PHYSIOLOGY OF RESPIRATION

Respiration includes 2 processes:

1) **External respiration** – is the uptake of O₂ and excretion of CO₂ in the lungs
2) **Internal respiration** – means the O₂ and CO₂ exchange between the cells and capillary blood

The quality of these respiration processes depends on:

a) **pulmonary ventilation** – it means the inflow and outflow of air between the atmosphere and the lung alveoli
b) **diffusion** of oxygen and CO₂ between the alveoli and the blood
c) **perfusion** – of lungs with blood
d) **transport** of O₂ and CO₂ in the blood
e) **regulation** of respiration

Nonrespiratory functions:
- in voice production
- protective reflexes (apnoea, laryngospasm)
- defensive reflexes (cough, sneeze)
- in thermoregulation

**STRUCTURE OF THE RESPIRATORY TRACT**

Upper airways  - nose, nasopharynx - borderline - larynx
Lower airways - trachea, bronchi, bronchioles.
The airways divide 23 times to 23 generations between the trachea and:

**Alveoli** - 300 million - total surface area 70 m² lined pneumocytes
  - type I - flat cells
  - type II - producers of the surfactant
  - lymphocytes, plasma cells, alveolar macrophages, mast cells....

**Innervation:** Smooth muscles innervated by

**autonomic nervous system:**
- **parasympathetic** - muscarinic - bronchoconstriction
- **sympathetic** - beta₂ - receptors – bronchodilation - mainly to adrenalin
- **noncholinergic nonadrenergic** innervation - VIP
Inspiration - an active process - contraction of the inspiratory muscles:
- **Diaphragm** - accounts for 60-75% of the tidal volume
- **External intercostal muscles**
  - **Auxiliary**-accessory-inspiratory muscles: Scalene and sternocleidomasoid m.m.

Expiration - quiet breathing - passive process - given by elasticity of the chest and lungs
- forced expirium - active process – expiratory muscles:
  - Internal intercostal m.m.
  - Muscles of the anterior abdominal wall

**Innervation:** Motoneurons: Diaphragm – n. n. phrenici (C₃-C₅)
Others–lower segments o the spinal cord

**Pulmonary ventilation**
- the volume of the air inspired and expired per time unit
- mostly expressed as minute ventilation MV = Vₜ x f (6-8 l/min)

Increase in alveolar ventilation over the requirements of the metabolism – → hyperventilation (decrease in PA CO₂ and increase in PA O₂, the result - – hypocapnia
- it means – hyperventilation causes respiratory alcalosis

an opposite situation – hypoventilation – hypercapnia – respiratory acidosis

Maximum voluntary ventilation MVV 120 – 180 l/min

**Terminology**
eupnoe – normal quiet breathing
tachypnoe – breathing at higher frequency
bradypnoe – breathing with lower frequency
hyperpnoe – deeper br.
dyspnoe – laborious br.
ortopnoe – using auxilliary muscles
apnoe - cease of breathing

Pulmonary ventilation consists of:
1) alveolar ventilation
2) ventilation of dead space

**Alveolar ventilation**
- is the amount of air reaching the alveoli
- if the frequency of breathing is 12/min and \( V_T \) is 500 ml, than minute ventilation is 6 litres.
- If the dead space is 150 ml, than \( 500 - 150 = 350 \text{ ml} \times 12 = 4200 \text{ millilitres} \)
- alveolar ventilation is 4.2 l/min.
  Rapid, shallow respiration causes decrease of alveolar ventilation – see table

**Dead space**

- space of airways, in which does not occur the exchange of O\(_2\) and CO\(_2\) between the air and pulmonary capillary blood. It is important to distinguish between the **anatomic dead space (ADS)** and **total (physiologic – TDS) dead space**

In healthy individuals, the 2 dead space are identical.

- **ADS** – normal value is 150 ml is the volume of conductive zone of airways – from nose to terminal bronchioles
- **TDS** – is higher in disease states

the it is ADS + volume of air in alveoli, which are ventilated without blood perfusion.

The **ADS** can be measured by analysis of single – breath N\(_2\) curves
The **TDS** can be calculated from the PCO\(_2\) of alveolar gas and the tidal volume according to:

\[
\text{Bohr’s equation: } \quad P_{E CO_2} \times V_T = P_{A CO_2} \times (V_T - V_D)
\]

For example:  
\[
P_{E CO_2} = 28 \text{ mmHg} \\
P_{A CO_2} = 40 \text{ mmHg} \\
V_T = 500 \text{ ml} \\
\text{then } V_D = 150 \text{ ml}
\]

**LUNG VOLUMES**

- **Tidal volume** (\( V_T \)) – air that enters into lungs with each inspirium
- **Inspiratory reserve volume (IRV)** – the air inspired with a maximal insp. effort to normal inspiratory volume (in excess of the quiet \( V_T \))
- **Expiratory reserve volume** (ERV) – the volume expired by an active exp. effort after quiet passive expiration
- **Residual volume** – air left in the lungs after a maximal expirium
  - collapse air + minimal air
- **Total lung capacity** – air in the lungs after maximal inspiration

**The vital capacity** - the largest volume of the air that can be expired after a maximal inspiratory effort \( VC = ERV + V_T + IRV \)

**Timed-forced vital capacity** – FVC – information about the strength of the resp. m.m. FVC in 1 second – the fraction of the FVC expired
  - in 1 second (reduced in bronchoconstrictory disease – asthma)
**Pulmonary surfactant**

**Structure of the alveolar system:**

Total surface area – during exhalation – 80 m²
- inhalation -120 m²
= the largest body surface in direct contact with the external environment

300 million of alveoli in the human lungs of different sizes - instability of the system

2x surface tension

Laplace’s law – \[ P = \frac{2\sigma}{r} \]

P – pressure in the bubble
r - radius of the bubble

→ as air enters smaller bubbles – the pressure required to overcome surface tension increases. Smaller bubbles have a tendency to collapse to the bigger ones.

Stabilizing material in the lungs = a surface active agent – reducing the surface tension = pulmonary surfactant = substance lowering surface tension at the air-liquid interphase present in the alveoli and small airways with additional important physiological effects.

**Composition of the surfactant**

**Amount:** approx. 1 g (1 ml) in the whole adult lungs - monomolecular layer covering 80 m² of the lung inner surface

S = a complex mixture of phospholipids, proteins, ions.

- **Phospholipids** – 90% (tab. 1)
- **Proteins** - SP-A, SP-B, SP-C 8%
- **Carbohydrates** 2%
- **Ions** - Ca²⁺

Table

<table>
<thead>
<tr>
<th>Substance</th>
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<tbody>
<tr>
<td>Phosphatidylcholine</td>
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<tr>
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<tr>
<td>Phosphatidylinositol</td>
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<tr>
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</tr>
<tr>
<td>Phosphatidyletanolamine</td>
<td>3%</td>
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<tr>
<td>Others</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100%</td>
</tr>
</tbody>
</table>

**Proteins:** Specific proteins
- hydrophilic - SP-A, SP-D
  (structural changes of SF, regulatory functions in metabolism of SF, role in the pulmonary defence system)

- hydrophobic – SP-B, SP-C (promotion of rapid PL insertion into air-liquid interface - biophysical activity)

**Synthesis and secretion of SF**

In the lungs: 40 different cell types
The alveoli are lined by epithelial cells – of

- the type I. – Pneumocyte I. (cover 95% of the a. surface)
- the type II. – Pneumocyte II. (5%):
  Cuboidal (9 microns) singly, small groups. They lie flat on the basal lamella, contain microvilli and more organelles than that of the pneumocytes I.

**Pneumocyte II** = the producers of the surfactant.

**Biosynthesis of the surfactant**

**Pneumocytes II** – ribosomes, mitochondria, lysosomes, Golgi’s complex, multi-vesicular bodies, large lamellar bodies (up to 25% of the cytoplasm = dispersions of phospholipids and proteins.

SF is produced in the endoplasmatic reticulum, transformed to the lamellar bodies. Maturation – transport near of the margin of pneumocyte II cell – secretion by exocytosis.

**Alveolar metabolism of the surfactant**

Destruction of the surfactant:
1) Reuptake by pneumocytes II – reutilisation of substrates
2) Phagocytosis and degradation by alveolar macrophages
3) Elimination through lymphatic and vascular system, and
4) Mucociliary transport

**Structural forms of SF:** - lamellar bodies
  - tubular myelin
  - monomolecular film

**Control of synthesis and secretion of SF**

**Local**

**Local:**
Positive effect
-Ca$^{2+}$, -neutrophils,
- mechanical stretching of type II cells

**Negative effect**
- SP-A (negative biofeedback) – the more SP-A is present in alveoli, the less of SF is synthetized and secreted

**Neural control:** symphatetic
- parasympatetic
  - both positive effect

**Humoral control:**
**Positive effect**
- corticosteroids
- T₃, T₄, TRH
- estrogens,
- prostaglandins (PGE2)

**Negative effect**
- hyperglycaemia (children of diabetic mothers – higher incidence of RDS)
- hyperinsulinemia
- androgens - inhibition of corticosteroids action
  - general stimulatory effect for growth

**Surfactant functions**

1) **Mechanical stabilisation of alveoli and small airways decreasing surface tension at the air-liquid interphase.**

According to the Laplace law – by the same tension in the wall, the pressure inside the smaller alveoli is higher, and this is why when alveoli of different size are connected, alveoli with smaller diameter (and higher pressure inside) tend to empty to the larger alveoli. This would lead to instability in system of alveoli!

**Function of surfactant → to keep STABILITY in the lungs**

The surface tension is kept low, when the alveoli become smaller during expiration. The surfactant increases the lung compliance (the change in lung volume per unit change in pleural pressure) and decreases work of breathing. **Increase in lung compliance and reduction of the work of breathing**

2) **Prevention of the pulmonary edema**
   - The decrease of the surface tension diminishes a negative forces for transudation of fluid into the interstitium or alveoli.

3) **Role in the immune defence system of the lung**
   - Positive chemotactic effect for macrophages
   - The surfactant increases phagocytosis
   - Prevention against an adhesion of microorganisms – via a decrease of the surface tension of the pathogenic microbes
4) **Transports solid inhaled particles or damaged cells from alveolar compartment**
   - Transport of particles into the wall of alveoli – pulmonary macrophages

5) **Facilitation of the free airflow and low resistance in the airways**
   - Facilitation of the mucociliary transport and airflow through terminal bronchioles

**Surfactant disorders in some pulmonary diseases**

1) Idiopathic respiratory distress syndrome (IRDS)

**Surfactant in perinatal period**
- Pneumocytes II – start of the surfactant production in 30th – 32nd week of gestational age

   Immature surfactant – predominance of the phosphatidylinositol (mature – phosphatidylglycerol)

   Fetus secretes the surfactant through airways to the amniotic fluid –
   - determination of the maturity from the fluid.

The first breath – the increase of the surfactant secretion.

*Surfactant deficiency = idiopathic respiratory syndrome (IRDS) – in newborns. In adults ARDS.*

*Prematurely born children* – insufficient function of SF
   → development of respiratory distress syndrome (IRDS - idiopathic)

   Symptoms: tachypnoe, dyspnoe, expiratory grunting, decrease in compliance, increase of work of breathing, hypoxemia, acidosis, ...)

2) Adult respiratory distress syndrome (ARDS)
3) Pneumonia
4) Meconium aspiration syndrome
5) Congenital diaphragmatic hernia
6) Pulmonary edema, ...

**Surfactant replacement therapy**

**Aims:**
1) to deliver surfactant to the lungs
2) to stimulate metabolism of endogenous surfactant

**Types of exogenous surfactants:**
   - Natural: from amniotic fluid, bovinne, porcinne (Curosurf, Alveofact)
   - Artificial: synthetic (Exosurf)
Way of administration: intratracheally (bolus dose, nebulisation)

Timing of therapy: 1) prophylactic
2) rescue

Effects of surfactant replacement:
- immediate – increase in oxygenation, increase in the lung compliance
- later – reduction of FiO$_2$ and ventilatory pressure, to shorten oxygenotherapy and artificial ventilation

THE TRANSPORT OF OXYGEN AND CARBON DIOXIDE

Ventilation = the exchange of air between the environments and the lungs

Diffusion – of oxygen from the alveoli into the blood
- of CO$_2$ - in the opposite direction

The exchange of the gases – theories
1) active – secretory (Bohr, Haldane)
2) passive – diffusion on the basis of pressure differences – concentration gradients (Barcroft, Krogh)

1) The transport of oxygen

O$_2$ - dissolved in plasma
- bound to hemoglobin

a) Physically dissolved O$_2$:

1 l plasma – 3 ml O$_2$ (3 ml %)

Linear relationship – the amount of O$_2$ dissolved in plasma is proportional to the PO$_2$ (Henry’s law): „The amount of dissolved gas in fluids depends on the volume of the fluid, on the pressure of the gas and on the solubility coefficient (at constant temperature)."

C$_S$O$_2$ = 0.024
C$_S$O$_2$ = 0.51 (20-25 x more)

C$_S$ = amount of a gas (in 1) dissolved in 1 l of a fluid at P = 760 mmHg

b) O$_2$ combined with hemoglobin

1 g Hb ← 1.34 ml O$_2$ = Hufner’s coefficient
1 l of blood – 160 g of Hb = 160 x 1.34 = 214 ml O$_2$ =
= O$_2$ capacity = 100% (90-100 %)
Oxygen hemoglobin dissociation curve:

- the basic relationship between percentage of O₂ saturation of Hb and PO₂.

Factors affecting the affinity of Hb for O₂

1) CO₂ + H⁺ - shift the dissociation curve to the right – Bohr Effect
2) Body temperature
   - Increase of BT – evokes a decrease of the affinity between Hb and O₂ – shift of the curve to the right.
   - The decrease of BT – an opposite effect – hibernation.
3) 2,3-DPG – metabolit in red cells metabolism (Embden – Mayerhof pathway) – a product of glycolysis.
   2,3-DPG shifts the curve to the right – release O₂, reduction the affinity of Hb for O₂.

Carbon dioxide transport

PaCO₂ = 40 mmHg (5.3 kPa); P₉O₂ = 46 mmHg (6.1 kPa)
1) CO₂ dissolved in plasma
2) CO₂ dissolved in erythrocytes
3) Biocarbonate ions
4) CO₂ bound with proteins

1,2) CO₂ dissolved in plasma and in erythrocytes: 5% CO₂

\[
\text{CA} + \text{CA} \xrightarrow{\text{CO}_2 + \text{H}_2\text{O}} \text{H}_2\text{CO}_3 \xrightarrow{\text{H}^+} \text{H}^+ + \text{HCO}_3^- \\
\]

3) Bicarbonate ions: 75-80 % CO₂

\[
\text{NaHCO}_3 \xrightarrow{\text{plasma}} \text{KHCO}_3 \xrightarrow{\text{erythrocytes}} \frac{\text{H}_2\text{CO}_3}{1} = 20 \\
\]

4) CO₂ bound with proteins: 15-20 %
   - a) with free amino groups of various plasma proteins to form carbamino compounds
   - b) with the free amino (-NH₂) sites of the hemoglobin

\[
\text{HbNH}_2 + \text{CO}_2 \rightarrow \text{HbNHCOOH} \\
\]

Carbon dioxide dissociation curve

The relationship between CO₂ pressure and CO₂ content is nearly linear.

Factors affecting CO₂ transport:
O₂ – increasing the PO₂ – shift to the right = Haldane effect = analogy to Bohr effect.
Partial pressures of O\textsubscript{2}, CO\textsubscript{2}

Air – mixture of gases (O\textsubscript{2}, CO\textsubscript{2}, N\textsubscript{2} ...)
Pressure caused by one gas alone = partial pressure

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>Atmospheric air:</strong></td>
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<tr>
<td>O\textsubscript{2}</td>
<td>20.93</td>
<td>150 mmHg</td>
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<tr>
<td>CO\textsubscript{2}</td>
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<tr>
<td>N\textsubscript{2}</td>
<td>78.1</td>
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<td><strong>Alveolar air:</strong></td>
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<td>CO\textsubscript{2}</td>
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<tr>
<td>PaCO\textsubscript{2}</td>
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<tr>
<td><strong>Venous blood:</strong></td>
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<tr>
<td>PvO\textsubscript{2}</td>
<td>40</td>
<td>5.3</td>
</tr>
<tr>
<td>(mixed) PvCO\textsubscript{2}</td>
<td>46</td>
<td>6.1</td>
</tr>
</tbody>
</table>

**Oxygen Therapy**

= a lifesaving modality in clinical medicine

**Indications:** hypoxemia, hypoxia (mainly hypoxic hypoxia)

**Applications:** incubators, intranasal catheter, O\textsubscript{2} mask

When 100% O\textsubscript{2} (FiO\textsubscript{2} = 1.0) is inhaled – the Hb is fully saturated
and 5x is increased O\textsubscript{2} dissolved in plasma (from 3 to 14-15 ml/l).

PaO\textsubscript{2} = 700 mmHg
(93 kPa) – in healthy humans.

**Adverse effects of the oxygen therapy**

1) **Irritation of airways** mucosa with inhalation of dry (non humidified) and cold O\textsubscript{2}
2) **Changes in the lung**
   - a decrease of the surfactant production (exposure for 24-28 hours and more)
   - an inhibition of pulmonary macrophages activity
   - an inhibition of the mucociliary transport
   - lung edema
3) **Vasoconstriction**
   - cerebral
   - retinal – ischemia – formation of the fibrotic scares – visual defects –
   - blindness – retroental fibroplasia
4) Effect on the brain and other organs – experimental knowledges – a decrease of the brain GABA content, ATP.

**Hyperbaric oxygenation**

Application of the oxygen in hyperbaric conditions (2-3 atm. = 2-3 x 760 mmHg) –
- application of the pressure on the whole body.

Increase of O\textsubscript{2} in physical solution in plasma.

PaO\textsubscript{2} = 2000 mmHg – sufficient to supply tissues.
Method – in hyperbaric chambers, tanks
Indications – inactivation of Hb functions – intoxication with CO, methemoglobinemia, cyanide poisoning, treatment of Bürger’s disease, disturbances of vascularisation (ulcus cruris), surgery for certain forms of congenital heart disease, gas gangren.

Limitation of the hyperbaric oxygen exposure to less than 5 hours by 3 atm.

**ARTIFICIAL VENTILATION**

= artificial method ensures a flow of gas into (from) the alveoli

**Ventilator** – a device that replaces or augments the function of the inspiratory muscles – to ensure a flow of gas into the alveoli.

**Classification of artificial ventilation:**

**INNP = intermittent negative pressure ventilation** – by reducing the ambient pressure around the thorax.
Neg. P ventilators - acting on – the thorax - the whole body below the neck (tank respirator – „iron lungs“)

Principle: The pressure in the chamber is reduced cyclically by means of a large volume displacement pump, that causing the lungs to expand and contract.
In the past – for poliomyelitis victims – now for overnight support for patients with respiratory muscle weakness.
Disadvantages – it occupies much space, access to the patient – poor neck seal

**IPPV = intermittent positive pressure ventilation**

Principle: IPPV ventilators produce inspiration – inflation – expiration is usually passive.

Types: Time/pressure/volume/ combined cycled machines.
**Time cycled** ventilators switch between inspiration and expiration after a preset time interval.
**Pressure cycled** – switch when a preset airway pressure threshold has been reached.
**Volume cycled** – cycle when a preset tidal volume has been delivered.

**IPPV + retarded – delayed expirium**

**IPPV + PEEP !!!**

Benefit – the functional residual capacity can be maintained by leaving a constant standing pressure in the lungs, keeping them slightly inflated even at the end of expiration.
PEEP – causes – an increase in PaO₂

Disadvantage: increase in intrathoracic pressure – diminution in venous return to the heart, decrease in cardiac output
Special Techniques:

**MANDATORY VENTILATION**

- allows the patient to breathe spontaneously through the ventilatory circuit.

**Non-synchronised:**
At predetermined intervals a positive pressure **artificial breath** is provided by the ventilator independently of the patients spontaneous breathing = without synchronisation.

**Synchronised:**
For avoiding of the mandatory breath during the period of the spontaneous breath. Electronic control. Any spontaneous inspiratory activity by the patient is sensed by „trigger“ – pressure sensor and then expiratory valve is closed – inspiratory valve is opened. The flow of gas through the inspiratory valve is matched to the patient inspiratory flow. This allowed the patient to breath spontaneously through the ventilator. Synchronisation between patient and ventilator.

**High frequency ventilation**

- High frequency IPPV (60 – 120/min)
- HF jet ventilation HFJV (150 – 600/min)
- HFJV – brief, frequently repeated pulses of gas are directed from a high pressure generator down the airways. VT and Paw are low.
- HF oscillation ventilation HFOV (up to 5000/min)
- HFOV – oscillate gas in the airways using a piston pump or diaphragm pump. VT are very small, gas movement occurs by mechanisms other than VT.

**Non-invasive ventilation**

- **CNP** – continuous negative pressure – analogy to the „iron lungs“.
  Keeping the negative pressure around the chest (body) to hold alveoli opened.
  Premature newborns with RDS – Pulmarca. Spontaneous breathing on the shifted FRC level.

- **CPAP** – continuous positive airway pressure – spontaneously breathing patient in whom Paw is held positive (5 – 10 cm H$_2$O in relation to atmospheric pressure throughout the respiratory cycle.
  Nasal CPAP – in premature newborns with RDS, in adults – Sleep Apnea Syndrome, snoring).
  Benefit – keeping the alveoli to be opened in all phases of the respiratory cycle – anti atelectatic effect.

**Effects of different barometric pressures on organism**

A) Effects of high atmospheric pressure-hyperbaric conditions

- **Diving**
  Sea (water) depth – to each 10 m – barometric pressure increases by 1 atm. (760 mmHg) – subject in the depth is exposed to a P 2 atm (1 – by the air + 1 by the water).
  Effect of depth on the lung volume – Boyle, s Law: „The volume of gas is compressed in the higher P and the volume is inversely proportional to the pressure“.
Compression of gases – in the depth 10 m – half of the lung volume. Increased P can collapse alveoli.

Necessity to breath from the special devices (aqualungs) – to maintain the same pressure in the lungs than in environment. By the P outside is regulated P in the gas tanks and P in aw and alveolar compartment.

Effect of depth on the partial pressure of gas: Nitrogen, oxygen, carbon dioxide:

High nitrogen P:
At high pressure it is diluted in the plasma – at 4-5 atm. P Nitrogen euforia – like alcohol intoxication, at 35 and more atm. narcosis. N dissolves freely in the fats of the body and also in the membranes of the neurons.

High oxygen P:

Carbon dioxide toxicity at high P:
- no problem – the rate of the CO₂ production in the divers body is the same.

Effect of decompression

Decompression Sickness
(Caisson Disease, divers paralysis)

In the depth the large amount of nitrogen have dissolved in his body and then sudden return to normal atm. P can develop production of N bubbles intracellularly (extracellularly – Boyle’s Law. The plug the small blood vessels.

Symptoms: 1) Pain in the joints and muscles of the legs and arms 2) CNS symptoms: dizziness, paralysis, collapse, coma, unconsciousness 3) Shortness of breath, pulmonary edema, death

Treatment: By special decompression tables – return to previous depth in hyperbaric chamber – and return slowly to normal P.

REGULATION OF BREATHING

1/ NEURAL
2/ HUMORAL

Neural for: -regulation of ventilation - protection and defence of the RS

Humoral for: modification of ventilation according to
- oxygen needs
- elimination of carbon dioxide
NEURAL REGULATION OF BREATHING

a/ Medullary respiratory centers
Primary respiratory centers:

- **Inspiratory part:** dorsal respiratory group (ventro-lateral nucleus of tractus solitarius)
- **Expiratory part:** area of ncl. retrofacialis, Bötzinger’s complex
- **Mixed area:** inspiratory + expiratory neurons – ventral respiratory group – innervation of larynx – ncl. ambiguus, ncl. para – and retroambigualis

b/ Pontine respiratory centers

1) **The apneustic center** (ncl. reticularis, area vestibularis)
2) **The pneumotaxic center** (ncl. parabrachialis, ncl. Kölliker – Fusse)

Modifications of respiratory centers activities

a) **Modification by higher CNS centers**

1) **Cerebral cortex** – voluntary control (hyperventilation, apnoea, vocalization, speech...)
2) **Limbic structures and hypothalamus** (changes in emotions – crying, laughing, panting ...)

Voluntary and automatic control of respiratory muscle function are separately.

Voluntary control of breathing:
Corticospinal pathway – in dorsolateral spinal medulla (damaged = syndrome of the automatic breathing)

Automatic control of breathing:
Bulbospinal pathway – in ventrolateral tract (damaged = Ondine’s curse).

b) **Modification of breathing by peripheral receptors**

1) **Receptors of the nose**
Olphactoric and trigeminal endings – mechanical, chemical and thermal stimuli
Involved in:
Regulation of the quiet breathing (nasothoracic reflex)
Protective and defensive airway reflexes

2) **Receptors of the naso – and oropharynx**
The endings of the n. Vth, VIth, IXth, Xth
Stimuli: Mechanical, thermal
Involved in: Regulation of the quiet breathing (stimulation of the inspirium?)

3) **Receptors of the larynx**
a/ **Mechanoreceptors** – pressure sensitive, drive receptors (proprioceptors)
b) **Cold receptors** – inspiratory airflow  
c) **Laryngeal irritant receptors** (chemical and mechanical stimuli)  
d) **Chemosensitive – fluid receptors**  
e) Others – nonspecific

**Lower airways and lung receptors**

1) **Pulmonary stretch receptors** – mechanoreceptors of the airway in smooth muscles
   **Slowly adapting receptors**
   - Low – threshold (tonic) receptors  
   - High – threshold (phasic) receptors

   **Stimuli:** Increase in volume and pressure in airways and lungs
   **Effects:**
   **Hering – Breuer inflation reflex**
   a) inhibiting inspirium  
   b) promoting expirium

2) **Irritant receptors** – C-fiber receptors of the airways - cough receptors
   **Rapidly adapting receptors**

   **Stimuli:** Inhaled irritants, mechanical deformation of the airway mucosa
   **Effects:**
   Coughing, hyperpnoea, bronchoconstriction, laryngoconstriction, hypersecretion of mucus.

3) **C-fiber receptors** of the lungs
   **J-receptors** (juxtapulmonary capillary)

   **Stimuli:**
   Mechanical: an increase in interstitial lung pressure (edema, embolism, „wet lungs“ ...)  
   Chemical: smoke (cigarette), capsaicin, PDG, histamine, serotonin, prostaglandins

   **Effects:**
   **Pulmonary chemoreflex** – 2 phases: depressive and excitatory  
   Bronchoconstriction, laryngoconstriction

   **J - reflex** (Paintal) – the inhibition of mono- and polysynaptic reflexes – in extreme physical effort

4) **Non – specific receptors** affecting respiration
   - Proprioreceptors, muscle spindles (thorax, abdomen)  
   - Cutaneous receptors (thermo-, tactile ...)  
   - High pressure receptors in circulation  
   - Mechanoreceptors of the eye  
   - Senses – visual, acustic, vestibular ...

**CHEMICAL – HUMORAL REGULATION OF BREATHING**

Regulation of ventilation by PO₂, PCO₂, pH
Sensors-monitors: chemoreceptors: - peripheral
- central

Peripheral chemoreceptors:
- glomus caroticum
- glomus aorticum (n. Xth)

Tonic activity

Effects on ventilation:
A decrease in PaO₂ and / or an increase in PaCO₂ – the frequency of nerve impulses increases:
Effect: hyperventilation

Interaction of chemical factors affecting ventilation – positive hypoxic - hypercapnic relationship

Effects on cardiovascular system: redistribution of the blood into the vital most important organs, hypertensive reaction, bradycardia.

Central chemoreceptors:
Location: ventrolateral surfaces of the medulla (H⁺, Mitchell, Loeschke and Schlaefke zone)

Stimulus: An increase in PCO₂ and H⁺ (a decrease in pH) in the cerebrospinal and cerebral interstitial fluid

Effects: hyperventilation in respiratory and metabolic acidosis

PROTECTIVE AND DEFENSIVE REFLEXES OF THE AIRWAYS

Protective (preventive) reflexes:

- Kratschmer´s apnoeic reflex: nasal origin (n.Vth)
  Stimuli: chemical irritation of nasal mucosa
  Effects:
  - inhibition of ventilation
  - laryngoconstriction
  - peripheral vasoconstriction – redistribution of the blood
  - bradycardia

- Diving reflex (n.Vth) nasal and perioral region
  Stimuli: cold (water, air)
  Effects: the same as in Kratschmer´s reflex

Defensive reflexes:
**Sneezing** – mechanical stimulation of nasal mucosa (n.V.)

1) deep inspirations (intensification through HB reflex)
2) expiratory effort – compressive phase
   - expulsive phase

**Coughing** – laryngo-pharyngeal / tracheobronchial

1) preparatory inspiration
2) expiratory effort – compressive phase (P_{i.p.} = 100-200 mmHg)
   - function of glottis
   - expulsive phase – airflow velocity – 120 m/s (hurricane 50 m/s)

**Expiration reflex** – medial margin of vocal folds – only expiratory effort

**Aspiration reflex** - naso – oropharynx – only inspiratory effort.
Sniff-like reflex.