GOMEL STATE MEDICAL UNIVERSITY
Normal and Pathological Physiology Department

PHYSIOLOGY OF RESPIRATION

EXTERNAL RESPIRATION

Lecture 1

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Lecture plan:

1. External respiration.
2. Respiratory movements.
3. Intrapleural pressure and its change during respiration.
4. Lung ventilation. Pulmonary volumes.
5. Dead space.
6. Alveolar ventilation.
7. Gas exchange in the lungs.

1. *External respiration.*

A set of processes providing the O_2 intake by the organism, its delivery and consumption by tissues and excretion of the respiration end-product CO_2 into the environment, is called respiration.

The complex process of gas exchange with the environment is formed by a number of consecutive processes (Figure).

***External respiration (pulmonary)*:**

- *Gas exchange between pulmonary air and atmospheric air (lung ventilation).*
- *Gas exchange between pulmonary air and the capillary blood of pulmonary circulation.*

Internal respiration:

- *O_2 and CO_2 transport in the blood.*
- *Gas exchange between blood and cells.*
- *Tissue respiration i. e. O_2 consumption and CO_2 excretion during metabolism (in mitochondria).*

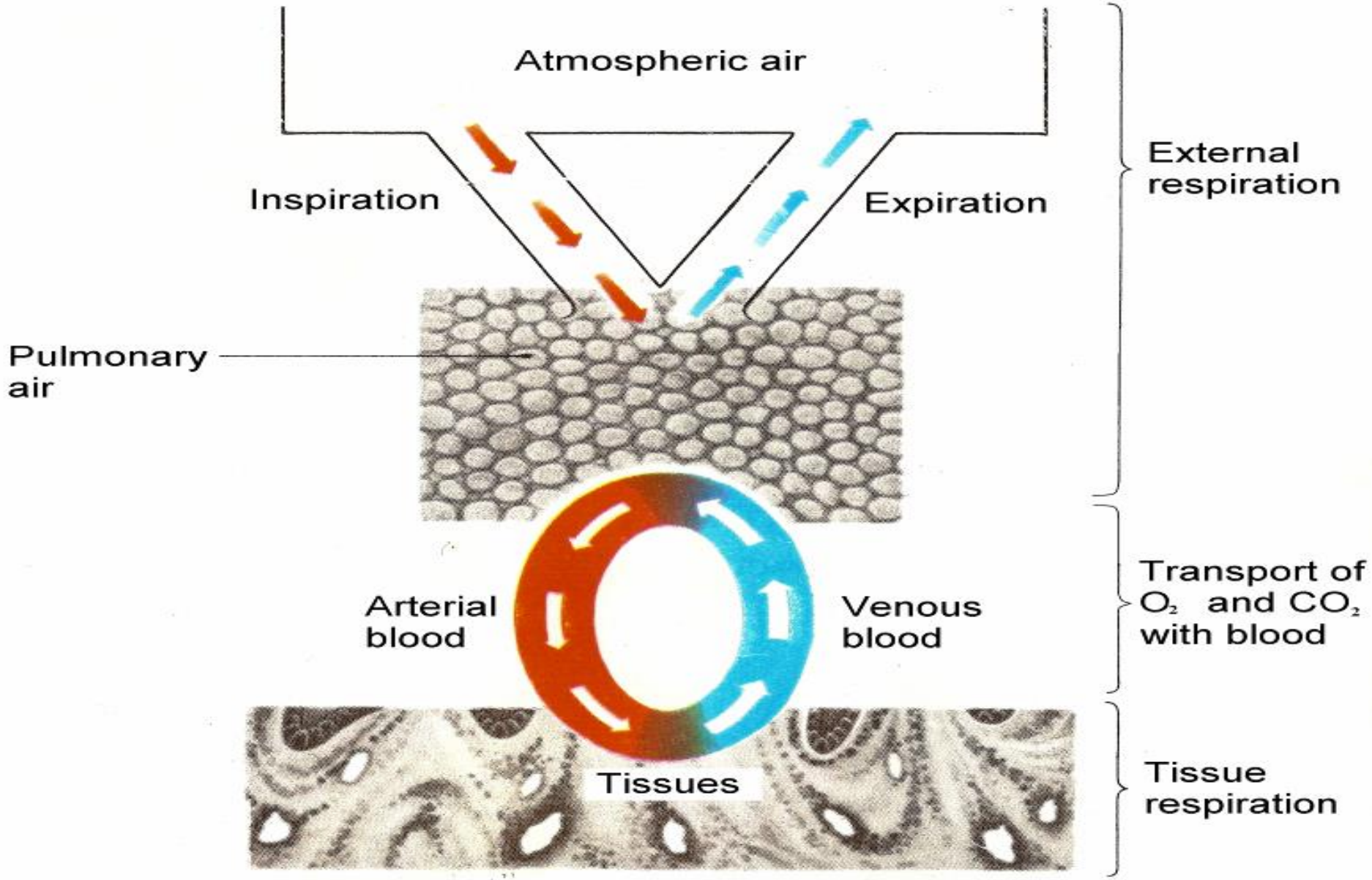


Figure — Process of gas exchange between the environment and the organism

In humans the function of external respiration and renewal of the gas composition of blood is performed by the ***upper and lower airways*** or ***respiratory tract*** *(nasal and oral cavity, larynx, trachea, bronchi, bronchioles, alveolar ways*) and the ***lungs***.(Figure).

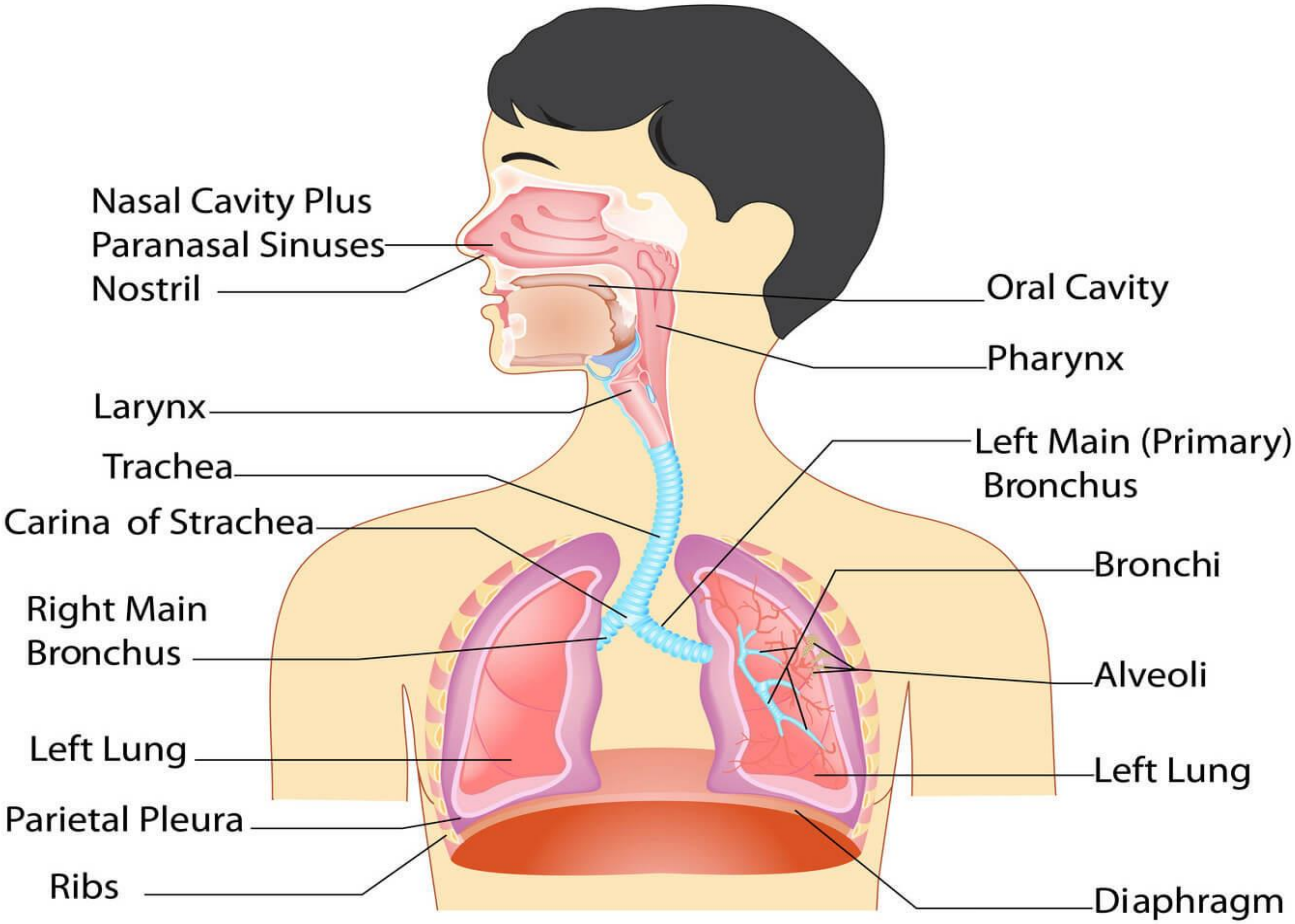


Figure — Anatomy of the respiratory system

A number of adaptive features of the lung structure allow to realize the gas exchange processes:

1. The ***extensive respiratory area of the lungs is 50–90 m^2***.

2. Presence of the special ***small (pulmonary) circle of blood circulation***.

3. Presence of ***elastic tissue*** in the lungs ensuring lung expansion and compression during inspiration and expiration. The lungs have the property of elastic recoil, i. e. the rebound of the lungs after their stretching by inhalation.

4. **Presence of support cartilage tissues** as of the cartilage bronchi in the airways. It prevents collapse of the airways and promotes fast and easy passage of air.

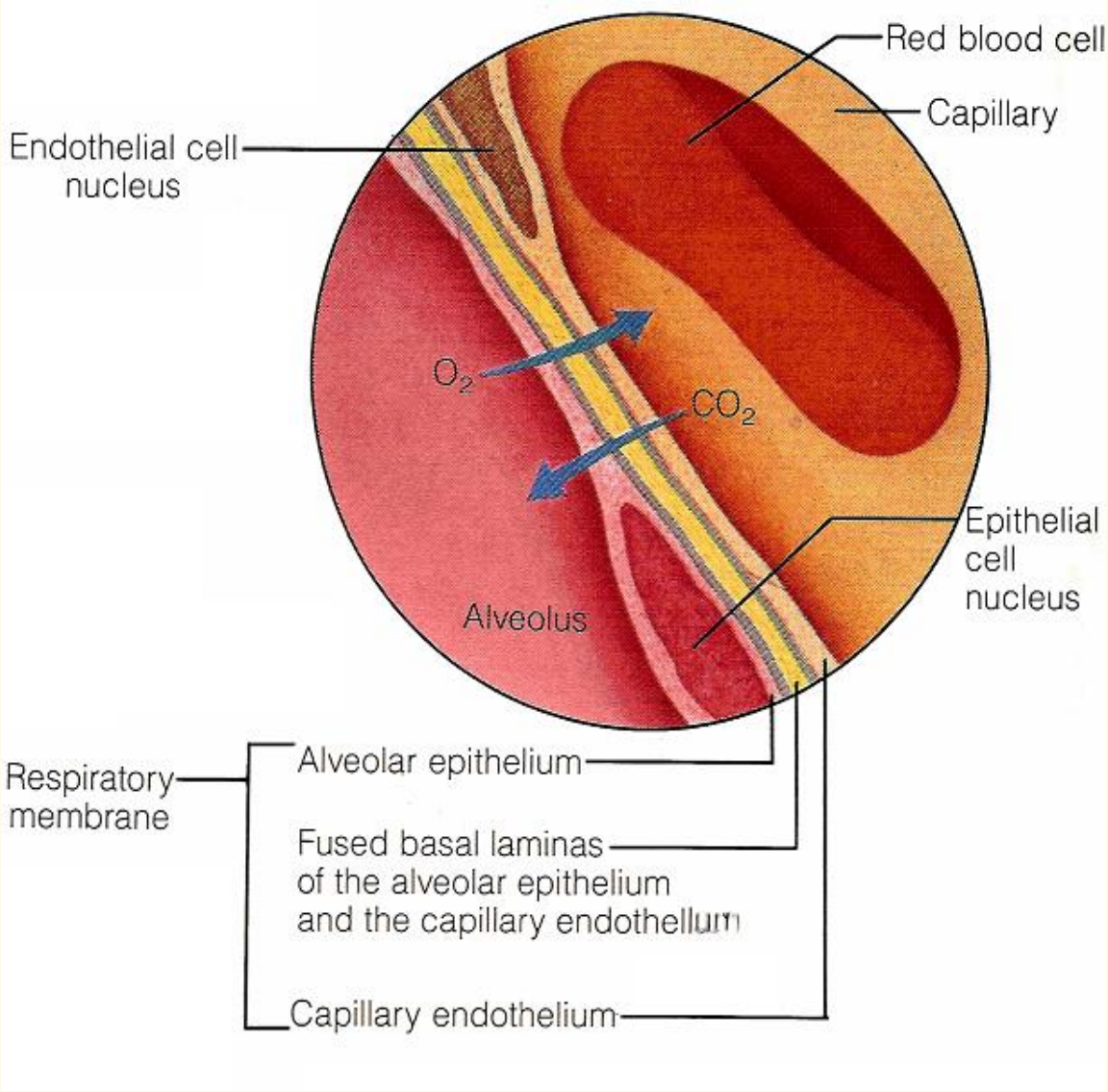


Figure — Anatomy of the respiratory membrane

5. Presence of the ***air and blood channel***, separated by the thinnest (0.004 mm) membrane consisting of a double layer — an alveolar itself and a capillary. Through this **aerohematic barrier** gases diffusion occurs.

Non-respiratory functions of the lungs

The primary function of the lungs is gas exchange. However, the lungs perform several important *non-respiratory functions*.

1. Protective function. The lungs are a barrier between the internal and external environment. In the lungs many immune factors are produced (interferon, lysozyme, immunoglobulins, lactoferrin) which protect the organism from infections.

2. Excretory. During respiration not only carbon dioxide, but also other substances are excreted (acetone, ethanol). Besides, about 500 mL of water is removed due to evaporation from the alveolar surface per day.

3. Blood deposition. The lungs are the physiological depot of blood.

4. Regulation of the aggregate state of blood. When blood passes through the small (pulmonary) circle of circulation, small clots and emboli are removed. The lungs contain a large number of basophils containing heparin. Also, some coagulation and anticoagulation factors are synthesized in the lungs (tromboplastin, factors II, VIII, etc.).

5. Production of biologically active substances. This function is provided by the cells of the diffuse endocrine system which are present in the lungs.

6. Metabolic. In the endothelial cells of the pulmonary capillaries the transformation of biologically active substances takes place. Such substances as serotonin, bradykinin, noradrenaline are exposed to absorption and ferment transformation in the lungs. On the internal surface of the pulmonary capillaries a large amount of angiotensin-converting enzyme is localized, which catalyzes the process of the transformation of angiotensin I into angiotensin II.

7. The lungs participate in thermoregulation (due to water evaporation from the alveolar surface).

8. The lungs play a role in the regulation of the acid-base balance of blood (mainly due to CO_2 excretion).

2. *Respiratory movements.*

Alveolar ventilation necessary for gas exchange is carried out due to the constant alternation of inspiration and expiration. During inspiration the air saturated with O_2 gets into the alveoli. During expiration, the air poor in O_2 but rich in CO_2 is released from the alveoli. **The phase of inspiration and the following phase of expiration make the *respiratory cycle*.**

Air movements are caused by the alternate increase and decrease of the volume of the thorax.

The mechanism of inspiration. Inspiration is ***an active* process**.

During inspiration, the diaphragm contracts and pulls downward while the muscles between the ribs contract and pull upward. This increases the size of the thoracic cavity in the vertical, sagital, frontal planes and decreases the pressure inside. As a result, air rushes in and fills the lungs. During expiration, the diaphragm relaxes, and the volume of the thoracic cavity decreases, while the pressure within it increases. As a result, the lungs contract and the air is forced out.

Rib movement. The ribs form mobile connections with the vertebral bodies and transverse processes of vertebras. As the ribs go upward, the size of the thorax increases in the anteroposterior and lateral dimensions. The elevation of the ribs is caused by contractions of ***inspiration muscles***. They include: ***external intercostal, internal intercartilaginous muscles*** (Figure).

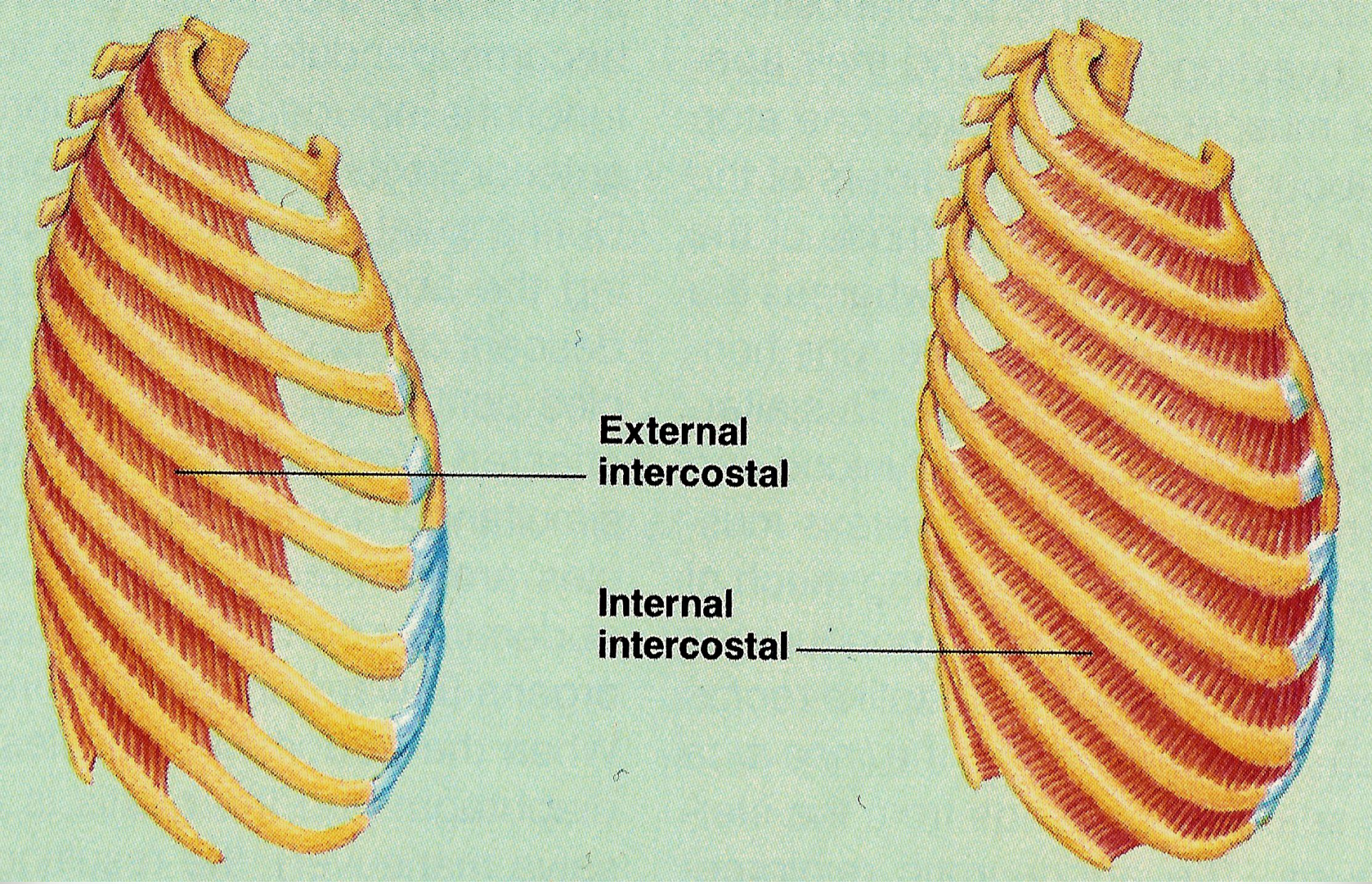


Figure — Intercostal muscles

The movement of the inferior ribs has a big influence on the volume of the thorax, that is why the inferior lobes of the lungs are ventilated better than the superior ones.

In a healthy young ***male*** the difference between the circumference of the thorax during inspiration and expiration ***(thoracic excursion) is 7–10 cm***, ***in a healthy young female — 5–8 cm***. Forced respiration involve *auxiliary inspiration muscles:*

- **greater and smaller pectoral muscles;**
- **scalene muscle;**
- **sternocleidomastoid muscle;**
- **trapezius muscle, etc.**

Movement of the diaphragm. The diaphragm has the form of a dome protruding into the thoracic cavity. During expiration it adjoins the internal wall of the thorax. During inspiration the diaphragm flattens as a result of ***contractions of its muscle fibers*** (Figure).

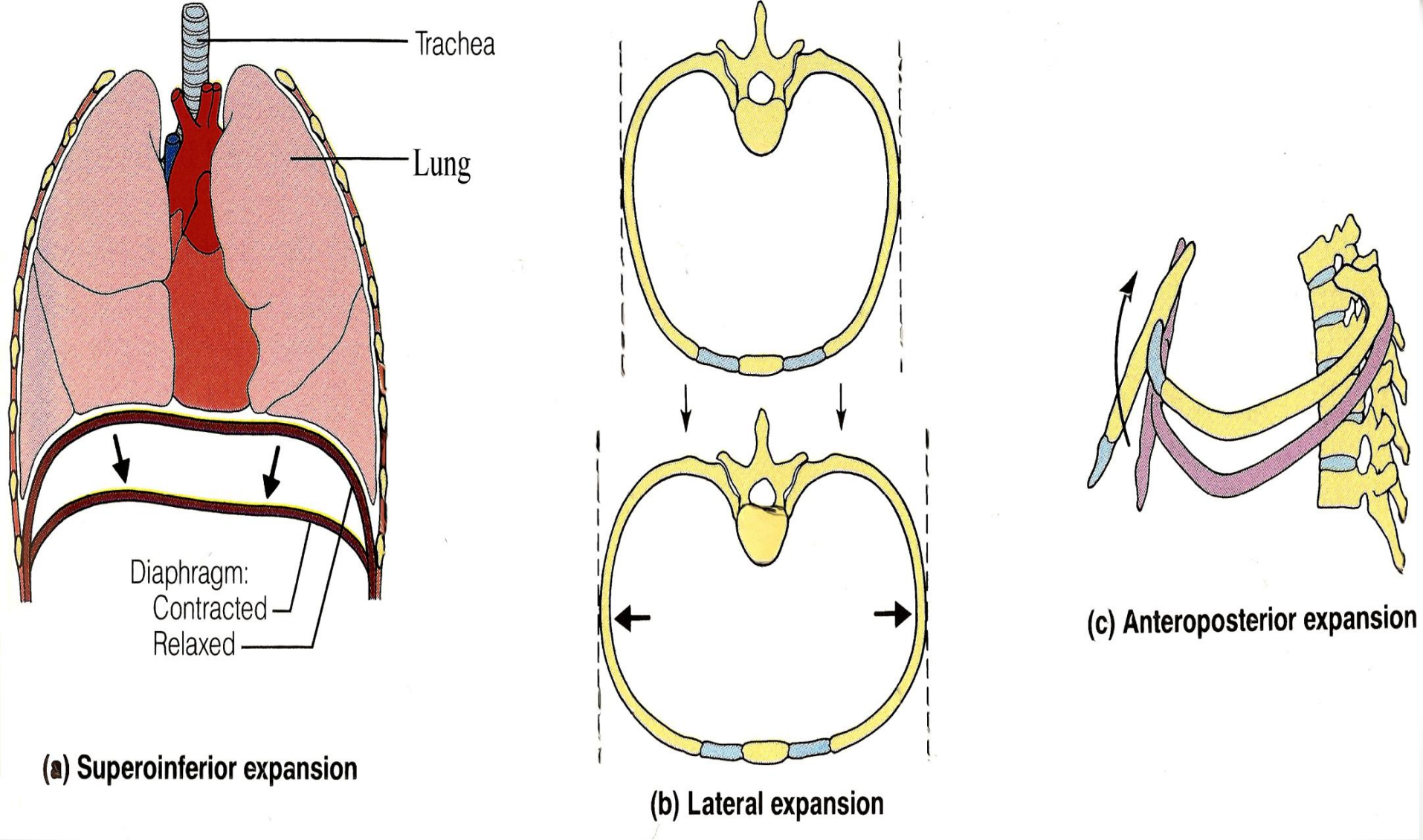


Figure — Changes in the thoracic volume during breathing

Notes: (a-c) Ways in which the volume of the thorax is increased during inspiration. The diaphragm descends as it contracts, increasing the superiorinferior dimension (a). Due to the contraction of the external intercostal muscles the ribs are elevated, the thorax expands laterally (b) and in the anteriorposterior plane (c).

In a person at rest expiration is *passive*.

The mechanism of expiration is ensured by:

- **weight of the thorax;**
- **elasticity of the costal cartilages;**
- **elasticity of the lungs;**
- **pressure of the organs of the abdominal cavity on the diaphragm.**

The following expiration muscles take part in forced respiration: internal ***intercostal muscles*** and *auxiliary expiration muscles* (*backbone flexors, abdominal muscles).*

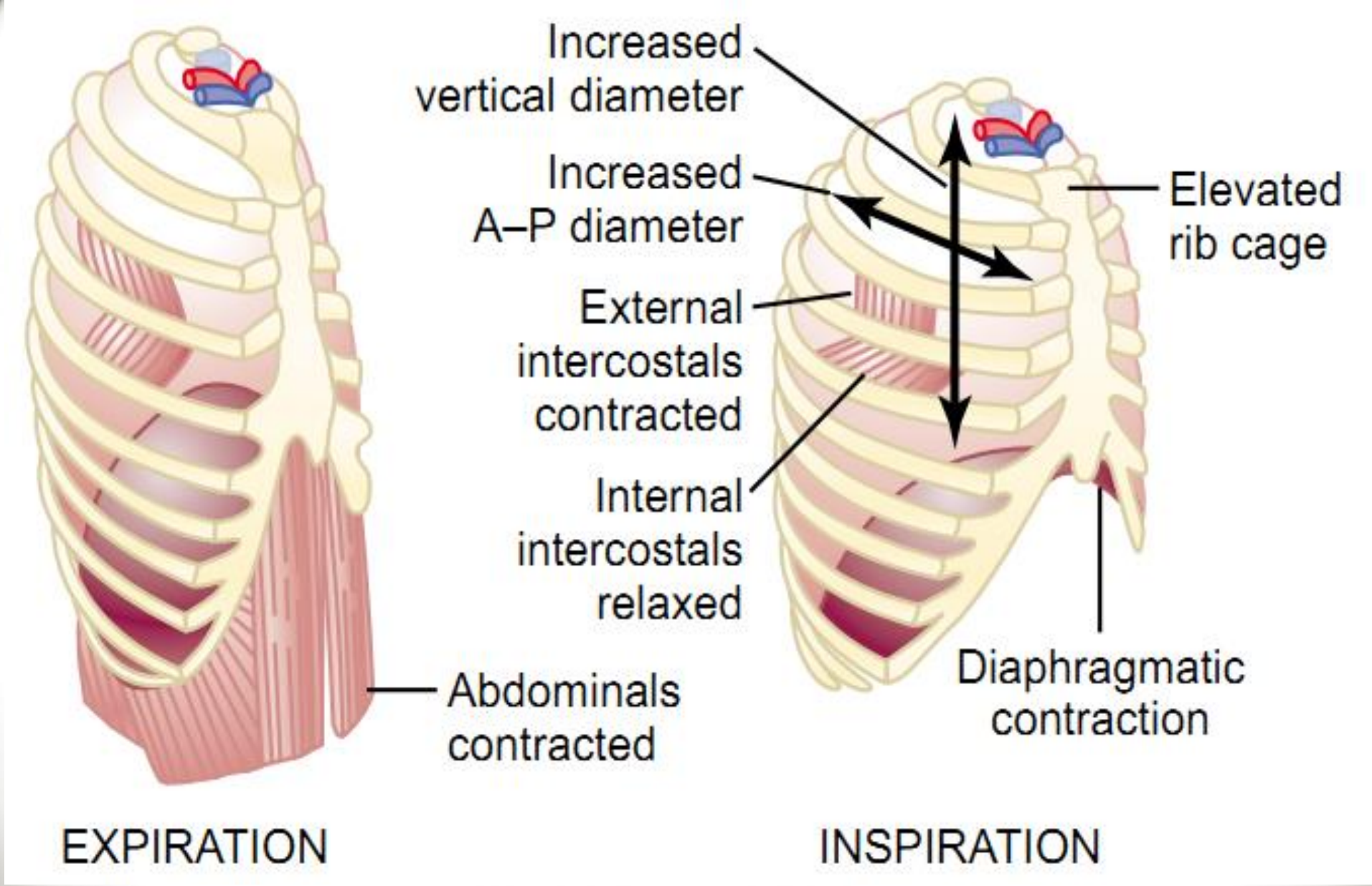


Figure — Contraction and expansion of the thoracic cage during expiration and inpiration

Types of respiration. There are 3 types of respiration depending on which component (elevation of the ribs or lowering of the diaphragm) causes an increase in the thoracic volume:

- **Thoracic** (the main mechanism is *rib movements*).
- **Abdominal** (the m*ovement of the diaphragm*).
- **Mixed**.

To a greater extent the type of respiration depends on age (the mobility of the thorax increases), clothes, profession. As abdominal respiration becomes difficult during the last months of pregnancy, at this period thoracic respiration is involved.

The abdominal type of respiration is the most effective:

- lung ventilation is the deepest.
- return of venous blood to the heart is ensured.

Abdominal respiration prevails in physical workers, opera singers, etc. After birth a baby has abdominal respiration, by the age of 7 it is changed into thoracic.

3. Intrapleural pressure and its change during respiration.

The lungs are covered with the ***visceral pleura***, and the internal surface of the thoracic cavity is covered with the ***parietal pleura***. A thin film of serous fluid fills the space between the two pleurae. The narrow gap (5–10 μm) between the parietal and the visceral pleura is known as the **pleural cavity or space**.

If to insert a needle into the pleural cavity and connect it with a water manometer, the pressure there will be:

during inspiration — 6–8 cm H_2O (4–5 mm Hg);

during expiration — 3–5 cm H_2O (2–3 mm Hg) lower than atmospheric pressure.

This difference between the pressure in the pleural cavity and atmospheric pressure is usually called ***intrapleural pressure (also called intrathoracic pressure).***

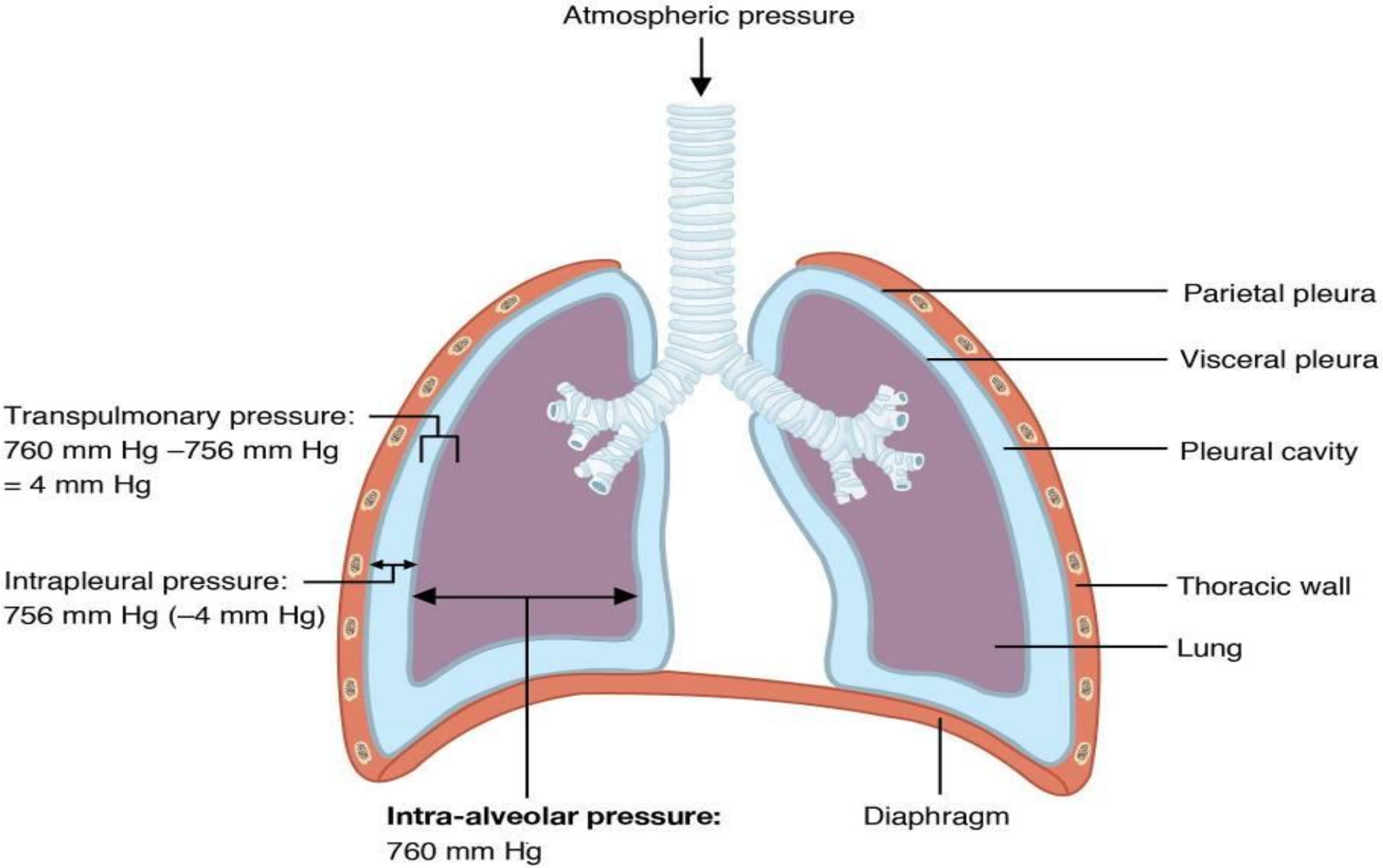


Figure — Intrapleural and transpulmonary pressures

Negative intrapleural pressure is caused by the ***elastic recoil*** of the lungs***, i. e. a tendency of the lungs to collapse.***

During inspiration an increase of the negative pressure in the thoracic cavity leads to an increase of negative intrapleural pressure (Figure).

The accumulation of liquid in the pleural cavity is interfered by the lower oncotic pressure of pleural liquid (it has less amount of protein) than in plasma.

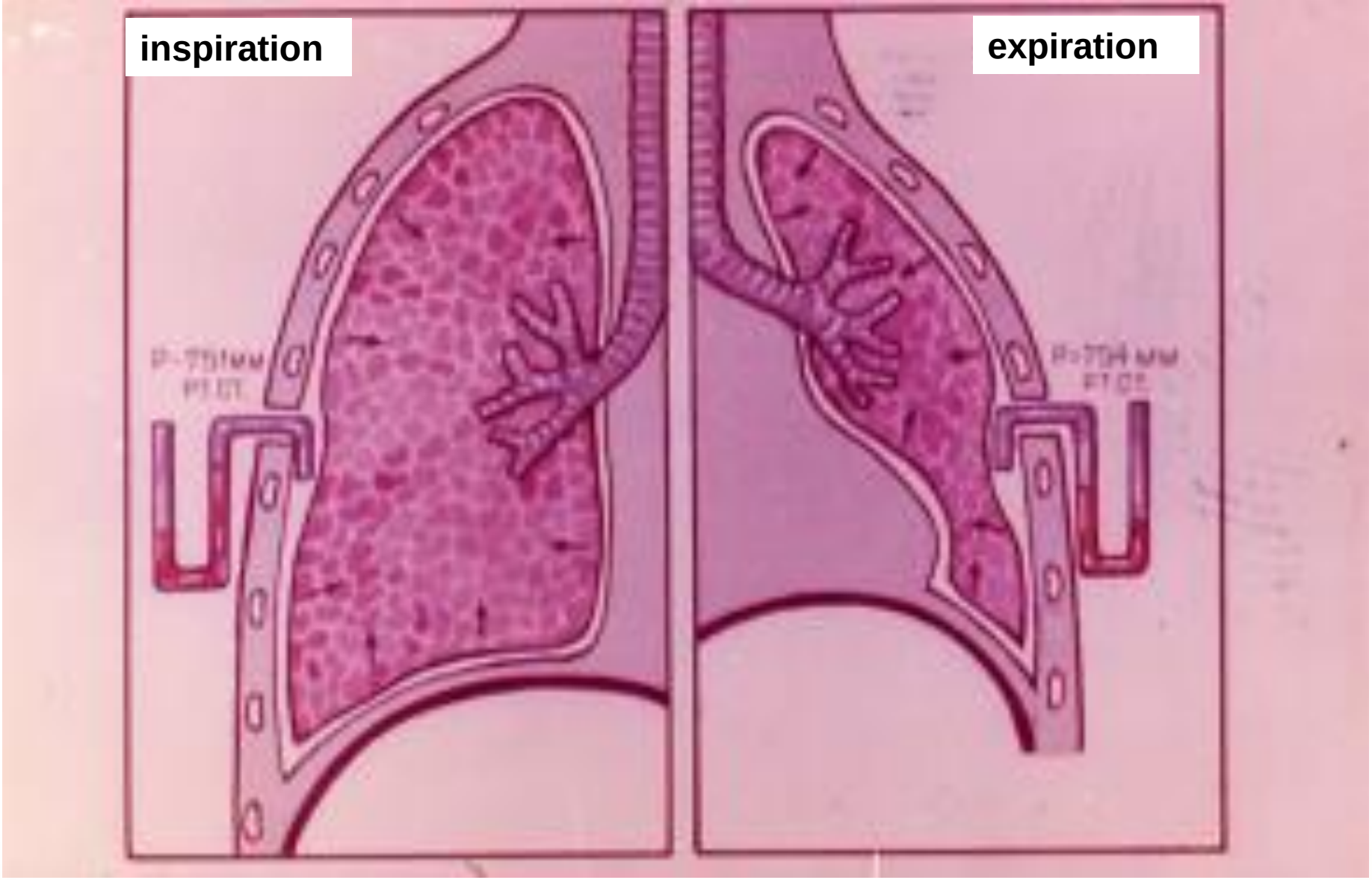


Figure — Pressure in pleural cavity and its change at respiration

The elastic recoil of the lungs is caused by **3 factors:**

- **Surface tension of the liquid covering the internal surface of the alveoli.**
- **Elasticity of the alveolar walls (contain elastic fibers).**
- **Tone of bronchial muscles.**

At liquid–air interfaces there are ***intermolecular forces (forces of surface tension)***. Influenced by these forces the alveoli tend to collapse. The forces of surface tension make 2/3 of the elastic recoil of the lungs.

If the internal surface of the alveoli was covered with a water solution, the surface tension would have to be **5–8 times higher**. In these conditions alveolar collapse would be observed.

A strong influence on the volume of pulmonary compliance and elastic recoil is performed by **surfactant** — a substance composed of phospholipids and proteins, which are formed by the pneumocytes of the 2^{-nd} type. The surfactant is located on the internal surface of the alveoli.

***The role of the surfactant*:**

1) it reduces superficial tension in the alveoli and thus increases lung compliance;

2) it stabilizes the alveoli, interferes adhesion of their walls (interfering atelectasis);

3) it reduces resistance to gas diffusion through the wall of the alveolus;

4) it interferes pulmonary edema by decreasing the force of superficial tension in the alveoli;

5) it facilitates the lung widening in the first inspiration of a newborn;

6) it promotes activation of phagocytosis by alveolar macrophages.

If the size of the alveolus is reduced, the molecules of the surfactant become closer and the surface tension is reduced — the alveolus does not collapse (Figure).

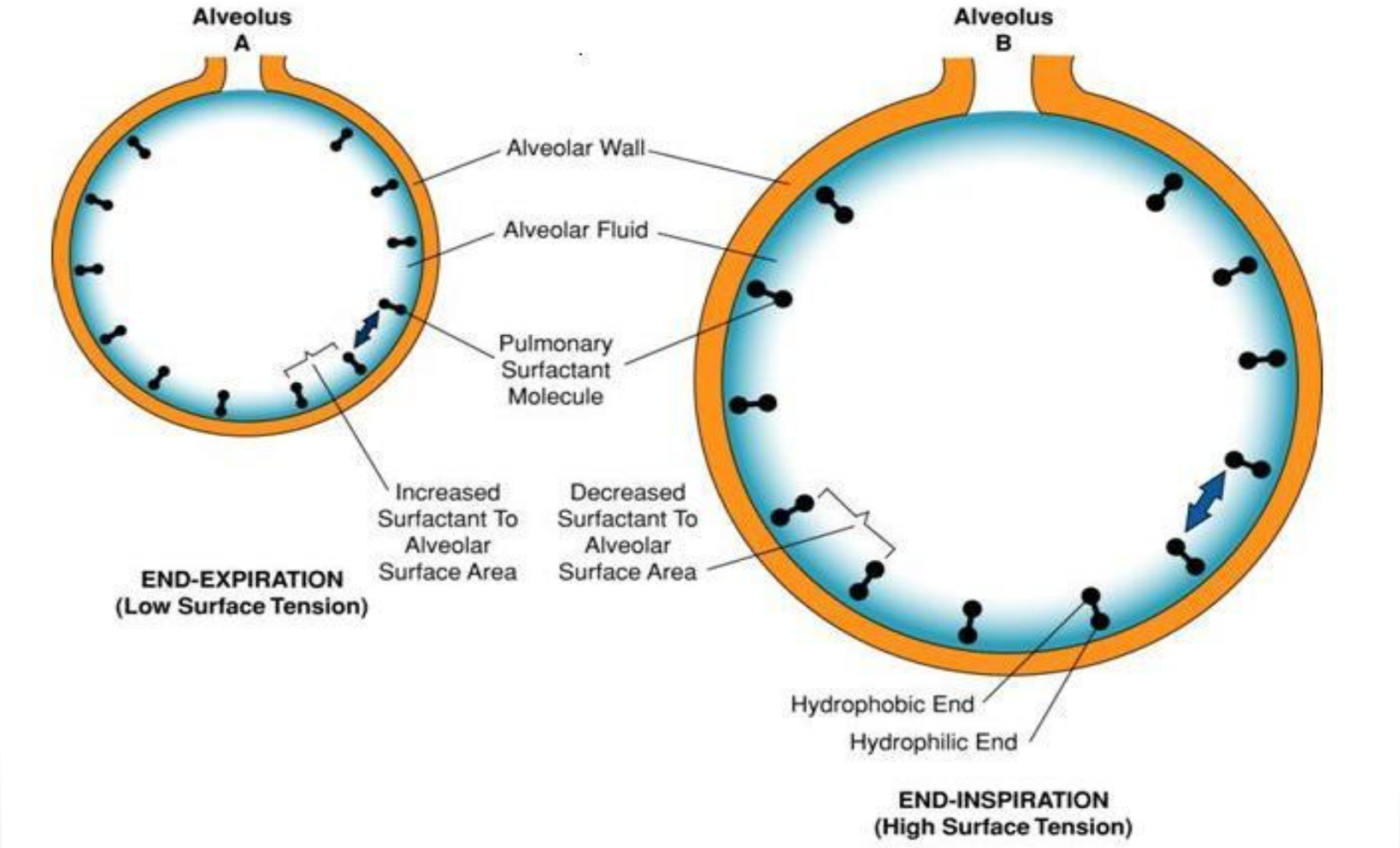


Figure — Pulmonary surfactant regulates alveolar surface tension

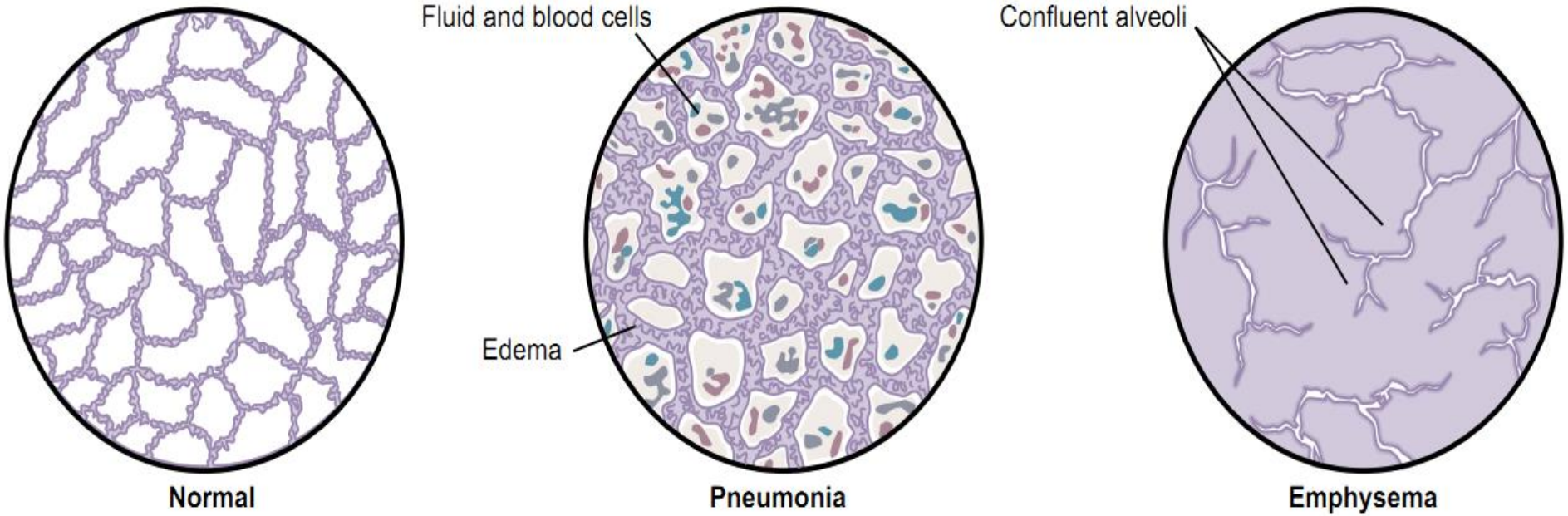


Figure — Lungs alveolar changed at pneumonia and emphyzema

The expansion of the alveoli leads to an increase of their surface tension, which strengthens the elastic recoil of the lungs.

Surfactant deficiency results in collapse of a great number of alveoli — **atelectasis**, or absence of ventilation of large portions of the lungs , i. e. incomplete expansion of the lungs.

In newborns the surfactant is necessary for the lungs to expand during respiration.

The abnormal presence of air in the pleural cavity (through the damaged thorax or lung occurring as a result of disease or injury) is called ***pneumothorax***. Due to their elasticity the lungs collapse into 1/3 of their volume.

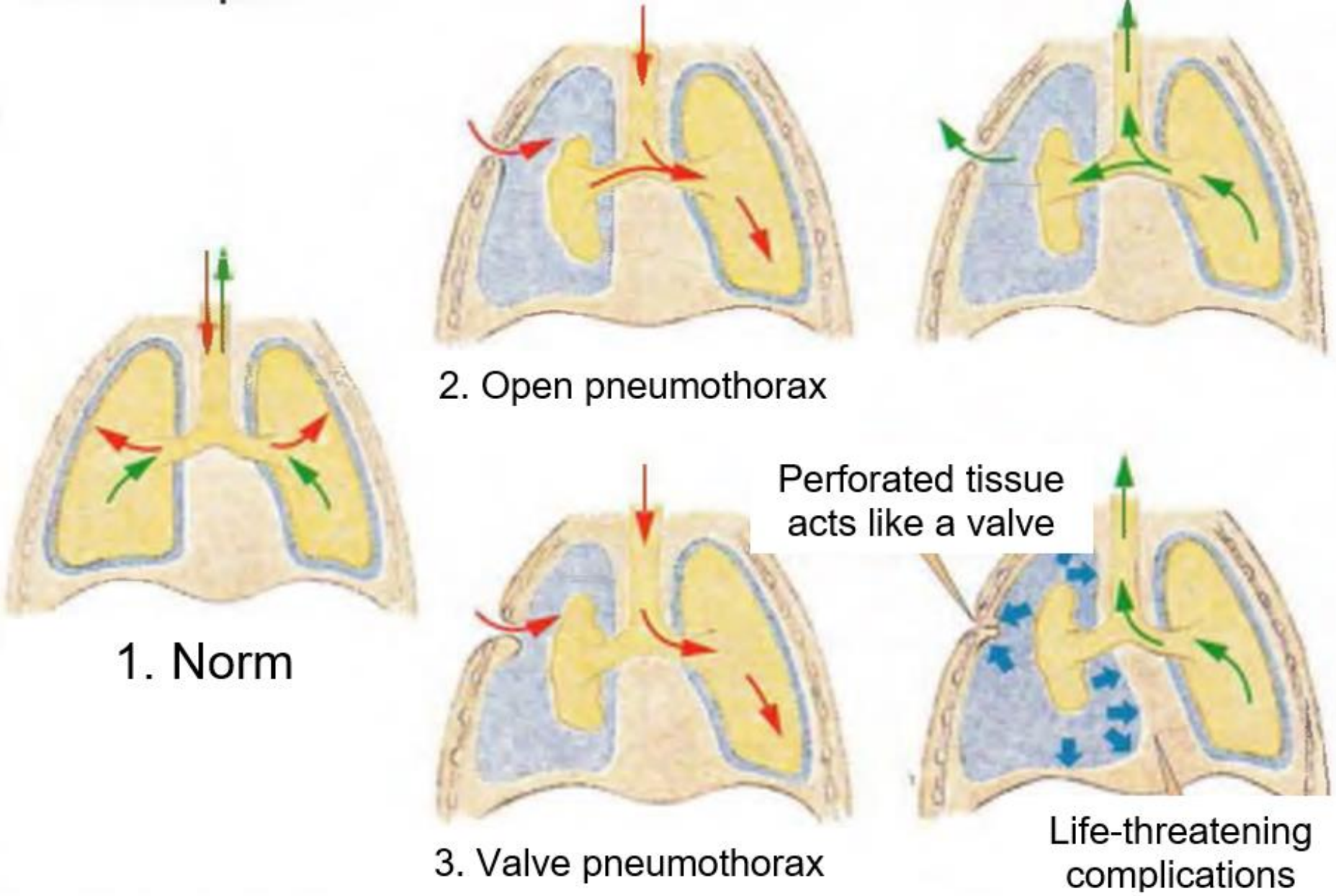


Figure — Types of pneumothorax

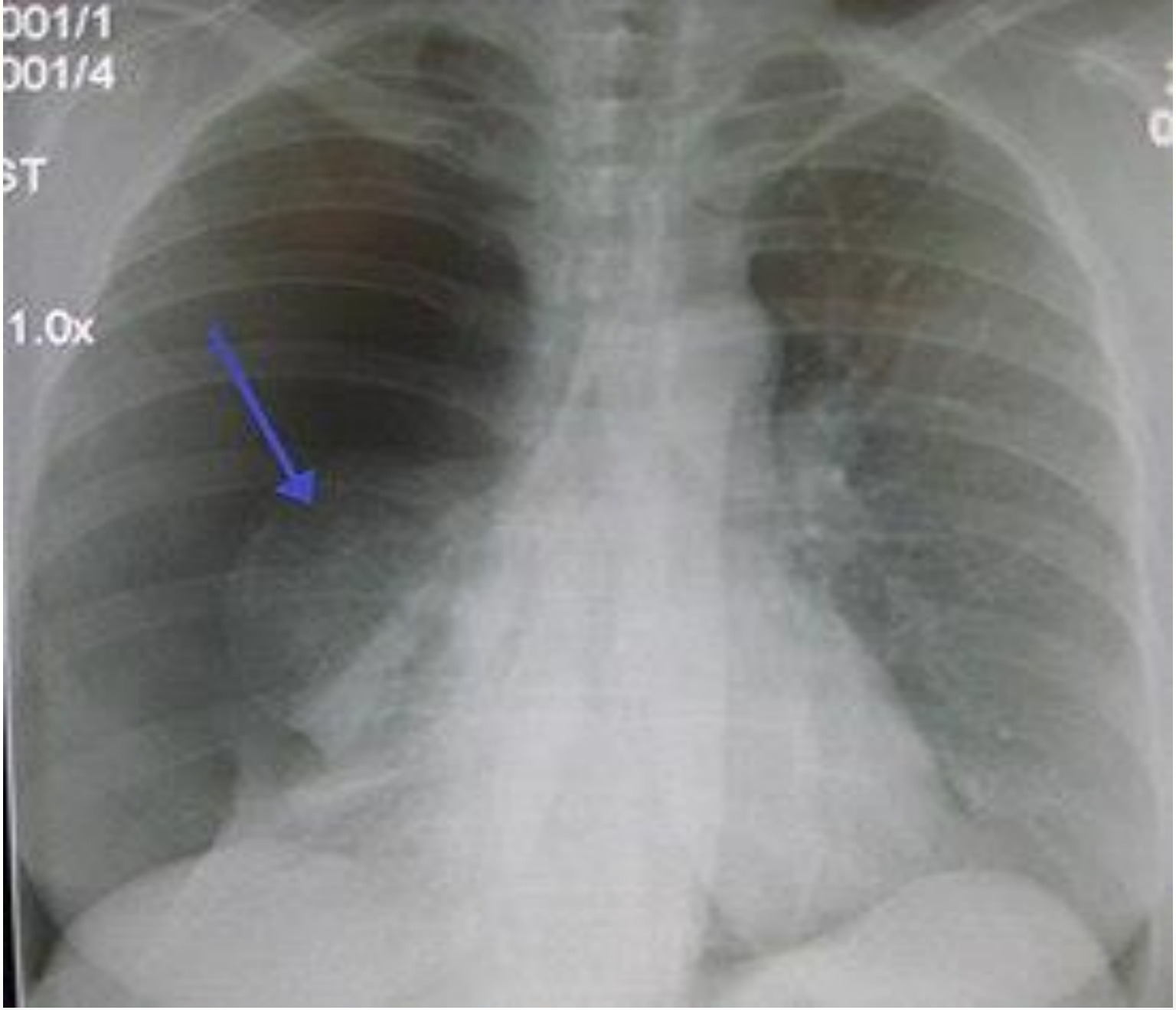


Figure — Pneumothorax

4. *Lung ventilation. Pulmonary volumes.*

Thus, there are 4 initial respiratory volumes and 4 capacities of the lungs (Figure):

1. ***Tidal (respiratory) volume (TV)*** — the amount of air inspired and expired by a person when extra effort is not applied (quiet respiration) (***0.3–0.9 L, approximately 500 mL***).

2. ***Inspiratory reserve volume (IRV)*** — the amount of air which can be inspired after quiet inspiration (***1.5–2.0 L***).

3. ***Expiratory reserve volume (ERV)*** — the amount of air which can be expired after quiet expiration (***1.0–1.5 L***).

4. ***Residual volume*** — the amount of air remaining in the lung after maximal expiration (***1.0–1.5 L***).

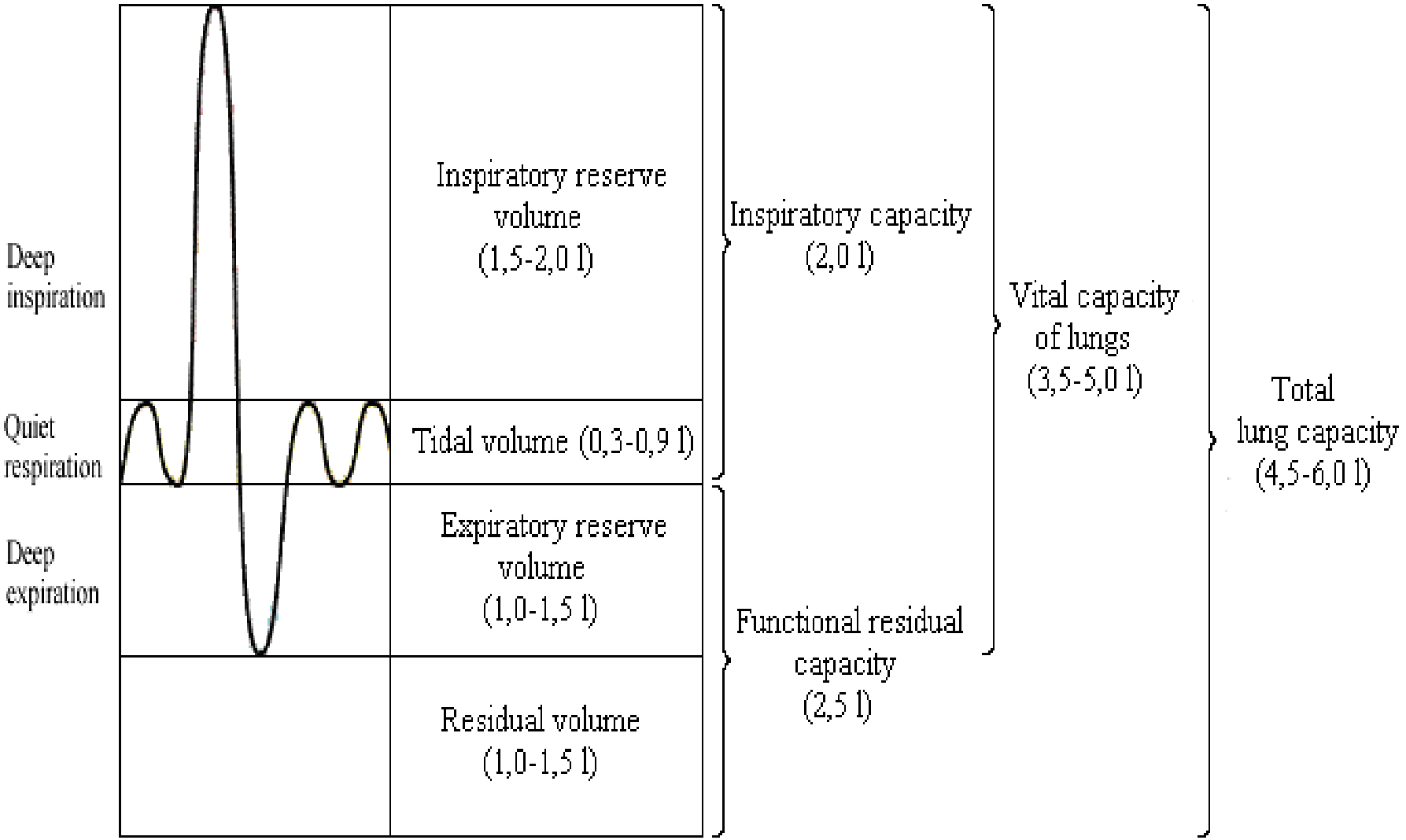


Figure — Spirographic record. Pulmonary volumes and capacities

1. *Vital capacity of the lungs (VCL)* = TV + IRV + ERV (0.5 + 1.5 + 1.5) = 3.5 L (***3.5–5 L***). It indicates the force of respiratory muscles, lung compliance, the area of the respiratory membrane.

2. *Functional residual capacity (FRC),* or alveolar air — the amount of air remaining in the lungs after quiet expiration (***2.5 L***).

3. Total lung capacity (TLC) — the amount of air contained within the lungs in the maximal inhalation (***4.5–6.0 L***).

4. *Inspiratory capacity (IC)* includes the tidal volume + inspiratory reserve volume (***2.0 L***).

VCL determines the maximal volume of air which can come or go out of the lungs during one inspiration or expiration. This is the indicator of the mobility of the lungs and the thorax.

Factors influencing VCL:

Age. VCL declines after 40 (due to decreased lung elasticity and thoracic mobility).

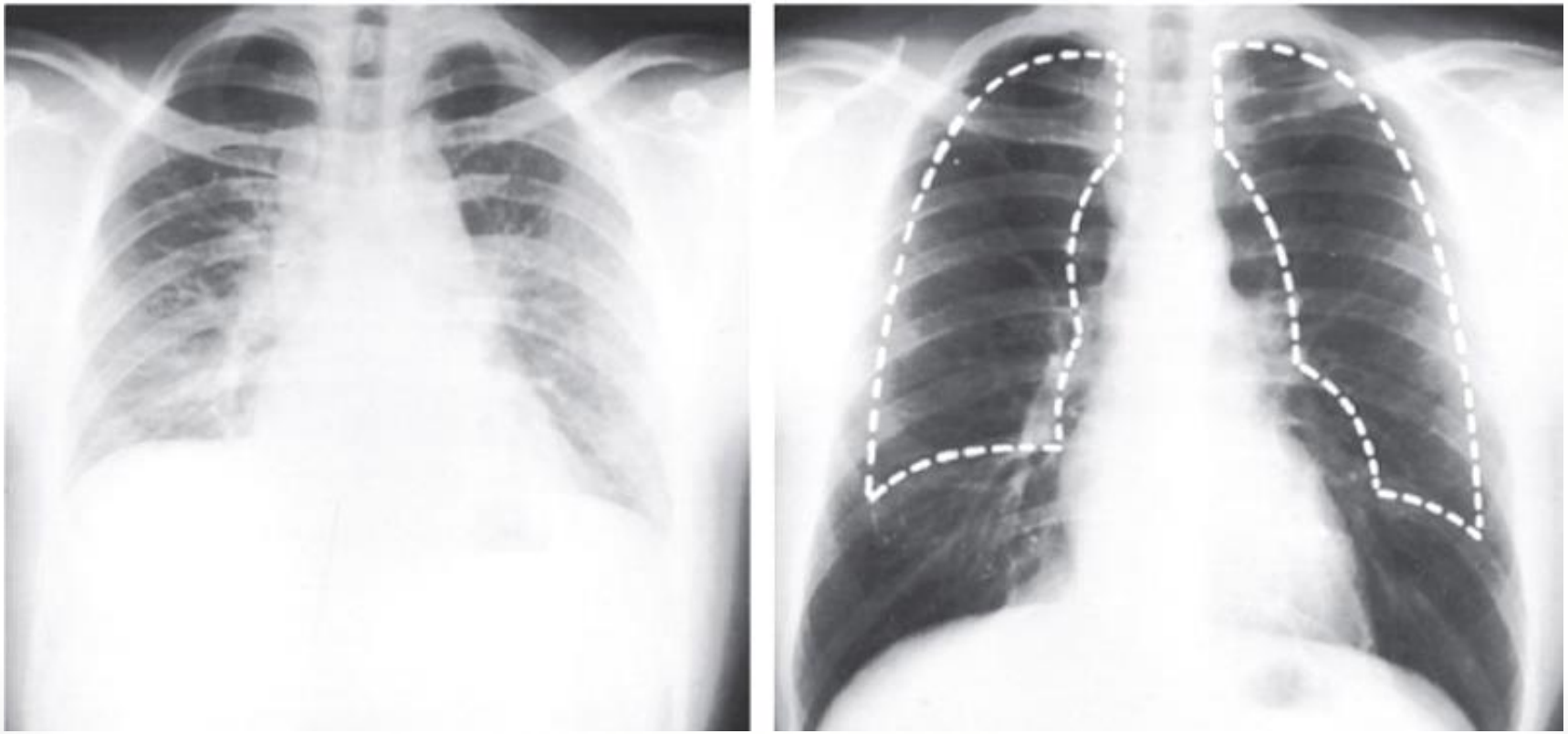
Sex. In women VCL on average is in 25 % lower than in men.

Body size.

Body position. In the vertical position it is higher than in horizontal (due to the greater filling of the pulmonary blood vessels).

Degree of physical activity. In physically fit people VCL increases (especially in swimmers).

Figure — Reserve volumes of the lungs



X-ray of chest in full expiration and full inspiration

5. Dead space

There are two types of dead space:

Anatomic dead space.

Functional (physiological) dead space.

Dead space refers to the space in which oxygen (O2) and carbon dioxide (CO2) gasses are not exchanged in the respiratory tract. ***Anatomic dead space*** specifically refers to the volume of air located in the segments of the respiratory tract that are responsible for air conduction to the alveoli and respiratory bronchioles but do not take part in the process of gas exchange itself (nasal and oral cavities, larynx, trachea, bronchi, bronchioles, alveolar ways).

Its physiological roles are:

- **Air cleaning (the mucous membrane catches fine particles of dust, bacteria).**
- **Air humidifying (secret of the epithelial glandular cells).**
- **Air warming (the temperature of expired air is approximately 37 °C).**

The ***volume of anatomic dead space*** is on average 150 ml (***140–170 mL***).

Therefore, out of 500 mL of the respiratory volume only 350 mL will get into the alveoli. The volume of alveolar air is 2,500 mL. ***The pulmonary ventilation coefficient thus is 350: 2,500 = 1/7***, i. e. as a result of 1 respiratory cycle only 1/7 part of air of FRC is refreshed, or its complete refreshing occurs of not less than 7 respiratory cycles.

***Physiologic (functional)* dead space** is the sum of anatomic and alveolar dead spaces. *Alveolar dead space* refers to the volume of air in the alveoli that are ventilated but not perfused, and thus gas exchange does not take place. Usually such alveoli are few, therefore the volume of anatomic dead space is almost equal to functional dead space.

6. Alveolar ventilation

The average normal respiratory rate in an adult is 14 ***(12–18) breaths per minute***.

In children it is more frequent: in infants — 30–40 breaths per minute, ***in newborns — 40–55 per minute***.

The respiratory minute volume (RMV), or minute ventilation – the minute volume of breathing, i. e. the total volume of gas inhaled (inhaled minute volume) or exhaled (exhaled minute volume) from the lungs per minute.

The respiratory minute volume can be calculated by the following formula:

$$\mathbf{RMV = TV \times RR;}$$

where TV is the tidal volume and RR is the respiratory rate per minute.

For example,

RMV = 500 mL × 14 = **7 L**.

Respiratory minute volume at rest is 6–8 L/min. During physical activity RMV can increase up to 120 L/min.

Deep and infrequent respiration is more effective than superficial and frequent respiration.

Minute ventilation is regulated so that it can provide constant gas composition of alveolar air.

If normal RMV is 7 L/min, but the respiratory rate is too frequent (35 breaths per minute) and superficial (TV = 0.2 L), mainly the dead space will be ventilated and inspired air will not reach the alveoli. Such a condition is dangerous for life.

Alveolar ventilation **is the total volume of new air reaching the alveoli during a breath per minute**. It can be calculated by the formula:

$$\mathbf{V_A = RR \times (TV\text{-}V_D);}$$

where V_A is alveolar ventilation per minute, RR — respiratory rate per minute; TV — tidal volume; V_D — dead space volume.

Normally, **alveolar ventilation** is **4.2–5.6 L/min.**

One of the indicators of the respiratory system reserves ***is the maximal ventilation of lungs (MVL) or maximal voluntary ventilation*** — volume of air passing through the lungs within a certain time interval during respiration with the maximal possible frequency and depth.

MVL varies within 120–170 L/min and depends on age, sex, body size.

Alongside with the respiratory volumes and capacities, some additional parameters are determined for the evaluation of pulmonary function.

Forced vital capacity (FVC) is defined as the amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible (which depends on height, weight, and other factors). *The normal difference between VCL and* ***FVC*** *is* ***100–300 mL.*** In bronchial obstruction FVC is increased.

Forced expiratory volume (FEV1) refers to the maximal volume of air that can be exhaled during a forced breath per second. It averages around three liters, which makes **70–80 % of VCL** (the parameter FEV1/FVC or FEV1 %, Tiffeneau index). This parameter is decreased in bronchial obstruction.

Peak expiratory flow (PEF) or peak expiratory flow rate is the maximal flow rate of air achieved during a forced expiration. It is usually measured with a peak flow meter.

In clinical practice pneumotachometers are widely used. They allow to perform continuous registration of the flow rate of expired air during expiration of forced vital capacity. Due to this it is possible to evaluate the parameters of **forced expiratory flow (FEF)** — the flow rate of air coming out of the lungs during the middle portions of forced expiration which is determined at the moments of expiration of the deferent fractions of the forced vital capacity. The usual intervals are 25, 50, and 75 % of FVC (FEF 25 %, FEF 50 %, and FEF 75 %).

The «flow — volume» curve reflects the change of the expiratory flow during the process of forced expiration (Figure 6.8). The form of the curve has a certain diagnostic value. The part of the curve corresponding to 0–25 % of FVC depends on the passage of air through the large bronchi, trachea, and upper airways. The part from 50 to 85 % of FVC reflects the passage through the distal bronchi and bronchioles.

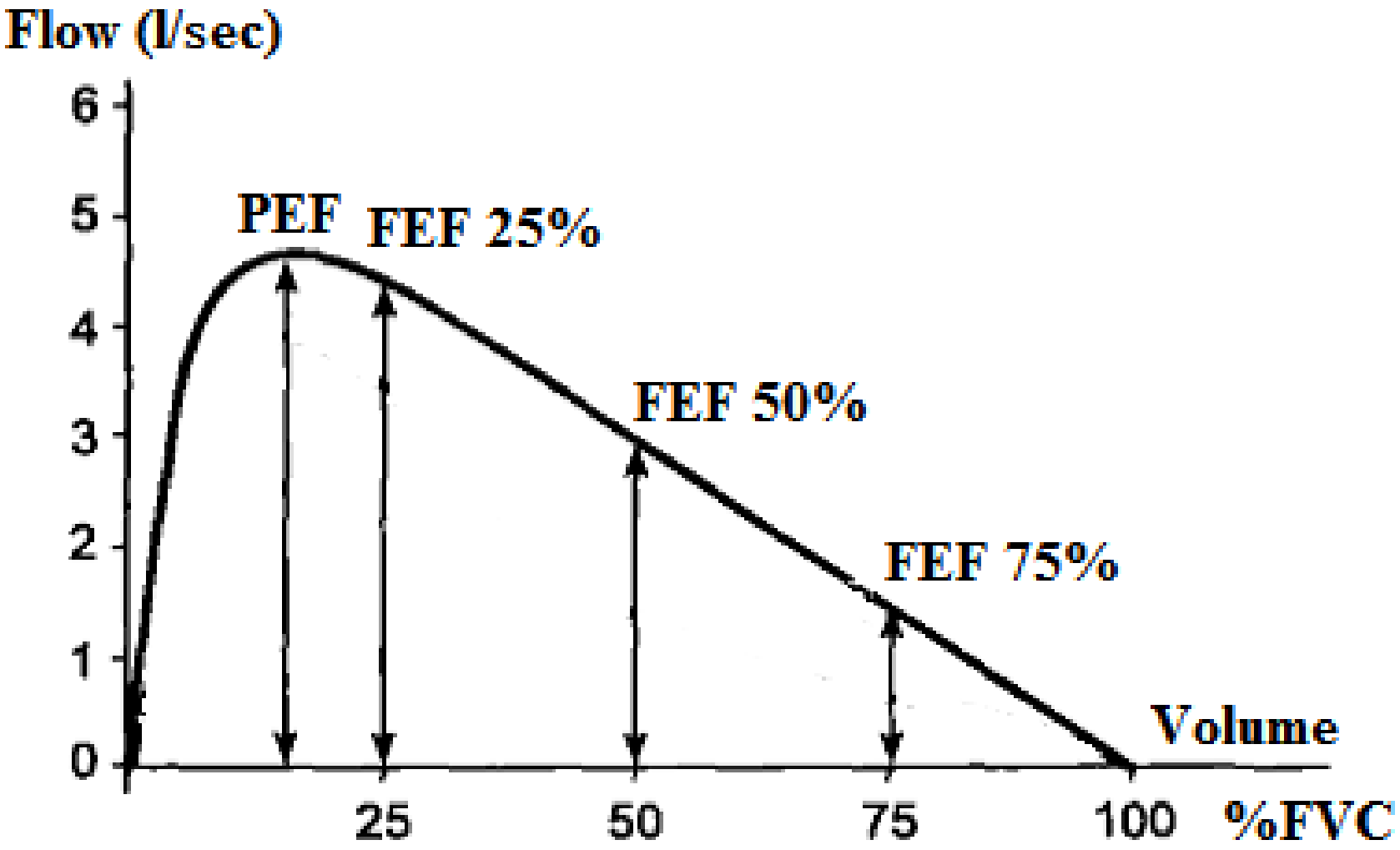


Figure — The «flow–volume» curve in a healthy person

Note: PEF — peak expiratory flow; FEF 25 % — forced expiratory flow during expiration of 25 % of FVC; FEF 50 % — forced expiratory flow during expiration of 50 % of FVC; FEF 75 % — forced expiratory flow during expiration of 75 % of FVC

The determination of all the above listed parameters is used for the evaluation of the function of external respiration.

There are two basic types of disorders of external respiration.

1) Obstructive type is characterized by the increased resistance of the respiratory passageways for air flow. They can be caused by the increased tone of the smooth muscles of the bronchioles, hypertrophy of the mucous membrane, mucus accumulation, tumors, and other factors. Obstructive type is characterized by decreased PEF, FEV1, FEF 25 %, FEF 50 %, FEF 75 %, Tiffeneau and MVL indices. Also, in obstructive disorders the residual volume, functional residual capacity, and total lung capacity are increased.

2) Restrictive type usually occurs due to decreased lung compliance and lung expansion during inspiration. The causes are pulmonary fibrosis, accumulation of fluid in the pleural cavity and others. The main sign of restrictive disorders is decreased VCL (by 20 % and more from the due vital capacity), total lung capacity, functional residual capacity, and residual volume.

The mixed type of external respiratory failure is also observed.

7. Gas exchange in the lungs.

Gas exchange is the delivery of oxygen from the lungs to the bloodstream, and the elimination of carbon dioxide from the bloodstream back to the lungs. The exchange of gases occurs between the alveoli and capillaries by O_2 diffusing from the air of the alveoli into the blood (approximately **500 L of O_2**) and CO_2 diffusing from the blood into the alveolar air (**450 L of CO_2**).

1. The **partial pressure of gases** is a measure of great importance for pulmonary gas exchange.

Atmospheric air inhaled during respiration has a relatively constant composition (Table).

Table — Composition of air

Air	O_2, %	CO_2, %
Inhaled	21.0	0.02–0.03
Exhaled	16.0	4.5
Alveolar	14.0	5.5

Partial pressure **is the pressure of gas in gas mixture. It is proportional to the concentration of gas** (in %) and general pressure of gas mixture.

The example of the measurement of pO_2 и pCO_2 in atmospheric air:

$$pO_2 = \frac{760 \text{ mm Hg} \times 21{,}0}{100} = 159 \text{ mm Hg.}$$

$$pCO_2 = \frac{760 \text{ mm Hg} \times 0{,}03}{100} = 0.23 \text{ mm Hg.}$$

For the measurement of the partial pressure of gases in alveolar air the vapor pressure of water (47 mm Hg) should be taken into account:

$$pO_2 = \frac{(760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 14}{100} = 100 \text{ mm Hg}$$

$$pCO_2 = \frac{(760 \text{ mm Hg} - 47 \text{ mm Hg}) \times 5{,}5}{100} = 40 \text{ mm Hg}$$

The partial pressure of each gas in the alveolar gas mixture tends to force the molecules of this gas into the blood of the alveolar capillaries.

Gas diffusion occurs due to the difference of the partial pressure of these gases in alveolar air and their pressure in the blood (partial pressure of gas in a liquid) (Figure).

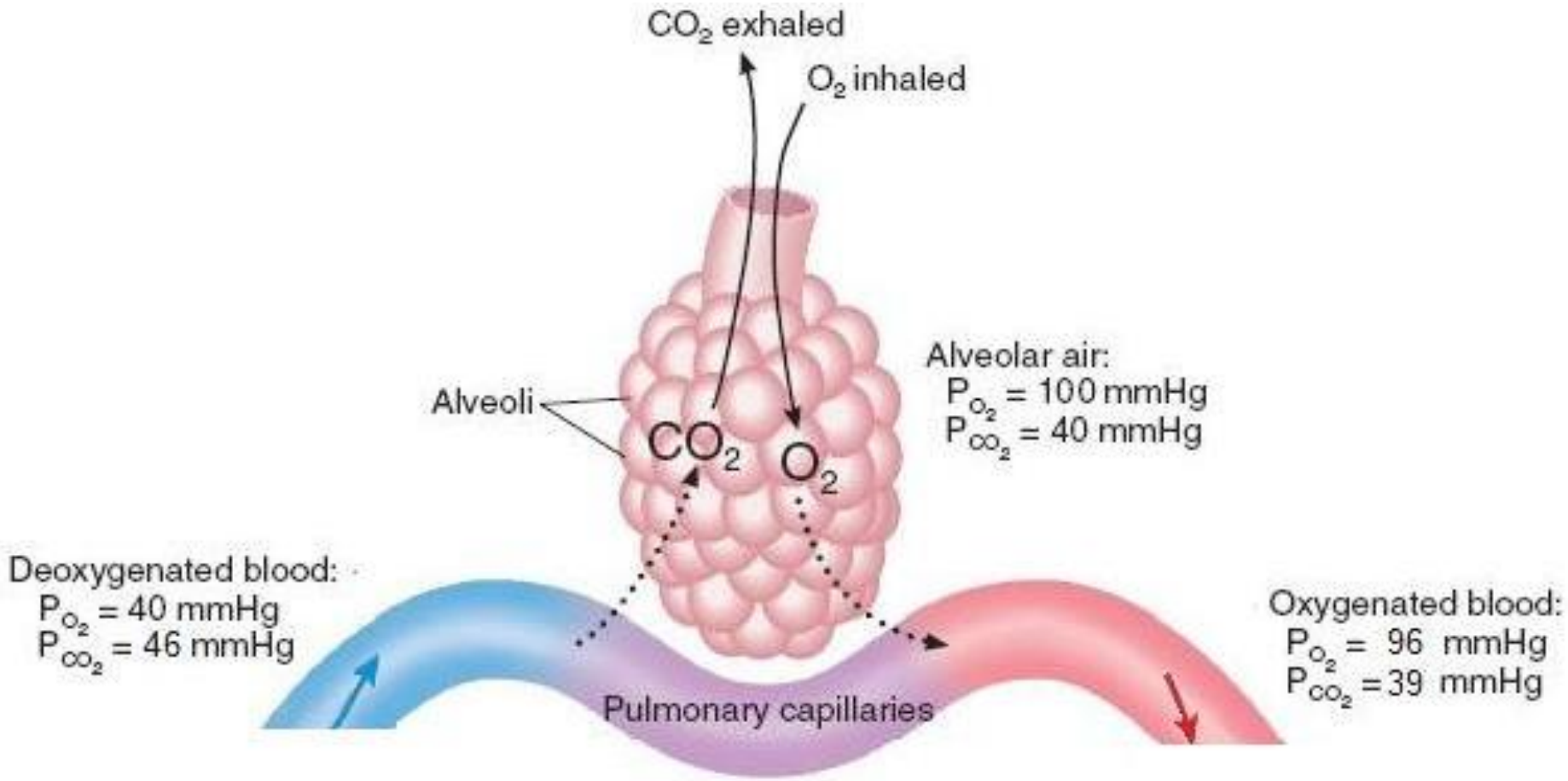


Figure — Gas exchange in the lungs between the alveolus and capillary

In the blood gases are in dissolved and chemically bound conditions. The force with which a molecule of gas tends to enter a gas environment is called **the partial pressure of gas in a liquid**.

The amount of gas dissolved in a liquid depends on:

- **the composition of the liquid;**
- **the volume and pressure of the gas over the liquid;**
- **the temperature of the liquid;**
- **the nature of the gas.**

If the partial pressure of gas is *greater in the gas phase* in the alveoli, (which is normally true for oxygen), more *gas molecules diffuse into the blood.* Alternatively, if the pressure of gas is greater *in the dissolved state* in the blood, (which is normally true for CO_2), the *diffusion occurs towards the gas phase in the alveoli.*

The diffusion of O_2 is provided by the difference of its partial pressures equal to 60 mm Hg (p O_2 in alveolar air is 100 mm Hg and pO_2 in venous blood is 40 mm Hg, table). The diifference of partial pressures for CO_2 is 6 mm Hg (pCO_2 in venous blood is 46 mm Hg and pCO_2 in alveolar air is 40 mm Hg). CO_2 diffusion into alveolar air occuring at the relatively low difference of the pressures is explained by the high diffusion capacity of this gas.

Table — Partial pressure of gases (mmHg)

Gas	Venous blood	Alveolar air	Arterial blood
O_2	40	100	96
CO_2	46	40	39

The constancy of the gas composition of alveolar air is a necessary condition of normal gas exchange. Dead space, which carries out the function of a buffer smoothing fluctuations of the composition of alveolar air during the respiratory cycle, plays an essential role in the maintenance of the given constancy.

The diffusion of oxygen and carbon dioxide occurs passively, according to their concentration differences across the alveolar-capillary barrier. These concentration differences must be maintained by ventilation of the alveoli and perfusion of the pulmonary capillaries. ***Ventilation-perfusion relationships*** reflect the conformity of the respiratory minute volume to cardiac output during the pulmonary circle of blood circulation. The normal **ventilation-perfusion coefficient (VPC)** is ***0.8–1.0***.

$$VPC = \frac{\text{RMV (L/min)}}{\text{CO}_2\text{ (L/min)}} = 0.8\text{-}1.0$$

Smooth muscles of the majority of the vessels of the systemic circle of blood circulation dilate if there is low O_2. On the contrary, smooth muscles in the vessels of the pulmonary circulation constrict, which causes the narrowing of the vessels in poorly ventilated parts of the lungs and reduction of the blood flow.

The human requirement for O_2 is 250–300 mL/min (in physical exertion — up to **5000 mL**).

2. A comparatively thin **aerohematic barrier (0.4–1.5 μm)** (Figure) between the air and blood vessels including:

1) the surfactant layer (surfactant is one of the factors promoting O_2 diffusion);

2) the alveolar epithelium;

3) two basal membranes;

4) the endothelium of capillaries.

Apart from this barrier, during diffusion O_2 goes through:

- the layer of blood plasma;
- the membrane of erythrocytes.

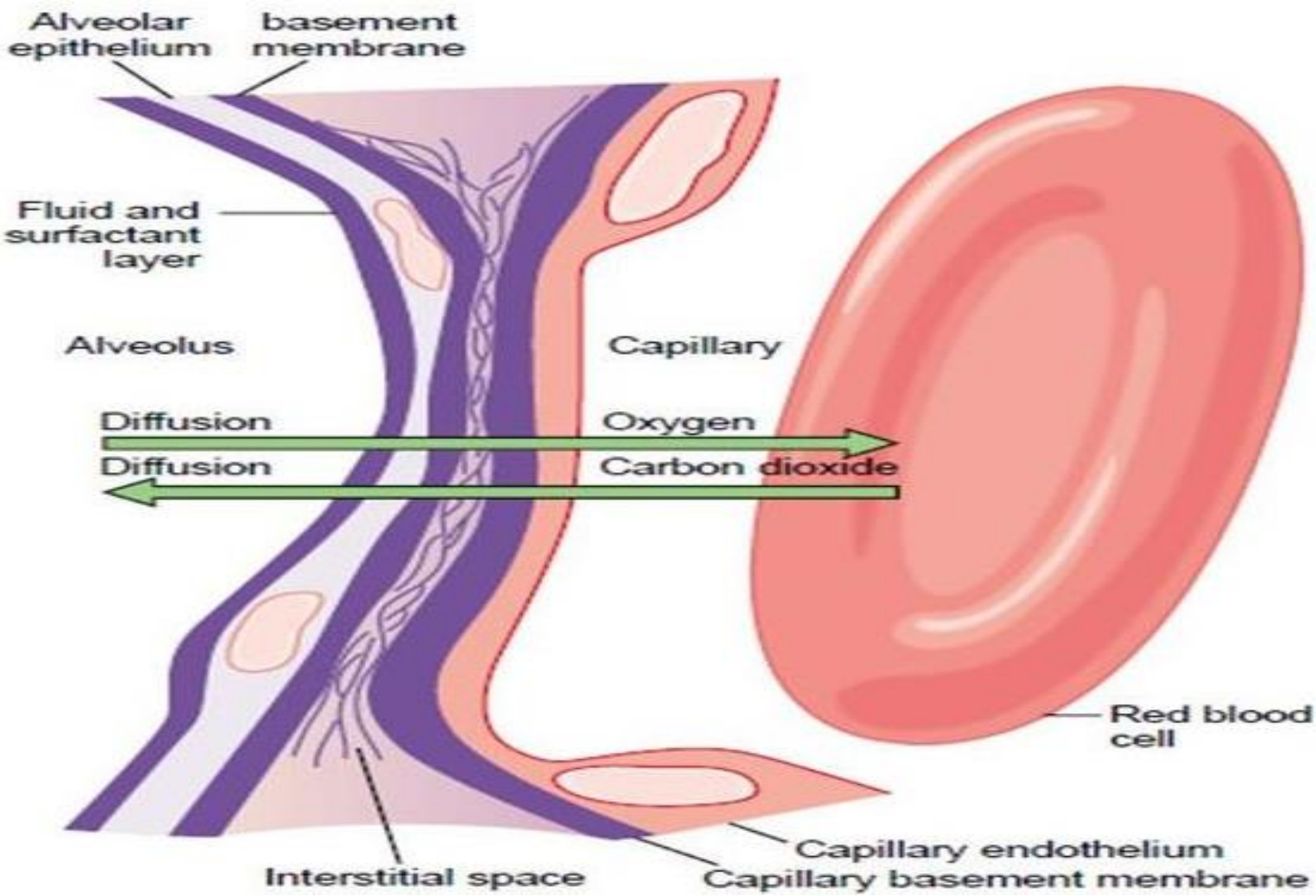


Figure — Structure of the aerohematic barrier

3. High **diffusion capacity of the lungs**. It is defined by the amount of gas penetrating through the lung membrane per minute for 1 mm Hg of gradient of pressure.

For O_2 it is 25 mL/min. x mm Hg.

For CO_2 the diffusion ***capacity is 24 times more*** (CO_2 has high solubility).

4. Great total alveolar surface (approximately 90 m^2).