Objectives

The lung volumes and capacities
Ventilation and its changes, hyper and hypoventilation
The dead volume and its function, alveolar ventilation
Composition of the atmospheric and the alveolar air, partial pressure of a gas
Diffusion of $O_2$ and $CO_2$ in lungs and their transport in blood
Regulation of breathing

Practical tasks

1. Functional lung examination
2. Examination with the SanoScope spirometer
3. The effect of increasing $CO_2$ and decreasing $O_2$ content in the inspired air on respiration
4. Measurement of haemoglobin oxygen saturation by the pulse oxymeter
Task 1. The functional lung examination (spirometry)

- the most common pulmonary function test
- the patient is breathing into a spirometer - he follows the doctor’s instructions how to breathe: quiet breathing, maximum inspiration, hold the breath, ....
- a record is obtained and evaluated (manually or by a computer)
1. **Perform the examination – get a record**
   - patient is in sitting position
   - he/she is exhaling into the spirometer
2. analyse the record

- read the patient's values and write them into the result sheet

- you will determine specific values for the patient, based on his/her age, weight and height

- please **do not copy the normal values from the slides** (unless recommended by teacher)

- a special ruler with 3 scales is used for the analysis

  a) 60 mm / 1 minute (for reading the **time variables**)

  b) litres – for reading the **volumes**

  c) 50 mm / 1 second (for reading the FEV$_1$, FEV$_3$)
The record includes measurement of:

- tidal volume ($V_T$)
  - volume of a normal inspiration (quiet breathing)
  - typical value: 500 ml

- frequency of breathing ($f$)
  - number of breaths (=peaks) in quiet breathing per minute
  - normal value: 10 – 18/min (write down the value into the result sheet)
• expiratory reserve volume (ERV)
  – largest additional volume that can be forcefully exhaled after tidal expiration
  – normal value: 1000 ml

• inspiratory reserve volume (IRV)
  – largest volume that can be forcefully inspired over normal inspiration
  – normal value: 2500 ml

• vital capacity (VC)
  – maximum volume that can be expired after maximum inspiration
  – normal value: 4000 ml
Minute lung ventilation (\( \dot{V} \))
– is the amount of air a person breathes (ventilates) in a minute

\[
\dot{V} = f \times V_T \quad 5 - 9 \text{ l/min}
\]

- Maximum ventilation Vent_{max} (Maximum breathing capacity) – is the amount of air a person breathes in a minute when an individual is breathing forcefully - as deep and as quickly as possible (120 – 170 l)

- can be calculated if we know
  - maximum frequency per minute
  - maximum tidal volume (of an inspiration)

\[
\text{Vent}_{max} = \text{frequency}_{max} \times \text{Volume}_{max}
\]

- breathing reserve – ratio

\[
\text{Vent}_{max \text{ per minute}} = \frac{\text{Vent}_{max}}{\dot{V}} (\text{minute ventilation})
\]

- normal value 5 or more, sportsmen 15 and more
- indicates how many times the ventilation can be increased
**forced expiratory volume per 1s (FEV<sub>1</sub>)**

- the volume expired in the first second of maximal expiration after a maximal inspiration

- normal value: min 80 % of VC (read in litres, recalculate to % of the VC)

- an indicator with a major clinical importance (for making diagnosis)

**forced expiratory volume per 3s (FEV<sub>3</sub>)**

- the volume expired in the first 3 seconds of maximal expiration after a maximal inspiration

- normal value: 97-100 % of VC (read in litres, recalculate to % of the VC)
maximal voluntary apnea during inspiration  \( Api \)

- cessation of breathing in inspiratory position of the chest
- normal value: 40 – 60 s

maximal voluntary apnea during expiration  \( Ape \)

- cessation of breathing in expiratory position of the chest
- normal value: 20 – 40 s

minute consumption of oxygen \( V_{O_2} \)

- normal value during quiet breathing: 250 – 300 ml
3. determine the normal values

- lung volumes depend on the metabolic rate
  (metabolic rate ↔ requirements for O₂, production CO₂)
- read the normal values from the tables and copy them into the result sheet

4. make the final evaluation

- compare the patient’s results with normal values
- values close to 100 % can be considered as normal

Conclusion

- indicate which values were normal, which were higher or lower
Spirometry examination using Sanoscope device

- Computer spirometry

**Procedure**

- Provide your personal data (date of birth, age, height, gender, smoking status..)

1. 2x normal in/ex
2. normal in and then maximum inspiration at normal pace (not quick)
3. immediately forceful/quick inspiration (as quick as possible)
4. immediately forceful expiration (as quick as possible)
Flow Volume Loops

• a graphical analysis of inspiratory and expiratory flow from various inspired lung volumes

• subjects inhale to TLC -> rapidly exhale to RV

• airflow from TLC is maximal at the beginning of forced exhalation (PEF) where:
  (1) elastic traction of alveolar septa on airway is greatest
  (2) expiratory muscle strength is greatest
  (3) airway resistance is lowest

• airway resistance increases as forced expiration proceeds due to progressive reduction in airway calibre
### Sanoscope - results

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Result</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced Vital Capacity in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRV – inspiratory reserve V</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ERV – expiratory reserve V</td>
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<td></td>
<td></td>
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<tr>
<td>VT - tidal volume</td>
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<tr>
<td>Forced Vital Capacity Expir.</td>
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<td></td>
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<tr>
<td>FEV 1</td>
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<td></td>
<td></td>
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<tr>
<td>FEV 1/VC max</td>
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<tr>
<td>MEF25 Max Exp Flow at 25% VC</td>
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<tr>
<td>MEF 50 Max Exp Flow at 50 % VC</td>
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<tr>
<td>MEF 75 Max Exp Flow at 75 % VC</td>
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<td></td>
<td></td>
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<tr>
<td>MEF 75 – 85</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PEF peak expiratory flow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIF peak inspiratory flow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area AEx</td>
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</tbody>
</table>

**Conclusion:** are the results normal?
Flow Volume Loops - most common abnormalities

Flow volume loops

Obstructive lung volumes > normal (↑ TLC, ↑ FRC, ↑ RV); restrictive lung volumes < normal. In obstructive, FEV₁ is more dramatically reduced compared with FVC → decreased FEV₁/FVC ratio. In restrictive, FVC is more reduced or close to same compared with FEV₁ → increased or normal FEV₁/FVC ratio.
Ventilation and its changes

- **eupnea**
  - easy, free respiration, as observed normally under resting conditions
  - normal frequency (12-18/ min)
  - normal tidal volume (500 ml)

Changes in frequency of breathing

- **tachypnea** – increased frequency of breathing, rapid breathing
- **bradypnea** – decreased frequency of breathing, slow breathing

Changes in tidal volume

- **hyperpnea** – an increase of tidal volume, deep breathing
- **hypopnea** – a decrease of tidal volume, shallow breathing
• **hyperventilation**
  - ventilation exceeds metabolic requirements
  - $\text{CO}_2$ is removed at higher than normal rates
  - decrease of $\text{CO}_2$ in blood ($\text{CO}_2$ is transported by blood from tissues to lung)
  - may result in respiratory alkalosis
    - excess of basic substances
    - pH of blood exceeds 7.44

• **hypoventilation**
  - ventilation is slower than required by metabolism
  - $\text{CO}_2$ production is higher than its elimination
  - $\text{CO}_2$ content in blood is increased
  - respiratory acidosis may occur
    - excess of acidic substances
    - pH of blood is lower than 7.36
Respiratory passageways

A/ Conducting zone
- upper respiratory tract (passageways)
  - nasal cavity, nasopharynx, larynx
- lower respiratory tract
  - trachea, bronchi, bronchioles (most)

B/ Respiratory zone (gas exchange)
- lower respiratory tract
  - respiratory bronchioles
  - alveolar ducts
  - alveolar saccules
  - alveoli
**Dead space (V_D)**

- parts of respiratory passageways where no significant gas exchange occurs between lungs and blood

1. **anatomical dead space** – approx **150 ml**
   = conductive part of airways
   - function: the inspired air is heated, cleaned, moisturized

2. **alveolar dead space**
   - involves alveoli where no gas exchange takes place
   - in a healthy human:
     - all alveoli serve for gas exchange
     - alveolar dead space ⇒ 0
   - in people with a lung disease - alveoli are malfunctioning
     - alveolar dead space > 0 (e.g. in pneumonia, fibrosis)

Physiological dead space = anatomical dead space + alveolar dead space
Alveolar ventilation (VA)

- volume of air that reaches alveoli per minute (and serves for the gas exchange)
- it can be calculated as:

\[
\text{alveolar ventilation} = \text{alveolar volume} \times \text{frequency of breathing} \\
= (\text{tidal volume} - \text{dead space}) \times \text{frequency of breathing}
\]

The gas exchange zone
- in normal quiet breathing - approx. 70 % of the tidal volume arrive into alveoli
- i.e. 70 % of the tidal volume serve for gas exchange

Example

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume ($V_T$)</td>
<td>500 ml</td>
</tr>
<tr>
<td>Frequency of breathing</td>
<td>12/ min</td>
</tr>
<tr>
<td>Dead space ($V_D$)</td>
<td>150 ml</td>
</tr>
<tr>
<td>Minute ventilation ($V$)</td>
<td>$V_T \times f = 500 \times 12 = 6000$ ml</td>
</tr>
<tr>
<td>Alveolar ventilation ($V_A$)</td>
<td>$(500 - 150) \times 12 = 4200$ ml</td>
</tr>
</tbody>
</table>

1200 ml – remain in dead space
– alveolar ventilation depends on frequency of breathing and the tidal volume

<table>
<thead>
<tr>
<th>$V_T$/ml</th>
<th>frequency</th>
<th>min. ventilation/ml</th>
<th>$V_D$-dead space/ml</th>
<th>alveolar ventilation/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>12</td>
<td>6000</td>
<td>150x12=1800</td>
<td>350x12 = 4200</td>
</tr>
</tbody>
</table>

Ventilation can be increased by an increase of
- the inspiratory volume (deeper breathing)
- frequency of breathing (faster breathing)
- both frequency and volume

**Question:** Does it matter whether there is an increase in frequency or inspiratory volume?

<table>
<thead>
<tr>
<th>min. ventilation/ml</th>
<th>$V_D$-dead space/ml</th>
<th>alveolar ventilation/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 000</td>
<td>150 x 12=1800</td>
<td>11 200</td>
</tr>
<tr>
<td>12 000</td>
<td>150 x 24=3600</td>
<td>8 400</td>
</tr>
</tbody>
</table>

- more air is supplied for gas exchange if the inspiratory volume is higher (increase is less pronounced if the breathing rate gets higher)
Oxygen transport in blood

A/ Physically dissolved O₂
- the amount depends on the partial pressure of O₂ in lungs
- 3 ml / 1l of blood – under normal pressure conditions
  (more in hyperbaric chambers)
- it exerts the partial pressure of O₂ in blood

B/ Chemically bound O₂
- bound to haemoglobin (oxygenated Hb) – attached to Fe²⁺

oxygen haemoglobin saturation - % of oxygenated Hb from total Hb

Normal values
1. arterial blood 95%
2. venous blood 75%
Oxygen association – dissociation curve

- shows saturation of Hb in relation to partial pressure of O\(_2\) (pO\(_2\))
- sigmoidal shape
- the higher pO\(_2\), the more O\(_2\) is bound to Hb
- beginning of the curve is slow
  - the first molecule of O\(_2\) binds with difficulties
  - afterwards the spatial configuration of Hb is changed and next molecules of O\(_2\) are more readily bound
- then steep rise of the curve – i.e. already under low pO\(_2\) is blood well saturated with O\(_2\) (high affinity of Hb to O\(_2\))
- high altitudes
  - low $pO_2$
    - 6000 m: 4.5 kPa = 34 mm Hg
  - therefore lower Hb saturation
  - as a compensation the Er count increases
Factors that influence the oxygen-hemoglobin association curve

**Affinity of Hb to O\(_2\) is decreased**
- O\(_2\) is more easily released from the bond with Hb
- pCO\(_2\)* ↑
- pH ↓
- temperature ↑
- 2,3 DPG ↑

= shift to right and down (e.g. in tissues)

**Affinity of Hb to O\(_2\) is increased**
- O\(_2\) is released from bound with Hb less easily
  - pCO\(_2\) ↓
  - pH ↑
  - temperature ↓
  - 2,3 DPG ↓

= shift to left and up (e.g. in the lungs)

* **Bohr effect:** increasing concentration of CO\(_2\) will reduce the oxygen affinity of Hb

![Graph showing the oxygen-hemoglobin association curve](image-url)
CO₂ - main product of metabolism (98%)
- diffuses from tissues into blood, transported as:

1. Physically dissolved CO₂ – arterial blood 30 ml, venous 35 ml/liter (5%)
2. Chemically bound (30%)
   - to haemoglobin - carbaminohaemoglobin

3. Bicarbonate ions CO₂ (65%)
   - after diffusion into erythrocytes CO₂ reacts with water
     \[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \] (catalyzed by bicarbonate dehydratase)
   - \( \text{H}^+ \) is bound by Hb (Hb buffer)
   - \( \text{HCO}_3^- \) diffuses into plasma (and functions as a part of bicarbonate buffer)
     (and Cl⁻ from plasma enters erythrocytes, this ion change is referred to as \textbf{Hamburger effect})
   - in lung the reaction occurs in reverse order
The CO₂ equilibrium curve
- shows the relationship between partial pressure of CO₂ and its amount in blood
- the higher the blood partial pressure of CO₂, the more CO₂ is transported

- an inverse association with pO₂
- the higher the pO₂ in blood the less CO₂ is bound in blood (Christiansen-Douglas-Haldane effect)
- less O₂ allows more CO₂ to load in the tissues and more CO₂ unload in the lungs
- more O₂ shifts the curve downwards and to the right

Normal values of pCO₂
normocapnia - arterial blood – 5,3 kPa (40 mm Hg)
  - venous blood – 6,1 kPa (45 mm Hg)
hypercapnia – increase of pCO₂
hypocapnia – decrease of pCO₂

hyperventilation - excessive ventilation causing ↓ of pCO₂ and ↑ of pO₂
hypoventilation - excessive ventilation causing ↑ of pCO₂ and ↓ of pO₂
Task: Determination of haemoglobin saturation by a pulse oximeter

**Saturation of Hb** = % oxy Hb from the total Hb (% of Hb in blood that carries $O_2$)

- arterial blood: 96 – 100 %
- venous blood: 75 %

The pulse oximeter can be used in measuring the pulse oxygen saturation and pulse rate through finger.
Determination of haemoglobin saturation
Procedure

- Clean the fingernail with disinfection agent on whatever finger (best - 2nd or 3rd)
- Put the pulse oximeter probe on a finger with display facing up.
- Press the ON button
- Read the values of saturation and heart rate about 10 seconds after they appear on the display (values need to get stable)

Do the following measurements and make the report

A. Write down the heart rate and haemoglobin saturation of you and your colleagues
B. Evaluate your results in regard to the physiological values.
C. Are there any differences in the values of the smokers and non-smokers?
   (are any differences expected?)
D. How are the values affected if you hold the breath?
   (are any differences expected?)
E. How does the fingernail polish affect the results?
Regulation of respiration – the respiratory centre

pneumotaxic centre - inhibits the apneustic centre

apneustic centre – stimulates inspiratory neurons

medulla oblongata and pons – the respiratory centre

**inspiratory neurons** (dorsal and ventral respiratory group)
- their stimulation causes inspiration
- **generator of respiratory activity**

**mutual inhibition**

**expiratory neurons** (ventral respiratory group)
1. inhibit inspiratory neurons,
2. cause active expiration
Activity of respiratory centre is influenced by

cortex (voluntary control of breathing)

subcortical structures (limbic system - emotions, hypothalamus - temperature)

pneumotaxic centre
apneustic centre
respiratory centre

inspiratory neurons
expiratory neurons

receptors in respiratory system, lung (mechano, thermo, chemo)

hormones

peripheral and central chemoreceptors

Tr. corticospinalis

respiratory muscles

Tr. bulbocospinalis
Chemical regulation of respiration

Peripheral chemoreceptors
- receptors that monitor amount of $O_2$ and $CO_2$ in blood
  (partial pressure - $pO_2$ and $pCO_2$)
  = small islets of sensory cells in
  - aorta – glomus aorticum (aortal bodies)
  - a. carotis – glomus caroticum (carotid bodies)
  - active already under conditions of normal $pO_2$ a $pCO_2$ (generate action potentials)
  - hypoxia and hypercapnia increase stimulation of the receptors that subsequently
    stimulate inspiration centre
  - $O_2$ - weak stimulant (cause less pronounced change in ventilation)
  - $CO_2$ - strong stimulant (cause more pronounced change in ventilation)
  - more pronounced stimulation if both hypoxia and hypercapnia occurs
Central chemoreceptors

- ventral part of medulla oblongata
- sensitive to changes of $H^+$ concentration in cerebrospinal fluid
- $H^+$ indirect indicator of $CO_2$ concentration in blood/cerebrospinal fluid
- $CO_2$ diffuses from blood to cerebrospinal fluid and reacts with water

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

- central chemoreceptors
  - indirect and delayed effect (after 20-30 s)
  - more powerful than peripheral chemoreceptors
  - stronger effect – 80% of response (i.e. change in ventilation)

- in very high concentrations of inspired air, $CO_2$ has inhibitory effect – decrease of ventilation – death may occur (vineyards)
Receptors in the respiratory passageways

• **mechanoreceptors** – sensitive to stretching, speed of air, etc.

The Hering Breuer reflexes

• **Inflation reflex**
  – passive inflation of air into the lungs – inhibits ventilation
  – a reflex triggered to prevent overinflation of the lungs
  
  – inflation stimulates the **lung** – **inflation receptors**
  – their activity increases (produce more action potentials that travel via n. vagus to the inspiratory neurons in respiratory centre)
  – if lung inflation is large - the inspiratory neurons are inhibited (reflex)
  – inspiratory muscles relax - expiration starts

• **Deflation reflex**
  – passive deflation of air from the lungs – stimulates ventilation

• **chemoreceptors** – sensitive to chemical substances (unpleasant odours)
• **free nerve endings** (cranial nerves)– chemical, mechanical, thermal stimuli
Protective reflexes

Includes

• Cough
• Sneezing

fast expiration aimed at removing of irritating agents from respiratory passageways

– stimulus – mechanical, chemical irritation of mucosa
  • larynx and lower passageways - cough
  • nose - sneezing
– receptors – free nerve endings
– centres – in medulla and pons
– executive organs – respiration muscles
cough/sneezing = very strong expiration
Voluntary regulation of respiration

- frequency and depth of breathing – can be voluntarily regulated
  (action potential travels by tr. corticospinalis, involuntary breathing – tr. bulbospinalis)
- voluntary apnoea – is eventually broken by autonomous regulatory mechanism, that stimulate inspiration (chemoreceptors)
- breaking point
  - hypoxia $pO_2$ 9,3 kPa (in arterial blood)
  - hypercapnia $pCO_2$ 6,6 kPa (in venous blood)

Ondine’s curse
- congenital respiratory disorder of automatic breathing
- patient can breathe only voluntarily
- problems during sleep – tracheotomy, mechanical ventilation
Task: The influence of increasing CO$_2$ concentration and decreasing O$_2$ concentration on respiration
Task
- observe and describe the effect on ventilation in:

1. decreasing content of O₂ in the inhaled air
2. increasing content of CO₂ in the inspired air
3. both increasing content of CO₂ and decreasing content of O₂

Principle
→ less O₂ and/or more CO₂
→ lower partial pressure of O₂/ higher partial pressure of CO₂ partial in the blood
→ stimuli from the peripheral /central chemoreceptors
→ will reach a regulatory effect of the respiration centre and subsequent
→ change in ventilation (volume, frequency) order to regain balance of O₂/CO₂ in the body

O₂ – weak stimulant (weak and delayed response)
CO₂ stronger stimulant (more powerful and faster change in ventilation)
both O₂ and CO₂ strongest stimulus (the most pronounced response)
Procedure

1. atmospheric air with absorber of CO₂
   - with every inspiration the content of O₂ decreases
   - expired CO₂ is absorbed, therefore content remains unchanged

2. pure oxygen with soda lime – without absorber of CO₂
   - since it is 100% O₂, the decrease caused by inspiration is not detectable
   - with every expiration CO₂ content is increasing

3. atmospheric air, without absorber (soda lime)
   - with every inspiration the content of O₂ decreases
   - with every expiration CO₂ content is increasing

the breathing is recorded
measurement is stopped when changes in ventilation are observed (f or V)
**Result and conclusions**
- for each out of 3 parts determine:
  A. change in frequency of breathing – at the beginning/after stimulation
  B. depth of breathing (volume) – at the beginning/after stimulation
  C. time, when changes occurred
  D. calculate ventilation - at the beginning/after stimulation
  E. conclude if the response is normal

<table>
<thead>
<tr>
<th>Time when change in ventilation is observed</th>
<th>Tidal volume (l)</th>
<th>Frequency /min</th>
<th>Minute ventilation (l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning</td>
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<td></td>
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</tr>
<tr>
<td>↓ ( \text{O}_2 )</td>
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<tr>
<td>Beginning</td>
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</tr>
<tr>
<td>↑ ( \text{CO}_2 )</td>
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<tr>
<td>↑ ( \text{CO}_2 ) ↓ ( \text{O}_2 )</td>
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