or excitement. In ill persons it can occur already during moderate physical effort or even at rest. Dyspnoea is always a subjective feeling of breathlessness or of dificulty in breathing. A variable clinical pattern of this condition is described. Some patients describe dyspnoea as lack of air or impossibility to get a breath.. Higher effort and breathing with a greater participation of respiratory muscles can be observed. **Dyspnoea does not reflect directly the condition of oxygenation. It is rather a symptom expressing the disproportion between the requirement of respiration and the ability of respiratory organs and the organism as a whole to maintain the required respiration**. Dyspnoea can be a permanent condition, or it can occur in episodes. The afferent information plays a certain role in the dyspnoea development. An episode of dyspnoea can arise during the night. The nocturnal, paroxysmal dyspnoea can be very dramatic as it can be accompanied by cough and a subjective feeling of breathlessness. In other cases dyspnoea can be associated with a certain enforced position – orthopnoea. Orthopnoea is a severe degree of breathlessness, during which the patient is not able to stay in a recumbent position, just in sitting position, or is for a short time not able to stay in standing position. In patients with cardiopulmonary diseases can often be the so called panic dyspnoea observed. There are probably more mechanisms which are responsible for the arise of dyspnoea. But almost regularly during dyspnoea a congestive pulmonary circulation can be observed. The changes of the pulmonary circulation have greater participation in arise of dyspnoea than the single.

It is not possible to measure directly the condition of oxygenation in the tissues. There are however several possibilities of indirect estimation of the cellular oxygenation degree. Firstly, the determination of blood saturation with gases of respiration is performed, furthermore the condition of ventilation, perfusion and the lung volumes are determined, and in addition, the cardiovascular system functions are measured. The transport of oxygen to the tissues depends on the efficiency of circulation and thus on the heart performance. The capacity of blood to transport oxygen has an important role. Together with the patientd's subjective sensations these methods represent a better possibility to approach to the conception of the supply of tissues with oxygen.

1.2 Pathophysiology of respiration and respiratory organs

Respiratory organs from pathophysiological point of view can be considered as two parts of one system. The first part is represented by organs in which gas exchange takes place, i.e. airways and lungs. The other part is represented by all structures and their functions responsible for the air transport from the external environment into the gas exchange units. This "pumping" is performed by the chest, respiratory muscles, nerves, nervous centers, and neurohumoral control.

1.2.1 Pulmonary ventilation and its disorders

Ventilation of the lungs is a complex of processes ensuring the transport of air into the lungs and the expiration of air enriched in carbon dioxide with low oxygen content. The complex of these processes which are the basis of ventilation depends on the intact chest, perfectly working airways, neurochemical regulative control of breathing, and lung tissue itself.

During inspiration the thoracic cavity enlarges due to the contraction of the respiratory muscles. When the diaphragm contracts, it moves downward into the abdominal cavity. The elevation of sternum and of ribs causes enlargement of the thoracal cavity in the back to front diameter. The inspiration is an active process which depends on several factors. **The expiration** is a passive process, depending on relaxation of inspiratory muscles. The elastic properties of chest and lungs are important factors. The chest and the lungs have generally a permanent tendency to restriction. The intrapleural pressure is negative and keeps the lungs distended. During inspiration the intrapleural pressure becomes more negative thus distending the lungs. The distension of the lungs during more negative intrapleural pressure depends on elastic fibres and the total elastic properties of the lungs. Alveoli have a tendency to collapse. It is caused by the moist surface of alveoli tending to

connect the opposite sides together. This connection is hindered by a secrete produced by specialized cells known as pulmonary surfactant. It is a lipoprotein lowering the surface tension of the alveolar fluid and hindering the potential collapse of alveoli. **Inspiration and expiration take place according to the principle of pulmonary distension and compression**. During inspiration is the pressure in the lungs lower than the atmospheric pressure and during the expiration the situation is reverse. During regular (quiet) breathing some alveoli are collapsed. Distensibility of the lungs is in relation to the intraalveolar pressure which is necessary for attaining a certain distension of lungs. Distensibility during the elevation of the intraalveolar pressure is a property of the lungs. This property is called compliance. The lung compliance expresses the change in lung volume due to increase in intraalveolar pressure. During distension of the lungs energy is spent to overcome the viscosity of the pulmonary tissue and the airways resistance to the air flow during inspiration. The respiratory work is the sum of the effort spent during inspiration and expiration to overcome the airways resistance to the air flow. Decrease in the lung compliance, increase in airway resistance and the requirement of active expiration increase the respiratory work.

The rhythm and frequency of breathing is regulated by nervous and chemical mechanisms. The respiratory centre is localized in the medulla oblongata and in pons Varolii in the medulla oblongata. The respiratory centre controls the frequency of breathing, the rhythm, the depth of breath and the level of alveolar ventilation. During inspiration and expiration afferent impulses come to the centre having alternating stimulatory or inhibitory effects. The efferent fibres transfer impulses from the respiratory centre to the respiratory muscles via the phrenic and intercostal nerves.

The respiratory centre is influenced by afferent impulses from the pulmonary receptors being sensitive to tension (distension), from central and peripheral chemoreceptors, from cerebral cortex and thalamus, and from arterial and venous baroreceptors. Receptors sensitive to tension are situated at several sites in the lungs. Many of them are situated in the bronchi and bronchioles. They are stimulated during distension of the lungs. During stimulation the impulses are transferred via afferent fibres of nervus vagus to the respiratory centre. Afferent impulses elicit a reflex inhibition of inspiration (it hinders the further air flow into the lungs). The reflex inhibition of inspiration is termed Hering-Breuer reflex. Essentially, it protects the lungs against excessive distension. The saturation of blood with oxygen and carbon dioxide influences the frequency and the depth of breathing so that they can comply with the actual requirements. The chemosensitive receptors are situated in the medulla oblongata. They are sensitive to changes of carbon dioxide and H^+ concentrations in the surrounding fluid. Under physiological conditions, the concentration of carbon dioxide is a primary stimulus for ventilation. The increase in CO_2 causes a raise in H^+. It results from the formation of carbonic acid from CO_2 and water and its subsequent dissociation to H^+ and HCO_3^-. The increase in carbon dioxide or hydrogen ion levels stimulates directly the neurons of respiratory centre. This process results in increased frequency and depth of breathing and with a subsequent decrease in CO_2. When the concentration of hydrogen ions decreases, the respiratory centre slows down the respiration and CO_2 can be retained, so that equilibrium between bicarbonates and carbonic acid in the body fluids can be attained. Hypoxia, under usual circumstances, acts as a secondary stimulus for the ventilation.

Peripheral chemoreceptors, situated in the carotid arteries and aorta are connected with the respiratory centre by afferent nerve fibres. These receptors are sensitive to a low oxygen and high CO_2 levels in blood. Impulses from these receptors stimulate the respiratory centre. The respiratory centre is also stimulated from the cerebral cortex and thalamus. The stimulation from the cerebral cortex induce the state of vigilance. The stimulation from thalamus acts especially during emotions. The stimulation of baroreceptors due to increased blood pressure results in a moderate suppression of the respiratory centre.

When there is a marked decrease in **alveolar ventilation** (e.g. by an half), the blood saturation with oxygen decreases just about 10 per cent in comparison with the normal values. Alveolar ventilation participates in regulation of respiration by means of carbon dioxid level in blood. The decrease in alveolar ventilation manifests itself more markedly in the increase of CO_2 level in blood rather than in decrease of oxygen. Therefore it is physiologically useful that the alveolar ventilation takes part in regulation of respiration by means of CO_2 level in blood.

The acinus is the essential functional unit of the lungs. It consists of terminal and respiratory bronchioles, alveolar ducts and alveoli. The inspiration is performed by the enlargement of the thoracic cavity by aid of respiratory muscles. In this situation the air flows from the outside into the lungs and to alveoli. The airways are arranged in such a way that they form in fact a biological filter for the air flow. The air in the upper airways is warmed up to the body temperature. It becomes saturated with water vapours to 100 per cent and is cleansed by adhesion of various particles to the airways walls. The air entering the alveoli is free of almost all undesirable components, including the pathogenic microbes. The lung tissue is thanks to these useful mechanisms, kept *clean and sterile*. The function of the mucociliary system, the reflex mechanisms (cough, bronchospasm), secretion of lactoferrin, lysosyme, IgA and the presence of macrophages aid to this cleanliness.

The primary role in the continuous cleansing of airways plays the mucociliary system. Besides the motion of cilia, the secretion of the mucous membranes and the production of periciliary fluid participate in the cleansing. The motion of cilia is directed towards the nose and the mouth cavities. The mucous membrane of trachea, bronchi and bronchioles contain cylindrical ciliated cells. Among these cells there are situated cells producing mucus. The secretion in airways is produced also in the submucous glands of the cartilaginous airways. During one day about 100 ml of mucus is produced. The majority of mucus is reabsorbed. About 10 ml of mucus in the airways is removed by expectoration and swallowing.

The mucous or gelous layer *is swimming like icefloe* upon the surface of the periciliary fluid in the form of sol which surrounds the cilia. The mucous layer moves towards nasopharynx in coordination with the respiratory movements. This can take place providing the mucociliary system is intact. Firstly, the epithelial cells with the cilia have to be morphologically and functionally intact. The ciliar motion depends on the thickness and the rheologic qualities of the mucus and the periciliary fluid. The speed of the transport decreases: if the viscosity of mucus increases, if its elasticity decreases, if the amount of mucus is augmented, or if the mucociliary system is damaged. To ensure the cleaning of airways also under these conditions, cough is involved. **An effective cough** begins with a deep inspiration, which enlarges the airways, then the epiglottis closes the superior aperture of the pharynx, and a very vehement contraction of the expiratory muscles follows, the intrathoracic pressure increases, the epiglottis opens and the air is expelled explosively. During the contraction of muscles the intrapleural pressure remains high. Just then (after the opening of glottis) the pressure in airways decreases. That is the reason for the expulsion of air with secretion which resides on the airway walls. Problems arise when the neuromuscular function of respiratory muscles is disturbed, or if the thorax is injured, if the airway resistance is increased, or if the cough reflex is suppressed.

The pulmonary ventilation is provided by inspiration and expiration. The tidal volume (V_T) is the volume of air which enters and leaves the respiratory organs during normal inspiration and expiration. The minute ventilation is the volume of air moved in and out of the lungs per minute. It is the VT multiplied by the number of breaths per minute ($V_E = V_T \cdot f$). The amount of air which enters the respiratory organs consists of two parts. The first one represents the volume which reaches the alveoli, the other one is the volume of air in airways where the gas exchange does not take place (dead space). Therefore $V_E = V_A + V_D$, where V_A is the volume representing the alveolar ventilation and V_D is volume of air in dead space. Physiologically useful is only the alveolar or effective ventilation. It is that portion of the minute ventilation volume which enters the alveoli where gas exchange realizes. To determine precisely the air volume which represents the alveolar ventilation is not easy. The physiological parameter providing information on alveolar ventilation is the CO_2 pressure in arterial blood.

About 150 ml of air remain in the airways. This volume cannot be utilized in gas exchange. It represents **the ventilation of the dead space** (regarding the gas exchange it is of no value). The relation between the dead space and the tidal volume (V_D/V_T) is a convenient expression for the efficiency of ventilation. Respiration realizes *to ensure* the alveolar ventilation. The transport of oxygen and also the speed of CO_2 elimination depend **on the efficiency of alveolar ventilation**. The speed of CO_2 exhalation determines the magnitude of alveolar ventilation. Normal alveolar ventilation *is measured* by the level of arterial CO_2. The optimum alveolar ventilation has to be performed at a level which can manage

the exhalation of the necessary amount of CO_2. Under physiological circumstances the pressure of CO_2 in arterial blood cannot exceed 45 mm Hg during normal alveolar ventilation. In analysis of the blood gases it is of course the partial pressure of CO_2 (the total pressure of a certain volume of a mixture of gases is the sum of partial pressures of every component of the mixture forming the gas volume). The partial pressure of CO_2 can be determined from the total pressure by assessing the percentage of its participation in the mixture. Under physiological conditions, the pH of plasma ranges from 7,36 to 7,44. The saturation of blood with oxygen attains 93–98 per cent. In this case the partial pressure of CO_2 in arterial blood (pCO_2) is 35–45 mm Hg and that of O_2 (pO2) is 75–100 mm Hg during intact ventilation. By analysing the exhaled air the volume of CO_2 can be estimated. This value does not provide any information on alveolar ventilation.

Information about the mechanics of ventilation can be obtained by **measuring the pulmonary volumes and speed of the airflow**. Useful values can be obtained by spirometric examination. Simple and essential is the information on the value of vital capacity of the lungs (FVC). It is the volume of air expirated after maximal inspiration. Graphic illustration of expiration provides information on the volume of air which has been exhaled within 1, 2 and 3 seconds (FEV 1, FEV 2, FEV 3). These are the components of FVC, nevertheless they have a great importance in evaluation of pathological conditions. A very useful information provides the relation of FEV 1 and FVC (FEV 1/FVC), especially in cases of obstructive lung diseases.

The maximal minute ventilation is the volume of air which a person can exhale and inspire in one minute during maximally intented ventilation.

The level of ventilation must ensure the metabolic requirements of organism, especially regarding the carbon dioxide exhalation. The partial pressure of CO_2 in the arterial blood ought not exceed the limit of 45 mm Hg. Ventilation, which exceeds the metabolic requirements is called hyperventilation. Ventilation which is insufficient regarding the metabolic requirements of organism is called hypoventilation.

1.2.1.1 Hyperventilation

During hyperventilation the volume of CO_2 in the arterial blood decreases and that is why there is a minor possibility for the carbonic acid formation from water and CO_2. In fact it means a decrease in the carbonic acid level and a subsequent decrease in concentration of hydrogen ions. That is why the pH of plasma becomes alkaline. This condition is called respiratory alkalosis, hypocapnia or non-metabolic alkalosis. The kidneys compensate this condition by eliminating the bicarbonate ions, retaining the hydrogen ions and non-bicarbonate anions. It results in excretion of alkalic urine and improvement of the plasmatic pH.

During alkalosis the level of ionized calcium decreases. The reduced ionized calcium induces enhanced neuromuscular excitability because of the disturbed membrane potential. The decrease in ionized Ca^{2+} results from the fact that the protein bound calcium (CaPr) is in equilibrium with the hydrogen ions. When the H^+ concentration decreases, the amount of protein bound calcium increases to maintain the equilibrium. The amount of the ionized Ca^{2+} is reduced. The increased neuromuscular excitability can be manifested by several symptoms. It can lead to spasms and tetany. Tetany appears especially when alkalosis develops very quickly. The bloodflow through the vital organs is decreased. It is due to the vasoconstrictive effect of low carbon dioxid concentration. The release of oxygen from oxyhaemoglobin is impaired during alkalosis. As a result, tissue hypoxia develops. The brain is extremely sensitive to hypoxia, hence various symptoms of central nervous system disorders arise.

As mentioned above, **alveolar hyperventilation** leads to respiratory alkalosis because CO_2 is exhaled and the level of its concetration in arterial blood decreases. One of the most common causes of alveolar hyperventilation and of subsequent alkalosis is an abnormally rapid respiration, that accompanies psychical tension and extreme emotional conditions. Hyperventilation is also caused by severe pathological conditions such as high fever, encephalitis, meningitis, and several states leading to increased excitability of the respiratory centre. The result is an increased respiratory effort, which originates in physiological impulses. Drugs, e.g. salicylates, pathologic conditions as brain tumors and traumas of central nervous system can increase the sensitivity of the res-

piratory centre. Bleeding can cause hyperventilation in a similar way. Hyperventilation occurs also during pulmonary diseases (pneumonias, fibroses, oedema of the lungs) as a result of the stimulation of pulmonary J receptors.

Alveolar hyperventilation can occur **as compensatory mechanism** during metabolic acidosis, or it can be caused by hypoxaemia. Low arterial concentration of oxygen can stimulate the peripheral chemoreceptors, which in turn stimulate the respiratory centre. In this manner the increased input of oxygen is ensured, but CO_2 is exhaled simultaneously because of hyperventilation.

1.2.1.2 Hypoventilation

Alveolar hypoventilation is an insufficient ventilation, with regard to the metabolic processes. Hypoventilation can result from disturbed regulation of respiration or disorders of the respiratory system. **Alveolar hypoventilation leads to hypercapnia which is associated with hypoxaemia**. The increase in carbon dioxide concentration together with the decrease in O_2 is acompanied with a rise in carbonic acid. The condition is called respiratory acidosis or nonmetabolic acidosis, hypercarbia and hypercapnia.

The functioning kidneys react to this condition by compensation. Because of the increased level of carbonic acid in the extracellulary space they retain bicarbonate ions and excrete hydrogen ions and nonbicarbonate anions.As a result, **excretion of acide urine** and a useful retention of plasma bicarbonates take place. It is clear, that before this compensation, pH in the plasma has been shifted to the acid values. If the increase in carbon dioxide tension in the plasma persits for a long time period, the participation of kidneys in regulation of pH of the plasma becomes reduced. The increase in the carbon dioxide tension stimulates the receptors in the aorta and in the carotid arteries, resulting in an enhancement of heart rate and contraction force, and subsequent changes in circulation.

The increase in arterial carbon dioxide concentration causes vasodilatation in the cerebral circulation. The blood flow through the brain increases too. These changes cause a rise in cerebrospinal fluid pressure and create conditions for development of cerebral oedema. Patients complain of unconfortable feelings like nausea, headache, tension in the head and confusion. Papilloedema or its impact on the optic nerve can be found. The headache is usually localized in the occipital area.

The increase in hydrogen ions concentration in the extracellular fluid causes their penetration into cells. To maintain the electric equilibrium on membranes, potassium ions escape from the cells. The level of potassium in serum increases at the beginning, but later deficit in potassium stores of organism develops. The intracellular deficiency of potassium causes muscular weakness. A long lasting hypokalaemia leads to degenerative alterations in myocardial cells. The most important changes are those occuring in the nuclei of myocardial cells, and the development of myocardial fibrosis. As a consequence of hypoxia and hypercapnia effects on myocardial cells, arrhythmias may occur.

A very rapid increase in carbon dioxide concetration easily causes convulsions and unconsciousness. Prolonged hypercapnia combined with hypoxaemia causes behavioural changes, lethargy, desorientation and confusion of a varying degree.

Hypoxaemia and acidosis are the causes of vasoconstriction in the pulmonary circulation with a subsequent increase in the pressure. The purpose of these changes is to minimize the ventilation-perfusion inequalities. Chronic vasoconstriction with increased pressure is a load for the right ventricle, because it has to eject the blood against increased resistance. This leads to hypertrophy of the right ventricle, possible consequent failure. The right ventricle hypertrophy under changed circulatory conditions in the lungs produces a condition called cor pulmonale chronicum. This complex processes include also other changes being the consequences of primary chronic hypoxia due to hypoventilation. In patients with these changes a compensatory polycythaemia and increased vascularisation in peripheral parts of organism develops.

When there is pulmonary emphysema with an increased amount of CO_2 in arterial blood, it is the manifestation of the terminal phase which lasts for a relatively short time.

The increase in CO_2 during moderate hypoxia can cause a state with complete desorientation, lethargy or even unconsciousness and death. It is a *narcosis* induced by hypercapnia.

Hypoventilation can be caused by several drugs, which decrease the sensitivity of the respiratory centre. In this way act anaesthetics, sedatives, hyp-

notics and strong analgesics. The respiratory centre is depressed also by inhalation of pure oxygen. The changes in bloodflow in the brain stem can also cause depression of the respiratory centre.

Alveolar hypoventilation occurs in several pathological conditions. The underlying cause is the disturbance of respiration mechanisms. The causes can be classified as obstructive ventilatory disorders, restrictive ventilatory disorders and the defficiency of the pulmonary surfactant.

1.2.2 Distribution of ventilation and its disorders

During inspiration the inhaled air passes through the branching bronchi and bronchioles into the terminal respiratory units – the alveoli. These are situated at the end of the 26th generation of the bronchial and bronchiolar tree. Even in healthy poeple the airflow is not distributed and directed equally into all alveoli. In pulmonary diseases, the differences in the supply of air between the alveoli can enormously increase.

The inequality of ventilation is present also in healthy persons. There are marked differences between the highest and the lowest parts of the lungs. The causes of this *vertical gradient* are, first of all, the anatomical arrangement and the impact of gravitation on the blood in the pulmonary circulation. In addition, the mechanisms of ventilation are involved. During expiration, the lower parts of the lungs are drained more intensively. Therefore during inspiration the lower parts *receive* more air than the upper parts of the lungs. This mechanism acts during quiet respiration. During exercise (physical work) the ventilation of the lungs increases and is more uniform than during breathing at rest. The differences between the distribution of regional ventilation can be estimated by analysis of the expired air after preceding inhalation of pure oxygen. Another possibility is to measure the emission of the radionuclide of xenon after its inhalation in a low concentration.

Disturbances of regional ventilation arise easily. When the pulmonary parenchyma is damaged, the air flows predominantly into the intact parts of lungs, and the damaged areas receive air only to a limited extent. According to the character of lesion two categories of abnormal ventilatory function can be distinguished: restrictive and obstructive ventilatory disorders.

Restrictive ventilatory disorders arise when a certain lung volume is reduced. The hallmark of a restrictive disorder is a decrease in the vital capacity. It is necessary to exclude the diagnosis of obstructive ventilatory disease, because in this condition the lung volumes are also reduced. There are many pulmonary disorders, disturbances of the control system of respiration and alterations of the thorax, causing restrictive pattern of abnormal ventilatory function. In principle it involves the following conditions:

1. alterations of the chest and muscles of respiration (kyphoscoliosis, myasthenia gravis)
2. lung diseases and related condions (diffuse interstitial fibrosis, pulmonary oedema)
3. disorders of the pleura
4. restriction of the thoracic cavity (tumours, cardiomegaly, pneumothorax, haemothorax, pleural effusion)
5. pneumonectomy

Obstructive ventilatory disorders are caused by disturbances in airflow. The most frequent cause is the increase in the resistance in the airways. The test of the forced expiration and especially the ratio of the forced expiratory volume in 1 second to forced vital capacity (FEV 1/ FVC) provides very useful information.

Obstructive ventilatory disorders can be found in patients with asthma, bronchitis, emphysema, bronchiectasis or other diseases narrowing the tracheobronchial system.

1.2.3 Changes in diffusion

Diffusion can be defined as the movement of molecules from region of higher concentration to region of lower concentration. Diffusion is a passive process, which does not require any energy. Oxygen in the lungs diffuses, from the alveolar space into capillaries. The same principle is involved in tissues during the oxygen diffusion from capillaries into the adjoining cells. In the same way, however, in the reverse direction, CO_2 diffuses. For *the transfer* of oxygen and CO_2 chemical reactions are utilized. O_2 is binding with haemoglobin and carbon dioxide is binding with bicarbonates and partially with haemoglobin.

1.2.3.1 Diffusing capacity

The diffusing capacity of the lungs for any gas refers to the volume of gas diffusing across the alveolar capillary membrane per time unit in response to the difference in the gas pressures within the alveoli and pulmonary capillaries.

The diffusing capacity of the lungs can be measured just for oxygen and CO_2, because of their approximately equal ability to bind with haemoglobin. The diffusing capacity cannot be assessed separately without the presence of erythrocytes and haemoglobin. The volume of the diffusing gas (e.g. CO_2) and its bond to haemoglobin per unit of time depends on the difference between its pressure **in alveoli and that in capillaries**. The diffusion depends on:

1. solubility and diffusibility in each layer of alveolar capillary membrane
2. surface dimensions and thickness of the barrier
3. rate of chemical reaction of CO_2 with haemoglobin

When the pulmonary blood flow increases, e.g. during muscular exercise, it increases also in the previously nonperfused capillaries. As a result, they dilate and therefore the resultant diffusing capacity increases. Increased diffusing capacity and capillary perfusion in the lungs is physiological in people who live at high altitude.

1.2.3.2 Changes in diffusing capacity

The diffusing capacity can be changed in several lung diseases. In principle, the thickening of the alveolar capillary membrane or a decreased blood flow through the capillaries, or both of them, are considered to play an important role. The most common cause of reduced diffusing capacity is the decrease in blood flow through the capillaries. Embolism of the pulmonary artery or microemboli can exclude from function a part of the capillary vascular bed. Therefore diffusing capacity of the lungs is decreased in these conditions. Also infiltrative processes localized in the interalveolar septa are similarly manifested. They are responsible for destruction of the capillaries (interstitial fibrosis, collagenosis, sarcoidosis). Reduction of the diffusion surface together with the destruction of capillaries arise in emphysema or after simple pneumonectomy.

1.2.4 Changes in perfusion

In principle the pulmonary blood circulation has a single purpose. It is the adequate provision of blood for the pulmonary capillaries for the exchange of gases. The involved processes have to function in accordance so that the gas exchange can take place undisturbed. The blood flow has to be in accord with ventilation. Ventilation has to be in accord with the metabolic processes in organism. The ventilation and blood flow have to be proportionally distributed in the lungs. The processes of ventilation are under central control. **The pulmonary blood flow is not distributed uniformly**. There are obvious differences in the blood flow between single parts of the lungs. The differences in the blood flow under physiological conditions concern the upper and the lower parts of the lungs. In the regions with increased arterial pressure the flow is higher and vice versa. In standing posture the apical parts of the lungs are perfused minimally. The local perfusion is determined by regional factors. In areas with vasoconstriction induced by hypoxia, the blood flow is low. As a result, the blood is passed into the less ventilated areas. Changes in the distribution of the pulmonary blood flow can be also induced by disorders affecting the vessels, including the vasculitis, embolism or the compression of a larger vessel by e.g. tumour, cyst or emphysema. More often they result from vasoconstriction due to alveolar hypoxia. The alveolar hypoxia can occur in consequece of local changes in ventilation.

The perfusion of the lungs serves for the purpose of gas exchange. In addition, the pulmonary circulation has other very important roles regarding the functions of the whole organism. It represents a filter for the venous blood. It acts as a reservoir of blood for the left ventricle. It is involved in the endocrine regulation by changing some substances. Its surface is large enough for effective filtration and absorption of many substances.

1.2.5 Exchange of respiratory gases

The result of the complex activity of respiratory system, is a state, when pO_2 and pCO_2 in arterial blood are within the physiological limits. Respiration is ensured by ventilation of the lungs, the distribution of the inhaled air via the tracheobronchial system to the alveoli, by diffusion and perfusion, and by the control of respiration. These processes are mutually

linked in order to compensate actual deterioration of some of their parts by other activities.

During inspiration the air is warmed, and saturated with water vapours. In consequence, the partial pressures of N_2 and O_2 decrease proportionally. Under physiological conditions, a larger volume of O_2 is transferred to the alveoli than that of CO_2 *removed* from them. During all physiological changes the alveolar-arteriolar difference in pO_2 is maintained as an important factor for the respiratory gas exchange.

The distribution of inhaled air and the pulmonary blood flow are not equal or mutually proportional. That is the reason why during physiological actions in healthy people there is a moderate ventilation-perfusion disproportion. The most frequent cause of this imbalance is the arterial hypoxia. Almost every pulmonary disease is associated with certain ventilation – perfusion abnormalities.

If some parts of lungs are less ventilated in relation to their perfusion, the diffusion of O_2 decreases. At the end of capillaries the pO_2 is below the normal. The partial pressure of CO_2 tends to increase. The result is that pO_2 is lower than pCO_2. In the *hyperventilated* parts of lungs are opposite relations.

The gas exchange requires certain conditions to be effective and adequate to the actual metabolic situation in organism. The first requirement is the diffusion of O_2 from alveoli to the blood and from the blood to tissues. CO_2 passes in the same way, however in a reverse direction. The exchange of respiratory gases is dependent upon the adequate level of alveolar ventilation and perfusion, sufficient gradient of gases, intact alveolar-capillary membrane, and upon the surface on which the gas exchange takes place. In addition, the affinity of haemoglobin, especially to oxygen is a necessary factor.

The lung tissue contains an immense amount of capillaries localized in close vicinity to the alveoli. The alveolar-epithelial layer consists of flat type I cells. The function of these cells is to transfer the respiratory gases. These cells can be very easily damaged by other gases being toxic. It is of great importance that these cells are not able to regenerate after being damaged. In such case, they are replaced by cells of type II, which are able, in case of need, to transform themselves to cells of type I. The walls of capillaries and alveoli are separated by a narrow interstitial space. Together they form the alveolar-capillary membrane.The diffusion of oxygen and CO_2 is a continuous process which takes place within the alveolar-capillary membrane. The exchange of respiratory gases across **the alveolar-capillary membrane depends on several factors**:

1. adequate ventilation has to procure the necessary volume and concentration of oxygen in alveoli (ventilation)
2. normal blood flow through the pulmonary capillaries (perfusion)
3. thickness and quality of the alveolar-capillary membrane
4. total surface of the alveolar-capillary membrane
5. relative gradient and solubility of the gases on both sides of the alveolar-capillary membrane (diffusion)
6. normal affinity of oxygen to haemoglobin.

The effective exchange of the respiratory gases needs optimum conditions for ventilation and perfusion. If there is balance in these processes, their ratio is 1.0 or 0.8. Perfusion of poorly ventilated alveoli decreases the concentration of O_2 in arterial blood with a simultaneous increase in CO_2 concentration. When poorly perfused alveoli are well ventilated, the dead space becomes larger.

Several disorders in the lungs which affecting ventilation or perfusion, are manifested as **ventilation-perfusion disproportion**. Alveolar hyperventilation cannot increase the diffusion of oxygen. Oxygen is bound to haemoglobin and any intensification of ventilation cannot cause its further binding to haemoglobin. This is valid exclusively for oxygen. During alveolar hyperventilation, CO_2 can be exspired in a higher amount. In such parts of the lungs it leads to normal oxygenation with hypocapnia. The blood from such regions is mixed with the blood from other regions where this disproportion does not occur. And there is still another fact to be considered: the binding of oxygen to haemoglobin. The ability of haemoglobin to bind oxygen at different tensions of oxygen can be expressed by the known non-linear dissociation S curve. The affinity of haemoglobin to oxygen depends on pO_2, temperature, pH in erythrocytes and the concentration of 2,3-DPG.

The respiratory gas exchange disturbance is defined as a state, where a disproportion between saturation of blood with oxygen and elimination of CO_2 at the level of the alveolar-capillary membrane is present. The disorder of gas exchange results usually from changed ventilation-perfusion ratio. The disturbance of gas exchange may be caused by alterations of alveolar-capillary membrane, reduction of the capillary bed, or change in normal affinity between haemoglobin and oxygen.

1.2.6 Ventilation-perfusion abnormalities

The alveolus in connection with the capillary bed forms the essential functional unit for exchange of respiratory gases. On this level several states can arise:

- normal respiratory unit: ventilation and perfusion are in equilibrium
- respiratory unit as dead space: alveolus is ventilated but the blood flow is reduced or absent
- shunt respiratory unit: alveolus is not ventilated or the ventilation is reduced, the perfusion is normal
- excluded respiratory unit: the alveolus and capillaries are not functional

Extreme situations are presented by **respiratory units as dead space and shunt respiratory units**. Dead space is that part of ventilation which is a component of total capacity, yet does not participate in gas exchange. Total dead space participate in several states:

- anatomical dead space is represented by the conducting airways
- alveolar dead space is represented by alveoli which are ventilated, but not perfused with blood
- the dead space effect: arises when the ventilation is greater than perfusion; this condition arises when ventilation does not take appropriate part in the gas exchange (due to excessive ventilation or perfusion below average)

A shunt can be expressed as a part of the heart output blood volume, which does not participate in gas exchange. Following states may be involved:

- anatomical shunt: about 2–3 per cent of the right ventricular cardiac output passes the pulmonary circulation circuit and returns to the left ventricle without being oxygenated, it is the blood flowing particularly through the bronchi and pleura
- the capillary shunt: represents the blood which flows via entirely unventilated alveoli. It is the so called true or absolute shunt. The extent of this shunt cannot be affected by any measure, not even by therapy with oxygen.
- the shunt effect appears when the perfusion is greater than the ventilation; usually due to decreased ventilation or high blood flow velocity within the pulmonary circulation.

The essential issue in these conditions is that in bronchial and pulmonary diseases such changes arise which cause the enlargement of dead space and simultaneously the shunt of pulmonary blood flow. That is why in the initial phases hypoxaemia is present. pCO_2 is usually not increased at the beginning. If there is a low ventilation-perfusion ratio, an increased amount of CO_2 is *expired*. The progression of the disease leads later to CO_2 retention.

The perfusion of the lungs can be disturbed in consequence of haemodynamic changes. Pulmonary embolism, the decrease in heart output, reduction of the capillary circulation or the decrease in pulmonary circulation resistance can cause an enlargement of the dead space.