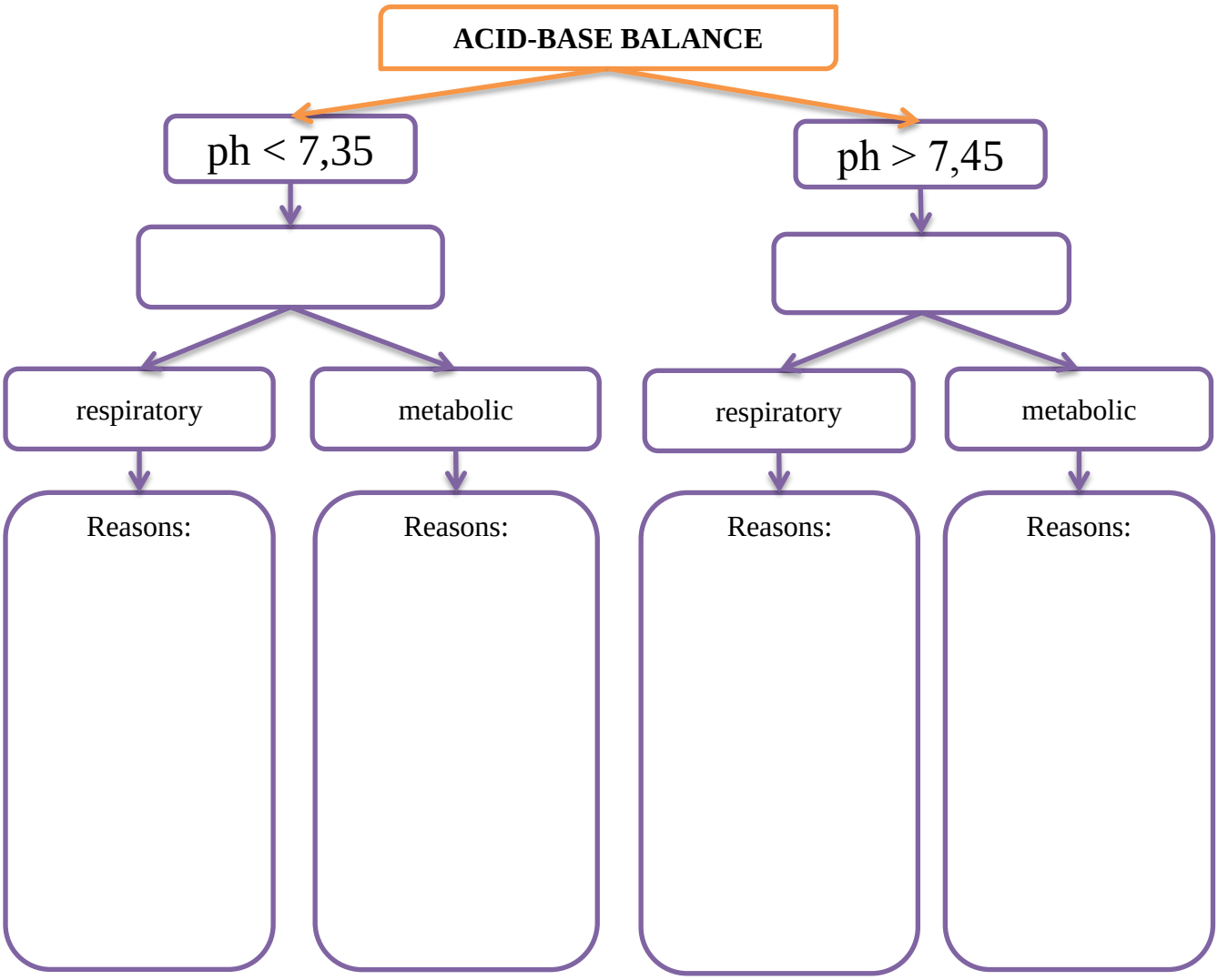
_____

Task 1.17. *pH limits compatible with life are: from _____ to _____*

Task 1.18. Complete the table to characterize buffer systems of an organism:

Name of buffer system	Its components	Properties

Task 1.19. *Complete the table. Maintainance the acid-base balance of organism.*



2. Physiology of erythrocytes and hemoglobin

Task 2.1. *Complete the table to define erythron*

ERYTHRON is _____

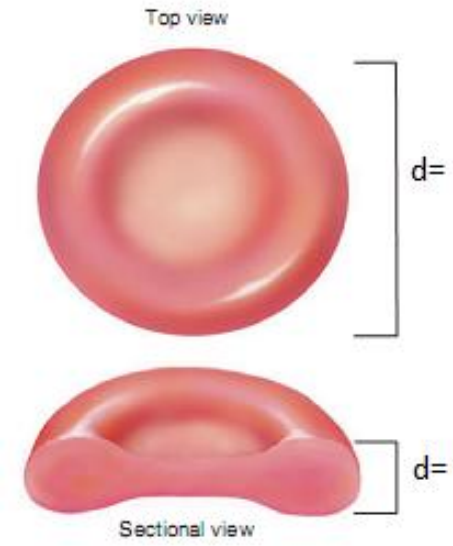
_____

_____

It includes:

Final adaptive result: _____

_____



Task 2.2. *Give structural and functional characteristics of RBC.*

Morphology: _____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Functions:

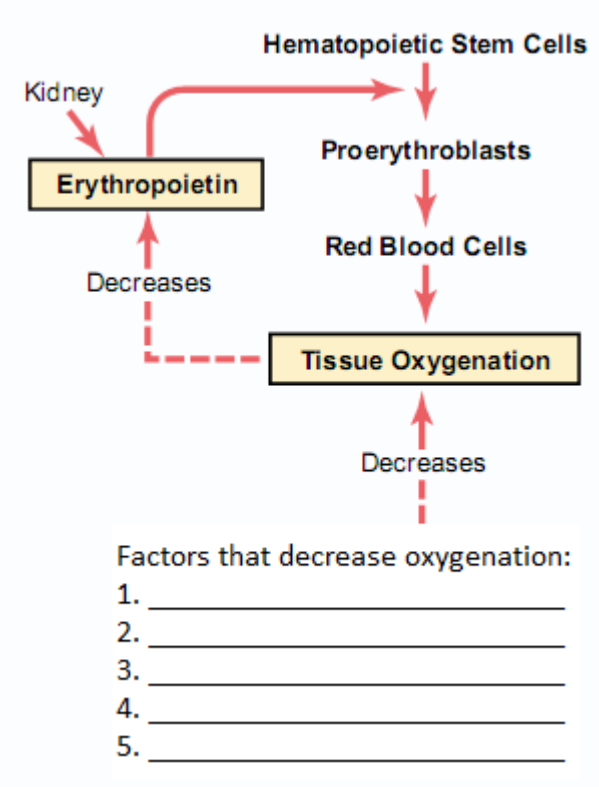
1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

Task 2.3. *Name the physiological properties of RBC:*

- _____
- _____
- _____
- _____

Task 2.4. *Define the factors influencing to erythropoesis.*

- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____



Task 2.5. *Study the scheme "**Functions of erythropoietin mechanism to increase production of RBC when tissue oxygenation decreases**" and complete it:*

Task 2.6. *Complete the following table*

Number of RBC		
Female adult	**Male adult**	**Newborn**

and explain the difference in male and female RBC contents. _____

_____

_____

Task 2.7. *Complete the table to define clinical significance of RBC content changes*

Erythrocytosis is _____ _____		**Erythropenia is** _____ _____	
relative	**absolute**	**relative**	**absolute**

Task 2.8. *Explain clinical significance of Erythrocyte Sedimentation Rate (ESR)*

_____
_____
_____
_____

Task 2.9. *Define the normal male and female ESR and explain differences:*
Male _____; female _____
_____
_____
_____

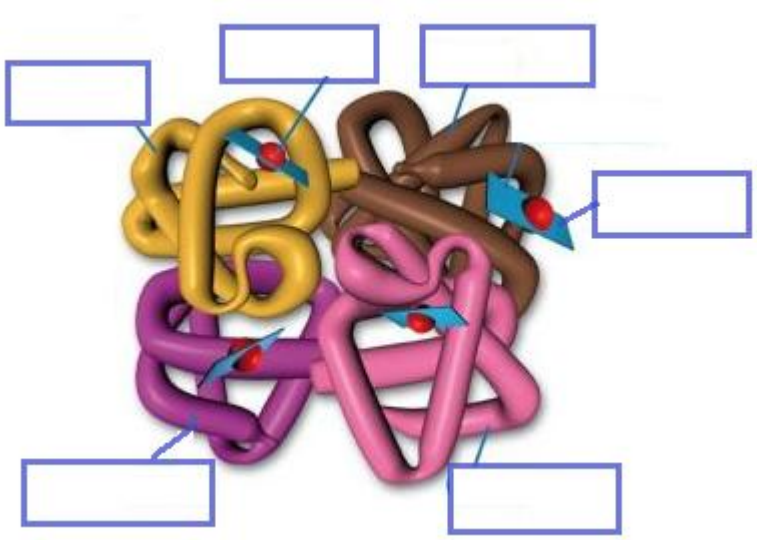
Task 2.10. *List factors influencing to the ESR*

Factors which increase ESR	**Factors which decrease ESR**

Task 2.10. *Explain clinical significance of Hematocrit; define its normal value in male and female*

_____
_____
_____
_____

Task 2.11. *Label the main structural components of hemoglobin molecule and describe its chemical structure*



_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Task 2.12. *Determine the types of Hb and complete the table*

Type	**Peculiarities of composition**	**Period of ontogenesis**	**Affinity to O_2**

Task 2.13. *Determine normal value of Hb in male and female and explain the differences:*
male _____; female _____
_____
_____
_____

Task 2.14. *Complete the following statements:*
Color index (CI) of erythrocytes is the ratio _____
_____
_____
If the CI is in the range 0.85-1.1, erythrocytes are called _____
If the CI is more than 1.1, erythrocytes are called _____
If the CI is in less than 0.85, erythrocytes are called _____

Task 2.15. *Define the hemoglobin compounds:*

Physiological compounds

Name	Formula	Compartment of formation and localization
1.		
2.		
3.		

Pathological compounds

Name	Formula	Reasons of their formation
1.		
2.		

Task 2.16. *Define the oxygen capacity of blood:*

_____

_____

1gramm of Hb can attach _____ *ml* of O_2

Calculate the oxygen capacity if

Hb is 140 g/l: _____

Hb is 120 g/l: _____

Hb is 100 g/l: _____

Task 2.17. *Types of hemolysis:*

1. _____
   _____
2. _____
   _____
3. _____
   _____
4. _____
   _____

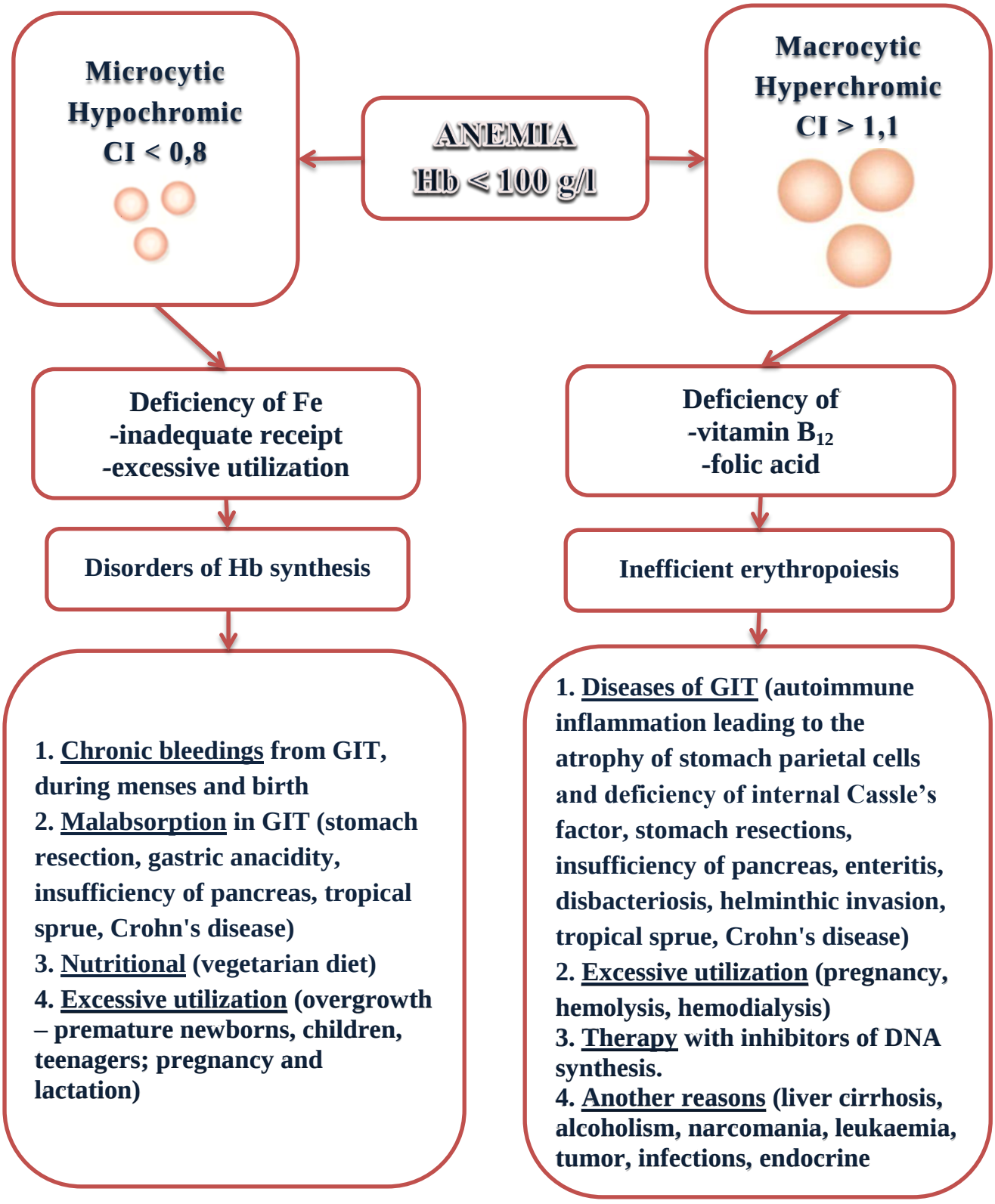


Figure 2. **Morphological classification of anemia, their etiology and genesis**

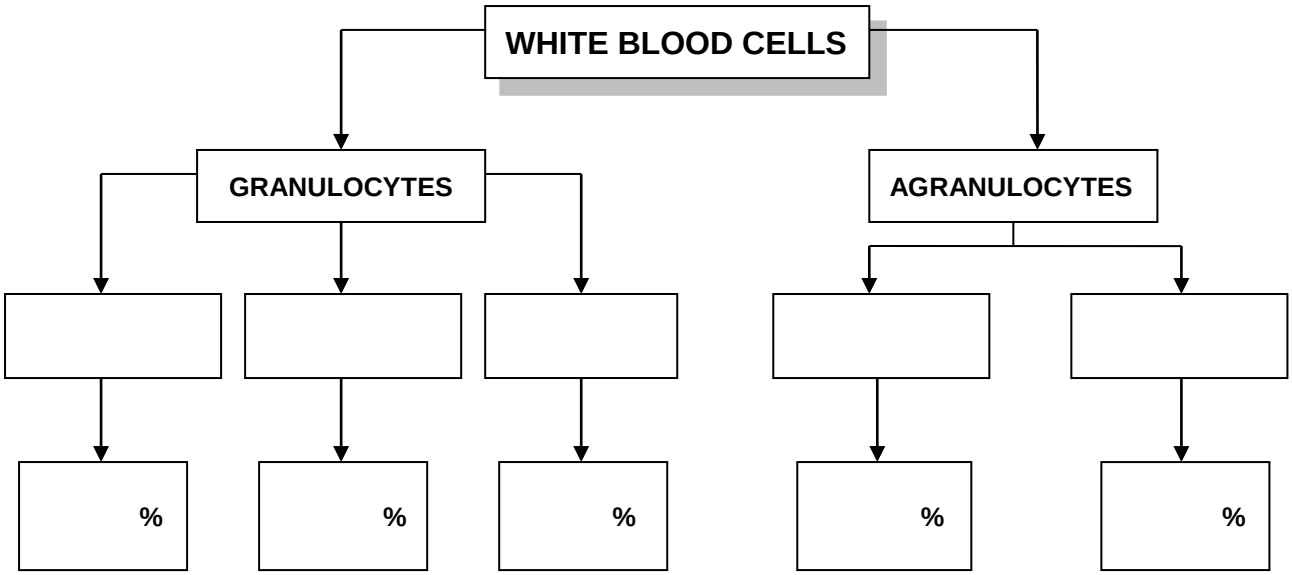
3. Blood protective functions: physiology of leukocytes.

Task 3.1. *Determine the normal content of leukocytes in blood*

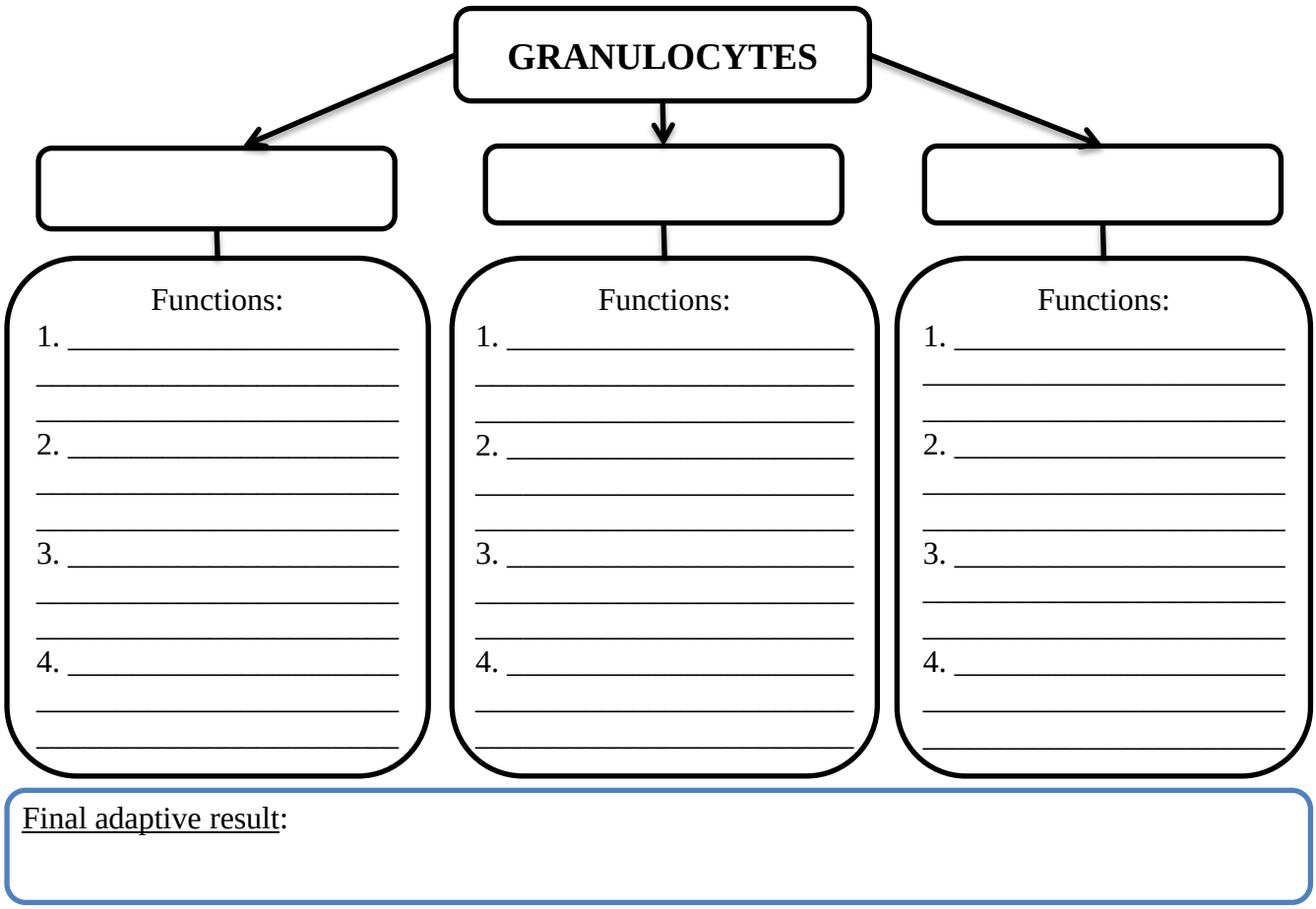
_____

_____

Task 3.2. *Complete the following table*



Task 3.3. *Complete the following table*



Final adaptive result:

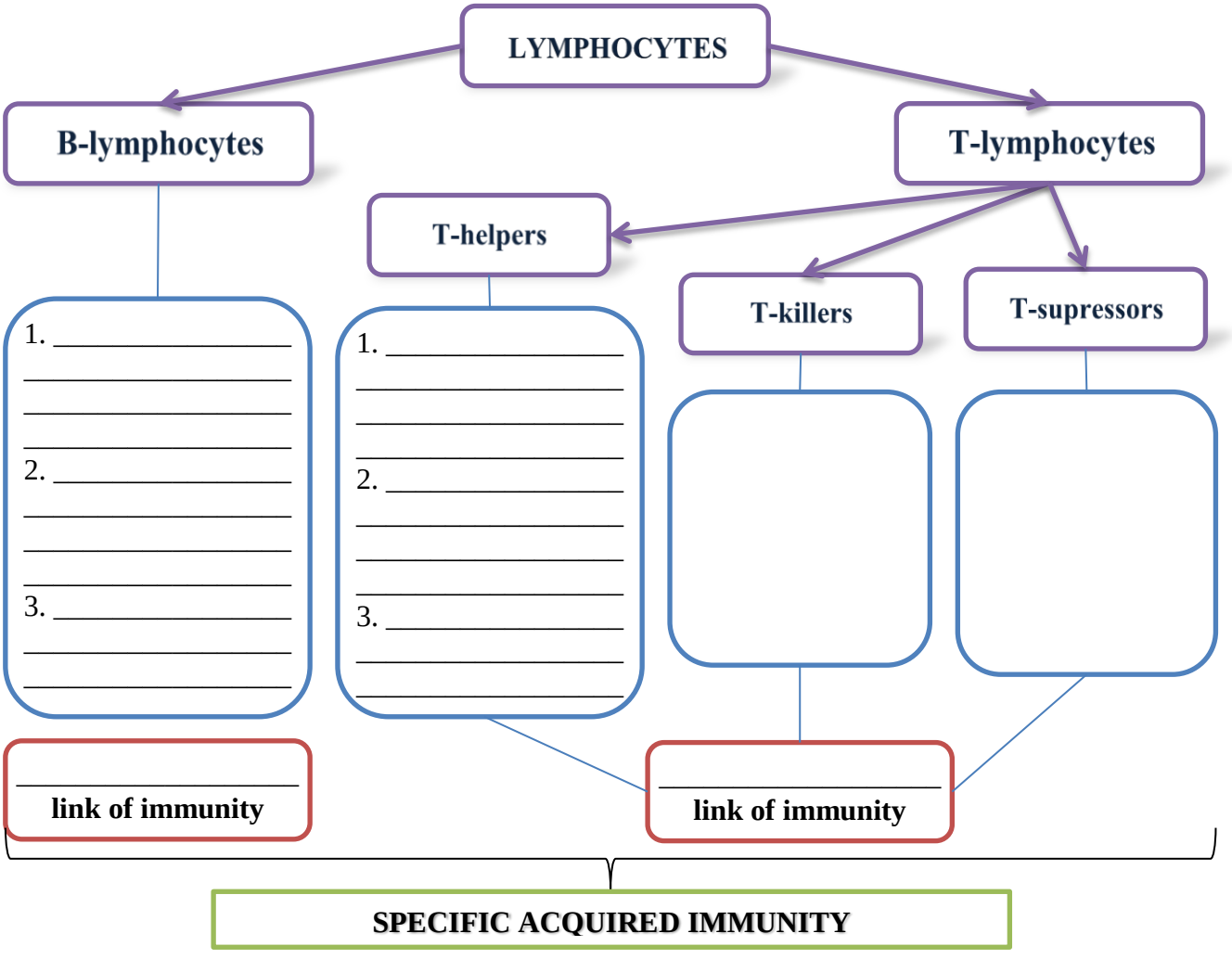
Task 3.4. *Complete the following statements:*

Agranulocytes are of 2 types. They are _____ and _____. _____ make up 0-10 per cent of blood leucocytes. They are capable of _____ movement and manifest _____ _____.

They are able to phagocytize up to _____ bacteria. Because of these they perform the following functions: *(use the Table 6 p. 61 of manual "Physiology of blood system")*

1. _____
2. _____
3. _____
4. _____
5. _____

Task 3.5. *Complete the following scheme describing functions of lymphocytes:*



Task 3.6. *Complete the following table to compare the mechanisms of immunity:*

Humoral immunity	***Cellular immunity***

Task 3.7. *Explain the mechanism of antibodies production:*

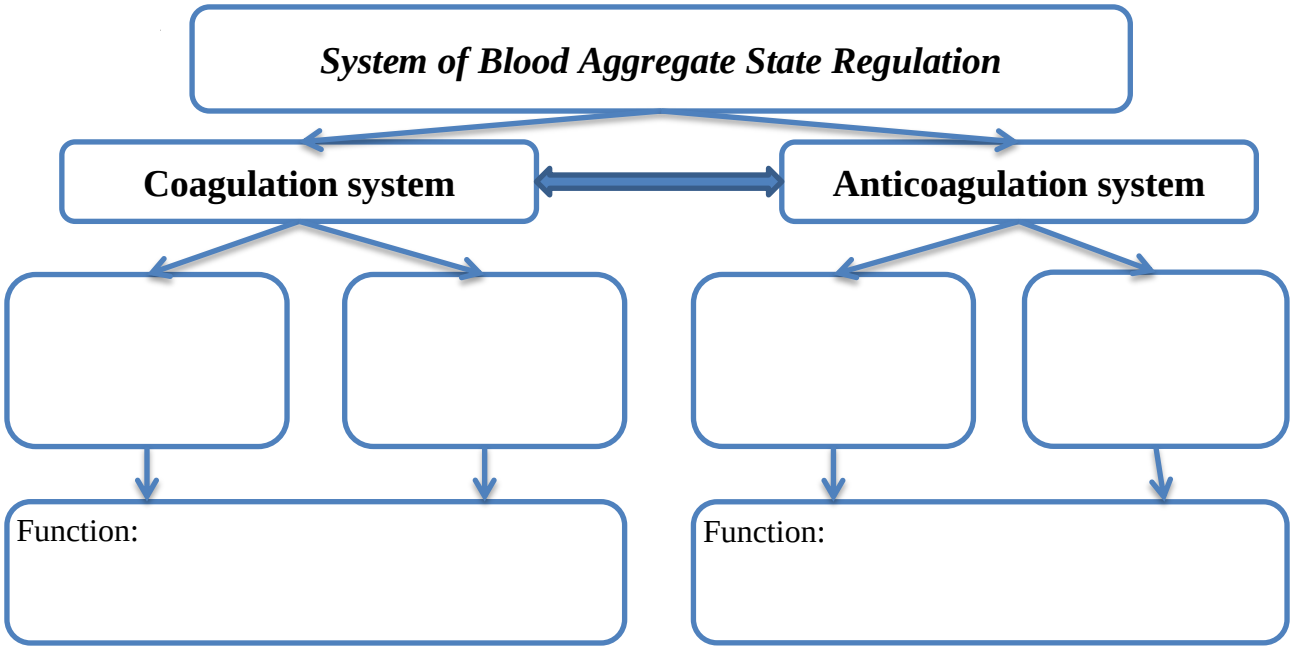
_____
_____
_____
_____
_____
_____
_____
_____

Task 3.8. *Complete the following table to define the types of leukocytes content changes:*

Leukocytosis is _____ _____		**Leukopenia is _____** _____	
physiological	**reactive**	**physiological**	**pathological**

4. Types and physiological mechanisms of the blood coagulation. Physiology of platelets.

Task 4.1. *Complete the scheme "The System of Blood Aggregate State Regulation" and define the functions of its components*



Task 4.2. *Complete the following table "Factors of blood coagulation"*

Main factors of thrombocytes

Nomenclature	Name	Functions
P_3		
P_5		
P_6		
P_9		
P_{10}		
P_{11}		
Factor of Willebrandt		

Plasma coagulation factors

Nomen-clature	Name	Organ producing	Functions
I			
II			
III			
IV			
V			
VI			
VII			
VIII			
IX			
X			
XI			
XII			
XIII			
XIV			
XV			

Task 4.3. *Complete the table "Vascular-platelet hemostasis" and describe its stages*

	Name of stage	Description of processes
1		
2		
3		
4		
5		

Final adaptive result is _____
_____

Task 4.4. *Complete the table "Coagulation hemostasis" and describe its stages*

Name of stage	Duration	Description of processes
I._____ _____		
Extrinsic (tissue) mechanism		
Intrinsic (blood) mechanism		
II. _____ _____		
III. _____ _____		

Final adaptive result is _____
_____
_____
_____

Task 4.5. *Draw the scheme "Coagulation Hemostasis"*

Task 4.6. *Complete the scheme "After-phase of blood clotting"*

Retraction	***Fibrinolysis***
	I.
	II.
	III.

Task 4.7. *Explain the significance of anticoagulation system*

_____

_____

Task 4.8. *Define the factors of blood fluidity maintaining*

1. _____

   _____

2. _____

   _____

3. _____

   _____

4. _____

   _____

5. _____

Task 4.9. *Complete the scheme "Blood Anticoagulants"*

Primary anticoagulants are _____ _____ _____		**Secondary anticoagulants are _____** _____ _____	
substance	**effect**	**substance**	**effect**

Task 4.1. *Complete the normal value of the following hematology repots. Analyze these blood tests and make the conclusion*

HEMATOLOGY REPORT

HOSPITAL:

NAME:

CODE: DATE:

Parameter	Result	Unit	N Range
WBC	12,5	10^9/L	
GR	82,0	%	
Mye	2,0	%	
MetM	5,0	%	
Stb	15,0	%	
Seg	60,0	%	
Eos	0,0	%	
Bas	0,0	%	
LY	12,0	%	
MO	6,0	%	
RBC	4,2	10^12/L	
CI	0,9		
HGB	135,0	g/L	
HTC	42,0	%	
PLT	240,0	10^9/L	
ESR	25	mm/h	

HEMATOLOGY REPORT

HOSPITAL:

NAME:

CODE: DATE:

Parameter	Result	Unit	N Range
WBC	8,6	10^9/L	
GR	37,0	%	
Mye	0,0	%	
MetM	0,0	%	
Stb	3,0	%	
Seg	32,0	%	
Eos	1,0	%	
Bas	1,0	%	
LY	48,0	%	
MO	15,0	%	
RBC	4,6	10^12/L	
CI	0,85		
HGB	132,0	g/L	
HTC	40,0	%	
PLT	238,0	10^9/L	
ESR	8	mm/h	

HEMATOLOGY REPORT

HOSPITAL:

NAME:

CODE: DATE:

Parameter	Result	Unit	N Range
WBC	7,6	10^9/L	
GR	64,0	%	
Mye	0,0	%	
MetM	0,5	%	
Stb	5,0	%	
Seg	55,0	%	
Eos	3,0	%	
Bas	0,5	%	
LY	26,0	%	
MO	10,0	%	
RBC	3,0	10^12/L	
CI	0,77		
HGB	96,0	g/L	
HTC	33,0	%	
PLT	250,0	10^9/L	
ESR	31	mm/h	

HEMATOLOGY REPORT

HOSPITAL:

NAME:

CODE: DATE:

Parameter	Result	Unit	N Range
WBC	6,4	10^9/L	
GR	70	%	
Mye	0	%	
MetM	0	%	
Stb	3	%	
Seg	58	%	
Eos	8	%	
Bas	1	%	
LY	22	%	
MO	8	%	
RBC	4,4	10^12/L	
CI	0,82		
HGB	122	g/L	
HTC	39	%	
PLT	130	10^9/L	
ESR	18	mm/h	

5. Blood protective functions. Blood types.

Task 5.1. *Complete the following statements:*
Different blood types are determined by the hereditary presence or absence of antigens on the surface of erythrocytes. They are called _____ and they are of 2 types: _____ and _____.
In the blood serum the antibodies against these antigens are present. They are called _____ and they are also of 2 types: _____ and _____.

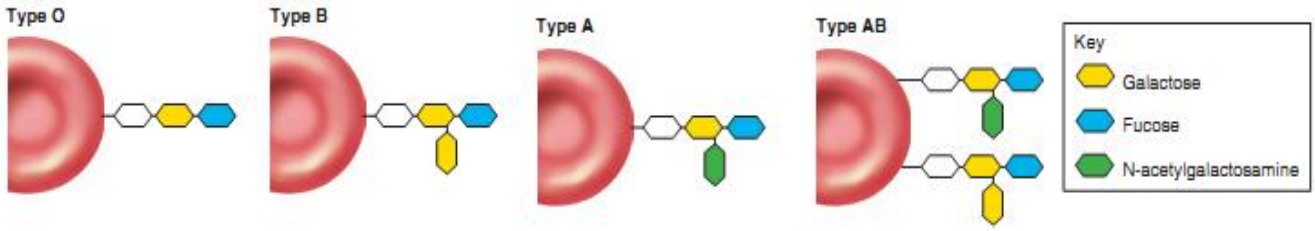


Figure 3. **Chemical Basis of the ABO Blood Types.** *The terminal carbohydrates of the antigenic glycolipids are shown. All of them end with galactose and fucose (not to be confused with fructose). In type A, the galactose also has an N-acetylgalactosamine added to it; in type B, it has another galactose; and in type AB, both of these chain types are present.*

When the same _____ and _____ are present the phenomenon of _____ is observed which is the clumping of RBCs bond together by antibodies.

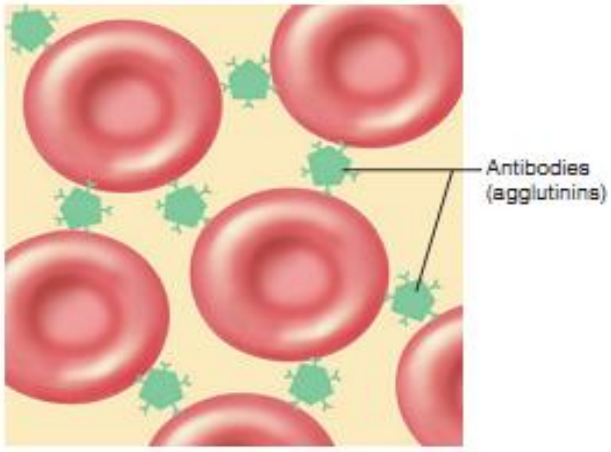


Figure 4. **Agglutination of RBCs by Antibodies.** *Anti-A and anti-B have 10 binding sites, and can therefore bind multiple RBCs to each other.*

Task 5.2. *Complete the following table to classify blood groups according to ABO-system:*

Blood group	***RBCs agglutinogens***	***Serum agglutinins***	***SI***
I			
II			
III			
IV			

Task 5.3. *Study the illustration of the ABO blood typing and explanation for it.*

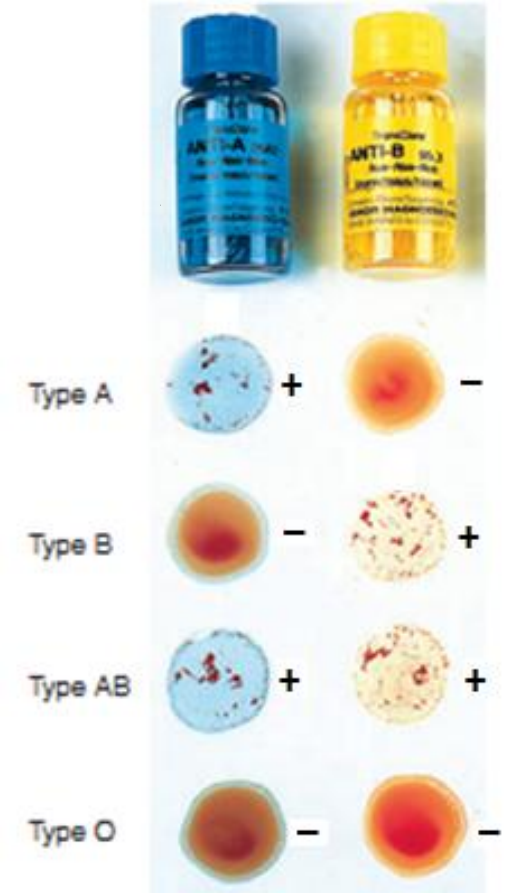


Figure 5. **ABO Blood typing with monoclonal antibodies.**

Each row shows the appearance of a drop of blood mixed with anti-A and anti-B monoclonal antibodies. Pay attention that anti-A reagent is actually the solution of α agglutinins, correspondently Anti-B is the solution of β ones. Blood cells become clumped if they possess the antigens for the antibodies (top row left, second row right, third row both) but otherwise remain uniformly mixed. Thus type A agglutinates only in anti-A; type B agglutinates only in anti-B; type AB agglutinates in both; and type O agglutinates in neither of them.
When standard sera are used for blood typing you have to represent exactly that serum of II group contents β agglutinins and reacts with RBCs of groups possessing B agglutinogens (III and IV). A serum of III group has α agglutinins and reacts with erythrocytes of groups which content A agglutinogens (II and IV). RBCs of I group possess no agglutinogens and never can agglutinate with any sera. In contrast erythrocytes of IV group with sera of all groups I, II and III.

Use this information to complete the table "Blood typing showing agglutination of different blood types RBCs". Label with "+" agglutination and "–"if it's absent.

Serum Group	**Erythrocytes group**			
	I (O)	**II (A)**	**III (B)**	**IV (AB)**
I (α and β)				
II (β)				
III (α)				
IV (0)				

Task 5.4. *Explain the blood typing with help of standard sera*

_____
_____
_____
_____

Task 5.5. *Explain the blood typing with help of anti-A and anti-B reagents*

_____
_____
_____
_____

Task 5.4. *Define the blood types according to the Rh-factor (pay attention that there are no natural antibodies to the Rhesus-agglutinogens)*

Blood type	***RBCs agglutinogens***	***Serum agglutinins***
Rh (+)		
Rh (−)		

Task 5.5. *Explain the blood typing in Rh-factor system*

_____
_____
_____
_____

Task 5.6. *Study the illustration of the Rhesus conflict between mother and fetus*

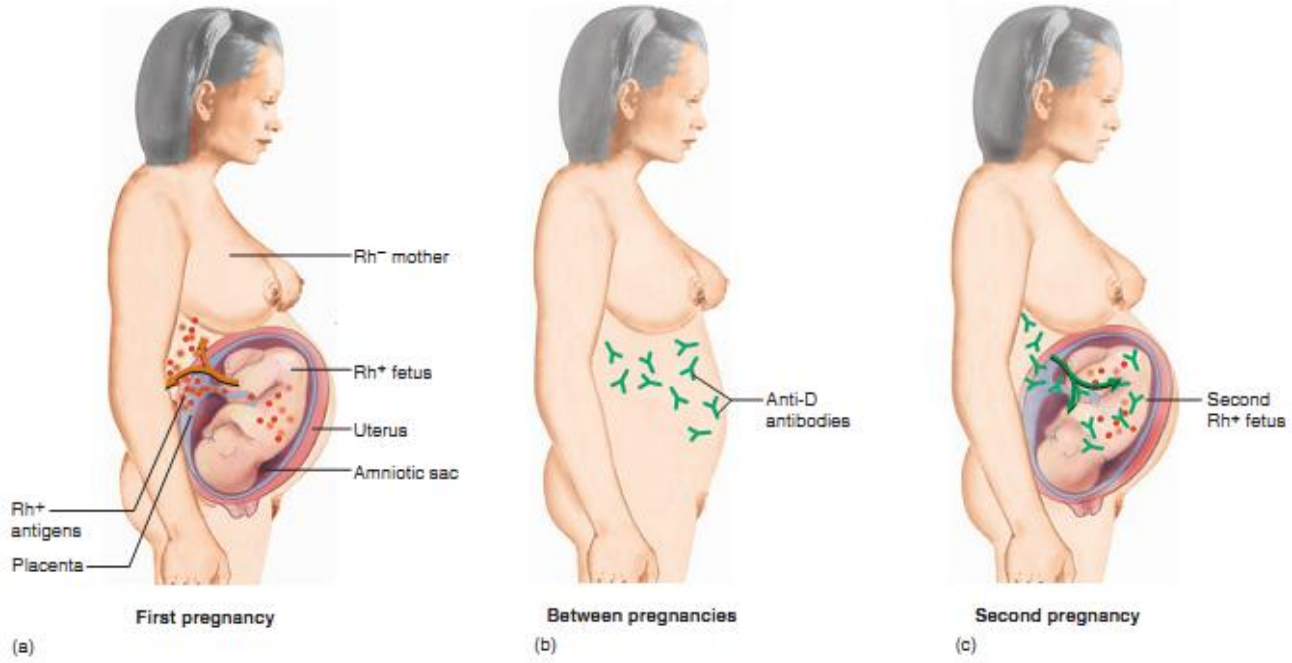


Figure 6. Hemolytic Disease of the Newborn (HDN).

Explain the mechanism of rhesus-conflict during pregnancy _____
_____
_____
_____
_____

Explain why ABO-system don't cause the immune conflict between mother and fetus

_____
_____
_____

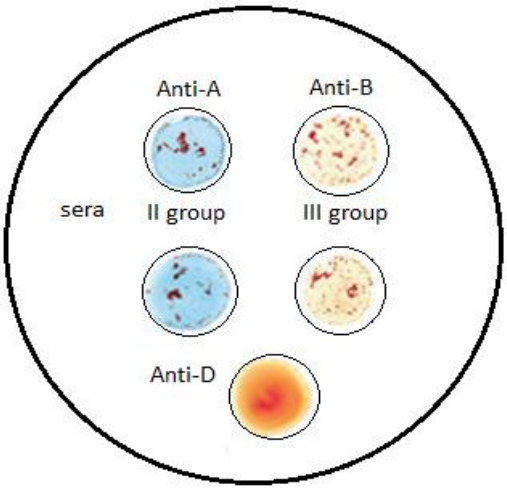
Task 5.7. *List the general rules of hemotransfusion*

1. _____
_____
2. _____
_____
3. _____
_____

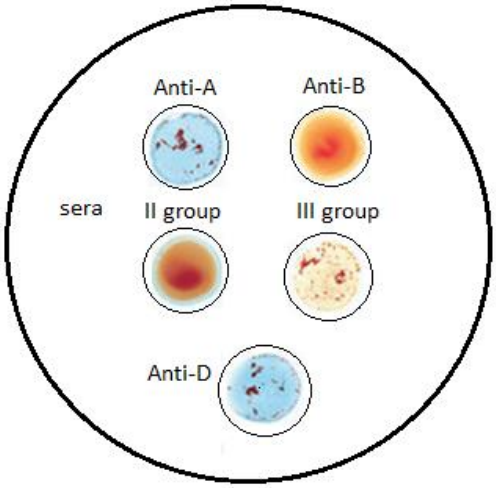
Task 5.8. *List the obligatory tests before the blood transfusion*

1. _____
_____
2. _____
_____
3. _____
_____
4. _____
_____

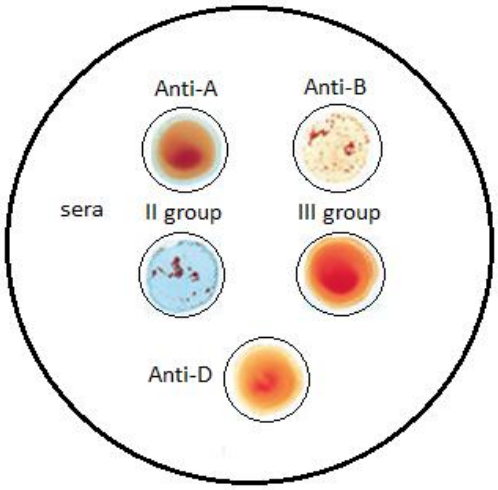
Task 5.8. *Determine the blood group and Rh-factor on the pictures*



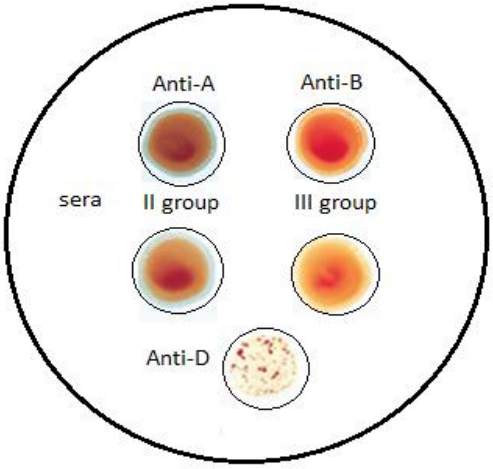
Blood type _____



Blood type _____



Blood type _____

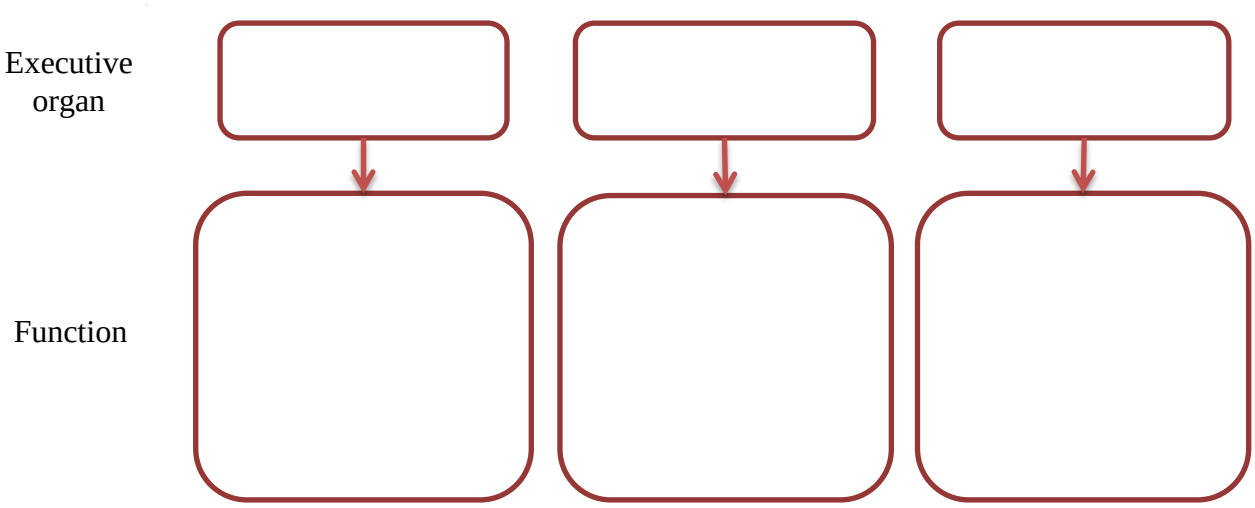


Blood type _____

PHYSIOLOGY OF HEART

6. General characteristic of blood circulation system. Physiological properties of myocardium. Physiological basis of ECG

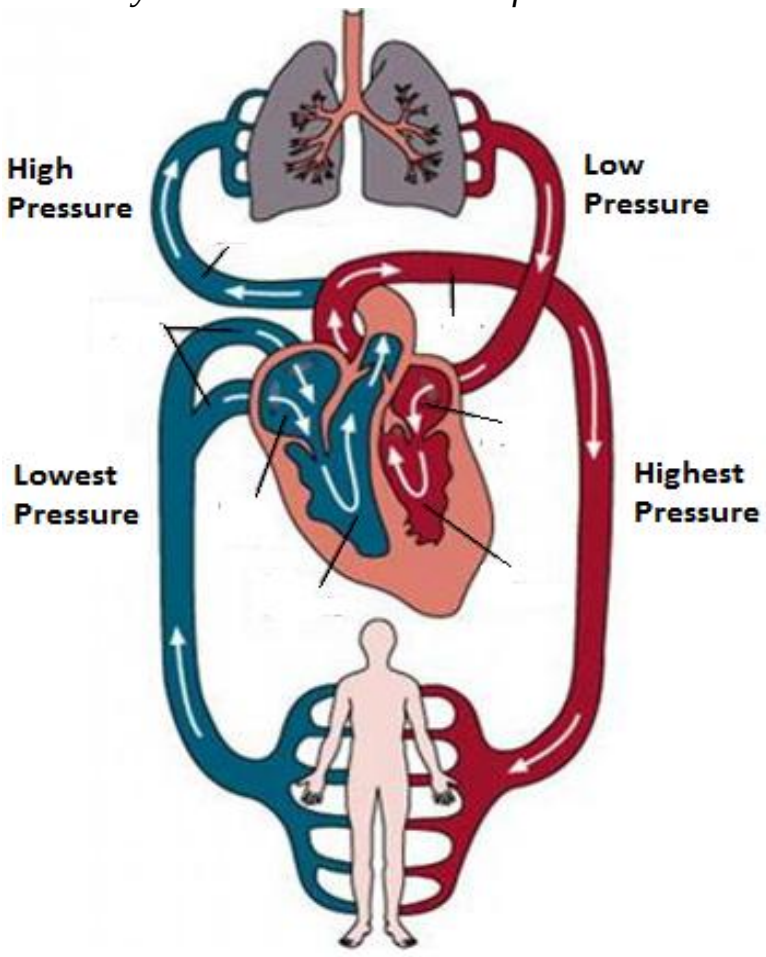
Task 6.1. *Draw the scheme of* ***functional system of circulation***



Final adaptive result: _____

_____

Task 6.2. *Cardiovascular system has 2 divisions. Define them and complete the scheme.*



Task 6.3. *Define the stages of grater (systemic) circulation*

✓ _____
_____

✓ _____
_____

✓ _____
_____

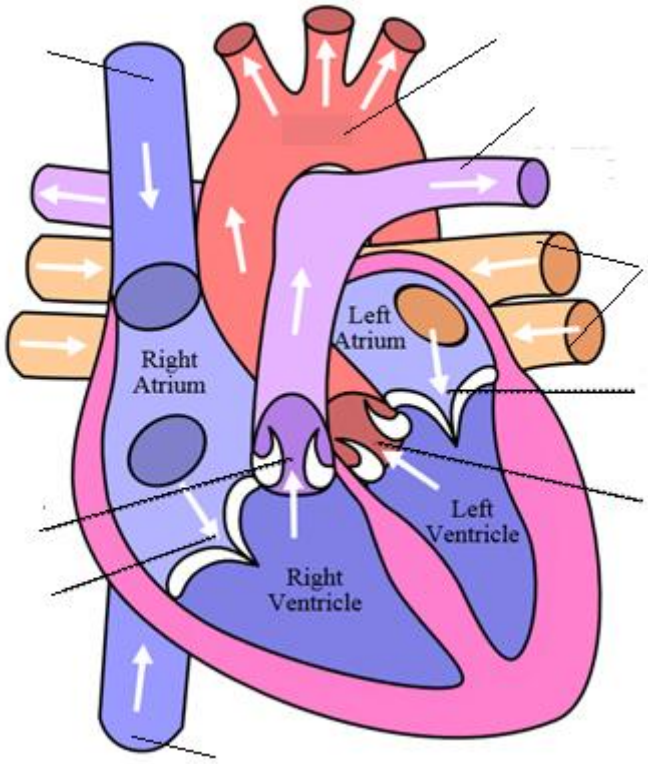
Task 6.4. *Define the stages of lesser (pulmonary) circulation*

✓ _____
_____

✓ _____
_____

✓ _____
_____

Task 6.5. *Describe anatomical structures of heart.*

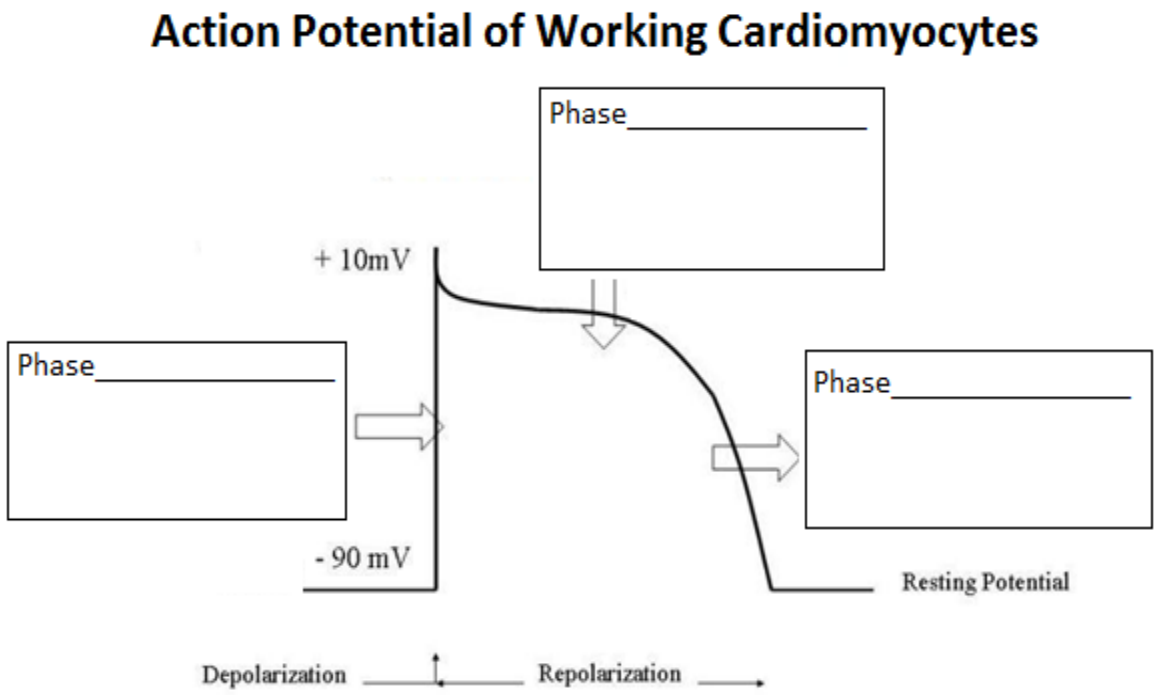


Task 6.6. *List and give definition of physiologic properties of myocardium.*

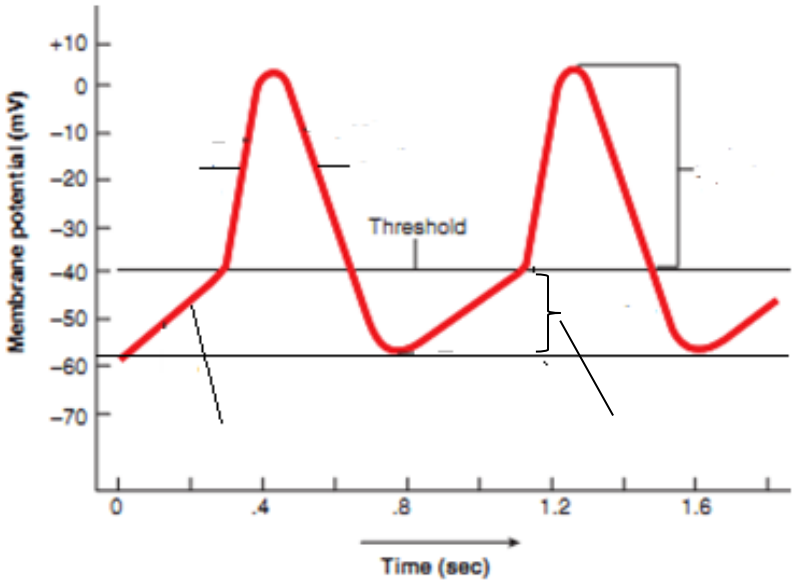
- _____
_____
_____
- _____
_____
- _____
_____

- _____
  _____
- _____
  _____

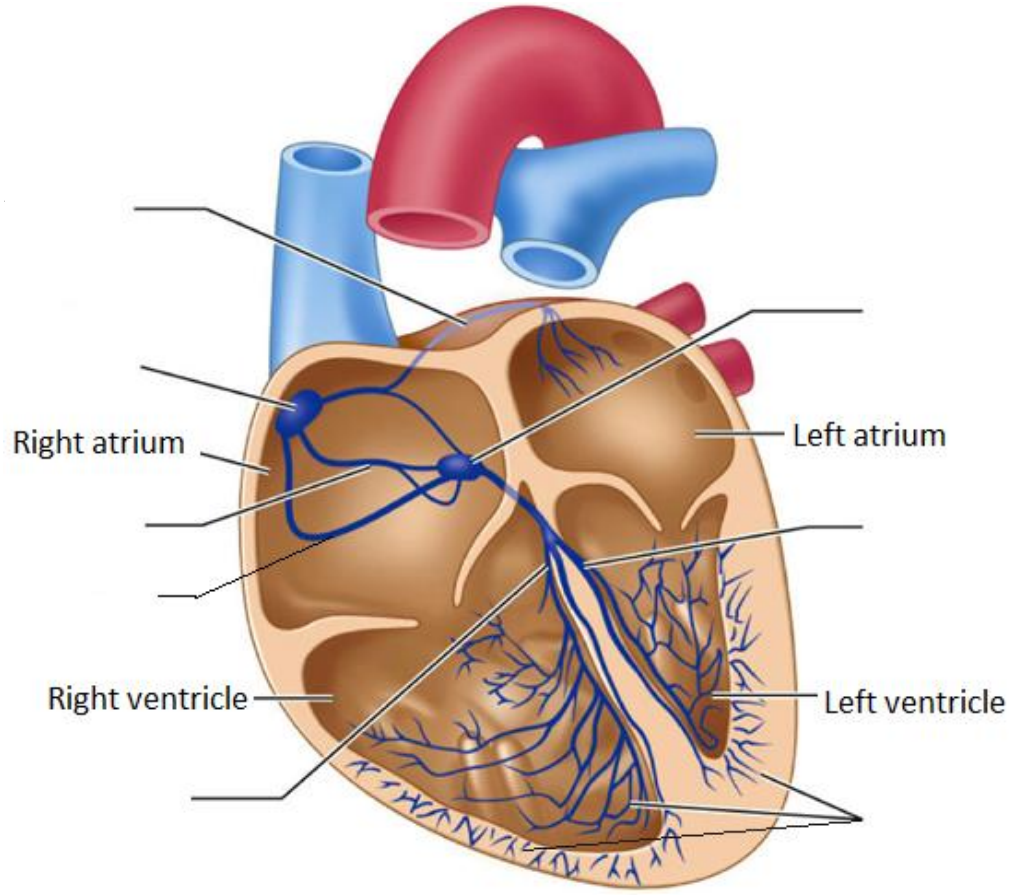
Task 6.7. *Name the phases of action potential of ventricular myocytes and describe the processes in every phase of AP. Define duration of absolute refractory phase and its significance.*



Task 6.8. *Name the phases of action potential of SA node and describe the processes in every phase of AP.*



Task 6.9. *Label the structures of heart's conduction system.*



Task 6.10. *Complete the table.*

Localization of excitable cells	*Frequency (AP/min)*	*Velocity of conduction (m/s)*
SA-node		
AV-node		
His' bundle		
Purkinje fibers		
Working cardiomyocytes of atria and ventricles		

Task 6.11. *Name the important physiological functions of the conductive system of heart:*

- _____
- _____
- _____
  _____

Task 6.12. *Define the importance of atrioventricular delay.*

_____

_____

_____

Task 6.13. *Describe excitation-contraction coupling by stages.*

1._____

_____

2._____

_____

3._____

_____

4._____

_____

5._____

_____

6._____

_____

7._____

_____

8._____

_____

9._____

_____

10._____

_____

Task 6.14. *Give definition of electrocardiography*.

_____

_____

_____

_____

Task 6.15. *Give definition of electrocardiogram.*

_____

_____

_____

_____

Task 6.16. *Define and describe different leads of ECG. Use illustration to decide this task*

1. **Classical leads (*Einthoven, 1913*)** are _____
   _____
   _____
   I lead _____
   II lead_____
   III lead_____
2. **Intensified leads *(Goldberger, 1942)*** are _____
   _____
   _____
   aVR_____
   aVL_____
   aVF_____
3. **Chest leads *(Wilson, 1934)*** are _____
   _____
   _____
   V_1_____
   V_2_____
   V_3_____
   V_4_____
   V_5_____
   V_6_____

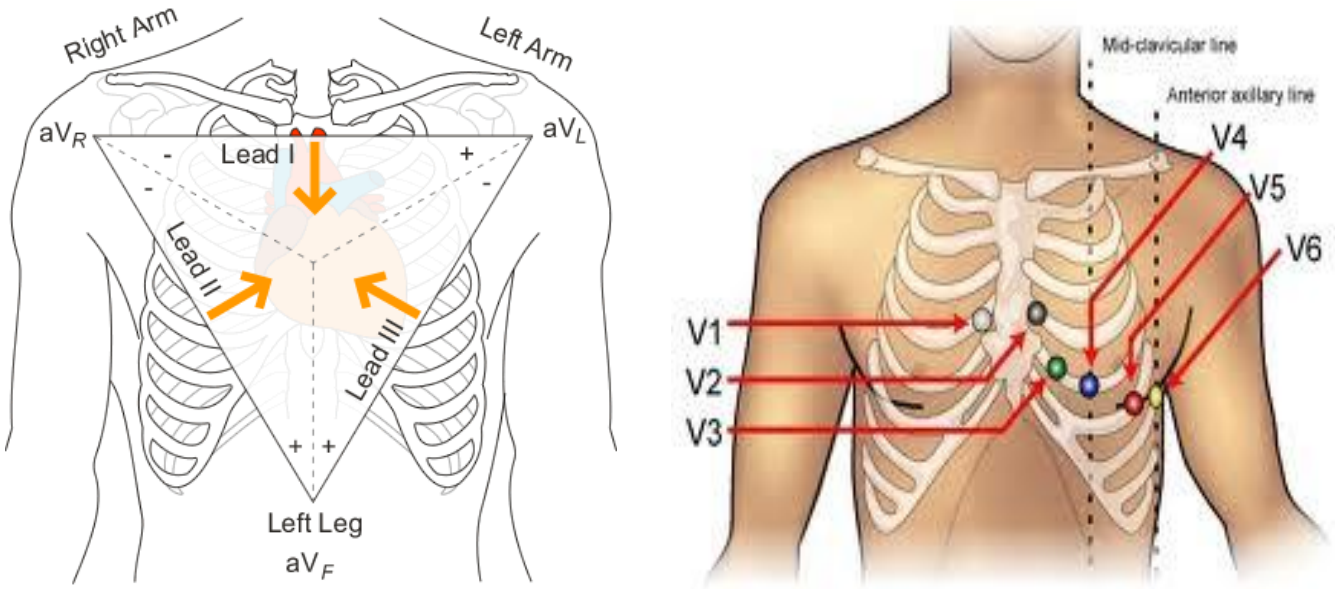
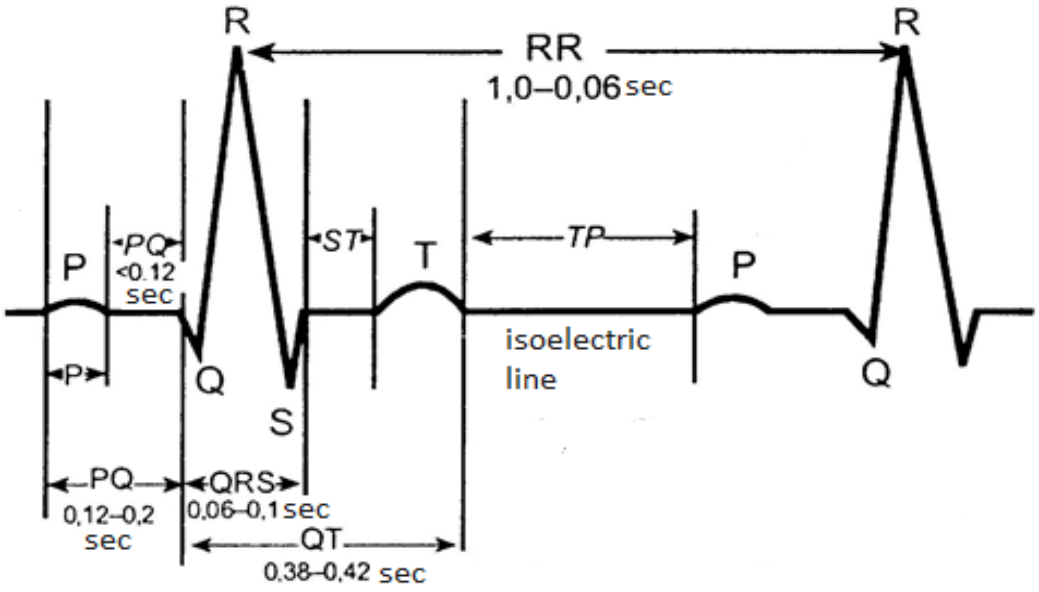


Figure 7. **Different leads used for ECG registration**

Task 6.17. *Study the illustration of ECG and complete the following statements*



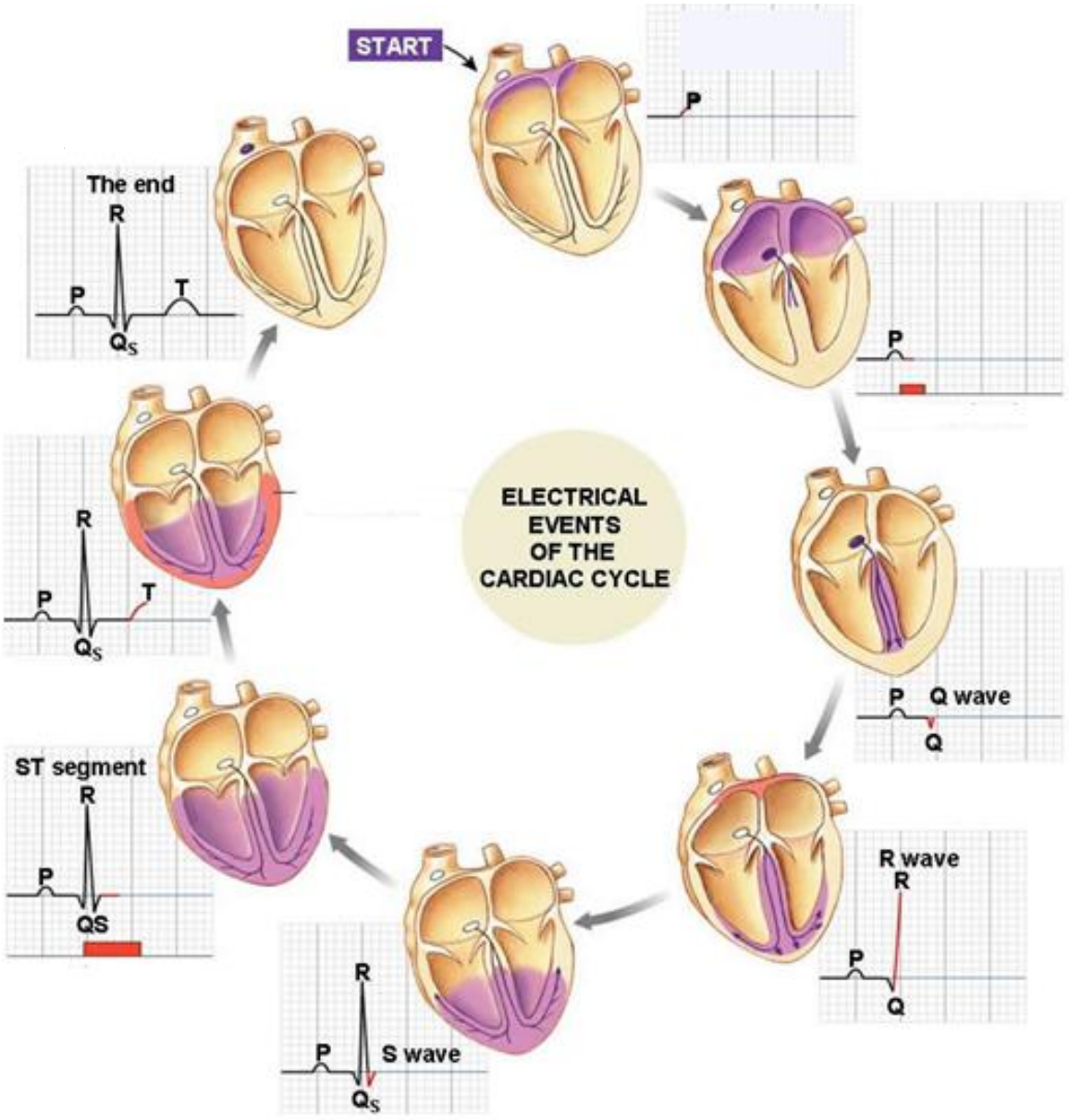
During cardiac cycle these parameters of ECG are recorded:

1) waves. They are _____
2) segments. They are _____
3) intervals. They are _____

Task 6.18. *Complete the table for II standard lead using the previous illustration.*

Index	***Electrical activity***	***Duration***	***+ or -***	***Amplitude***
P wave				
P-Q interval				
Q wave				
R wave				
S wave				
QRS complex				
R-R interval				
S-T segment				
T wave				
Q-T interval				

Task 6.19. *Define the stages of electrical activity of the heart.*



7. Heart pumping function

Task 7.1. *Give definition of cardiac cycle.*

_____

_____

_____

Task 7.2. *Calculate the duration of cardiac cycle if heart rate is*

75bpm _____

80bpm_____

60bpm_____

Task 7.3. *Explain why cardiac cycle starts from excitation of right atrium?*

_____

_____

Task 7.4. *Complete the table to characterize systole and diastole of atria and ventricles.*

Atrial systole

	Duration	***Pressure***	***Veins sphincters***	***AV valves***	***Direction of blood flow***
Right atrium					
Left atrium					

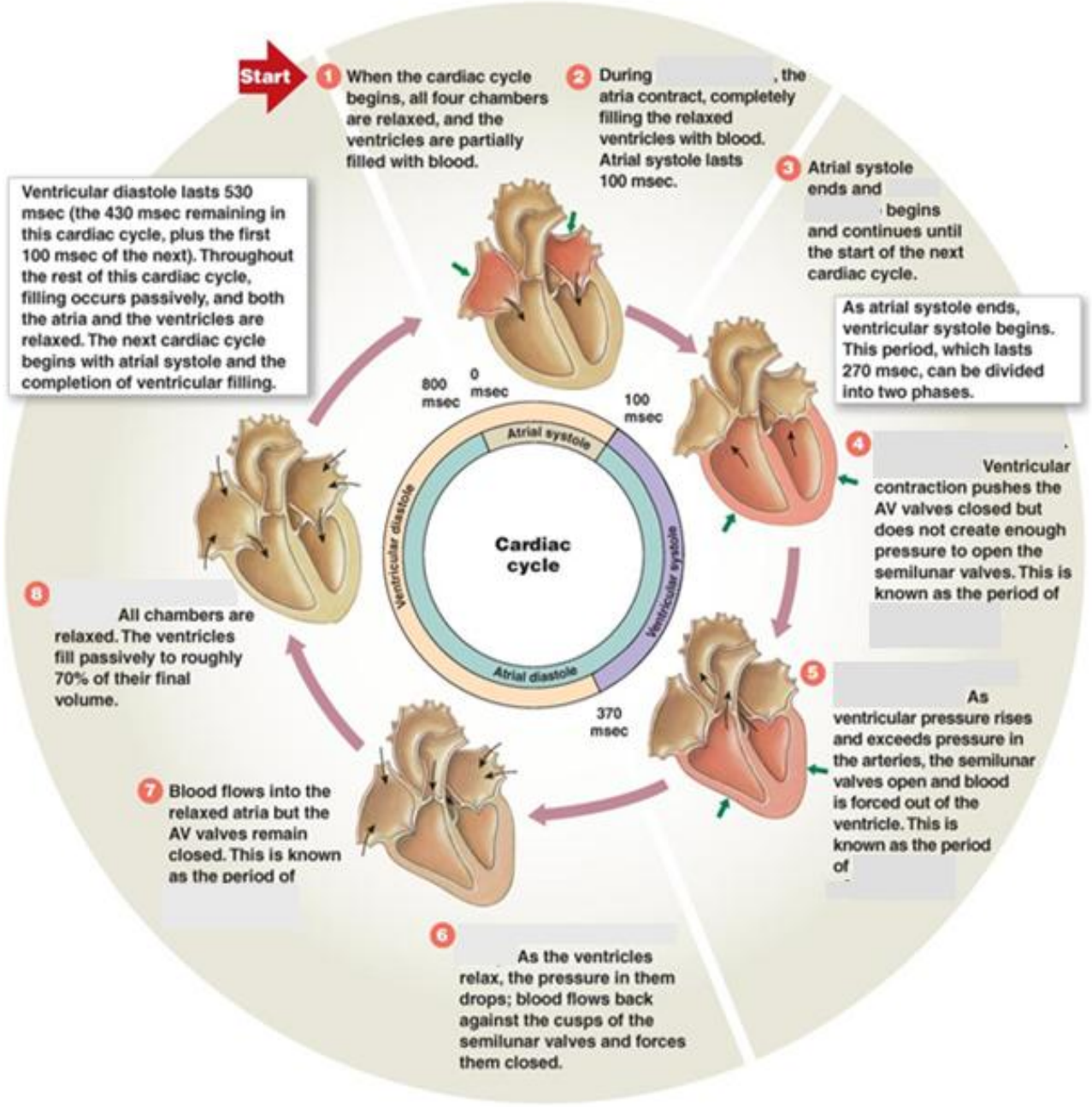
Ventricular systole

	Duration	***Pressure***	***Veins sphincters***	***AV valves***	***Direction of blood flow***
Tension period					
Phase of asynchronous contraction					
Phase of isometric contraction					
Ejection period					
Rapid phase					
Slow phase					

Ventricular diastole

	Duration	***Pressure***	***Veins sphincters***	***AV valves***	***Direction of blood flow***
Protodiastolic period					
Period of isometric relaxation					
Period of ventricular filling:					
Maximal filling					
Reduced filling					

Task 7.5. *Name the phases of cardiac cycle using the description of events in heart chambers*



1_____

2._____

3._____

4._____

5._____

6._____

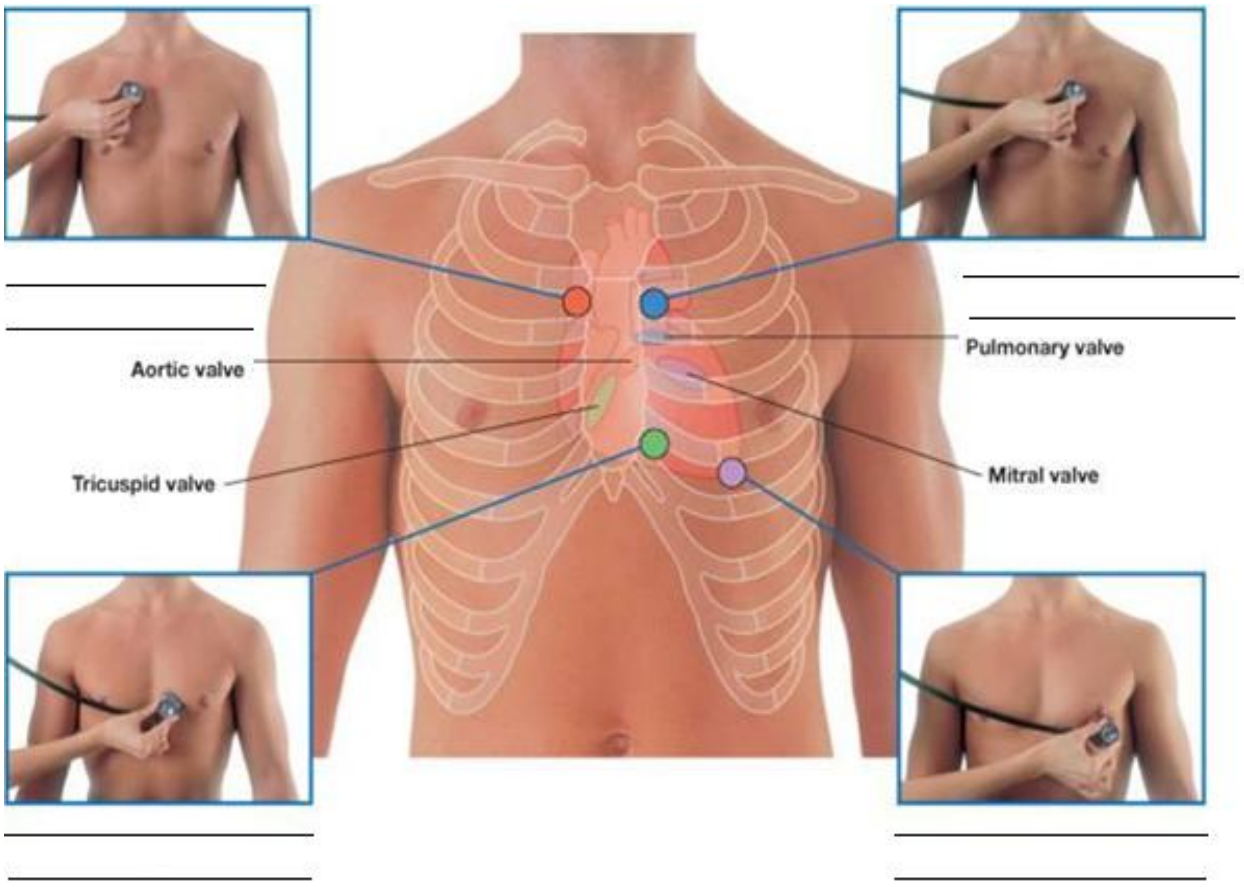
7._____

8._____

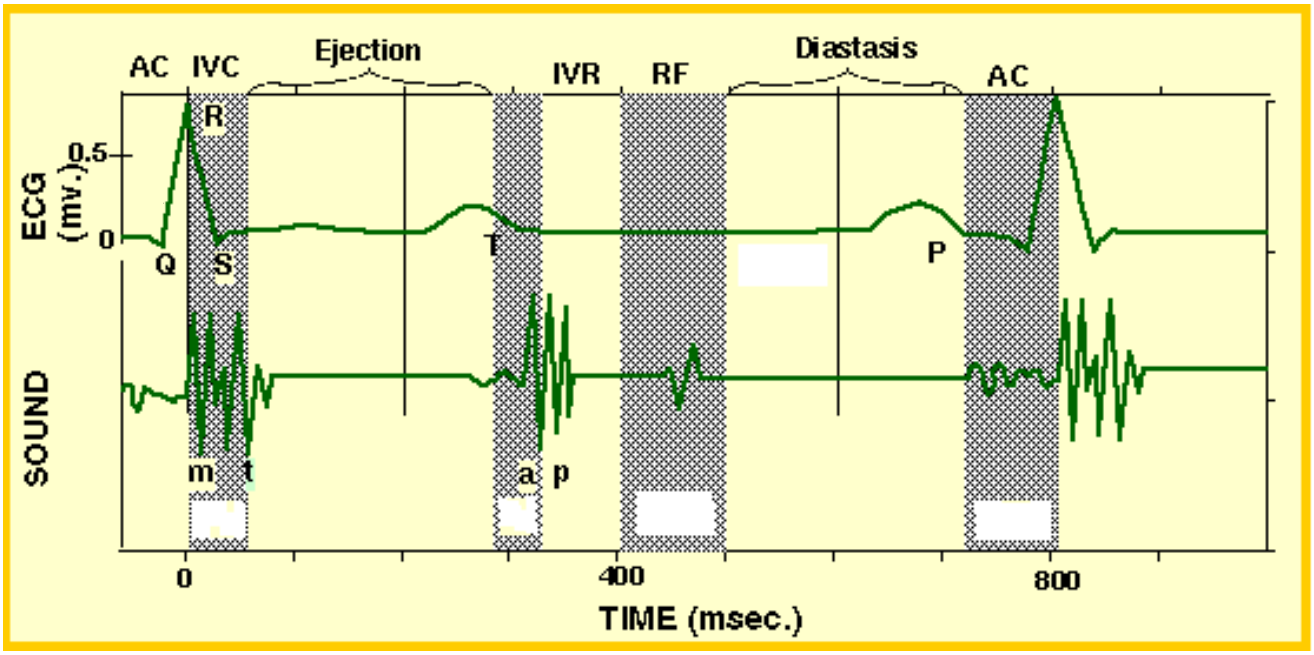
Task 7.6. *Define relationship of the heart sounds to heart pumping.*

	Reasons of formation	***Characteristics***
I heart sound		
II heart sound		
III heart sound		
IV heart sound		

Task 7.7. *Define the chest surface areas for auscultation of normal heart sounds*.



Task 7.8. *Define relationship of phonocardiogram and electrocardiogram.*



8. Regulation of heart activity

Task 8.1. *Study and memorize the mechanisms of cardiac activity regulation.*

Neuronal regulation		***Humoral regulation***
Intrinsic	***Extrinsic***	
1. Myogenic - homeometric mechanism (Anrep's effect); - heterometric mechanism (Frank-Starling law). **2. Intracardiac peripheral reflexes** - cardiostimulation; - cardioinhibition	1. Autonomic nerves 2. Baroreceptors' reflex 3. Bainbridg reflex 4. Respiratory effect 5. Chemoreceptors' reflex	1. **Hormones**: - renin-angiotensin-aldosterone system (RAAS), - natriuretic peptide, - endothelin, - ADH, - thyroid hormones, - glucocorticoids, - mineralocorticoids, - catecholamines 2. **Ions**: Na^+, K^+, Ca^{2+}

Task 8.2. *Define the law of the heart (Frank-Starling law or heterometric mechanism).*

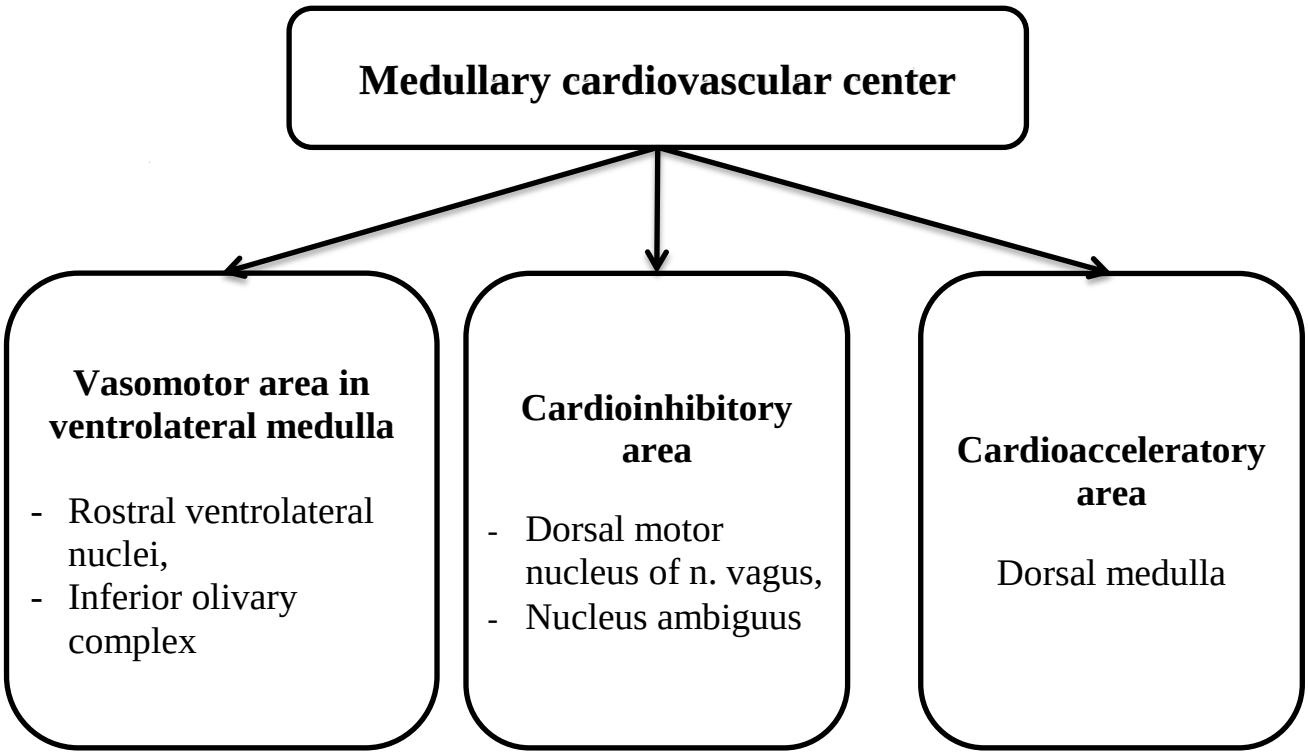
_____
_____
_____

Task 8.3. *Define the Anrep's effect or homeometric mechanism*

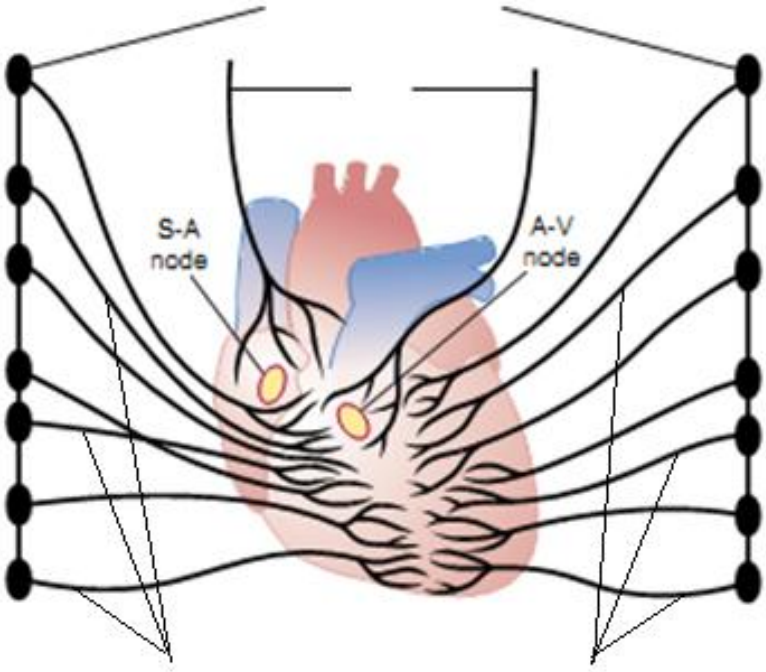
_____
_____
_____

Task 8.4. *Draw the scheme of intracardiac reflex*

Extrinsic neuronal regulation is provided by cardiovascular center of medulla oblongata.



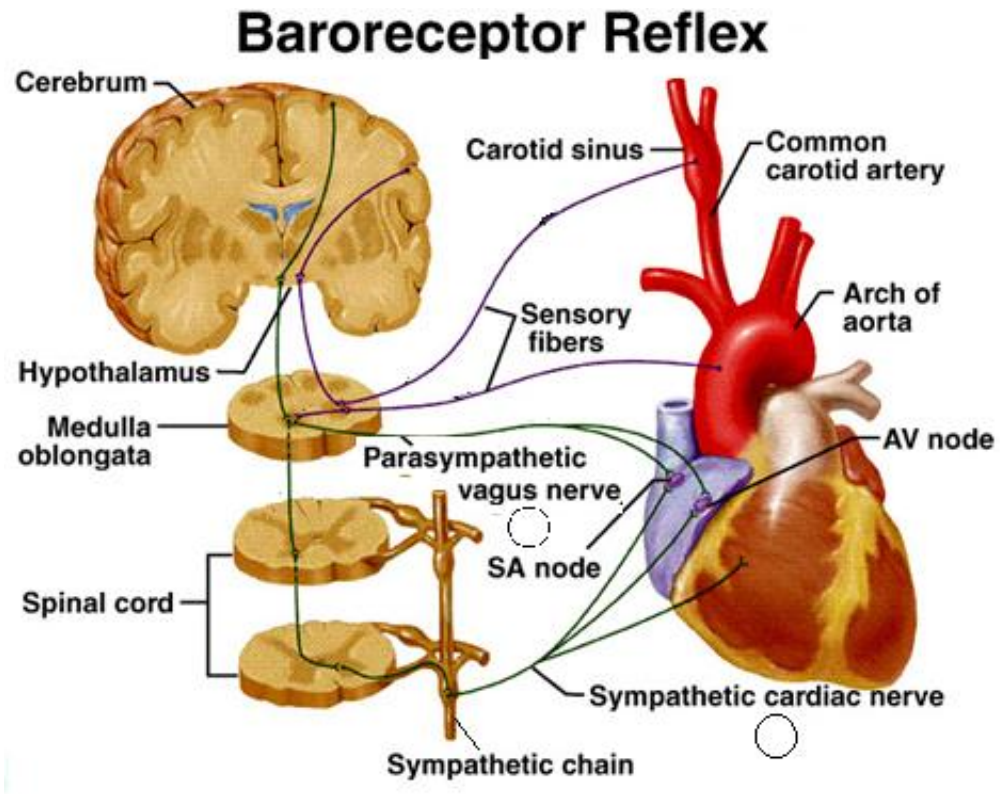
Task 8.5. *Complete the figure. Define the parasympathetic right and left vagal innervation and right and left sympathetic nerves innervation*



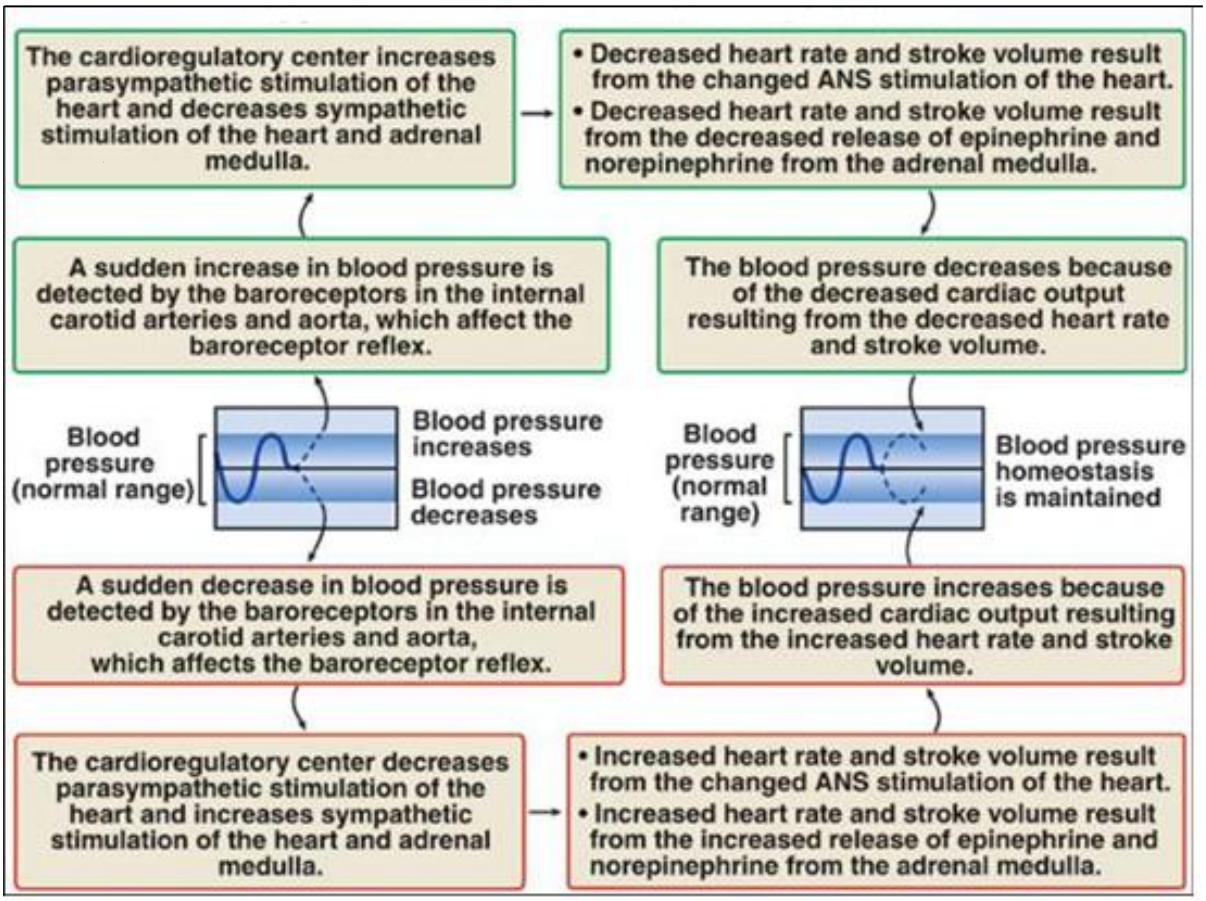
Task 8.6. *Complete the table* ***"Efferent pathways of cardiac activity neuronal regulation"***

	Parasympathetic	***Sympathetic***
Nervous center		
Efferent nerve		
Innervated structures		
Mediator		
Receptors		
Response		
Electrical state		
Effect		

Task 8.7. *Baroreceptor reflex. Define on the picture direction of impulses conduction and effects of parasympathetic and sympathetic nerves by "+" or "–".*



Task 8.8. *Memorize the mechanism of cardiac activity regulation in case of blood pressure changes.*

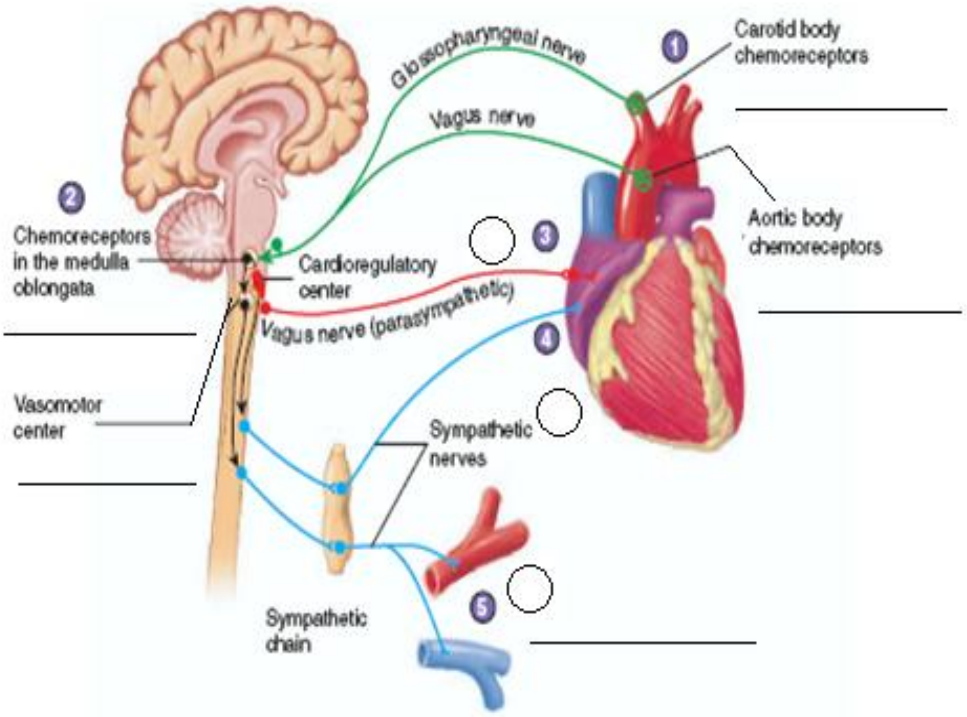


Task 8.9. *Draw the scheme Bainbridge and baroreceptor reflexes.*

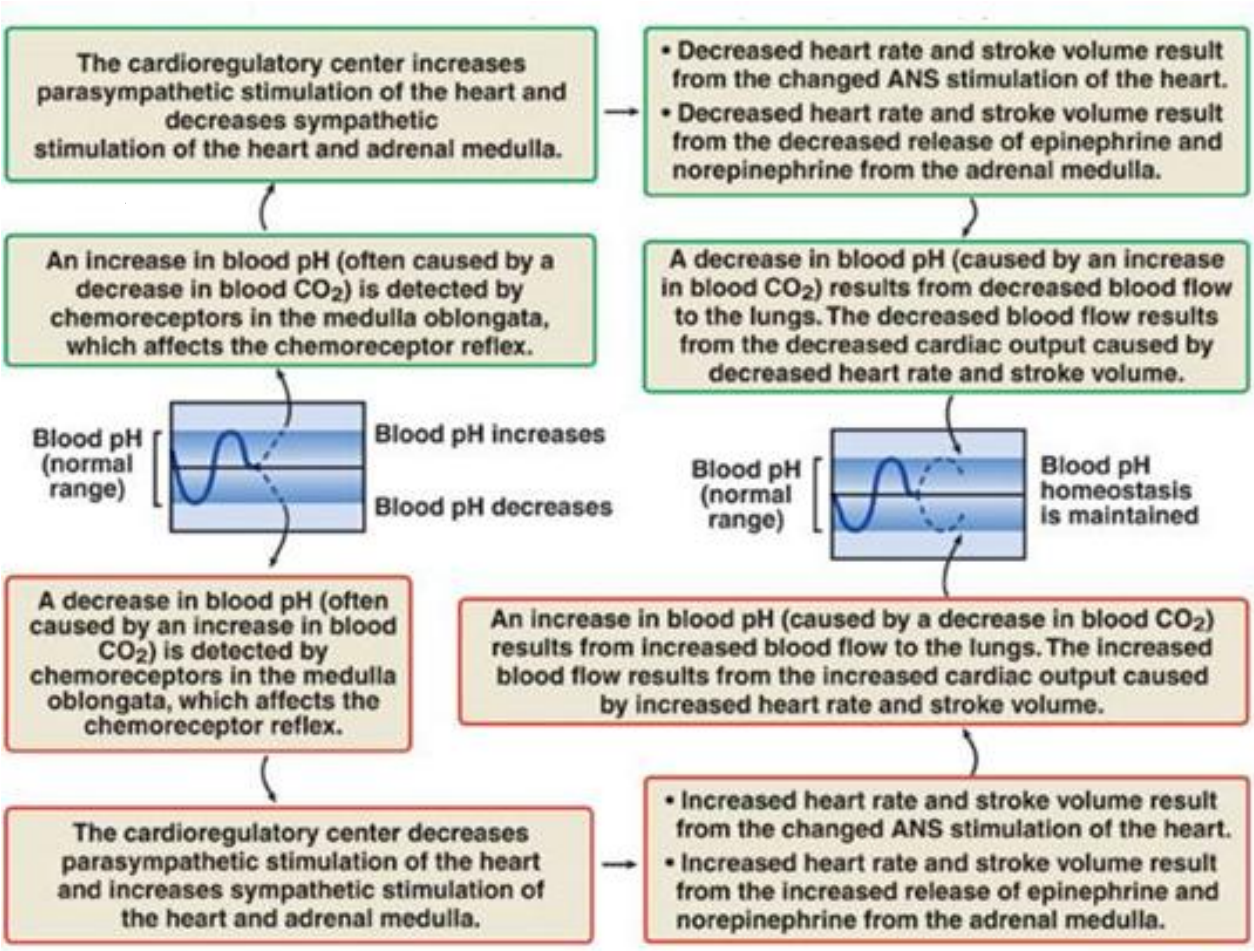
Task 8.10. *Draw the scheme of respiratory regulation of cardiac activity*.

Task 8.11. *Study the picture illustrating chemoreceptor reflex. Define 1) adequate stimuli for peripheral and central receptors; 2) direction of excitation conduction and 3) effects ("+" or "−") to the target organs*.

1. Chemoreceptors in the carotid and aortic bodies monitor blood O_2, CO_2, and pH.
2. Chemoreceptors in the medulla oblongata monitor blood CO_2 and pH.
3. Decreased blood O_2, increased CO_2, and decreased pH decrease parasympathetic stimulation of the heart, which increases the heart rate.
4. Decrease blood O_2, increased CO_2, and decreased pH increase sympathetic stimulation of the heart, which increases the heart rate and stroke volume.
5. Increased sympathetic stimulation of blood vessels increases vasoconstriction.



Task 8.12. *Memorize the mechanism of cardiac activity regulation in case of pH changes.*



Task 8.13. *Humoral regulation refers to the effect of hormones in the heart and how hormones that are released into the bloodstream under certain physiological states may regulate cardiac function. Name these hormones.*

_____

_____

_____

_____

_____

_____

_____

_____

PHYSIOLOGY OF THE VASCULAR SYSTEM

9. General circulation, haemodynamics laws, blood vessels role in the blood circulation

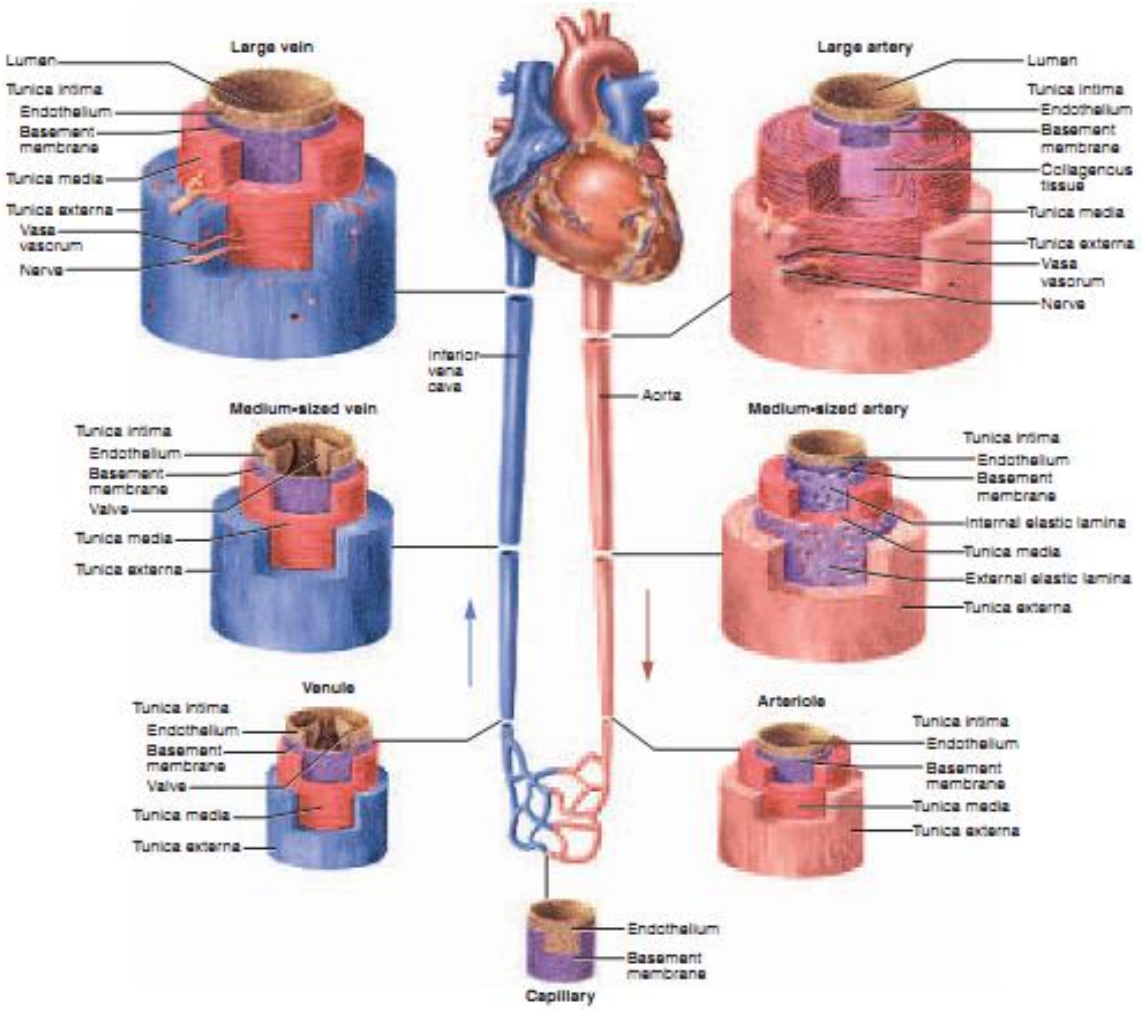
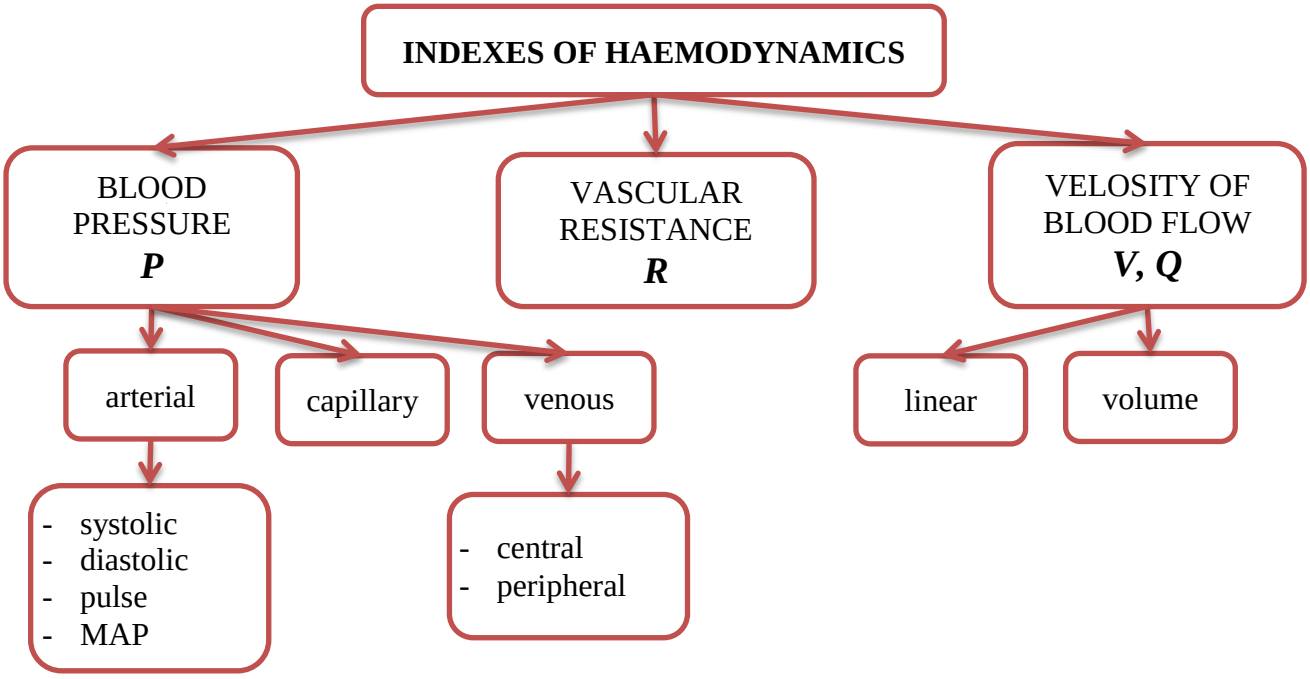


Figure 8. **Structure of the wall in different types of vessels**

Task 9.1. *Complete the table "Functional classification of the vascular system"*

Functional type of vessels	***Anatomical type of vessels***	***Physiological function of the vessels***
1.Elastic vessels		
2.Resistance vessels (Distributing vessels)		
3. Sphincters		
4.Exchange vessels		
5.Capacitance vessels (Reservoir**)**		
6. Shunts, including various types of anastomoses.		

Task 9.2. *Memorize the indexes of hemodynamics*



Task 9.3. *Give definition of volume velocity of blood flow and explain the dependence.*

$$Q = \frac{(P_1 - P_2)}{R} \qquad Q = \frac{\Delta P}{R}$$

Define the parameters

*Q is*_____

*ΔP is*_____

*R is*_____

_____

_____

_____

Task 9.4. *Give definition of linear velocity of blood flow and explain the dependence.*

$$V = \frac{Q}{\pi r^2}$$

Define the parameters:

*V is*_____

*Q is*_____

πr^2 is_____

_____

_____

_____

Task 9.5. *Give definition of peripheral vascular resistance and explain the dependence.*

$$R = \frac{8l\eta}{\pi r^4}$$

Define the parameters:
*R is*_____
*l is*_____
*η is*_____
*πr^4 is*_____

Task 9.6. *Explain the factors influencing to the arterial blood flow:*

1. _____
_____

2. _____
_____

3. _____
_____

Task 9.7. *Explain factors influencing to the venous blood flow:*

1. _____
_____

2. _____
_____

3. _____
_____

4. _____
_____

5. _____
_____

Task 9.8. *Characterize indexes of hemodynamics in capillaries.*

Liner velocity of blood flow _____
Pressure
in arterial part _____
in venous part _____

Resistance_____ _____

Task 9.9. *Define the types of capillaries, their location and function.*

Type	***Location***	***Function***

Task 9.10. *Define the processes providing the water and substances exchange in capillaries bed*

- ✓ _____
- ✓ _____
- ✓ _____
- ✓ _____
- ✓ _____

Task 9.11. *Give definition of filtration.*

_____
_____
_____

Task 9.12. *Complete the formula of filtration pressure.*

FP = P____ + P____ – P____ = _____ + ____ – ____ = ____ *mm Hg*

Filtration pressure depends on the following factors:

1. _____
2. _____
3. _____

Task 9.13. *Complete the statements:*

*The higher hydrostatic pressure in capillaries the filtration is*_____
*The higher oncotic pressure of interstitial fluid the filtration is*_____
*The higher oncotic pressure of blood the filtration is*_____

Task 9.14. *Give definition of reabsorption* _____
_____
_____
_____

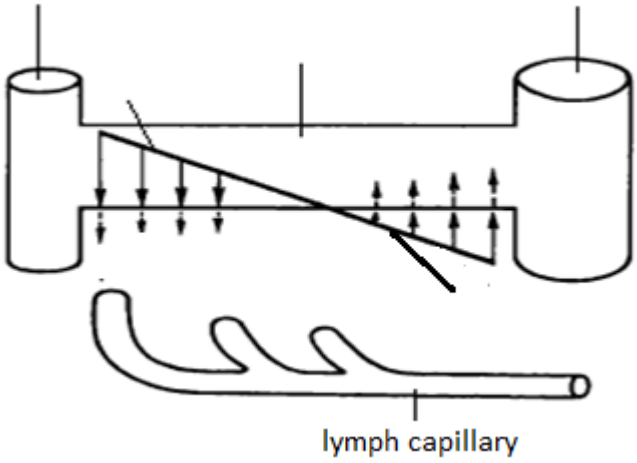
Task 9.15. *Complete the formula of reabsorption pressure.*

RP = P____ – P____ – P_____ = ____ – ____ – _____ = _____ *mm Hg*

Reabsorption pressure depends on the following factors:

1. _____
2. _____
3. _____

Task 9.16. *Label the picture to illustrate filtration and reabsorption processes*



Task 9.17. *Give definition of arterial pulse*

_____

_____

_____

Task 9.18. *List the arterial pulse characteristics. Complete the table.*

Index	***Significance***

Task 9.19. *Draw the scheme to demonstrate the dependence of pulse filling***.**

Filling of pulse

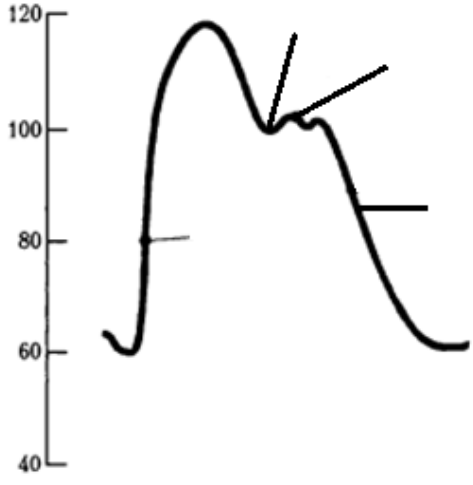
Task 9.20. *Draw the scheme to demonstrate the dependence of pulse tension.*

Tension of pulse

Task 9.21. *Draw the scheme to demonstrate the dependence of pulse rhythm, quickness and rate (frequency)*

Rhythm, quickness, rate (frequency)

Task 9.22. *Give definition of sphygmogram and mark the phases*



Sphygmogramm is _____

_____

_____

_____

1) _____

_____

2)_____

_____

3)_____

_____

4)_____

_____

_____

Task 9.23. *Explain the origin of:*

- *Anacrotic rise* _____

_____

_____

_____

- *Catacrotic descend* _____

_____

_____

_____

- *Incisure* _____

_____

_____

_____

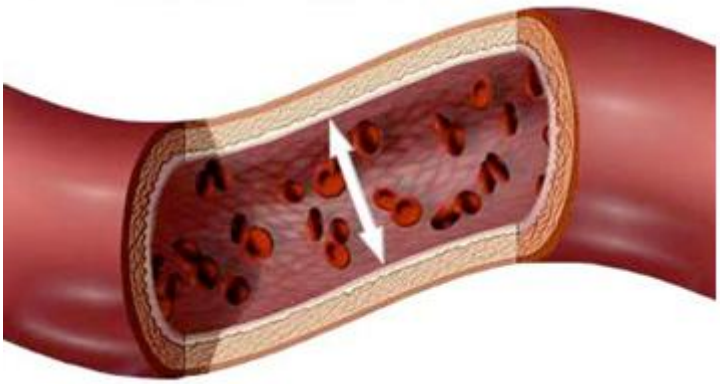
- *Dicrotic rise* _____

_____

_____

_____

Task 9.24. *Give definition of blood pressure*



Blood pressure is

_____

_____

_____

_____

_____

_____

_____

_____

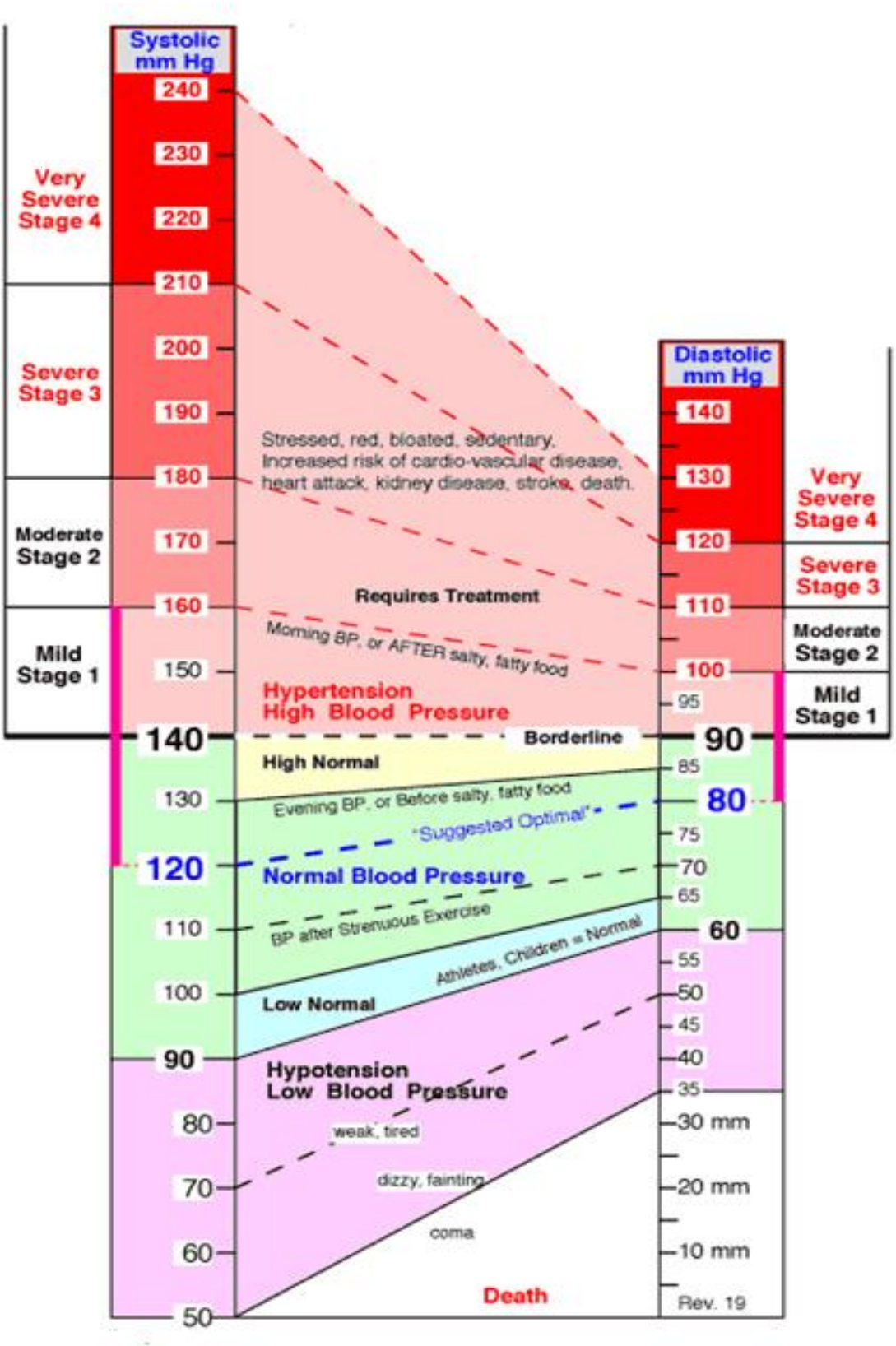
Task 9.25. *Define the types of blood pressure*

✓ _____

✓ _____

✓ _____

Task 9.26. *Memorize the levels of normal and abnormal arterial blood pressure.*



Task 9.27. *Give definition and name the normal values of arterial pressure types.*

1. *Systolic pressure* − _____

_____

_____

2. *Diastolic pressure* − _____

_____

_____

3. *Mean arterial pressure (MAP)* − _____

_____

_____

4. *Pulse pressure* − _____

_____

_____

Task 9.28. Calculate the MAP and PP and make conclusion about their values:

1) 120/80 −_____

_____

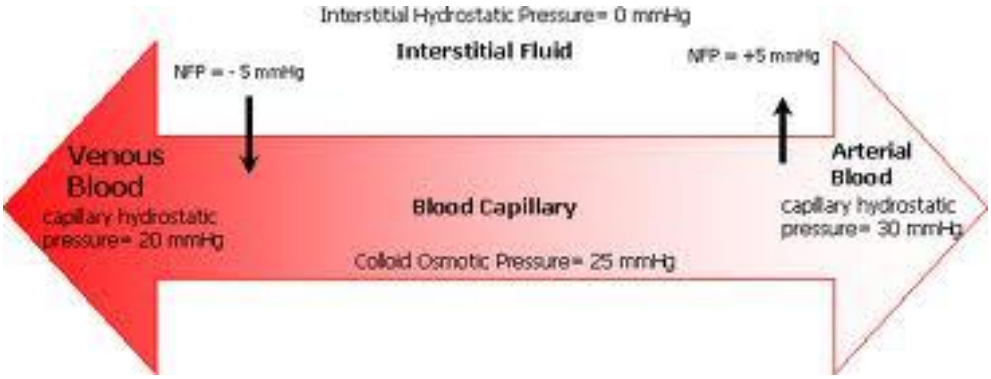
2) 100/60−_____

_____

3) 150/90−_____

_____

Task 9.29. *Define the capillaries pressure and give its characteristic*



_____

_____

_____

_____

_____

Task 9.30. *Define the normal central venous pressure and factors influencing to it.*

_____
_____
_____
_____
_____
_____

Task 9.31. *Study the following illustration and its description. Define the waves of phlebogram and their formation*

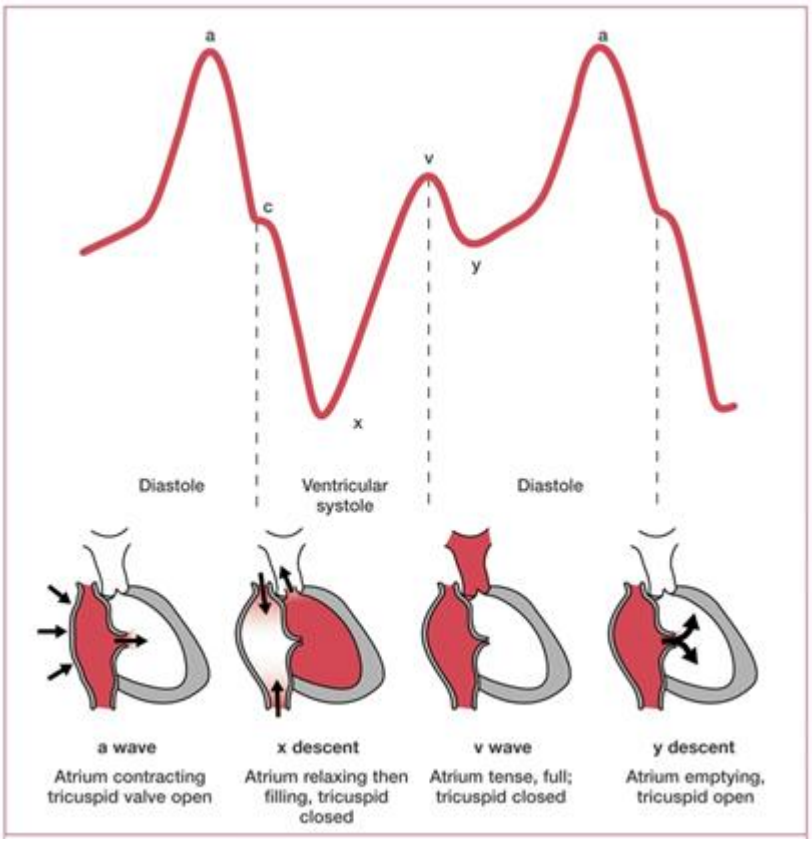


Figure 9. **Central venous pressure waveform**:

1) *a-wave* due to atrial contraction during diastole (absent in atrial fibrillation, but enlarged in tricuspid stenosis, pulmonary stenosis and pulmonary hypertension);

2) *c-wave* due to bulging of tricuspid valve back into the right atrium at the onset of systole;

3) *v-wave* due to rise in atrial pressure from venous return through the vena cavae during systole and before the tricuspid valve opens at the onset of diastole (enlarged in tricuspid regurgitation);

4) *x-descend* due to atrial relaxation;

5) *y-descend* due to atrial empting into the ventricle during diastole

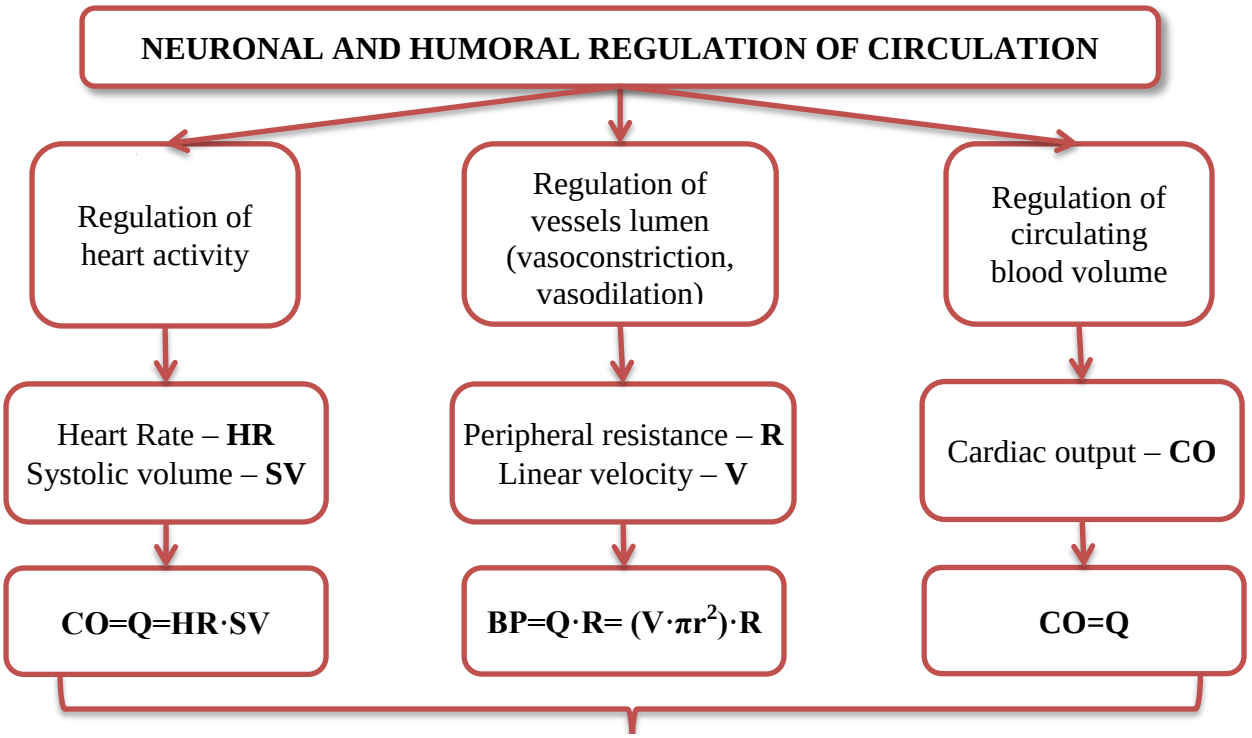
Phlebogram is _____
_____
_____

1)_____
_____

2)_____
_____

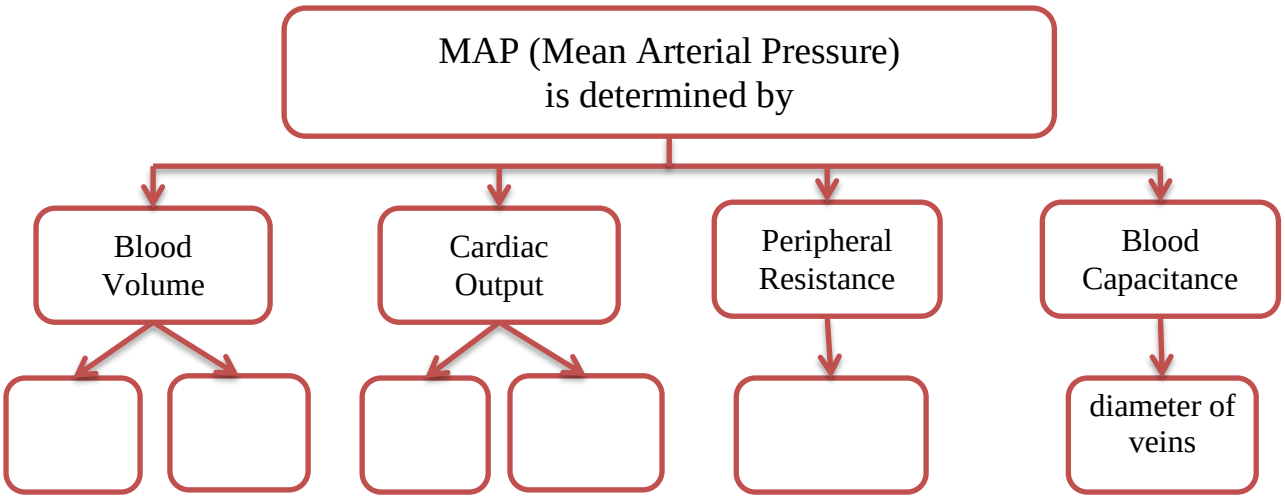
3)_____
_____

10. Regulation of circulation



Correspondence of blood flow to the needs of organs and systems

Task 10.1. *Complete the scheme and define the factors influencing to the arterial pressure*



Task 10.2. *Short-term regulation of BP is mediated by neural reflex. As you know, each reflex arch is composed of these components: receptors, afferent nerves, center, efferent nerves and organ-effector. Complete the table and define the adequate stimulus for each type of receptors*

Receptors	***Afferent nerves***	***Nervous center***	***Efferent nerves***	***Target structures***
1) Baroreceptors				
2) Chemoreceptors				
3) Low pressure receptors				

Task 10.3. *Give characteristic of baroreceptors*

_____

_____

_____

Task 10.4. *Describe short-term regulation of MAP by baroreceptors*

Regulation of MAP in case of hypertension

MAP	***BR***	***Afferent nerve***	***Nerve center***	***Efferent. nerves***	***Target organ and effect***
↑					

Regulation of MAP in case of hypotension

MAP	*BR*	*Afferent nerve*	*Nerve center*	*Efferent nerves*	*Target organ and effect*
↓					

Task 10.5. *Give characteristic of low-pressure receptors and define their role in regulation of BP*

_____

_____

_____

_____

Task 10.6. *Give characteristic of chemoreceptors and define their role in regulation of BP.*

_____

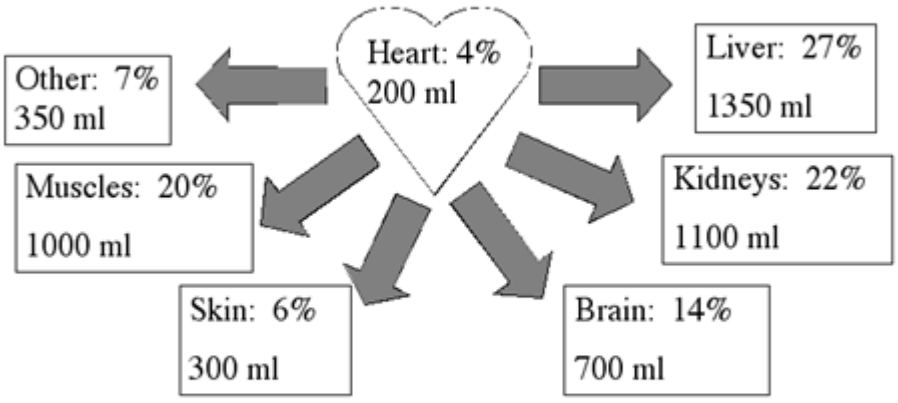
_____

_____

_____

Task 10.7. *Baroreceptors control the MAP by altering the CO and PR. Give definition of cardiac output and define normal value at rest state and in state of physical activity*

Cardiac Output at Rest = _____ L/min



Cardiac Output during Physical Loading = _____ L/min

Cardiac output is _____
_____
_____

Task 10.8. *Give definition of stroke volume and define normal value at rest state and in state of physical activity*
Stroke volume is _____
_____
_____
SV at rest state _____
*SV in physical activity*_____

Task 10.9. *Describe a dependence of cardiac output (CO) and venous return (VR)*

↓ VR → ↓ firing of _____ → ↑_____↑_____↑____

↑ VR → ↑ firing of _____ → ↑_____ (*Bainbridge reflex*) → ↑ ____↑____

Task 10.10. *Describe a dependence of peripheral vascular resistance and BP*
_____
_____
_____
_____
_____

Task 10.11. *Intermediate and long-term control of the circulation.*
Humoral control operating within hours and days:

- *Vasoactive substances are* _____
- *Nonvasoactive substances* _____

Task 10.12. *Complete the table "Vasoactive substances"*

Vasoconstrictors		***Vasodilators***	
substance	***influence***	***substance***	***influence***

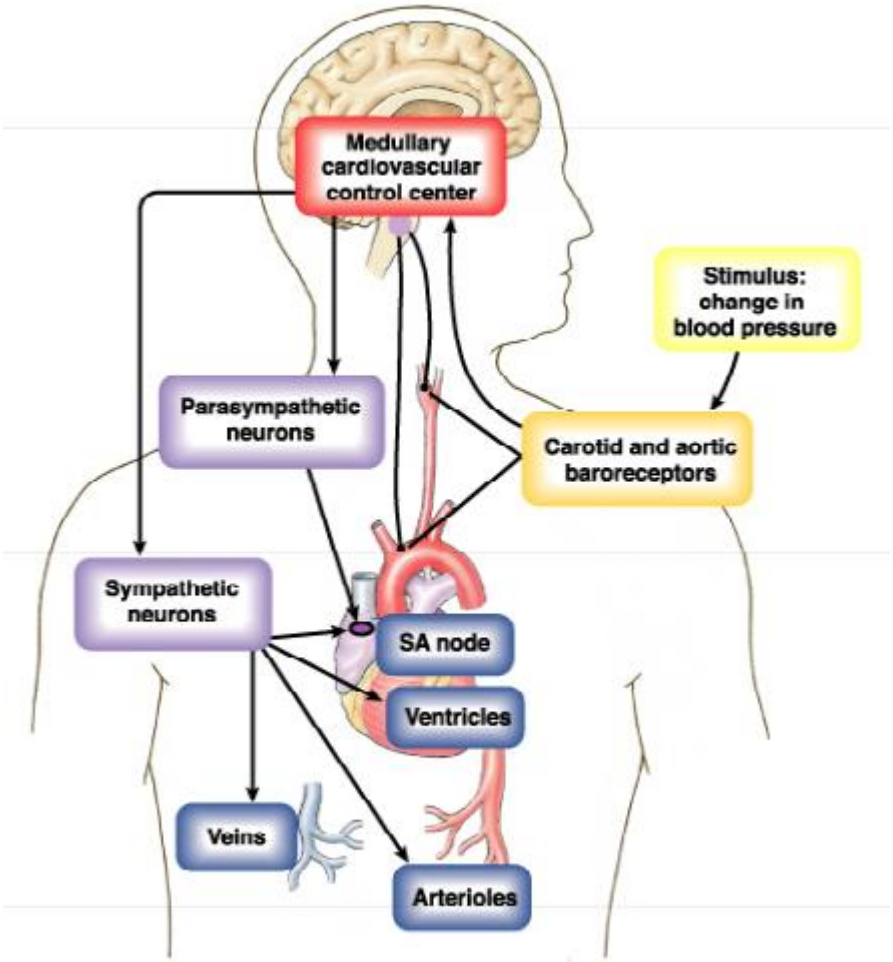
Task 10.13. *Complete table "Renin-Angiotensin-Aldosterone System".*

Definition of RAAS	***Stimulus to activate***	***Effect***

Task 10.14. *Draw the scheme of RAAS activation and influences to the target organs.*

Task 10.15. *Draw the scheme of conditioned regulation of cardiac activity and vascular tone.*

Task 10.16. *Labe the picture. Name the neurotransmitters and receptors to each of the target tissue.*



EFFECTS OF SYMPATHETIC AND PARASYMPATHETIC PATHWAYS ON THE CARDIOVASCULAR SYSTEM

EFFECTOR RESPONSE	ANATOMIC PATHWAY	NEURO-TRANSMITTER	RECEPTOR
Tachycardia	Sympathetic	Norepinephrine	β_1 on cardiac pacemaker
Bradycardia	Parasympathetic	Acetylcholine	M_2 on cardiac pacemaker
Increase cardiac contractility	Sympathetic	Norepinephrine	β_1 on cardiac myocyte
Decrease cardiac contractility	Parasympathetic	Acetylcholine	M_2 on cardiac myocyte
Vasoconstriction in most blood vessels (skin, kidney)	Sympathetic	Norepinephrine	α_1 on VSMCs
Vasodilation in most blood vessels (muscles, myocardium)	Adrenal medulla	Epinephrine	β_2 on VSMCs
Vasodilation in "fight or flight" response	Sympathetic	Acetylcholine	M_2 receptor
Vasodilation in blood vessels of salivary glands and erectile blood vessels	Parasympathetic	Acetylcholine	M_2 receptor

Functional system of respiration

Respiration - is a totality of processes ensuring consumption of oxygen and elimination of carbon dioxide.

Final adaptive result – functional system of respiration supplies all tissues with optimal quantity of oxygen and eliminate carbon dioxide to get optimal gas exchange; it takes part not only in gas exchange but also in maintenance of acid-base balance, water-ion balance, excretion and thermoregulation.

Functional system of respiration consists of:

1. Anatomical apparatus:
- lungs
- auriferous tract

2. Auxiliary apparatus:
- respiratory muscles
- pleural cavity
- blood, heart, vessels

3. Regulatory apparatus:
- humoral mechanism
- neural mechanism

Respiratory system is divided into the 2 sections:

1. upper RS includes: nose, nasal cavity, paranasal sinuses, pharynx
2. lower RS includes: larynx, trachea, bronchi, bronchioles, alveoli.

Importance of the airways

- exchange of gases does not take place
- inspired air is moistened, warmed and freed of dust and microorganisms
- Air is most thoroughly freed of dust when breathing through the nose
- The walls of airways are covered with mucous secretion it gradually moves (7-19 mm/min) toward the nasopharynx by the action of ciliated epithelium of the nasal cavity, trachea and bronchi. Mucus contains a bactericidal substance lysozyme.

Functions of respiratory system includes:

1. Gases exchange between air and circulating blood.
2. Movement of air to the exchange surface of the lungs which are alveoli.
3. Production of sound (vocalization of speech).
4. Provision for olfactory system.

Non respiratory functions

1. Production of heparin, prostaglandins, thromboplastin, histamine, coagulation factors VII and VIII, serotonin.
2. Protective function: antibodies production, phagocytosis, production of lyzocim, interferon.
3. Alter the pH of blood by facilitating alterations in the partial pressure of carbon dioxide
4. Filter out small blood clots formed in veins
5. Filter out gas micro-bubbles occurring in the venous blood stream such as those created during decompression after underwater diving.
6. Influence the concentration of some biologic substances and drugs used in medicine in blood

7. Convert angiotensin I to angiotensin II by the action of angiotensin-converting enzyme
8. Immunoglobulin-A is secreted in the bronchial secretion and protects against respiratory infections.
9. Maintain sterility by producing mucus containing antimicrobial compounds (mucins, lactoferrin, lysozyme, lactoperoxidase)
10. Ciliary escalator action is an important defence system against air-borne infection. (the dust particles and bacteria in the inhaled air are caught in the mucous layer present at the mucosal surface of respiratory passages and are moved up towards pharynx by the rhythmic upward beating action of the cilia)
11. Provide airflow for the creation of vocal sounds.
12. The lungs serve as a reservoir of blood in the body. The blood volume of the lungs is about 450 milliliters on average, about 9 percent of the total blood volume of the entire circulatory system. This quantity can easily fluctuate from between one-half and twice the normal volume. Loss of blood from the systemic circulation by hemorrhage can be partially compensated for by shunting blood from the lungs into the systemic vessels
13. Thermoregulation

Protective respiratory reflexes

- Stimulation of the nasopharynx, larynx and trachea receptors by dust particles and accumulated mucus causes ***cough*** which is necessary to remove the foreign material from the respiratory tract before it reaches the lungs
- stimulation of the receptors of nasal cavity causes ***sneezing***. The function of sneezing is to expel mucus containing foreign particles or irritants and cleanse the nasal cavity.

The cough reflex has both sensory (afferent) and motor (efferent) components:

1. mechanical and chemical stimuli act to the pulmonary irritant receptors (cough receptors) in the epithelium of the respiratory tract, receptors are located mainly on the posterior wall of the trachea, pharynx, and at the main carina, the point where the trachea branches into the main bronchi and are less abundant in the distal airways, and absent beyond the respiratory bronchioles.

2. Impulses travel via the vagus nerve (CN X), to the medulla of the brain.

3. The efferent neural pathway then follows via the vagus and superior laryngeal nerves to the glottis, external intercostals, diaphragm, and other major inspiratory and expiratory muscles.

Sneezing

1. Foreign particles or sufficient external stimulants reach the nasal mucosa.
2. Release of histamines, which irritate the nerve cells in the nose.
3. Signals being sent to the brainstem through the trigeminal nerve .
4. Initial signal activates the pharyngeal and tracheal muscles and creates a large opening of the nasal and oral cavities, resulting in a powerful release of air and bioparticles.

The sneeze reflex involves contraction of a number of different muscles and muscle groups throughout the body, typically including the eyelids.

Respiration is a process of O_2 utilization in metabolic reactions which is possible through following stages of respiration:

1. External respiration:

1.1. Gas exchange between alveoli and external environment – pulmonary ventilation

1.2. Exchange of gases in the lungs between blood of lesser circulation and alveolar space

2. Transport of gases by blood

3. Internal respiration:

3.1. Gas exchange between blood and tissues

3.2. Utilization of oxygen in the tissues and elimination of carbon dioxide.

Respiratory cycle includes inspiration, expiration and pause.

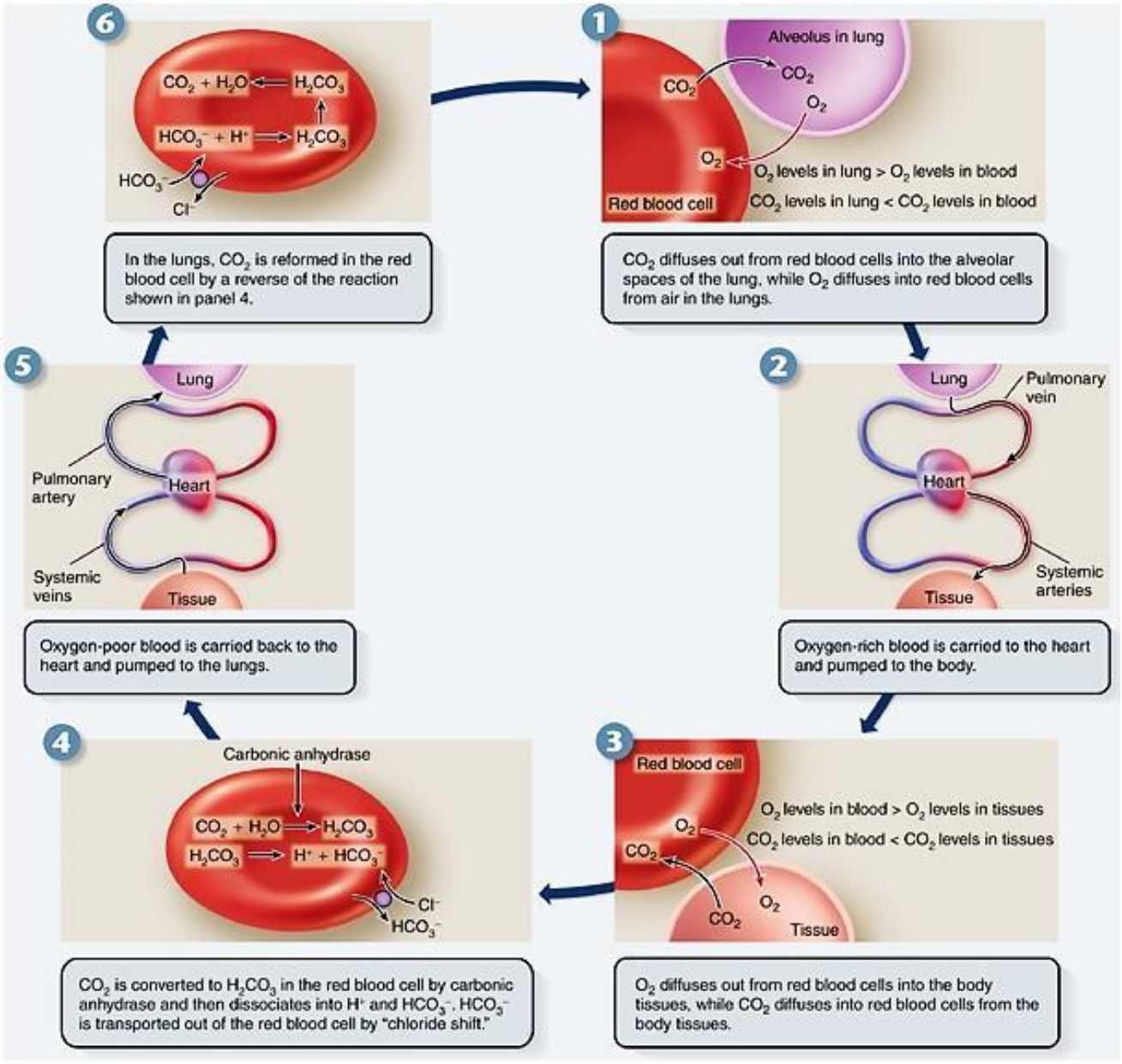


Figure 1. Stages and processes of respiration

Oxygen Respiratory chain:

1. Transport of Oxygen into the alveoli during inspiration.
2. Diffusion of Oxygen into the blood.
3. Oxyhemoglobin formation.
4. Transport of Oxygen from lesser circulation to the tissues.
5. Dissociation of Oxyhemoglobin.
6. Diffusion of Oxygen into the tissues
7. Utilization of oxygen in the tissues.

Carbon dioxide respiratory chain:

1. Carbon dioxide formation in the tissues.
2. Diffusion of Carbon dioxide into the blood.
3. Carbaminohemoglobin formation.
4. Transport of Carbon dioxide from greater circulation to the lungs.
5. Dissociation of Carbaminohemoglobin.
6. Diffusion of Carbon dioxide into the alveolar space.
7. Elimination of carbon dioxide.

Pressure and Flow

Airflow is governed by the same principles of flow, pressure, and resistance as blood flow. The pressure that drives respiration is **atmospheric (barometric) pressure**—the weight of the air above us. At sea level this pressure, called *1 atmosphere* (1 atm), is enough to force a column of mercury 760 mm up an evacuated tube; therefore, 1 atm - 760 mmHg. This is the average atmospheric pressure at sea level; it fluctuates from day to day and is lower at higher altitudes. One way to change the pressure of a gas, and thus to make it flow, is to change the volume of its container.

Boyle's law states that *the pressure of a given quantity of gas is inversely proportional to its volume* (assuming a constant temperature). If the lungs contain a quantity of gas and lung volume increases, their **intrapulmonary pressure**—the pressure within the alveoli—falls. If lung volume decreases, intrapulmonary pressure rises.

To make air flow into the lungs, it is necessary only to lower the intrapulmonary pressure below the atmospheric pressure. Raising the intrapulmonary pressure above the atmospheric pressure makes air flow out again. These changes are created as skeletal muscles of the thoracic and abdominal walls change the volume of the thoracic cavity.

Pulmonary ventilation is a physical movement of air into and out of the lungs. The movement of air depends upon a few things:

1. ***Boyle's law*** – it says that pressure and volume are inversely related.

↑ *volume* ---------- ↓ *pressure*

↓ *volume* ---------- ↑ *pressure*

We use this principle to understand how breathing actually happens. Relationship between intrapulmonary pressure and atmospheric pressure determines direction of air flow.

3. Pressure inside **(*intrapulmonary pressure***) and outside are equal, so no air movement occurs (between each respiratory cycle)

$$P\ out = P\ in$$

4. ***Contraction of diaphragm*** it moves down so
↑ volume ---- ↓ pressure and air flows inside ---- inspiration

$$P\ out \geq P\ in$$

5. ***Diaphragm relaxing*** --- it will push up the lungs so
↓ volume ---- ↑ pressure so air flows out ---- expiration

$$P\ out \leq P\ in$$

Each lung is covered by pleura. Pleura is serous membrane lining the pleural cavity which made by parietal and visceral pleura. A narrow space between the layers of the visceral and parietal pleura contains serous fluid which resembles lymph in composition.

The pleurae and pleural fluid have three functions:

1. **Reduction of friction.** Pleural fluid acts as a lubricant that enables the lungs to expand and contract with minimal friction. In some forms of *pleurisy*, the pleurae are dry and inflamed and each breath gives painful testimony to the function that the fluid should be serving.

2. **Creation of pressure gradient.** Pressure in the pleural cavity is lower than atmospheric pressure; as explained later, this assists in inflation of the lungs.

3. **Compartmentalization.** The pleurae, mediastinum, and pericardium compartmentalize the thoracic organs and prevent infections of one organ from spreading easily to neighboring organs.

Pressure in pleural cavity is called ***intrapleural pressure*** which is below atmospheric. Atmospheric pressure is 760 mm Hg; negative pressure in the pleural space is –4 - –8 mm. Hg (so, value of intrapleural pressure is 752 – 756 mm.Hg).

During inspiration the volume of the thoracic cavity increases because of contraction of inspiratory muscles. The pleural pressure becomes 'more negative'. At the end of quiet inspiration it reduces to –6 mm Hg. In deep inspiration, the intrapleural pressure can be reduced to –20 mm Hg. At the end of a quiet expiration, when almost all the respiratory muscles are relaxed, the pleural pressure (P_{pl}) approximates –3 mm Hg. The alveolar pressure (P_A) at the same time is equal to atmospheric. During forced expiration it can become positive but still it is below alveolar pressure by the magnitude created by the elastic recoil force of the lungs. The difference P_A - Ppl = 3 mm Hg is known as the ***transpulmonary pressure*** (P_L). Thus, ***pressure in the pleural space is less than that in the alveoli by the magnitude created by the elastic recoil force of the lungs.***

Owing to increase in transpulmonary pressure the lungs become expanded, their volume increases at the expense of atmospheric air.

When the inspiratory muscles are relaxed, the elastic forces of expanded lungs and abdominal walls reduce the transpulmonary pressure and lung volume decreases, thus giving rise to expiration. So $P_{pl} = P_{alv} – P_{elas}$

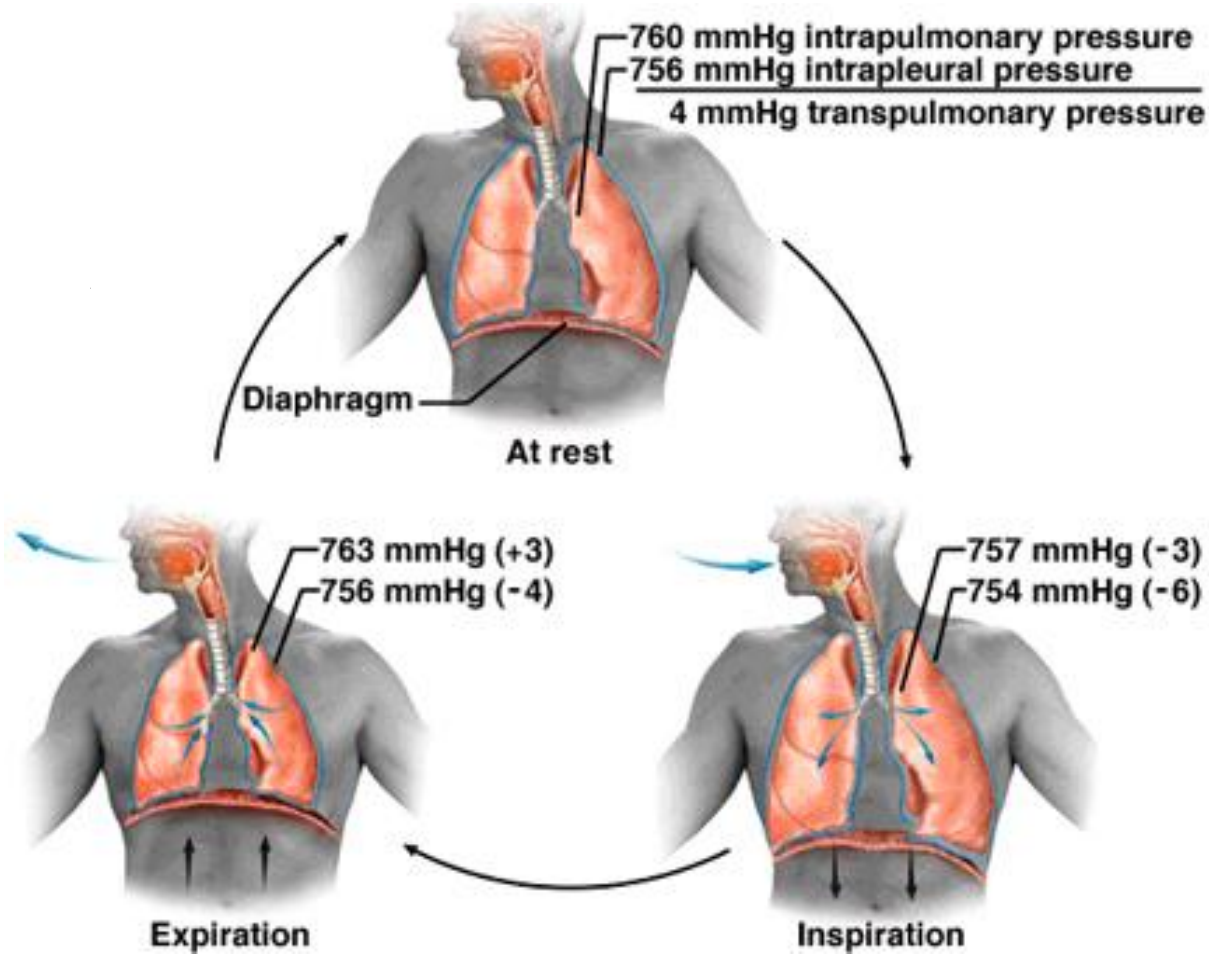


Figure 2. The cycle of pressure changes causing ventilation of the lungs

Elastic properties of the lungs.

The elastic recoil force of the lungs is conditioned by two factors:

1) surface tension in the alveolar fluid film lining the alveoli

2) tissue elasticity of the alveolar walls due to the presence in them of elastic fibres.

Removal of forces of surface tension (by introducing saline solution into the lungs) reduces the elastic recoil force of the lungs by two-thirds.

In the alveolar wall there is an aqueous layer contains the so-called surfactants i.e. surface active substances with low surface tension, it is formed by special alveolar cells, the pneumocytes of type II.

Surfactant reduces surface tension, so that the alveoli in the lungs are able to expand. Without surfactant, the wet surfaces of the alveoli in lungs would stick together and lungs would not be able to expand - so, you would not be able to breath.

The alveoli are the tiny sacs in the lungs and are have moist surfaces. Wet surfaces stick together due to surface tension, which is caused by the attraction that water has for itself.

About three to four weeks before birth, lungs begin to produce surfactant. When you are born and take your first breath, you have to open the fluid-filled alveoli to allow air in. Without surfactant, this would be nearly impossible, which is why very premature infants have so much difficulty breathing.

Following functions except mentioned above are typical for surfactant:

1) antibacterial effect;
2) protection of alveolar wall;
3) decreases permeability of pulmonary membrane (prevent edema of lungs);
4) facilitate diffusion of oxygen.

Some medical conditions cause loss of surfactant. Reasons for surfactant deficient:

- insufficiency of pulmonary circulation;
- acidosis;
- fever;
- artificial pulmonary ventilation;
- narcotic drugs (that is why after surgical operation high risk of pneumonia development);

In pulmonary edema, fluid from the blood invades and floods the alveoli, this causes dilution and washout of the surfactant, so that alveoli are more likely to collapse. Inflammation of the lungs also causes reduced surfactant production, so again the alveoli collapse due to increased surfaced tension.

Mechanism of inspiration

1. Inspiration results from contraction of the inspiratory muscles:
   - The muscular part of the diaphragm, on contraction of its lateral parts, it is pulled downward. During quiet inspiration the diaphragm descends by approximately 1.5 cm to increase vertical dimension of the thoracic cavity.
   - Contraction of external intercostals and intercartilaginous parts of the internal intercostal muscles causes displacement of the six lower ribs, which increases the volume of the thoracic cavity.
2. The volume of the lungs is increased because of action of atmospheric pressure just from one side through auriferous tract.
3. Transport of air into the lungs because alveolar pressure decreases about 1,5 mm. Hg (gradient of pressure).

Mechanism of expiration

During quiet breathing expiration proceeds in a passive manner at the expense of elastic energy accumulated during the preceding inspiration.

1. Relaxation of inspiratory muscles.
2. The volume of the thoracic cavity is decreased.
3. The volume of the lungs is decreased.
4. Passage of air from the lungs into the external environment because alveolar pressure increases becomes more than atmospheric pressure

On deep expiration the expiratory muscles contract, which is known as active expiration. The abdominal muscles (the external and internal oblique, transversus abdominis and rectus abdominis) contract in active expiration.

On contraction, the internal intercostal muscles cause the ribs to descend, their sides come closer to each other since the moment of force is greater for the upper than for the lower rib.

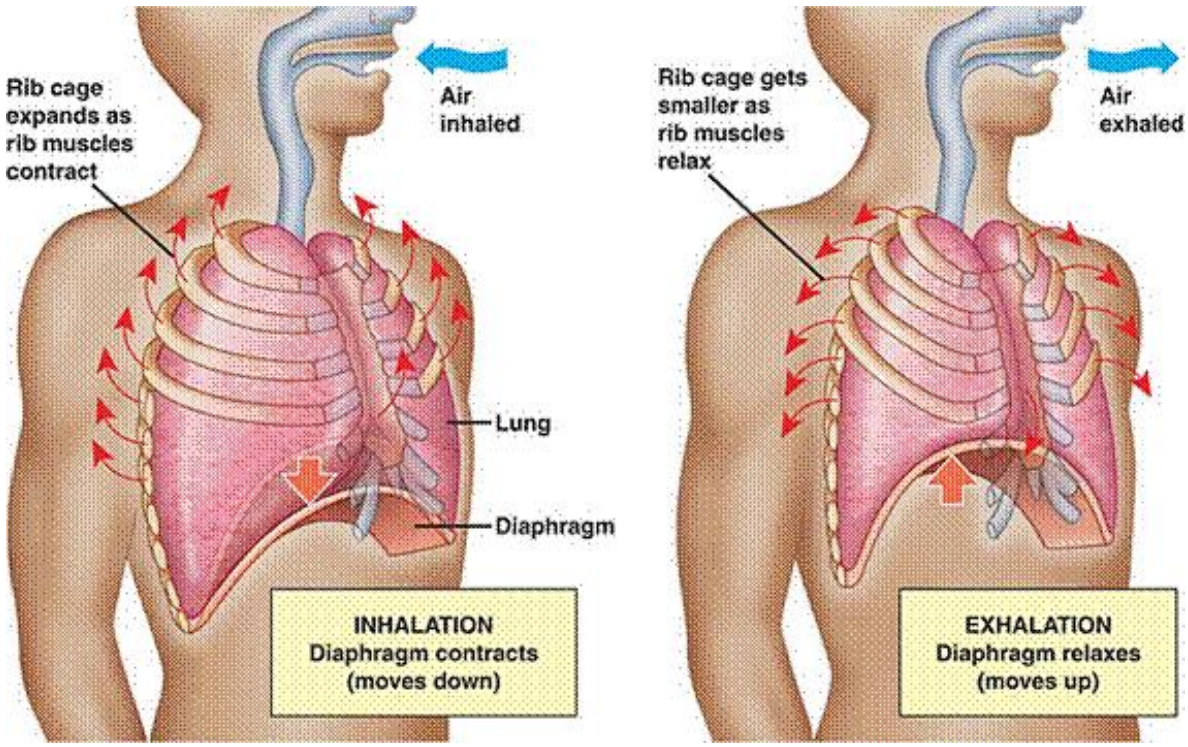


Figure 3. Mechanism of respiratory movements

Research of external respiration parameters

Simple method for studying pulmonary ventilation is to record the volume movement of air into and out of the lungs, a process called *spirometry*.

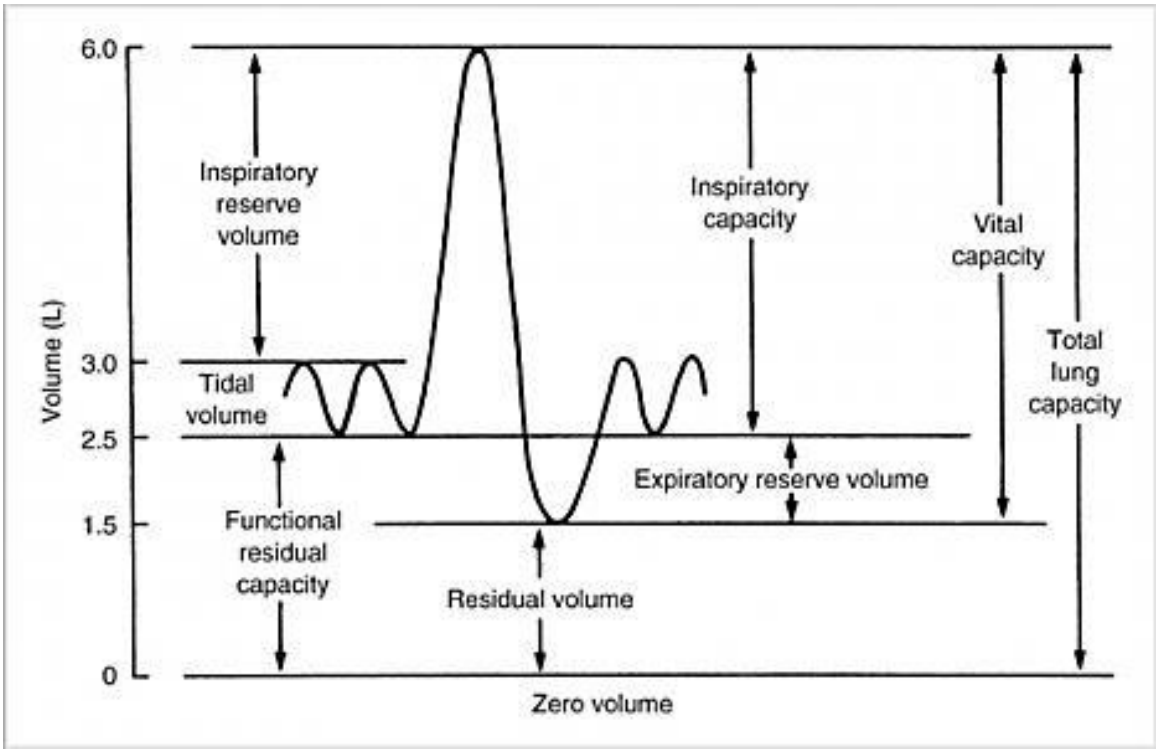


Figure 4. Spirogram: respiratory volumes and capacities

Spirogram is a curve indicating changes in lung volume under different conditions of breathing. For ease in describing the events of pulmonary ventilation, the air in the lungs has been subdivided into the 4 volumes and 3 capacities.

Lung volumes and ***lung capacities*** refer to the volume of air associated with different phases of the respiratory cycle. Lung volumes are directly measured; Lung capacities are inferred from lung volumes.

The average total lung capacity of an adult human male is about 6 litres of air, but only a small amount of this capacity is used during normal breathing.

The average human respiratory rate is 30-60 breaths per minute at birth, decreasing to 12-20 breaths per minute in adults.

Lungs volumes

1. **TV - Tidal volume**: that volume of air moved into or out of the lungs during quiet breathing – 500 ml

2. **RV - Residual volume**: the volume of air remaining in the lungs after a maximal exhalation – 1,2 L

3. **ERV - Expiratory reserve volume**: the maximal volume of air that can be exhaled by the forceful expiration after the end of normal expiration – 1,3 L

4. **IRV - Inspiratory reserve volume**: the maximal volume that can be inhaled by the forceful inspiration above the normal inspiration – 1,5-2,5 L

Lungs Capacities:

1. VC – Vital capacity is a maximal volume of air which can be expired after maximal inspiration.

$$VC = TLC - RV \text{ or } VC = TV + IRV = ERV \text{ (men – 3,5 L, women – 3,4 L)}$$

2. FRC - Functional residual capacity is volume of air remains in the lungs after quiet expiratory.

$$FRC = RV + ERV \text{ (2-3 L)}$$

3. TLC - Total lung capacity: the volume in the lungs at maximal inflation

$$TLC = VC + RV \text{ (4-6 l)}$$

4. Minute pulmonary ventilation (MPV) – Minute or total ventilation is the amount of air moved in or out of the lungs per minute. Quantitatively, the amount of air breathed in per minute is slightly greater than the amount expired per minute. MPV is also the sum of two other ventilations, alveolar ventilation and dead space ventilation.

5. Minute alveolar ventilation (MAV) – Alveolar ventilation is the volume of air breathed in per minute that: 1) reaches the alveoli and 2) takes part in gas exchange. Alveolar ventilation is often misunderstood as representing only the volume of air that reaches the alveoli. Physiologically, MAV is the volume of alveolar air/minute that takes part in gas exchange (transfer of oxygen and carbon dioxide) with the pulmonary capillaries. Air that reaches the alveoli, but for one reason or other does not take part in

gas exchange, is not considered part of VA (for example, air that goes to an unperfused alveolus). Such alveolar regions lacking gas exchange constitute alveolar dead space. Clinically, the terms hyperventilation and hypoventilation apply to alveolar ventilation only.

6. Dead space ventilation is that part of minute ventilation that does not take part in gas exchange; it is also referred to as "wasted ventilation". Dead space ventilation (VD) includes: 1) air that enters only conducting airways (referred to as anatomic dead space) and 2) air that reaches alveoli but does not exchange carbon dioxide or oxygen with the capillary blood. The combined volume of these two areas is often referred to as physiologic dead space.

EXCHANGE OF GASES IN THE LUNGS

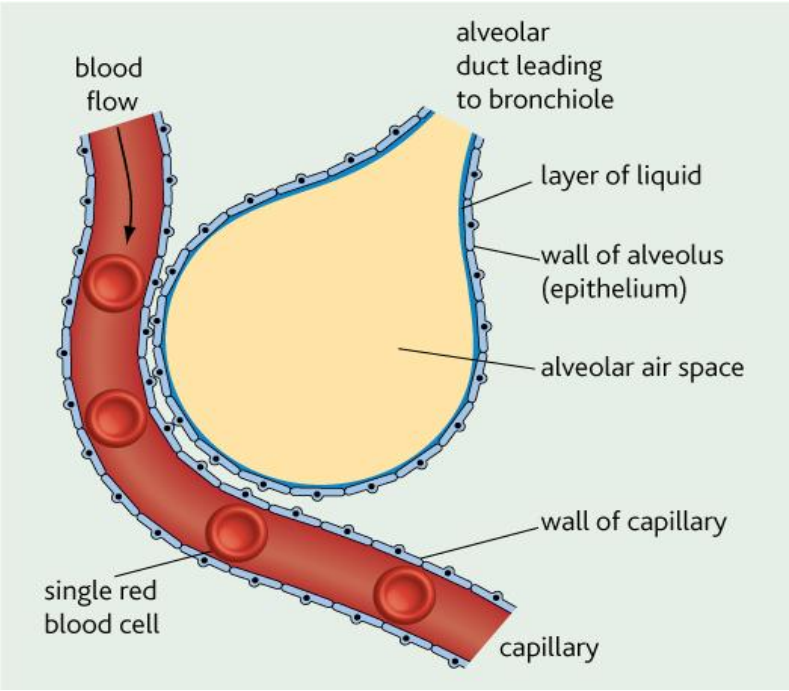
One human lung averages 300 mln of alveoli. Most of the outer surface of alveoli communicates with lung capillaries.

Exchange of gases in the lungs occurs as a result of diffusion of oxygen from the alveolar air into the blood (about 500 1 per day) and of carbon dioxide from the blood into the alveolar air (approximately 430 1 per day).

Diffusion occurs due to:

1. partial pressure difference of these gases in the alveolar air
2. blood tension of gases
3. small diffusion distance between alveolar space and capillary
4. surface area of all alveoli
5. coordination of blood flow and diffusion
6. Solubility of the gases.

Diffusion rate directly proportional to partial pressure gradient, surface area of pulmonary membrane and reversed proportional to thickness of pulmonary membrane. The thickness of the lung membrane is 1-3 mkm, diffusion rate is 0.3 s, S – 50-80 m^2.



During diffusion oxygen passes thought following layers and they are:

1. surfactant
2. pneumocytes
3. basement membrane
4. interstitial fluid
5. basement membrane of capillary
6. endothelial cells
7. plasma
8. RBC
9. Hb

Figure 5.Respiratory membrane

There are 3 types of alveolar cells:

- type I – respiratory epitheliocytes
- type II – septal cells – produce surfactant – oily secretion – decreases surface area of alveoli so they will not collapse.
- alveolar macrophages – duct cells - wander the lumens of the alveoli and the connective tissue between them. They are the last line of defense against inhaled matter. Particles over 10 _m in diameter are usually strained out by the nasal vibrissae or trapped in the mucus of the upper respiratory tract. Most particles 2 to 10 _m in diameter are trapped in the mucus of the bronchi and bronchioles, where the airflow is relatively slow, and then removed by the mucociliary escalator. Many particles smaller than 2 _m, however, make their way into the alveoli, where they are phagocytized by the macrophages. In lungs that are infected or bleeding, the macrophages also phagocytize bacteria and loose blood cells. Alveolar macrophages greatly outnumber all other cell types in the lung; as many as 50 million perish each day as they ride up the mucociliary escalator to be swallowed.

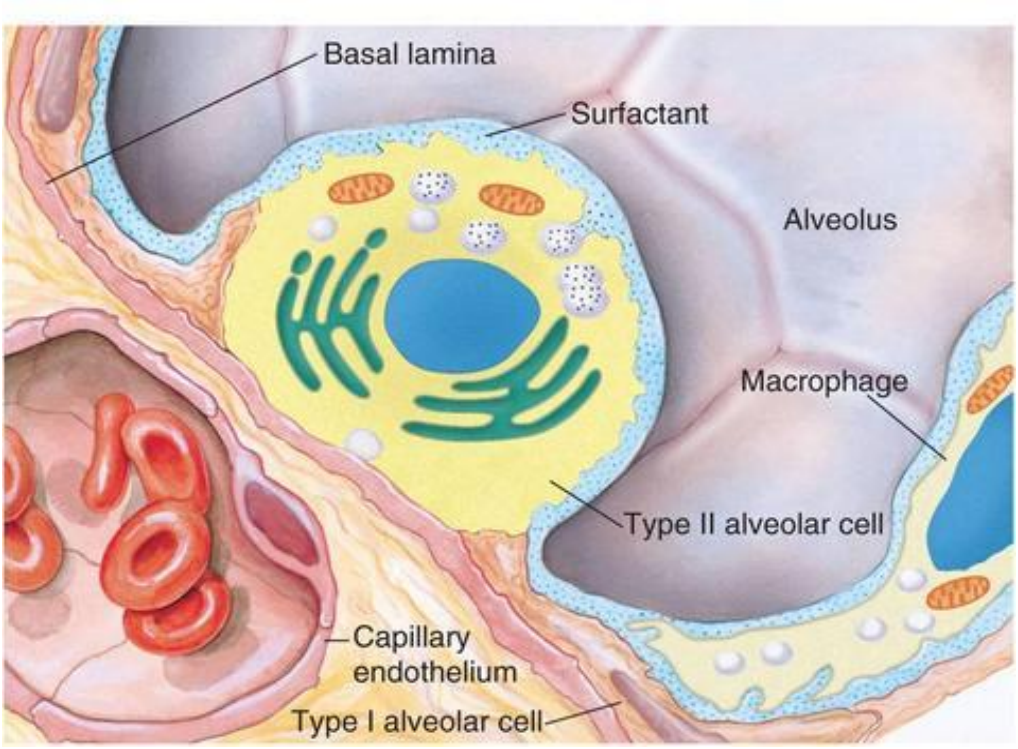


Figure 6. Types of alveolar cells.

Concentration gradients of the gases

Table 1. Atmospheric air, expired air and alveolar air have different composition (%)

Component	Atmospheric air	Expired air	Alveolar air
O_2 (%)	20,93	16	14
CO_2 (%)	0,04	4	5,5
N_2 (%)	78,5	74,9	74,5
Water vapour	0,5	5,5	5,6

Partial pressure of gas is part of pressure in gas mixture (760 mm Hg) taken for one gas and it is proportional to the percentage gas content and the total pressure of a mixture.

In the alveolar partial pressure it should be kept in mind that here the water vapour pressure is about 47 mm Hg at 37°C

$$(760 – 47) \times 14 / 100 = 100 \text{ mm Hg.}$$

At the CO_2 content of 5.5 %, its partial pressure will be 39.2 mm Hg (about 40 mm Hg).
!!! The O_2 and CO_2 partial pressures in the alveoli are the driving force for diffusion of their molecules through the alveolar membrane into the blood.

Table 2. Parameters of O_2

Parameter	Alveolar space	Venous blood	Arterial blood	Tissues
O_2, %	14	6-8	13	2-4
PO_2 (mm Hg)	100	40	100	20-40
HbO_2, %	---	60	96	----

Table 3. Parameters of CO_2

Parameter	Tissues	Arterial blood	Venous blood	Alveolar space
CO_2, %	2-4 (6)	5,5	5,7	5,5
PCO_2 (mm Hg)	60	40	46	40
$HbCO_2$, %	-------	52	58	-----

Diffusion of O_2 is provided by partial pressure difference which is about 60 mm Hg; for CO_2 it is only about 6 mm Hg. Passage of CO_2 into the alveolar air at a relatively small pressure difference is explained by high diffusing capacity of the lungs for this gas.

Ventilation-Perfusion Relationship

The relationship between alveolar ventilation (MAV) and blood flow via the pulmonary circulation (or lung perfusion, Q) is of paramount importance for exchange of gases in the lungs.

MAV/Q is close to 0.8. Hence, alveolar ventilation is slightly less than lung perfusion per unit of time.

The pattern of ventilation and perfusion of various parts of the lungs is non-uniform. This can be examined by the following:

1) Presence of the anatomical dead space;
2) The effective alveolar space (the ventilated and perfused alveoli);
3) Ventilated but unperfused alveoli (the alveolar dead space);
4) The unventilated but perfused alveoli (the alveolar veno-arterial shunt).

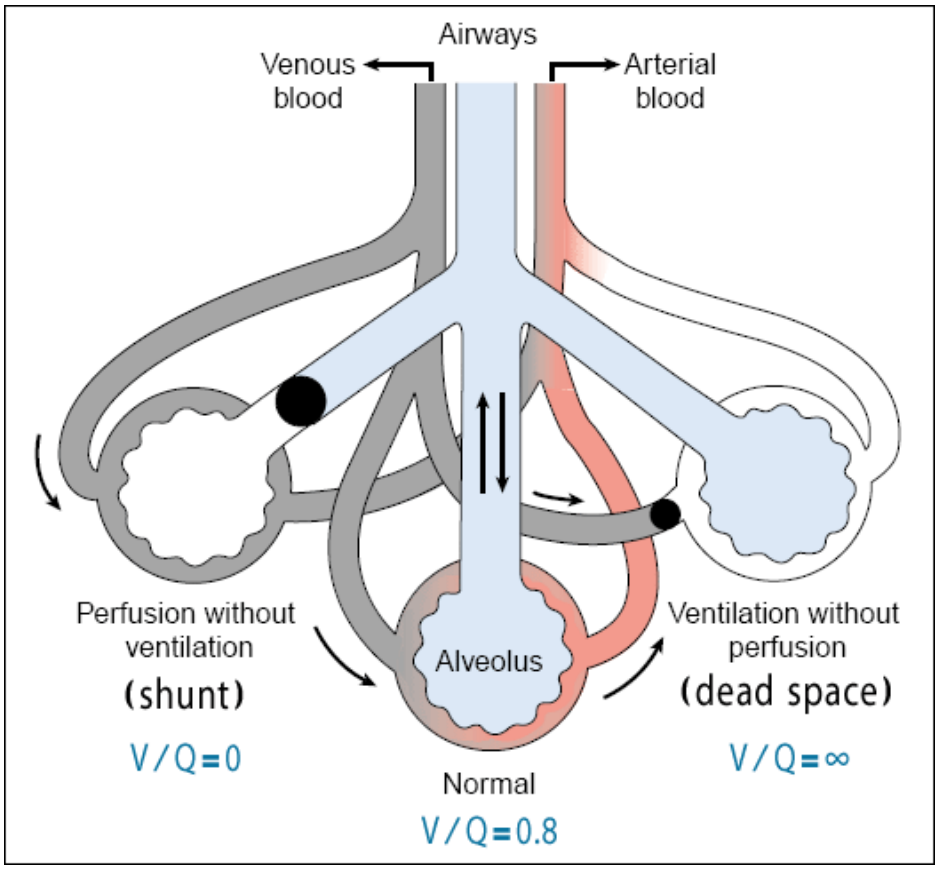


Figure 7. Ventilation and perfusion in lungs alveoli

Oxygen Transport

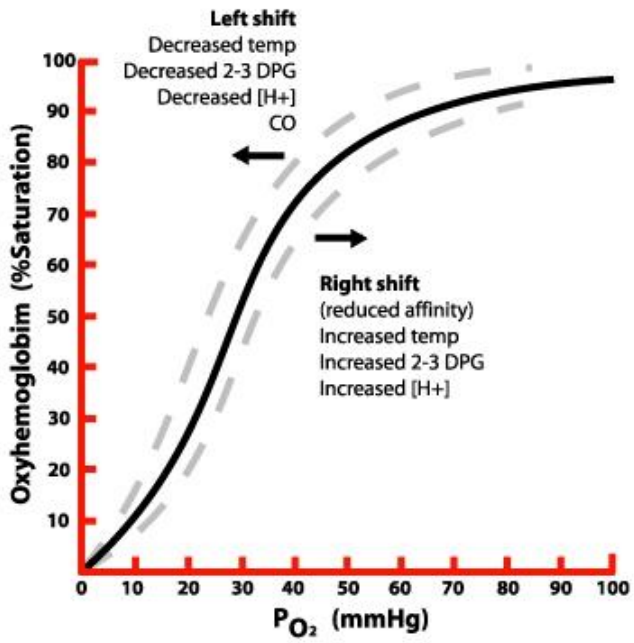
Only 0.3 ml of oxygen is dissolved per 100 ml of blood at 37°C. Oxygen dissolved in blood plasma of lung capillaries diffuses into erythrocytes. Here it is immediately bound by haemoglobin to form oxyhaemoglobin.

Oxygen capacity of blood is 190ml/L of blood (1g Hb binds to 1.36 ml O_2). In alveolar capillaries with adequate ventilation and perfusion practically all haemoglobin is converted to oxyhaemoglobin.

The concentration of oxygen in arterial blood, by volume, is about 20 ml/dL. About 98.5% of this is bound to hemoglobin and 1.5% is dissolved in the blood plasma. Each heme group can bind 1 O_2 to the ferrous ion at its center; thus, one hemoglobin molecule can carry up to 4 O_2. If even one molecule of O_2 is bound to hemoglobin, the compound is called **oxyhemoglobin (HbO_2)**, whereas hemoglobin with no oxygen bound to it is **deoxyhemoglobin (HHb).** When hemoglobin is 100% saturated, every molecule of it carries 4 O_2; if it is 75% saturated, there is an average of 3 O_2 per hemoglobin molecule; if it is 50% saturated, there is an average of 2 O_2 per hemoglobin; and so forth. The poisonous effect of carbon monoxide stems from its competition for the O_2 binding site. The relationship between hemoglobin saturation and PO_2 is shown by an *oxyhemoglobin dissociation curve*.

Oxyhaemoglobin dissociation curve.

At O_2 tension equal to zero, blood contains only deoxyhaemoglobin; as the O_2 tension increases, the amount of oxyhaemoglobin increases too.



When the O_2 tension rises to 40 mm Hg, the level of oxyhaemoglobin grows particularly rapidly (to 75 per cent). The O_2 saturation (SO_2 of haemoglobin at 60 mm Hg reaches 90 per cent but with further increase in O_2 tension full saturation of haemoglobin proceeds very slowly.

The sloping part of the curve corresponds to high O_2 tension (more than 60 mm Hg) and provides evidence that the level of oxyhaemoglobin under these conditions does not depend much on the O_2 tension and partial pressure in inspired and alveolar air. For example, in ascent to the height of 2 km above sea level, atmospheric pressure falls from 760 to 600 mm Hg, the O_2 partial pressure in the alveolar air is reduced from 105 to 70 mm Hg, while the level of oxyhaemoglobin decreases by only 3 per cent. Thus, the upper part of the curve reflects the ability of haemoglobin to bind large amounts of O_2, despite a moderate decrease in its partial pressure in inspired air. Tissues are sufficiently supplied with oxygen even in these conditions.

A steep part of the curve corresponds to O_2 tension which is inherent in body tissues (35 mm Hg and lower). Dissociation of oxyhaemoglobin is higher and sometimes almost complete in tissues that consume much oxygen, e.g. working muscles, liver, kidneys. In tissues with mild intensity of oxidation processes dissociation of the greater part of oxyhaemoglobin does not occur. When tissues are switched from rest to activity (muscle contraction, secretory activity of glands), favourable conditions are created to enhance oxyhaemoglobin dissociation and O_2 supply to the tissues.

Haemoglobin affinity for oxygen reflected by the oxyhaemoglobin dissociation curve is not constant and is influenced by the following factors.

1) Erythrocytes contain ***2,3-disphosphoglycerate*** (2,3-DPG) whose content is increased, in particular when the blood O_2 tension is reduced. A molecule of 2,3-DPG can enter the central part of a haemoglobin molecule to decrease haemoglobin affinity for oxygen. The curve is shifted to the right; oxygen enters tissues with more ease.
2) Haemoglobin affinity for oxygen decreases with increase in the ***CO_2*** and ***H+*** concentration (Bohr effect). In these circumstances the curve is also shifted to the right.
3) ***Temperature*** rise has the same effect on dissociation. In tissues with high metabolic rate the concentration of CO_2 and acid products increases and temperature rises. As a result, dissociation of oxyhaemoglobin is enhanced.

Oxygen content of the blood

The O_2 content in venous blood at rest is about 120 ml/L. The part of O_2 consumed by the tissues from arterial blood is known as the ***oxygen utilization coefficient***. It can be determined by dividing the arteriovenous oxygen difference by O_2 content in arterial blood and multiplying by 100.

For instance, (200 – 120) / 200 × 100 = 40 per cent.

At rest, the O_2 utilization coefficient varies from 30 to 40 per cent and increases to 50-60 per cent in muscular exertion.

Carbon Dioxide Transport

Carbon dioxide is transported in three forms—as carbonic acid, carbamino compounds, and dissolved gas:

1. About 90% of the CO_2 is hydrated (reacts with water) to form **carbonic acid,** which then dissociates into bicarbonate and hydrogen ions.
2. About 5% binds to the amino groups of plasma proteins and hemoglobin to form **carbamino compounds** – chiefly, **carbaminohemoglobin (HbCO$_2$)**. The reaction with hemoglobin can be symbolized Hb + CO_2 → $HbCO_2$. Carbon dioxide does not compete with oxygen because CO_2 and O_2 bind to different sites on the hemoglobin molecule – oxygen to the heme moiety and CO_2 to the polypeptide chains. Hemoglobin can therefore transport both O_2 and CO_2 simultaneously.
3. The remaining 5% of the CO_2 is carried in the blood as **dissolved gas**, like the CO_2 in soda pop.

The relative amounts of CO_2 exchanged between the blood and alveolar air differ from the percentages just given. About 70% of the *exchanged* CO_2 comes from carbonic acid, 23% from carbamino compounds, and 7% from the dissolved gas. That is, blood gives up the dissolved CO_2 gas and CO_2 from the carbamino compounds more easily than it gives up the CO_2 in bicarbonate.

Venous blood may yield about 58 volume per cent (580 ml/L) of CO_2 in which about 2.5 volume per cent are transported in physical solution in the blood. The

remainder is chemically bound and is contained in the form of bicarbonates (51 volume per cent) and carbaminohaemoglobin (4.5 volume per cent).

Carbon dioxide is produced in cells and continuously diffuses into the blood of tissue capillaries. In erythrocytes it is combined with water to form carbonic acid (H_2CO_3). This process is catalyzed (accelerated by 20 000 times) by the enzyme carbonic anhydrase. Since this enzyme is present in erythrocytes, while blood plasma is devoid of it, the CO_2 hydration occurs only in erythrocytes. Depending on the CO_2 tension, carbonic anhydrase catalyzes both the production of carbonic acid and its breakdown into CO_2 and water (in lung capillaries).

Some of the CO_2 molecules are combined in erythrocytes with globin amino groups to form carbaminohaemoglobin.

Owing to these processes of binding, the CO_2 tension in erythrocytes is not high. Therefore, new and new amounts of CO_2 diffuse inside the erythrocytes. Thus, concentration of HCO_3^- ions produced in bicarbonate dissociation is increased. The erythrocyte membrane is highly permeable to anions, so part of HCO_3^- ions enters the blood plasma. Ions of Cl^- enter erythrocytes from the plasma in exchange for HCO_3^- ions. The negative charge of Cl^- ions is equilibrated by K^+ ions. The blood plasma content of sodium bicarbonate ($NaHCO_3$) is enhanced.

Haemoglobin serves as the source of cations (K^+) which are necessary for H_2CO_3 binding in the form of bicarbonates.

Thus, the additional amounts of potassium bicarbonate and carbaminohaemoglobin are produced in the erythrocytes of tissue capillaries, while the amount of sodium bicarbonate enhances in the blood plasma. In this form CO_2 is transported to the lungs.

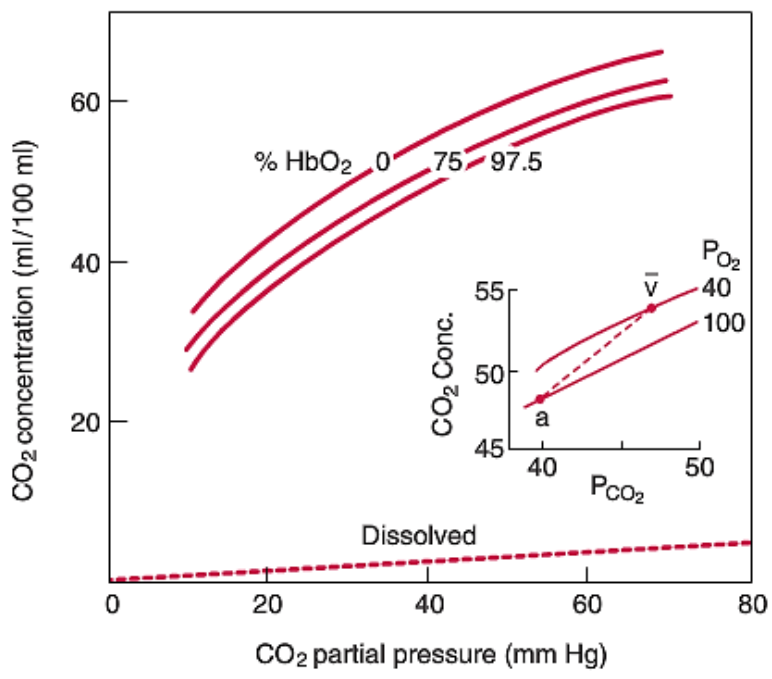


Figure 8.

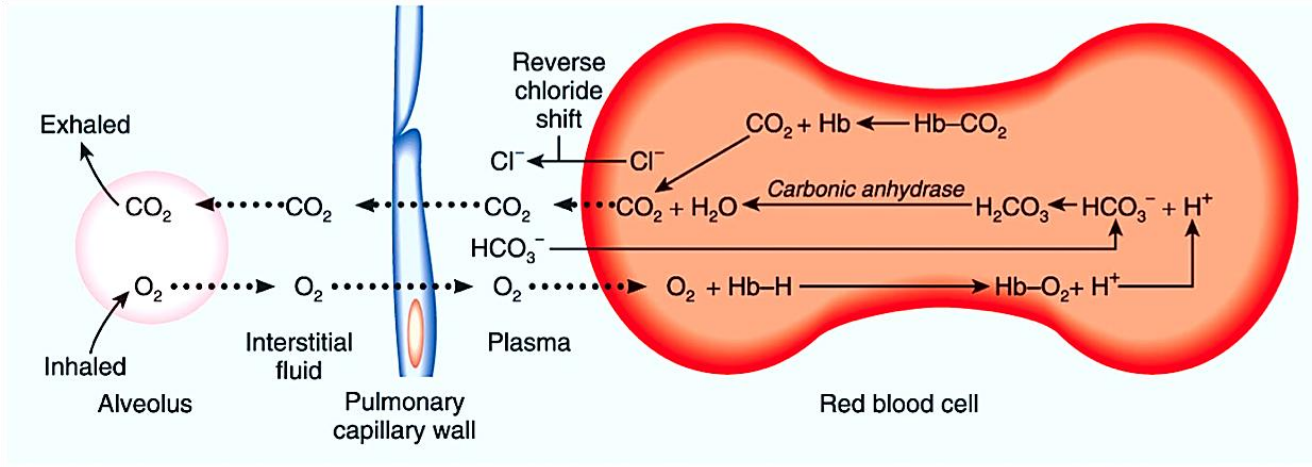
CO_2 Dissociation Curve

Much more linear than the O_2 dissociation curve; Curve moves rightwards with deoxygenation - Haldane Effect - due to:

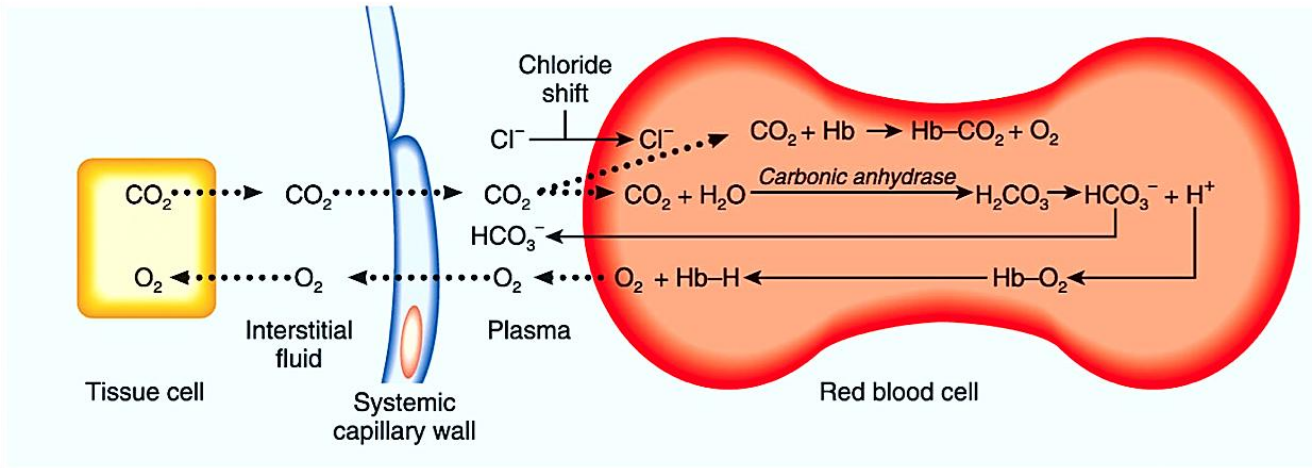
- *Improved ability of reduced Hb to mop up H^+ ions when carbonic acid dissociates;*
- *Improved ability of reduced Hb to form carbaminohaemoglobin.*

The CO_2 tension is decreased in lung capillaries. Carbaminohaemoglobin gives off CO_2. Production of oxyhaemoglobin occurs at the same time and its dissociation constants as of an acid increase.

Oxyhaemoglobin replaces potassium in bicarbonates. Carbonic acid in erythrocytes (in the presence of carbonic anhydrase) is rapidly decomposed into water and carbon dioxide. The HCO_3 ions enter erythrocytes and Cl^- ions are liberated into the blood plasma where the amount of sodium bicarbonate is reduced. Carbon dioxide diffuses in the alveolar air.



(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)



(b) Exchange of O_2 and CO_2 in systemic capillaries (internal respiration)

Figure 9. Exchange of O_2 and CO_2 in pulmonary and systemic circulation

GAS EXCHANGE IN THE TISSUES

The O_2 tension reaches the lowest value in the immediate vicinity of its consumption, i.e. in the mitochondria where O_2 is utilized for processes of biological oxidation. As a result of oxyhaemoglobin dissociation, the O_2 molecules are liberated along the capillary blood flow and diffuse in the direction of low O_2 tension. The O_2 tissue tension depends on many factors among which are the blood flow rate, geometry of capillaries and distance between them, arrangement of cells in relation to capillaries, intensity of oxidation processes, and so on.

The O_2 tension in interstitial fluid near the capillaries is much lower (20-40 mm Hg) than that in the blood. It is especially low in tissue areas which are located at an equal distance from the neighbouring capillaries. The O_2 tension in cells can approach zero at high intensity of oxidation processes. With increase in the blood flow rate, the O_2 tissue tension sharply rises. For instance, twice as much increase in the blood flow rate can cause a 10 mm Hg increase in the O_2 tension in a nerve cell. When the so-called reserve capillaries open, blood supply to the muscles is enhanced.

The CO_2 tension is the highest (up to 60 mm Hg) in cells since CO_2 is formed in the mitochondria. It undergoes variation in interstitial fluid (46 mm Hg on the average) and is 40 mm Hg in arterial blood. CO_2 diffuses to capillaries due to a tension gradient and is transported to the lungs with blood.

Carbon Dioxide Loading

Aerobic respiration produces a molecule of CO_2 for every molecule of O_2 it consumes. The tissue fluid therefore contains a relatively high PCO_2 and there is typically a CO_2 gradient of 46 → 40 mmHg from tissue fluid to blood. Consequently, CO_2 diffuses into the bloodstream, where it is carried in the three forms noted.

Most of it reacts with water to produce bicarbonate (HCO_3^-) and hydrogen (H^+) ions. This reaction occurs slowly in the blood plasma but much faster in the RBCs, where it is catalyzed by the enzyme *carbonic anhydrase.* An antiport called the *chloride-bicarbonate exchanger* then pumps most of the HCO_3^- out of the RBC in exchange for Cl^- from the blood plasma. This exchange is called the **chloride shift.** Most of the H^+ binds to hemoglobin or oxyhemoglobin, which thus buffers the intracellular pH.

Oxygen Unloading

When H^+ binds to oxyhemoglobin (HbO_2), it reduces the affinity of hemoglobin for O_2 and tends to make hemoglobin release it. Oxygen consumption by respiring tissues keeps the PO_2 of tissue fluid relatively low, and so there is typically a concentration gradient of 95 → 40 mmHg of oxygen from the arterial blood to the tissue fluid. Thus, the liberated oxygen – along with some that was carried as dissolved gas in the plasma – diffuses from the blood into the tissue fluid. As blood arrives at the systemic capillaries, its oxygen concentration is about 20 mL/dL and the hemoglobin is about 97% saturated. As it leaves the capillaries of a typical resting tissue, its oxygen concentration is about 15.6 mL/dL and the hemoglobin is about 75% saturated.

Thus, it has given up 4.4 mL/dL – about 22% of its oxygen load. This fraction is called the **utilization coefficient.** The oxygen remaining in the blood after it passes

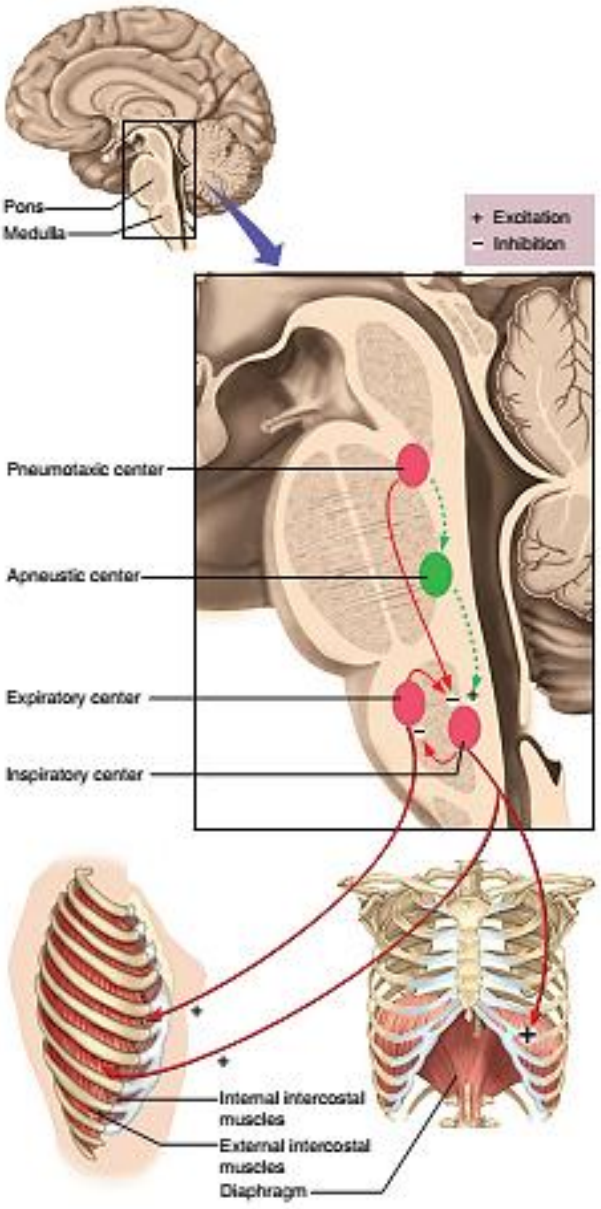
through the capillary bed provides a **venous reserve** of oxygen, which can sustain life for 4 to 5 minutes even in the event of respiratory arrest. At rest, the circulatory system releases oxygen to the tissues at an overall rate of about 250 mL/min.

REGULATION OF RESPIRATION

As we defined above the final result of functional respiratory system is to supply all tissues with optimal quantity of oxygen and eliminate carbon dioxide to get optimal gas exchange which satisfies current metabolic needs where the object of management is respiratory muscles. There are two links of regulation: internal and external.
Internal link regulates respiration through:

1. Change of RBC content;
2. Change of Hb content;
3. Change of Hb affinity to O_2 (due to temperature, ph, O_2 concentration changes);
4. Change tone of vessels, heart rate.

External link regulates external respiration (pulmonary ventilation) through the activity of respiratory center in brain.



The heartbeat and breathing are the two most conspicuously rhythmic processes in the body. The heart has an internal pacemaker and goes on beating even if all nerves to it are severed. Breathing, by contrast, depends on repetitive stimuli from the brain. There are two reasons for this:

1) Skeletal muscles do not contract without nervous stimulation.

2) Breathing involves the coordinated action of multiple muscles and thus requires a central coordinating mechanism to ensure that they all work together.

Control Centers in the Brainstem

The medulla oblongata contains **inspiratory (I) neurons,** which fire during inspiration, and **expiratory (E) neurons,** which fire during forced expiration (but not during eupnea). Fibers from these neurons travel down the *spinal cord* and synapse with lower motor neurons in the cervical to thoracic regions. From here, nerve fibers travel in the *phrenic nerves* to the *diaphragm* and *intercostal nerves* to the *intercostal muscles*. No pacemaker neurons have been found that are analogous to the

autorhythmic cells of the heart, and the exact mechanism for setting the rhythm of respiration remains unknown despite intensive research.

The medulla has two respiratory nuclei. One of them, called the **inspiratory center,** or **dorsal respiratory group (DRG),** is composed primarily of I neurons, which stimulate the muscles of inspiration. The more frequently they fire, the more motor units are recruited and the more deeply you inhale. If they fire longer than usual, each breath is prolonged and the respiratory rate is slower. When they stop firing, elastic recoil of the lungs and thoracic cage produces passive expiration.

The other nucleus is the **expiratory center,** or **ventral respiratory group (VRG).** It has I neurons in its midregion and E neurons at its rostral and caudal ends. It is not involved in eupnea, but its E neurons inhibit the inspiratory center when deeper expiration is needed. Conversely, the inspiratory center inhibits the expiratory center when an unusually deep inspiration is needed.

The pons regulates ventilation by means of a **pneumotaxic center** in the upper pons and an **apneustic center** in the lower pons. The role of the ***apneustic center*** is still unclear, but it seems to prolong inspiration. The ***pneumotaxic center*** sends a continual stream of inhibitory impulses to the inspiratory center of the medulla. When impulse frequency rises, inspiration lasts as little as 0.5 second and the breathing becomes faster and shallower. Conversely, when impulse frequency declines, breathing is slower and deeper, with inspiration lasting as long as 5 seconds.

Afferent Connections to the Brainstem

The brainstem respiratory centers receive input from the limbic system, hypothalamus, chemoreceptors, and lungs themselves.

Input from the *limbic system* and *hypothalamus* allows pain and emotions to affect respiration – for example, in gasping, crying, and laughing. Anxiety often triggers an uncontrollable bout of hyperventilation. This expels CO_2 from the body faster than it is produced. As blood CO_2 levels drop, the pH rises and causes the cerebral arteries to constrict. The brain thus receives less perfusion, and dizziness and fainting may result. Hyperventilation can be brought under control by having a person rebreathe the expired CO_2 from a paper bag.

Chemoreceptors in the brainstem and arteries monitor blood pH, CO_2, and O_2 levels. They transmit signals to the respiratory centers that adjust pulmonary ventilation to keep these variables within homeostatic limits.

The most potent stimulus for breathing is the pH of the body fluids, followed by PCO_2 and, least significant, PO_2.

These conditions are monitored by chemoreceptors in two general locations: **peripheral chemoreceptors** located outside the central nervous system (CNS) and **central chemoreceptors** located in the brainstem. The *peripheral chemoreceptors* are **aortic bodies** and **carotid bodies** located in the aortic arch and near the branch of the carotid arteries (**These are not to be confused with the aortic and carotid *sinuses,* which harbor the baroreceptors that monitor blood pressure!**). Although very small, the aortic and carotid bodies are richly supplied with capillaries and receive almost 40 times as much blood per gram of tissue as the brain does. The aortic bodies send signals

to the medulla by way of the vagus nerves and the carotid bodies transmit by way of the ***glossopharyngeal nerves***. The *central chemoreceptors* are paired areas close to the surface of the medulla oblongata, ventral to the inspiratory center. They *primarily monitor the pH of the cerebrospinal fluid* (CSF) and the tissue fluid of the brain.

The ***vagus nerves*** transmit sensory signals from the respiratory system to the inspiratory center. Irritants in the airway, such as smoke, dust, noxious fumes, or mucus, stimulate vagal afferent fibers. The medulla then returns signals that result in bronchoconstriction or coughing.

Stretch receptors in the bronchial tree and visceral pleura monitor inflation of the lungs. Excessive inflation triggers the **inflation (Hering–Breuer) reflex,** a protective somatic reflex that strongly inhibits the I neurons and stops inspiration. In infants, this may be a normal mechanism of transition from inspiration to expiration, but after infancy it is activated only by extreme stretching of the lungs.

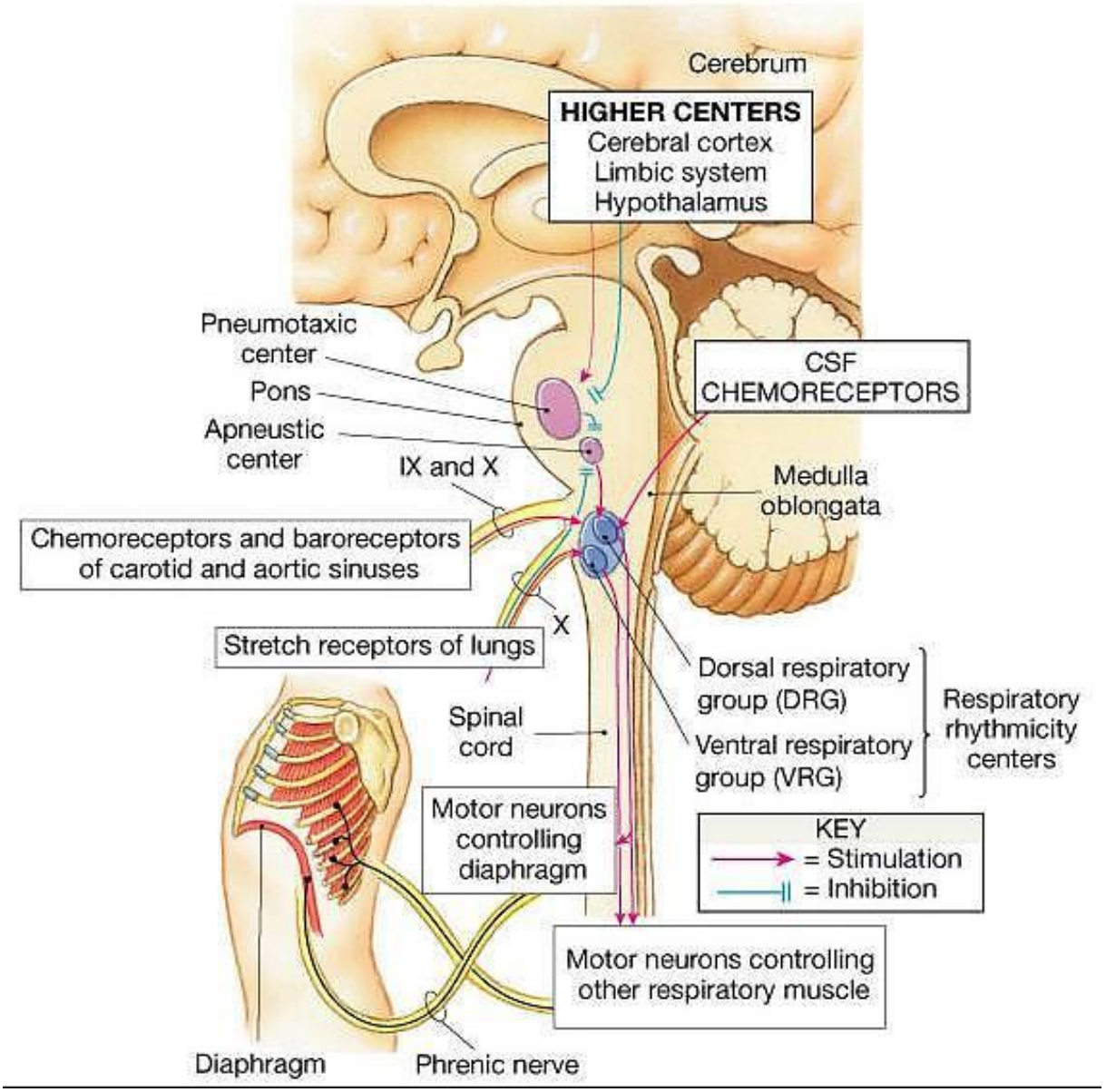


Figure 10. Regulation of respiration

The hydrogen ions, carbon dioxide, and oxygen individually affect respiration

Hydrogen Ions

Ultimately, pulmonary ventilation is adjusted to maintain the pH of the brain. Hydrogen ions cannot freely cross the blood-CSF barrier, but CO2 does. In the CSF, CO2 reacts with water and releases H^+. Protons then strongly stimulate the central chemoreceptors, which transmit signals to the inspiratory center.

Normally the blood has a pH of 7.40 ± 0.05. Deviation from this range is called **acidosis** when the pH falls below 7.35 and **alkalosis** when it rises above 7.45. The normal PCO_2 of the blood is 40 ± 3 mmHg. The most common cause of acidosis is **hypercapnia,** a PCO2 > 43 mmHg; the most common cause of alkalosis is **hypocapnia,** a PCO2 < 37 mmHg. Whenever, there is a CO_2 imbalance in the blood, CO_2 diffusion across the blood–CSF barrier creates a parallel shift in the pH of the CSF. Therefore, even though the brain responds primarily to pH changes, it is CO_2 that usually causes those changes. When these pH imbalances are due to a failure of pulmonary ventilation to match the body's rate of CO_2 production, they are called *respiratory acidosis* and *respiratory alkalosis*.

The corrective homeostatic response to acidosis is ***hyperventilation***, "blowing off" CO_2 faster than the body produces it. This shifts the carbonic acid reaction to the left:

$$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$$

The CO_2 at the left is expired in the breath. The H^+ on the right is consumed as this reaction proceeds toward the left, and as H^+ concentration declines, the pH rises.

The corrective response to alkalosis is hypoventilation, which allows the body to produce CO_2 faster than it exhales it. Hypoventilation shifts the reaction to the right, raises the H^+ concentration, and lowers the pH to normal:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$

Although pH changes usually result from PCO_2 changes, they can have other causes. In diabetes mellitus, for example, fat oxidation releases acidic ketone bodies, causing an abnormally low pH called *ketoacidosis*. Ketoacidosis tends to induce a form of dyspnea called *Kussmaul respiration*. Hyperventilation cannot reduce the level of ketone bodies in the blood, but by blowing off CO_2, it reduces the concentration of CO_2, generated H+ and compensates to some degree for the H^+ released by the ketone bodies.

Carbon Dioxide

Although the arterial PCO_2 has a strong influence on respiration, we have seen that it is mostly an indirect one, mediated through its effects on the pH of the CSF. Yet CO_2 has some effect even when pH remains stable. At the beginning of exercise, the rising blood CO_2 level may directly stimulate the peripheral chemoreceptors and trigger an increase in ventilation more quickly than the central chemoreceptors do.

Oxygen

Oxygen concentration usually has little effect on respiration. Even in eupnea, the hemoglobin is 97% saturated with O_2; therefore, increased ventilation cannot add very much. Only if the arterial PO_2 drops below 60 mmHg does it significantly affect ventilation, and such a low PO_2 seldom occurs even in prolonged holding of the breath. A moderate drop in PO_2 does stimulate the peripheral chemoreceptors, but another effect

overrides this: as the level of HbO_2 falls, hemoglobin binds more hydrogen ions. This raises the blood pH, which indirectly inhibits respiration. Only at a PO_2 60 mmHg does the stimulatory effect of hypoxemia override the inhibitory effect of the pH increase. Long-term hypoxemia can lead to a condition called **hypoxic drive,** in which respiration is driven more by the low PO_2 than by CO_2 or pH. This occurs in situations such as emphysema and pneumonia, which interfere with alveolar gas exchange, and in mountain climbing of at least 2 or 3 days' duration.

In summary, the main chemical stimulus to pulmonary ventilation is the H^+ in the CSF and tissue fluid of the brain. These hydrogen ions arise mainly from CO_2 diffusing into the CSF and brain and generating H^+ through the carbonic acid reaction. Therefore the PCO_2 of the arterial blood is an important driving force in respiration, even though its action on the chemoreceptors is indirect. Ventilation is adjusted to maintain arterial pH at about 7.40 and arterial PCO_2 at about 40 mmHg. This automatically ensures that the blood is at least 97% saturated with O_2 as well. Under ordinary circumstances, arterial PO_2 has relatively little effect on respiration. When it drops below 60 mmHg, however, it excites the peripheral chemoreceptors and stimulates an increase in ventilation.

Hering-Breuer reflex

Sensory nerve signals from the lungs also help control respiration. They are located in muscles portion of the walls of bronchi and bronchioles – they are **strerch receptors** that transmit signals though the vagi into the dorsal respiratory group when lungs become overstretched. This reflex is called **Hering-Breuer inflation reflex** acts as a PTC (inhibits inspiration). In human being this reflex is not activated until the TV increases to more than 3 times normal (greater than about 1.5 L). It has a protective mechanism for the preventing excess lung inflation rather than an important ingredient in normal control of ventilation. In *vagotomy* reflex disappears and breathing becomes *less frequent and deep*.

Respiration during exercise

In strenuous exercise, oxygen consumption and carbon dioxide formation can increase as much as 20-fold, but arterial PO_2 and PCO_2 and pH remains almost exactly normal but pulmonary ventilation is intensified. It is believed that the brain on transmitting motor impulses to the exercising muscles transmits at the same time collateral impulses into the brain stem to excite the respiratory center (analogous to the stimulation of the vasomotor center during exercises to increase blood pressure).

The role of other receptors in regulation of respiration

1. Effect of irritant receptors in the airways

The epithelium of trachea, bronchi and bronchioles is supplied with sensory nerve ending called **pulmonary irritant receptors**, this cause coughing and sneezing, the mechanism of these reflexes discussed earlier.

2. A few sensory nerve ending are in the alveolar walls in *juxtaportion* to the pulmonary capillaries are called **J-receptors**. They are stimulated when the pulmonary capillaries become engorged with blood or when pulmonary edema occurs in such

conditions as congestive heart failure and cause bronchospasm and frequent superficial breathing.

3. **Receptors of pleura** are activated in case of inflammation of pleura.
4. Irritation of **olfactory receptors** by odorants in moderate concentration causes sniffing. Strong irritation of them causes excitation of trigeminal nerve and sneezing with possible apnoe.
5. **Apnoe reflex** (diver reflex) – action of water to lower nasal meatus causes closure of larynx by epiglottis and prevents passage of water to the airways.

Regulation of respiration by cerebral cortex and subcortical structures

Although breathing usually occurs automatically, without our conscious attention, we obviously can hold our breath, take a deep breath, and control ventilation while speaking or singing. This control originates in the motor cortex of the frontal lobe of the cerebrum, which sends impulses down the corticospinal tracts to the respiratory neurons in the spinal cord, bypassing the brainstem respiratory centers. There are limits to voluntary control. Temperamental children may threaten to hold their breath until they die, but it is impossible to do so. Holding one's breath lowers the O_2 level and raises the CO_2 level of the blood until a *breaking point* is reached where automatic controls override one's will. This forces a person to resume breathing even if he or she has lost consciousness.

Any factor can increase disturbances in the respiratory center, which pass from many other functional CNS structures (behavioral regulation). Changes in the rate and depth of breathing accompany practically every behavioral act in human being. Breathing can be changed by various external influences, including light and sound. Psychological processes such as thinking, attention and emotions are attended by changes in breathing. Complex respiratory changes occur during speech and singing since passage of air through the upper airways during expiration is responsible for sound formation. Breathing during sleep is marked by specific alterations. The particular role of the cerebral hemispheres is that they are responsible for the finest adjustment of breathing to changing conditions in the body functioning. Their direct effect is accomplished though the cortico-bulbar pathway with participation of the subcortical structures – the limbic system, hypothalamus and reticular formation.

Experiments with transection of brain stem in different levels

1. Transection above pons – breathing is unchanged.
2. Transection below medulla oblongata – breathing standstill.
3. Transection between pons and medulla oblongata
   - apneusis – prolonged inspiration followed by short inefficient expiration,
   - gasping

Carbon Monoxide Poisoning

The lethal effect of carbon monoxide (CO) is well known. This colorless, odorless gas occurs in cigarette smoke, engine exhaust, and fumes from furnaces and space heaters. It binds to the ferrous ion of hemoglobin to form *carboxyhemoglobin (HbCO).* Thus, it competes with oxygen for the same binding site. Not only that, but it binds 210

times as tightly as oxygen. Thus, CO tends to tie up hemoglobin for a long time. Less than 1.5% of the hemoglobin is occupied by carbon monoxide in most nonsmokers, but this figure rises to as much as 3% in residents of heavily polluted cities and 10% in heavy smokers. An atmospheric concentration of 0.1% CO, as in a closed garage, is enough to bind 50% of a person's hemoglobin, and an atmospheric concentration of 0.2% is quickly lethal.

Respiratory Components of Visceral Reflexes

Inhibition of respiration and closure of the glottis during vomiting, swallowing, and sneezing not only prevent the aspiration of food or vomitus into the trachea but, in the case of vomiting, fix the chest so that contraction of the abdominal muscles increases the intra-abdominal pressure. Similar glottic closure and inhibition of respiration occur during voluntary and involuntary straining.

Hiccup is a spasmodic contraction of the diaphragm and other inspiratory muscles that produces an inspiration during which the glottis suddenly closes. The glottic closure is responsible for the characteristic sensation and sound. Hiccups occur in the fetus in utero as well as throughout extrauterine life. Their function is unknown. Most attacks of hiccups are usually of short duration, and they often respond to breath holding or other measures that increase arterial PCO_2. Intractable hiccups, which can be debilitating, sometimes respond to dopamine antagonists and perhaps to some centrally acting analgesic compounds.

Yawning is a peculiar "infectious" respiratory act whose physiologic basis and significance are uncertain. Like hiccuping, it occurs in utero, and it occurs in fish and tortoises as well as mammals. The view that it is needed to increase O_2 intake has been discredited. Underventilated alveoli have a tendency to collapse, and it has been suggested that the deep inspiration and stretching them open prevents the development of atelectasis. However, in actual experiments, no atelectasis-preventing effect of yawning could be demonstrated. Yawning increases venous return to the heart, which may benefit the circulation. It has been suggested that yawning is a nonverbal signal used for communication between monkeys in a group, and one could argue that on a different level, the same thing is true in humans.

Respiratory Effects of Baroreceptor Stimulation

Afferent fibers from the baroreceptors in *the carotid sinuses*, *aortic arch*, *atria*, and *ventricles* relay to the respiratory neurons, as well as the vasomotor and cardioinhibitory neurons in the medulla. Impulses in them inhibit respiration, but the inhibitory effect is slight and of little physiologic importance. The hyperventilation in shock is due to chemoreceptor stimulation caused by acidosis and hypoxia secondary to local stagnation of blood flow, and is not baroreceptor-mediated. The activity of inspiratory neurons affects blood pressure and heart rate, and activity in the vasomotor and cardiac areas in the medulla may have minor effects on respiration.

Effects of low oxygen pressure on the body

Barometric pressures at different altitudes

This decrease in barometric pressure is the basic cause of all the hypoxia problems in high-altitude physiology because, as the barometric pressure decreases, the atmospheric oxygen partial pressure decreases proportionately, remaining at all times slightly less than 21 per cent of the total barometric pressure – PO_2 at sea level about 159 mm Hg, but at 15240 m only 18 mm Hg.

Table 4. Effects of acute exposure to low atmospheric pressures on alveolar gas concentrations and arterial oxygen saturation

Altitude, m	Pressure, mm Hg	PO_2 in air, mm Hg	PCO_2 in alveoli, mm Hg	PO2 in alveoli, mm Hg	Arterial O2 saturation, %
0	760	159	40	104	97
~3000	523	110	36	67	90
~6100	349	73	24	40	73
~9200	226	47	24	18	24
~12200	141	29			
~15250	87	18			

Alveolar PO_2 at different elevations

Carbon dioxide and water vapor decrease the alveolar oxygen. Even at high altitudes, carbon dioxide is continually excreted from the pulmonary blood into the alveoli. Also, water vaporizes into the inspired air from the respiratory surfaces.

These two gases dilute the oxygen in the alveoli, thus reducing the oxygen concentration. Water vapor pressure in the alveoli remains 47 mm Hg as long as the body temperature is normal, regardless of altitude.

In the case of carbon dioxide, during exposure to very high altitudes, the alveolar PCO_2 falls from the sea-level value of 40 mm Hg to lower values. In the *acclimatized* person who increases his or her ventilation about fivefold, the PCO_2 falls to about 7 mm Hg because of increased respiration.

Acclimatization to low PO_2

A person remaining at high altitudes for days, weeks, or years becomes more and more *acclimatized* to the low PO_2, so that it causes fewer deleterious effects on the body. And it becomes possible for the person to work harder without hypoxic effects or to ascend to still higher altitudes.

The principal means by which acclimatization comes about are 1) a great increase in pulmonary ventilation, 2) increased numbers of red blood cells, 3) increased diffusing capacity of the lungs, 4) increased vascularity of the peripheral tissues, and 5) increased ability of the tissue cells to use oxygen despite low PO_2.

Increased Pulmonary Ventilation—Role of Arterial Chemoreceptors. Immediate exposure to low PO_2 stimulates the arterial chemoreceptors, and this increases alveolar ventilation to a maximum of about 1.65 times normal. Therefore, compensation occurs within seconds for the high altitude, and it alone allows the person to rise several thousand meters higher than would be possible without the increased ventilation. Then, if the person remains at very high altitude for several days, the chemoreceptors increase ventilation still more, up to about five times normal.

The immediate increase in pulmonary ventilation on rising to a high altitude blows off large quantities of carbon dioxide, reducing the PCO_2 and increasing the pH of the body fluids. These changes *inhibit* the brain stem respiratory center and thereby *oppose the effect of low PO_2 to stimulate respiration by way of the peripheral arterial chemoreceptors in the carotid and aortic bodies*. But during the ensuing 2 to 5 days, this inhibition fades away, allowing the respiratory center to respond with full force to the peripheral chemoreceptor stimulus from hypoxia, and ventilation increases to about five times normal. The cause of this fading inhibition is believed to be mainly a reduction of bicarbonate ion concentration in the cerebrospinal fluid as well as in the brain tissues. This in turn decreases the pH in the fluids surrounding the chemosensitive neurons of the respiratory center, thus increasing the respiratory stimulatory activity of the center.

The kidneys respond to decreased PCO_2 by reducing hydrogen ion secretion and increasing bicarbonate excretion. This metabolic compensation for the respiratory alkalosis gradually reduces plasma and cerebrospinal fluid bicarbonate concentration and pH toward normal and removes part of the inhibitory effect on respiration of low hydrogen ion concentration. Thus, the respiratory centers are much more responsive to the peripheral chemoreceptor stimulus caused by the hypoxia after the kidneys compensate for the alkalosis.

Increase in red blood cells and hemoglobin concentration during acclimatization

Hypoxia is the principal stimulus for causing an increase in red blood cell production. Ordinarily, when a person remains exposed to low oxygen for weeks at a time, the hematocrit rises slowly from a normal value of 40 to 45 to an average of about 60, with an average increase in whole blood hemoglobin concentration from normal of 15 g/dl to about 20 g/dl. In addition, the blood volume also increases, often by 20 to 30 per cent, and this increase times the increased blood hemoglobin concentration gives an increase in total body hemoglobin of 50 or more per cent.

Increased diffusing capacity after acclimatization

It will be recalled that the normal diffusing capacity for oxygen through the pulmonary membrane is about 21 ml/mm Hg/min, and this diffusing capacity can increase as much as threefold during exercise. A similar increase in diffusing capacity occurs at high altitude. Part of the increase results from increased pulmonary capillary blood volume, which expands the capillaries and increases the surface area through which oxygen can diffuse into the blood. Another part results from an increase in lung air volume, which expands the surface area of the alveolar-capillary interface still more. A final part results from an increase in pulmonary arterial blood pressure; this forces

blood into greater numbers of alveolar capillaries than normally—especially in the upper parts of the lungs, which are poorly perfused under usual conditions.

Peripheral circulatory system changes during acclimatization

The cardiac output often increases as much as 30 per cent immediately after a person ascends to high altitude but then decreases back toward normal *over a period of weeks as the blood hematocrit increases*, so that the amount of oxygen transported to the peripheral body tissues remains about normal.

Another circulatory adaptation is *growth of increased numbers of systemic circulatory capillaries* in the nonpulmonary tissues, which is called *increased tissue capillarity* (or *angiogenesis*). This occurs especially in animals born and bred at high altitudes but less so in animals that later in life become exposed to high altitude. In active tissues exposed to chronic hypoxia, the increase in capillarity is especially marked. For instance, capillary density in right ventricular muscle increases markedly because of the combined effects of hypoxia and excess workload on the right ventricle caused by pulmonary hypertension at high altitude.

Respiration in conditions below the sea level

When human beings descend beneath the sea the pressure around them increases tremendously. To keep the lungs from collapsing, air must be supplied at very high pressure to keep them inflated. This exposes the blood in the lungs also to extremely high alveolar gas pressure, a condition called *hyperbarism*. Beyond certain limits, these high pressures can cause tremendous alterations in body physiology and can be lethal.

Relationship of pressure to sea depth

A column of seawater 10 m deep exerts the same pressure at its bottom as the pressure of the atmosphere above the sea.

Therefore, a person 10 m beneath the ocean surface is exposed to 2 atmospheres pressure, 1 atmosphere of pressure caused by the weight of the air above the water and the second atmosphere by the weight of the water itself. At 20 m the pressure is 3 atmospheres, and so forth, in accord with the table.

Table 5. Change of barometric pressure at the different depth below the sea level

Depth, m	Barometric pressure, atm
Sea level	1 (760 mm Hg)
10	2
20	3
30	4
40	5
50	6

Effect of high partial pressures of individual gases on the body

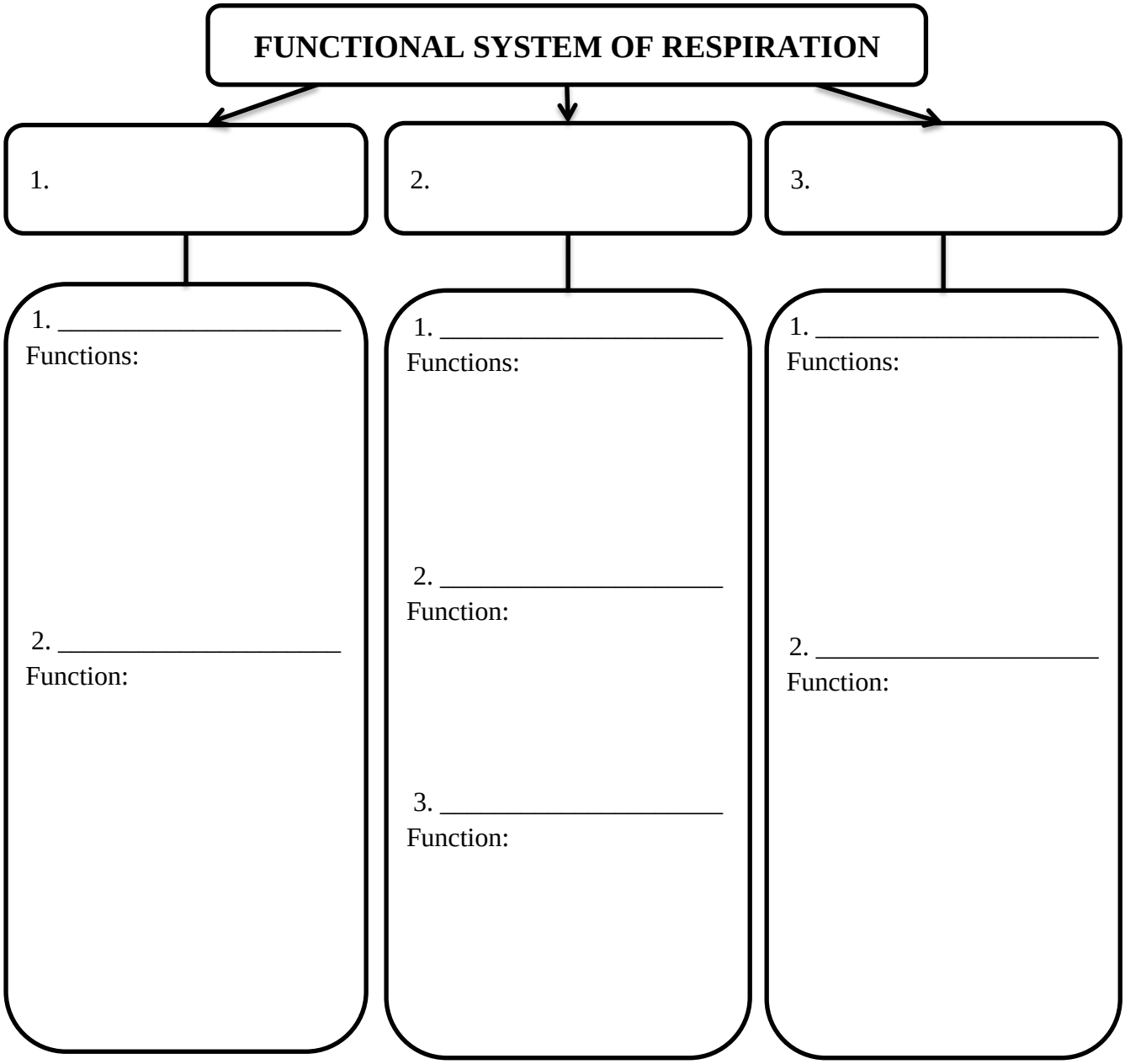
The individual gases to which a diver is exposed when breathing air are *nitrogen*, *oxygen*, and *carbon dioxide;* each of these at times can cause significant physiologic effects at high pressures.

Nitrogen narcosis at high nitrogen pressures

About four fifths of the air is nitrogen. At sea-level pressure, the nitrogen has no significant effect on bodily function, but at high pressures it can cause varying degrees of narcosis. When the diver remains beneath the sea for an hour or more and is breathing compressed air, the depth at which the first symptoms of mild narcosis appear is about 36 m. At this level the diver begins to exhibit joviality and to lose many of his or her cares. At 45-60 m, the diver becomes drowsy. At 60 to 76 m, his or her strength wanes considerably, and the diver often becomes too clumsy to perform the work required. Beyond 76 m (8.5 atmospheres pressure), the diver usually becomes almost useless as a result of nitrogen narcosis if he or she remains at these depths too long.

Nitrogen narcosis has characteristics similar to those of alcohol intoxication, and for this reason it has frequently been called "raptures of the depths." The mechanism of the narcotic effect is believed to be the same as that of most other gas anesthetics. That is, it dissolves in the fatty substances in neuronal membranes and, because of its *physical* effect on altering ionic conductance through the membranes, reduces neuronal excitability.

Task 11.1. Complete the scheme «*Functional system of respiration*» *and define functions of all its components.*



Task 11.2. Draw the scheme of cough reflex. Define afferent, central and efferent links.

Task 11.3. Draw the scheme of sneezing reflex. Define afferent, central and efferent links.

Task 11.4. List main stages of external and internal respiration.

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3. _____
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10. _____
11. _____
12. _____
13. _____
14. _____

Task 11.5. Define the values of P_{AL}, P_{pl} and P_L relating to the phase of respiration.

	P_{AL}, mmHg	**P_{pl},** mmHg	**P_L,** mmHg
Quite inspiration			
Forced inspiration			
Quite expiration			
Forced expiration			

Task 11.6. Complete the table *"Indexes of external respiration"*

№	Index	Definition	Normal value
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			

Task 11.7. List the factors accelerating the HBO_2 dissociation.

1._____
2._____
3._____
4._____
5._____
6._____
7._____

Task 8. Explain the inspiration and expiration processes step by step.

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