RESPIRATORY FUNCTIONS

OTHER FUNCTIONS OF RESPIRATORY SYSTEM

PULMONARY DEFENCE FUNCTIONS (e.g. mucociliary clearance, function of pulmonary macrophages, …)

METABOLIC AND **ENDOCRINE FUNCTIONS** (e.g. production of surfactant, conversion of angiotensin I to angiotensin II, …)

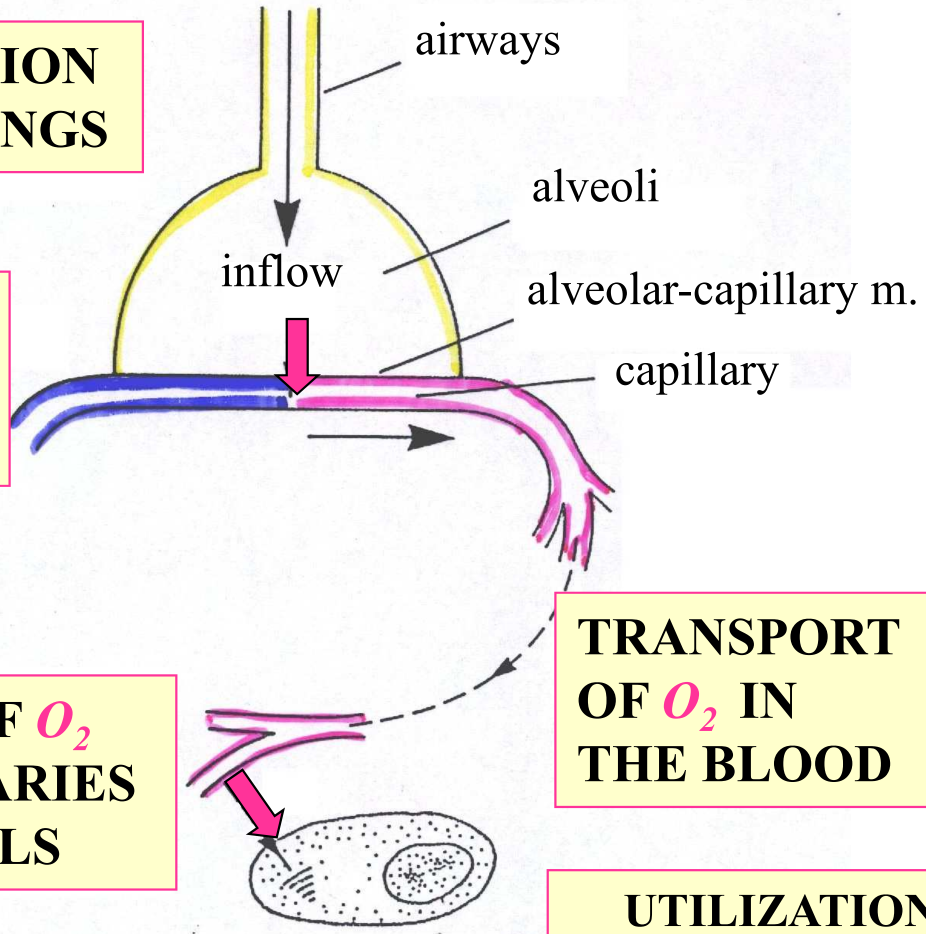
RESPIRATORY SYSTEM

- **AIR PASSAGES (CONVECTION)**
- **LUNGS AS GAS EXCHANGING ORGAN**
- **PUMP THAT ENABLES VENTILATION OF THE LUNGS (*chest wall with respiratory muscles*)**
- **TRANSPORT OF O_2 AND CO_2 IN THE BLOOD**
- **NERVOUS SYSTEM CONTROLLING THE RESPIRATORY MUSCLES (*areas in CNS, efferent motor neurons to respiratory muscles, and afferent neurons from various receptors*)**

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 CAPILLARIES TO THE CELLS

UTILIZATION OF O_2 BY MITOCHONDRIA
via oxidative phosphorylation

AT REST

O_2 INTAKE ~300 ml / min

CO_2 OUTPUT ~250 ml / min

RESPIRATORY QUOTIENT

$$\frac{250}{300}$$

INTERNAL RESPIRATION

PLAN

I BASIC PHYSICAL FEATURES OF GASES

II AIR PASSAGES

III MEASURABLE PARAMETERS

- **DEAD SPACE**
- **LUNG VOLUMES**
- **FUNCTIONAL INVESTIGATIONS**
- **CHARACTERISTIC PRESSURES**

IV COMPOSITION OF ALVEOLAR AIR

V ALVEOLAR-CAPILLARY MEMBRANE

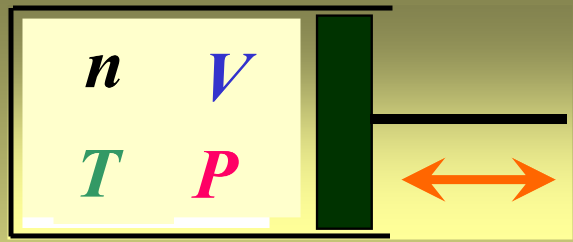
GENERAL CHARACTERISTICS OF GASES

- **RAPID PRESSURE EQUILIBRATION in the closed volume**
- **MOVEMENT proceeds from the areas of high pressure to the areas of low pressure -DOWN THE PRESSURE GRADIENT**
- **Diffusion of a gas ACROSS a BARRIER (between two areas) depends on the PROPERTY of the barrier**

IN A MIXTURE OF GASES

- **RATE of DIFFUSION of GAS COMPONENTS depends on the INDIVIDUAL PARTIAL PRESSURE GRADIENTS**
- **In a mixture of gases EQUILIBRATED WITH A LIQUID each component DISSOLVES independently in proportion to its:**
  - **PARTIAL PRESSURE in the gaseous phase**
  - **SOLUBILITY in the fluid**

RELATIONS BETWEEN MEASURED QUANTITIES



IDEAL GAS EQUATION

$$P = \frac{nRT}{V}$$

P - **pressure** [Pa] [mm Hg]

n - **amount of substance** [mol]

V - **volume** [m^3] [l]

T - **absolute temperature** [K]

R - **universal gas constant** [J/K.mol]

$$PV = nRT$$

If *n* and *T* do not change then

$$PV = \text{constant}$$

physical unit of work and energy **[J]**

PARTIAL PRESSURES IN A MIXTURE OF GASES

Dalton´s law - law of partial pressures

Mixture of two gas components (in a given volume)

n_1, n_2 - amounts of gas substances $\Rightarrow n_{tot} = n_1 + n_2$

$$F_1 = \frac{n_1}{n_{tot}}, \qquad F_2 = \frac{n_2}{n_{tot}}$$

$$F_1 + F_2 = 1$$

According to Dalton´s law:

PARTIAL PRESSURES can be expressed in terms of fractions:

$$P_1 = F_1 P_{tot} \qquad P_2 = F_2 P_{tot}$$

$$P_1 + P_2 = P_{tot}$$

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 GASES 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)*

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AIR PASSAGES

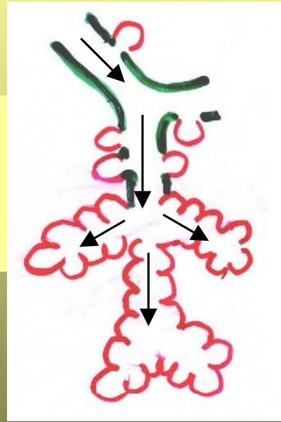
ANATOMICAL DEAD SPACE – CONDUCTING ZONE

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

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

TRANSITIONAL ZONE

- RESPIRATORY BRONCHIOLES
- ALVEOLAR DUCTS

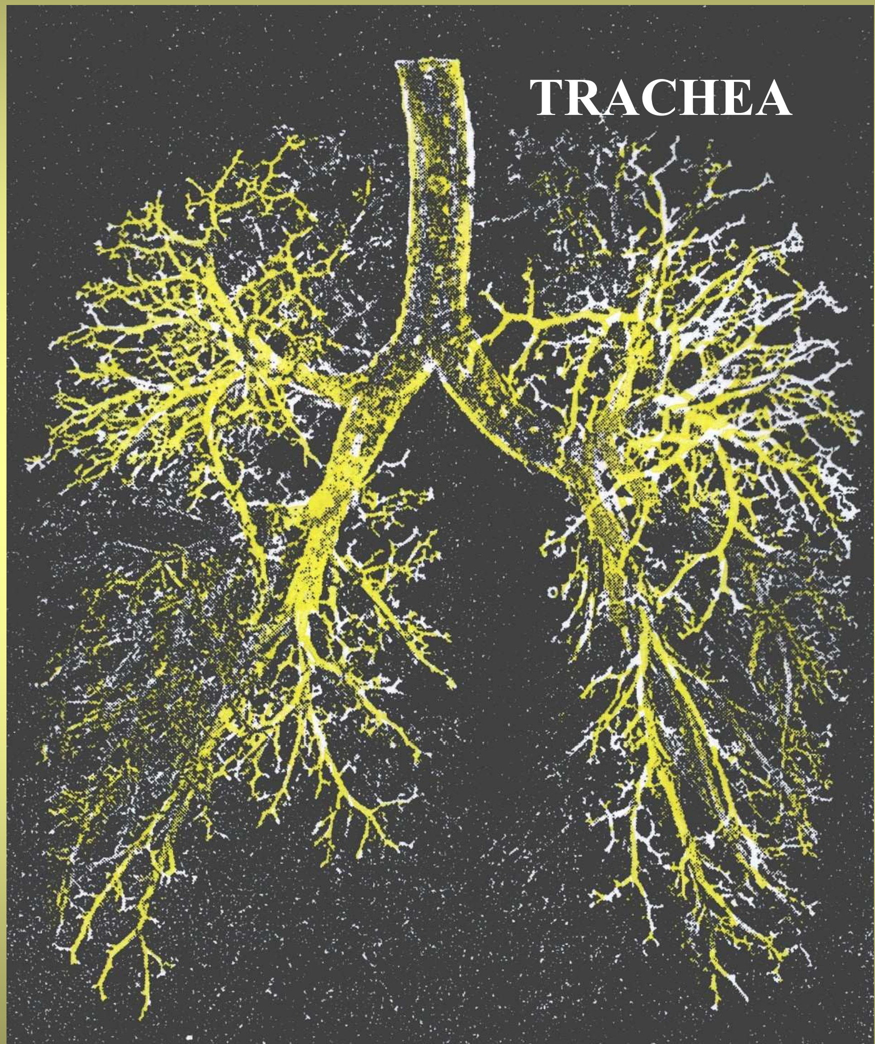


RESPIRATORY ZONE

TOTAL ALVEOLAR VOLUME at the end of quiet expiration ~3 l

TOTAL AREA ~ 100 m^2

CAST OF HUMAN AIR PASSAGES

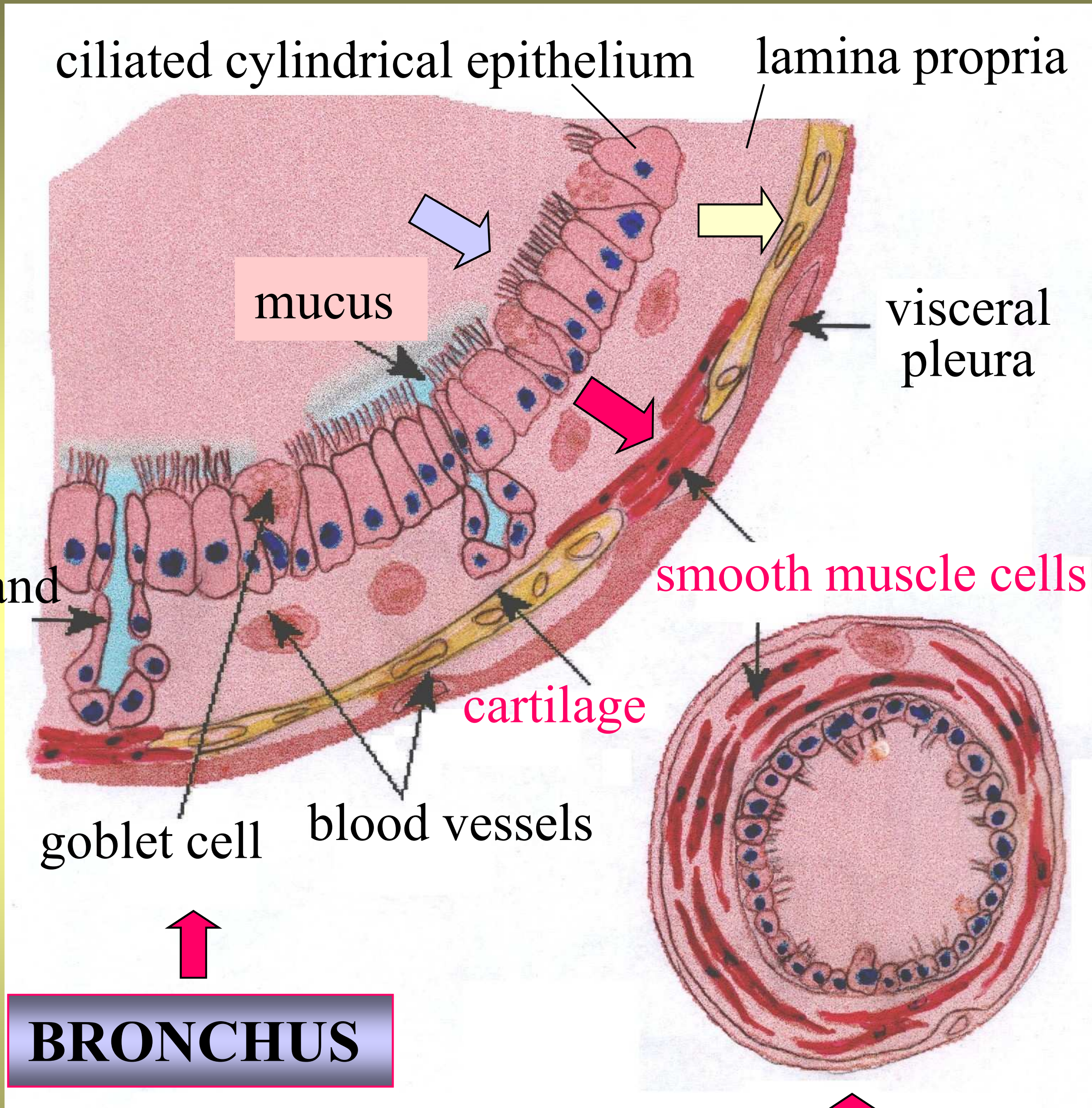


BRONCHI

BRONCHIOLES

TERMINAL BRONCHIOLES

AERODYNAMIC RESISTENCE



BRONCHUS

TERMINAL BRONCHIOLE ∅ < 1 mm

AUTONOMIC INNERVATION of smooth muscle cells

muscarinic receptors
activation ⇒ bronchoconstriction

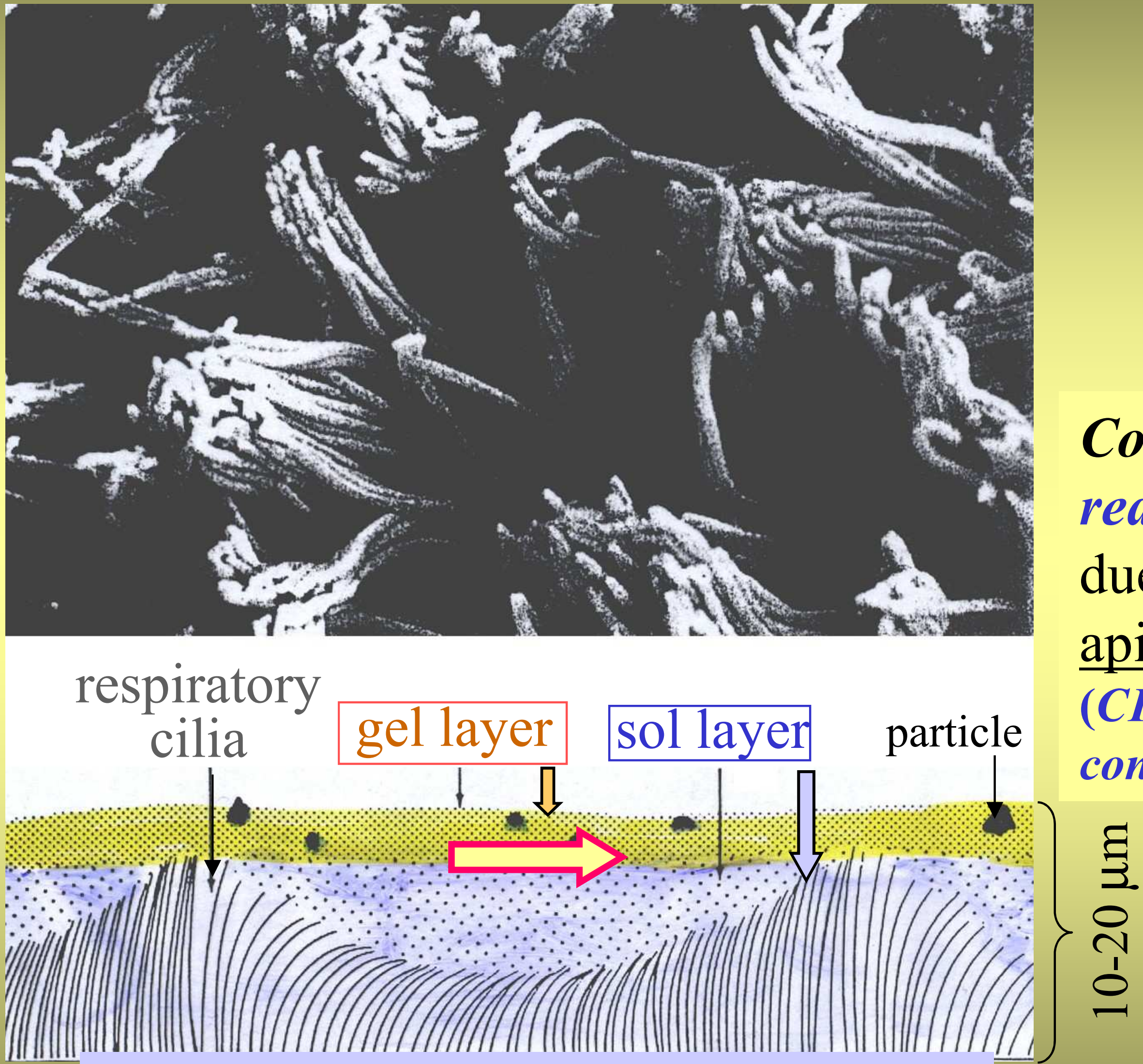
β_2-adrenergic receptors
activation ⇒ bronchodilatation

BRONCHIAL TONE DURING RESPIRATION

INSPIRATION - bronchodilatation (sympathetic discharge prevails)

EXPIRATION - bronchoconstriction (parasympathetic discharge prevails)

MUCOCILIARY CLEARANCE



movement of the mucus with particles

CHRONIC BRONCHITIS

CYSTIC FIBROSIS
mucoviscidosis

Complex genetic disorder ⇒ ***reduction of the sol layer*** mainly due to the defective ***Cl^- channels*** <u>in apical membrane</u> of epithelial cells (***CFTR - Cystic Fibrosis Transmembrane conductance Regulator***).

COLLOID SOLUTIONS
WITH DIFFERENT VISCOSITY

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V ALVEOLAR-CAPILLARY MEMBRANE

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

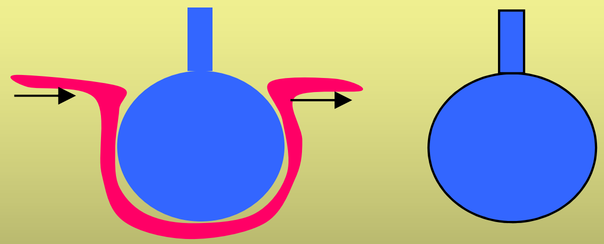
At the same **PULMONARY VENTILATION** (6 l/min) **ALVEOLAR VENTILATION** at **RAPID SHALLOW BREATHING** can be **SIGNIFICANTLY REDUCED** and **INADEQUATE** in comparison with **SLOW DEEP BREATHING**

DEAD SPACE IN RESPIRATORY SYSTEM

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

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

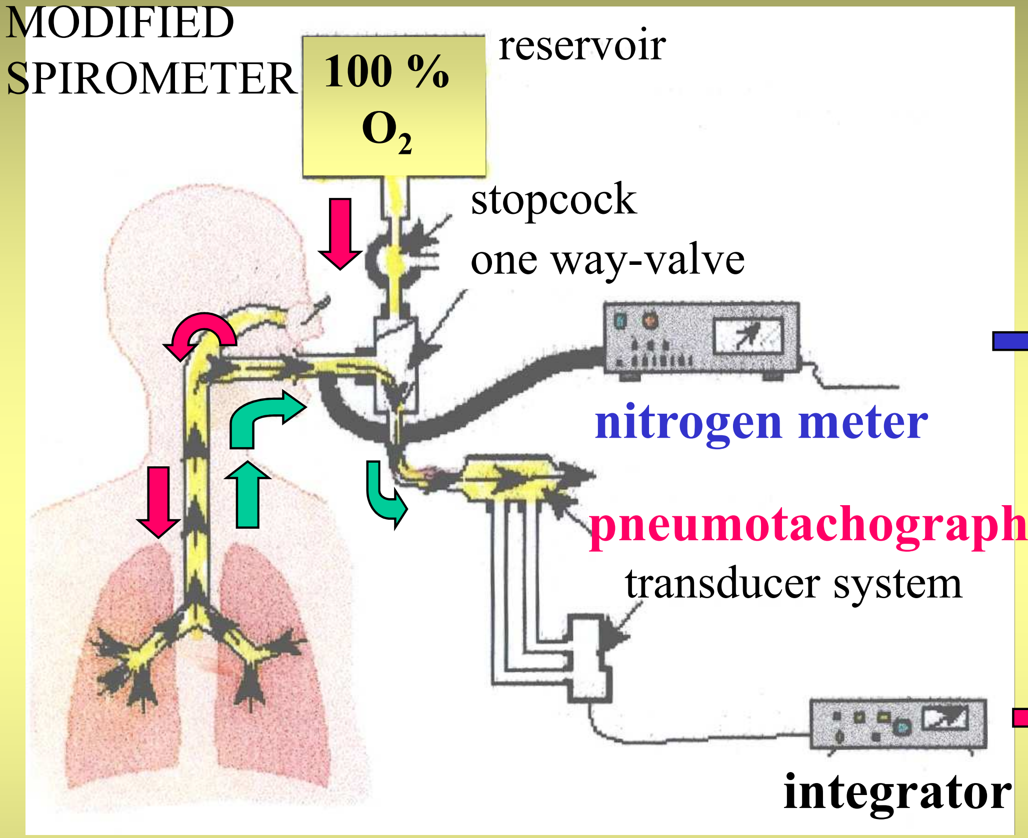
ANATOMICAL dead space + total VOLUME of ALVEOLI without functional capillary bed



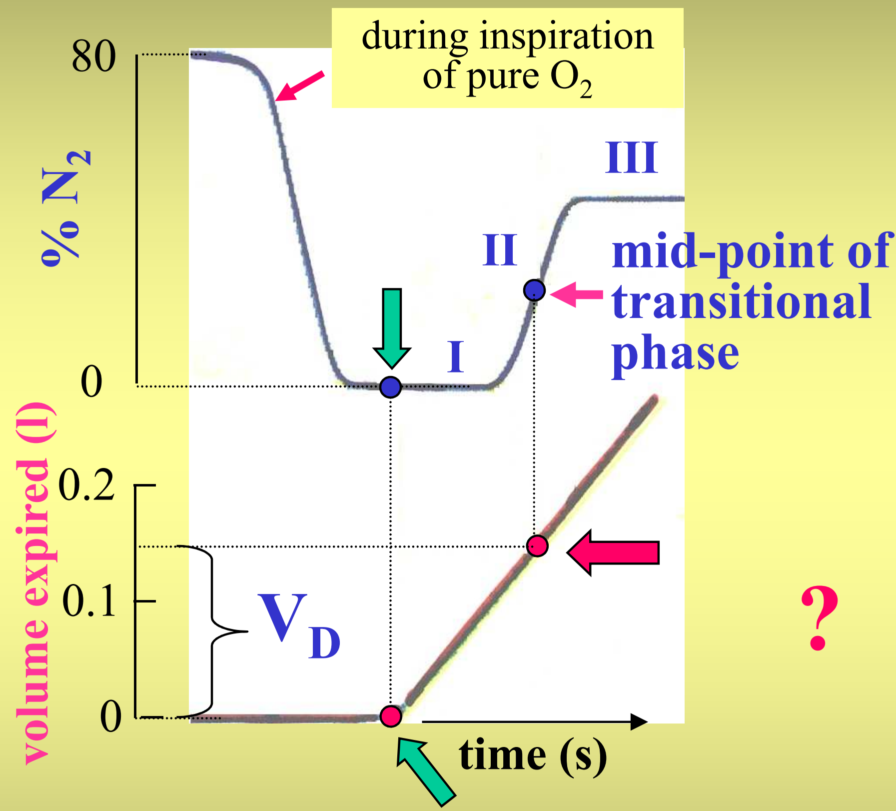
IN HEALTHY INDIVIDUALS
both spaces are practically identical

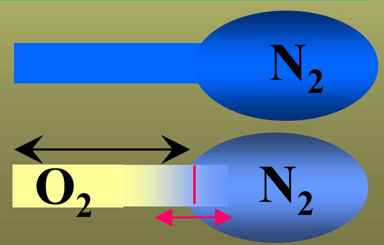
ANATOMICAL DEAD SPACE MEASUREMENT

(single breath N_2 test)



$V = \int Q\,dt$





NITROGEN CURVE

Phase I – expired air with pure O_2

Phase II - transitional phase (mixture of gasses due to diffusion)

Phase III - alveolar phase (alveolar air with **decreased value of N_2**)

ANATOMICAL DEAD SPACE

BOHR´S EQUATION

$$V_D = V_E \frac{P_{CO_2A} - P_{CO_2E}}{P_{CO_2A}}$$

$$P_{CO2} = F_{CO2} \cdot P_{total}$$

V_E ……. *expired tidal volume in reservoir*

$P_{CO2\ E}$ … *partial pressure of CO_2 in expired air (in reservoir)*

$P_{CO2\ A}$ … *partial pressure of CO_2 in alveolar part of expired air*

P_{CO2A} *can be measured in the last **10 ml** of the expired gas*

?

$$V_E = V_D + V_A$$

$$P\,V = n\,R\,T \Rightarrow n_{CO2} \sim P_{CO2}\,V$$

$$n_{CO2\ E} = n_{CO2\ D} + n_{CO2\ A}$$

……….?

FUNCTIONAL (TOTAL) DEAD SPACE

BOHR´S EQUATION

$$V_D = V_E \frac{P_{CO_2a} - P_{CO_2E}}{P_{CO_2a}}$$

FUNCTIONAL DEAD SPACE is obtained if alveolar P_{CO2A} is replaced by arterial partial pressure P_{CO2a}

$$P_{CO_2a} \geq P_{CO_2A}$$

HELTHY SUBJECTS - both ***partial pressures*** are nearly identical ⇒ **FUNCTIONAL** dead space equals **ANATOMICAL** dead space

RESPIRATORY DISEASES - numerous alveoli are without ***functional capillary bed*** ⇒ $P_{CO2A} < P_{CO2\,a}$

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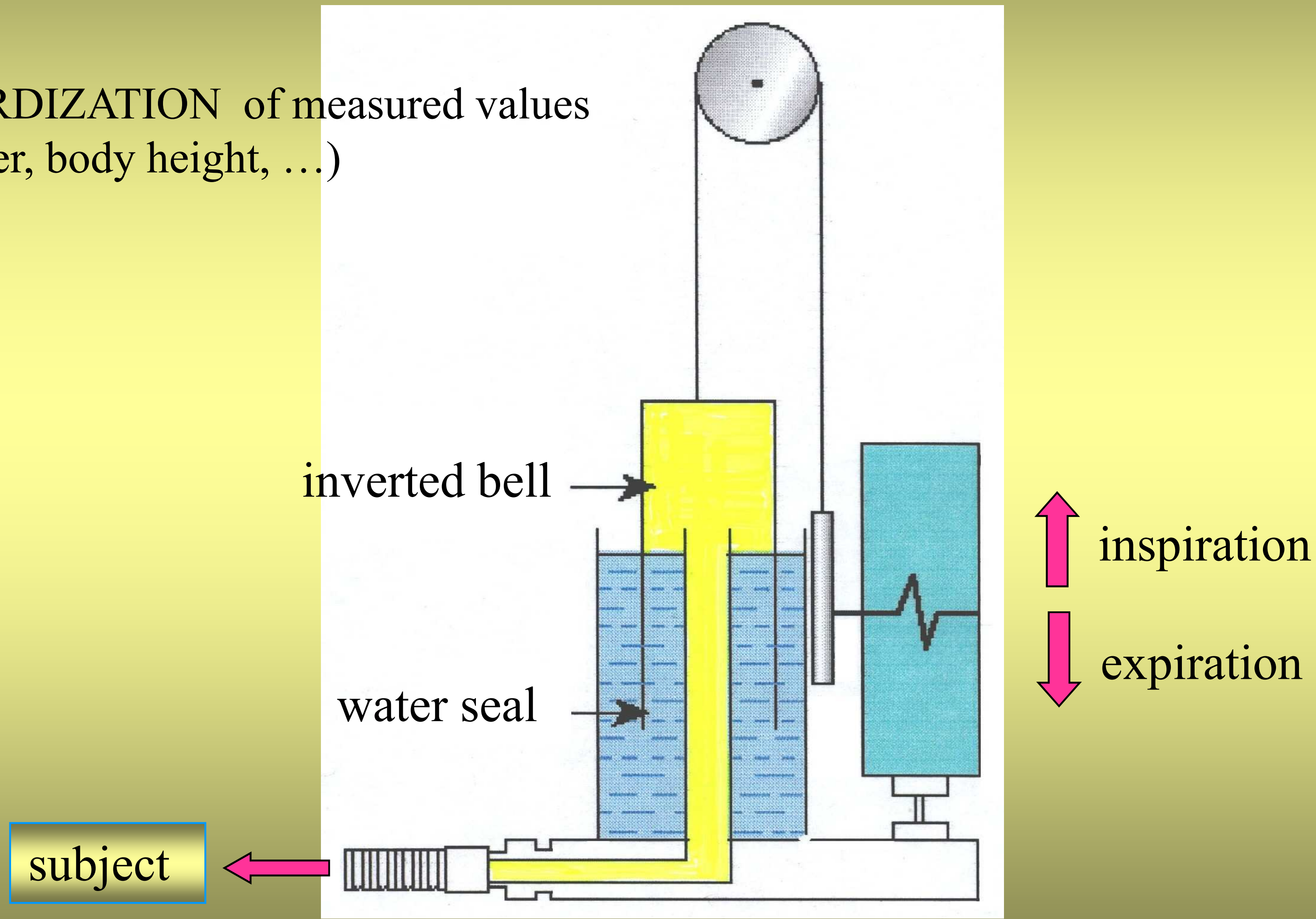
SPIROMETRY

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

STANDARDIZATION of measured values
(age, gender, body height, …)



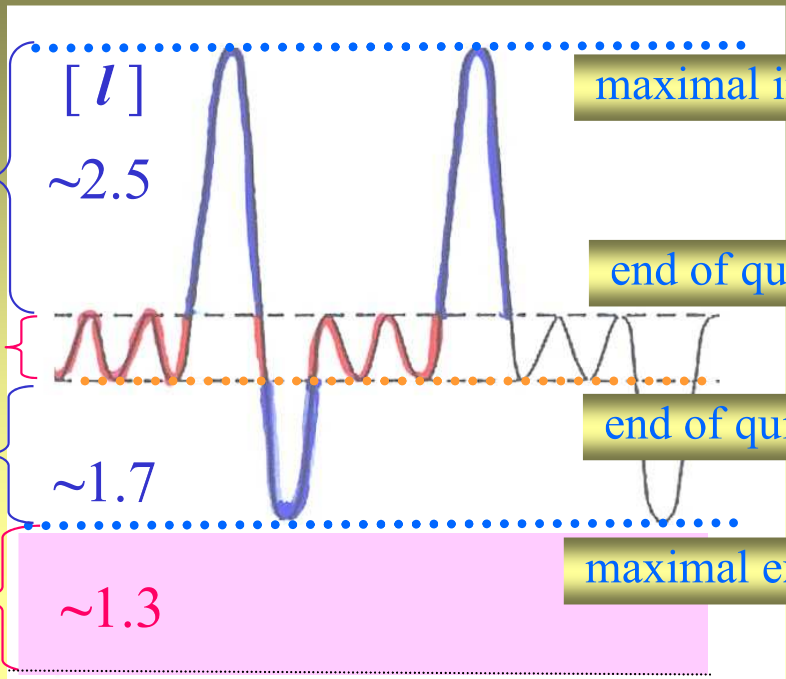
LUNG VOLUMES

INSPIRATORY RESERVE VOLUME *IRV*

TIDAL VOLUME V_T

EXPIRATORY RESERVE VOLUME *ERV*

RESIDUAL VOLUME *RV*



maximal inspiratory level

end of quiet inspiration

end of quiet expiration

maximal expiratory level

DILUTION METHOD
He

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

V_r ....reservoir volume

$c_{i\ He}$ ...known initial concentration of *He*

$c_{f\ He}$ ...final measured concentration of *He*

$$n = c\,V$$

$$n_{RV\ He} = n_{i,r\ He} - n_{f,r\ He}$$

(difference between initial and final amounts of *He* in reservoir)

RV ⇄ He reservoir (V)

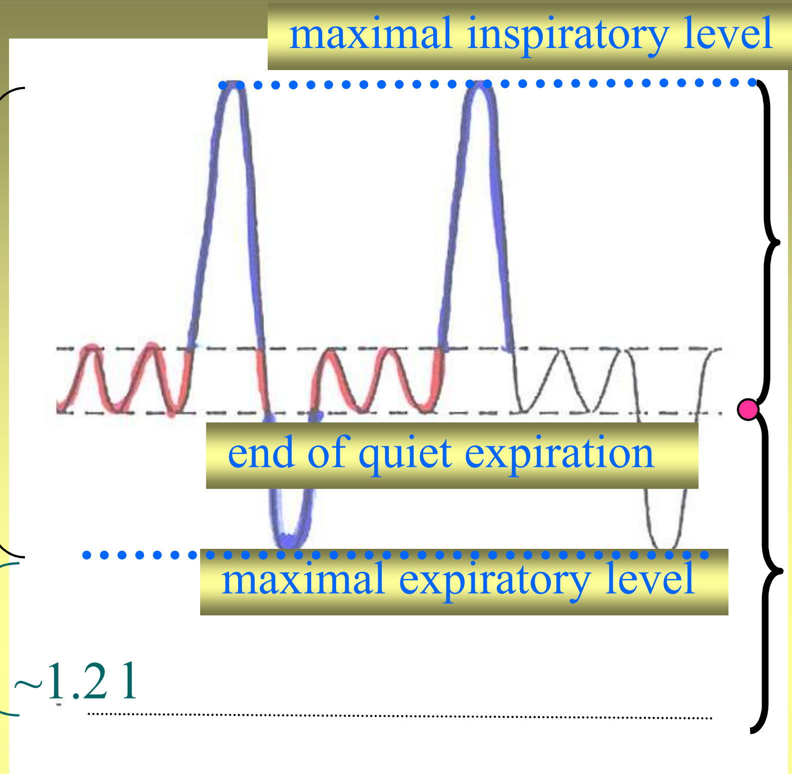
RV ⇄ reservoir (V)

TLC

VC

RV

$$\frac{RV}{TLC} \leq 25\%$$



INSPIRATORY CAPACITY

>3.0 l

FUNCTIONAL RESIDUAL CAPACITY

<3.0 l

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

The largest amount of air that can be expired after maximal inspiration

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

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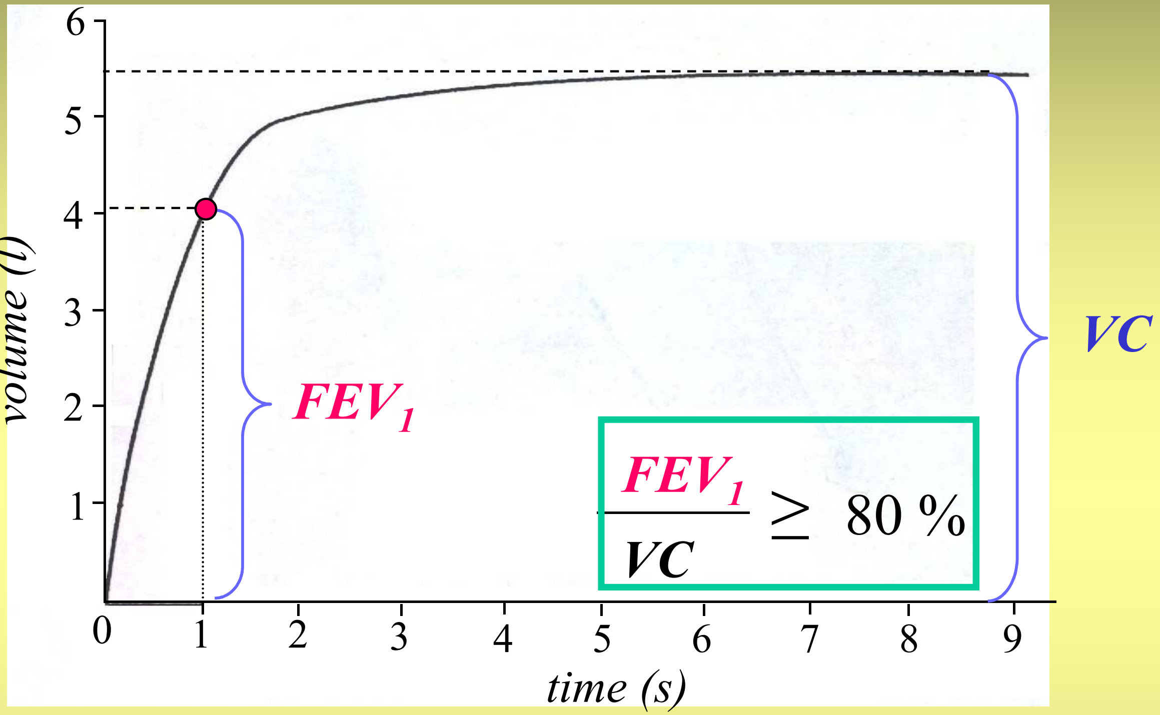
FUNCTIONAL INVESTIGATION OF THE LUNGS

- **TIMED VITAL CAPACITY** (*FEV_1* - forced expiratory volume per 1 *s*)

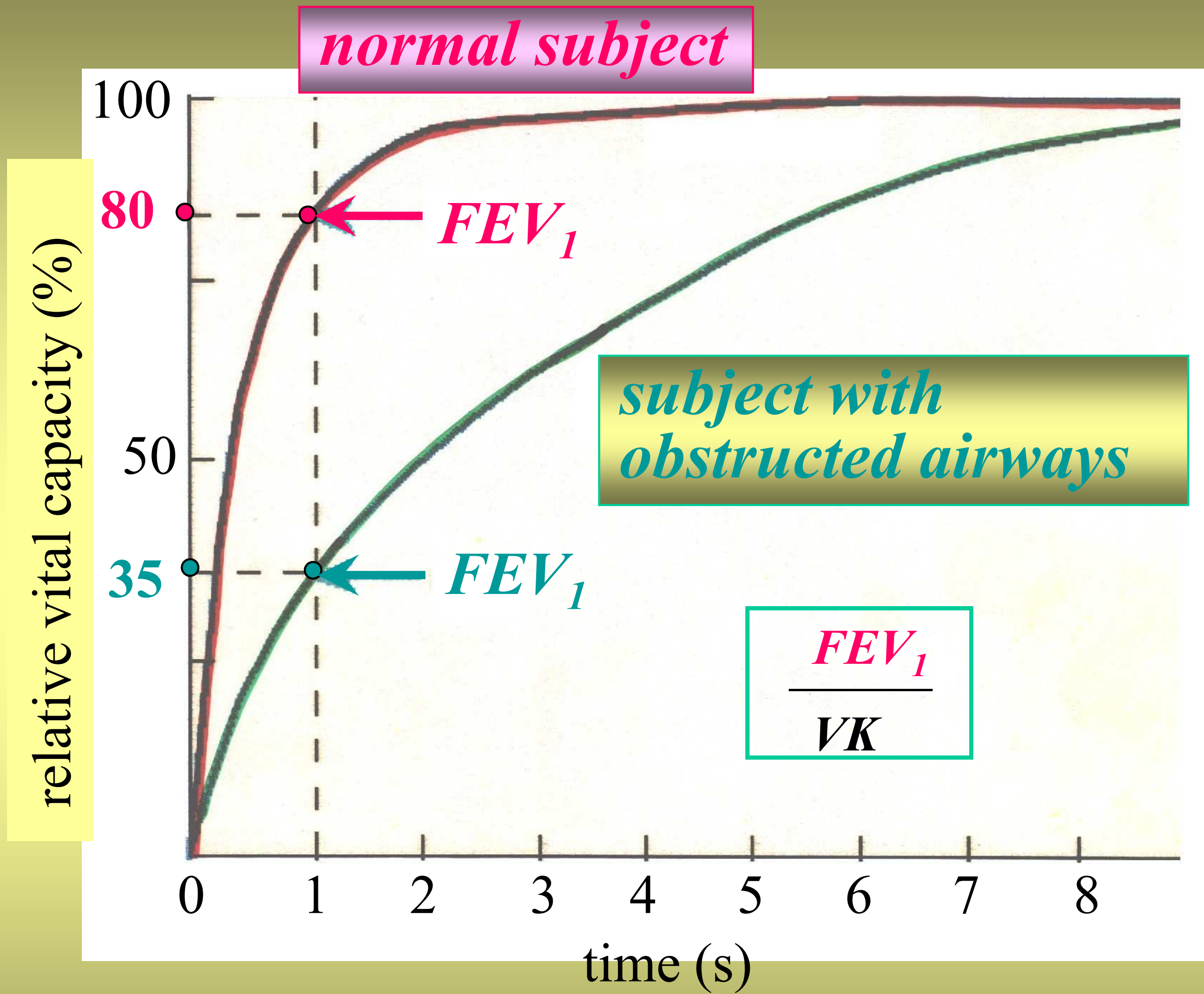


- **PULMONARY VENTILATION** ***RMV*** **(respiratory minute volume)**
(0.5 l x 12 breathes/min = 6 *l/min*)

- **MAXIMAL VOLUNTARY VENTILATION (*MVV*)** during time interval 10 s (125-170 *l/min*)

- **PEAK EXPIRATORY FLOW RATE (*PEFR*) measured by means of pneumotachograph** (~10 *l/s*)

TIMED VITAL CAPACITY FEV_1



TIMED VITAL CAPACITY enables to distinguish **RESTRICTIVE disorders** (e.g. pulmonary fibrosis) from **OBSTRUCTIVE disorders** with increased airway resistance (e.g. asthma bronchial).

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$P.V = const \Rightarrow P = \frac{const}{V}$

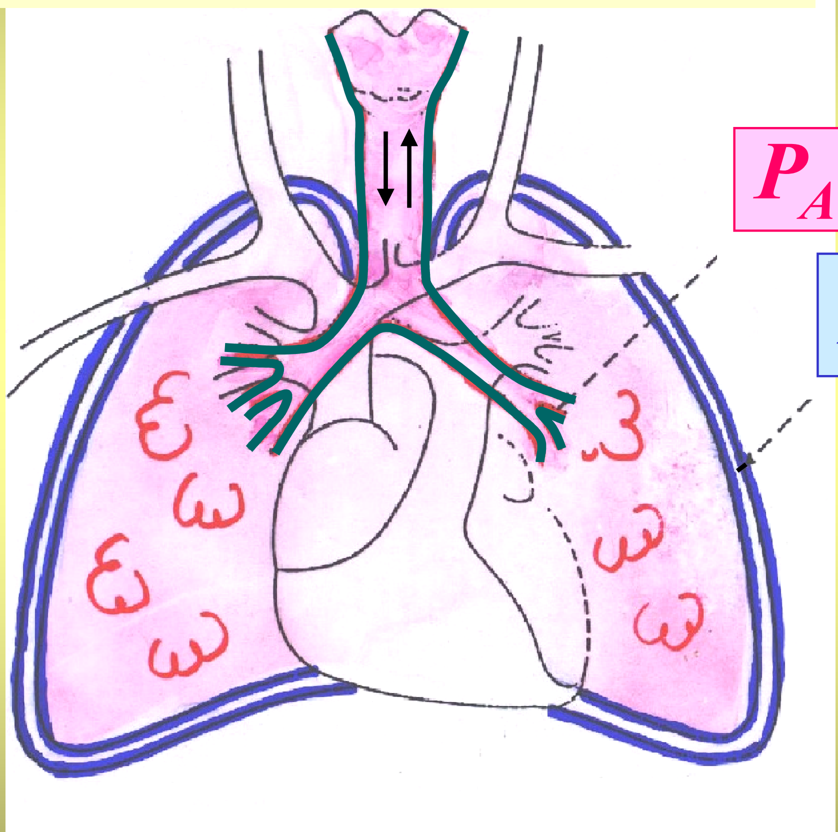
$\Delta P = Q.R$ POISEUILLE´S LAW

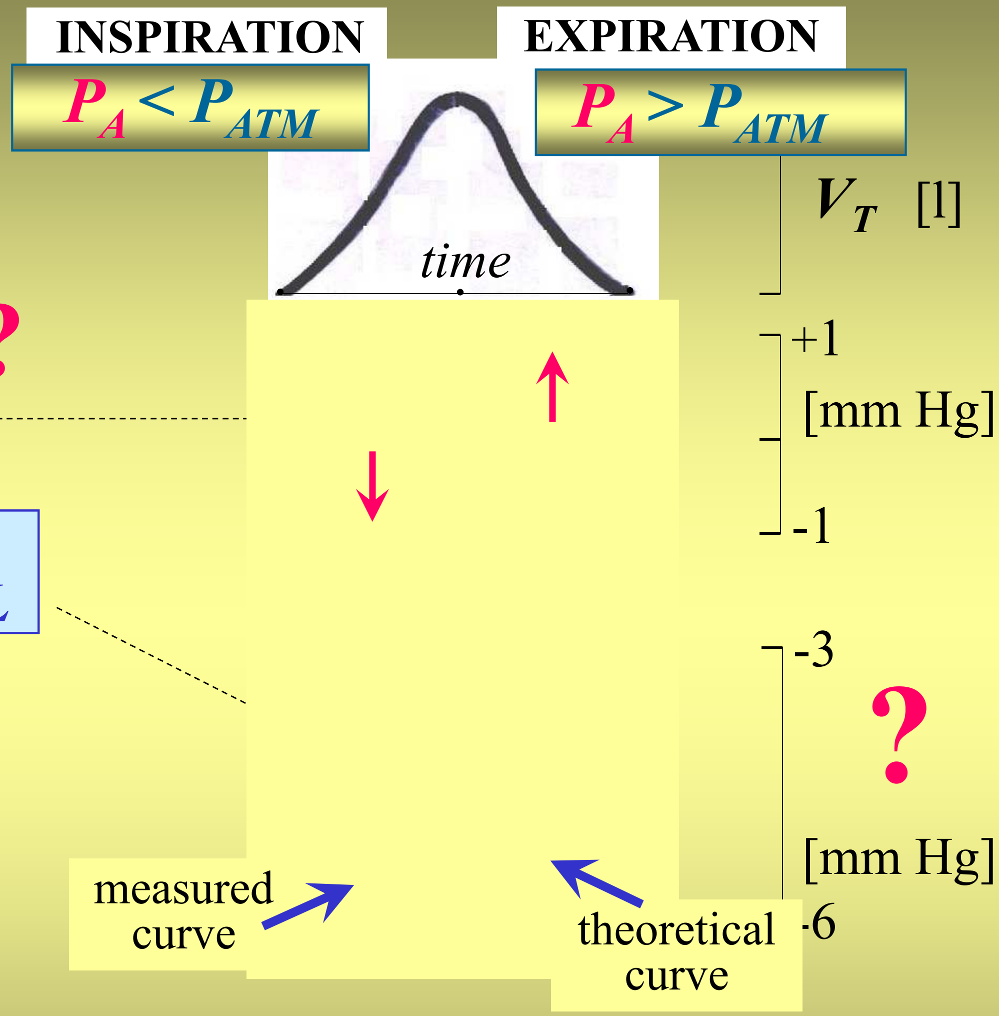
analogy to Ohm´s law

Q … flow rate

R ... aerodynamic resistance of air passages

TIME COURSES OF PRESSURES at quiet respiration





P_A **ALVEOLAR (INTRAPULMONARY, LUNG)**

P_{PL} **INTRAPLEURAL (INTRATHORACIC)**

$P_{TP} = P_A - P_{PL}$

TRANSPULMONARY

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COMPOSITION OF ALVEOLAR AIR

partial pressures in mm Hg

INSPIRED AIR

O_2	158.8
CO_2	0.3
N_2	601.0
…	

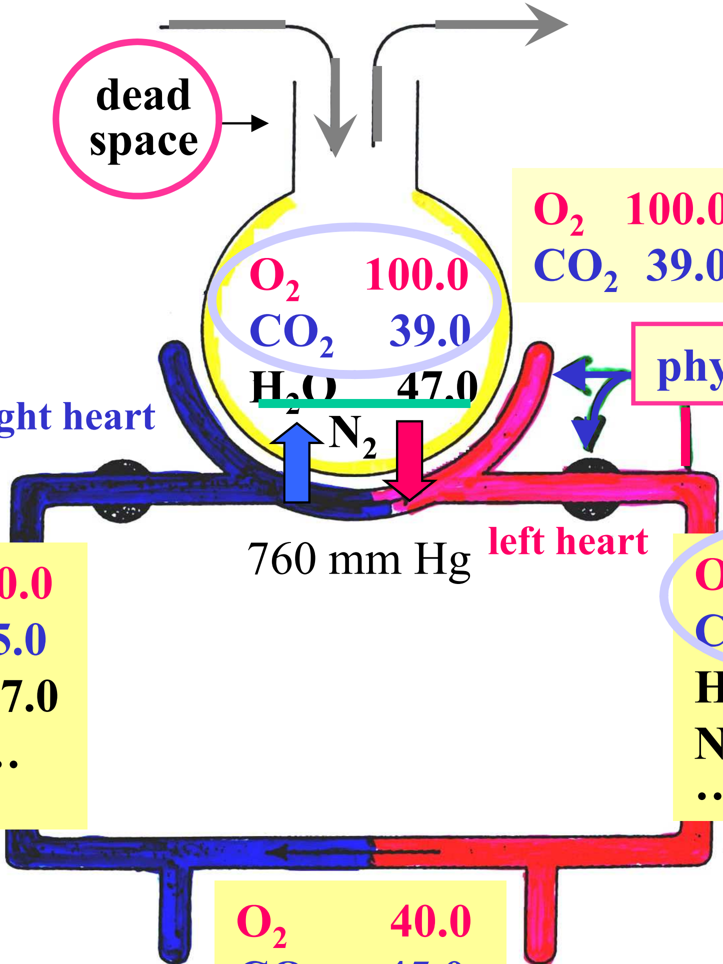
760 mm Hg

EXPIRED AIR

O_2	115.0
CO_2	33.0
H_2O	47.0
N_2	564.0
…	

760 mm Hg

?



O_2	100.0
CO_2	39.0

physiological shunts

?

veins

O_2	40.0
CO_2	45.0
H_2O	47.0
N_2	…
…	

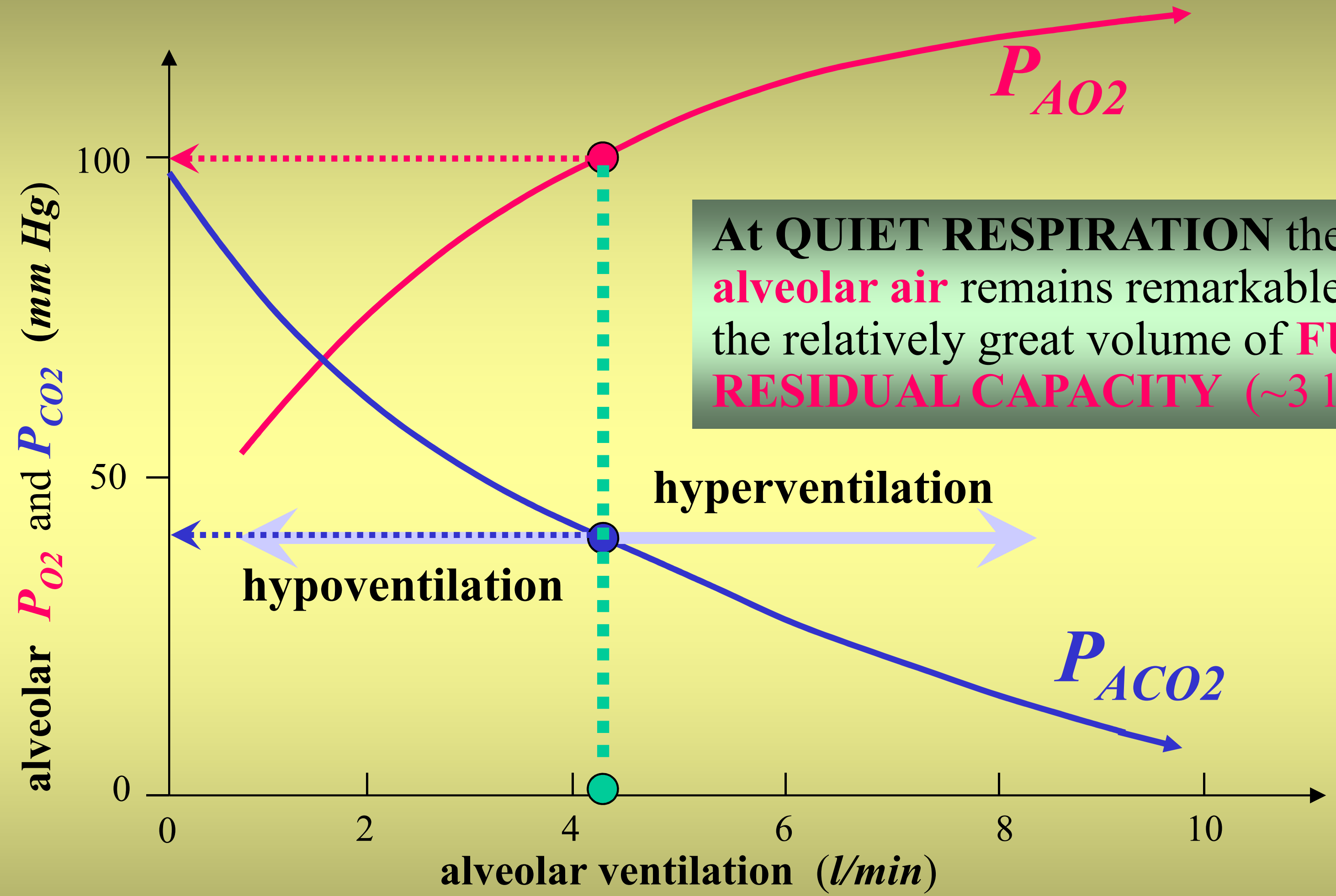
arteries

O_2	95.0
CO_2	41.0
H_2O	47.0
N_2	…
…	

periphery capillaries

O_2	40.0
CO_2	45.0
H_2O	47.0
N_2	…
…	

Alveolar P_{O2} and P_{CO2} at voluntary hypo- and hyperventilation



hyperventilation → hypocapnia → respiratory alkalosis

hypoventilation → hypercapnia → respiratory acidosis

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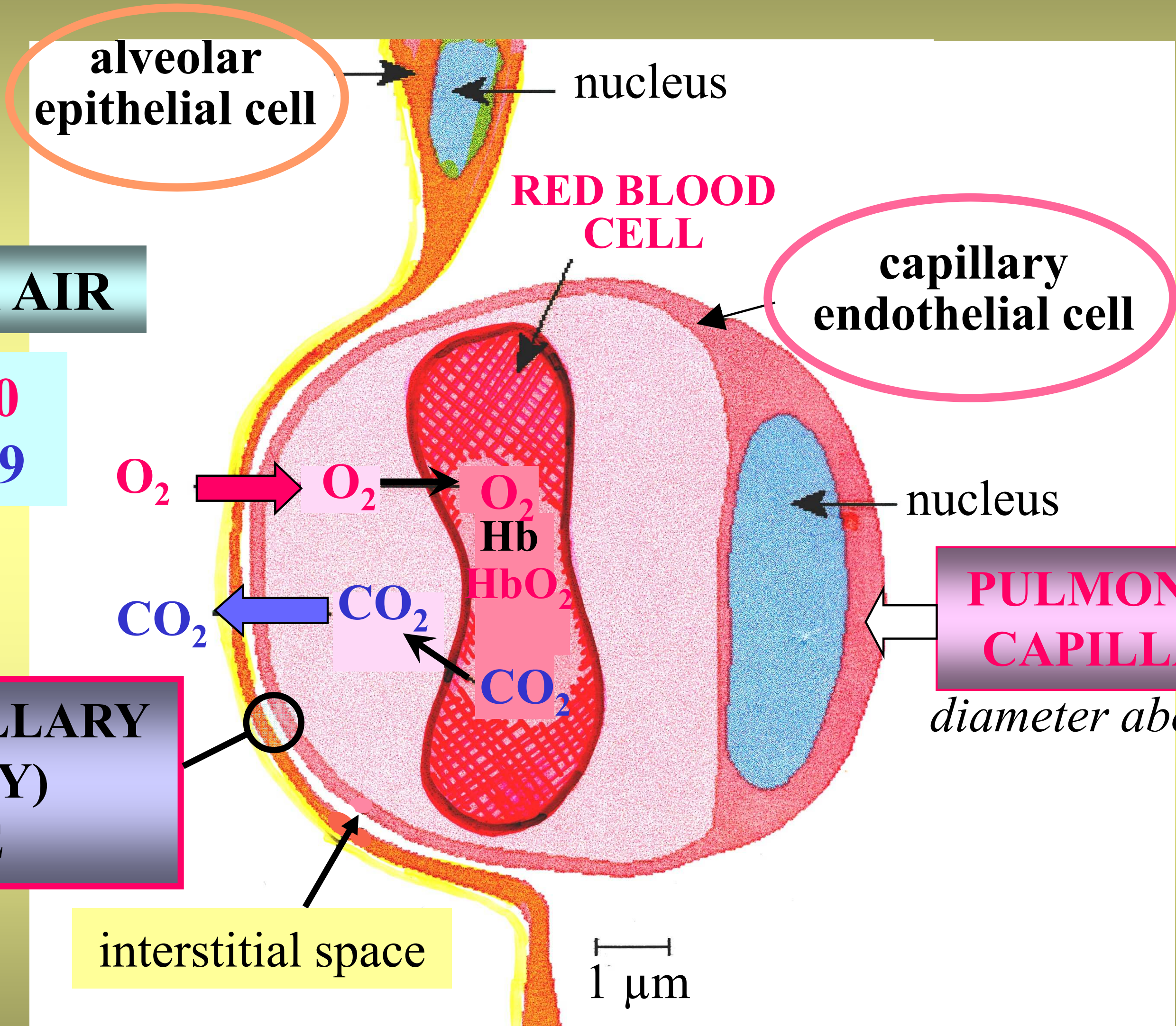
DIFFUSION OF GASES ACROSS RESPIRATORY MEMBRANE

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

FACTORS AFFECTING RATE OF DIFFUSION OF GASE IN THE LUNGS (O_2 or CO_2)

FICK´S LAW – LAW OF DIFFUSION

$$\dot{V} = \frac{k_D A}{l}(P_A - P_c) \quad (ml/min)$$

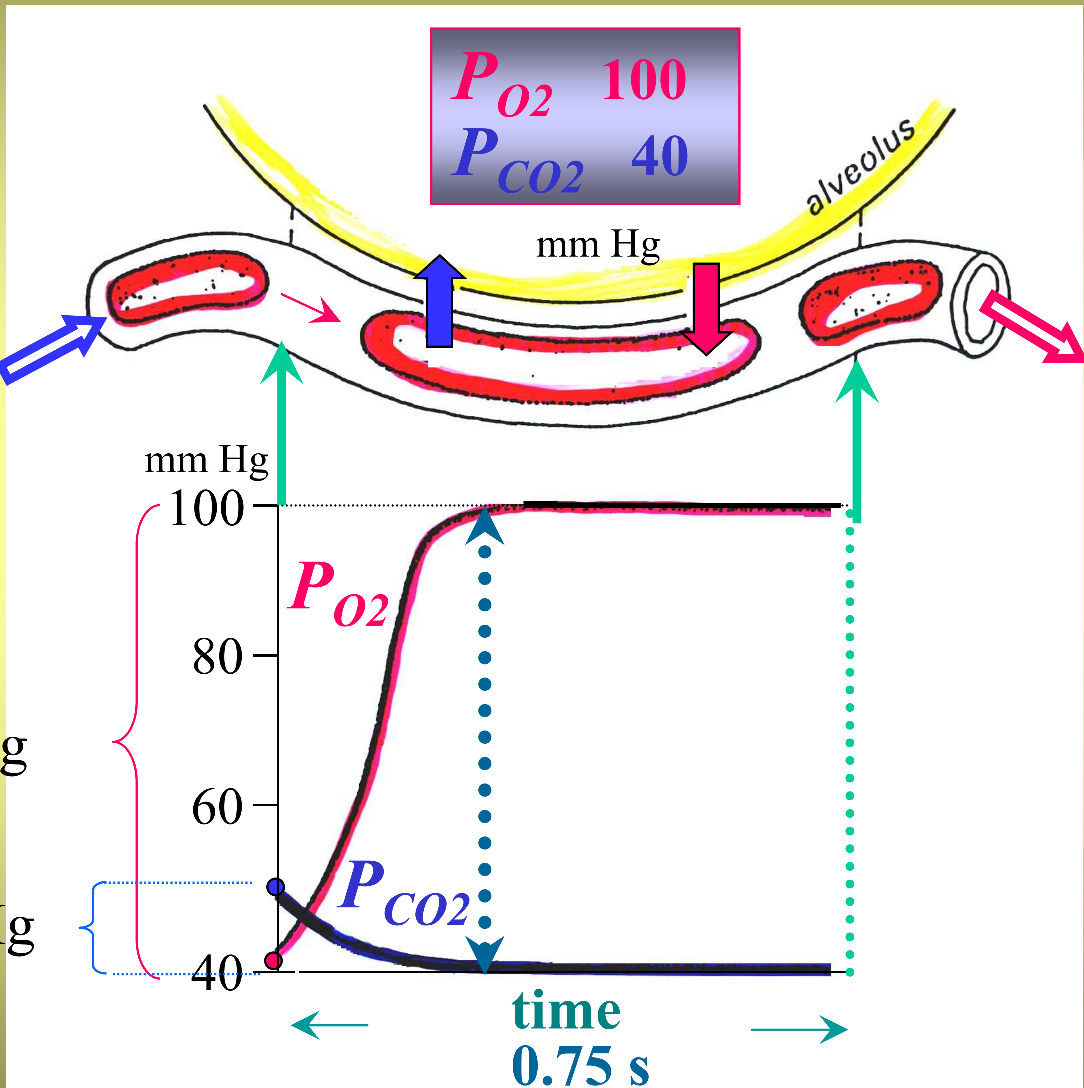
- **TOTAL SURFACE AREA OF THE ALVEOLAR-CAPILARY MEMBRANE** ***A*** **(~ 100 m^2)** (↓ ***A*** **:** *emphysema*)
- **DIFFUSION DISTANCE - THICKNESS OF THE BARRIER** ***l*** **(~1 μm)** (↑ ***l*** **:** *inflammation, pulmonary edema*)
- **PARTIAL PRESSURE DIFFERENCE** **(P_A - P_c)**
- **DIFFUSION COEFFICIENT OF THE GAS** **k_D** determined by molecular mass, solubility of the gas in the respiratory membrane (↓ k_D: *pulmonary fibrosis*).

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

venous blood

P_{O2} 40
P_{CO2} 46

mm Hg



P_{O2} 100
P_{CO2} 40

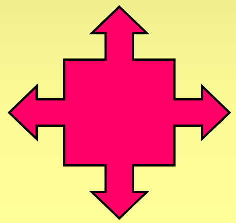
mm Hg

equilibrated 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



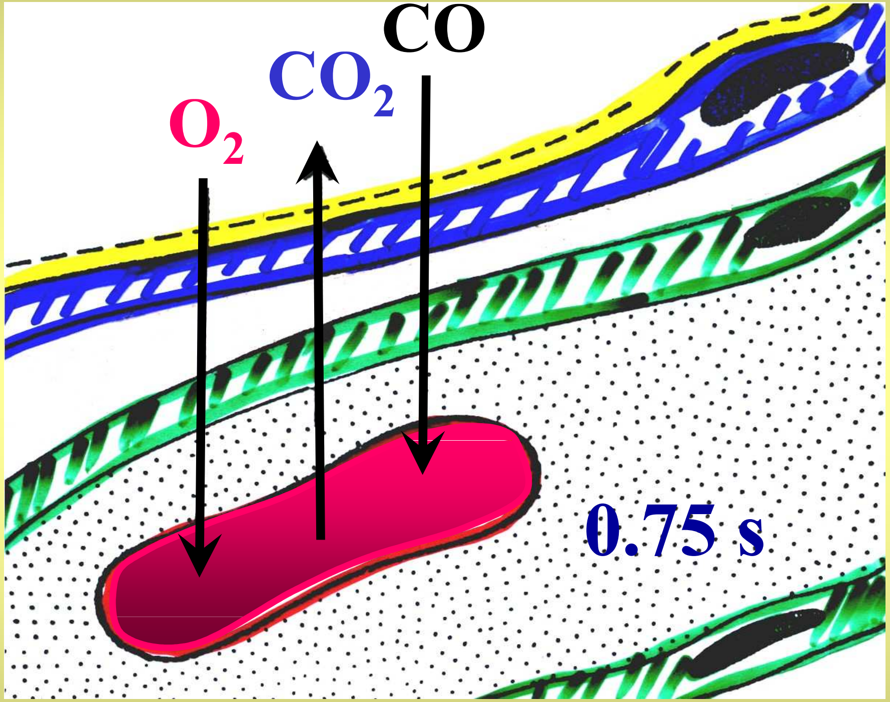
DIFFUSING CAPACITY OF THE LUNGS D_L

$$D_L = \frac{\dot{V}_{gas}}{P_A - P_c} \quad \left[\frac{ml/min}{mm\,Hg}\right]$$

$$\dot{V} = \frac{k_D A}{l}(P_A - P_c) \Rightarrow D_L = \frac{k_D A}{l}$$

$\dot{V}_{gas}$ – flow of the gas (*ml/min*)

$P_A - P_c$ – partial pressure difference (DRIVING FORCE FOR DIFFUSION)



INDEX OF DIFFUSING CAPACITY

Gas ***CO*** is suitable for measurement of D_L because P_{CO} in plasma is negligible. P_{ACO} and the decrease in amount of ***CO*** per unit of time in alveoli are measured ($\dot{V}_{CO}$).

$$D_{LCO} \approx \dot{V}_{CO}/P_{ACO}$$

$D_{LCO} \approx 17$ *ml/ min/ mm Hg*

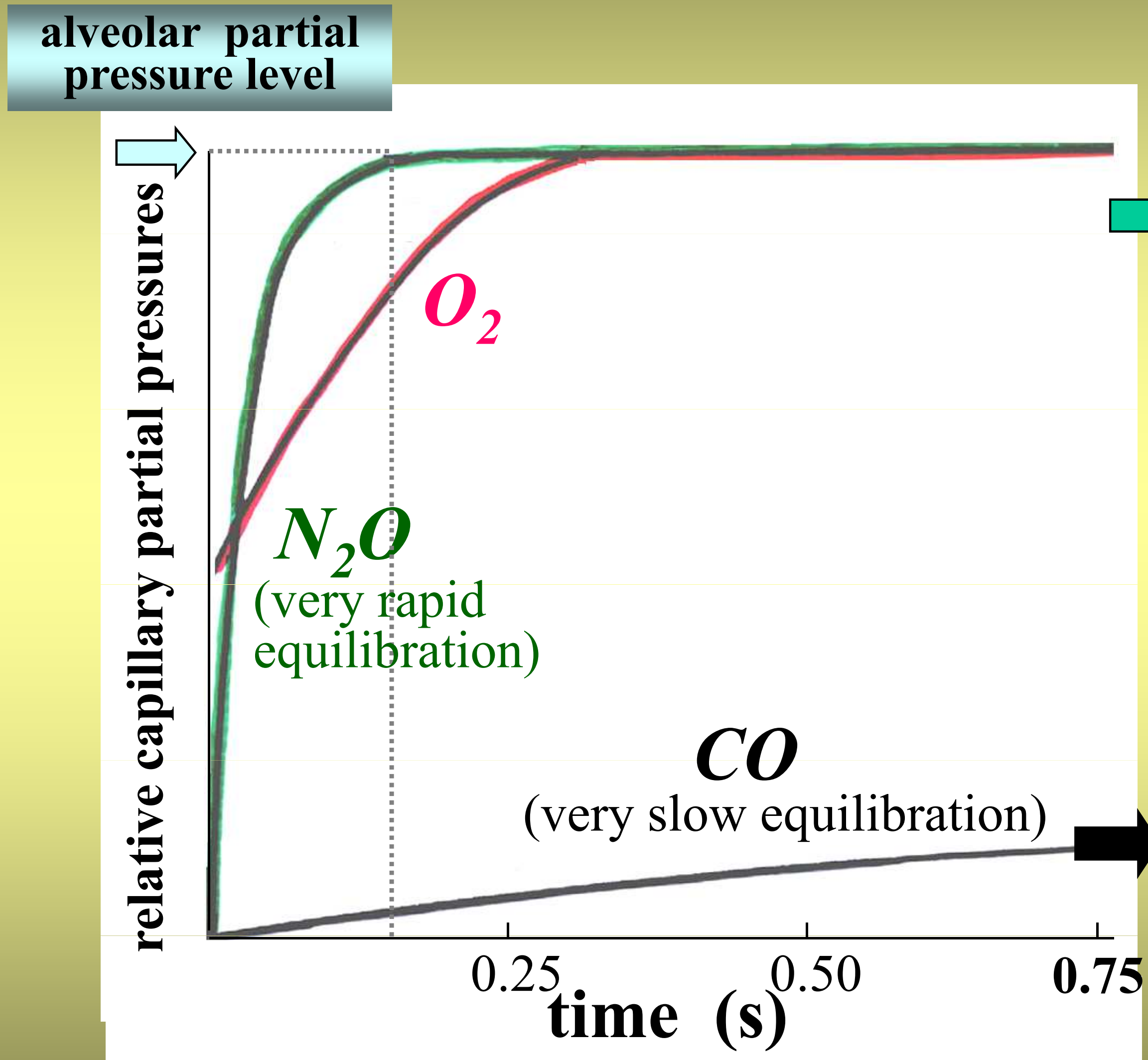
$D_{LO2} \approx 21$ *ml/ min/ mm Hg*

D_{LO2} **increases** during exercise ($\uparrow \dot{V}_{O2}$) and **is reduced** in pulmonary diseases ($\downarrow A$, $\uparrow l$)

$D_{LCO2} \gg D_{LO2}$

$k_{DCO2} \gg k_{DO2}$

EQUILIBRATION OF O_2, N_2O, AND CO PARTIAL PRESSURES IN CAPILLARY BLOOD WITH ALVEOLAR PRESSURES



time interval of erythrocyte contact with respiratory membrane

N_2O (nitrous oxide)

INERT GAS

used for cerebral and coronary blood flow measurements

CO (carbon monoxide)

AVIDLY BOUND IN ERYTHROCYTE

used for assessment of diffusing capacity of the lungs D_L

FICK´S LAW OF DIFFUSION

END