**(Slide 1) Lecture 9**

**Respiratory physiology**

**(Slide 2)** Lecture plan:

1. What is breathing?
2. Stages of respiration.
3. Basic Terms of Lung Ventilation.
4. Pulmonary Respiratory Mechanism.
5. Diffusion Processes in Lungs and Tissues and Transport of oxygen and carbon dioxide by Blood.
6. Transport of Gases by Blood.
7. Methods of Investigation of Respiration.
8. Non-respiratory functions of the lungs.

**(Slide 3)** Hold your breath. Really! See how long you can hold your breath as you continue listening to me. How long can you do it? Chances are you are feeling uncomfortable already. A typical human cannot survive without breathing for more than 3 minutes, and even if you wanted to hold your breath longer, your autonomic nervous system would take control. This is because every cell in the body needs to run the oxidative stages of cellular respiration, the process by which energy is produced in the form of adenosine triphosphate (ATP). For oxidative phosphorylation to occur, oxygen is used as a reactant and carbon dioxide is released as a waste product. You may be surprised to learn that although oxygen is a critical need for cells, it is actually the accumulation of carbon dioxide that primarily drives your need to breathe. Carbon dioxide is exhaled and oxygen is inhaled through the respiratory system, which includes muscles to move air into and out of the lungs, passageways through which air moves, and microscopic gas exchange surfaces covered by capillaries. The circulatory system transports gases from the lungs to tissues throughout the body and vice versa. A variety of diseases can affect the respiratory system, such as asthma, emphysema, chronic obstruction pulmonary disorder (COPD), and lung cancer. All of these conditions affect the gas exchange process and result in labored breathing and other difficulties.

Respiration in higher animals and humans is understood as a complex of processes that provide delivery of oxygen to the internal environment of the body, utilization of oxygen for oxidation of organic substances with production of carbon dioxide, and release of carbon dioxide from the body into the external environment.

**(Slide 4)** Stages of respiration:

**1st stage.** Ventilation of lungs – exchange of gases between alveolar gas and atmospheric air;

**2nd stage.** Exchange of gases between alveoli and blood;

**3d stage.** Transport of oxygen from lungs to tissues, and of carbon dioxide from tissues to lungs;

**4th stage.** Gas exchange between blood and tissues.

**5th stage.** Tissue, or internal, respiration.

**(Slide 5)** **Video. Phases of Respiration**

The last stage is the subject of biochemistry and molecular biology. The first four ones are traditionally studied by physiology and will be examined in this and in the following lecture.

**(Slide 6)** The thoracic cavity (the chest) is an air-tight cavity limited with the diaphragm from the bottom and with the rib cage from the sides. The diaphragm is a skeletal muscle consisting of radially arranged muscle fibers. Muscle fibers of the diaphragm are fixed with one end to the inner surface of the rib cage and with the other end to the central tendon of the diaphragm. The central tendon of the diaphragm has a hole for passage of the esophagus and of neurovascular fascicles. At relative physiological rest the diaphragm takes a dome-shaped configuration (with the convexity up) formed under influence of the abdominal pressure that exceeds the intrathoracic pressure. When muscles of the diaphragm contract, it flattens and descends, thus expanding the vertical volume of the chest. The bony framework of the chest is formed by the spine, ribs and the sternum. Ribs that form the basic structure of the framework, make two joints with the vertebrae: one with the vertebral body, and the other with its transverse process. In front, the ribs are sufficiently rigidly fixed to the sternum by cartilages. Contraction of external intercostal muscles changes the volume of the chest in the forward and sagittal directions: the ribs and the sternum go upward, and the ribs slightly diverge. The diaphragm and external oblique intercostal muscles provide inspiration at relative physiological rest. Expiration at physiological rest is a passive process resulting from relaxation of these muscles. When activity of an organism increases, metabolic demands in tissues increase, and breathing becomes deeper and more rapid and recruits accessory muscles. Accessory muscles participating in inspiration, include major and minor pectoral muscles, scalenes, sternocleidomastoid muscles and serrate muscles. Accessory muscles participating in forced expiration, include internal oblique intercostal muscles and muscles of the anterior abdominal wall.

**(Slide 7)** **Basic Terms of Lung Ventilation**

**Pleural cavity (pleural space)** is a gap between the visceral and parietal pleurae (the lung and the chest wall pleurae).

**Pleural pressure** is the pressure exerted by the contents of the pleural cavity on the organs of thoracic cavity and on the chest wall. Normally, the pleural pressure is several mm Hg lower than the atmospheric pressure.

**Elastic recoil of lungs (elastic resistance of lungs)** is a force with which the lung tissue resists stretch by the atmospheric pressure.

**Non-elastic resistance** is resistance of tissues of the airways and viscous resistance of tissues participating in breathing (tissues of thoracic and abdominal cavities). Non-elastic resistance plays a role in forced breathing and in different pathological conditions of respiratory organs. At relative physiological rest, non-elastic resistance does not produce any significant influence on the frequency and depth of respiratory movements.

**Negative pressure** is the difference between the pleural and atmospheric pressures. Since the pleural pressure is lower than the atmospheric pressure, this parameter is negative.

Pneg = Ppl – Patm

**(Slide 8)** **Ventilation of Lungs**

Breathing is a continuous cyclic process comprising three phases: inspiration, expiration and a breathing pause. Let us consider the process of ventilation of lungs using a schematic model and start with pause.

**(Slide 9)** **1. Breathing pause.** Forces acting on lung tissue in the breathing pause are equilibrated. These forces are: atmospheric pressure (Patm) acting from the outside through the airways, pleural pressure (Ppl 0) and elastic recoil (elastic force, Pel.r 0) acting from the thoracic cavity. Due to this equilibrium, the lung tissue does not move in breathing pause: lungs neither expand, nor collapse.

Patm = Ppl 0+ Pel.r 0; zero index indicates that these values are taken for the starting point.

**(Slide 10) 2. Inspiration.** Inspiration starts with contraction of respiratory muscles – the diaphragm and intercostals. The diaphragm flattens and descends increasing the vertical volume of the chest cavity. Contraction of the external intercostals forces the ribs to go up and diverge in the frontal plane. This causes expansion of the chest in the frontal and sagittal directions. With expansion of the chest the pleural cavity also expands in volume which results in decrease in the pleural pressure: Ppl1< Ppl0. Thus, the above expression takes the following form:

**Patm > Ppl 1+ Pel.r 0.**

The resultant vector of forces causes the lung tissue to stretch, and the lungs increase in volume. The pressure in the alveoli falls, and the atmospheric air starts to move from the region of high pressure (the environment) to the region of lower pressure (alveolar space).

**(Slide 11) 3. End of inspiration.** Stretch of the lung tissue during inspiration increases the elastic recoil, that is, Pel.r.1 > Pel.r.0. Besides, expansion of the lung decreases the volume of the pleural cavity with the resultant increase in the pleural pressure (Ppl2 > Ppl1). Finally, at some moment forces acting on the lung tissue from the chest cavity, again equilibrate with the atmospheric pressure that acts on the lung tissue through the airways, and inspiration stops.

**Patm = Ppl 2 + Pel.r. 1**

**(Slide 12) 4. Expiration.** Expiration begins with relaxation of respiratory muscles. The diaphragm resumes the dome-like configuration, ribs go down, and the chest returns to the size it had before inspiration. However, because the lungs still retain the maximal volume, the pleural cavity sharply decreases in volume with the resultant sharp increase in the pleural pressure: Ppl 3 >> Ppl 0. Therefore, the total sum of forces acting on the lung tissue from the chest starts to overbalance the atmospheric pressure:

**Patm < Ppl 3 + Pel.r. 1**

In result, the lungs begin to collapse until they return to the initial volume, that is, the volume of breathing pause. Here, since the lungs decrease in volume, pressure in the alveoli increases, and air starts to flow out of lungs down the pressure gradient.

Thus, following from the above, ventilation of lungs is a chain of events realized in accordance with the laws of physics. The main cause for change in the volume of lungs is contraction of respiratory muscles with the associated expansion of the chest volume and a change in the pleural pressure.

**(Slide 13)** The above statements are illustrated by the phenomenon of pneumothorax. Pneumothorax is breakage of air-tightness of the chest. Pneumothorax may be external and internal. In both cases pressure in the pleural cavity equals the atmospheric pressure and does not change with phases of breathing cycle. Here, the lungs collapse by force of elastic recoil, and their ventilation is no longer possible. Pneumothorax may result from different traumas of the rib cage and from pathological processes associated with destruction of tissues. To restore breathing, it is required to restore the air-tightness of the pleural cavity.

**(Slide 14) Video. Medical Mechanics of breathing.**

**Diffusion Processes in Lungs and Tissues and Transport of oxygen and carbon dioxide by Blood**

**(Slide 15)** Transport of oxygen from alveolar gas to arterial blood and of CO2 from venous blood to alveolar gas occurs due to difference in the partial pressures and partial tensions of gases between the alveolar gas and the blood. The difference in the partial tensions of gases in the blood and tissues causes directed movement of gases in the region of capillary exchange.

Partial pressure of any gas in a gas mixture is the pressure that could be produced by this gas at the same temperature, if it occupied the whole volume alone. For concentration of gases in liquids the term partial tension is used that is also evaluated in mm Hg.

O2 in blood binds with hemoglobin of erythrocytes to form oxyhemoglobin that is oxygen-containing (oxidized) form of hemoglobin. More than 99.9 % of oxygen is transported from lungs to tissues in this form. To characterize the function of blood to carry oxygen, the term “oxygen capacity of blood” is used.

Oxygen capacity of blood is the maximal amount of oxygen that can be bound to Hb in 100 ml of blood until its full saturation. Normally this value is 20 ml per 100 ml of blood.

**(Slide 16)** Hemoglobin turns into oxidized form depending on the partial pressure of O2 (PO2) which is shown by a curve of oxyhemoglobin dissociation. The diagram shows that at the partial pressure of oxygen from 60 to 80 mm Hg, hemoglobin is practically fully saturated with oxygen. Since the actual partial pressure of oxygen in the alveolar gas is about 100 mm Hg, there remains a reserve of 20 mm Hg, which can be used by the body in case of decrease in the atmospheric pressure and in the partial pressure of oxygen. For example, when an individual is climbing a mountain, this reserve permits him to do without additional adaptation and compensatory mechanisms within the first 1000 – 1500 m of elevation. However, further elevation requires activation of adaptation mechanisms consisting in increase in frequency and depth of breathing, increase in the heart rate and stroke volume, and in mobilization of erythrocytes from storages.

Long-term adaptation mechanisms lead to a steady increase in the amount of erythrocytes and hemoglobin in blood. As seen in the diagram, oxyhemoglobin dissociation curve changes its position depending on conditions. For example, at higher temperature the curve shifts to the right reflecting easier dissociation of oxyhemoglobin to oxygen and hemoglobin. At lower temperature the curve shifts to the left reflecting the opposite tendency.

**Transport of Gases by Blood**

**(Slide 17)** As mentioned earlier, more than 99.9% of oxygen is transported from lungs to tissues bound to hemoglobin. This is the main and, in fact, the only mechanism of transport of O2 by blood. Transport of CO2 is a more complicated matter. Hemoglobin transports only 30-35% of CO2 produced in tissues. About 3% of CO2 can be transported in a freely dissolved form, and the remaining 60-65% is transported as a monosubstituted salt of carbonic acid (NaHCO3) which mainly resides in blood plasma. CO2 produced in tissues in oxidation of nutrients goes to the blood plasma down the partial tension gradient, and finally to erythrocytes where it interacts with H2O (with participation of carbonic anhydrase enzyme) with the resultant production of carbonic acid:

CO2+H2O = H2CO3.

**(Slide 18)** In the aqueous phase carbonic acid dissociates to H+ ions and HCO3-. Negatively charged residue of carbonic acid (HCO3-) goes from erythrocytes to plasma, where it interacts with Na+ ion to form monosubstituted salt NaHCO3, which is the main transport for the most of CO2 (60-65%) from tissues to lungs.

**Methods of Investigation of Respiration**

**(Slide 19) Spirometry.** It is a method of measurement of respiratory volumes and capacities. There are the following respiratory volumes:

**Respiratory (tidal) volume** is the amount of air that can be inspired and expired by an individual at relative physiological rest. The tidal volume in a healthy individual is 0.4-0.5 l.

**Inspiratory reserve volume** is the maximal amount of air that can be additionally inspired after a quiet inspiration. The normal inspiratory reserve volume is 1.5–1.8 l.

**Expiratory reserve volume** is the maximal amount of air that can be additionally expired after a quiet expiration. The normal value is 1.0–1.4 l.

**Residual volume** is the amount of air that remains in lungs after maximal expiration, since the lungs cannot be completely emptied of gas. The residual volume in a healthy individual is 1.0-1.5 l.

**(Slide 20)** To characterize the function of the external respiration (breathing), respiratory capacities are often calculated which are sums of several respiratory volumes:

**Vital capacity of lungs (VCL)** is the total sum of the respiratory volume, inspiratory reserve volume and expiratory reserve volume. Normal VCL ranges from 3 to 5 liters. In males VCL is higher than in females.

**Inspiratory capacity** is the total sum of the respiratory volume and inspiratory reserve volume. Normal inspiratory capacity is 2.0–2.3 l.

**Functional residual capacity (FRC)** is the sum of the expiratory reserve volume and residual volume. This parameter can be calculated using gas dilution method and a closed-type spirograph. To determine FRC, helium noble gas is used incorporated into a respiratory mixture.

Vsp x CHe1 = Vsp x CHe2 + FRC x CHe2,

where Vsp – the volume of a spirometer; CHe1 – concentration of He in respiratory mixture in a spirograph before the test; CHe2 – concentration of He in respiratory mixture during the test. From here,

FRC = Vsp (CHe1 - CHe2)/ CHe2;

**The total capacity of lungs** is the total sum of all respiratory volumes.

Spirometry uses special devices – spirometers. There are dry and water spirometers.

**(Slide 21) Spirography** is a method which permits to record a respiratory curve (spirogram) with further evaluation of respiratory volumes and capacities using special measurements and calculations.

**(Slide 22) Video. Physiology practical demonstrations – Spirometry.**

**(Slide 23) Non-respiratory functions of the lungs:**

1. Trap for airborne particles: generally, nothing larger than 2.5μm gets to the alveoli.
2. Reservoir of blood: the lungs contain about 10% of the circulating blood volume.
3. Route of drug administration (eg. nebulised steroids and bronchodilators).
4. Route of drug elimination (eg. volatile anaesthetics).
5. Metabolism (eg. conversion of of angiotensin-I, and degradation of neutrophil elastase by α1-antitrypsin).
6. Modulator of acid-base balance by virtue of carbon dioxide elimination.
7. Modulator of the clotting cascade: the lungs contain thromboplastin, heparin and tissue plasminogen activator.
8. Filter for the bloodstream: particles larger than an RBC are trapped (~8 μm size barrier), which includes clots, tumour cells and other emboli.
9. Antimicrobial and immune functions: Alveolar macrophages and sequestered neutrophils, mast cells in the lung and bronchi, immunoglobulin in the respiratory mucus (IgA).
10. Modulation of body temperature: heat loss can occur by respiration.
11. Organ of speech: the lungs form a part of the system which permits communication by sound and language.

**(Slide 24)** Lesson assignment:

Kaplan Medical USMLE Step 1 Physiology: On the website of the department. Pages: 135 – 190.

Questions that we will analyze for a lesson on this topic:

1. Definition of breath, meaning.
2. 5 stages of the respiratory process.
3. The concept of external respiration.
4. The functional significance of the lungs, airways and chest during breathing.
5. Non-gas exchange functions of the lungs.
6. The mechanism of inhalation and exhalation.
7. Ventilation of the lungs: lung volumes and capacities (concepts, indicators). Minute volume of air, maximum ventilation of the lungs.
8. Gas exchange between alveolar air and blood: the driving force of gas exchange, indicators of the partial pressure of oxygen and carbon dioxide in the alveolar air and the tension of these gases in arterial venous blood and tissues.
9. Factors contributing to gas exchange in the lung.
10. Transport of oxygen and carbon dioxide by blood: compounds contained in arterial and venous blood, curve analysis, formation and dissociation of oxyhemoglobin and carbohemoglobin and factors influencing them (curve analysis).
11. Gas exchange between blood and tissues: driving force, auxiliary factors.

Finish for today

The full lecture is at the indicated website.

**Thank you for attention**