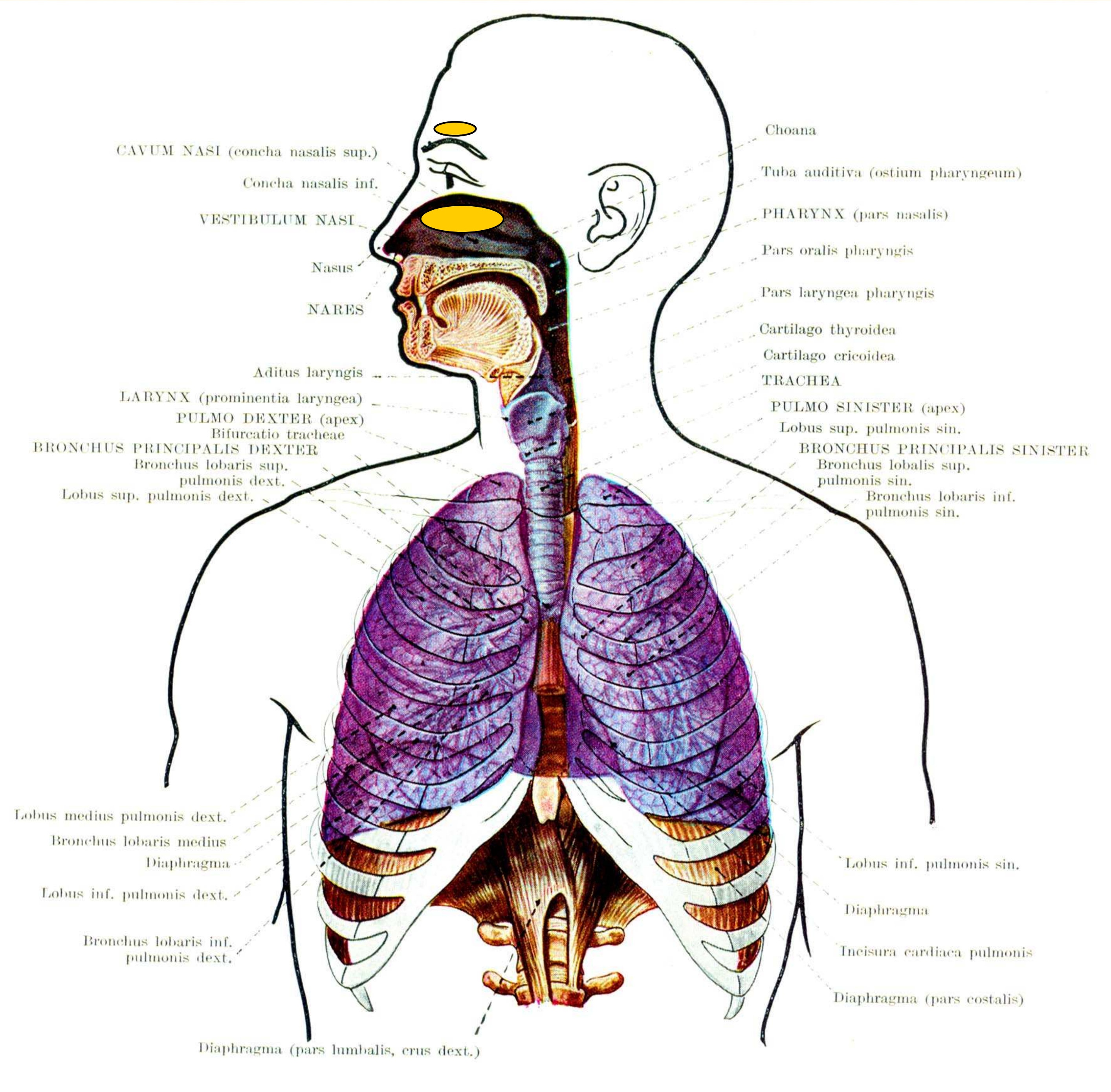
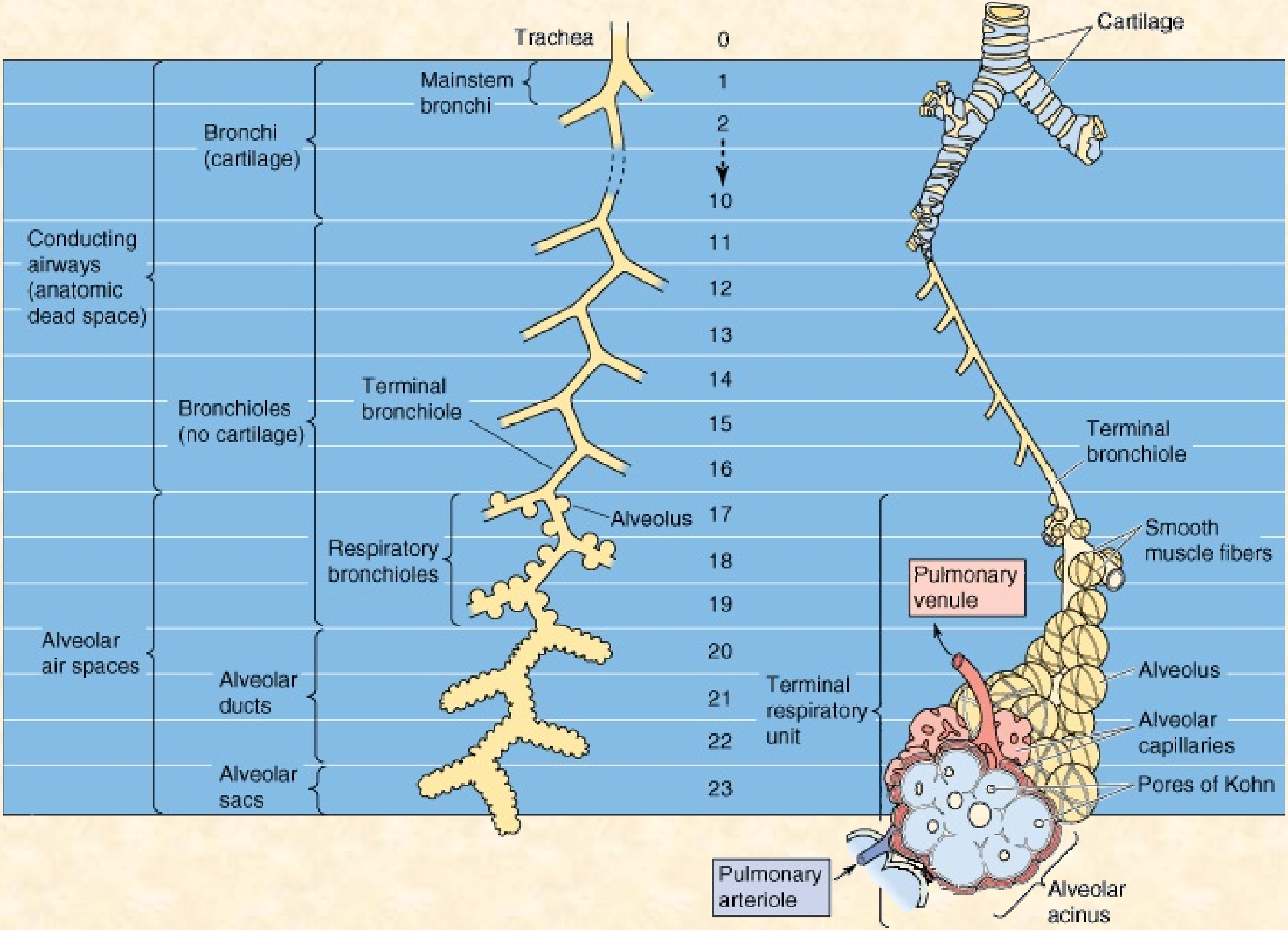
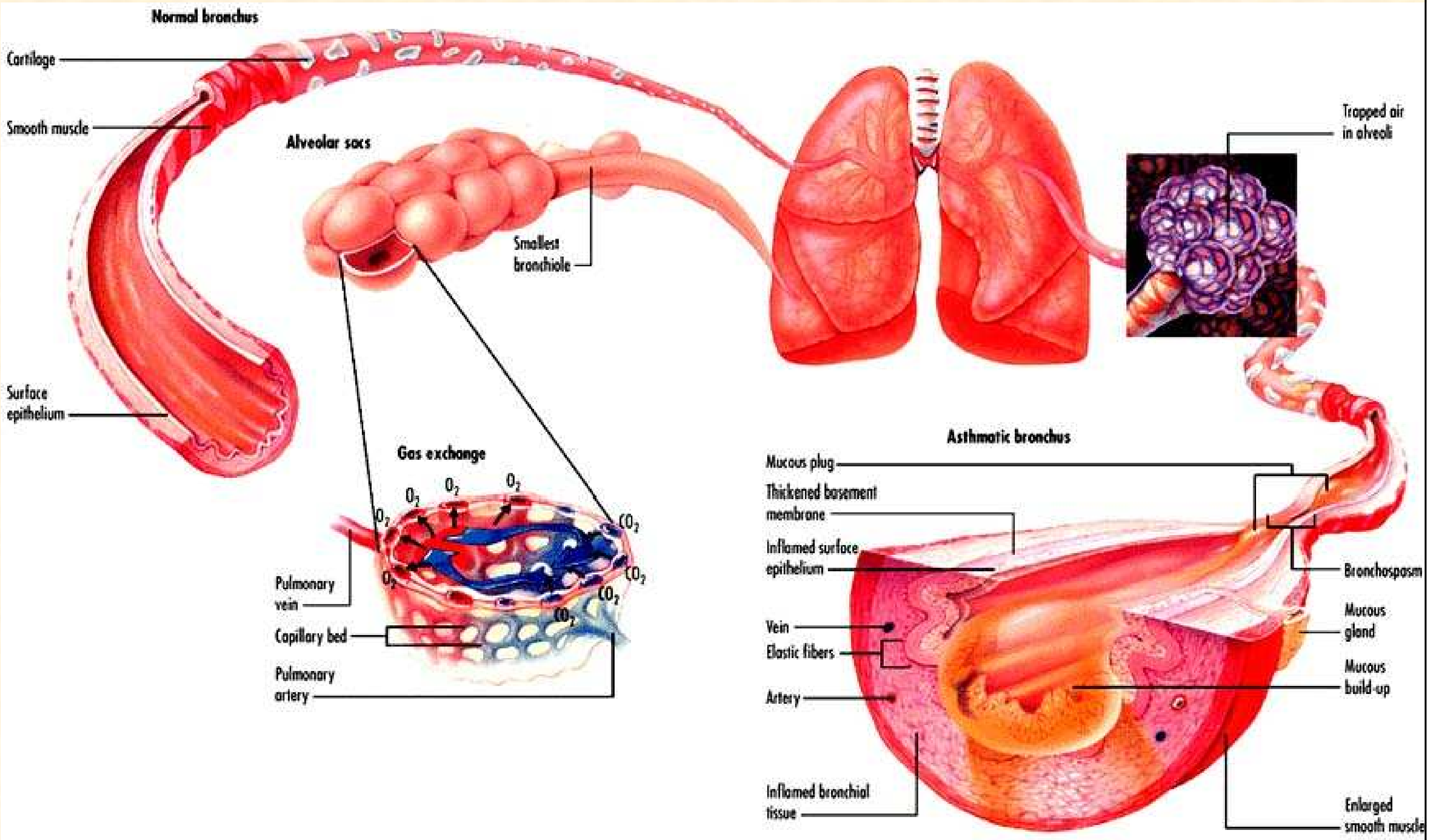
RESPIRATORY SYSTEM

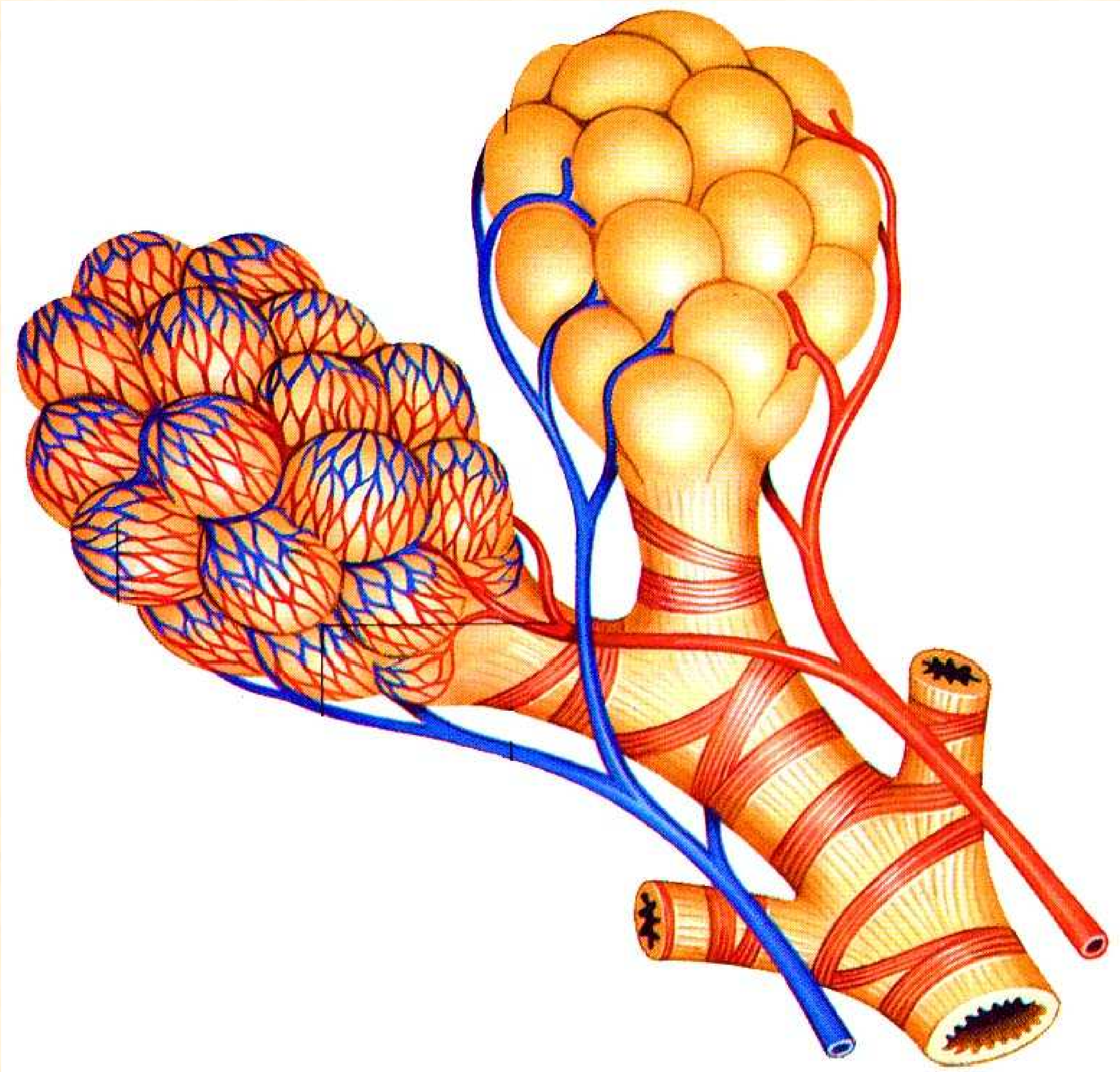
RESPIRATORY FUNCTIONS
MECHANICS OF RESPIRATORY SYSTEM
GAS TRANSPORT


CAVUM NASI (concha nasalis sup.)
Concha nasalis inf.
VESTIBULUM NASI
Nasus
NARES
Aditus laryngis
LARYNX (prominentia laryngea)
PULMO DEXTER (apex)
Bifurcatio tracheae
BRONCHUS PRINCIPALIS DEXTER
Bronchus lobaris sup. pulmonis dext.
Lobus sup. pulmonis dext.
Lobus medius pulmonis dext.
Bronchus lobaris medius
Diaphragma
Lobus inf. pulmonis dext.
Bronchus lobaris inf. pulmonis dext.
Diaphragma (pars lumbalis, crus dext.)
Choana
Tuba auditiva (ostium pharyngeum)
PHARYNX (pars nasalis)
Pars oralis pharyngis
Pars laryngea pharyngis
Cartilago thyroidea
Cartilago cricoidea
TRACHEA
PULMO SINISTER (apex)
Lobus sup. pulmonis sin.
BRONCHUS PRINCIPALIS SINISTER
Bronchus lobaris sup. pulmonis sin.
Bronchus lobaris inf. pulmonis sin.
Lobus inf. pulmonis sin.
Diaphragma
Incisura cardiaca pulmonis
Diaphragma (pars costalis)



Trachea
0
Cartilage
Mainstem bronchi
1
2
10
Bronchi (cartilage)
Conducting airways (anatomic dead space)
11
12
13
14
15
16
Terminal bronchiole
Bronchioles (no cartilage)
Terminal bronchiole
Alveolus
17
Smooth muscle fibers
Respiratory bronchioles
18
19
Pulmonary venule
Alveolar air spaces
20
Alveolar ducts
21
22
Terminal respiratory unit
Alveolus
Alveolar capillaries
Alveolar sacs
23
Pores of Kohn
Pulmonary arteriole
Alveolar acinus

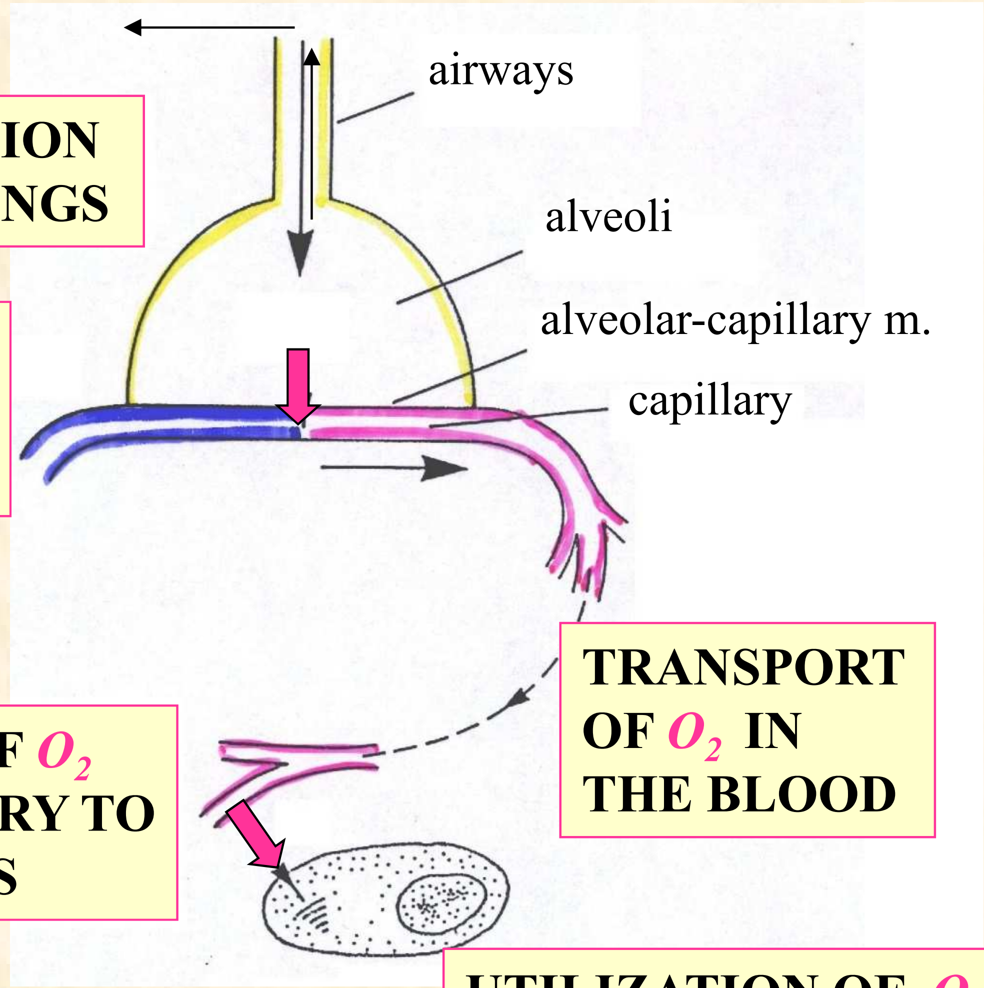

Normal bronchus
Cartilage
Smooth muscle
Surface epithelium
Alveolar sacs
Smallest bronchiole
Trapped air in alveoli
Gas exchange
O_2
CO_2
Pulmonary vein
Capillary bed
Pulmonary artery
Asthmatic bronchus
Mucous plug
Thickened basement membrane
Inflamed surface epithelium
Vein
Elastic fibers
Artery
Inflamed bronchial tissue
Bronchospasm
Mucous gland
Mucous build-up
Enlarged smooth muscle



STEPS IN THE DELIVERY OF O_2 TO THE CELLS

VENTILATION OF THE LUNGS

DIFFUSION OF O_2 ACROSS ALVEOLAR-CAPILLARY MEMBRANE



TRANSPORT OF O_2 IN THE BLOOD

DIFFUSION OF O_2 FROM CAPILLARY TO THE CELLS

UTILIZATION OF O_2 BY MITOCHONDRIA

AT REST

O_2	UPTAKE	~300 ml / min
CO_2	OUTPUT	~250 ml / min

INTERNAL RESPIRATION

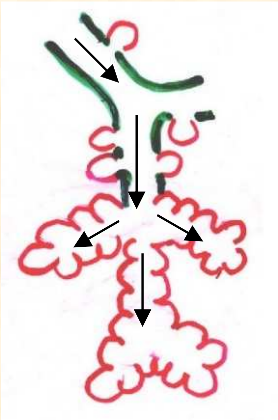
AIR PASSAGES

ANATOMICAL DEAD SPACE – CONDUCTING ZONE

- NASAL PASSAGES
- PHARYNX
- LARYNX
- TRACHEA
- BRONCHI
- BRONCHIOLES
- TERMINAL BRONCHIOLES

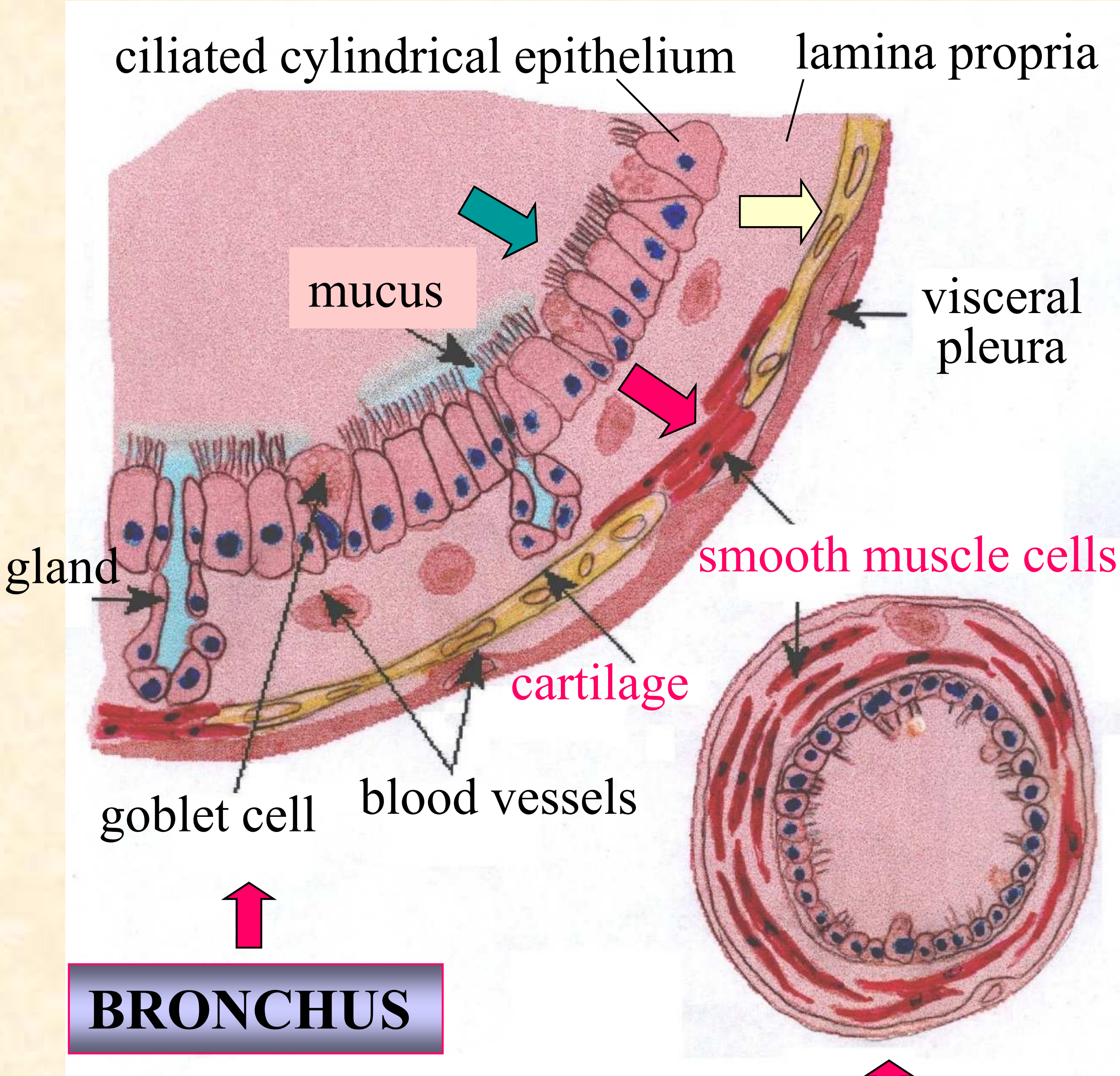
Other physiological functions:

- air is warmed, cleaned and takes up water vapour
- respiratory reflex responses to the irritants
- speech and singing (function of larynx)



RESPIRATORY ZONE (GAS EXCHANGE)

Total alveolar area ~100 m^2



AUTONOMIC INNERVATION of smooth muscle cells

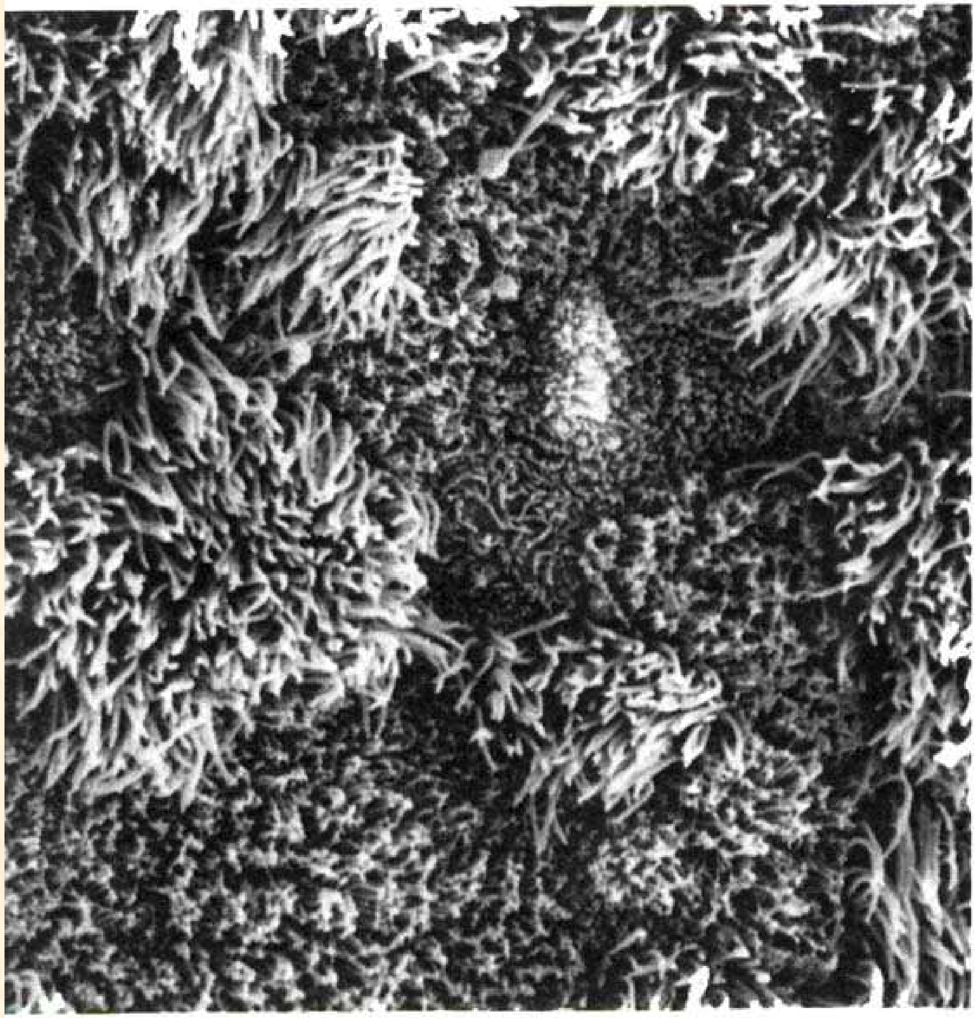
Stimulation via parasympathetic NS - n.vagus due to Muscarinic receptors: Acetylcholine activates bronchoconstriction

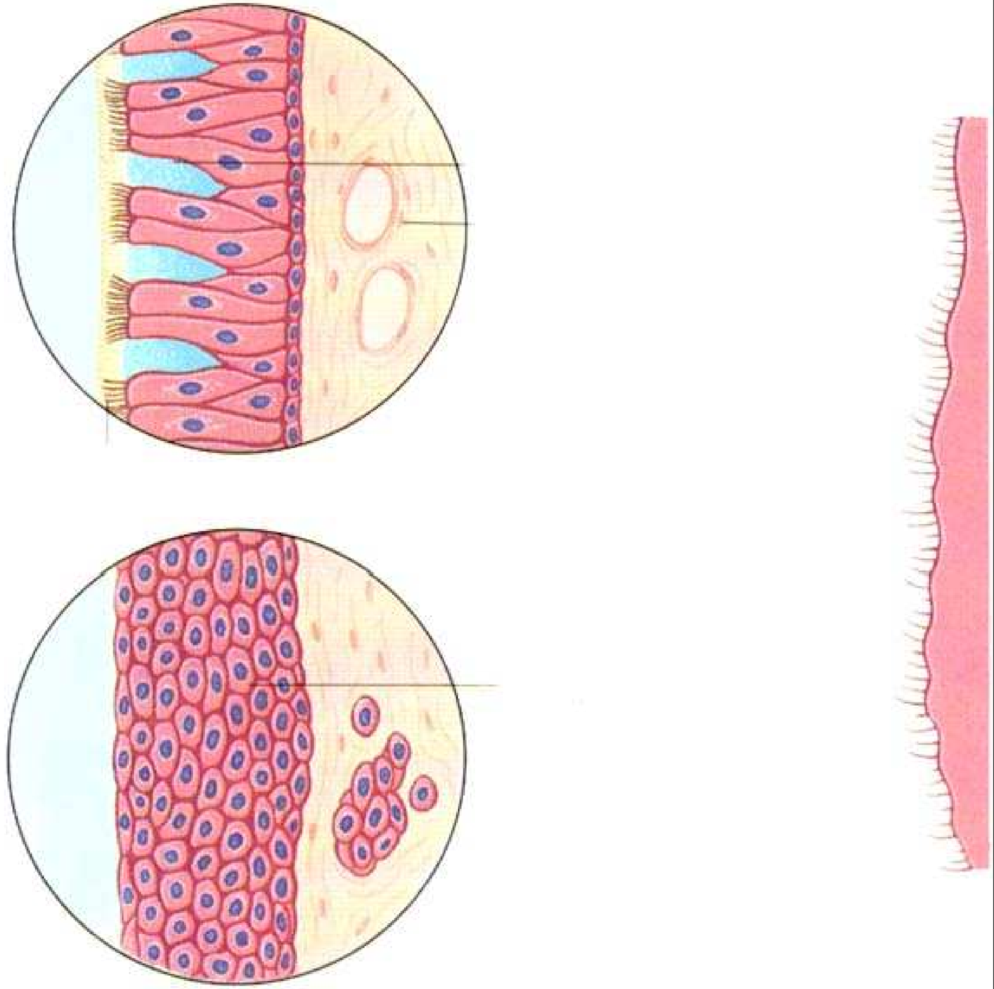
Stimulation via to sympathetic NS – due to catecholamins in circulation

β_2-adrenergic receptors: Noradrenaline activates bronchodilatation

TERMINAL BRONCHIOLE

∅ < 1 mm





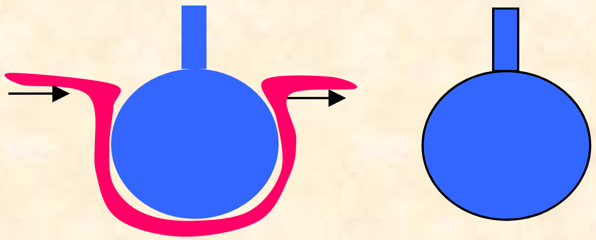
Cylindrical epithelium with cilia

DEAD SPACE

TOTAL GAS VOLUME NOT EQUILIBRATED WITH BLOOD
(without exchange of gasses)

- **ANATOMICAL dead space - volume of air passages**
- **FUNCTIONAL (total) dead space**

ANATOMICAL dead space + total VOLUME of ALVEOLI without functional capillary bed



IN HEALTHY INDIVIDUALS
both spaces are practically identical

V_T tidal volume ~ **500 ml**

V_A part of tidal volume entering alveoli ~ **350 ml**

V_D part of tidal volume remaining in the dead space ~ **150 ml**

$$V_T = V_A + V_D$$

f = 12/min

$$\dot{V} = V_T \times f$$

PULMONARY MINUTE VENTILATION

6 l/min

$$\dot{V}_A = V_A \times f$$

ALVEOLAR VENTILATION

4.2 l/min

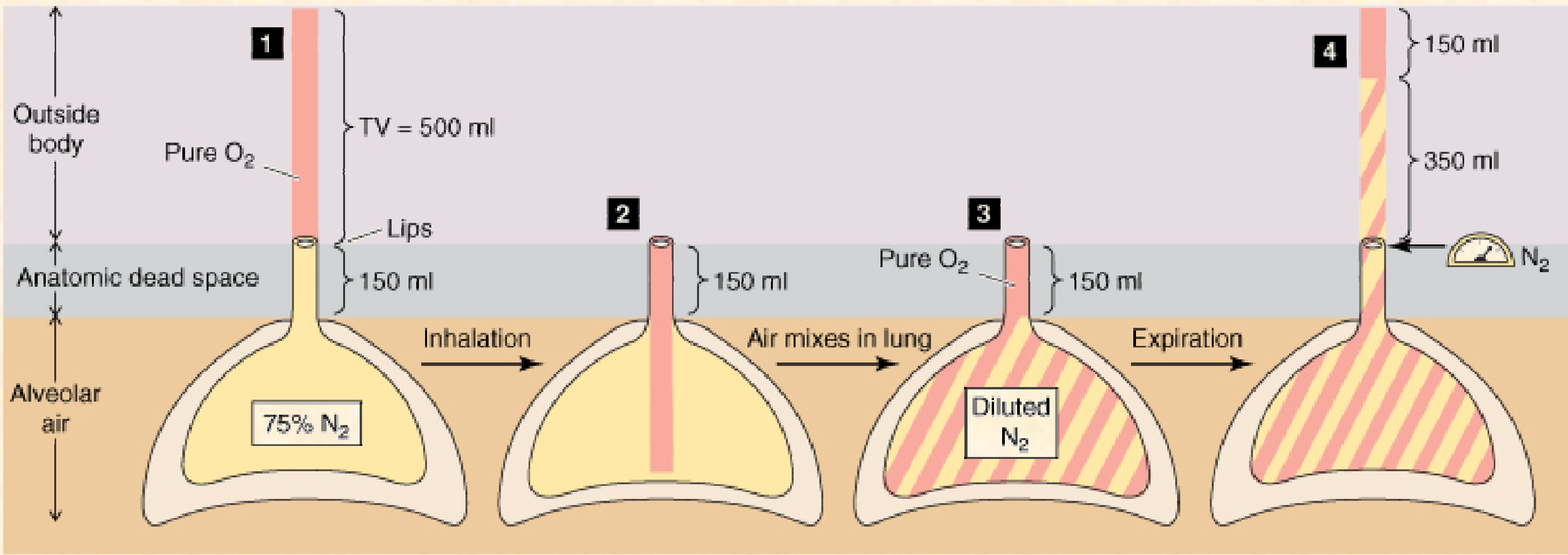
$$\dot{V}_D = V_D \times f$$

DEAD SPACE VENTILATION

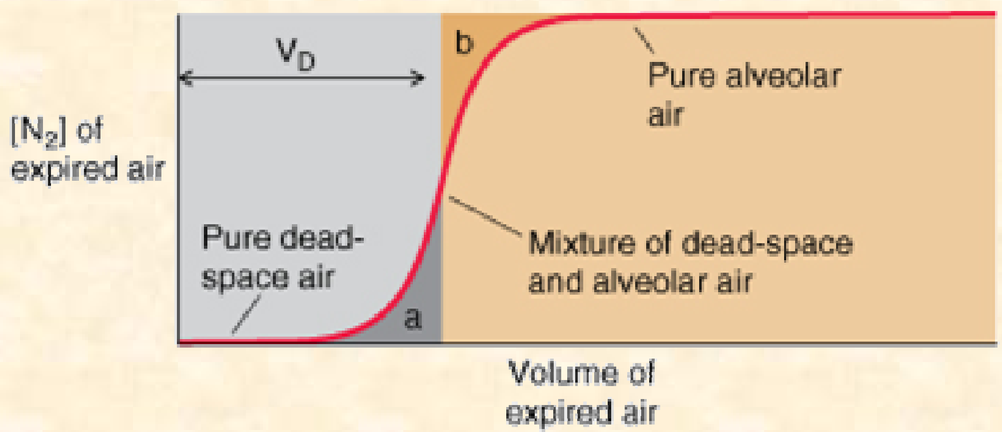
1.8 l/min

DEADSPACE – nitrogen test (force inspiration of pure O2, follow slowly expiration with monitoring of concentration of nitrogen)

A DILUTION OF INSPIRED 100% O_2

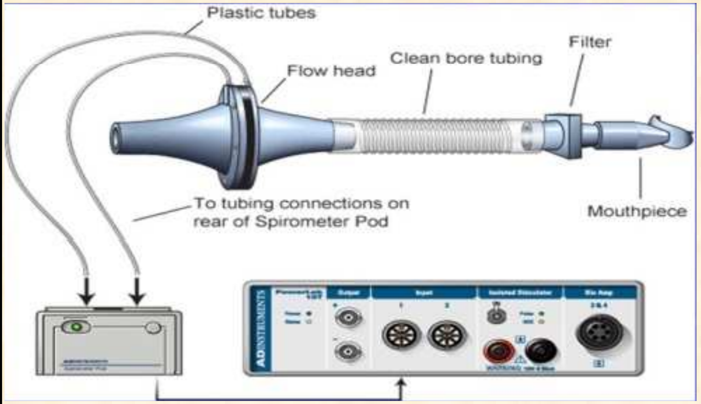


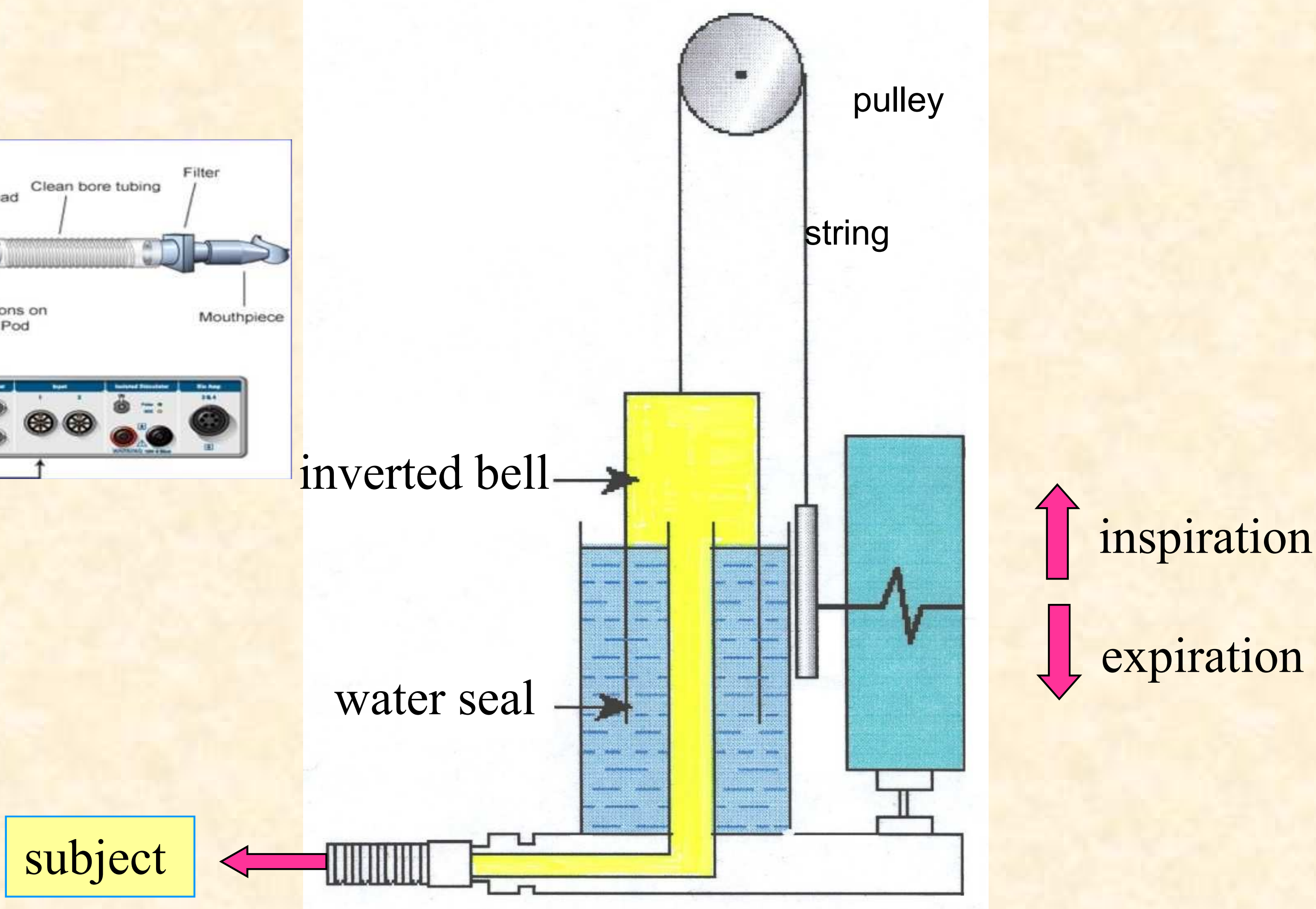
C MEASURED [N_2] PROFILE



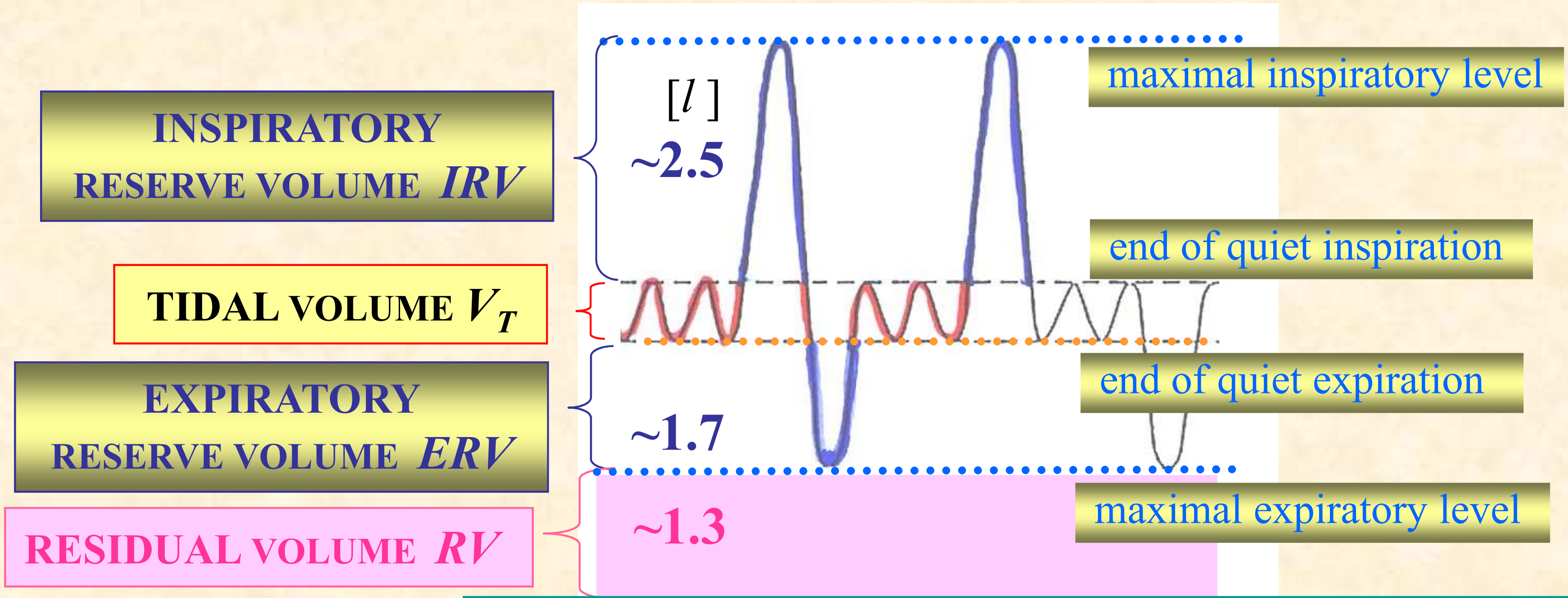
SPIROMETRY

(measurements of lung volumes, capacities, functional investigations, …)

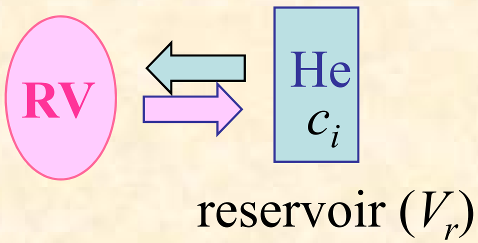




LUNG VOLUMES



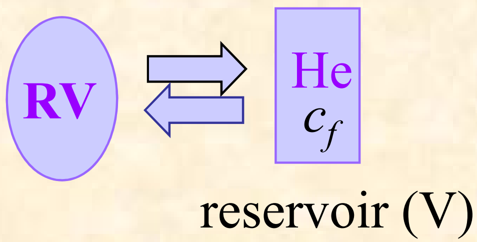
DILUTION METHOD
He



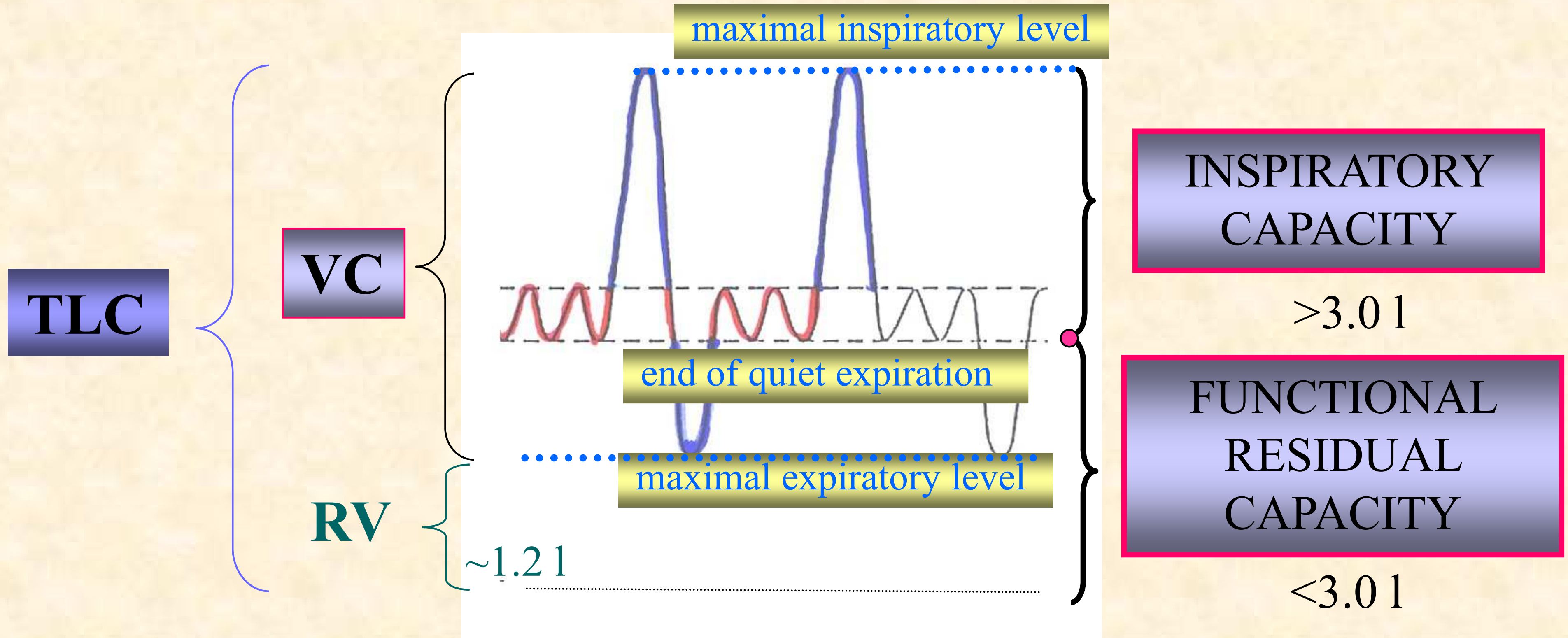
Principle of method: **1** Maximal expiration, **2** Repeated inspiration from and expiration into a reservoir (known **volume** V_r) with inert gas ***He*** (known concentration c_i)

⇒ Equilibration of the air in the residual volume and reservoir

3 Calculation of **residual volume *RV*** from the initial and final *He* concentrations in reservoir (c_i , c_f).



$$RV = V_r \frac{c_{i\,He} - c_{f\,He}}{c_{f\,He}}$$



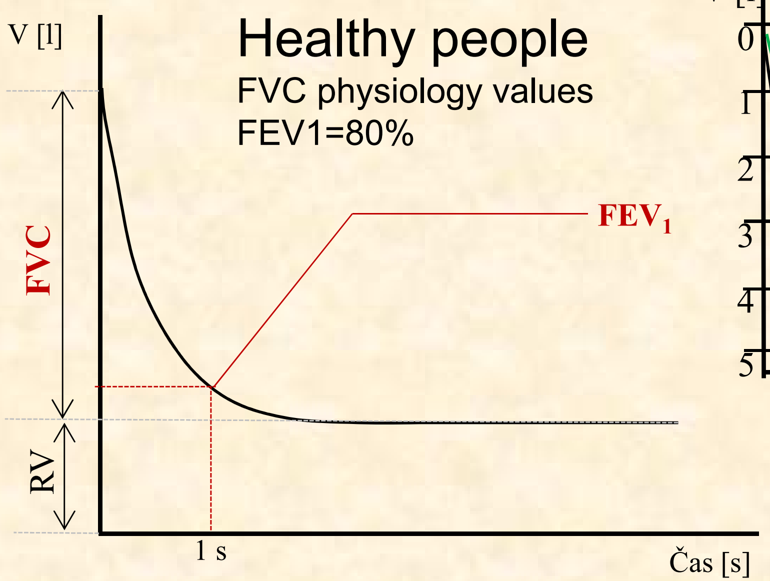
VC **VITAL CAPACITY** $= V_T + IRV + ERV$ ~ 4.7 l

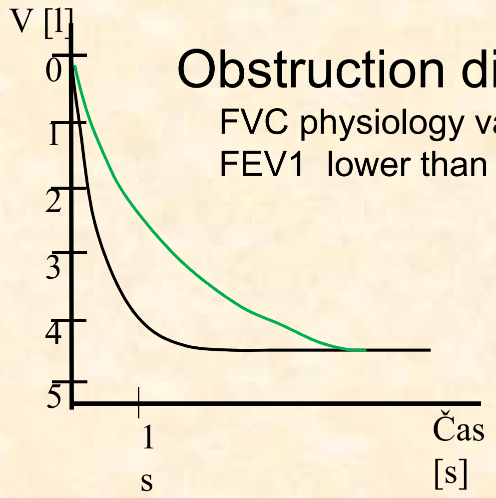
VC - the largest amount of air that can be expired after maximal inspiration

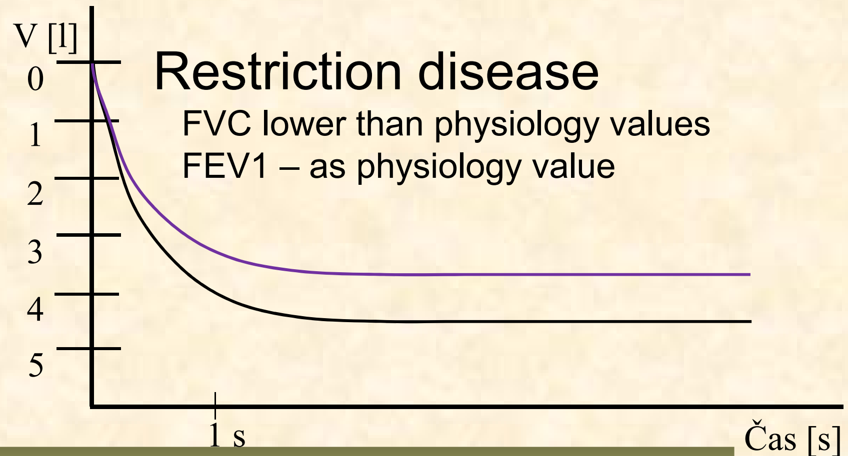
TLC **TOTAL LUNG CAPACITY** $= VC + RV$ ~ 6.0 l

FUNCTIONAL INVESTIGATION OF THE LUNGS

- **TIMED VITAL CAPACITY** (***FEV₁*** - forced expiratory volume per 1 s)





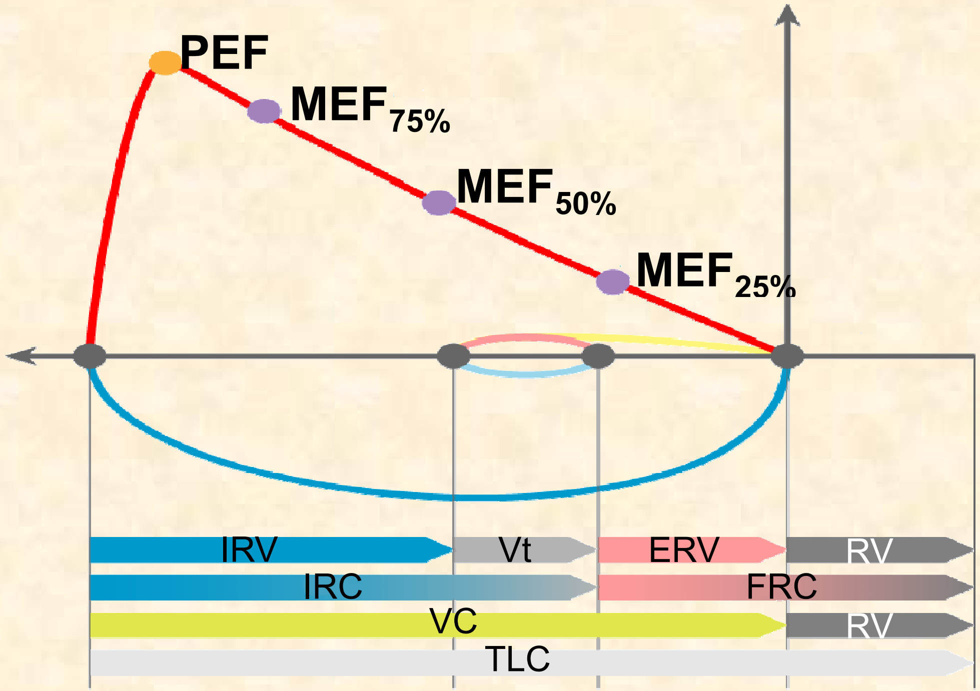


- **PULMONARY MINUTE VENTILATION** ***RMV*** **(respiratory minute volume) at rest** (0.5 l x 12 breathes/min = 6 l/min)
- **MAXIMAL VOLUNTARY VENTILATION (*MVV*)** (125-170 l/min)
- **PEAK EXPIRATORY FLOW RATE (*PEFR*)** (~10 l/s)

Flow – volume curve

Propeller spirometer

- **PEF** – peak expiratory flow
- **MEF** – maximální maximal expiratory flow on the differential levels of FVC - 75 %, 50 % a 25 % FVC



PNEUMOGRAPHY

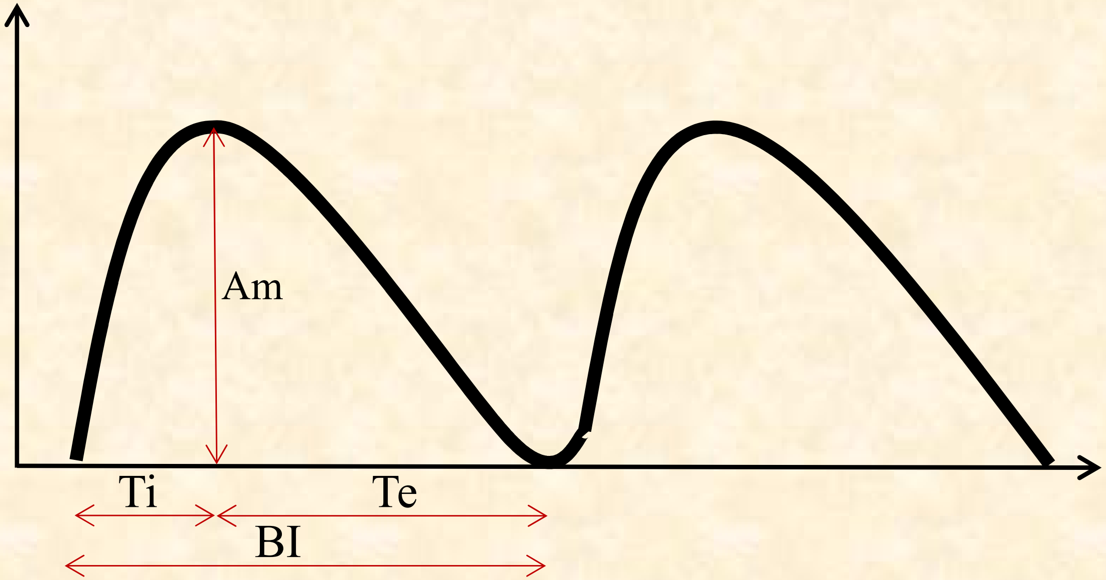
Principle

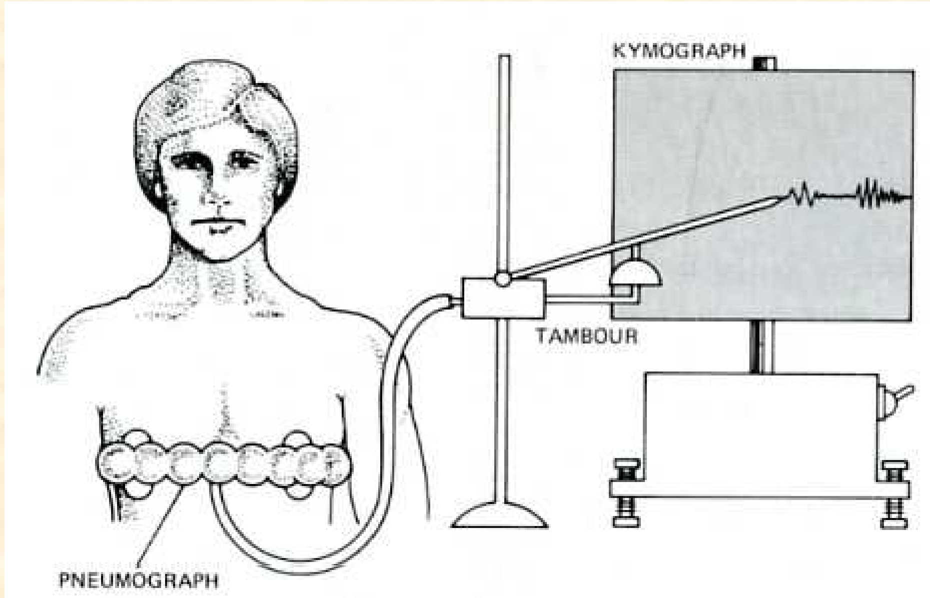
Pneumography – measurement of respiratory movements (via chest or abdomen)

- respiratory belt (piesoelectrical principle – is the ability of crystal to generate of electrical voltage during its deformation)

Record:

- Resting breathing
- Breathing after mild or intensive exercise
- Evaluation of record –Ti, Te, BI a Am

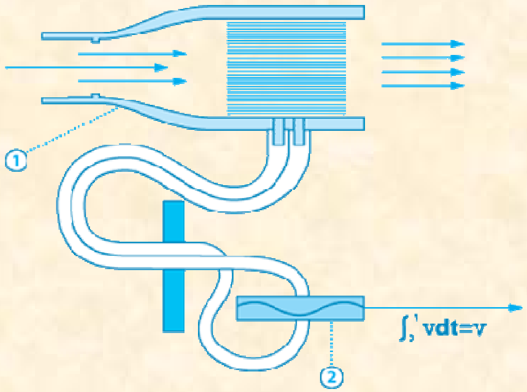


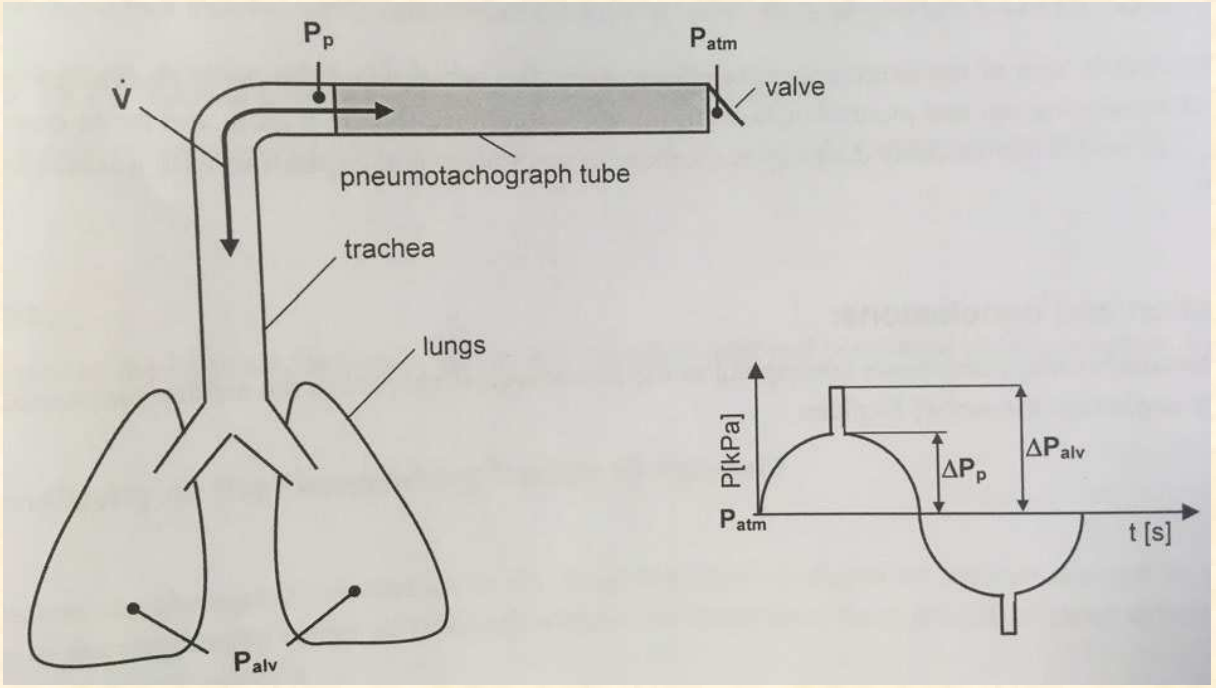


PNEUMOTACHOGRAPHY

Principle

Pneumotachograph - the device consists of tubes of the same diameter arranged in parallel. One of the tubes has branches with tubes near both its ends (oral and external). These are connected to a pressure sensor that allows you **to measure the differences in air pressure at the beginning and end of the pneumotachograph in proportion to the speed of the inhaled or exhaled air.**





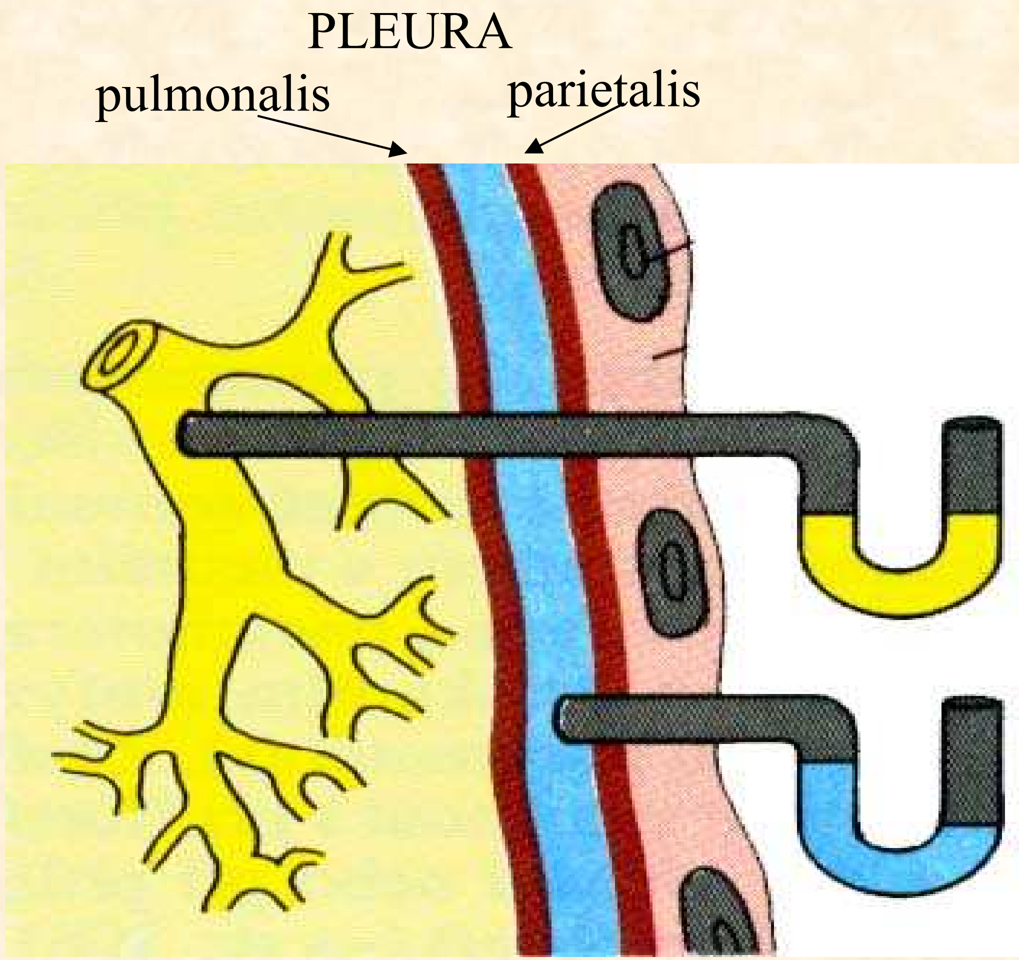
$$\Delta P_p = P_p - P_{atm}$$

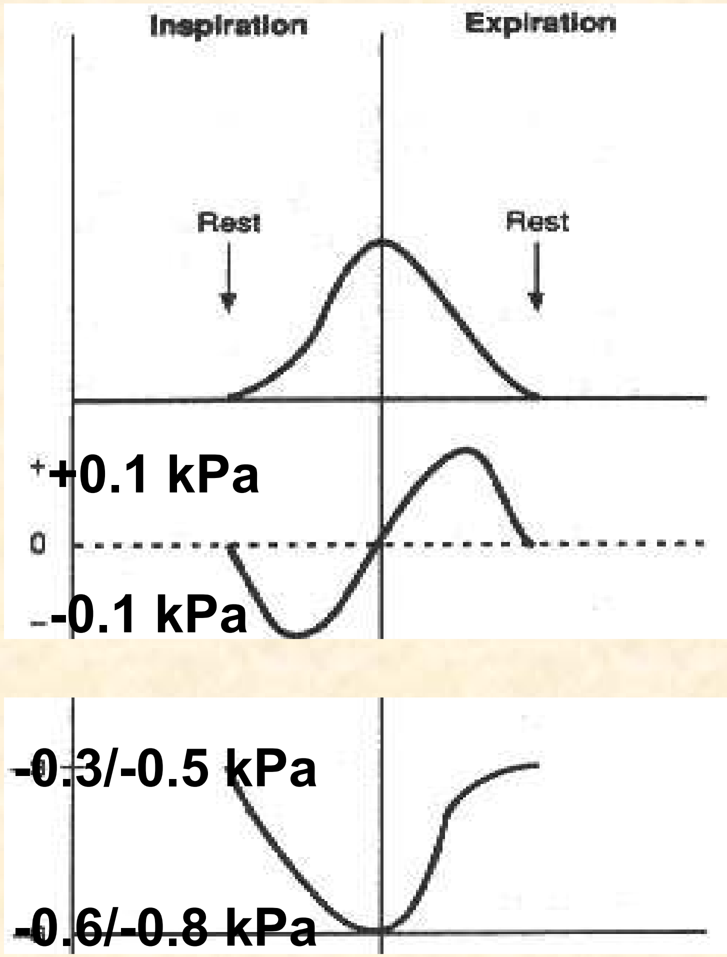
$$\Delta P_{alv} = P_{alv} - P_{atm}$$

$$\frac{P_p - P_{atm}}{R_p} = \dot{V} = \frac{P_{alv} - P_p}{R_d}$$

$$R_d = R_p \cdot \left(\frac{\Delta P_{alv}}{\Delta P_p} - 1 \right)$$

- Mechanics of breathing


PLEURA
pulmonalis
parietalis


Inspiration
Expiration
Rest
Rest
+0.1 kPa
0
-0.1 kPa
-0.3/-0.5 kPa
-0.6/-0.8 kPa

FORCES PARTICIPATING IN RESPIRATION

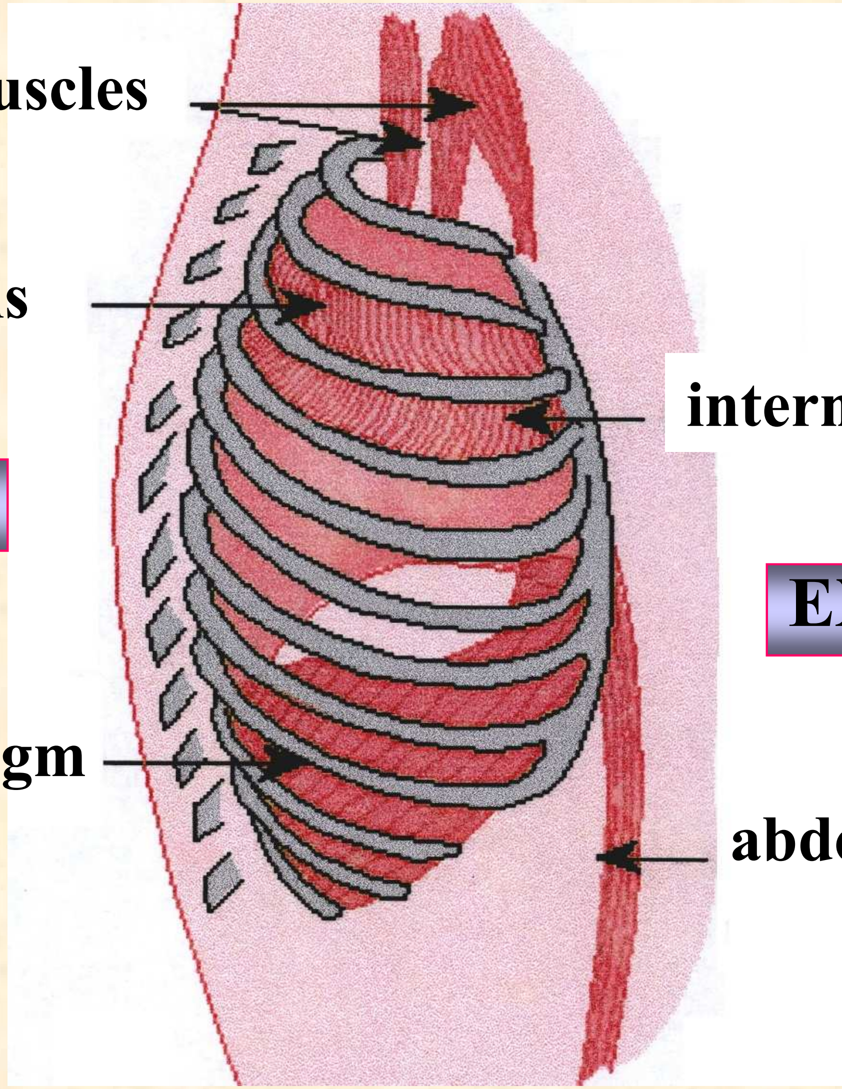
- **ACTIVE FORCES** performed by respiratory muscles
- **PASSIVE FORCES represented by:**
  - **lungs elasticity**
  - **chest elasticity**

QUIET RESPIRATION

INSPIRATION - active forces of inspiratory muscles prevail

EXPIRATION - only passive (elastic) forces are in action

RESPIRATORY MUSCLES



INSPIRATORY muscles

QUIET breathing

- *diaphragm* (> 80 %)
- ***external* intercostals** (< 20 %)

FORCED breathing in addition

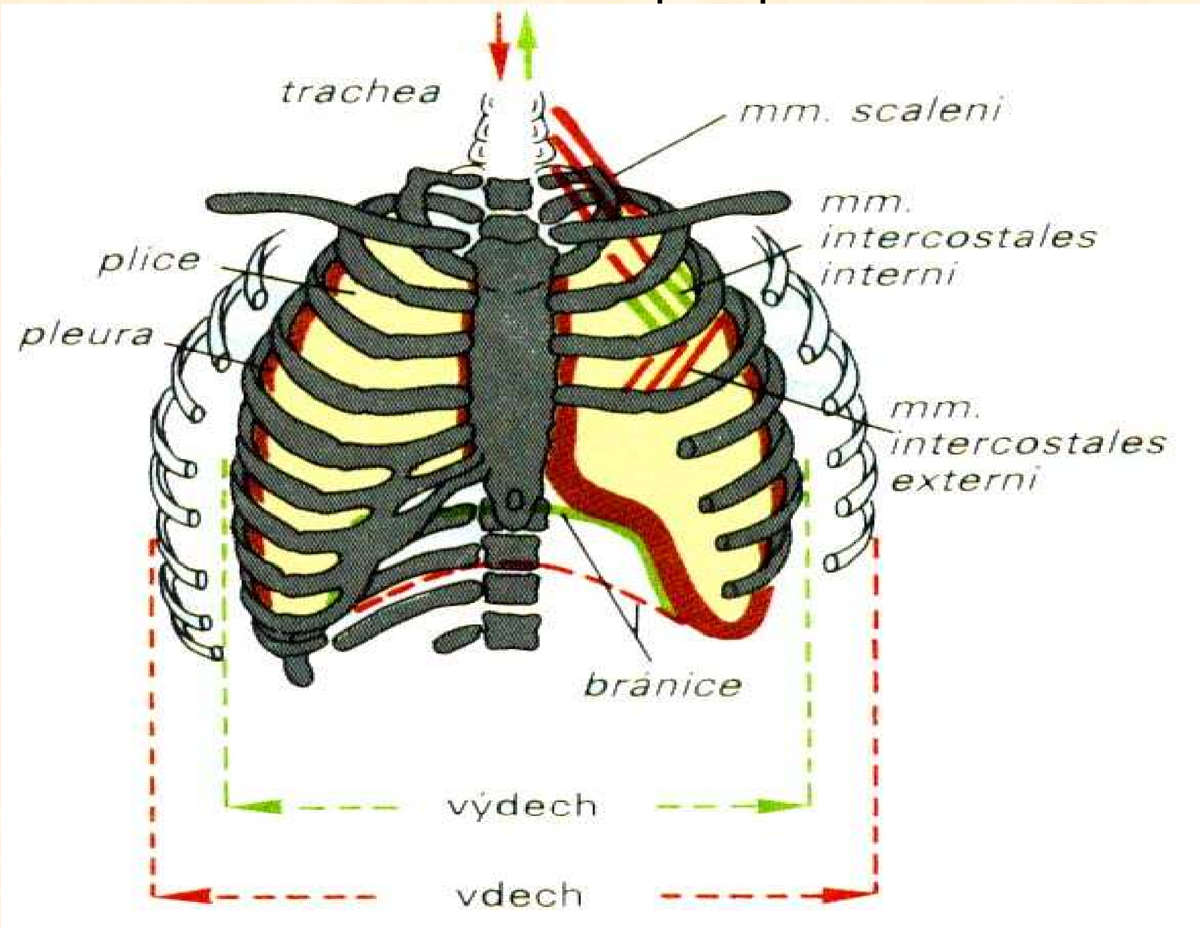
- ***accessory* inspiratory muscles** (mm. scalene)

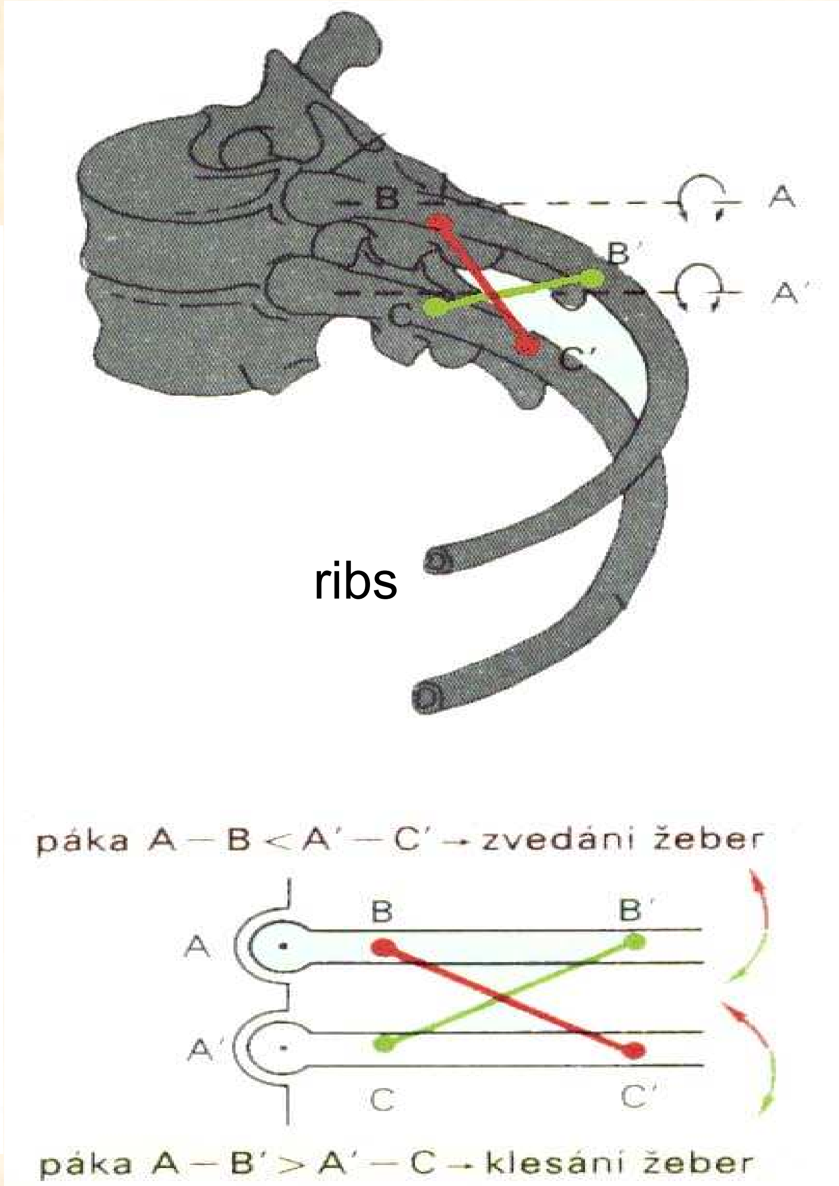
EXPIRATORY muscles

Only at FORCED breathing

- ***internal* intercostals**
- **muscles of the anterior *abdominal* wall** (abdominal recti, …)

Bucket-handle and water-pump handle effects





ribs

COMPOSITION OF DRY ATMOSPHERIC AIR

O_2	20.98 %	$F_{O2} \cong 0.21$
N_2	78.06 %	$F_{N2} \cong 0.78$
CO_2	0.04 %	$F_{CO2} = 0.0004$

Other constituents

BAROMETRIC (ATMOSPHERIC) PRESSURE AT SEA LEVEL

1 atmosphere = 760 mm Hg

PARTIAL PRESSURES OF GASSES IN DRY AIR AT SEA LEVEL

P_{O2} = 760 x 0.21 = ~160 mm Hg

P_{N2} = 760 x 0.78 = ~593 mm Hg

P_{CO2} = 760 x 0.0004 = ~0.3 mm Hg

1 *kPa* = 7.5 *mm Hg (torr)*

COMPOSITION OF ALVEOLAR AIR

partial pressures in mm Hg

INSPIRED AIR

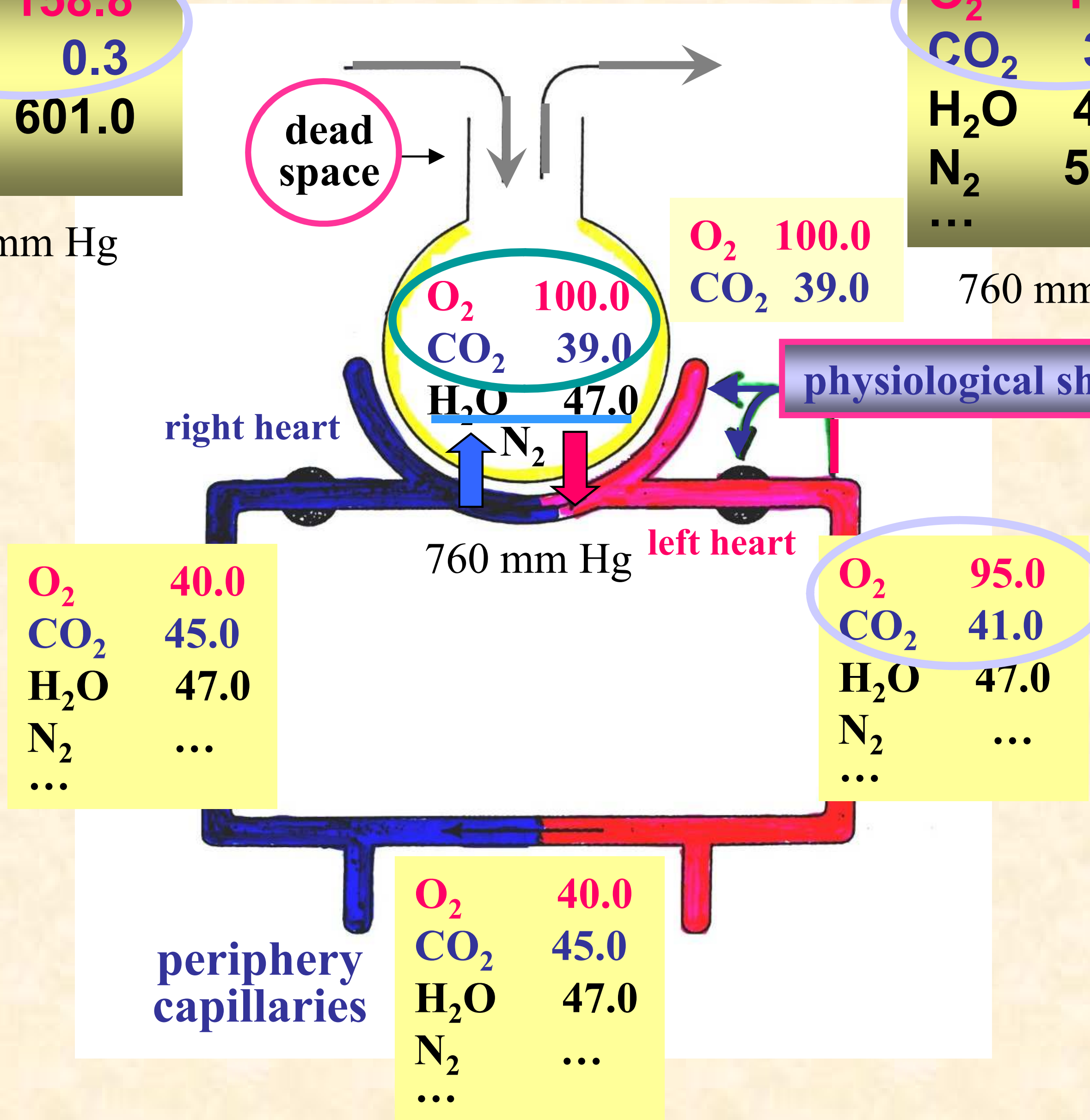
O_2	158.8
CO_2	0.3
N_2	601.0
…	

760 mm Hg

EXPIRED AIR

O_2	115.0
CO_2	33.0
H_2O	47.0
N_2	564.0
…	

760 mm Hg



veins

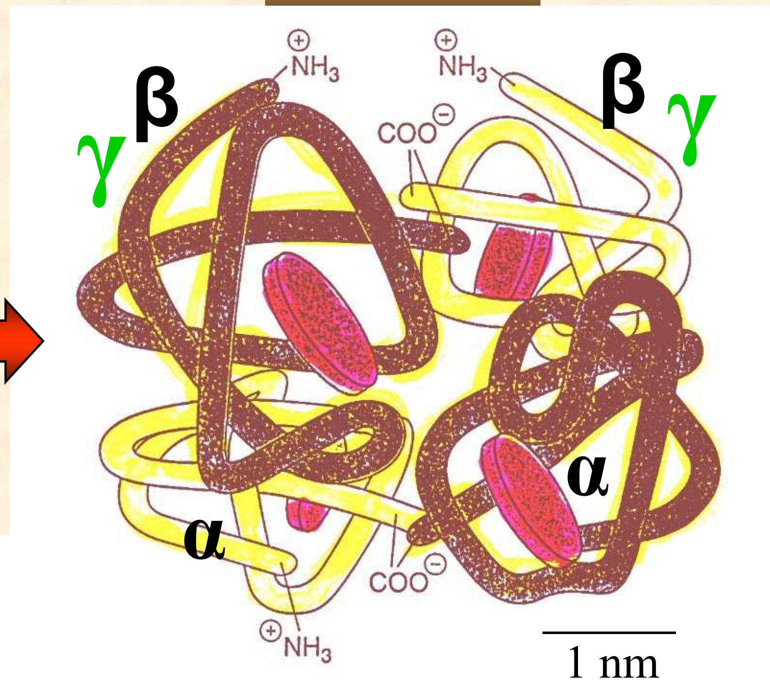
arteries

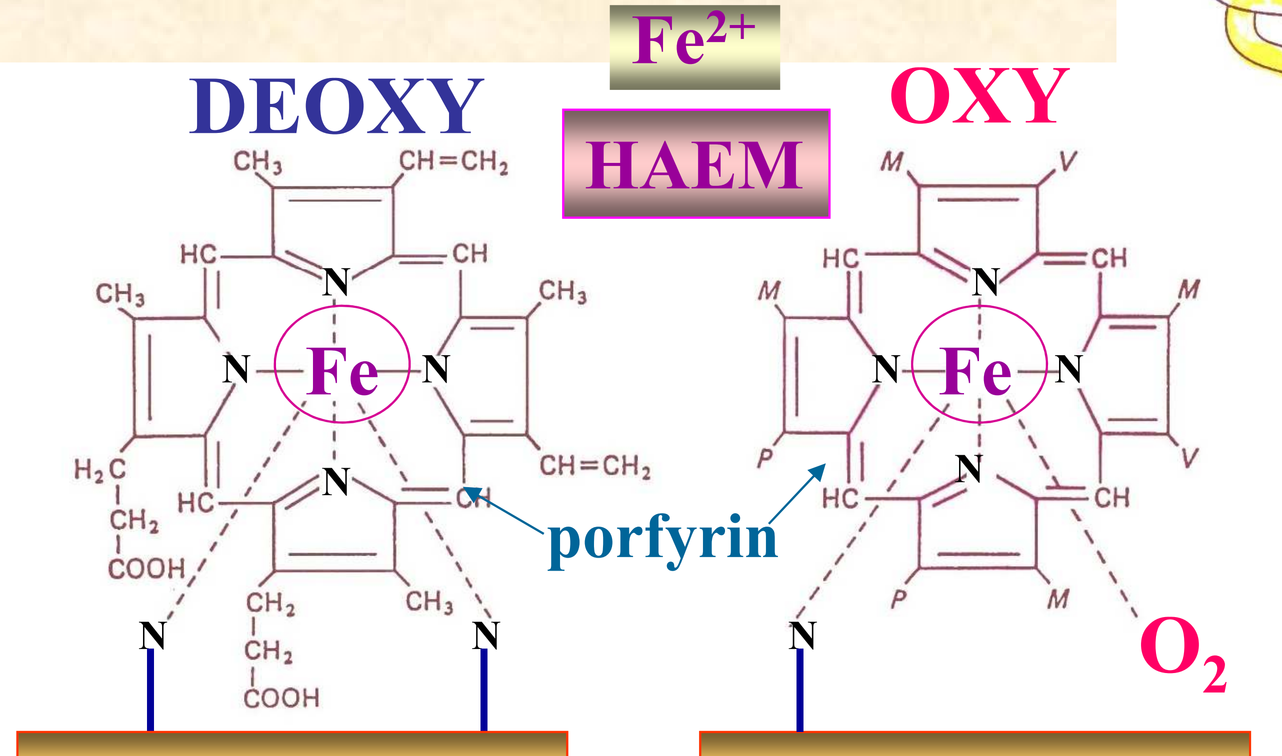
HAEMOGLOBIN

$Hb_4 + 4\ O_2 \leftrightarrow Hb_4O_8$

oxygenation

tetramer





polypeptide chain

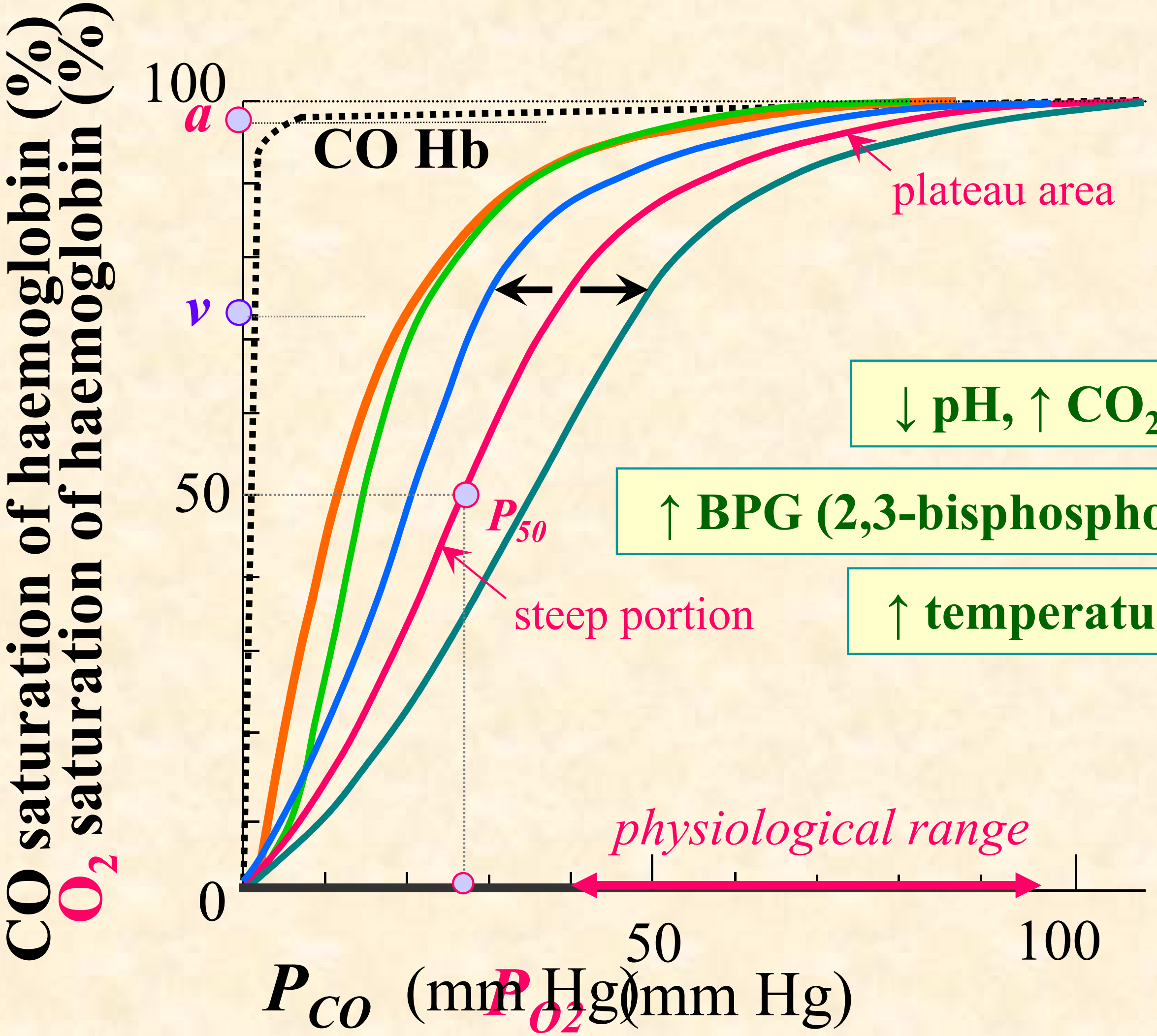
polypeptide chain

fetal Hb

Fe^{3+} (methaemoglobin)

oxidation

O_2–HAEMOGLOBIN DISSOCIATION CURVE



BOHR´S EFFECT
(↓ pH, ↑CO_2)

↓ pH, ↑ CO_2

↑ BPG (2,3-bisphosphoglycerate)

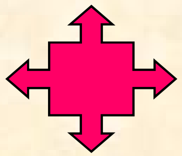
↑ temperature

fetal Hb

myoglobin

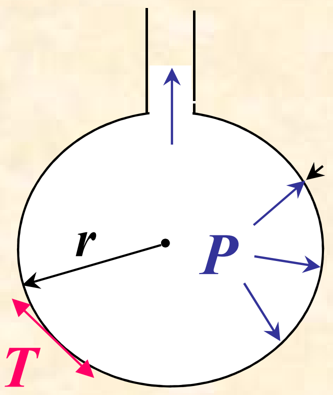
methaemoglobin

physically dissolved O_2 (1.4%)



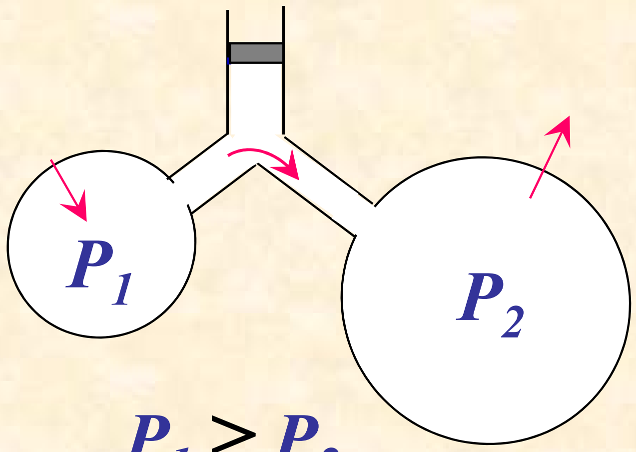
LAW OF LAPLACE

spherical structures



$$P = \frac{2T}{r}$$

?



$P_1 > P_2$

P pressure

r radius

T surface tension

PATHOLOGY

- COLLAPSE OF ALVEOLI - ATELECTASIS
- EXPANSION OF ALVEOLI

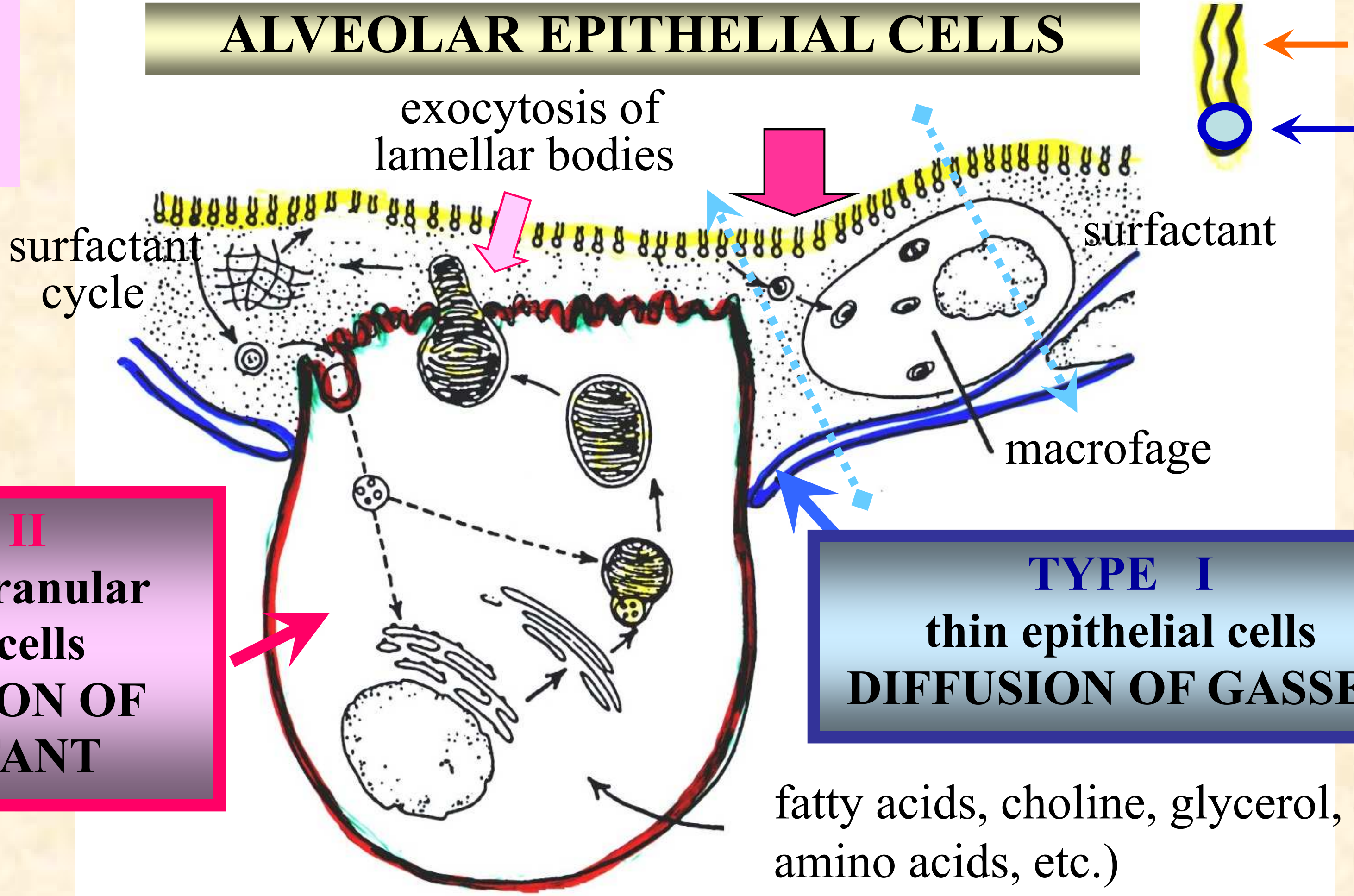
SURFACTANT

SURFACE TENSION LOWERING AGENT

EFFECT MAINLY IN THE EXPIRED POSITION

PHOSPHOLIPID
dipalmitoyl
fosfatidyl cholin

ALVEOLAR EPITHELIAL CELLS



TYPE II
specialized granular epithelial cells
PRODUCTION OF SURFACTANT

TYPE I
thin epithelial cells
DIFFUSION OF GASSES

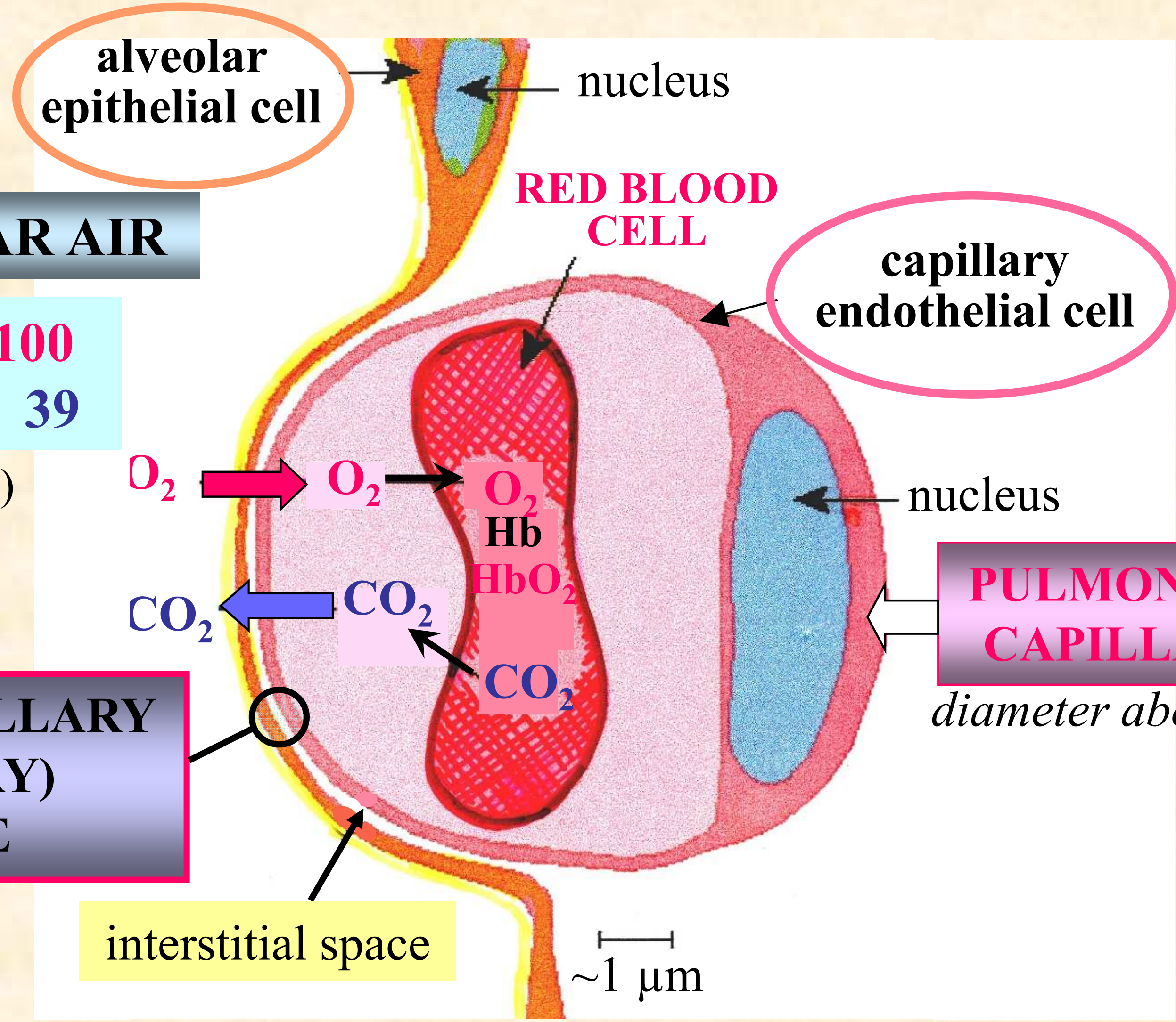
ALVEOLAR-CAPILLARY (RESPIRATORY) MEMBRANE

DIFFUSION OF GASES

ALVEOLAR AIR

P_{O2} = 100
P_{CO2} = 39

(mm Hg)



ALVEOLAR-CAPILLARY (RESPIRATORY) MEMBRANE

PULMONARY CAPILLARY

diameter about 5 µm

0.75 s

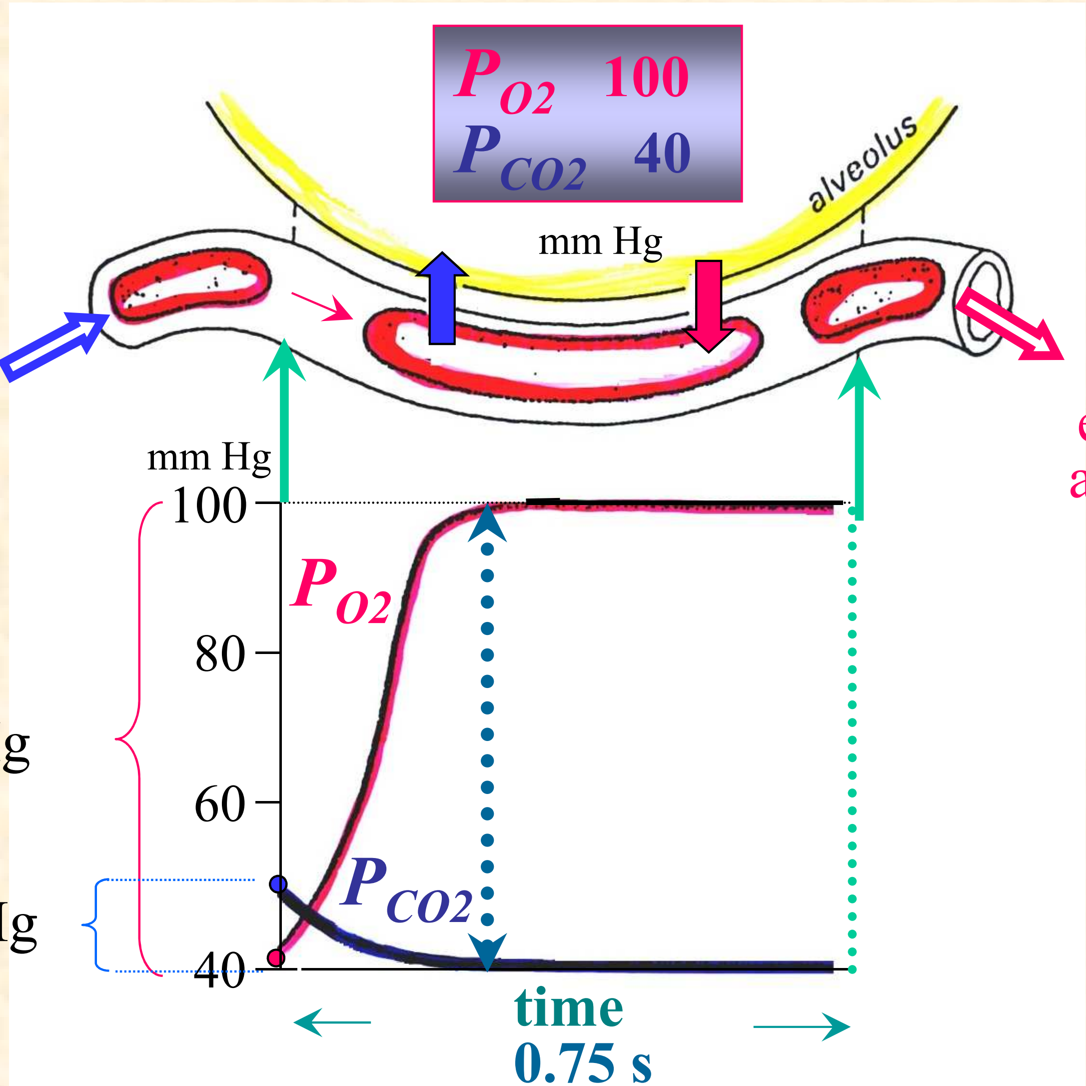
time interval of erythrocyte contact with respiratory membrane at rest

TIME COURSE OF CAPILLARY P_{O2} AND P_{CO2} DURING GRADUAL EQUILIBRATION WITH ALVEOLAR AIR

venous blood

P_{O2} 40
P_{CO2} 46

mm Hg



P_{O2} 100
P_{CO2} 40

mm Hg

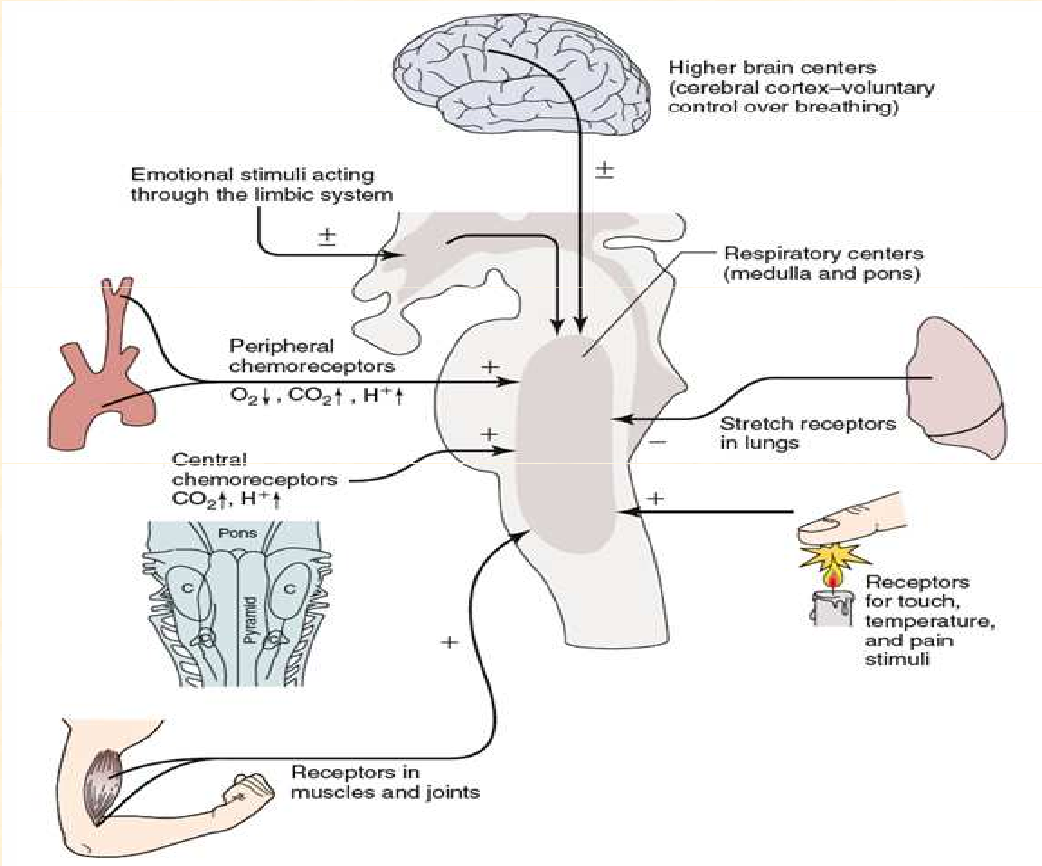
equalization with alveolar pressures

$\Delta P_{O2} \cong 60$ mm Hg

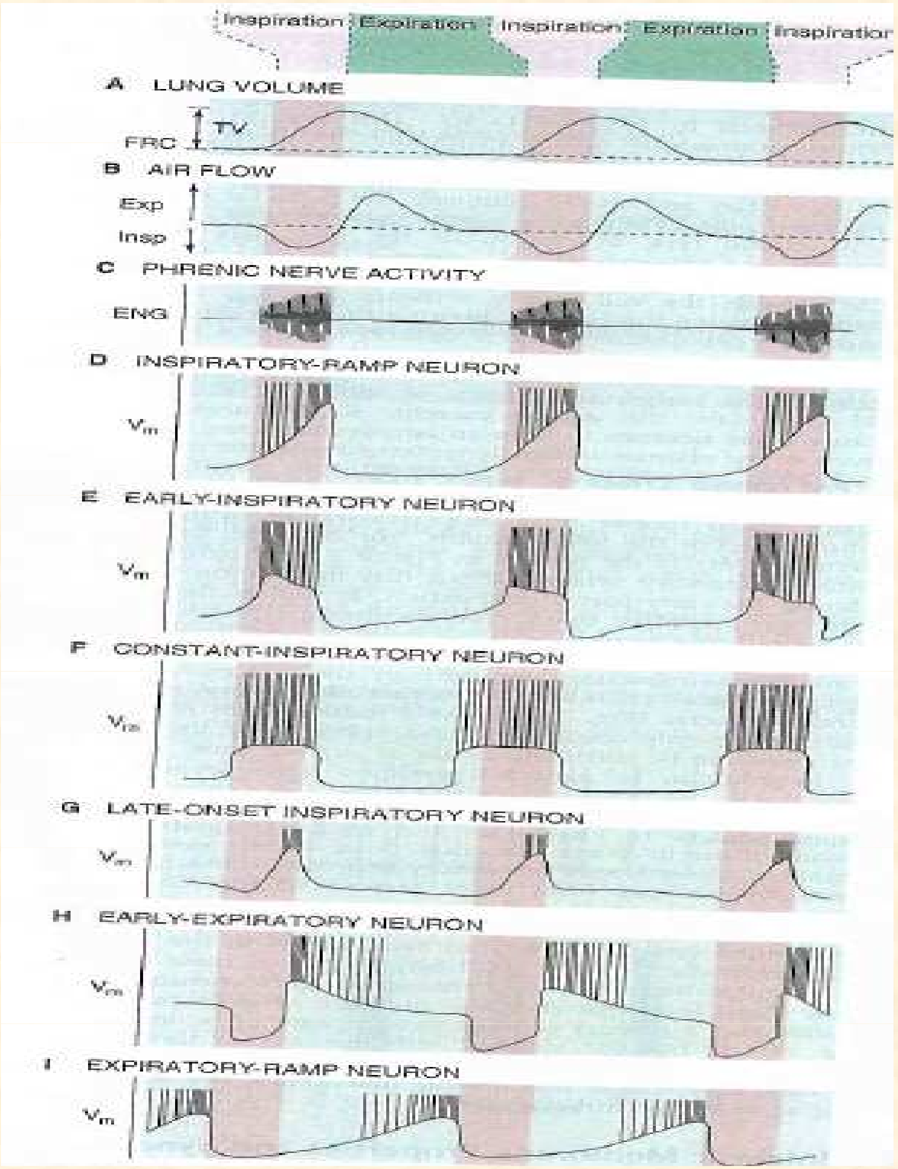
$\Delta P_{CO2} \cong 6$ mm Hg

time interval of contact of erythrocyte with respiratory membrane at rest

Control of ventilation



https://sleep.sharepoint.com/siteimages/Chapter%203.png


Inspiration
Expiration
Inspiration
Expiration
Inspiration
A LUNG VOLUME
TV
FRC
B AIR FLOW
Exp
Insp
C PHRENIC NERVE ACTIVITY
ENG
D INSPIRATORY-RAMP NEURON
Vm
E EARLY-INSPIRATORY NEURON
Vm
F CONSTANT-INSPIRATORY NEURON
Vm
G LATE-ONSET INSPIRATORY NEURON
Vm
H EARLY-EXPIRATORY NEURON
Vm
I EXPIRATORY-RAMP NEURON
Vm

- **Breathing is an automatic process that takes place unconsciously. Automaticity of breathing comes from regular (rhythmic) activity of groups of neurons anatomically localized in the medulla and its vicinity.**

- They can be divided into three **main groups:**

  - *dorsal respiratory group* – placed bilaterally on the dorsal side of the medulla oblongata, only inspiratory neurons, sending axons to motoneurons of inspiratory muscles (diaphragm, external intercostal muscles; their activation=inspiration, their relaxation=expiration; participates on inspiration at rest and forced inspiration

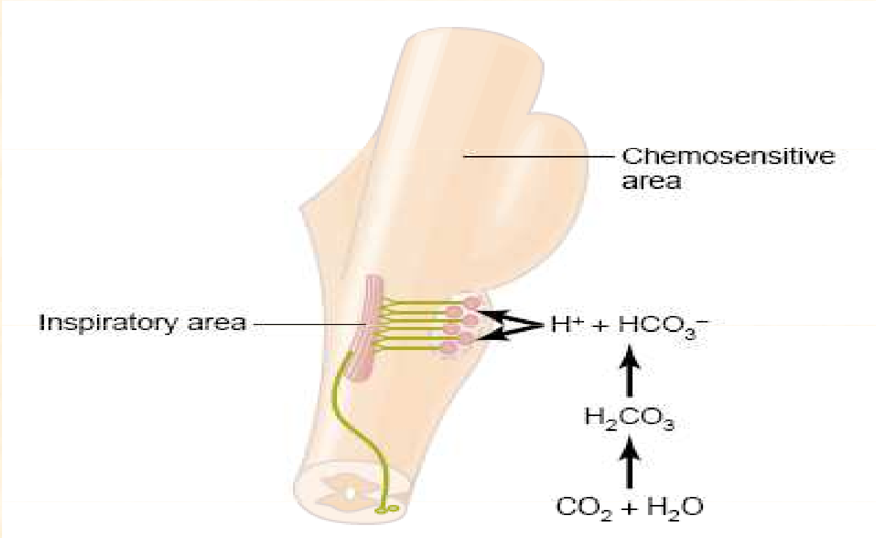
  - *ventral respiratory group* - located on the ventrolateral part of the medulla oblongata, the upper part: neurons whose axons of motor neurons activate the main and auxiliary inspiratory muscles; the lower part: expiratory neurons which innervate expiratory muscles (internal intercostal muscles). Neurons in this group operate only during forced inspiration and forced expiration.

  - *Pontine respiratory group* *- pneumotaxic center -* dorsally placed on top of the pont, contributes to the frequency and depth of breathing; affects the activity of respiratory neurons in the medulla oblongata.

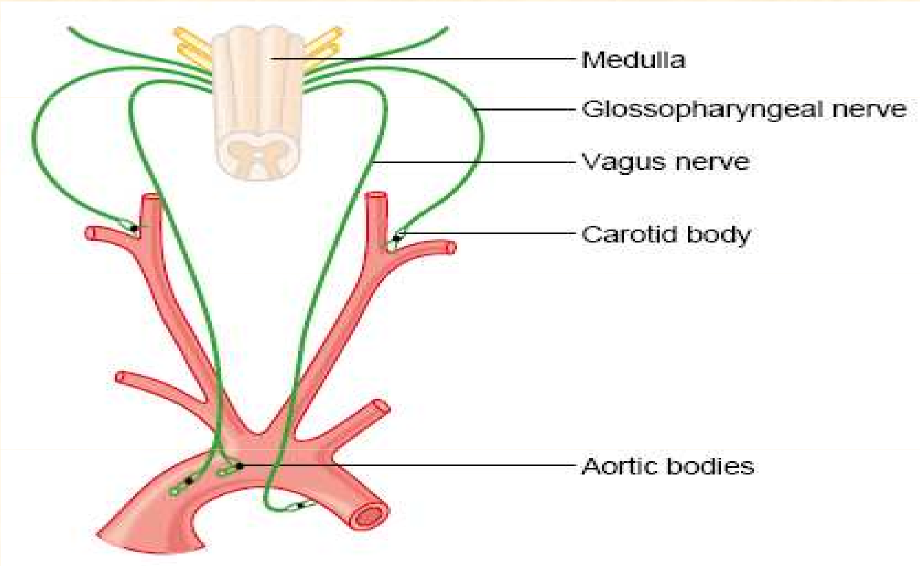
Chemical factors affecting the respiratory center:

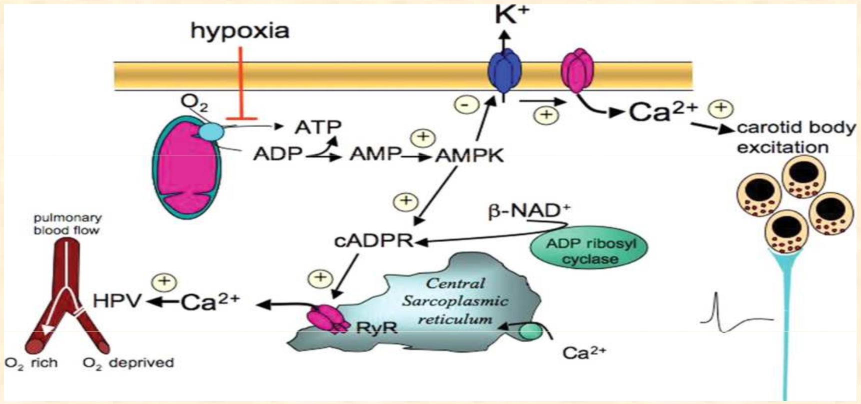
Central chemoreceptors

- on the front side of the medulla
- sensitive only to increase of arterial pCO_2 (by increasing H^+)



- Notice:
- central chemoreceptor are stimulated by other types of acidosis (lactate acidosis, ketoacidosis)





Peripheral chemoreceptors

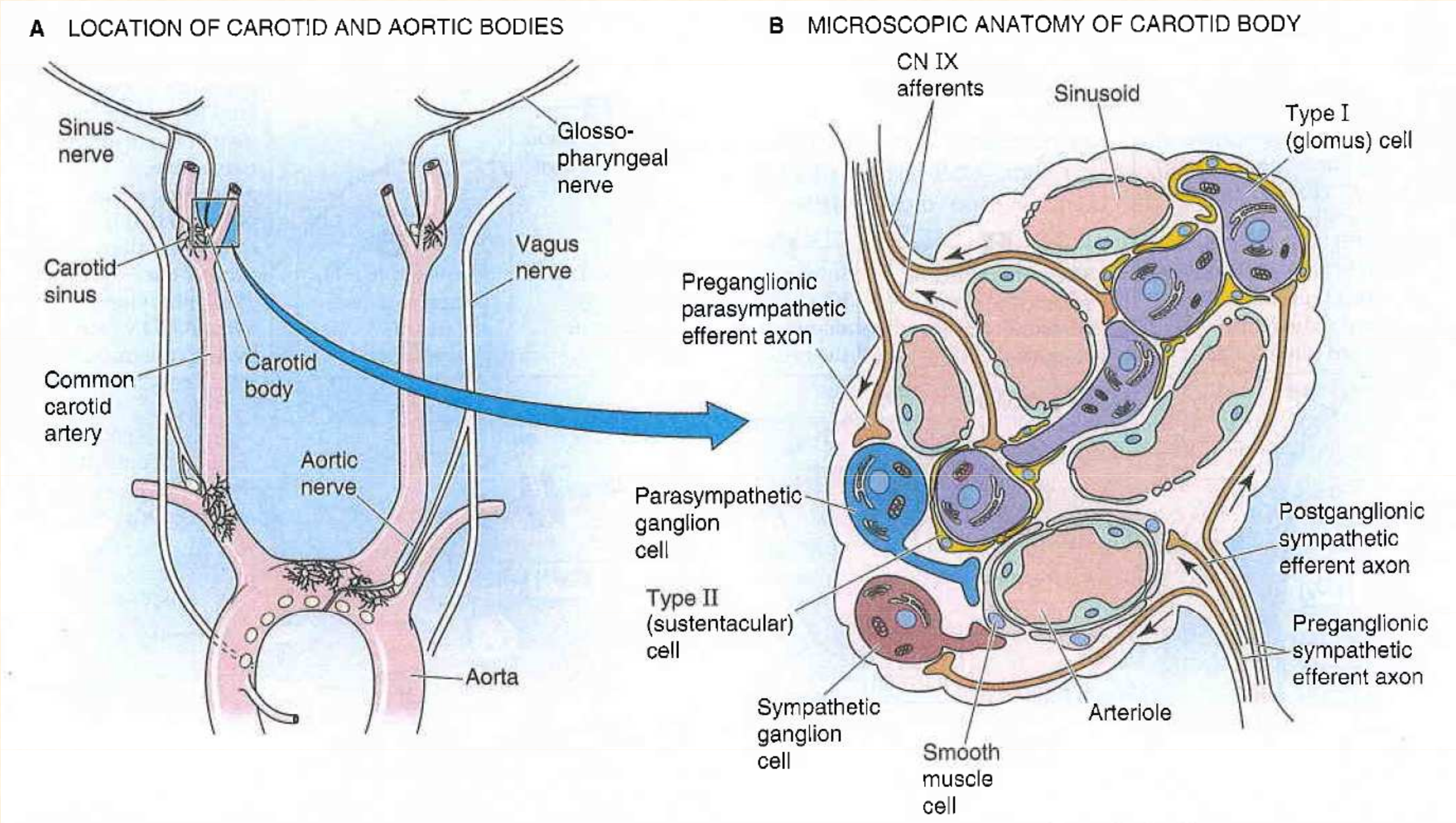
– located in the aortic and carotid bodies

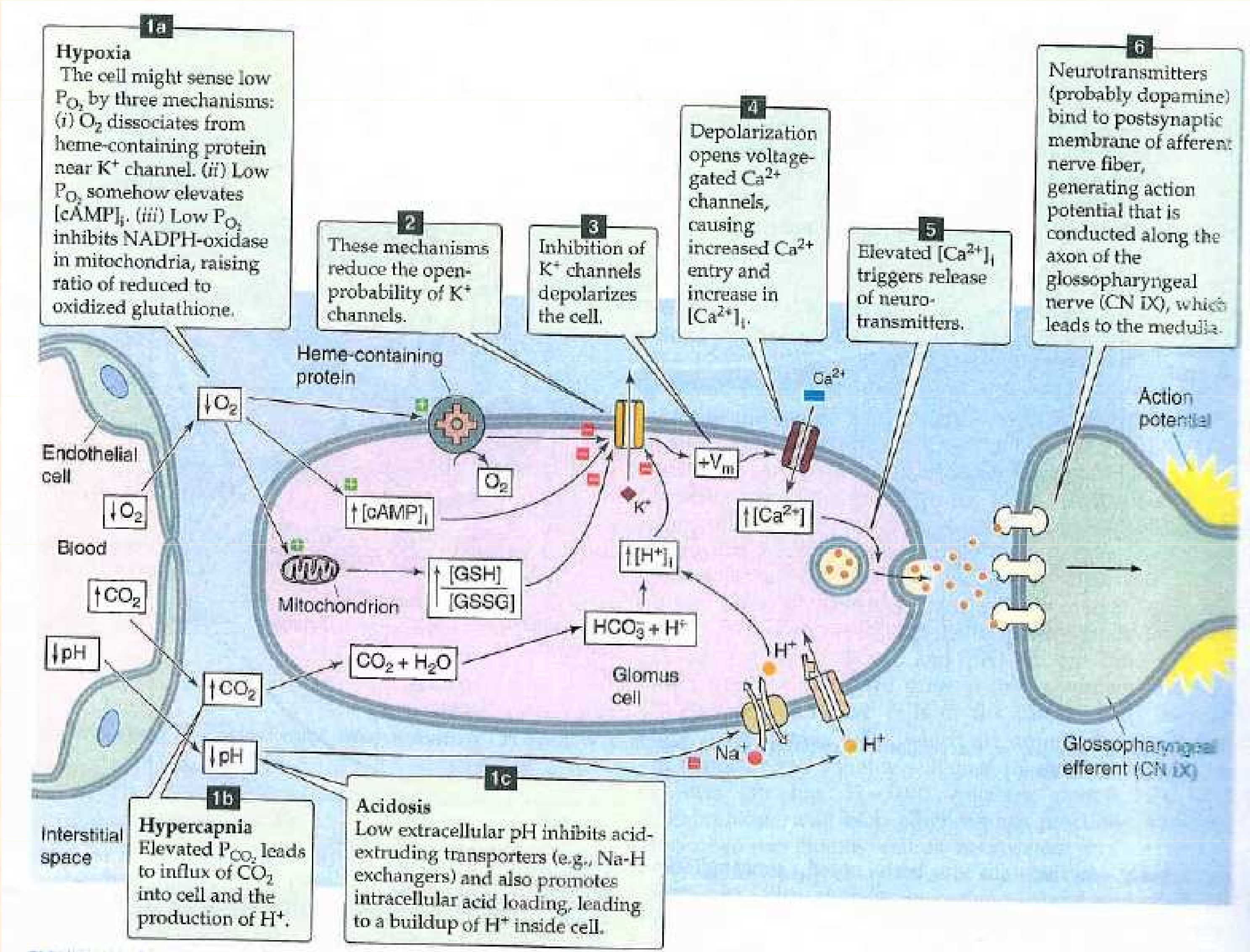
-primarily sensitive to decrease in arterial pO_2, particularly to decrease of O_2 under 10-13 kPa in the arterial blood.

They convey their sensory information to the medulla via the vagus nerve and glossopharyngeal nerve.

<u>Mechanism of action: D</u>ecreased ATP production in mitochondria leads to depolarization of receptors membrane and to excitation of chemoreceptor

http://www.medicine.mcgill.ca/physio/resp-web/sect8.htm,


A LOCATION OF CAROTID AND AORTIC BODIES
Sinus nerve
Glosso-pharyngeal nerve
Carotid sinus
Vagus nerve
Common carotid artery
Carotid body
Aortic nerve
Aorta
B MICROSCOPIC ANATOMY OF CAROTID BODY
CN IX afferents
Sinusoid
Type I (glomus) cell
Preganglionic parasympathetic efferent axon
Parasympathetic ganglion cell
Type II (sustentacular) cell
Postganglionic sympathetic efferent axon
Preganglionic sympathetic efferent axon
Sympathetic ganglion cell
Smooth muscle cell
Arteriole


1a
Hypoxia
The cell might sense low P_{O_2} by three mechanisms: (i) O_2 dissociates from heme-containing protein near K^+ channel. (ii) Low P_{O_2} somehow elevates $[cAMP]_i$. (iii) Low P_{O_2} inhibits NADPH-oxidase in mitochondria, raising ratio of reduced to oxidized glutathione.
2
These mechanisms reduce the open-probability of K^+ channels.
3
Inhibition of K^+ channels depolarizes the cell.
4
Depolarization opens voltage-gated Ca^{2+} channels, causing increased Ca^{2+} entry and increase in $[Ca^{2+}]_i$.
5
Elevated $[Ca^{2+}]_i$ triggers release of neuro-transmitters.
6
Neurotransmitters (probably dopamine) bind to postsynaptic membrane of afferent nerve fiber, generating action potential that is conducted along the axon of the glossopharyngeal nerve (CN IX), which leads to the medulla.
Heme-containing protein
Endothelial cell
Blood
Mitochondrion
Glomus cell
Interstitial space
Action potential
Glossopharyngeal efferent (CN IX)
$\downarrow O_2$
O_2
$\uparrow [cAMP]_i$
$\uparrow \frac{[GSH]}{[GSSG]}$
K^+
$+V_m$
Ca^{2+}
$\uparrow [Ca^{2+}]$
$\uparrow [H^+]_i$
$HCO_3^- + H^+$
$CO_2 + H_2O$
$\uparrow CO_2$
$\downarrow pH$
H^+
Na^+
1b
Hypercapnia
Elevated P_{CO_2} leads to influx of CO_2 into cell and the production of H^+.
1c
Acidosis
Low extracellular pH inhibits acid-extruding transporters (e.g., Na-H exchangers) and also promotes intracellular acid loading, leading to a buildup of H^+ inside cell.

Modulation of respiratory output

Major parameters for feedback control – classical gases:pO2, pCO2, pH

In additin to these, the respiratory system receives input from two other major sources:

1. **variety of stretch and chemical/irritant receptors** that monitor the size of airways and the presence of noxious agentsreceptors in respiratory system
2. **Higher CNS centers** that modulate respiratory activity for the sake of nonrespiratory activities

Irritants receptors on mucose of respiratory system – rapidly adapting
Stimulus: agens - chemical substances (histamin, serotonin, prostaglandins, ammonia, cigarette smoke).
Respons: increase mucus secretion, constriction of larynx and brochus

C-fibre receptors (juxtacapillary=J receptors)– free nerve ending of n.vagus (unmyelinated axon) in intersticium of bronchus and alveolus;
Stimulus: Mechanical irritans (pulmonary hypertension, pulmonary oedema)+chemical
Response: hypopnoe, rapid shallow breathing, bronchoconstriction, cough

Stretch receptors slowly adapting (mechanoreceptors in tracheobronchial tree that detect the changes in lung volume by sensing the stretch receptors of the airway wall), inform to brain about the lung volume to optimize respiratory; its irritants triggered decrese activity of respiratory centre – **Hering-Breuer´s reflexes**. (protecting the lungs from overinflation/deflation)

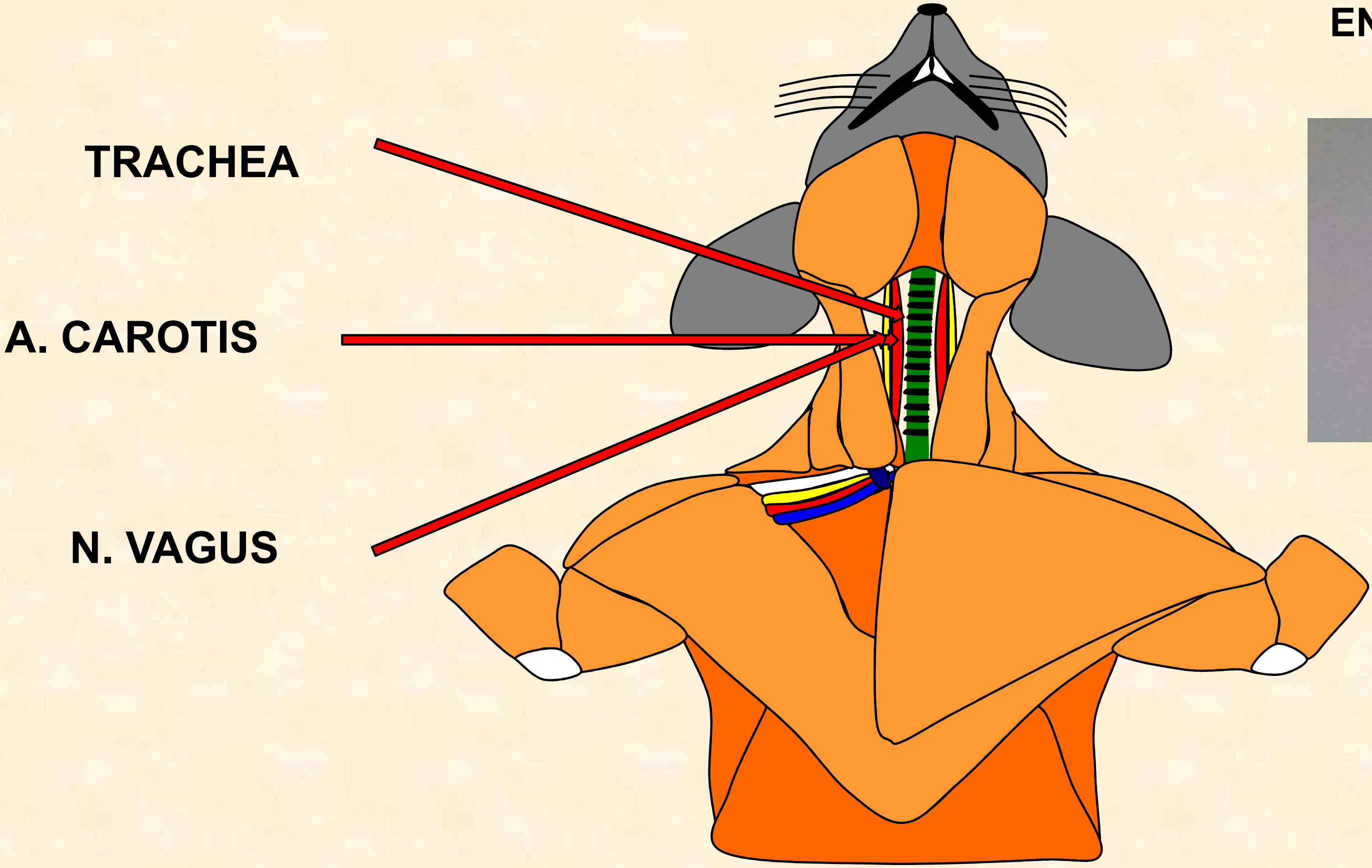
Baroreceptors – suppresses activity of respiratory centre

Irritants of **proprioreceptors of muscles, tendons** during active and pasive movements of limbs
Influenced activity of respiratory neurons (increase minute ventilation during work load)

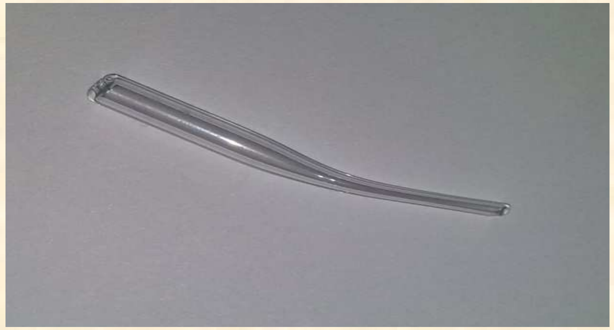
Limbic system, hypothalamus – strong pain, emotion
Tractus corticospinalis =cortex – activated RC during work load

temperature

- Hering – Breuer ´s reflex in animal experimentH

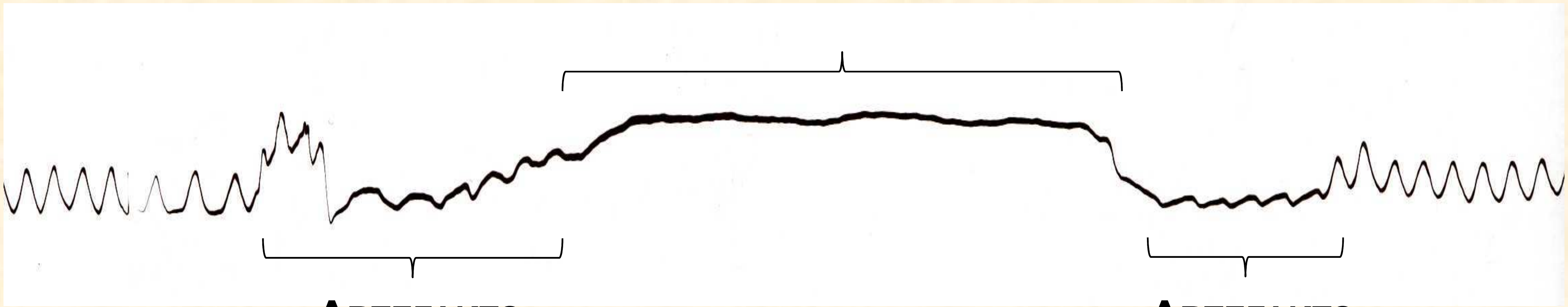


ENDOTRACHEAL CANNULA



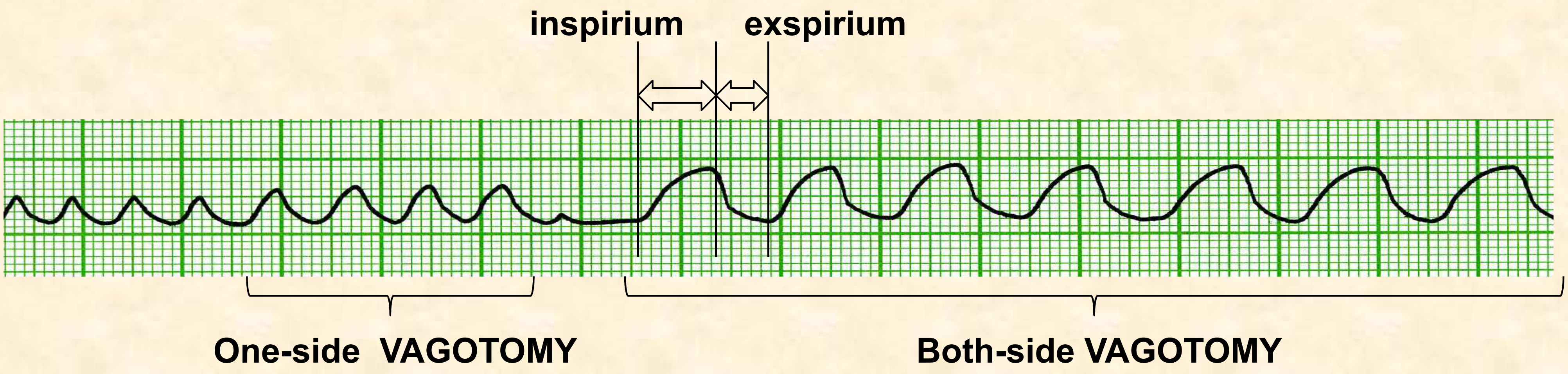
HERING-BREUER REFLEX

REFLEX STOP BREATHING



ARTEFAKTS ARTEFAKTS

Changes of breathing after VAGOTOMY



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.

<u>THANK YOU FOR YOUR ATTENTION</u>