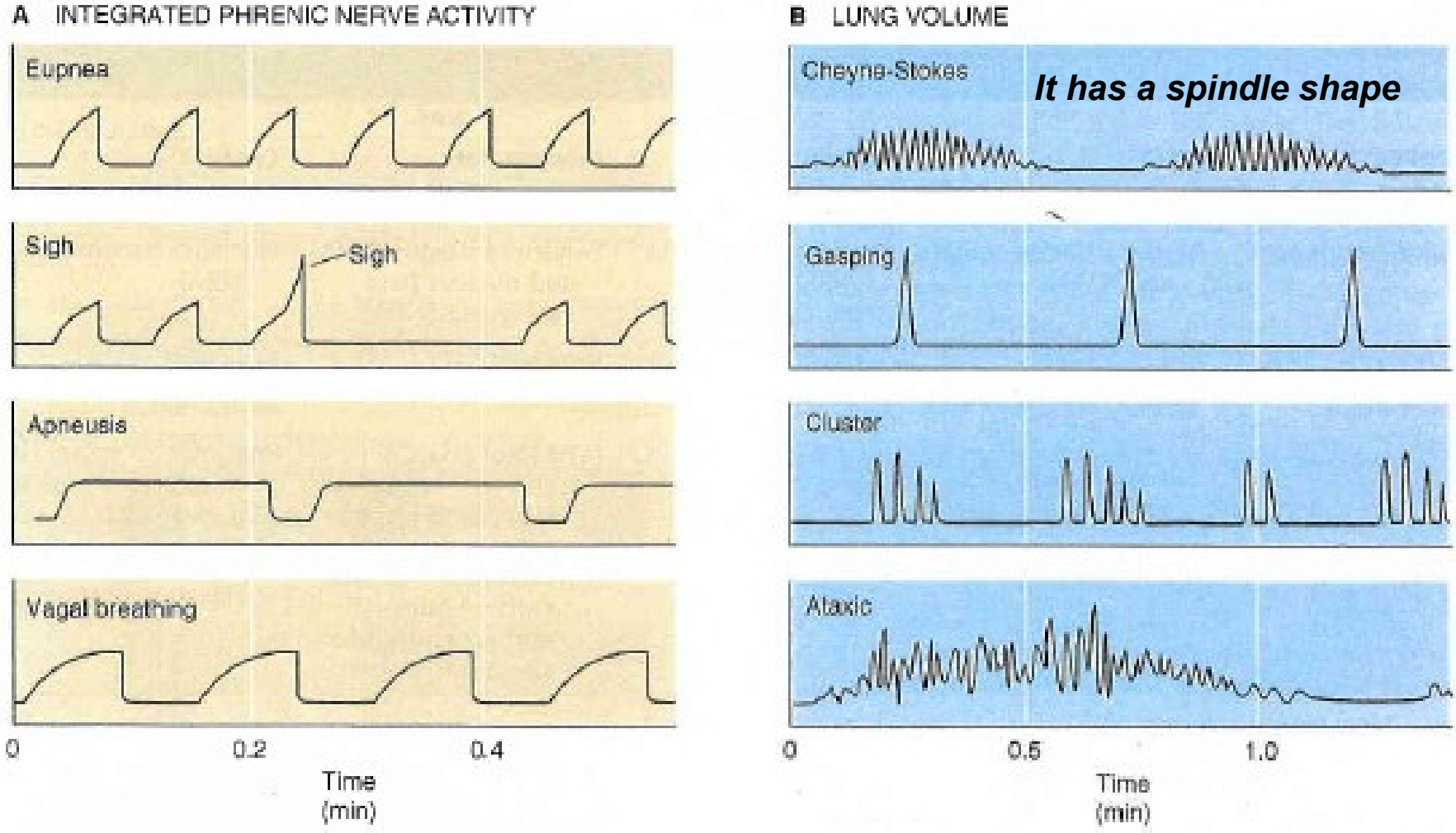
HYPOXIA

Periodic breathing

- It is not regular, rhythmic, but respiration occurs in periods ("a moment to breathe, take a moment to not breathe„)

- **CHEYNE-STOKES** The only one that can be physiological is that it occurs in young children in their sleep
- **BIOT‘S** Always pathological, in CNS diseases - meningitis, encephalitis, injuries
- **„gasping“**Most often in newborns with a disorder of cardiorespiratory reconstruction after birth, the baby "catches" the breath; one breath and nothing for a long time
- **KUSSMAUL** type of hyperventilation with the olfactory sensation of acetone


A INTEGRATED PHRENIC NERVE ACTIVITY
Eupnea
Sigh
Sigh
Apneusis
Vagal breathing
0
0.2
0.4
Time
(min)
B LUNG VOLUME
Cheyne-Stokes
It has a spindle shape
Gasping
Cluster
Ataxic
0
0.5
1.0
Time
(min)

Hypoxia, hypoxemia

- **Hypoxia is a general name for a lack of oxygen in the body or individual tissues.**
- **Hypoxemia** is lack of oxygen in arterial blood.
- Complete lack of oxygen is known as **anoxia.**

The most common types of hypoxia:

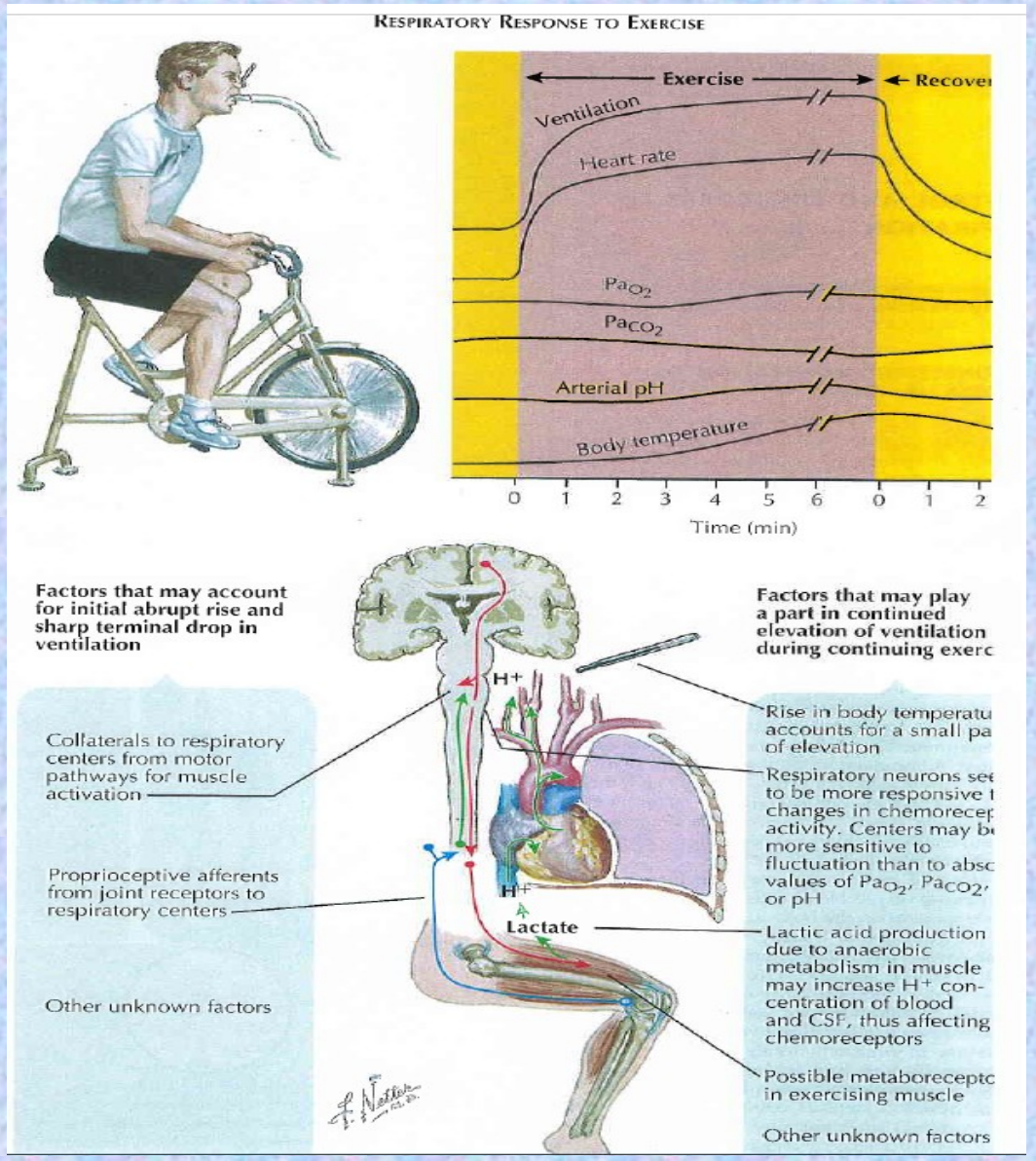
1. Hypoxic - physiological: stay at higher altitudes, pathological: hypoventilation during lung or neuromuscular diseases
2. Transport (anemic) - reduced transport capacity of blood for oxygen (anemia, blood loss, CO poisoning)
3. Ischemic (stagnation) - restricted blood flow to tissue (heart failure, shock states, obstruction of an artery)
4. Histotoxic - cells are unable to utilize oxygen (cyanide poisoning - damage to the respiratory chain)

Hypercapnia

- **Hypercapnia** - increase of concentration of carbon dioxide in the blood or in tissues that is caused by retention of CO_2 in the body
- possible causes: total alveolar hypoventilation (decreased respiration or extension of dead space)
- **mild hypercapnia (5 -7 kPa)** causes stimulation of the respiratory center (therapeutic use: pneumoxid = mixture of oxygen + 2-5% CO_2)
- **hypercapnia around 10 kPa** - CO_2 narcosis - respiratory depression (preceded by headache, confusion, disorientation, a feeling of breathlessness)
- **hypercapnia over 12 kPa** - significant respiratory depression - coma and death.

Spiroergometry

– combination of ergometry and analysis of breathing gases during work load on bicycle



- Change in ventilation immediately after the start of muscle work

  = a combination of chemical and other non-chemical influences.

Nervous regulation is probably decisive, chemical stimuli specify the setting of lung ventilation. Minute ventilation increases in direct proportion to oxygen consumption

- pO2, pCO2 and pH values in blood do not change significantly.

- **The respiratory center is activated from the motor areas of the cerebral cortex** (efferent corticospinal pathways to the motoneurons of the anterior horns of the spinal cord and at the same time by collaterals to the brainstem) . The lifelong learning process modulates these changes so that the amount of ventilation corresponds as closely as possible to the body's metabolic requirements

  Irritation of proprioceptors in working muscles, tendons and joint capsule (afferent pathways to the spinal cord, ascending pathways with collaterals activate respiratory centers)

HYPOXIA

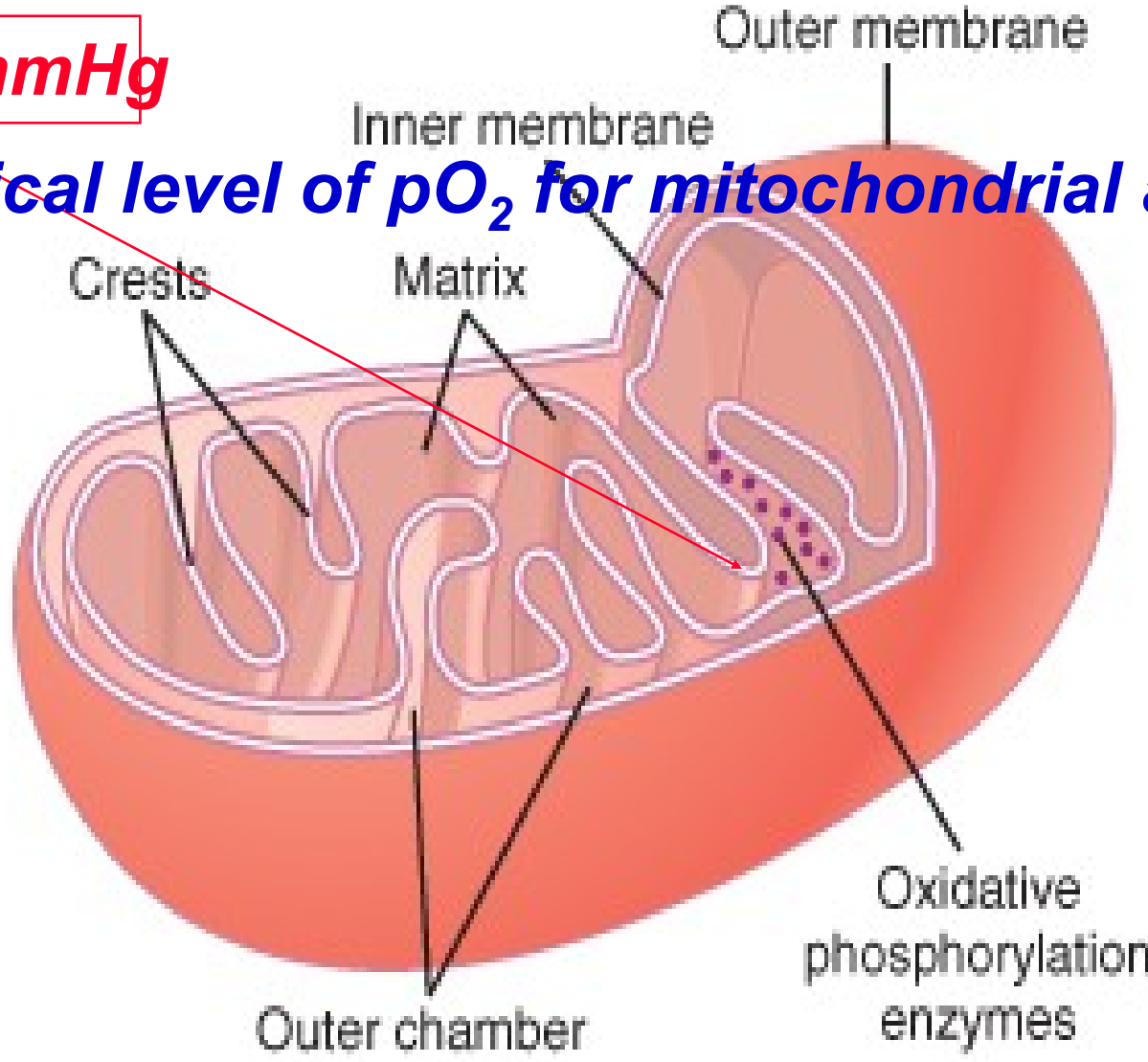
is oxygen deficiency at the cells or the tissue or the organs or the organism level

OXYGEN FALL

	pO_2 *in mmHg*
dry atmospheric air	*159*
humid atmospheric air	*149*
ideal alveolar gass	*105*
end-expirated air	*105*
Arterial blood	*77*
Cytoplasma – mitochondria	*3-10*
Mixed venous blood	*40*
Venous blood	*20*

pO_2 = 1 mmHg

= critical level of pO_2 for mitochondrial activity



This slide indicates that you will also encounter another distribution of hypoxia in the clinic

Hypoxia has been divided into following types:

1. *Decrease oxidation of blood in the lung*
2. *Pulmonary disease*
3. *Venous-arterial shorts in circulation*
4. *Oxygen transport disorder (blood – tissue)*
5. *Decrease utilization of oxygen by the tissue*

1. Decrease oxidation of blood in the lung

- *hypoxic hypoxia:*
  - *lower oxygen in atmospherical air*
  - *hypoventilation (neuromuscular diseases)*

2. Pulmonary disease

-hypoventilation :

We breathe superficially when we have
- narrowed airways - increase airway resistance (asthma bronchiale attack)
or
- due to lung fibrosis - decrease pulmonary compliance

3. Venous – arterial shunts

from fetal circulation: ductus arteriosus Botali
foramen ovale

Problems with pO_2 can occur in the above cases, especially in newborns after birth. However, the unrecognized imperfect closure of the foramen ovale may persist into adult and manifest as minor microembolizations with clinical signs in adult.

4. Oxygen transport disorder
(anemic hypoxia, stagnant hypoxia, ischemic hypoxia)

-Anemia

-Special type of hemoglobin (hemoglobin S-sickle cell anemia)

-Decrease of temperature

-Cardiovascular diseases

-Local disorder in circulation

5. Decrease utilization of oxygen by the tissue (histotoxic hypoxia)

-enzyme blocade of respiratory circle (poisoning)

- e.g. Cyanid poisoning – cyanid inhibits cytochromoxidase;
 treatment: methylen blue or nitrites
(methemoglobin + cyanid=cyanmetHg=nontoxic compound)

-lower capacity of cells for utilization of oxygen (deficit of vitamins)

Hypoxia is clearly associated with sympathetic activation, which then has other clinical implications (especially in the cardiovascular system)

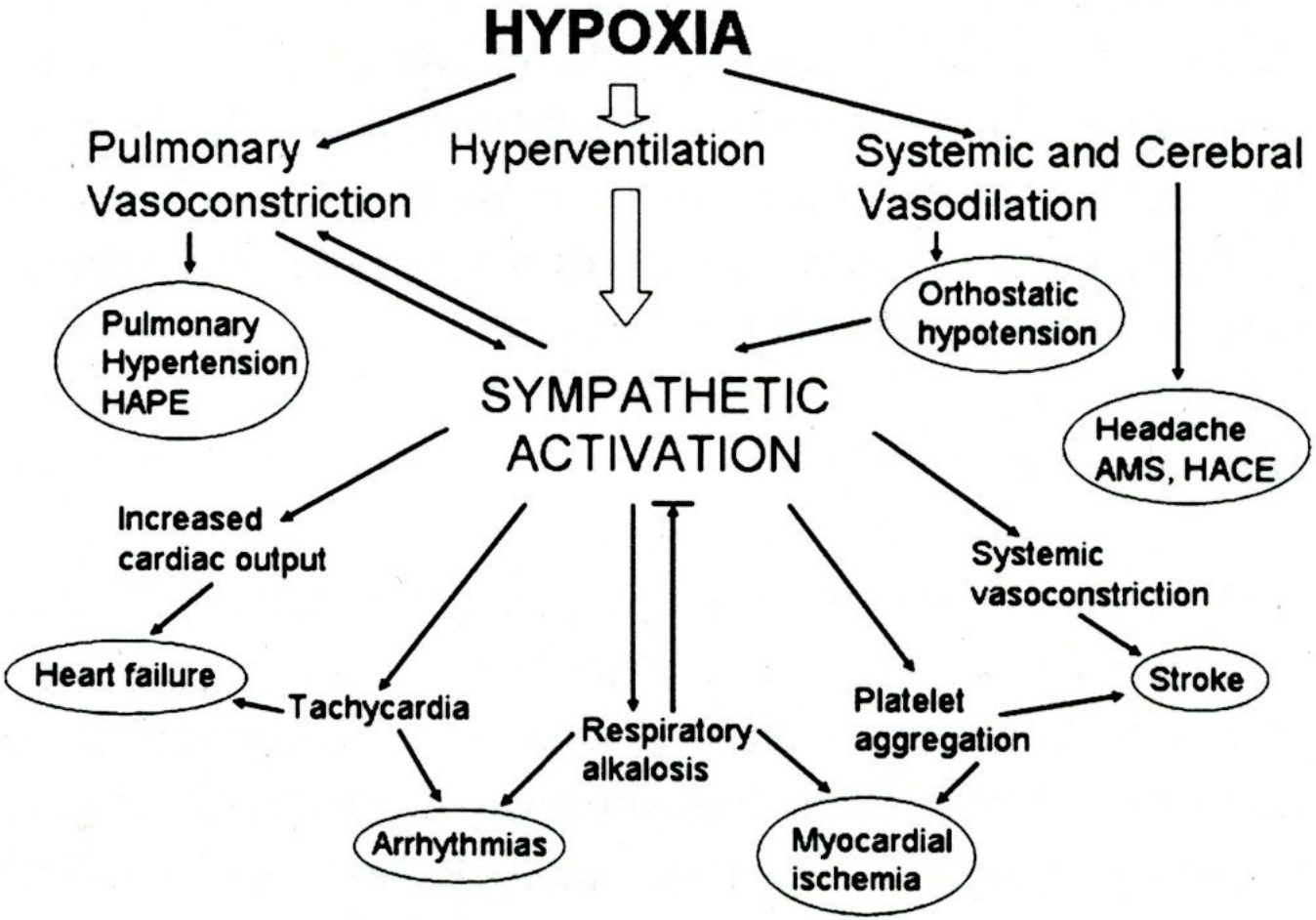
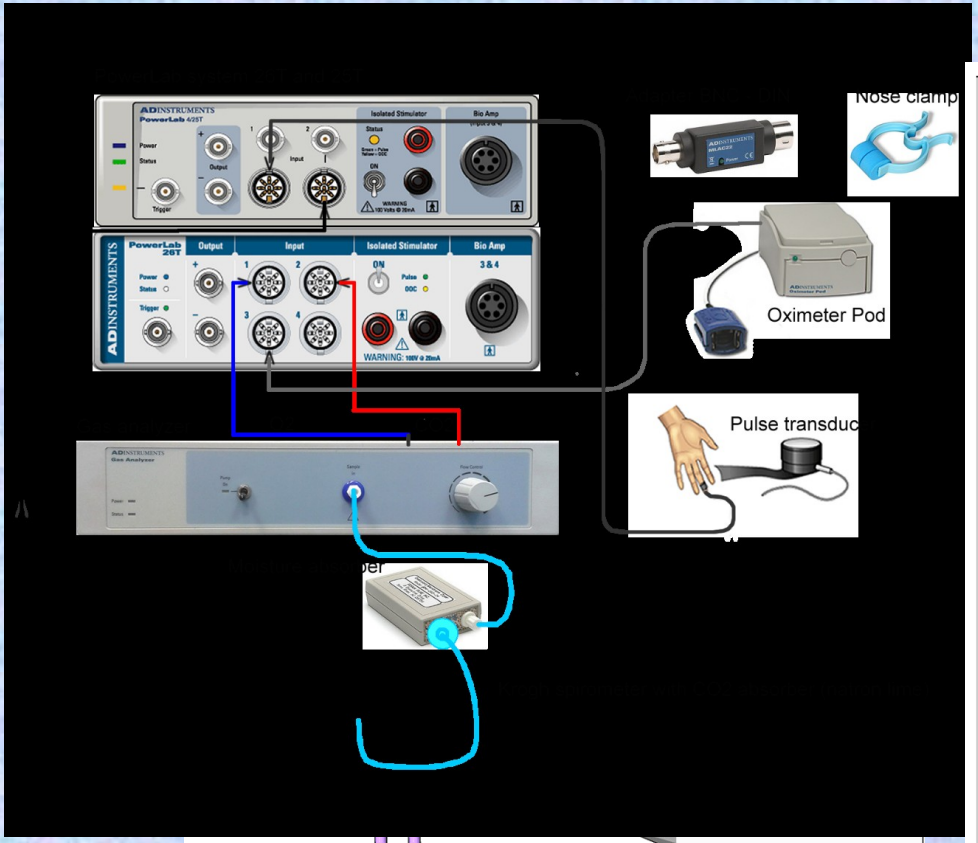


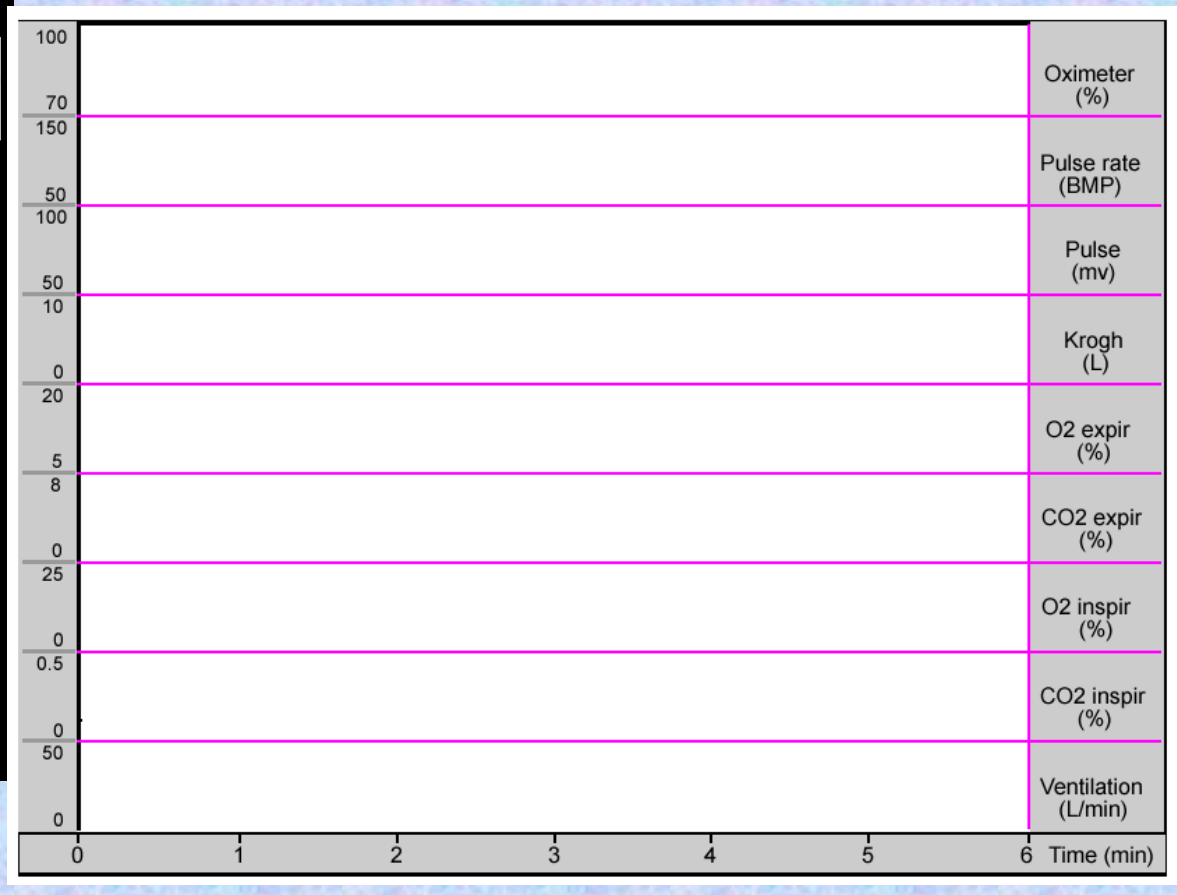
Fig. 3 Important physiological and pathophysiological effects during acute exposure to hypoxia and their potential associations with clinical conditions (modified after Rimoldi et al. 2010 [32]). *AMS* acute mountain sickness, *HACE* high-altitude cerebral edema, *HAPE* high-altitude pulmonary edema

EXPERIMENT - should be performed exactly **according to the instructions in the scripts**: Practical exercises in physiology and neuroscience, 2017;
Exercise: **Determining the sensitivity of the respiratory center to hypoxia**

- Note: we are creating an example of hypoxic hypoxia
- The Krogh respirometer in this case is filled only with ambient air, CO2 absorber (calcium hydroxide) is present. The volume of the respirometer is 10 l of air, one-fifth of which is oxygen - we have 2 liters of oxygen available. The test person is connected to a Krogh respirometer and the gas analyzer (see the following figure).
  We measure parameters: pO2, pCO2, movements of the respirometer show the respiratory rate and tidal volume, the computer calculates the minute ventilation. Using a pulse oximeter, we also read the oxygen saturation of hemoglobin from the finger of the hand. In addition, we have a record of the heart rate from the sphygmographic curve on the finger of the hand.
  The test person is connected to a respirometer and begins to breathe at rest. It takes about 2-5 minutes to achieve the effect of hypoxic hypoxia (depending on the intensity of the subject's metabolism, how fast and how much oxygen he consumes). **The effect of hypoxia begins to show an increase in minute ventilation as both parameters - pO2 and saturation - decrease.**
  We end the experiment when the saturation drops below 80%. We also notice responses to changes in heart rate.

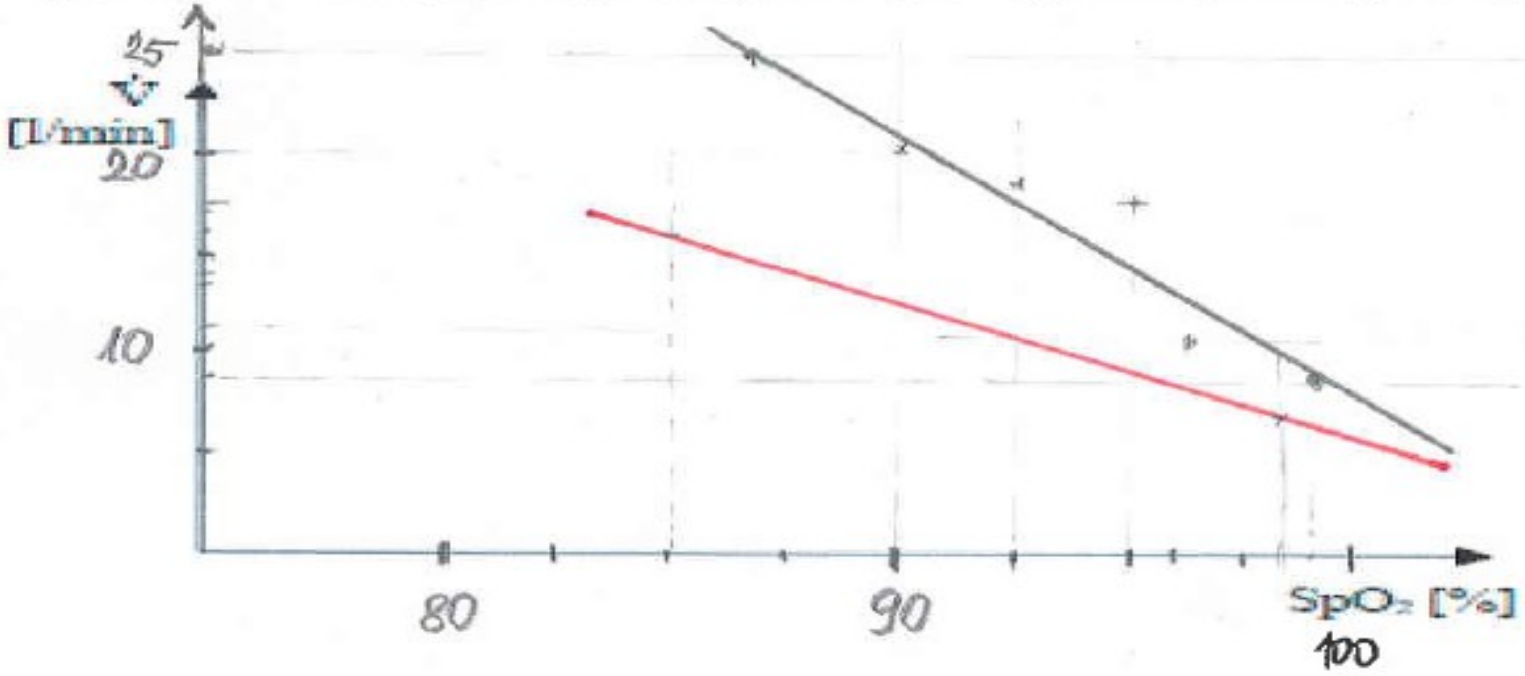
Hypoxia setup





Výsledky: *Results*

Hypoxie								
Osoba A	1.	2.	3.	4.	5.	6.	7.	8.
SpO_2 [%]	99	96	95	92	90	89	87	86
$\dot{V}$ [l/min]	8,1	13,2	14,8	18,1	20,3	19,8	21,2	25,6
Osoba B	1.	2.	3.	4.	5.	6.	7.	8.
SpO_2 [%]	98	96	95	92	90	89	86	85
$\dot{V}$ [l/min]	6,9	7,6	8,2	9,5	10,4	11,8	13,5	15,9



Hypoxic hypoxia

– during a trip to high mountains

e.g. with cable car to Mont Blanck

Effect of high altitude on arterial oxygen saturation
(numbers in parenthese are acclimatized value)

Altitude (m)	*barometric pressure (mmHg)*	*pO_2 in air (mmHg)*	*pCO_2 in alveoli (mmHg)*	*pO_2 in alveoli (mmHg)*	*arterial oxygen saturation (%)*
0	*760*	*159*	*40 (40)*	*104 (104)*	*97 (97)*
3 048	*523*	*110*	*36 (23)*	*67 (77)*	*90 (92)*
6 096	*349*	*73*	*24 (10)*	*40 (53)*	*73 (85)*
9 134	*249*	*47*	*24 (7)*	*18 (30)*	*24 (38)*
12 192	*141*	*29*			
15 240	*87*	*18*			

Classical distribution of barometric air pressure and the amount of pO2 and pCO2 with increasing altitude.

Breathing pure oxygen

altitude (m)	*barometric pressure (mmHg)*	*pCO2 in alveoli (mmHg)*	*pO2 in alveoli (mmHg)*	*arterial oxygen saturation (%)*
0	*760*	*40*	*673*	*100*
3 048	*523*	*40*	*436*	*100*
6 096	*349*	*40*	*262*	*100*
9 134	*349*	*40*	*139*	*99*
12 192	*141*	*36*	*58*	*84*
15 240	*87*	*24*	*16*	*15*

When climbers use oxygen bombs, their saturation at 6,000 m above sea level changes for the better.

Work capacity at high altitude

	work capacity (compare with normal condition) (%)
Unacclimatized	*50*
Acclimatized for 2 months	*68*
Native living at 4 023 m but working at 5 182 m above sea level	*87*

To evaluate the adaptation to alpine conditions, we can use the parameter of work capacity and its comparison: alpine environment versus work in the lowlands: newcomers, non-acclimatized individuals reach only half of their lowland work capacity, and even after 2 months of acclimatization are maximum 60-70%. However, people living permanently (from birth) in the high mountains have a much higher work capacity - (although it does not reach 100% lowland), but it is around 90%.

High altitude hypoxia – mountain sickness – alpine disease
clinical signs -- *mild step*

CNS	*disorientation*
Sensitivity	*headache*
Respiration	*increase (dyspnea, rapid breathing, hyperventilation)*
BP	*increase*
HR	*increase, arrhythmias*
muscle	*loss of co-ordination*
GIT	*nausea*

You read many times that there are injuries in the mountains - this is also a logical consequence of hypoxia - poor coordination of movements (you stumble where this would not normally happen to you).
Believe that hypoxia affects everyone a little differently - from my own experience I have a funny incident when we went to Mont Blanc as a family… the track there is very fast, because the cable car will take you there in about 45 minutes - up to 4000m above the sea (you will produce amazing acute hypoxia). The male half of the family had perfect euphoria, "nothing was a problem," running across the plateau from place to place, admiring the mountain and the snow; on the contrary, I could hardly move and lift my legs to one step, and coordinating the movement was almost beyond my power; my daughter was in such a headache that she refused to get back on the cable car, so we all walked from the middle of the hill on foot.

High altitude hypoxia – middle step

CNS	*dimness of vision, vertigo, anxiosity*
GIT	*nausea*
Sensitivity	*chest pain*
Respiration	*apnoe*
BP	*increase*
HR	*decrease, irregulary*
muscle	*spasmus*

High altitude hypoxia – severe step

CNS	*coma*
GIT	*nausea, vomiting*
Sensitivity	*chest pain*
Respiration	*Cheyn-Stokes breathing*
BP	*drop*
HR	*decrease*
Muscle	*muscle weakness*

Travelling by aircraft

The reason for all the problems described in the following pictures is the fact that we have pressure on board the aircraft as if we were at an altitude of 2000 meters above sea level.

Travelling by aircraft

This results in an increased risk for patients
with:

- ***Concentration of hemoglobin above 60 %***
- ***Atherosclerosis - severe step***
- ***Cardial insuficiency***
- ***Respiratory insuficiency***
- ***Hypertension - untreated (BP ower 200/100)***

(On board aicraft is pressure as on 2000 m above see level)

Reduced pO_2 in the air on board the aircraft affects the values of systolic and diastolic pressure:

- lower pO_2 - stimulated sympaticus

- increase periphery resistence - decrease stroke volume

- decrease pulse pressure - decrease perfusion in tissues - redistribution of blood in circulation

- increase of position of diaphragma

(decrease hemodynamics and respiration)

And this creates an increased risk
for patients with

- cardio – vascular diseases

- tromb – embolic diseases

Diving

during holidays - recreational

Caution: it is not recommended to dive in one morning and fly home in the afternoon

Diving

- **There is an increase in ambient pressure - hyperbaria (proportional to the depth of immersion); at every 10m depth the pressure increases by 100kPa The body must be able to cope with the unavailability of a normal supply of air to the lungs**
  - When breathing, the respiratory muscles must overcome the water pressure on the chest and at the same time develop sufficient lowpressure(vakuum) in the thoracic cavity for the inspiration to take place.
  - By strenuous contraction of the inspiratory muscles we reach a maximum vacuum of about 11kPa = depth 110cm (in greater depths it is not possible to breathe, it is necessary to use a breathing apparatus that adjusts the pressure of the inhaled air to the ambient water pressure - breathing with normal effort

Diving - risks

- The air contains 4/5 of nitrogen - harmless at normal atmospheric pressure
- At higher pressures, when the partial pressure of all gases in the inhaled mixture increases, the concentration of nitrogen in body fluids and tissues increases - the narcotic effect is applied
- Nitrogen anesthesia - is present to a depth of 30-40m, manifestations such as intoxication (euphoria, loss of judgment, inhibition, followed by fatigue, malaise, unconsciousness)
- Hyperbaria also increases pO2 in the inspiratory air - an increase in alveolar pO2, an increase in physically dissolved oxygen in the blood
- Hyperoxia – toxic effects of oxygen
- Increased ambient pressure reduces the volume of body cavities filled with air (middle ear, paranasal sinuses, lungs-alveoli - Boyle-Mariott law)
- Painful retraction of the eardrum if the pressure of the middle ear is not gradually equalized with the ambient pressure
- Alveolar collapse - prevention: breathing air under higher pressure using a breathing apparatus

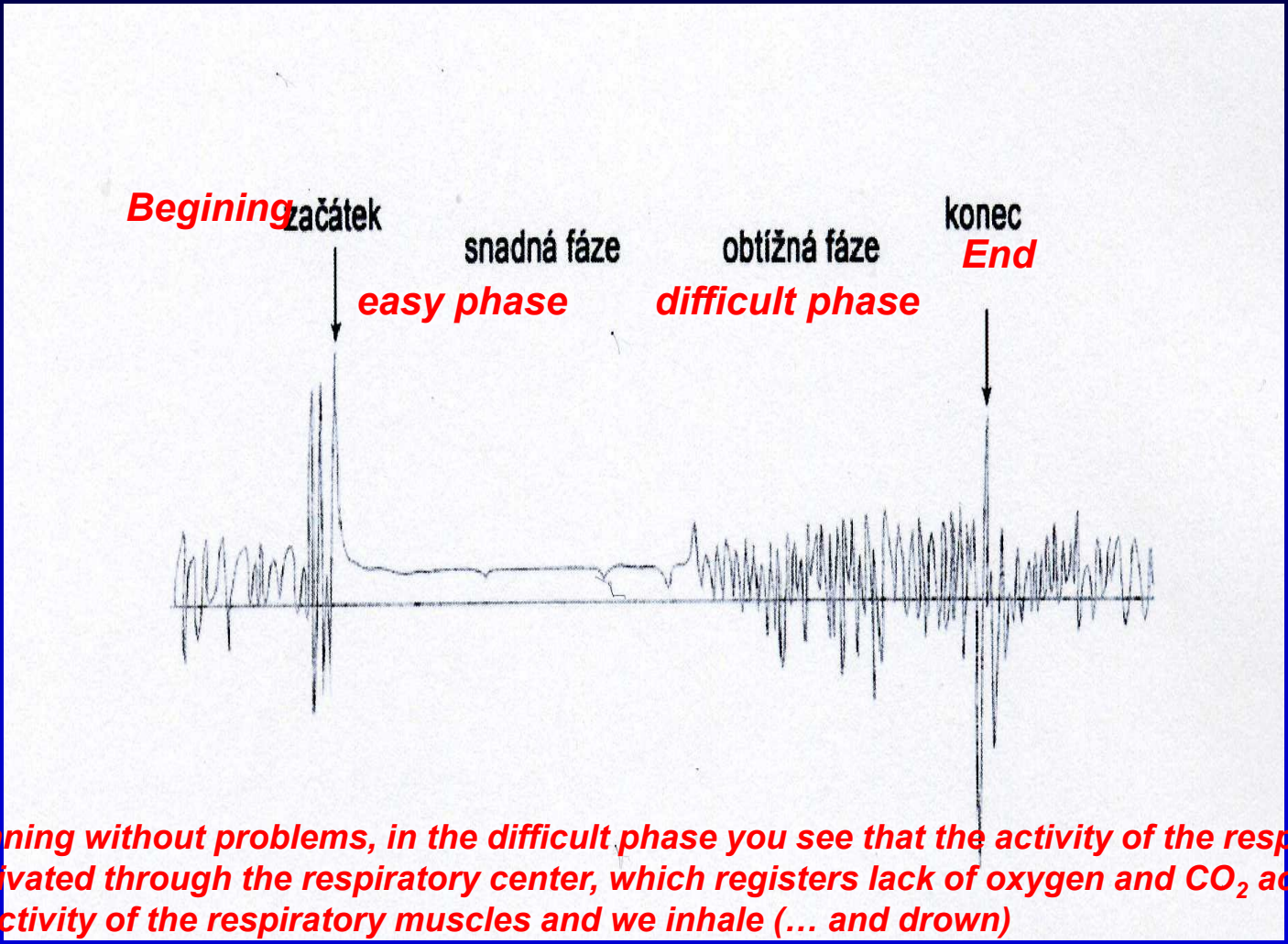
Diving

- **Short-term - breath holding, rise in pCO2 above 6.6 kPa - stimulation of the respiratory center, compulsion to inspiration**
- **Breathing using a snorkel**
  The volume of the anatomical dead space of the respiratory tract increases - the limitation of alveolar ventilation (maximum length 40cm, lumen 2 cm)
- **Long-term diving - with a breathing apparatus, the question is the content of the apparatus: pure oxygen (toxicity); compressed air - only to a depth of 30-40m (large proportion of nitrogen), to great depths - a mixture of oxygen and helium**
  - Helium is less soluble in tissues, has a smaller molecule than nitrogen - it is excreted faster from the body

- **Decompression sickness = Caisson disease**

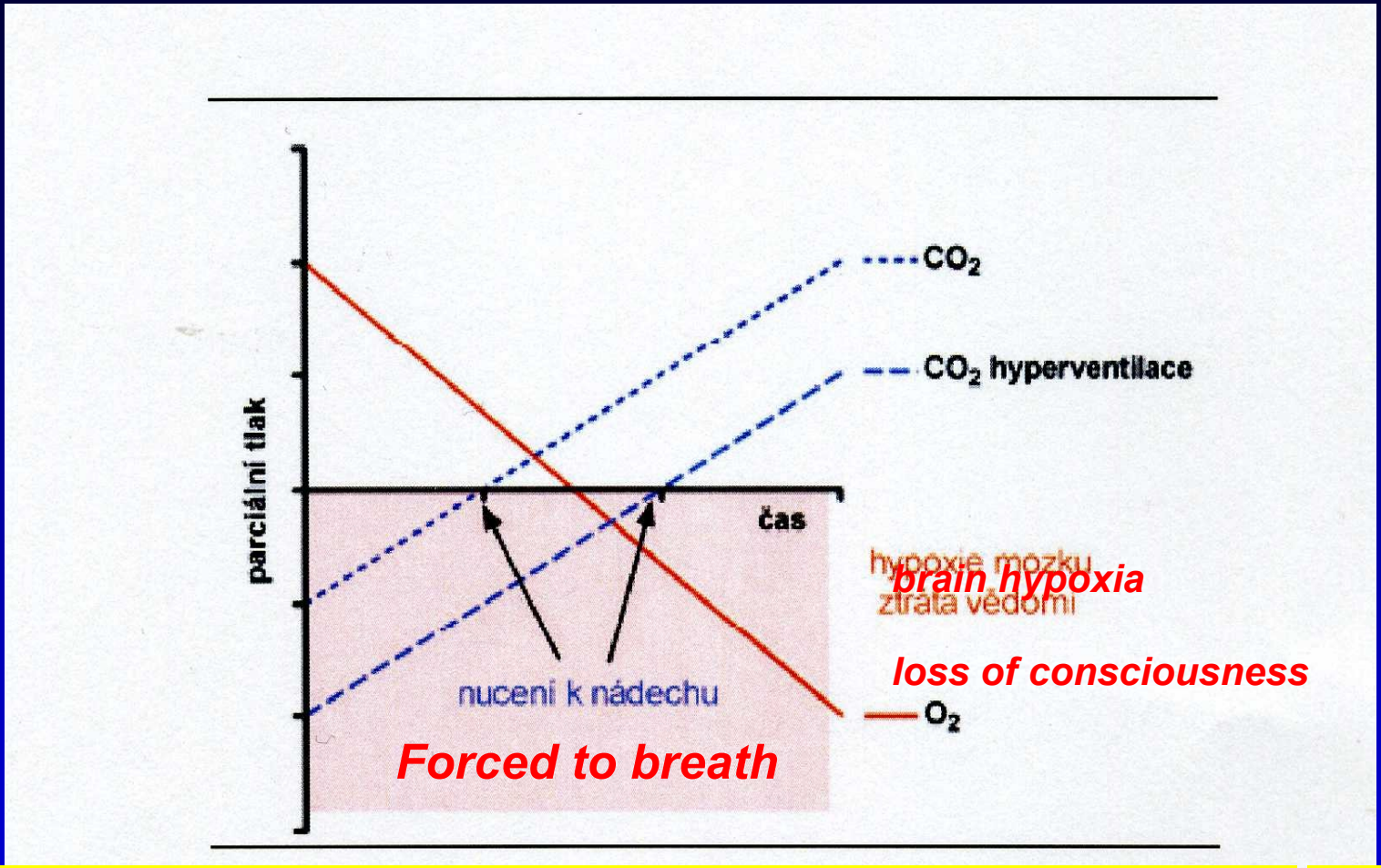
  If a person breathes air under higher pressure for a long time under water - the amount of nitrogen dissolved in body fluids and tissues (especially in adipose tissue) increases
  During a sufficiently slow emerging – oxygen diffuses from the tissues into the blood and is gradually exhaled
  Rapid emerging - there is no time to eliminate nitrogen and it accumulates in the form of bubbles in tissues and fluids
  Bubbles in the tissues cause pain (joint), bubbles in the circulation - blockage of small blood vessels – dyspnoe, damage to the myocardium or CNS
- **Prevention: slow emerging - 10m / min**
- **Treatment: immediate recompression in a pressure chamber followed by slow decompression**

The picture shows the activity of the respiratory muscles during breath holding during diving



… .in the beginning without problems, in the difficult phase you see that the activity of the respiratory muscles increases (activated through the respiratory center, which registers lack of oxygen and CO_2 accumulation; fails to maintain this activity of the respiratory muscles and we inhale (… and drown)

The danger of hyperventilation before diving



DO NOT hyperventilate! We must realize that the beginning of respiration is started mainly by the amount of pCO_2 in the body. If we hyperventilate before diving, we think that we will accumulate more oxygen in the body and thus stay under water for a longer time… BUT during hyperventilation, pCO2 is also exhaled and we put down the fuse to start breathing in time (you see a shift between the left arrow during normal breathing, and when it will force us to inhale after hyperventilation. This difference is whether we survive diving or drowning. We prolong the dive time, dive deeper, more inhaled oxygen and can affect the CNS euphorically, and loss of orientation below the surface, we won't know where it's up-where it's down, and our "forced breath" signal will be late and we may not be able to emerge.

Toxicity of oxygen

Toxicity of oxygen

The toxicity seems to be due to the production of the superoxid anion and H_2O_2

Causes:

- ***Loss of the ability to bind CO_2 in the venous blood***
  - CO_2 output through the lungs is hampered by the development of toxic pulmonary edema

Symptoms due to oxygen toxicity manifest themselves depending on the pressure under which we breathe oxygen and mainly depends on the time of exposure

Critical values occur when oxygen is exposed to> 40 kPa (300 mmHg) as a function of time

Toxicity of oxygen

When exposed around 8 hours, occurs

- *respiratory passages became irritated*
- *Substernal distress*
- *Nasal congestion*
- *Sore throat*
- *Cough*

When exposed around 24-48 hours, occurs:

- *damage of lungs*
  – *decrease production of surfactant*

Symptoms:

Pulmonary disorders with O_2 exposure

under pressure> 70 kPa will manifest within a few days - symptoms: cough, respiratory pain;

under pressure of 200 kPa for 3 - 6 hours with symptoms: convulsions, loss of consciousness

TOXICITY of OXYGEN

Recommendation:

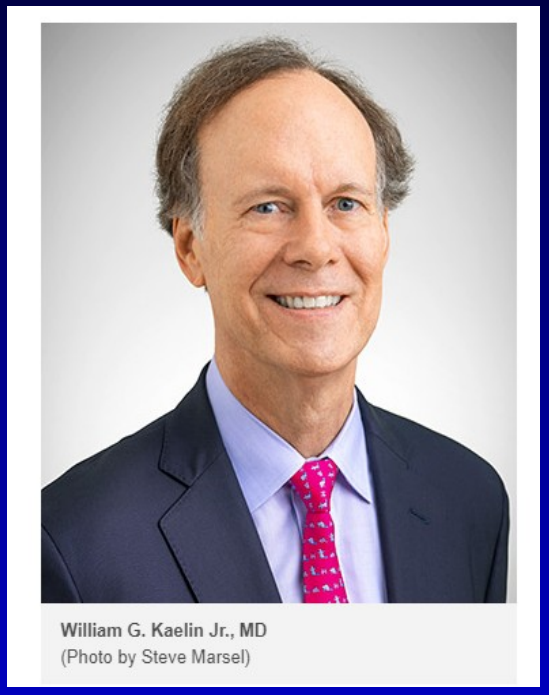
100 % - give discontinuosly

Best through the so-called "oxygen glasses" - when they add oxygen to the surrounding air

Nobel Prize in Physiology or Medicine 2019

© Nobel Media. Photo: A. Mahmoud

Gregg L. Semenza



Were awarded the Nobel Prize in Physiology or Medicine 2019

for delineating the biochemical details of elegant stress respons pathway

Complex of proteins „Hypoxia inducibile factor“ - HIF