RESPIRATORY PHYSIOLOGY

M. F. Din

Respiration

- All those processes that maintain the normal levels of oxygen and carbon dioxide in the body

- Internal (Cellular) respiration
  - This is the oxidation of substrate to release energy (and CO_2)
- 'External respiration'
  - This is the absorption of oxygen and the removel of carbondioxide from the body

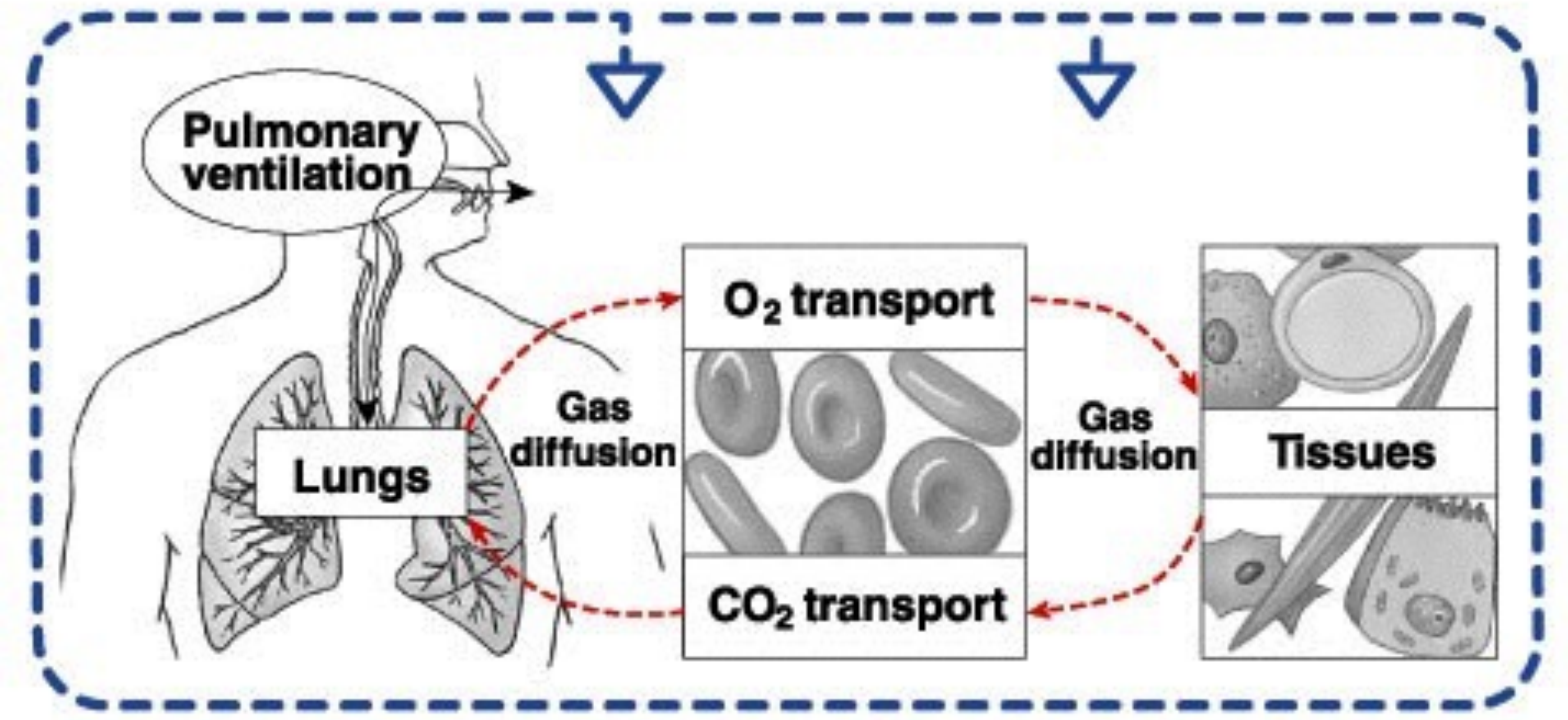
Aim of respiration

- To maintain
  - Pa O_2
  - Pa CO_2
  - pH (Arterial)

Steps of respiration

- Ventilation
- Diffusion
- Gas transport
- Tissue gas exchange

Control of all the above

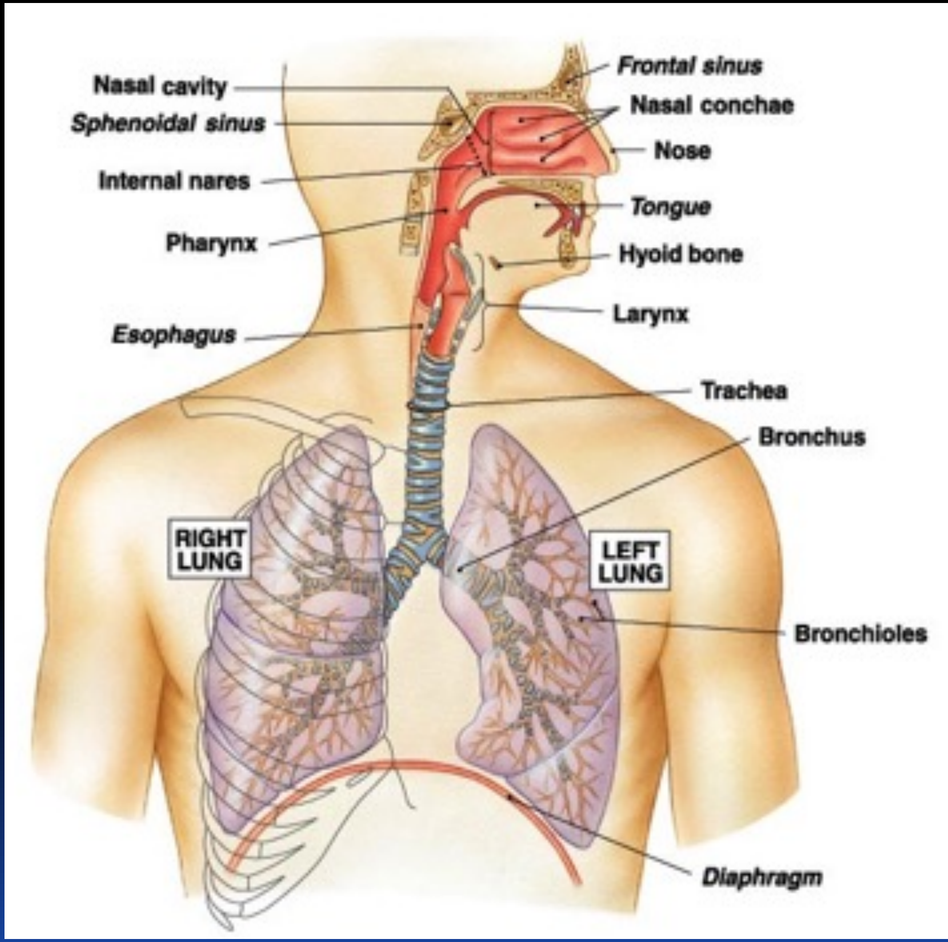


Pulmonary ventilation
Lungs
Gas diffusion
O_2 transport
CO_2 transport
Gas diffusion
Tissues

Physiological anatomy of the Respiratory system

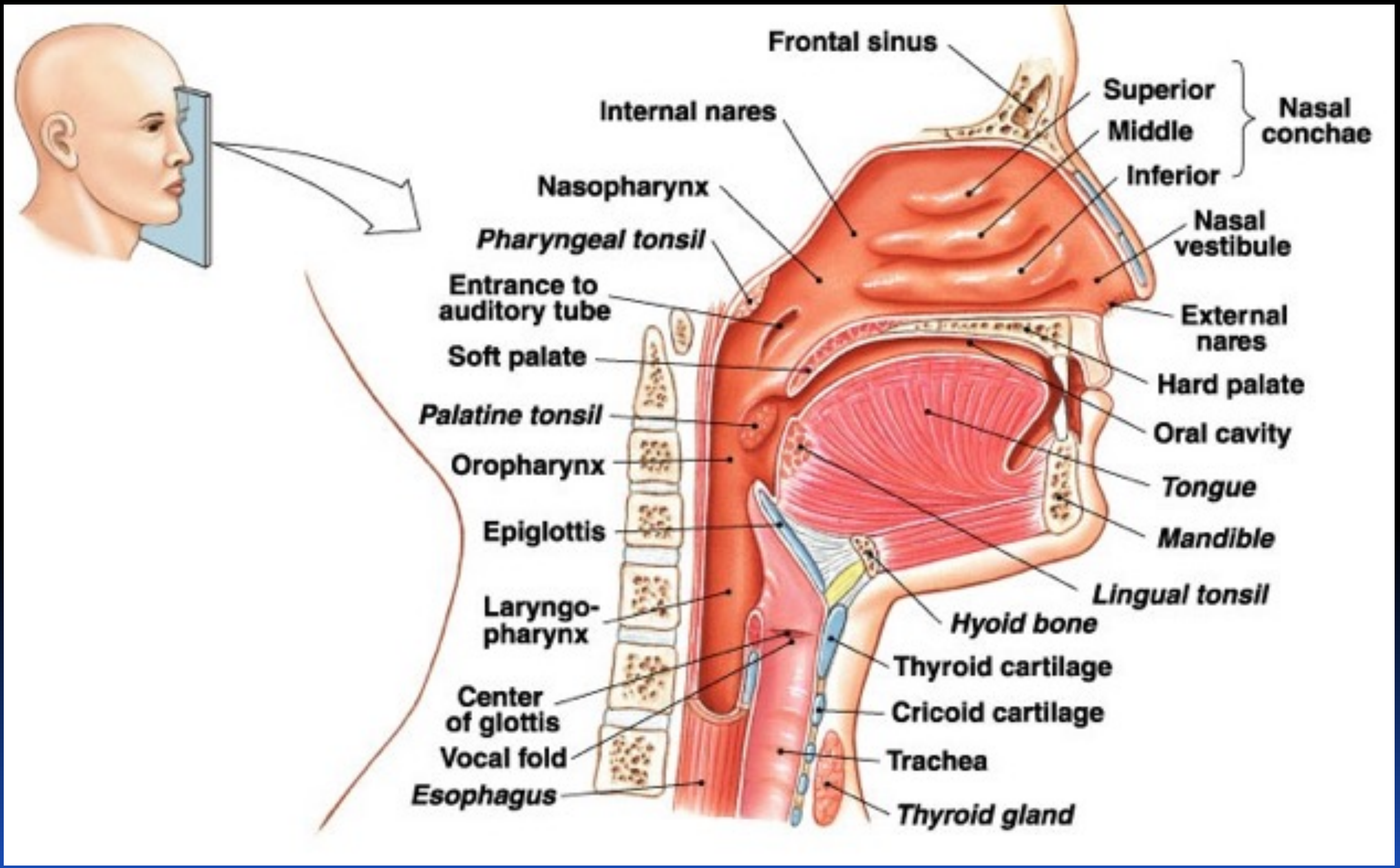
- Nose
- Pharynx
- Larynx
- Trachea
- Bronchii
- Lungs
- All assosiated, musculo-skelelatal apparatus, innervation

Respiratory System Divisions



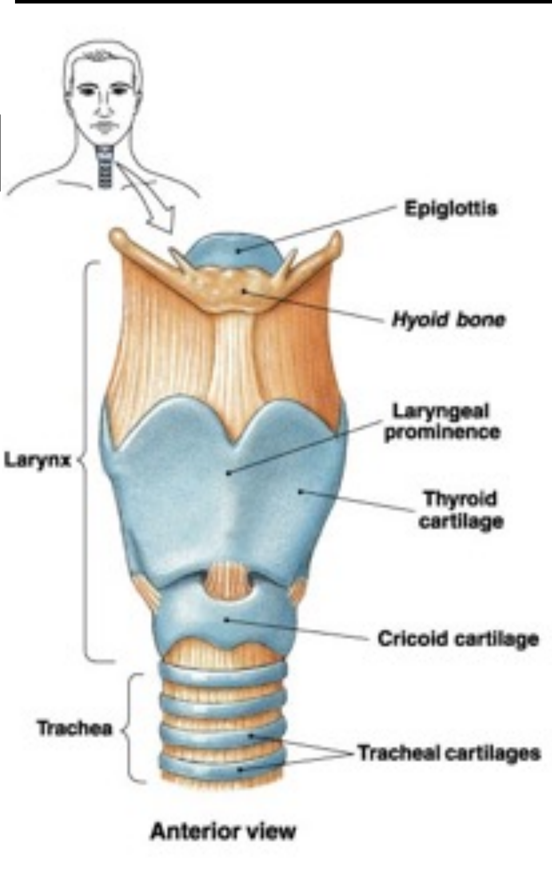
- Upper tract
  - Nose, pharynx and larynx
- Lower tract
  - Trachea, bronchi, lungs

Nasal Cavity and Pharynx

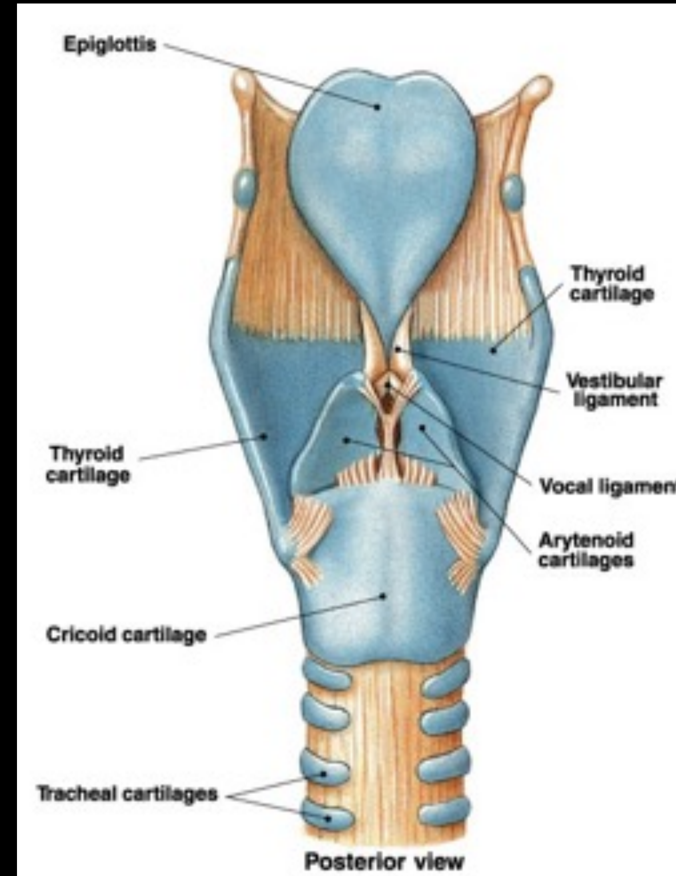


Nose and Pharynx

- Nose
  - External nose
  - Nasal cavity
    - Functions
      - Passageway for air
      - Cleans the air
      - Humidifies air
      - warms air
      - Olfaction
      - Along with paranasal sinuses are resonating chambers for speech
- Pharynx
  - Common passage for digestive and respiratory systems
  - Three regions
    - Nasopharynx
    - Oropharynx
    - Laryngopharynx
  - Humidification

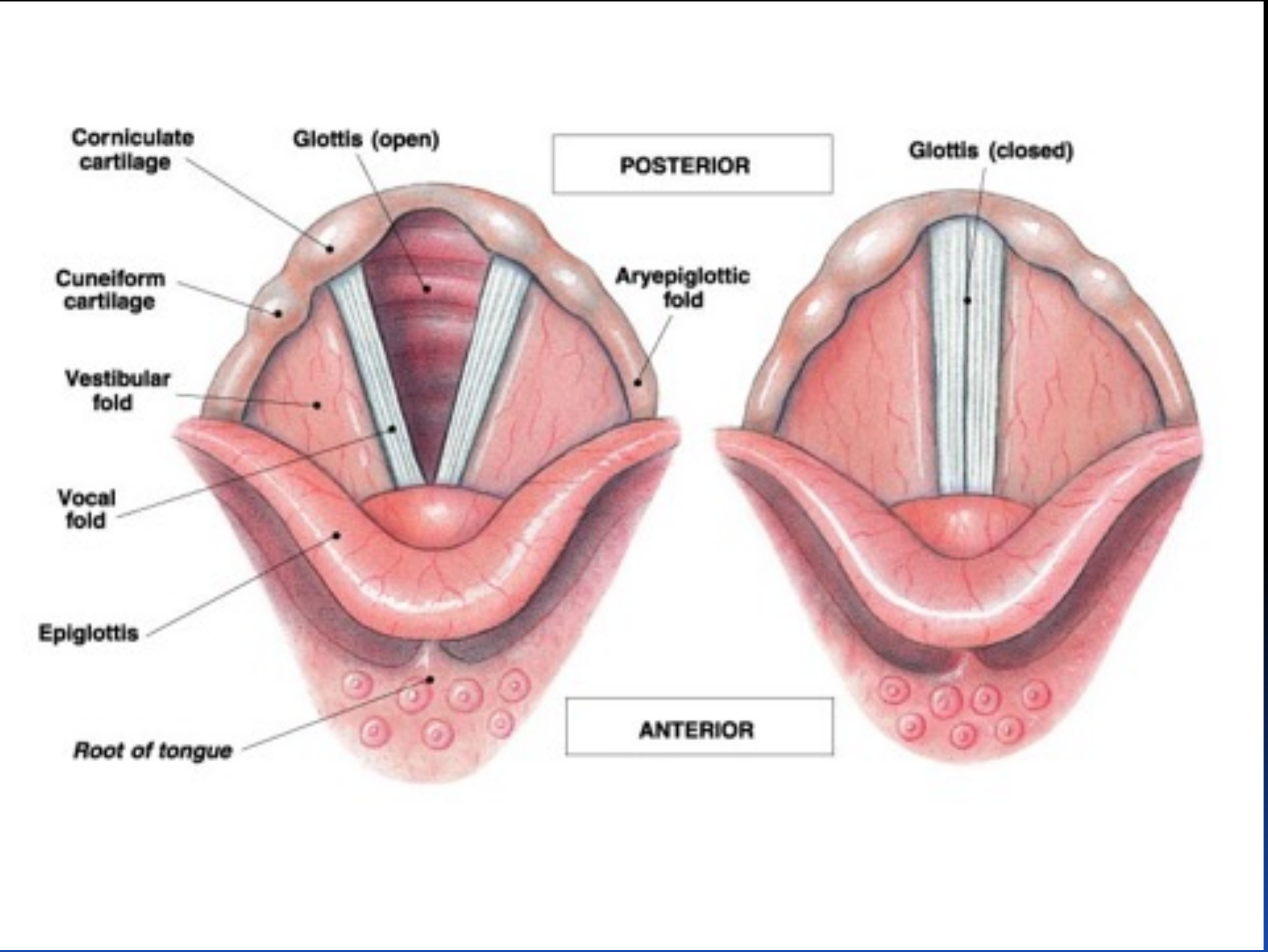


larynx



- Functions
  - Maintain an open passageway for air movement
  - Epiglottis and vestibular folds prevent swallowed material from moving into larynx
  - Vocal folds are primary source of sound production

Glottis

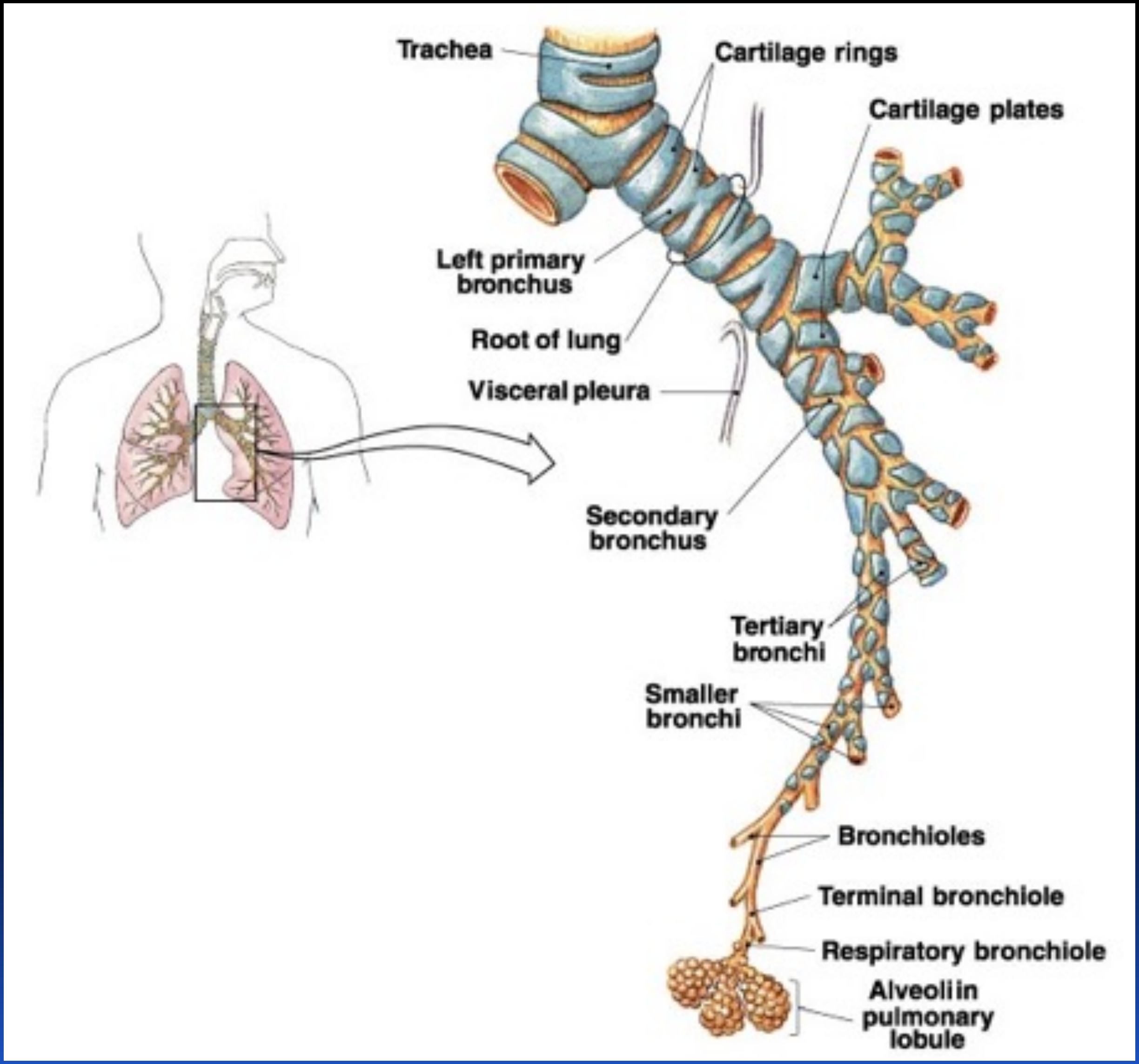


Corniculate cartilage
Glottis (open)
POSTERIOR
Glottis (closed)
Cuneiform cartilage
Aryepiglottic fold
Vestibular fold
Vocal fold
Epiglottis
Root of tongue
ANTERIOR

Tracheobronchial Tree

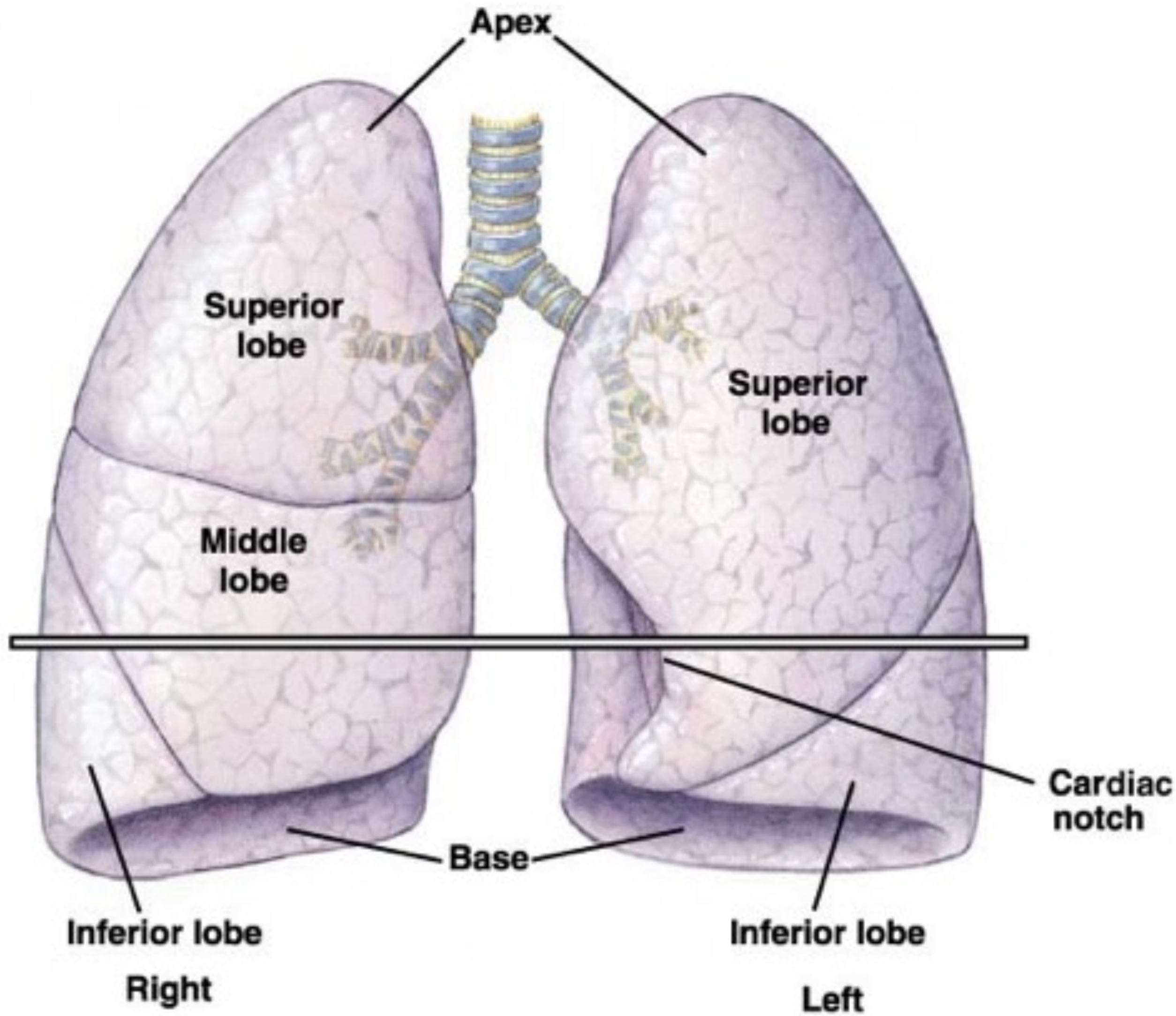
- Divides 23 times
- Conducting zone- 16 divisions
  - Trachea to terminal bronchioles which is ciliated for removal of debris
  - Passageway for air movement
  - Cartilage holds tube system open and smooth muscle controls tube diameter
- Respiratory zone
  - Respiratory bronchioles to alveoli
  - Site for gas exchange

Tracheobronchial Tree



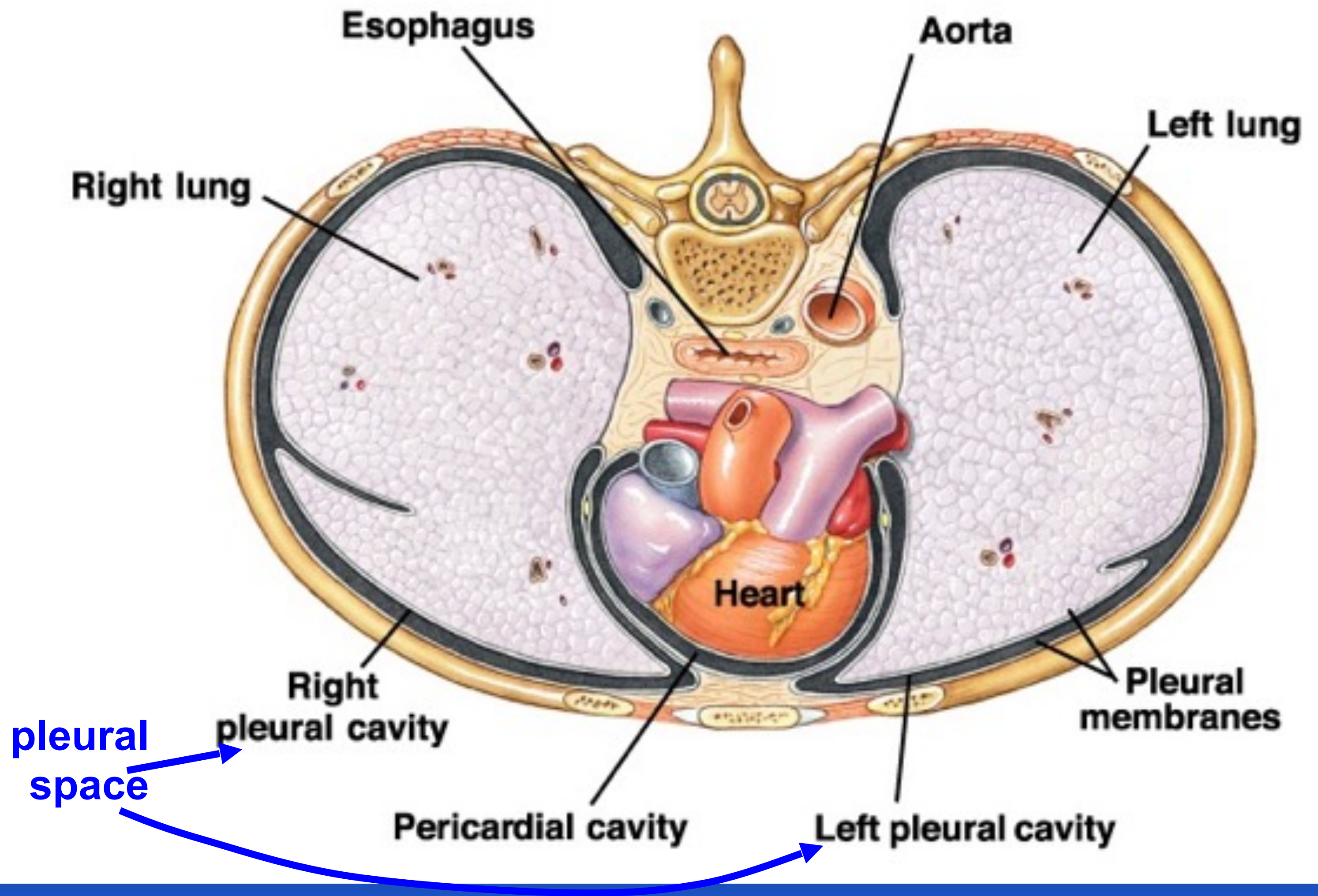
(c) External anatomy of lungs

Externally, the right lung is divided into three lobes and the left lung into two.

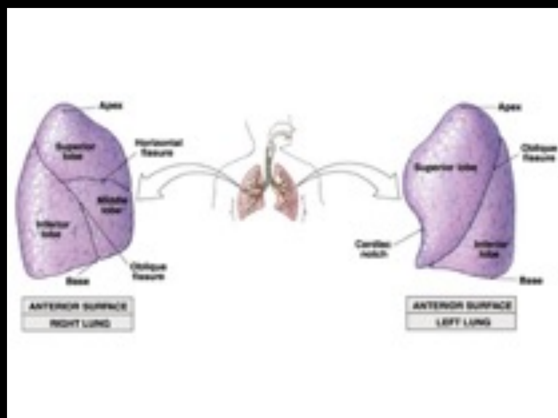


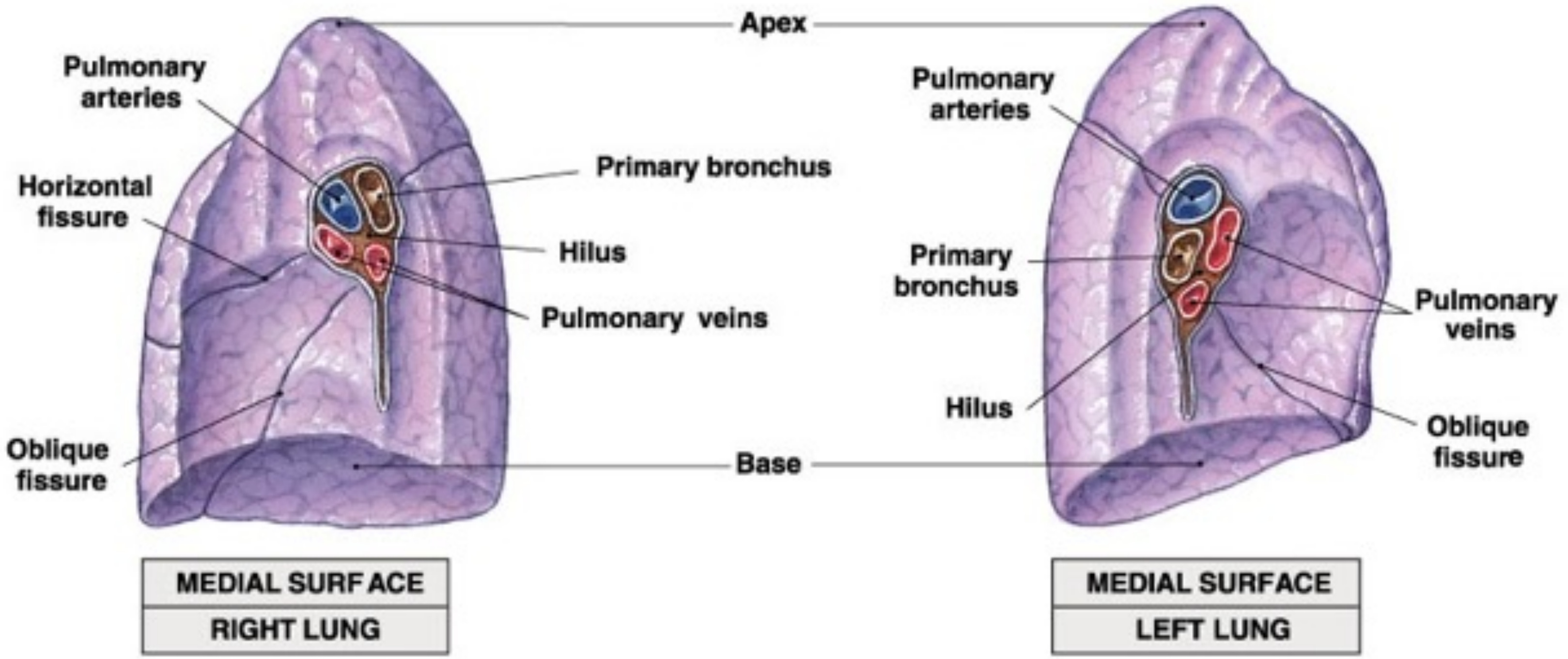
Sectional view of chest (Thoracic Cavity)

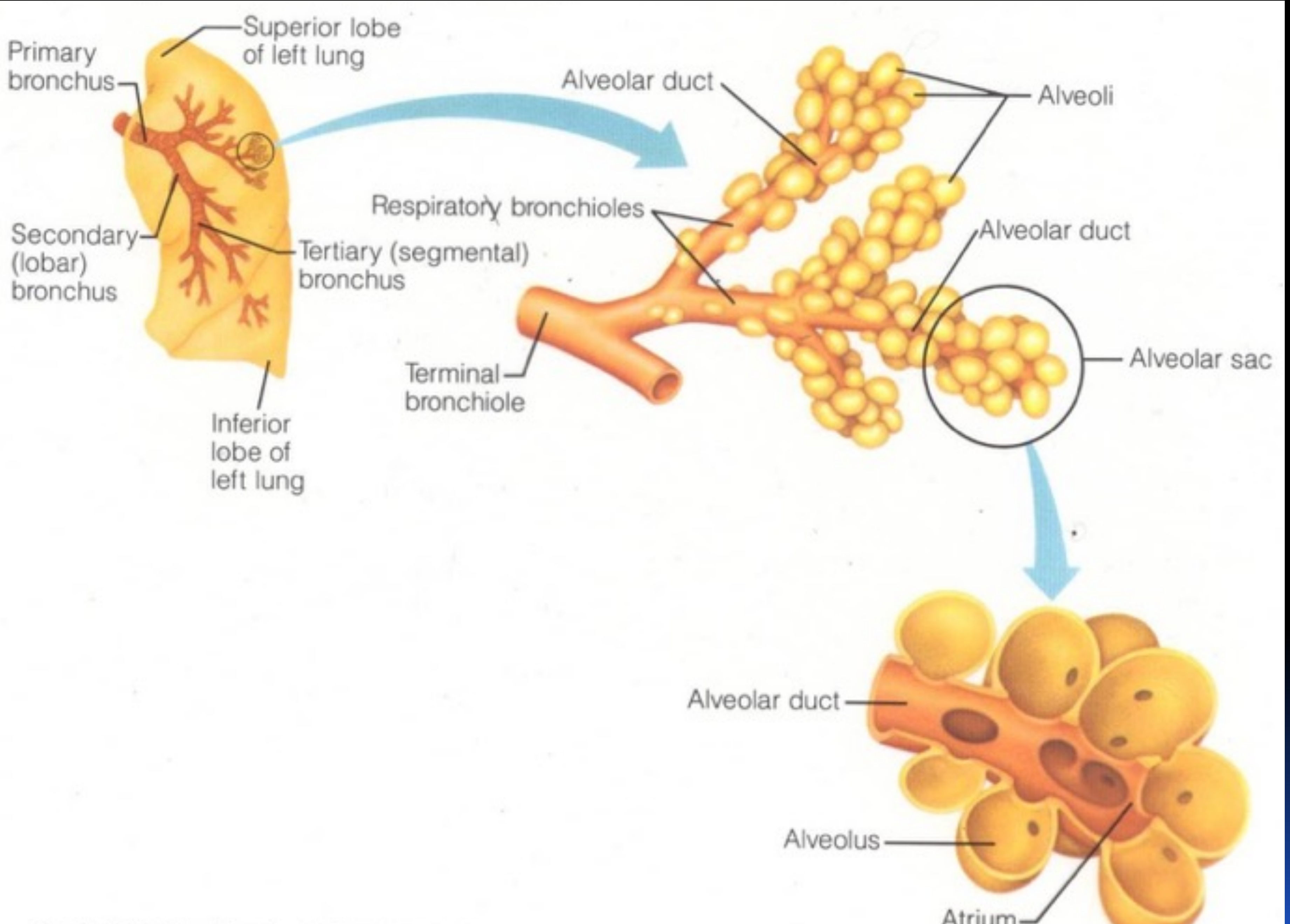
Each lung is enclosed in two pleural membranes. The pleural fluid and space are much smaller than illustrated. The esophagus and aorta pass through the thorax between the pleural sacs.



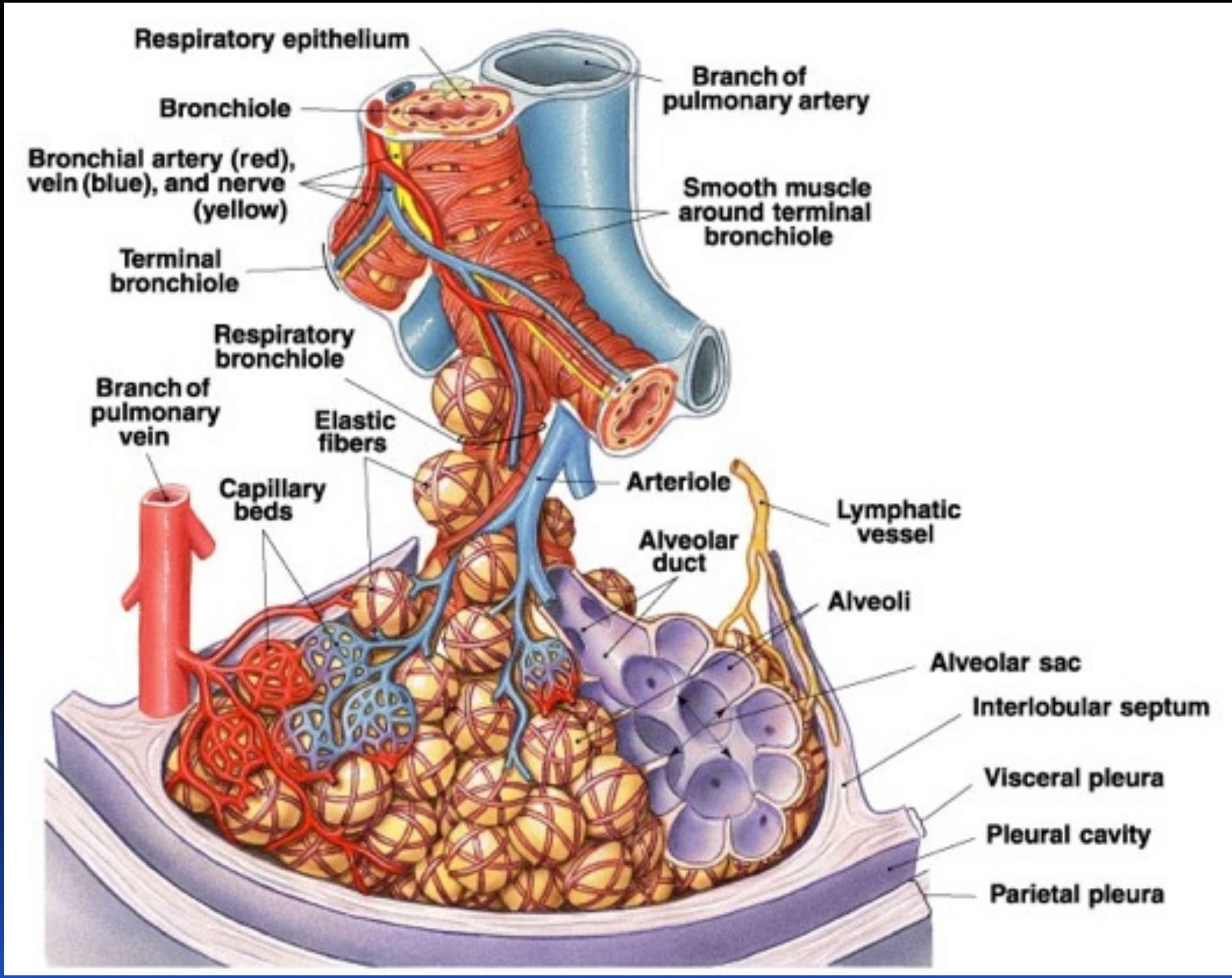
Lungs


Apex
Horizontal fissure
Oblique fissure
Base
ANTERIOR SURFACE
RIGHT LUNG
Apex
Oblique fissure
Superior lobe
Cardiac notch
Base
ANTERIOR SURFACE
LEFT LUNG

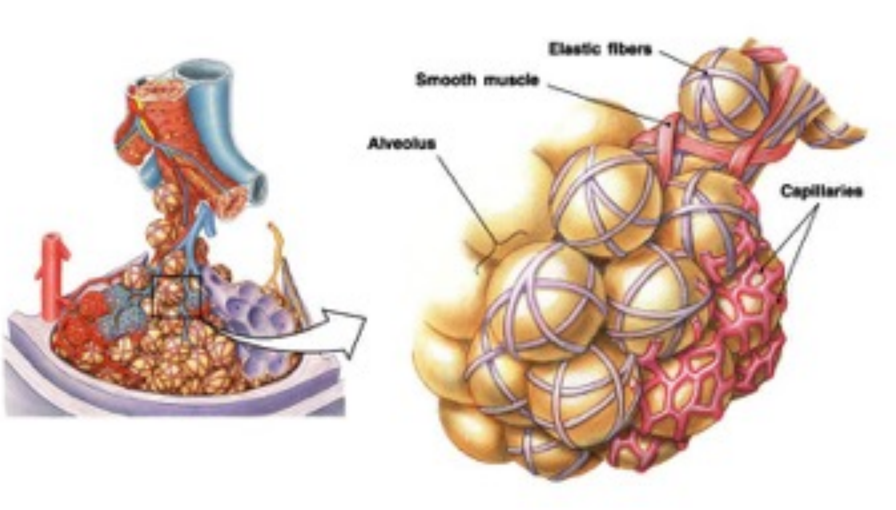

Apex
Pulmonary arteries
Horizontal fissure
Primary bronchus
Hilus
Pulmonary veins
Oblique fissure
Base
MEDIAL SURFACE
RIGHT LUNG
Pulmonary arteries
Primary bronchus
Hilus
Pulmonary veins
Oblique fissure
MEDIAL SURFACE
LEFT LUNG

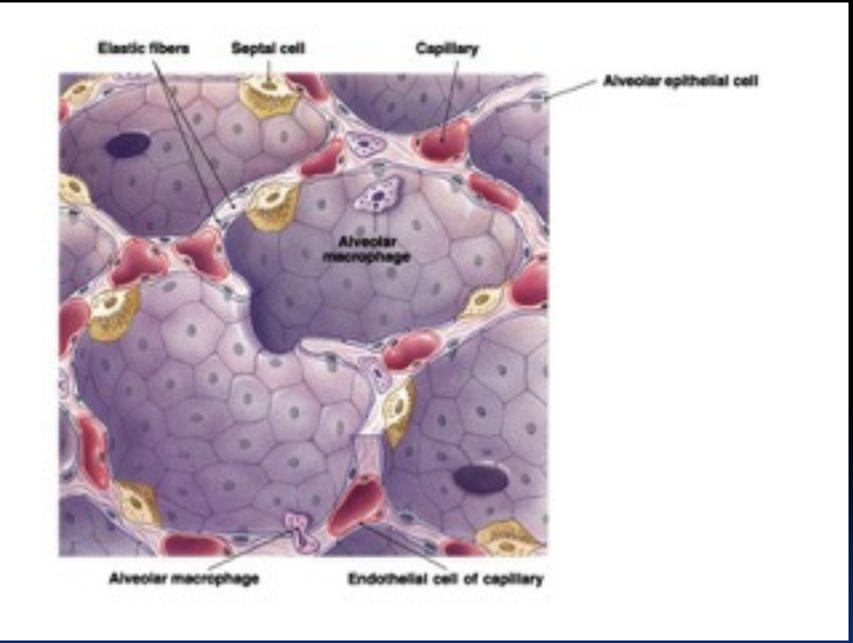

Superior lobe of left lung
Primary bronchus
Secondary (lobar) bronchus
Tertiary (segmental) bronchus
Inferior lobe of left lung
Alveolar duct
Alveoli
Respiratory bronchioles
Alveolar duct
Alveolar sac
Terminal bronchiole
Alveolar duct
Alveolus
Atrium

Bronchioles and Alveoli



Alveolus and Respiratory Membrane



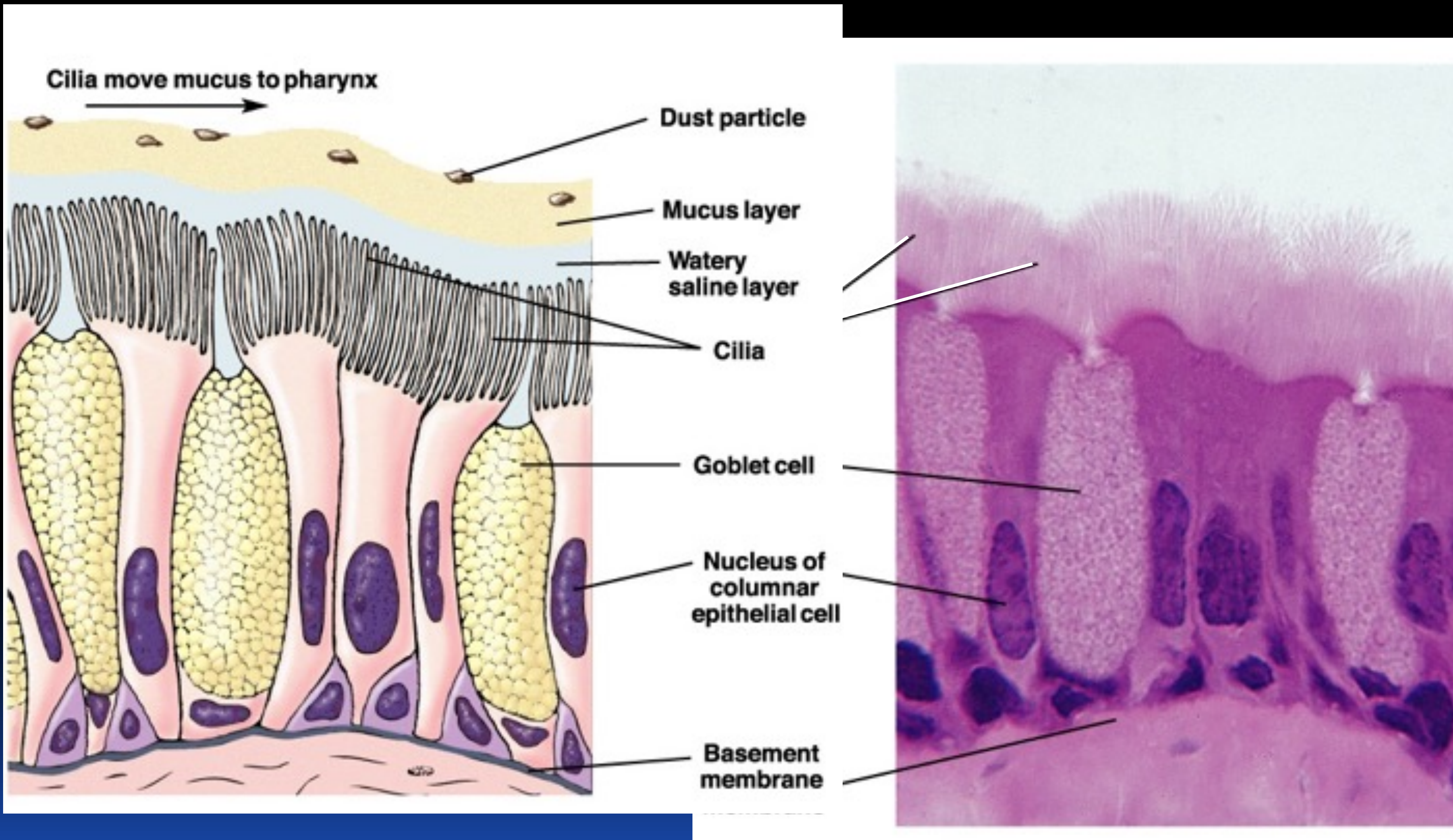


300 million alveoli

0.33mm diameter

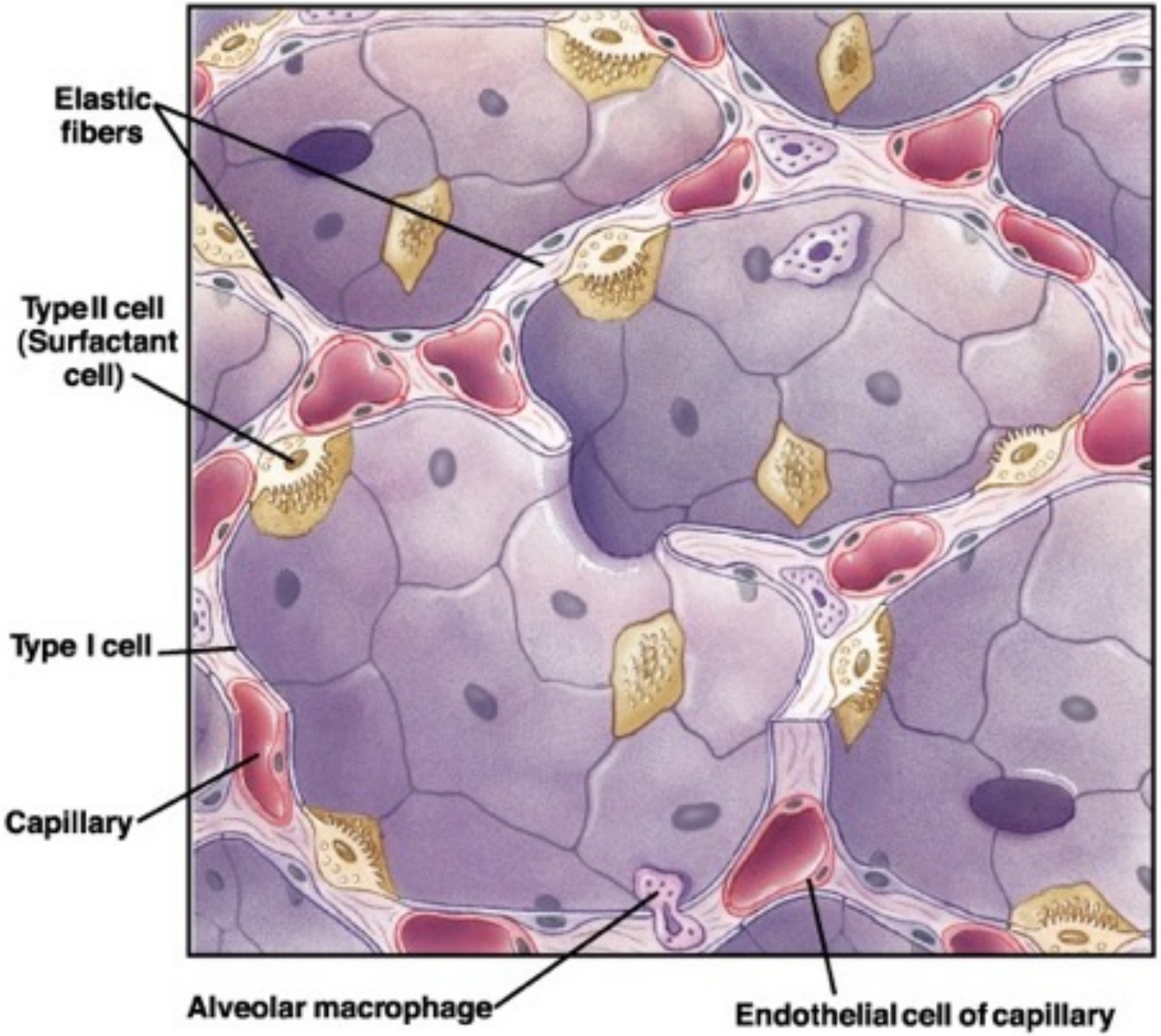
0.5 micron thickness

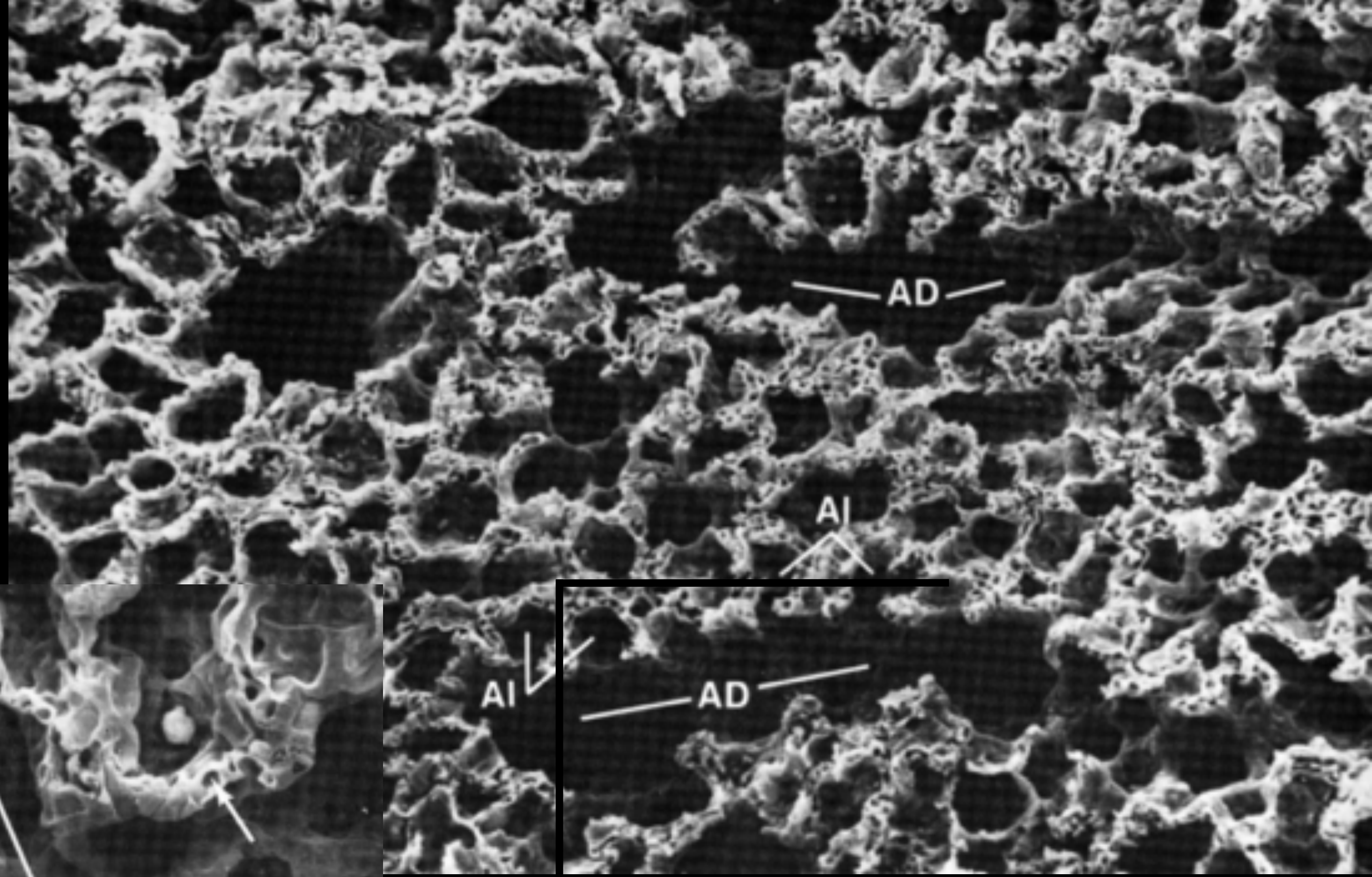
Large surface area- 70m^2

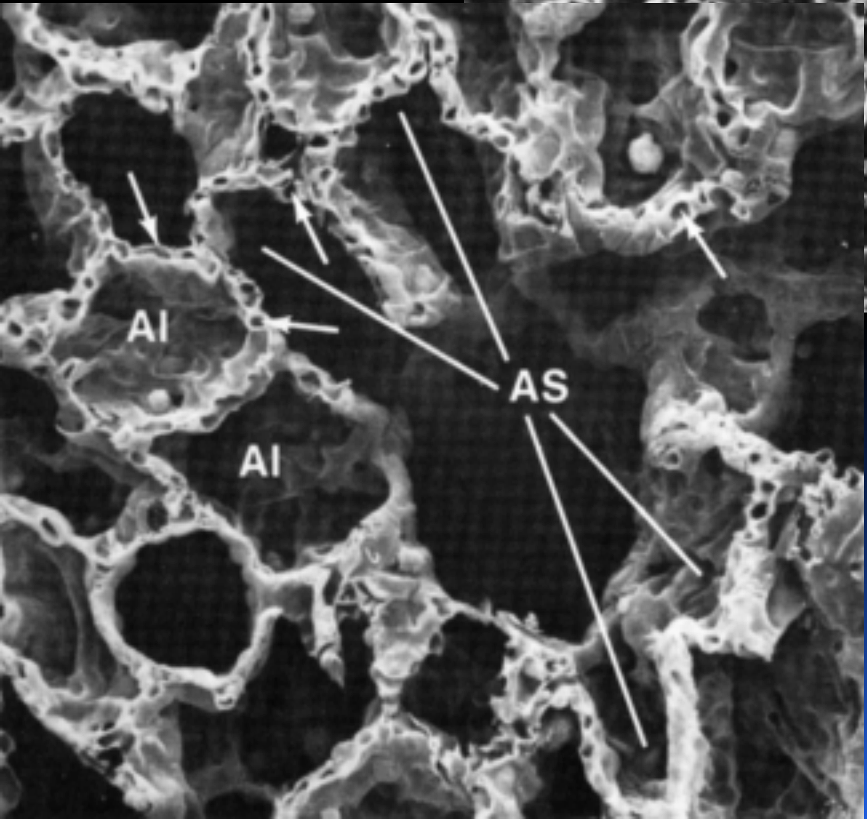

Cilia move mucus to pharynx
Dust particle
Mucus layer
Watery saline layer
Cilia
Goblet cell
Nucleus of columnar epithelial cell
Basement membrane

Alveolar structure

The alveoli are composed of type I cells for gas exchange and type II cells that synthesize surfactant. Alveolar macrophages ingest foreign material that reaches the alveoli.




AD
AI
AI
AD


AI
AS
AI


IS
Ca
Er
IP
AP
IP
AP
IP

Bronchial innervation

- Terminal bronchioles have high smooth muscle content
- ANS
  - Parasympathetic- Cholinergic bronchoconstriction
  - Sympathetic- adrenergic bronchodilation
- Non-cholinergic, non-adrenergic
  - VIP- mediates vasodilation
  - Leukotreines, Substance P- vasoconstriction

Other cellular components

- Macrophages
- Lymphocytes
- APUD cells
- Mast cells

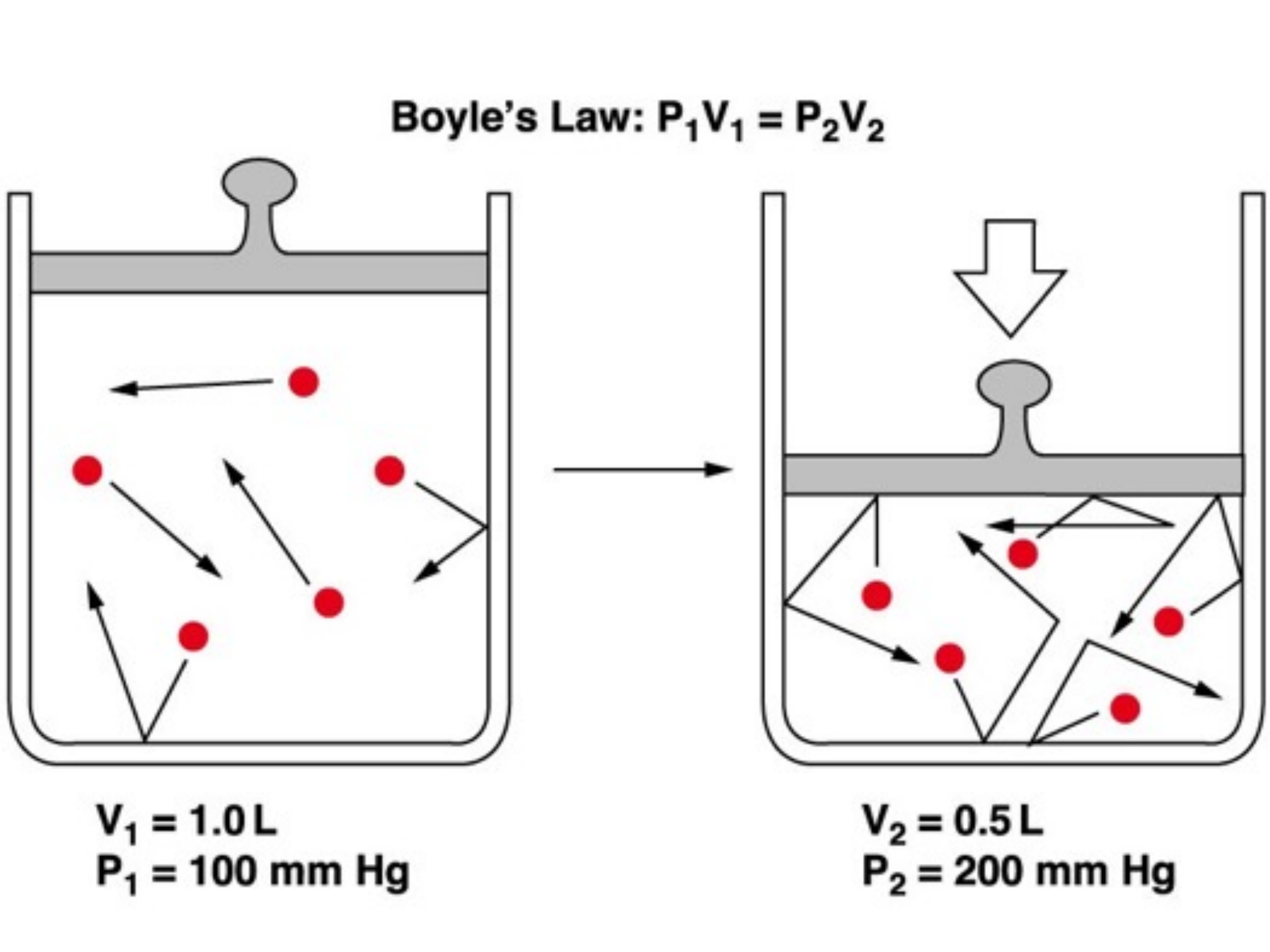
Non respiratory function of respiratory tract

- Olfaction
- Air conditioning
- Voice
- Defense:
  - Immune
    - Cellular
    - secretory
  - Reflexes
    - Cough
    - sneeze
- Metabolic
  - Secretion
  - conversion
- Circulatory
  - Filter
  - ‘reservoir’

Basic physics of gases

PHYSICAL PRINCIPLES OF GAS EXCHANGE
Properties of GASES

Boyle's Law: Presssure ∝ 1/V



Partial Pressure = pressure exerted by any one gas in a mixture

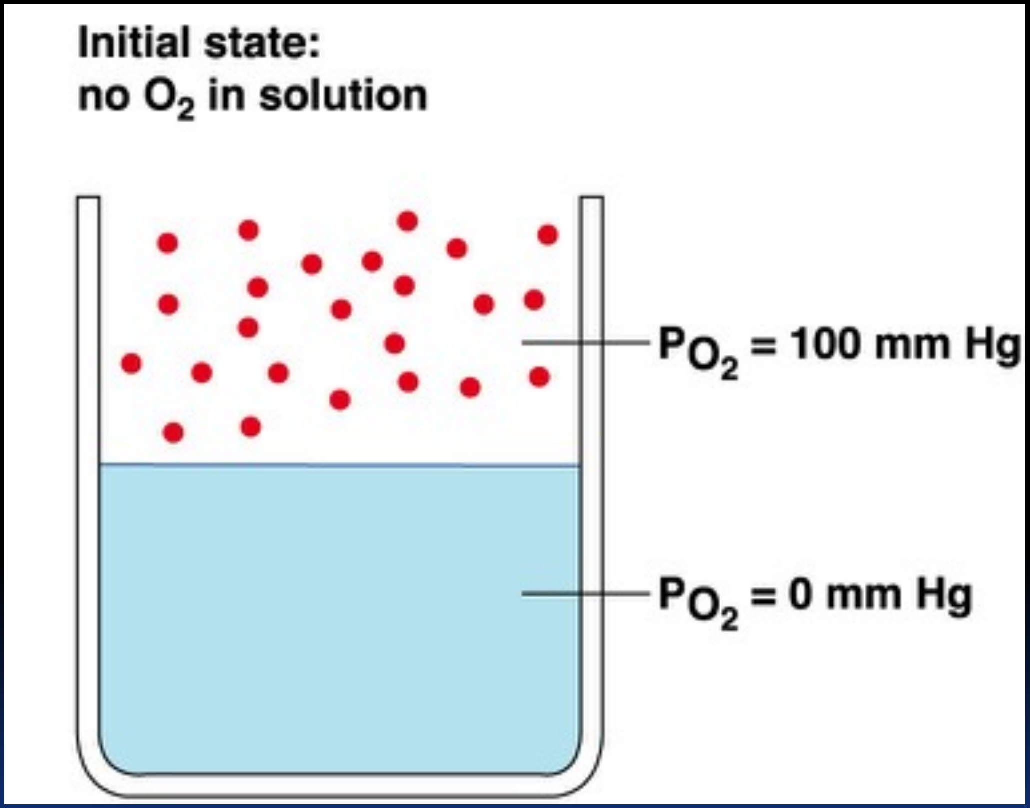
Partial Pressure = total pressure x fraction of total represented by the gas (Dalton's law), i. e.,

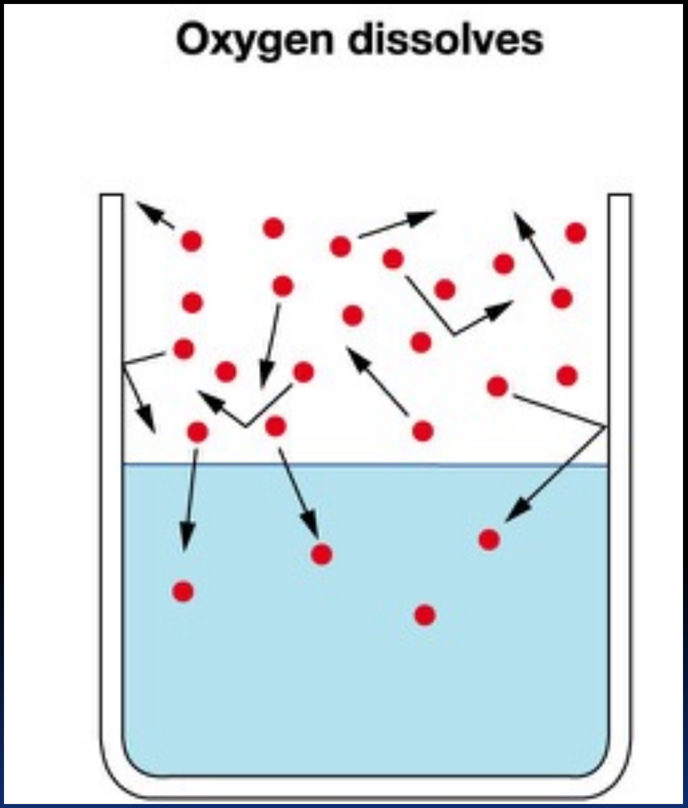
$$P_{gas} = P_{total} \times f_{gas}$$

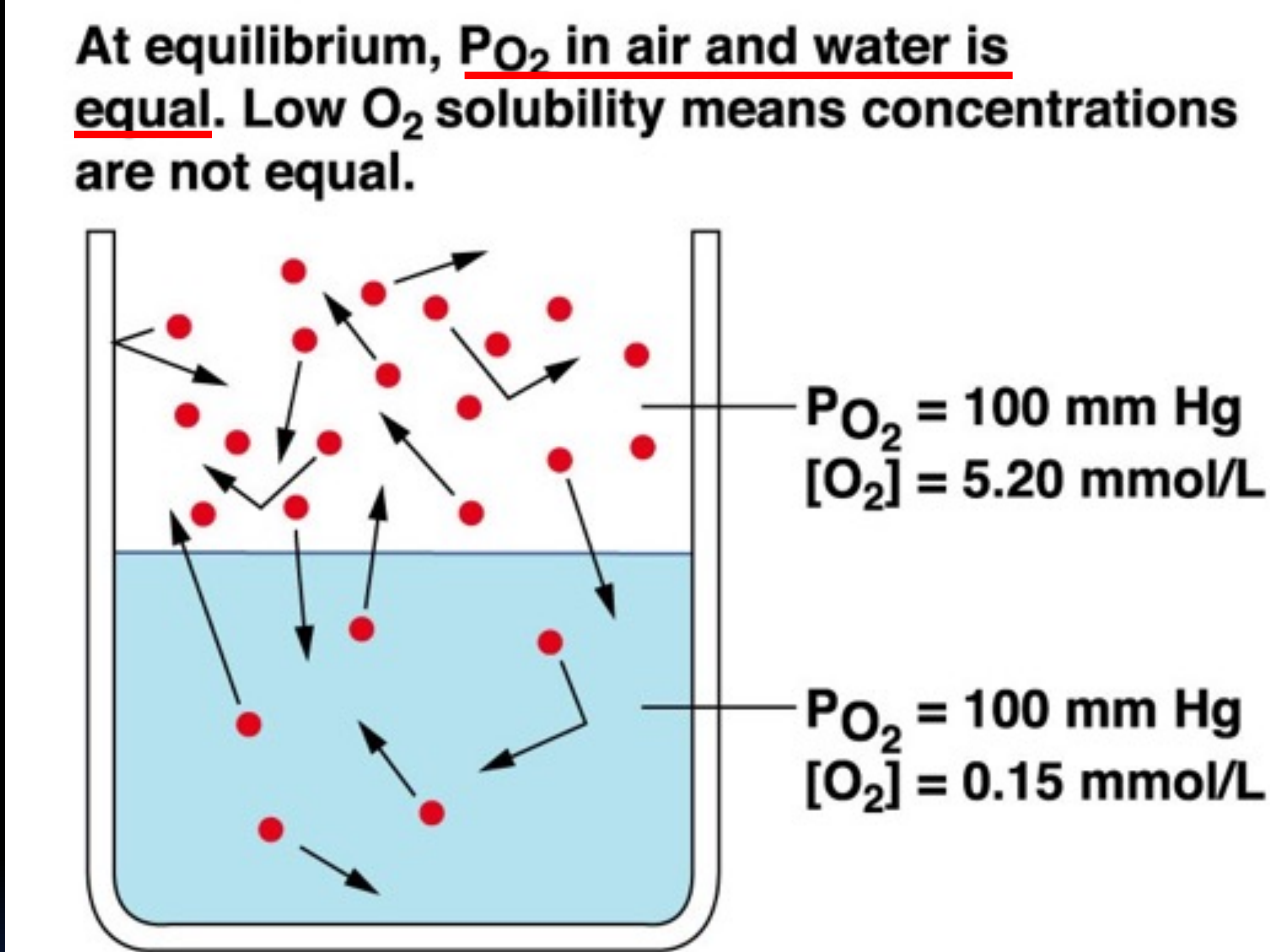
Composition of Air

	Dry atm. air %		Partial pressure mm Hg	Accounting for water vapor pressure = 47mmHg mm Hg
O_2	20.9	(0.21x760)	160	149
CO_2	0.04	(0.0004x760)	0.3	0.3
N_2 & other	79	(0.79x760)	600	564
total	100		760	713

Gases in solution



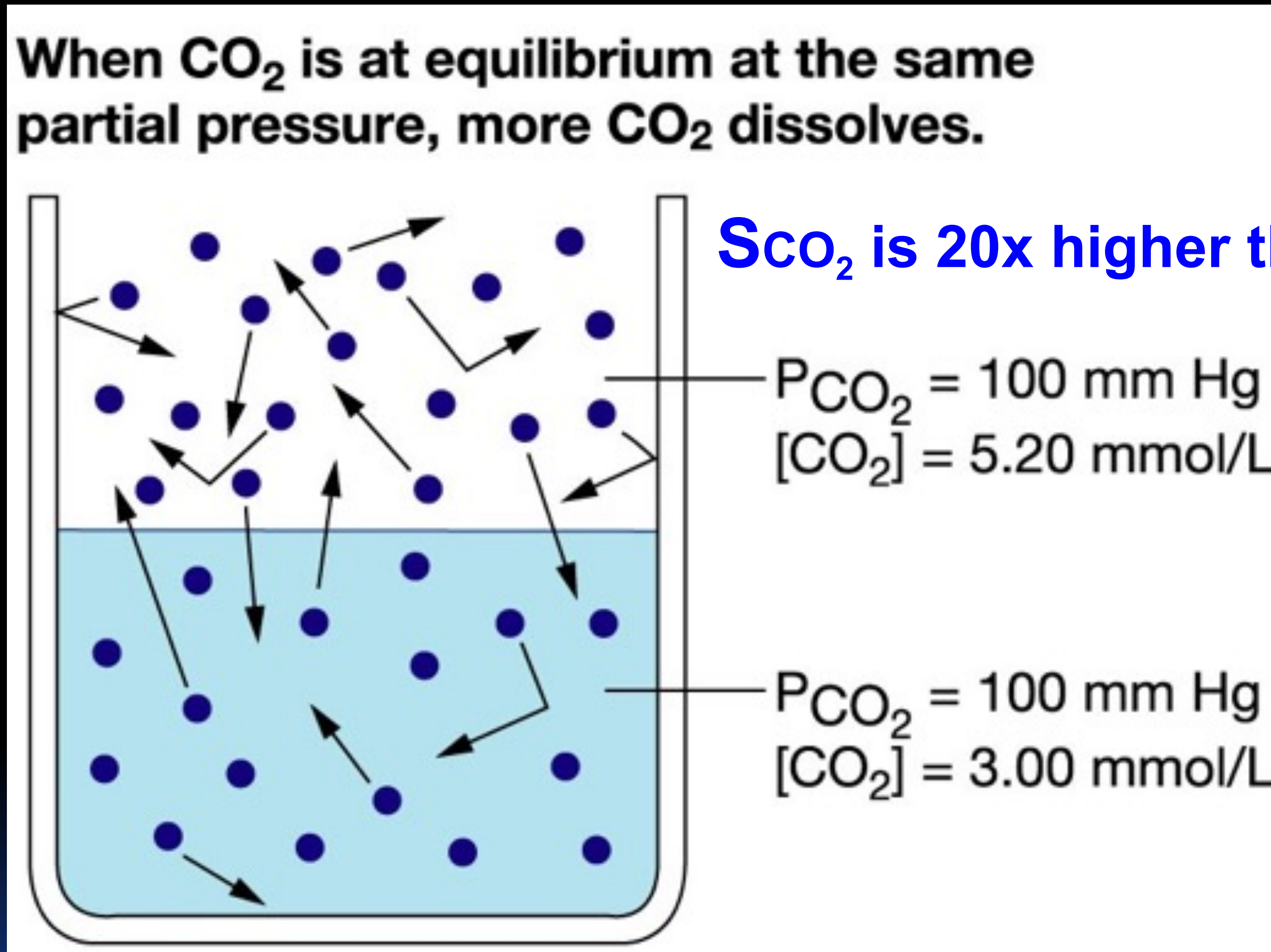




Henry's Law:

Conc. of gas in solution = partial pressure of gas X solubility coefficient

e.g., $[O_2]$ in moles/L: $[O_2] = P_{O_2} \times S_{O_2}$

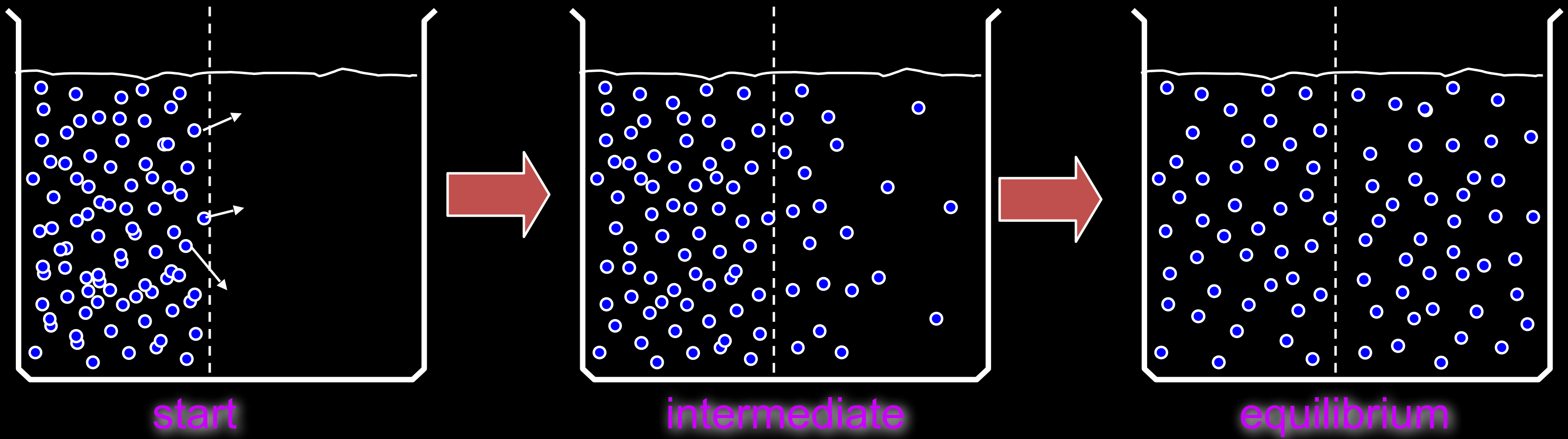


S_{CO_2} is 20x higher than S_{O_2}

mm Hg
n Hg

Therefore [Gas] depends on both P_{gas} and S_{gas}

What is DIFFUSION?

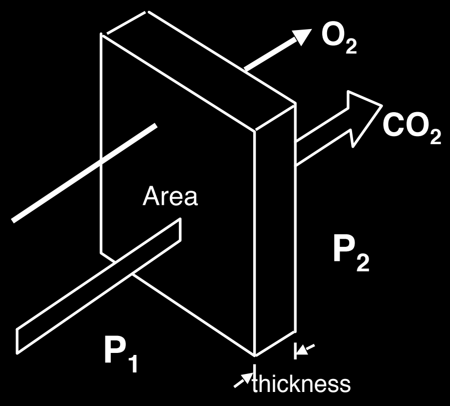


How fast is DIFFUSION?

Diffusion distance (µm)	Time required for diffusion
1	0.5 msec
10	50 msec
100	5 seconds
1,000 (1 mm)	8.3 minutes
10,000 (1 cm)	14 hours

Fick's 1st Law of Diffusion

Rate of diffusion = $dm/dt = D \cdot A \cdot \frac{dC}{dx}$



A = area available for diffusion

C = concentration of the substance

x = the distance for the diffusion

D = the diffusion coefficient

$$\text{Rate of Diffusion} \propto \frac{\text{Area x Concentration}}{\text{Distance}}$$

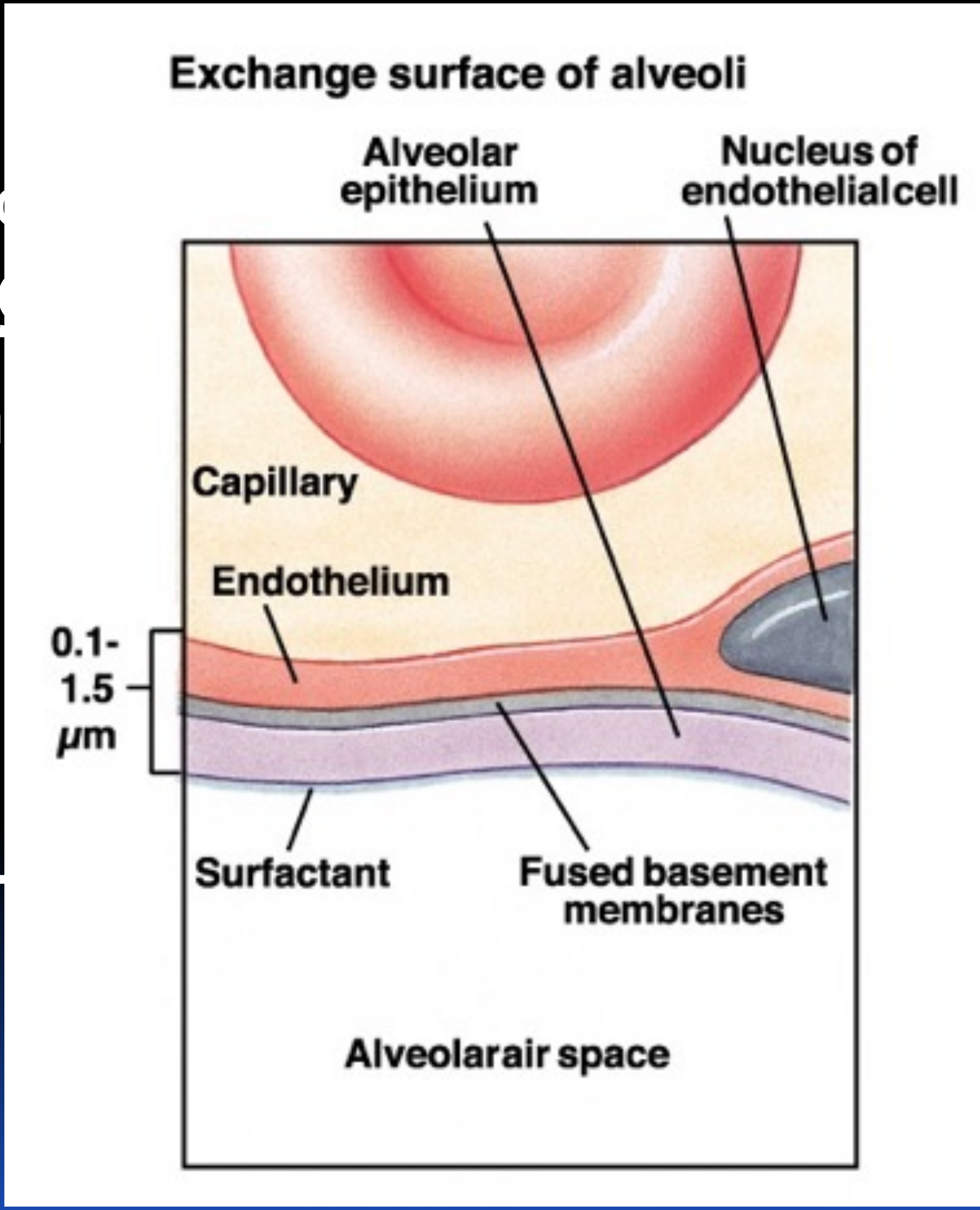
The strategy in the evolution of the respiratory apparatus

- ↑ available surface area
- ↓ distance required for diffusion (i.e., thickness)

Total **AREA** available f

diffusion of gases is **lar**

in human ~50-100 m



Diffusion **PATH LENGTH**

very **small**, <1 µm

- STPD
  - Standard temp, pressure, dry
  - 00 C,760mm Hg,
- BTPS
- ATPS

Other Gas laws

- Charles's law
  - If pressure constant,
  - $T \propto V$
- **General Gas law**
  - **PV/T = Constant**

Ventilation

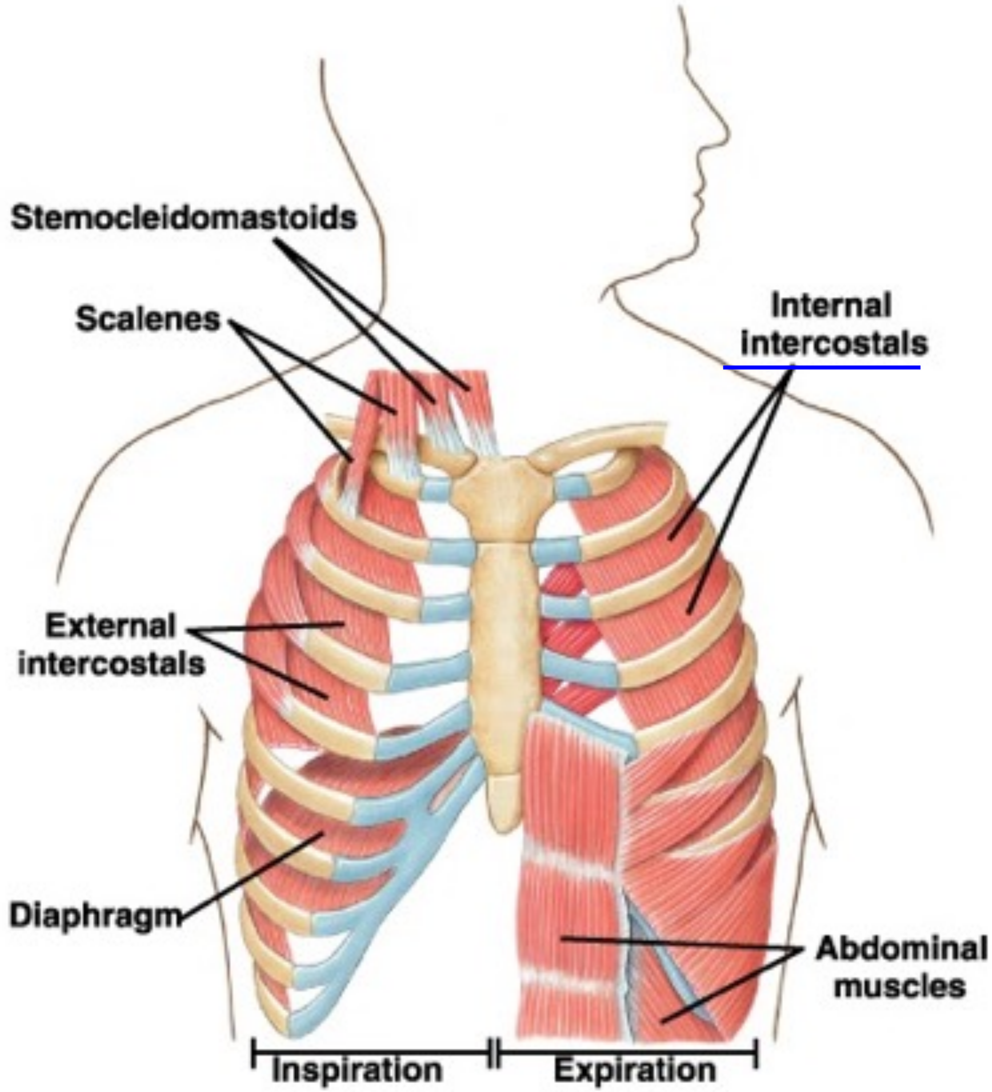
- The process of breathing in and out

Ventilatory apparatus

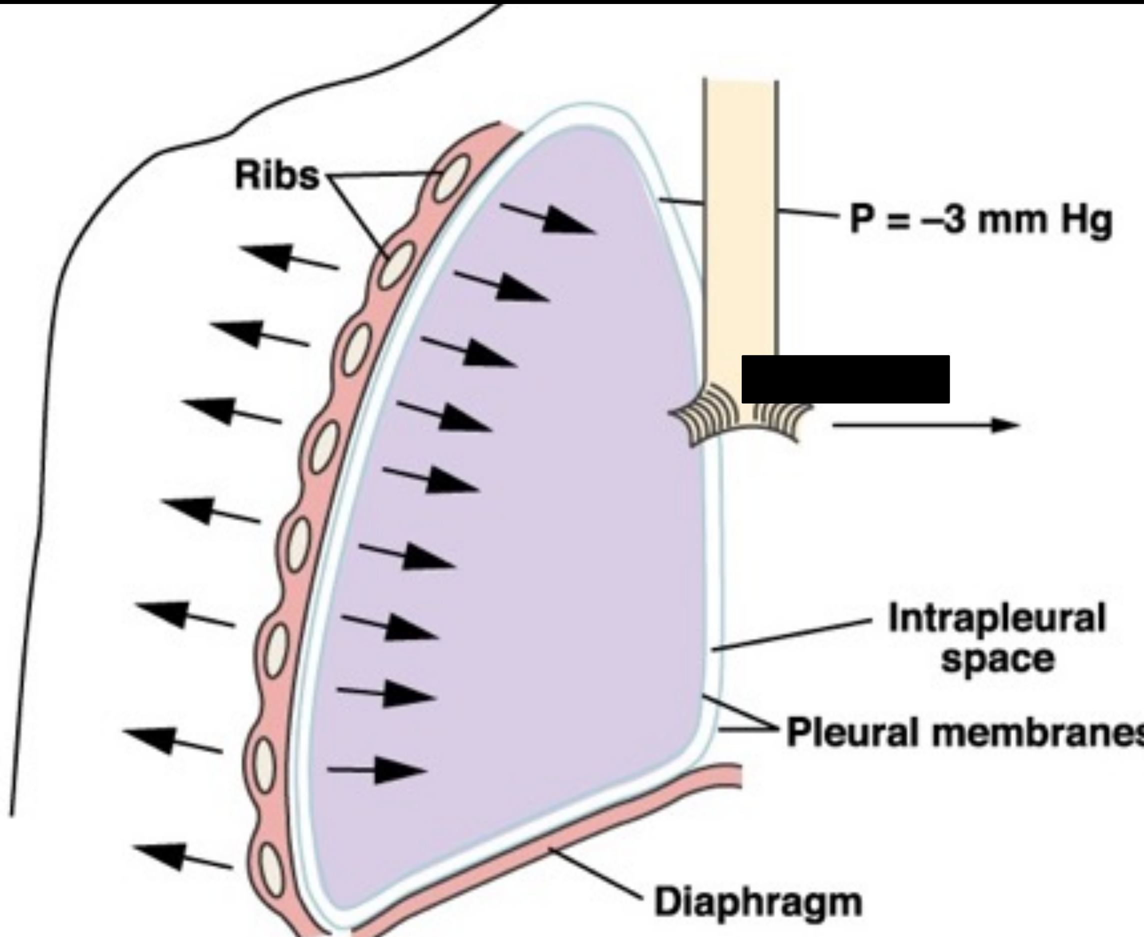
- Chest wall
  - Ribs
  - Intercostals
- The lungs
- The pleural space
- Muscles of respiration
  - Inspiratory
  - Expiratory

Muscles used for ventilation

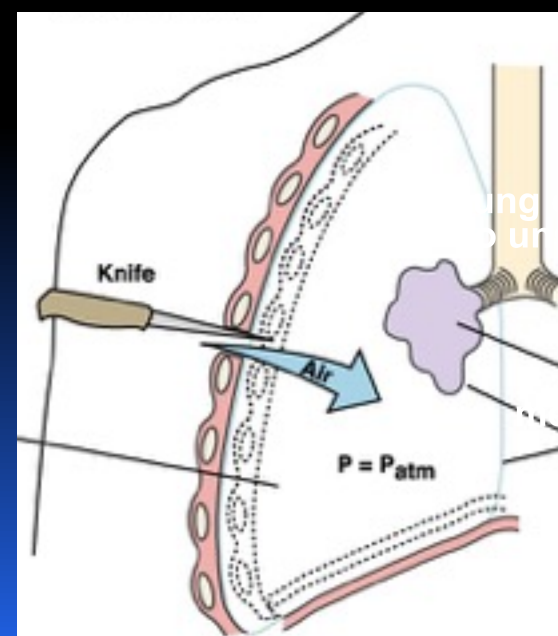
The muscles of inspiration include the diaphragm, external intercostals, sternocleidomastoids, and scalenes. The muscles of expiration include the internal intercostals and the abdominals.



Normal Lung at rest



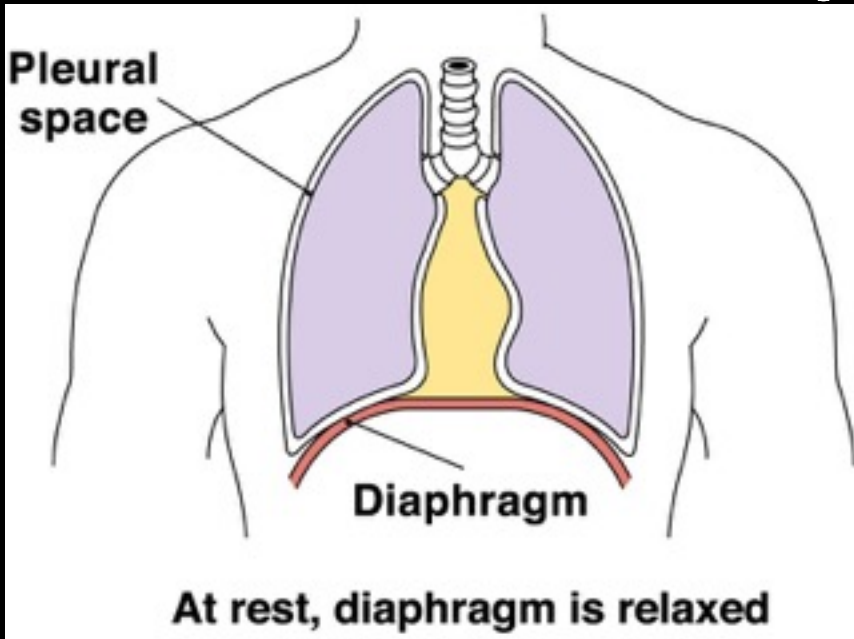
Pneumothorax

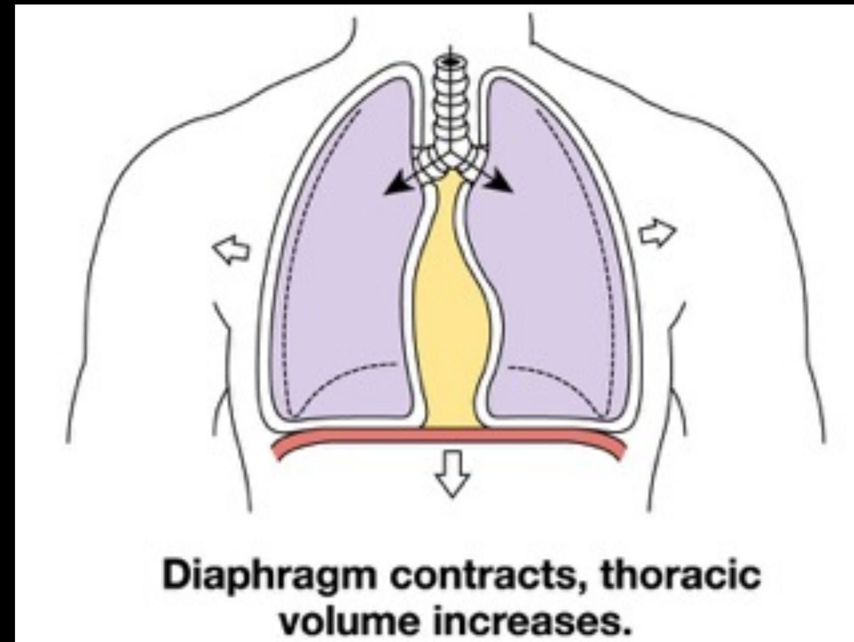


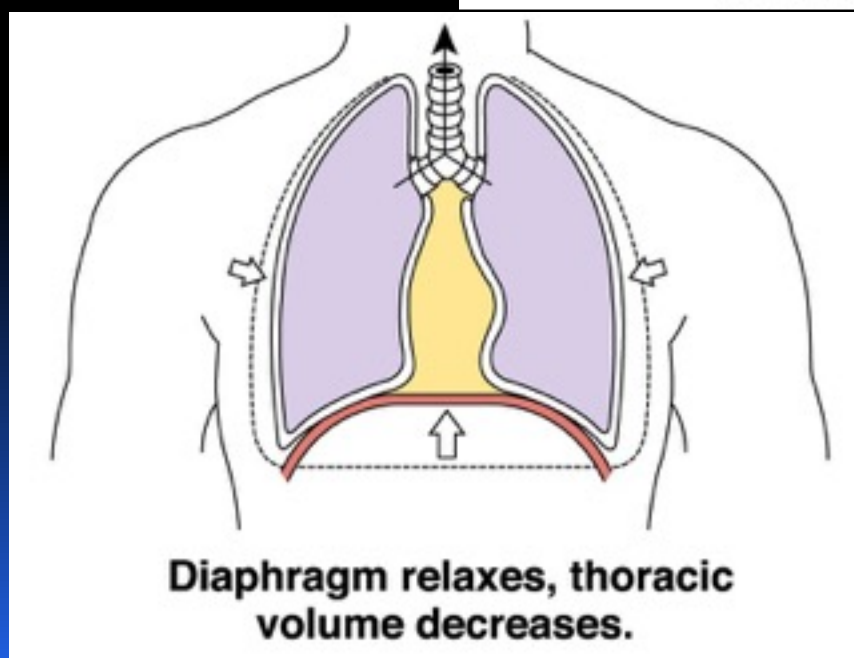
ng ollapses
o un tretched
size

Pleural
mbranes

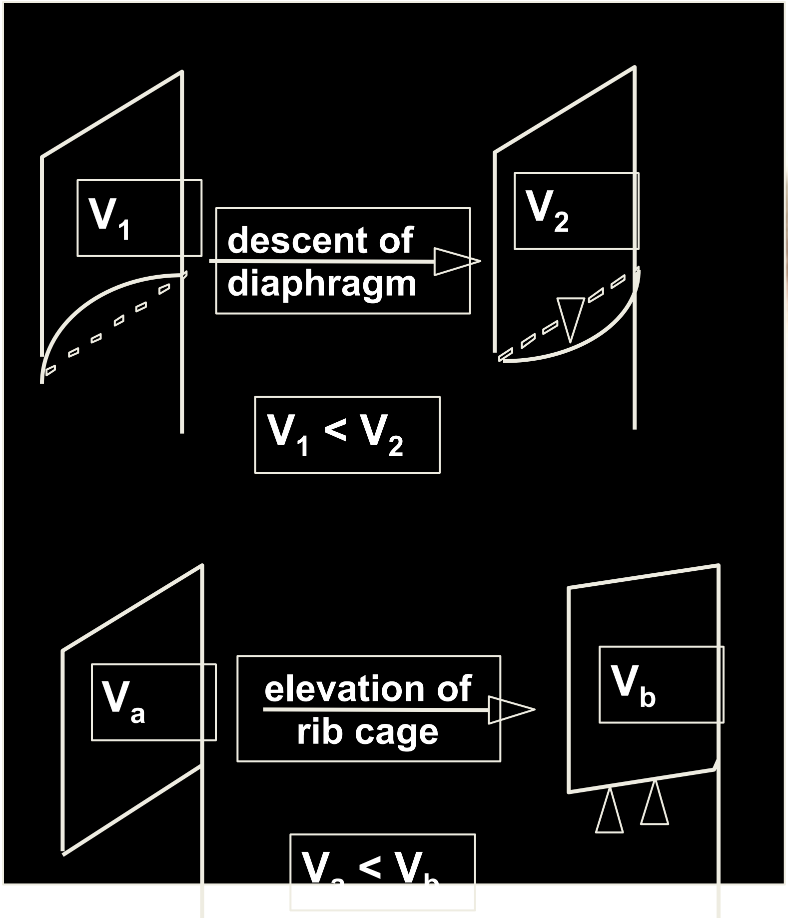
Quiet breathing- diaphragmatic

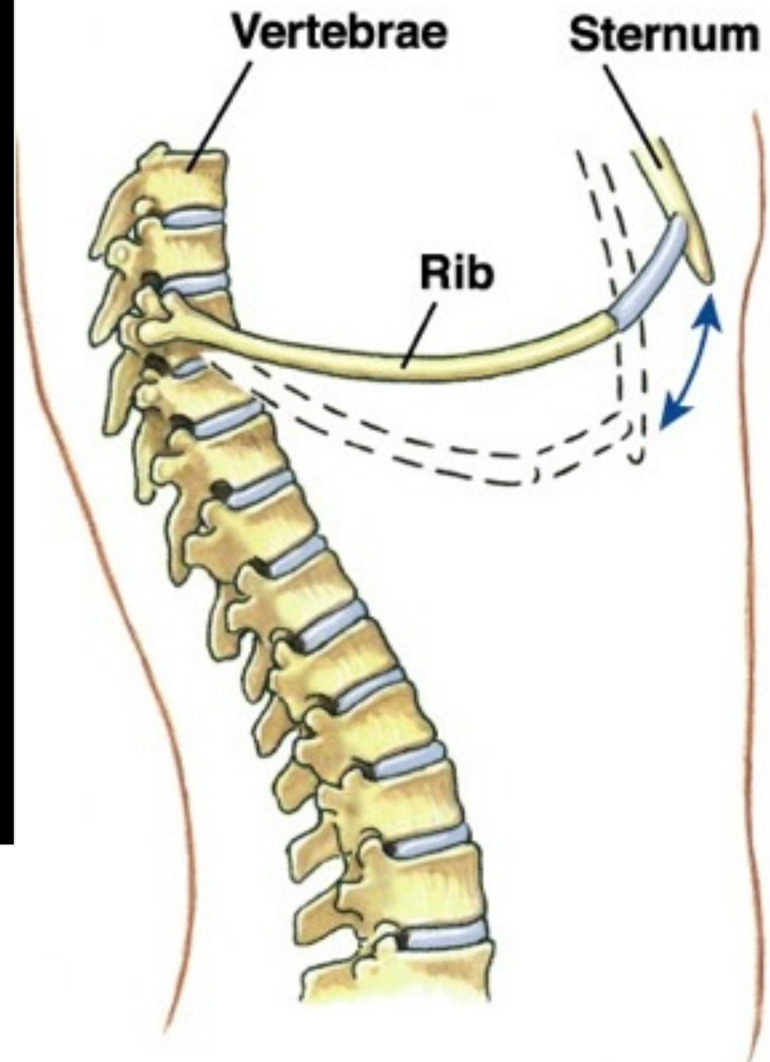




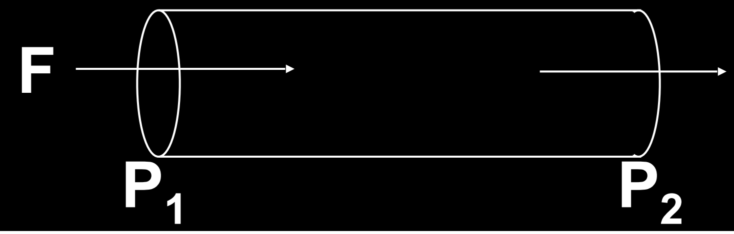


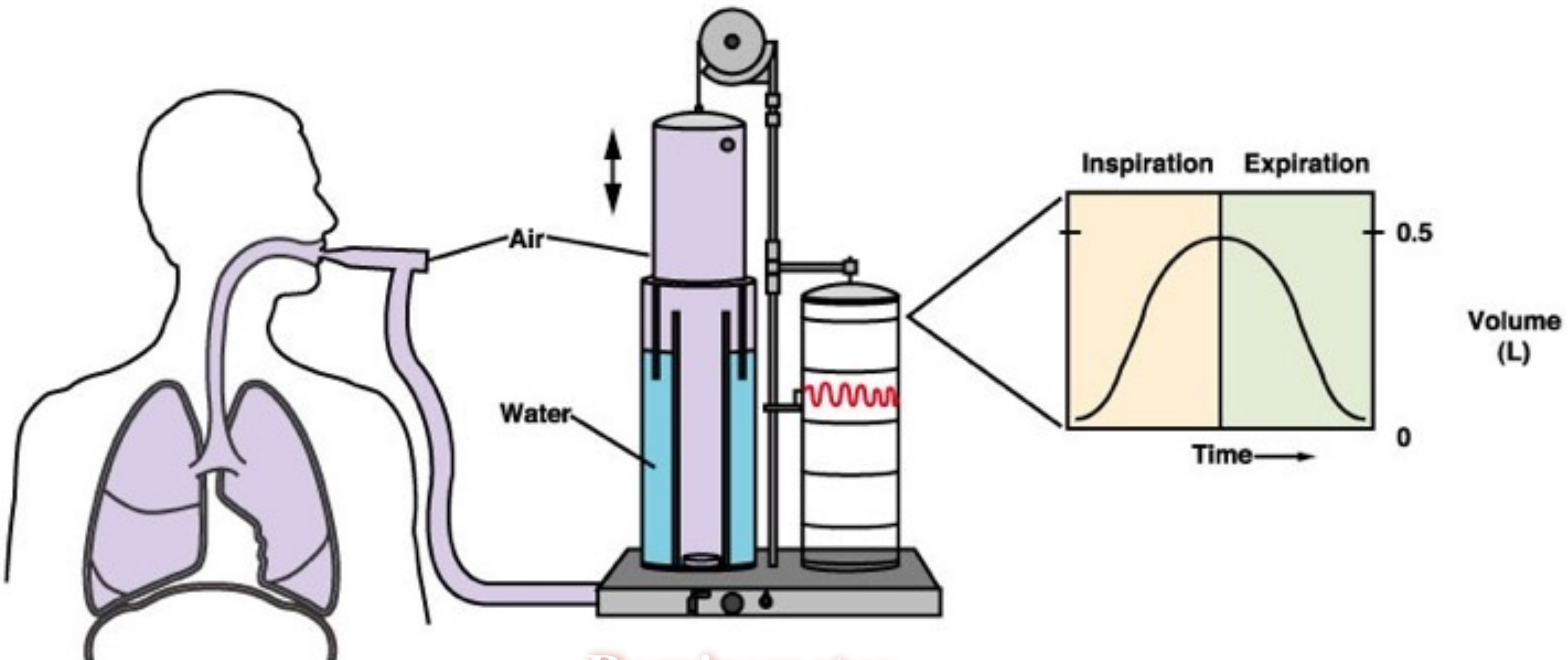
“Pump handle" motion increases anterior-posterior dimension of rib cage



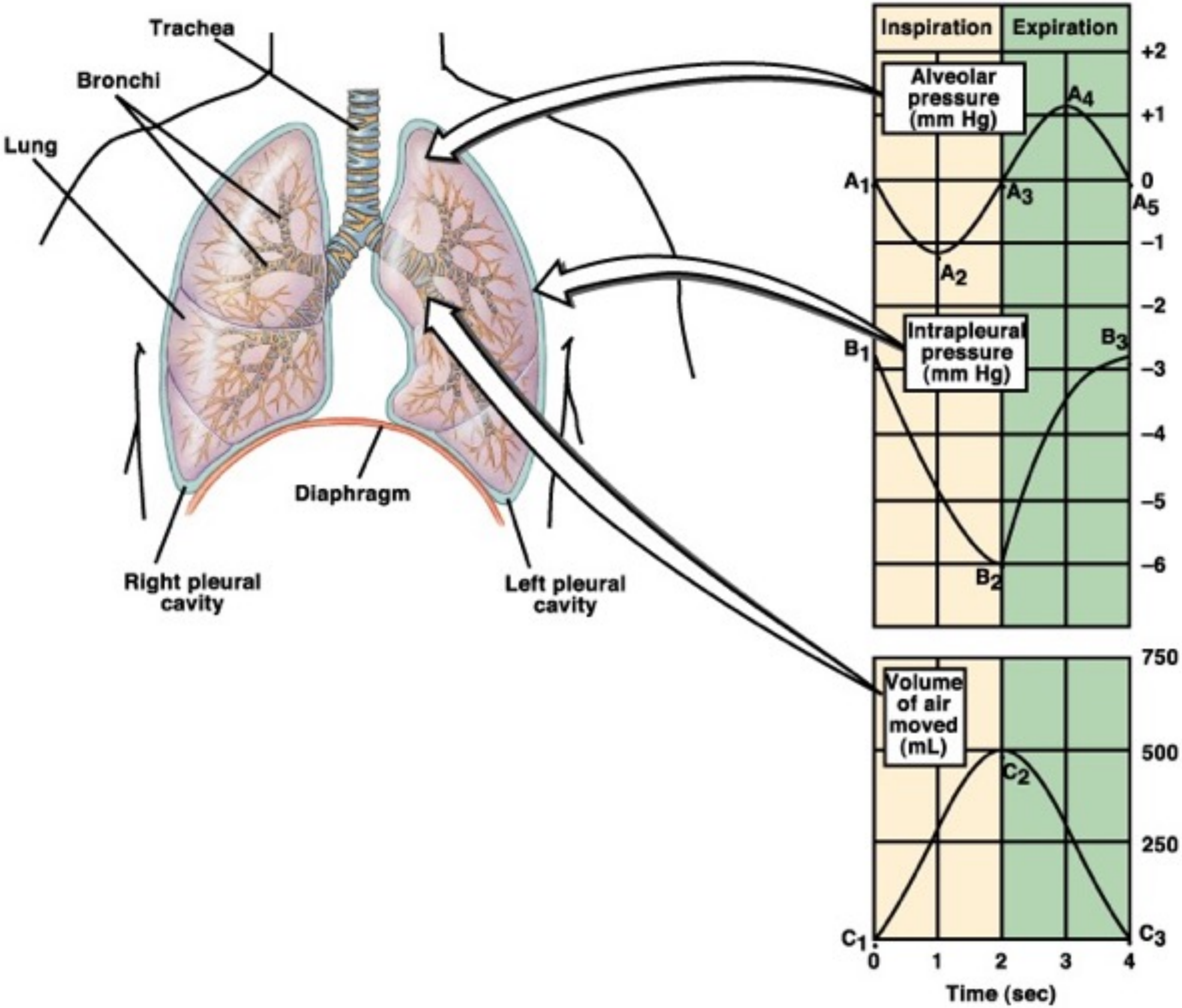


Flow (F) of air



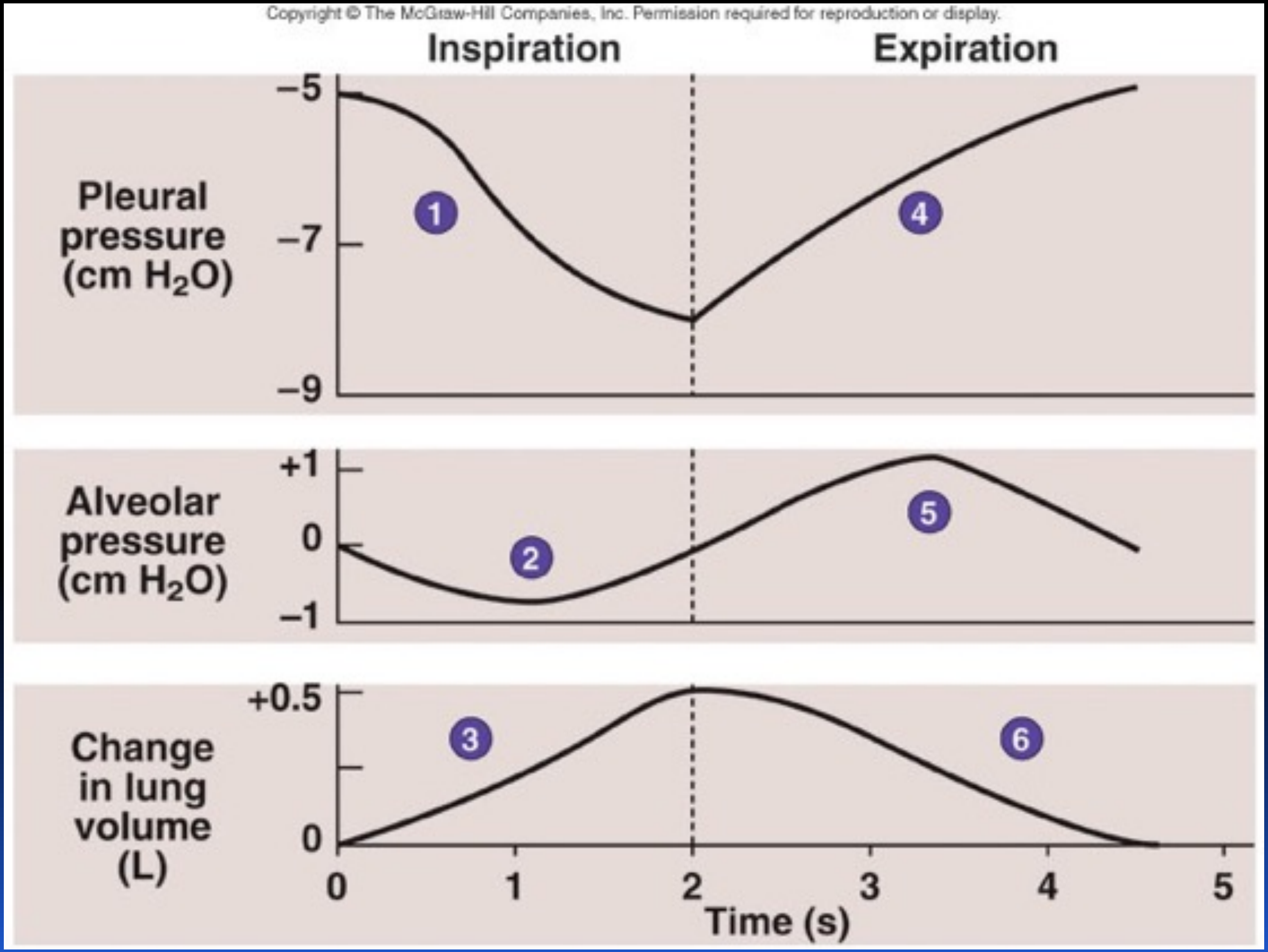


Respirometer

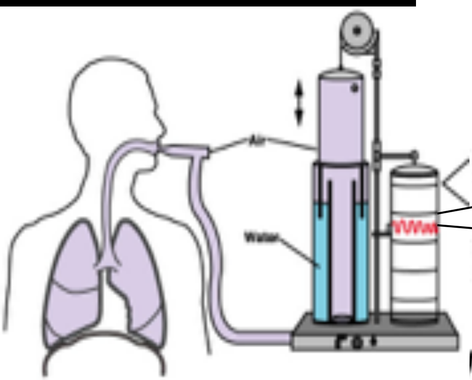


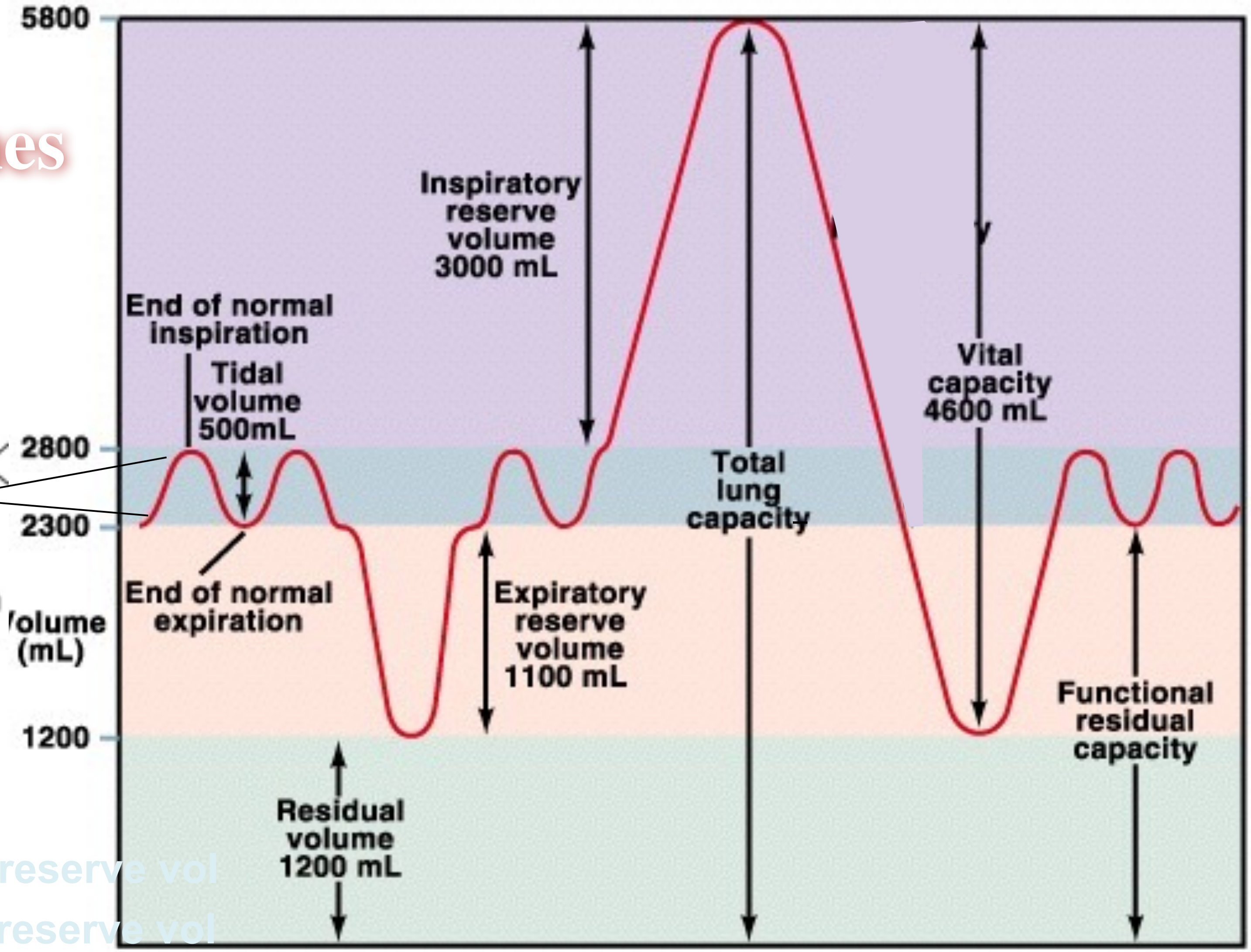
Trachea
Bronchi
Lung
Diaphragm
Right pleural cavity
Left pleural cavity
Inspiration
Expiration
Alveolar pressure (mm Hg)
Intrapleural pressure (mm Hg)
Volume of air moved (mL)
A1
A2
A3
A4
A5
B1
B2
B3
C1
C2
C3
+2
+1
0
−1
−2
−3
−4
−5
−6
750
500
250
0
1
2
3
4
Time (sec)

Normal Breathing Cycle



Lung Volumes





V_T = Tidal volume

ERV = expiratory reserve vol

IRV = inspiratory reserve vol

RV = residual vol

FRC = functional residual capacity

Vital capacity

Total lung capacity

Minute Volume = $\dot{V}$ = V_T x resp. rate

e.g., 0.5 L/breath x 12 breaths/min = 6 L/min

Pulmonary Volumes

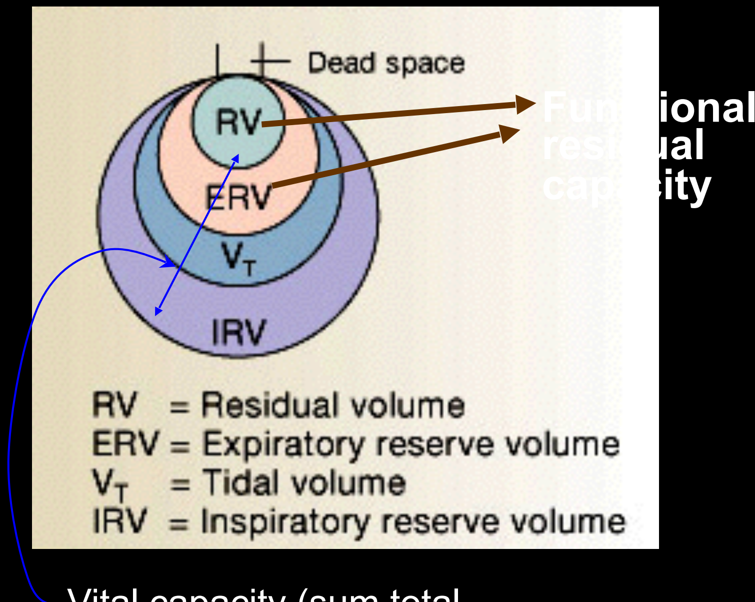
- Tidal volume
  - Volume of air inspired or expired during a normal inspiration or expiration
- Inspiratory reserve volume
  - Amount of air inspired forcefully after inspiration of normal tidal volume
- Expiratory reserve volume
  - Amount of air forcefully expired after expiration of normal tidal volume
- Residual volume
  - Volume of air remaining in respiratory passages and lungs after the most forceful expiration

Pulmonary Capacities

- Inspiratory capacity
  - Tidal volume plus inspiratory reserve volume
- Functional residual capacity
  - Expiratory reserve volume plus the residual volume
- Vital capacity
  - Sum of inspiratory reserve volume, tidal volume, and expiratory reserve volume
- Total lung capacity
  - Sum of inspiratory and expiratory reserve volumes plus the tidal volume and residual volume

Minute and Alveolar Ventilation

- Minute ventilation: Total amount of air moved into and out of respiratory system per minute
- Respiratory rate or frequency: Number of breaths taken per minute
- Anatomic dead space: Part of respiratory system where gas exchange does not take place
- Alveolar ventilation: How much air per minute enters the parts of the respiratory system in which gas exchange takes place



Vital capacity (sum total of all except RV)

Pulmonary volumes

		Males	Females	
Vital capacity	IRV	3000	1900	Inspiratory capacity
	V_T	500	500	
	ERV	1100	700	Functional residual capacity
Residual volume		1200	1100	
		5800 mL	4200 mL	

Factors affecting ventilation

- Lung compliance
- Surface tension
- Airway resistance
- Chest wall
- Regional differences

Work of Breathing

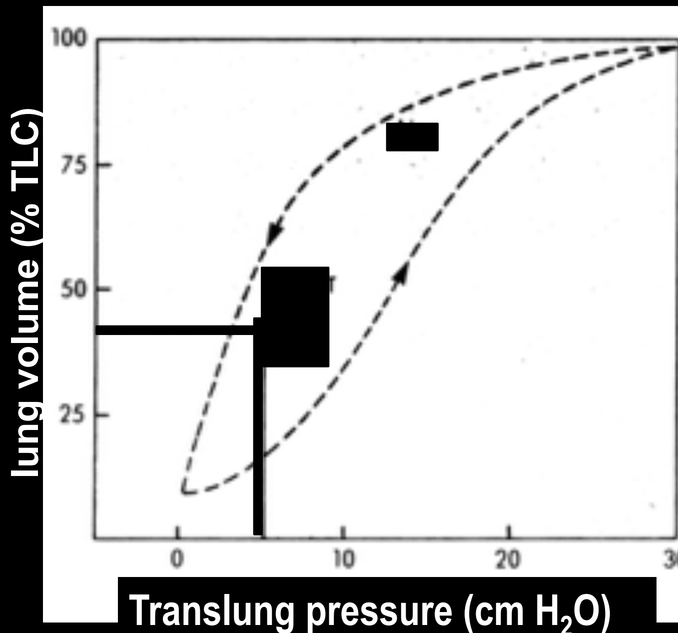
Compliance Work: force to expand lung against its elastic properties

Force to overcome viscosity of lung & chest wall

Airway Resistance Work: force to move air through airways

Compliance Work: Compliance of lung & chest wall

The ability of the lung to stretch is measured as the **COMPLIANCE, C**

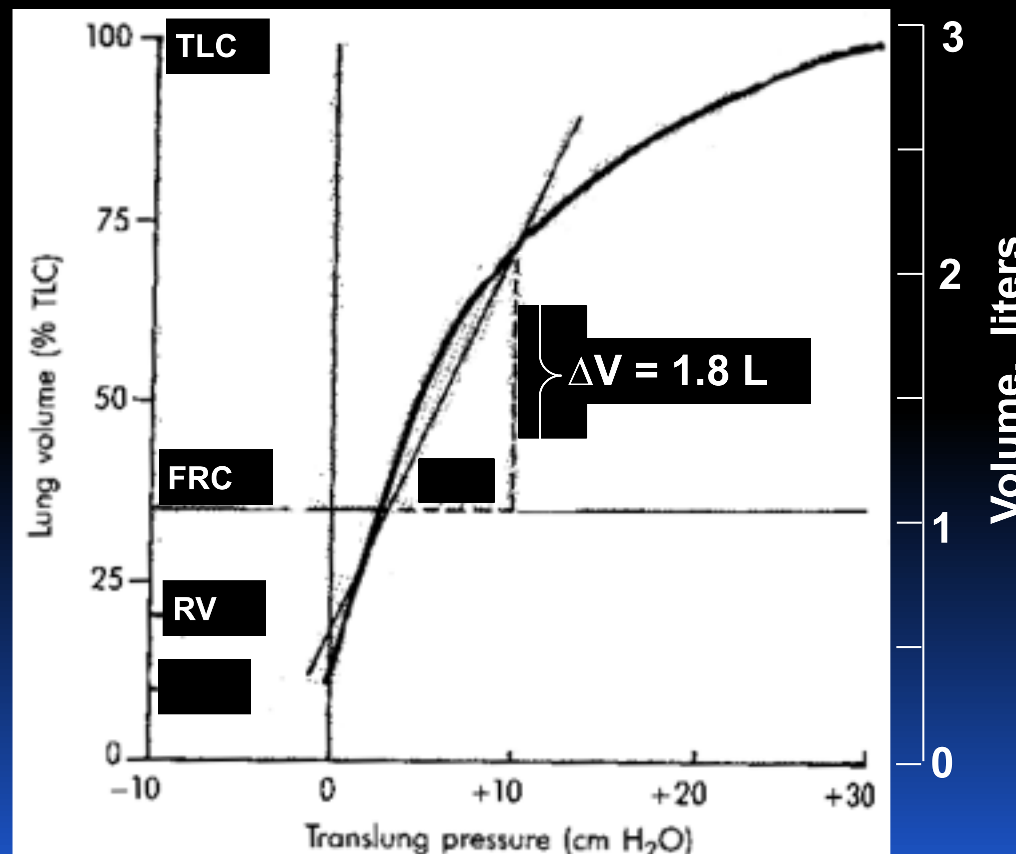


$C = \Delta V/\Delta P$

where V is lung volume and P is pressure

1. Curves are not linear

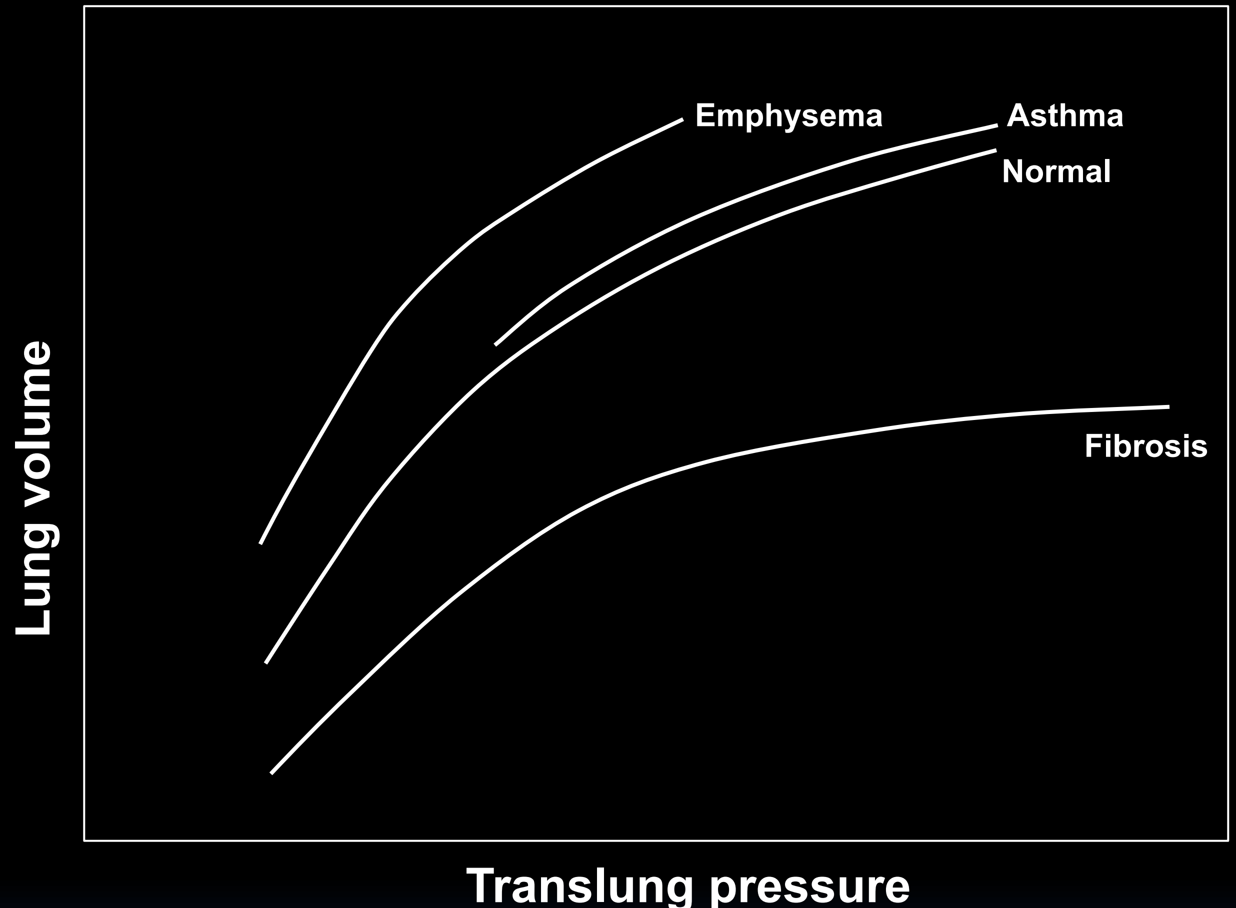
2. Difference between inspiratory & expiratory curves called <u>hysteresis</u>



$\Delta V/\Delta P = 1.8$ L/6.5 cm H_2O

$= 0.28$ L/cm H_2O

For comparison:
vein = 0.04 and artery = 0.002 L/cm H2O

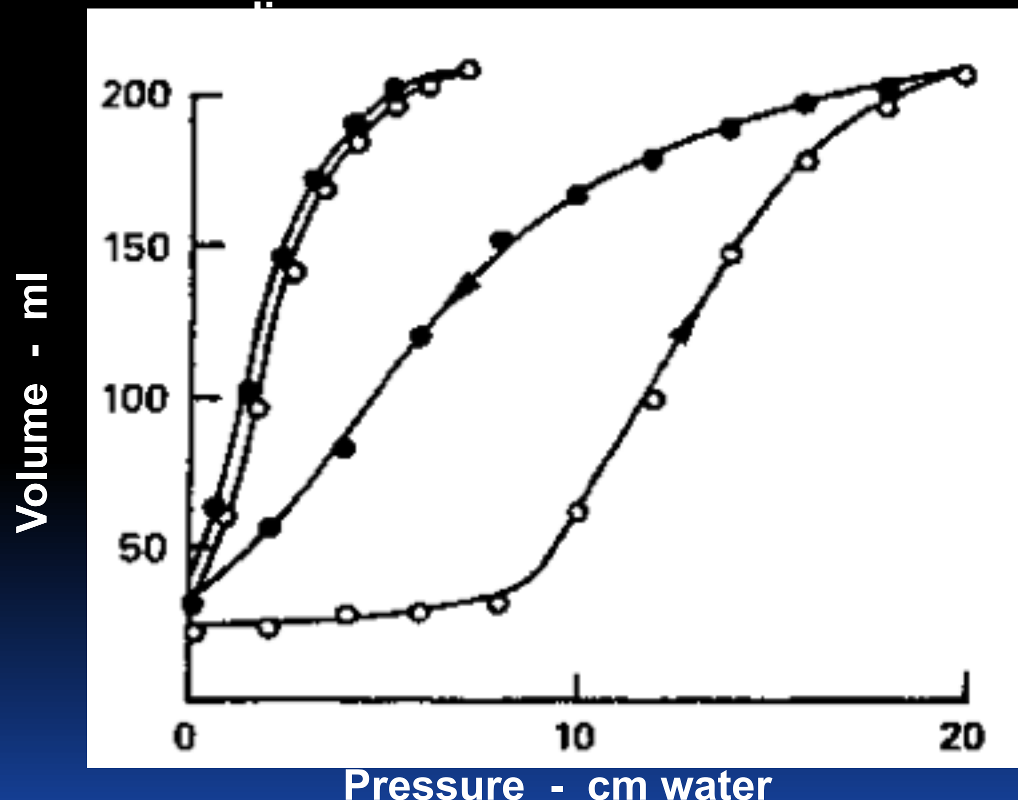


Deflation pressure volume curves of normal adult and three common chronic lung diseases

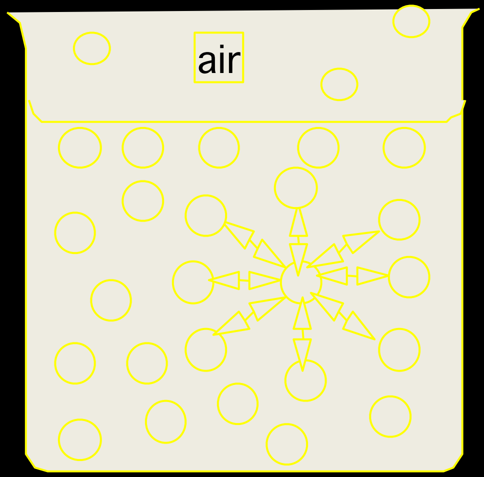
Question: How would the compliance change if the lung were filled with water instead of air??

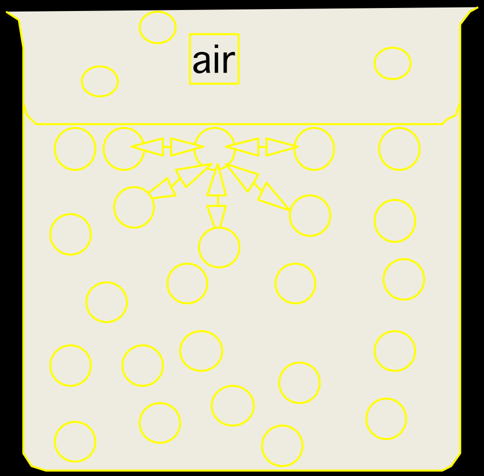
Question: Would the compliance of a lung filled with air be less than one filled with water??

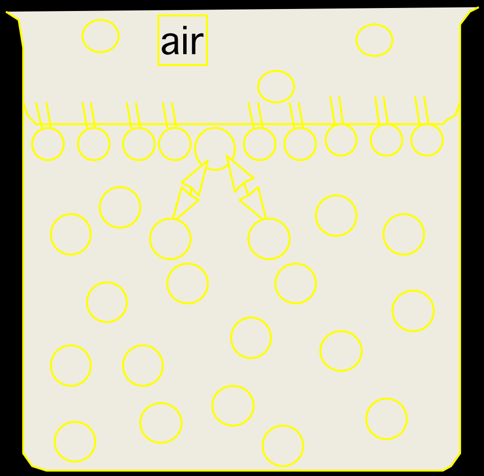
Experiment:



What is **surface tension**?







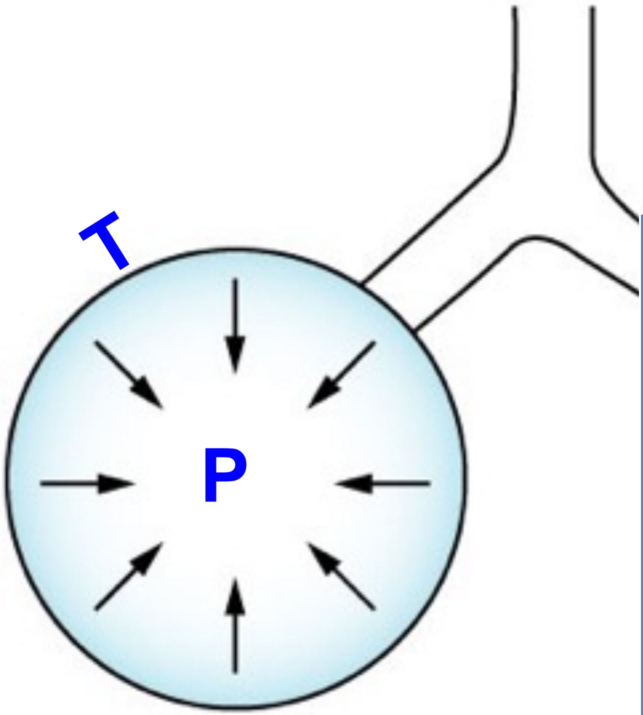
Law of LaPlace

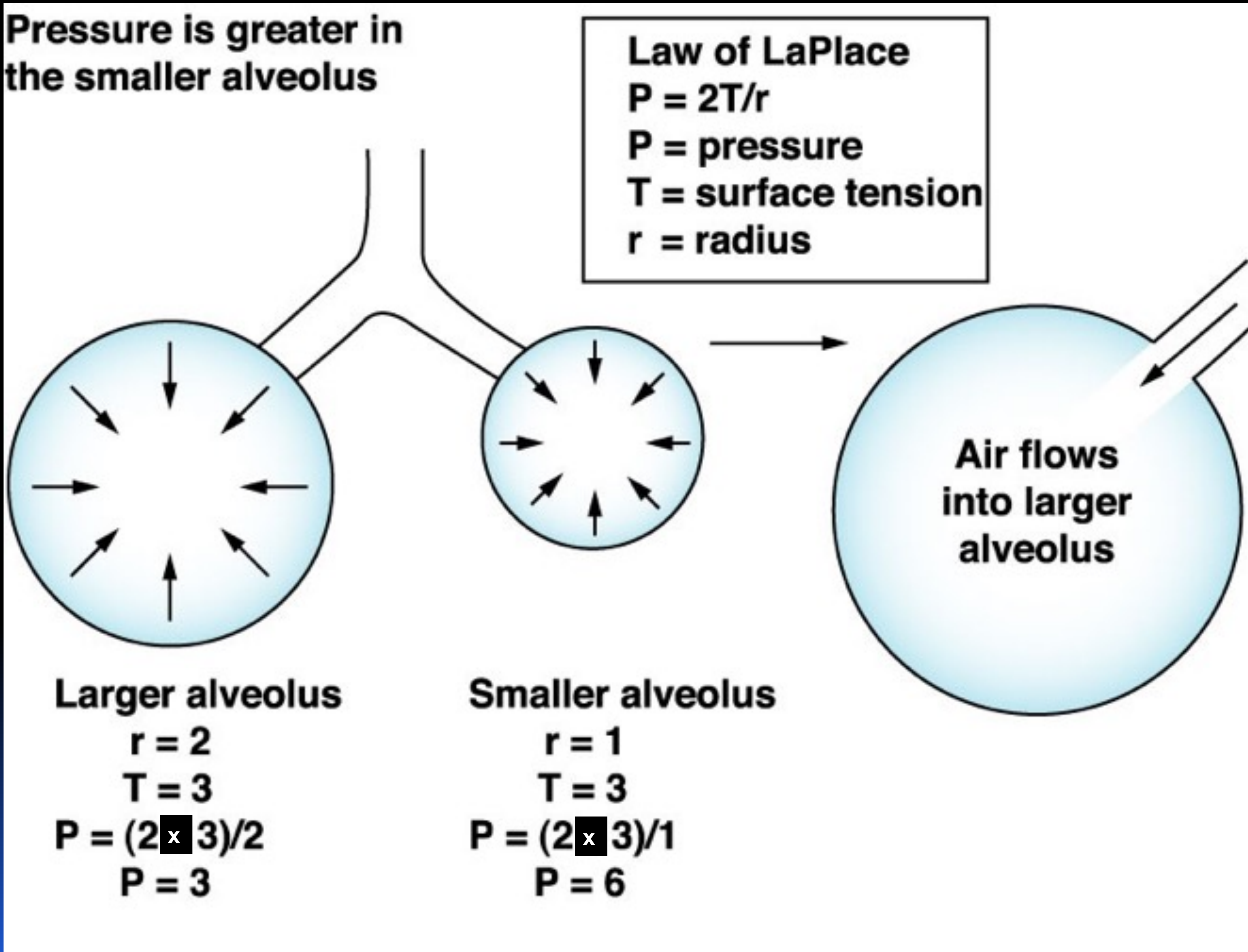
$P = 2T/r$

P = pressure

T = surface tension

r = radius

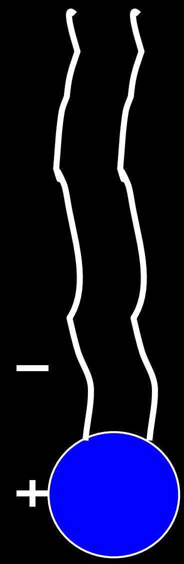


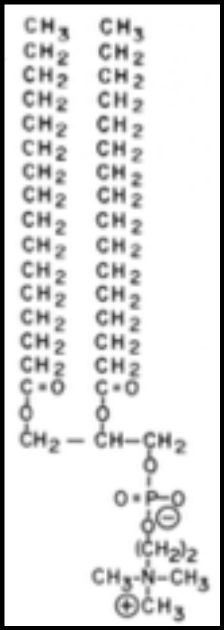

Pressure is greater in the smaller alveolus
Law of LaPlace
P = 2T/r
P = pressure
T = surface tension
r = radius
Air flows into larger alveolus
Larger alveolus
r = 2
T = 3
P = (2 x 3)/2
P = 3
Smaller alveolus
r = 1
T = 3
P = (2 x 3)/1
P = 6

Surface tension

- Causes the distention of the lund in the expiration stage to be very dificult
- May result in collapse of smaller alveoli
- The negative pressure may result in fluid entry into the alveoli

To counteract the effect of surface tension: Surfactant





A major component of lung surfactant is dipalmitoylphosphatidylcholine (DPPC). DPPC has typical phospholipid structure: two fatty acid residues are water insoluble, hydrophobic; phosphocholine at other end is charged and water soluble, hydrophilic.

What is the origin and composition of Lung Surfactant?

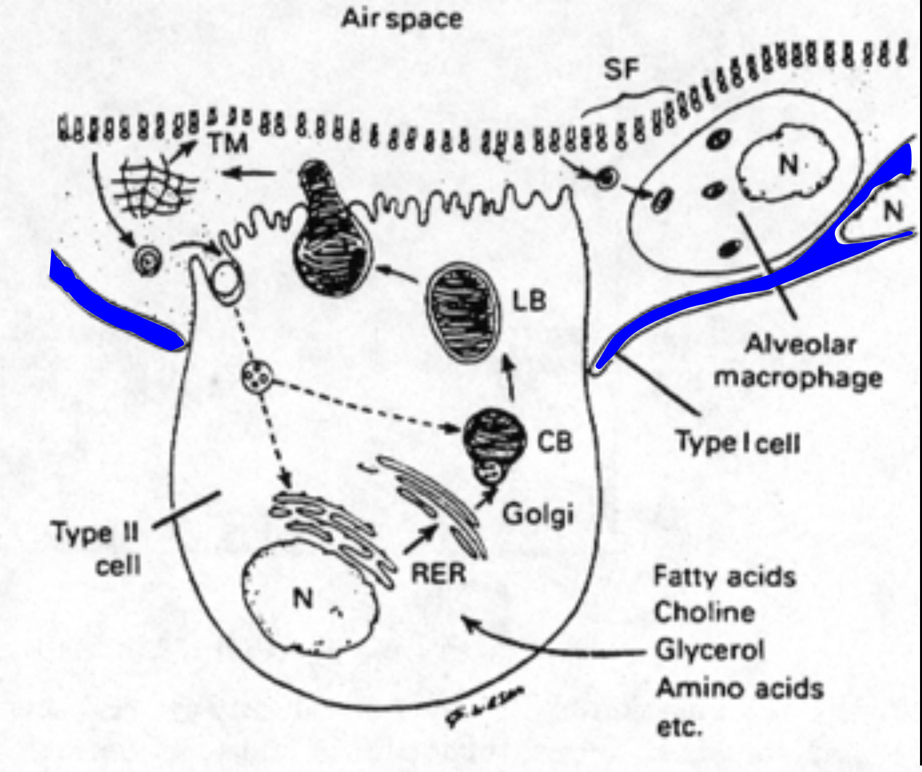
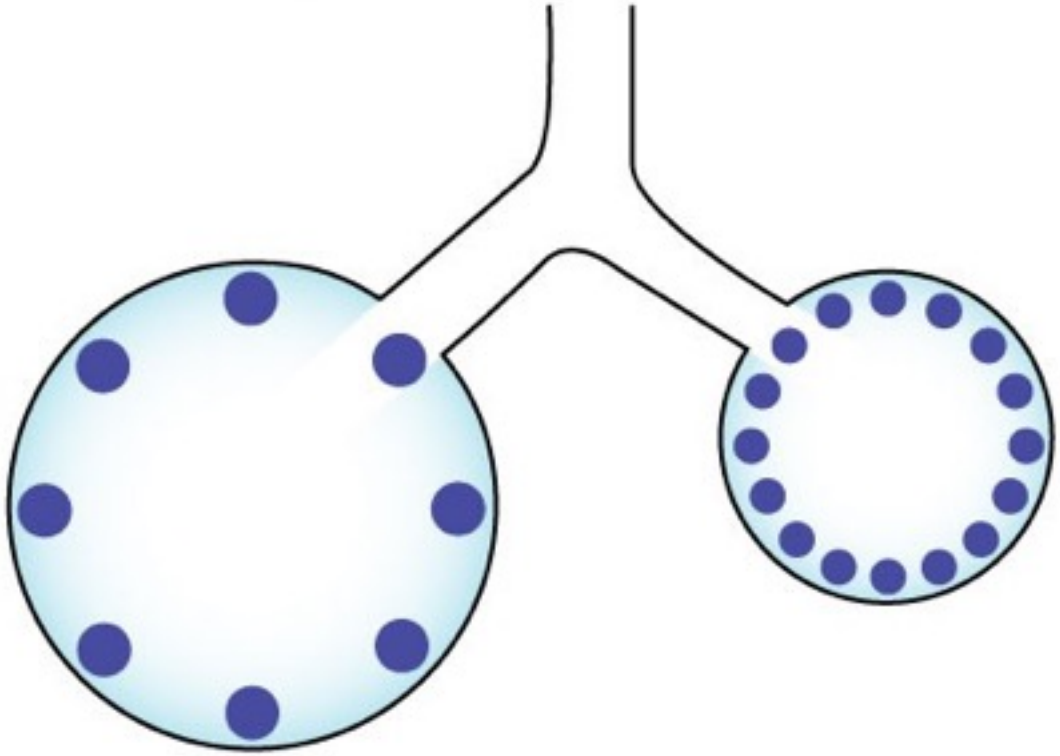


Figure 34–9. Formation and metabolism of surfactant. Lamellar bodies (LB) are formed in type II alveolar epithelial cells and secreted by exocytosis. The released lamellar body material is converted to tubular myelin (TM), and the TM is probably the source of the phospholipid surface film (SF). Some surfactant is taken up by alveolar macrophages, but more is taken up by endocytosis in type II epithelial cells. (Reproduced, with permission, from Wright JR: Metabolism and turnover of lung surfactant. *Am Rev Respir Dis* 1987;**135:**426.)

Approximate composition of surfactant

Component	percent composition
Dipalmitoylphosphatidylcholine	62
Other phospholipids	15
Neutral lipids	13
Proteins	8
Carbohydrates	2

Surfactant reduces surface tension (T). Pressure is equalized in the large and small alveoli



$r = 2$	$r = 1$
$T = 2$	$T = 1$
$P = (2 \times 2)/2$	$P = (2 \times 1)/1$
$P = 2$	$P = 2$

Importance of Surfactant:

1. Reduces surface tension, therefore increases compliance

2. Stability of alveoli; LaPlace

3. Helps keep alveoli dry; helps prevent pulmonary edema

4. Expansion of lungs at birth

Resistance Work:

Conductive Airway Resistance.

Remember: $\Delta P = R_{aw} \times \text{Flow}$

$$R_{aw} = (P_{alv} - P_{atm}) / \text{Flow}$$

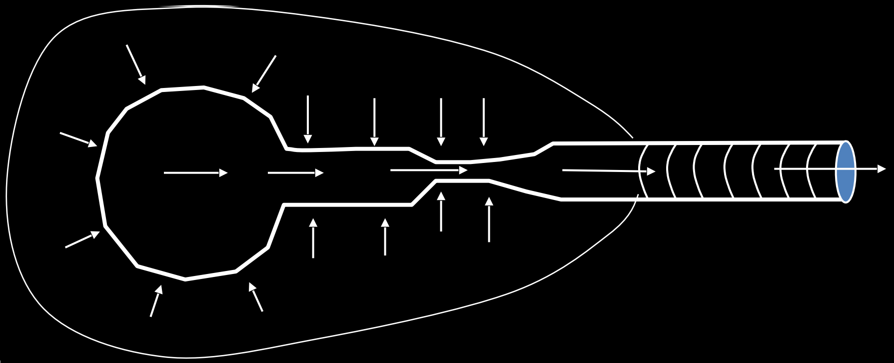
Like Poiseuille flow in blood vessels, i.e., inversely $\propto$ to r^4

$$R = \frac{8\eta l}{\pi r^4}$$

Agents that constrict vessels (bronchioles) or accumulate debris (e.g., mucus) increase resistance (makes airflow difficult).

Dynamic Compression of Airways

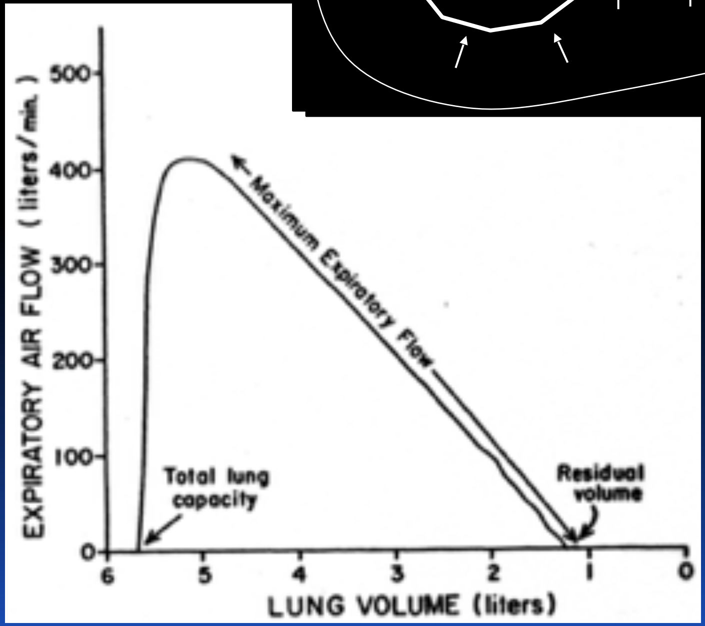
Very simply means that some conductive vessels are very collapsible. Since they are also enclosed within the thoracic cage, increased pleural pressure can sometimes lead to restrictive outflow (due to vessel collapse).

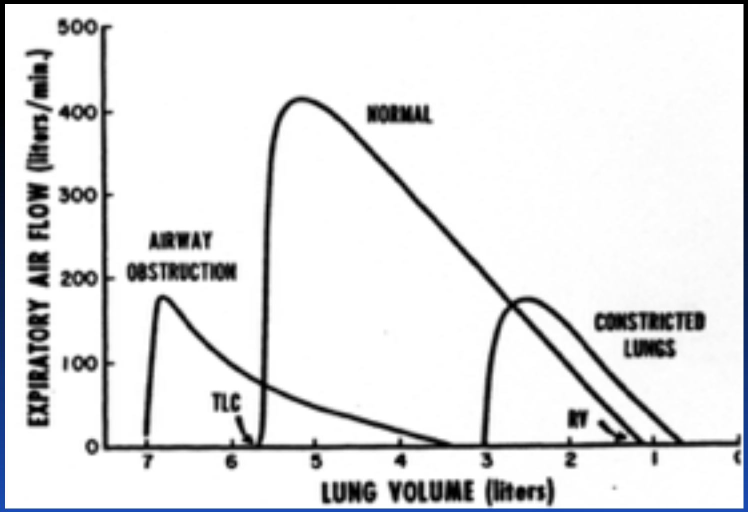


Flow = $\Delta P/R_{aw}$

should be linear

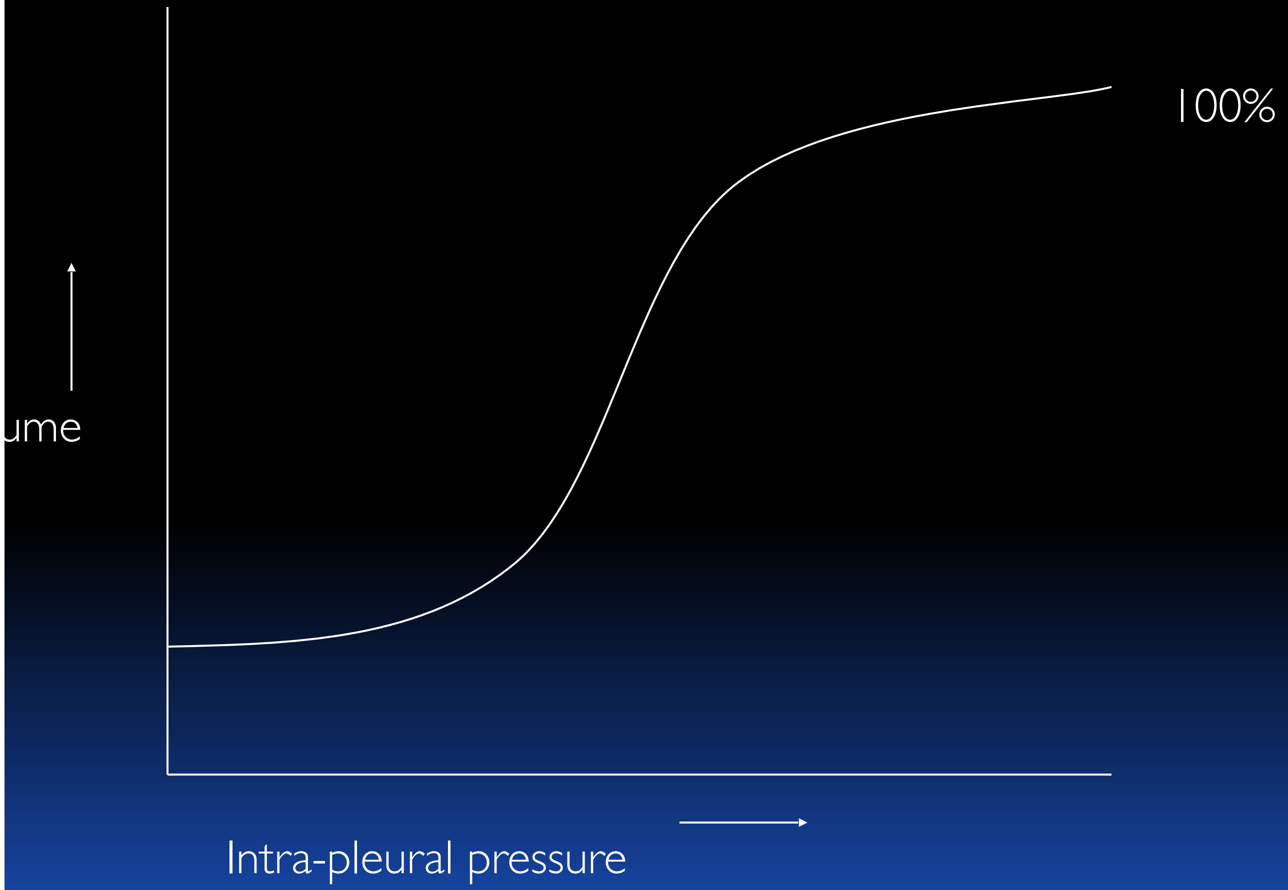
but it is not if airways are collapsible



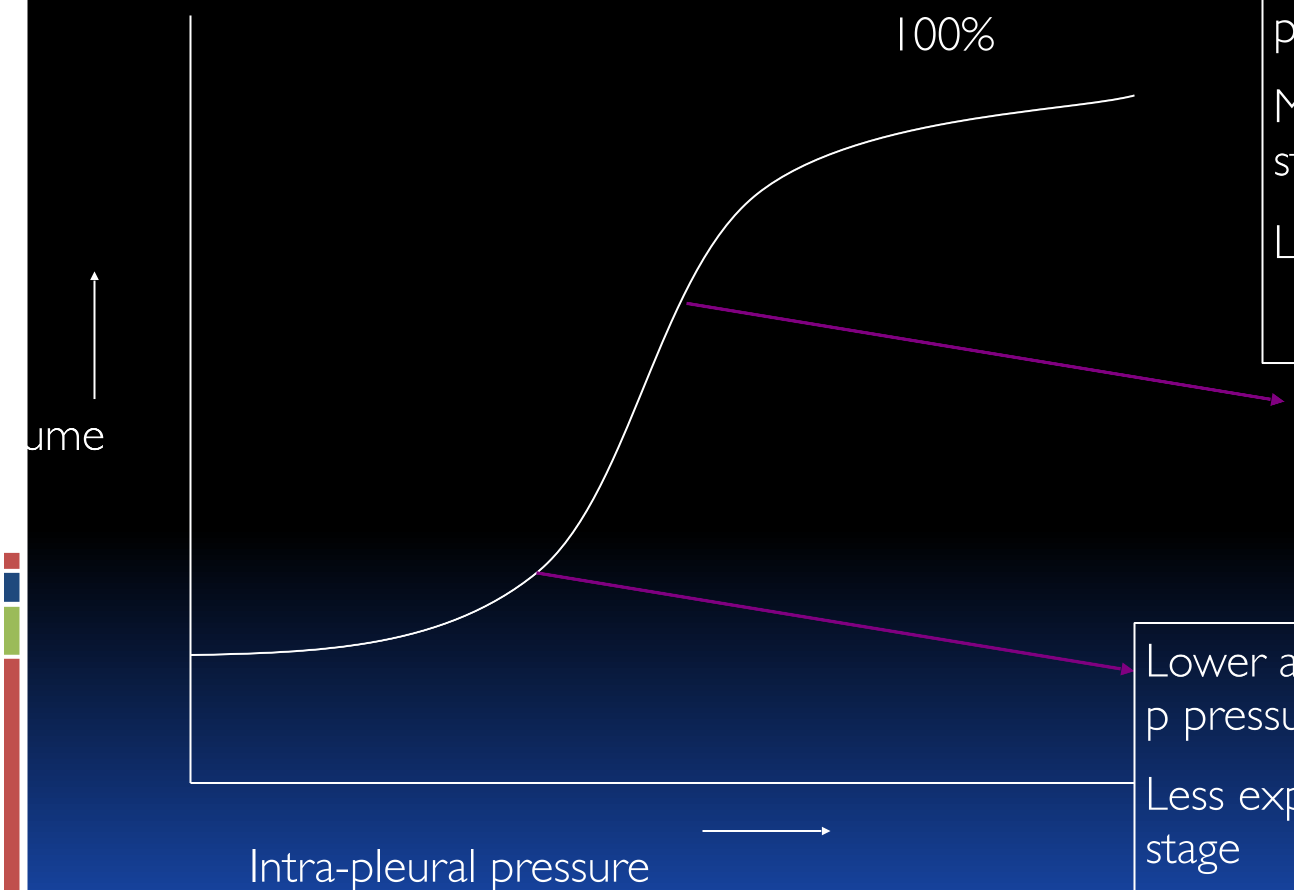


Regional differences

- If Erect
  - Upper area
    - Relatively less ventilation
  - Lower area
    - More ventilation
- If supine
  - Anterior
    - Less
  - Posterior
    - more



100%
ume
Intra-pleural pressure



Upper areas: less wt,Higher i/p pressure

More expanded at resting stage

Less change in ventilation

Lower areas: more wt, less i/p pressure

Less expanded at resting stage

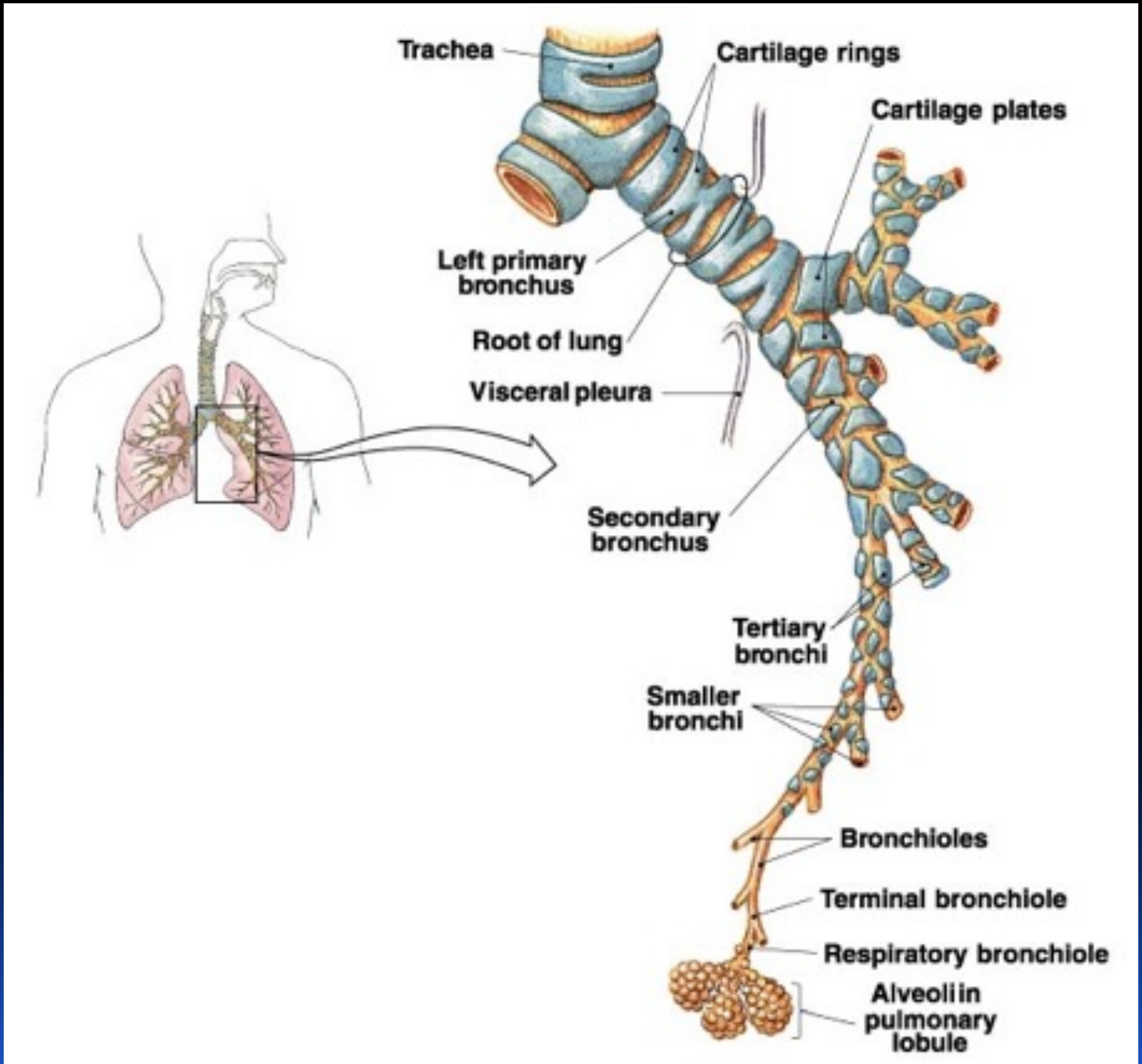
More change in ventilation

Dead space

- This is the portion of the airway that does not participate in gaseous exchange

- Anatomical dead space
  - this the portion of the airway that does not have alveoli and therefore cannot participate in gaseous exchange
  - 150ml

Tracheobronchial Tree



hysiological dead space= TOTAL EAD SPACE

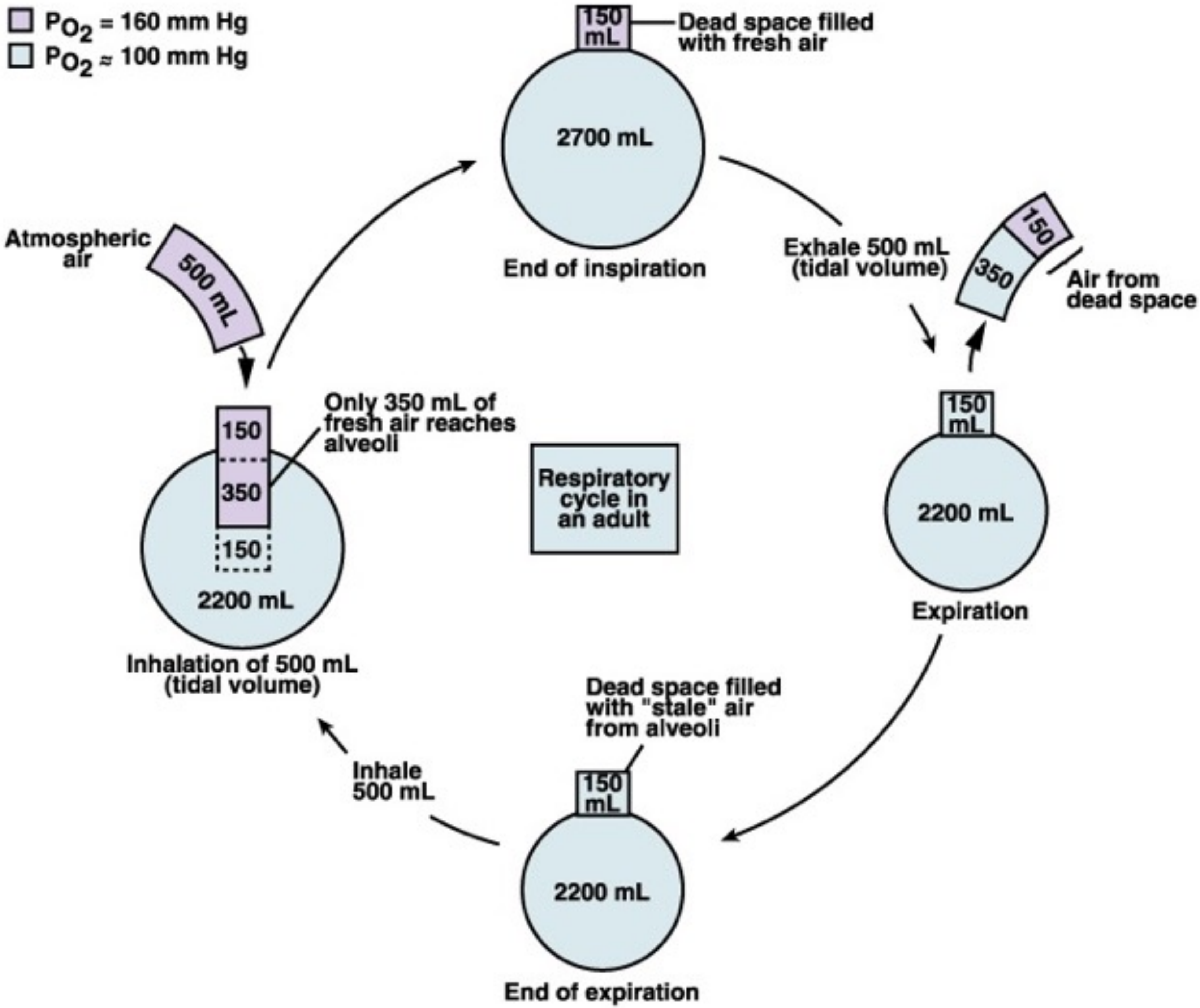
physiological V_D = anatomical V_D + alveolar V_D

The alveolar dead space would be those alveoli- bearing areas that are not participating in exchange.

This would be pathological

eg lack of circulation or very thick barrier

In the normal person, physiological dead space equals anatomical dead space



P_{O_2} = 160 mm Hg
P_{O_2} ≈ 100 mm Hg
150 mL
Dead space filled with fresh air
2700 mL
End of inspiration
Exhale 500 mL (tidal volume)
150
350
Air from dead space
Atmospheric air
500 mL
150
350
150
Only 350 mL of fresh air reaches alveoli
2200 mL
Inhalation of 500 mL (tidal volume)
Respiratory cycle in an adult
150 mL
2200 mL
Expiration
Dead space filled with "stale" air from alveoli
150 mL
2200 mL
End of expiration
Inhale 500 mL

How do we measure Dead Space?

Know how to distinguish between what is called Anatomical dead space and Physiological dead space

Bohr equation - uses P_{CO2} of expired air (PE_{CO2}) and alveolar air (PA_{CO2}), and tidal volume (V_T).

We can define the tidal volume (V_T) as being a composite of functional alveolar volume (V_A) and dead space volume (V_A), i.e.,

$$V_T = V_A + V_D$$

by definition

Amount CO_2 EXPIRED = Amount CO_2 from alveoli + Amount CO_2 from dead space

since Amount = concentration x volume, we can combine the two equations

$$PE_{CO2} \times V_T = [PA_{CO2} \times (V_T - V_D)] + [PI_{CO2} \times V_D]$$

and since PI_{CO2} = atmospheric air = 0.04% CO_2 , which is very low ≈ 0, we can simplify

$$PE_{CO2} \times V_T = PA_{CO2} \times (V_T - V_D)$$

$$V_D = V_T (PA_{CO2} - PE_{CO2}) / PA_{CO2}$$ Bohr Equation

Conc. of CO_2 in **alveolar** air

Conc. of CO_2 in **expired** air

$$V_D = V_T \frac{(PA_{CO2} - PE_{CO2})}{PA_{CO2}}$$

Bohr Eqn.

Conc. of CO_2 in **alveolar** air

Let's say we have a subject who is breathing with a V_T of 0.5 L, with a PE_{CO2} = 28 mm Hg and a PA_{CO2} = 40 mm Hg.

Why is PE_{CO2} less than PA_{CO2} ?

What is V_D ?

$$V_D = 0.5\ L \ \mathrm{x} \left(\frac{40 - 28 \quad 40}{\ } \right) = 0.5 \ \mathrm{x} \ (0.3) = 0.15\ L$$

Does Dead Space Matter? How?

$$V_T = V_A + V_T$$

It is necessary to correct for dead space to effectively measure ventilation rate

We have already been introduced to the **respiratory minute volume**, $\dot{V}$

$$\dot{V} = \text{freq} \times V_T$$

A more important "minute volume" is the **alveolar ventilation rate**

Alveolar vent. rate = total volume of "new air" entering alveoli each minute, $\dot{V}_A$

$$\dot{V}_A = \text{freq} \times (V_T - V_D)$$

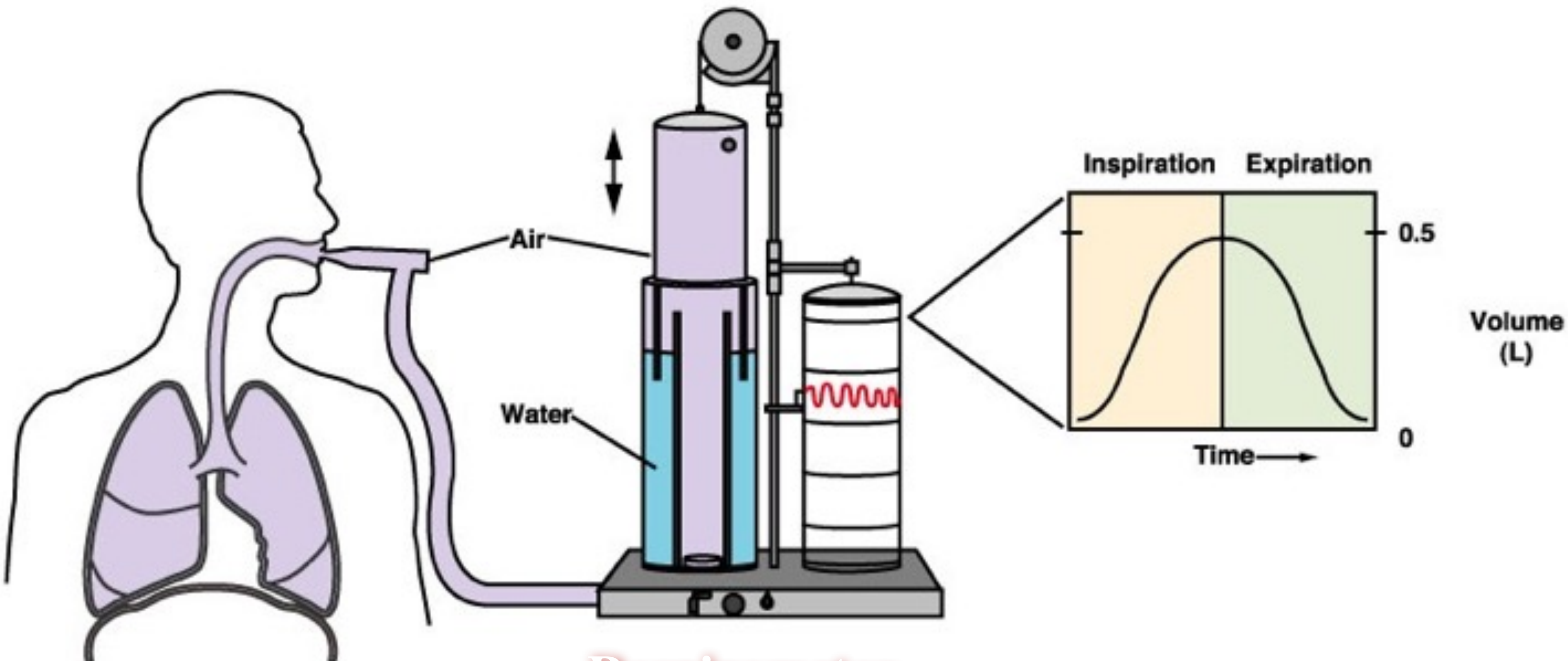
Is it more efficient to change $\dot{V}_A$ by ***frequency*** or by V_T?

What are the consequences of breathing through a long tube?

What is an absolute upper limit for the length of the tube?

Measurement of lung volumes

- Respiratory volumes:
  - Spirometry
- Residual volume
  - Helium dilution method
  - Body plethysmography
- Anatomoical dead space
  - Fowler's method



Respirometer

THE SPIROMETER

- Old version
  - spirometer bell
  - kymograph pen
- New version
  - portable

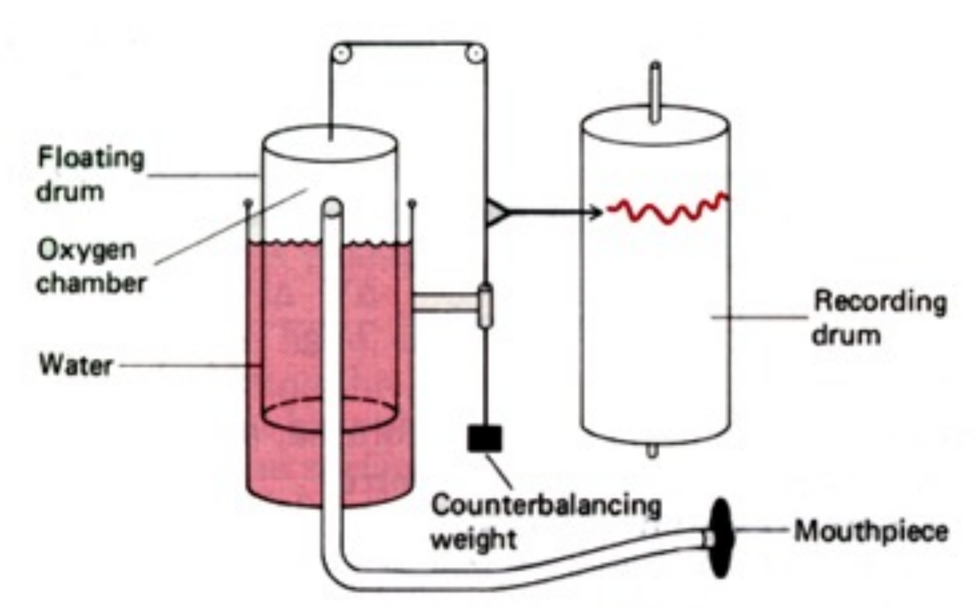
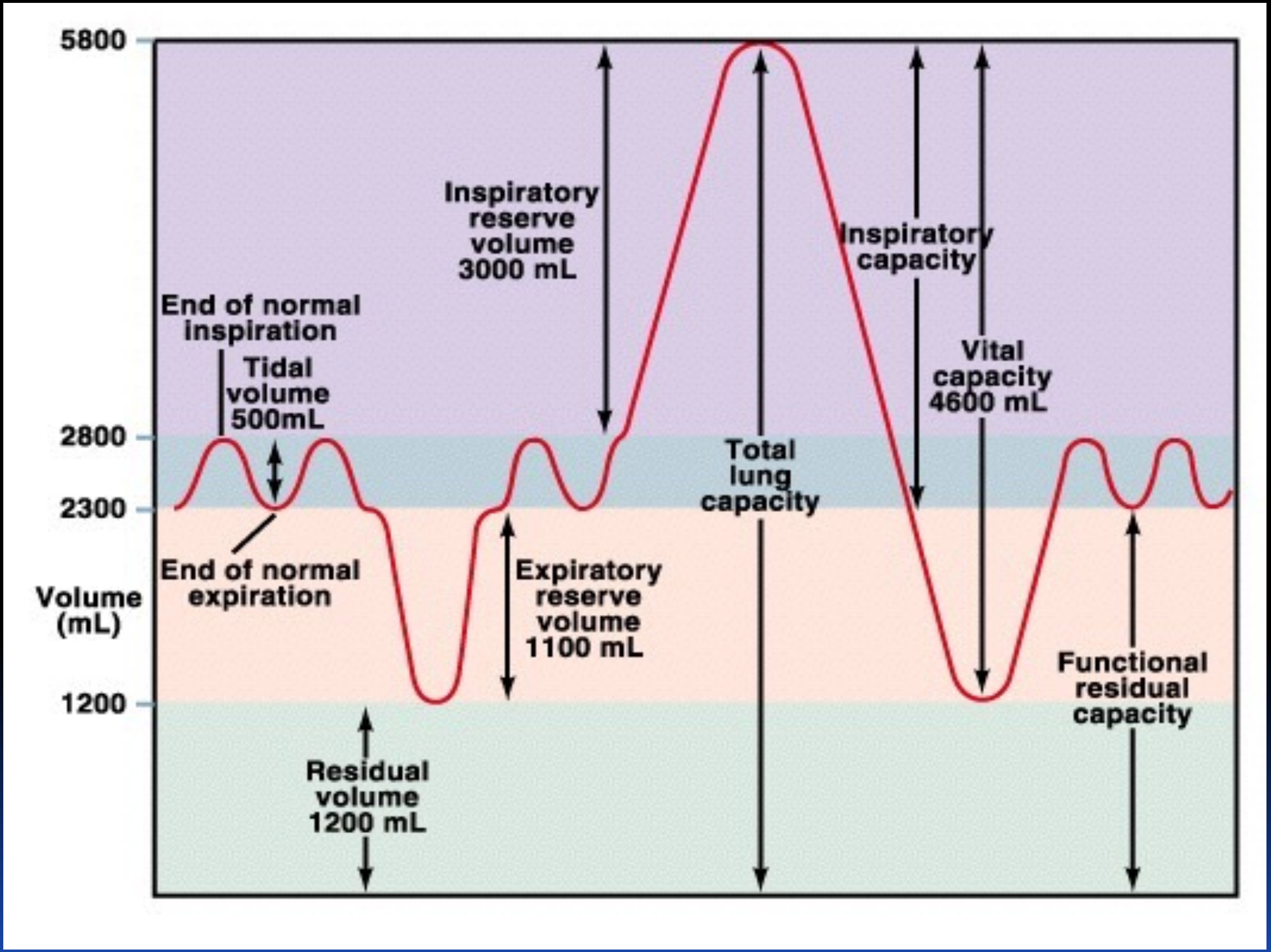


Figure 39—4. A spirometer.



5800
2800
2300
1200
Volume (mL)
Inspiratory reserve volume 3000 mL
End of normal inspiration
Tidal volume 500mL
End of normal expiration
Expiratory reserve volume 1100 mL
Residual volume 1200 mL
Total lung capacity
Inspiratory capacity
Vital capacity 4600 mL
Functional residual capacity

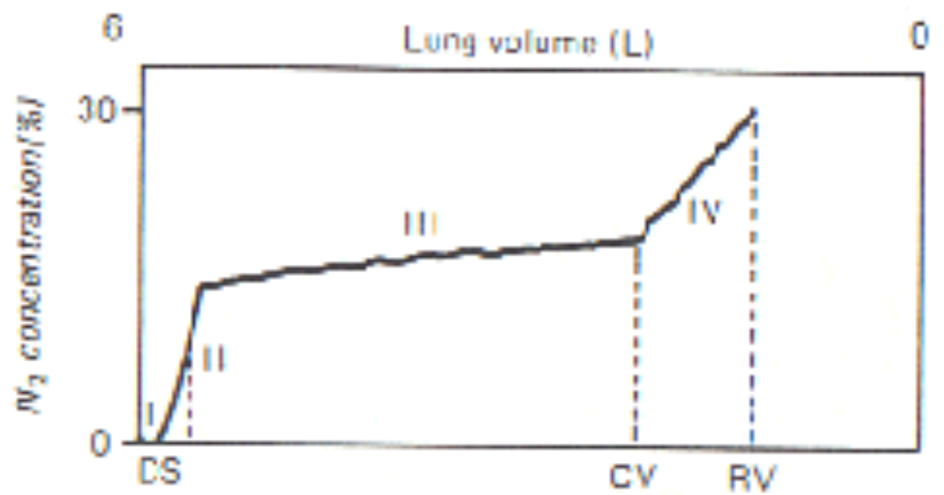


Figure 34–13. Single-breath N_2 curve. From midinspiration, the subject takes a deep breath of pure O_2, then exhales steadily. The changes in the N_2 concentration of expired gas during expiration are shown, with the various phases of the curve indicated by roman numerals. DS, dead space; CV, closing volume; RV, residual volume. (Modified from Buist AS: New tests to assess lung function: The single-breath nitrogen test. *N Engl J Med* 1975;**293**:438.)

I: ADS, oxygen only

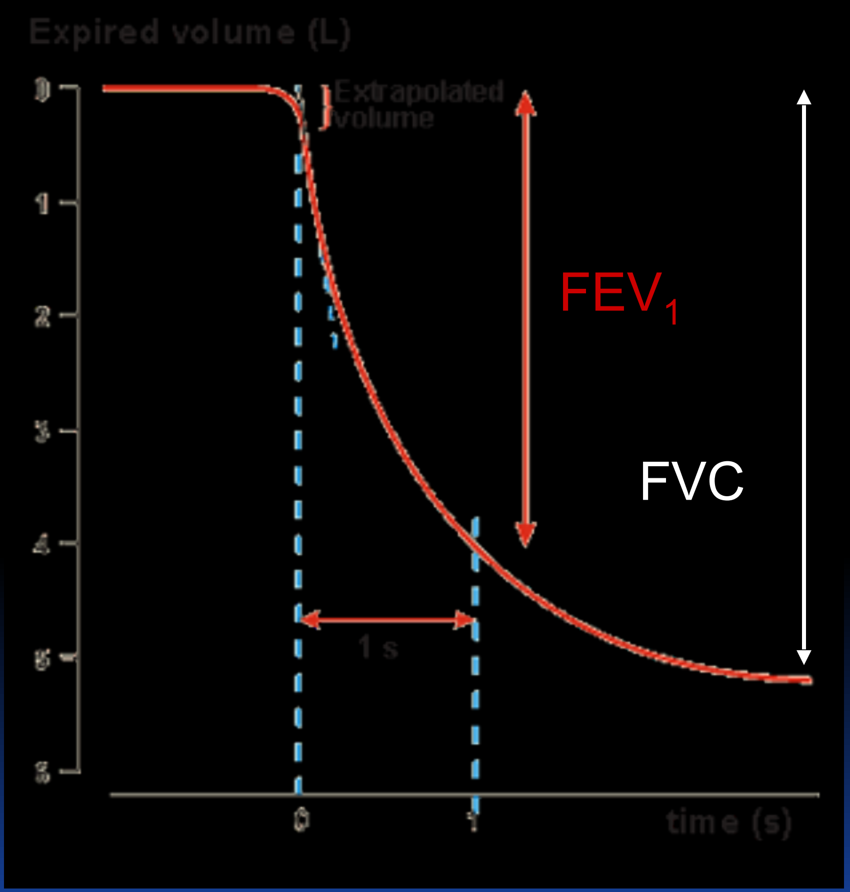
II: ALV air and DS mixture

III: Alveolar gas only

IV: Lower airways close, upper airways nitrogen rich

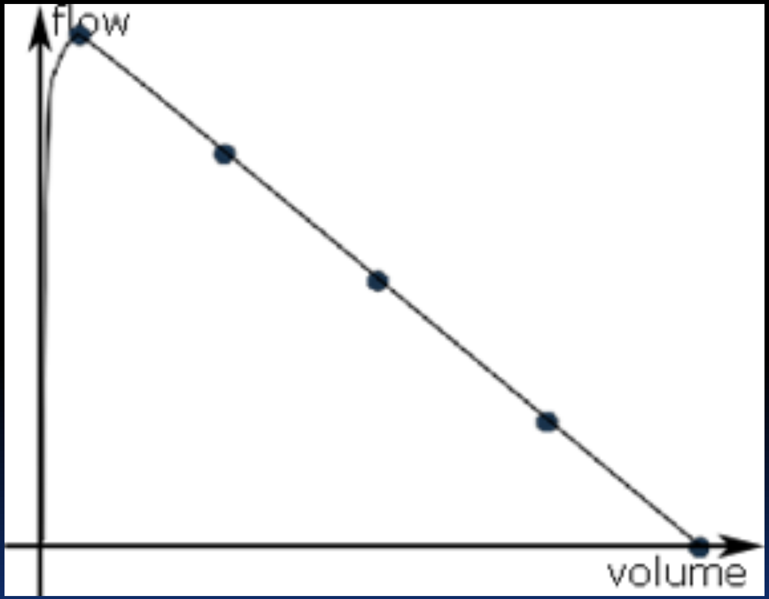
FEV_1 & FVC

- Forced expiratory volume in 1 second
  - 4.0 L
- Forced vital capacity
  - 5.0 L
  - usually less than during a slower exhalation
- FEV_1/FVC ratio = 80%



FLOW-VOLUME CURVE

in HEALTHY subjects

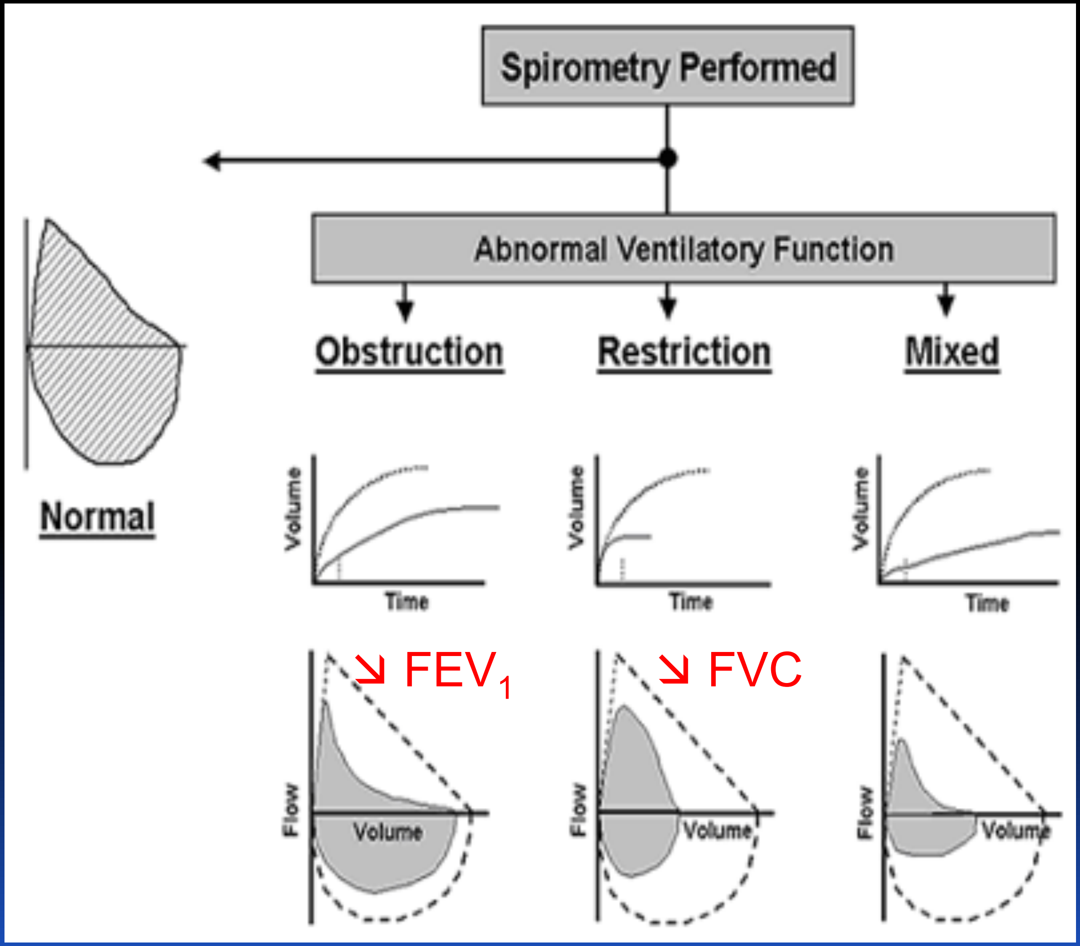


(in L)

FVC

FLOW-VOLUME CURVE

in respiratory patients



- Restrictive disease
  - ↘ expansion of the lung
  - e.g., interstitial fibrosis
- Obstructive disease
  - ↗ resistance to airflow
  - e.g., COPD, asthma

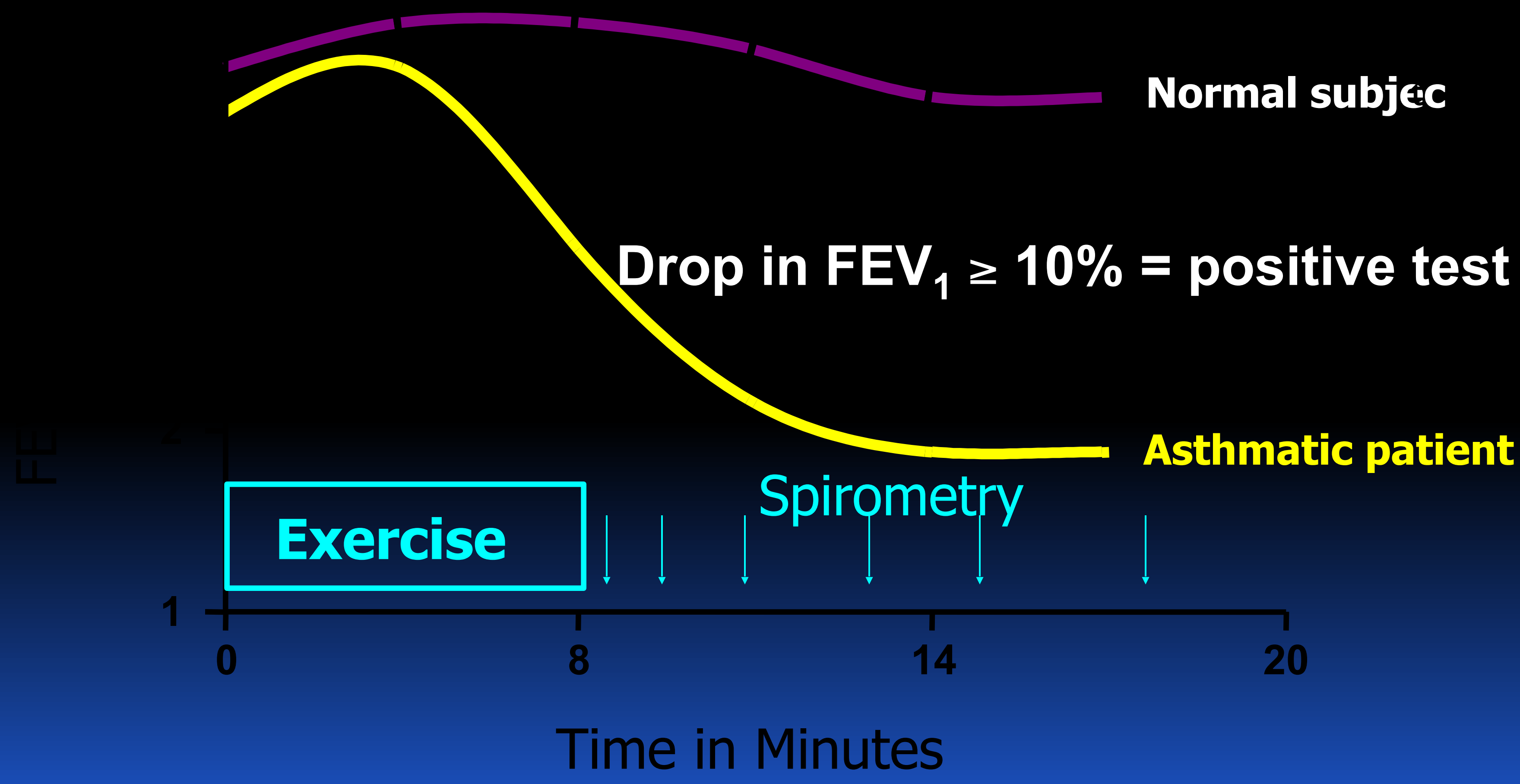
BRONCHIAL PROVOCATION TESTS

- Exposure of the airways to a **stimulus**
  - allergen
  - exercise
  - pharmacological bronchoconstrictive agent

- **Response of the smooth muscle ?**
  - baseline FEV_1
  - post-exposure FEV_1

➢ Airway hyperresponsiveness

EXERCISE TESTING



FUNCTIONAL RESIDUAL CAPACITY

- Measured by
  - body plethysmography
  - helium dilution

- **Body plethysmography**
  - mouthpiece obstructed
  - rapid panting

  Ä during inspiration ↘ pressure of the air in the lungs

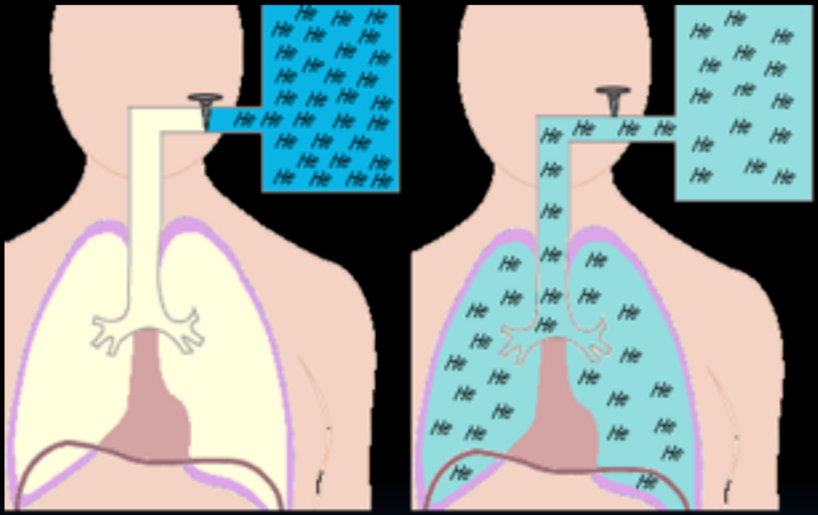
  Ä air in the box expands slightly

  ➥ ↗ pressure in the box

By applying Boyle's law (P · V = constant) → lung volume obtained

FUNCTIONAL RESIDUAL CAPACITY

- **Helium dilution**

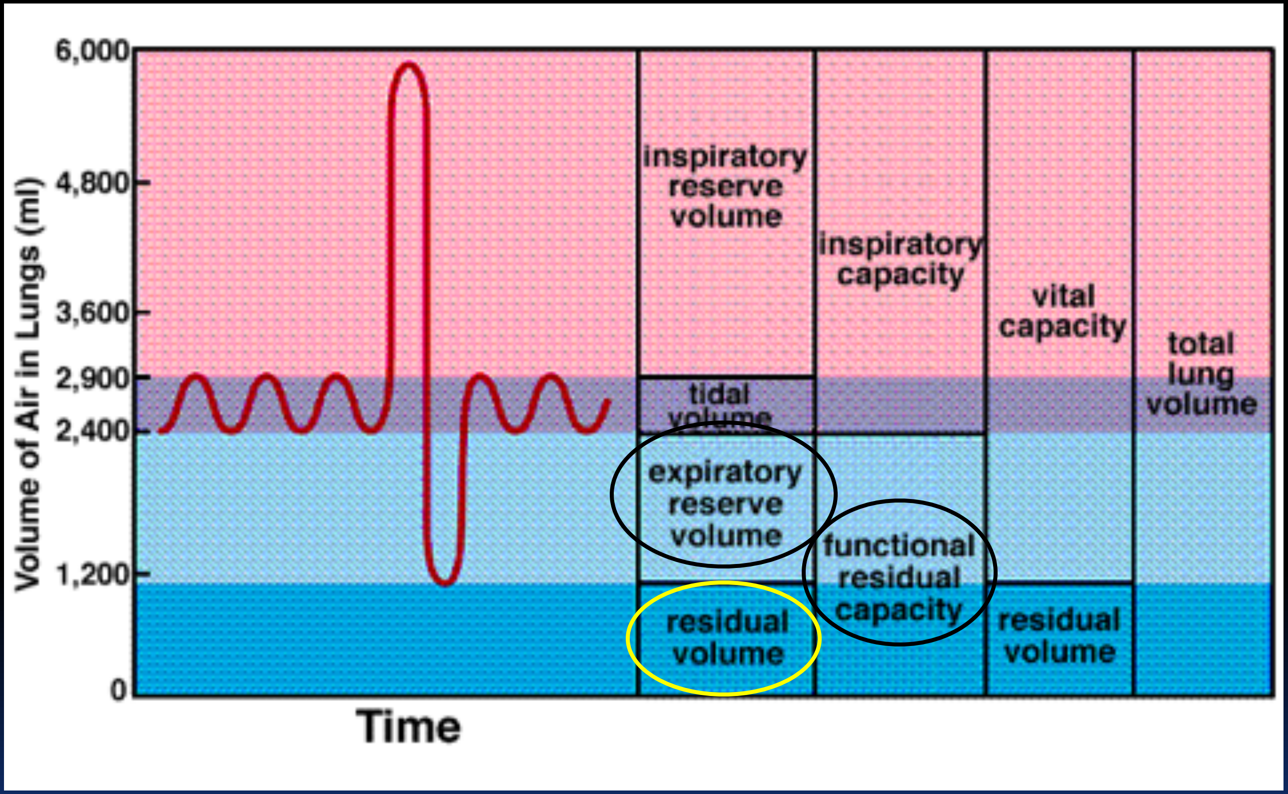


- Spirometer of known volume and helium concentration connected to the patient
- Closed circuit
- Law of conservation of mass

$$[\mathrm{He}]_{initial} \cdot V_s = [\mathrm{He}]_{final} \cdot (V_s + V_L)$$

↳ **Unknown lung volume can be calculated**

RESIDUAL VOLUME



RV = FRC - ERV

INTERPRETATION of RESULTS

- In patients with obstructive diseases
  - airway closure occurs at an abnormally high lung volume

    ↳ ↗ FRC (functional residual capacity)

    ↳ ↗ RV (residual volume)

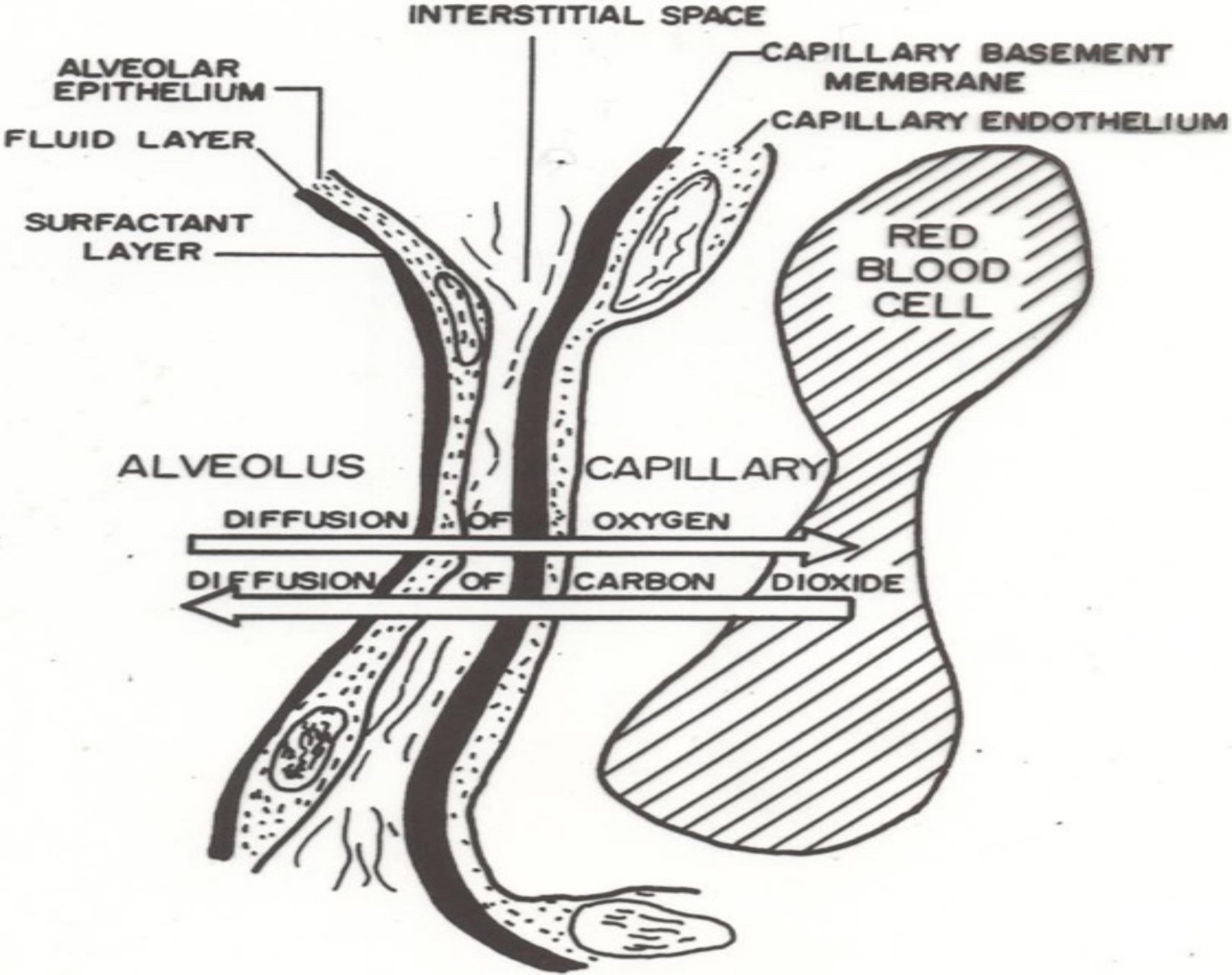
- Patients with reduced lung compliance (e.g., diffuse interstitial fibrosis)
  - stiffness of the lungs + recoil of the lungs to a smaller resting volume

    ↳ ↘ FRC

    ↳ ↘ RV

Blood Gas Exchange ‘diffusion’

- This is the exchange of gases across the Blood-gas barrier
- Is passive
- Occurs along the gas pressure gradients
- Is dependant on
  - Ventilation
  - Perfusion


INTERSTITIAL SPACE
CAPILLARY BASEMENT MEMBRANE
ALVEOLAR EPITHELIUM
CAPILLARY ENDOTHELIUM
FLUID LAYER
SURFACTANT LAYER
RED BLOOD CELL
ALVEOLUS
CAPILLARY
DIFFUSION OF OXYGEN
DIFFUSION OF CARBON DIOXIDE

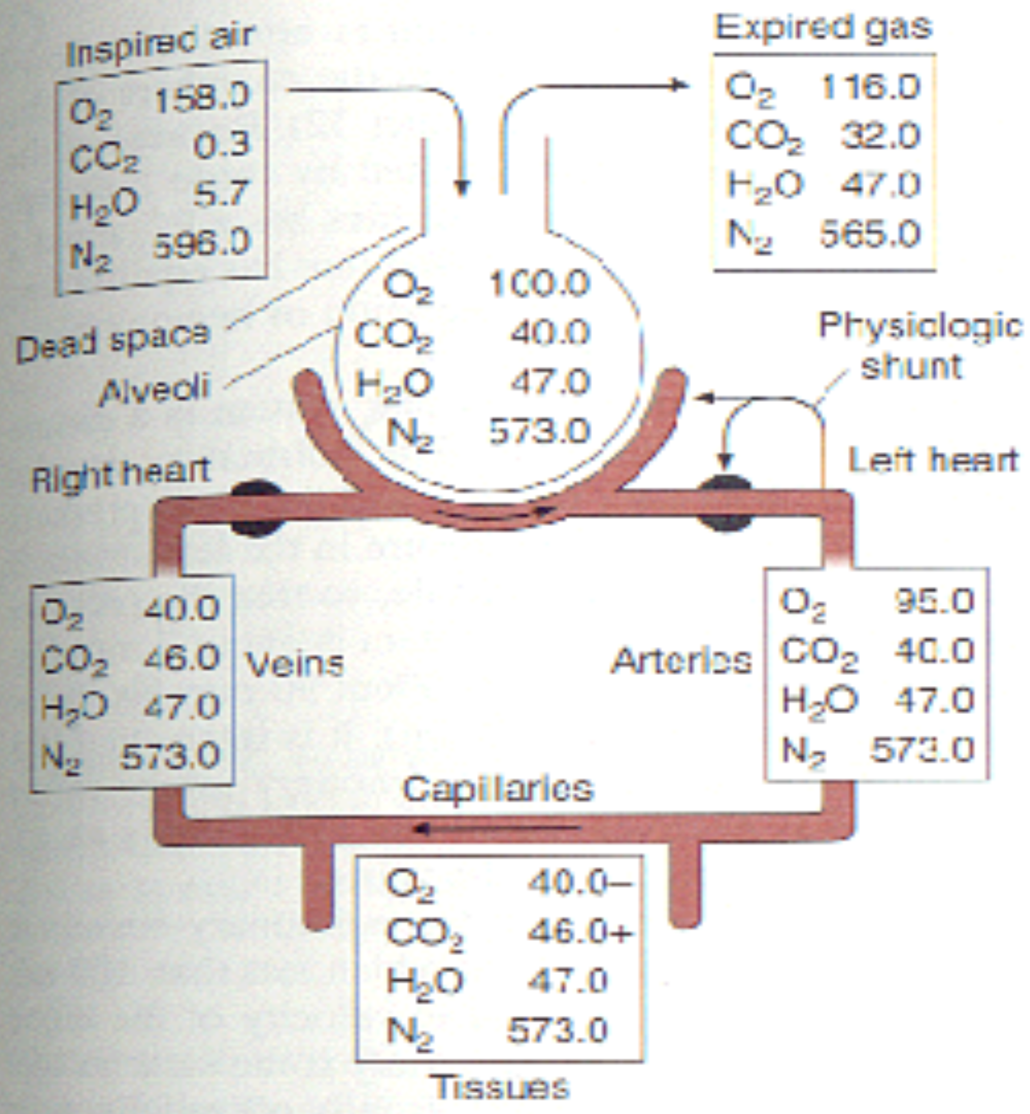


Figure 34–14. Partial pressures of gases (mm Hg) in various parts of the respiratory system and in the circulatory system.

Physical Principles of Gas Exchange

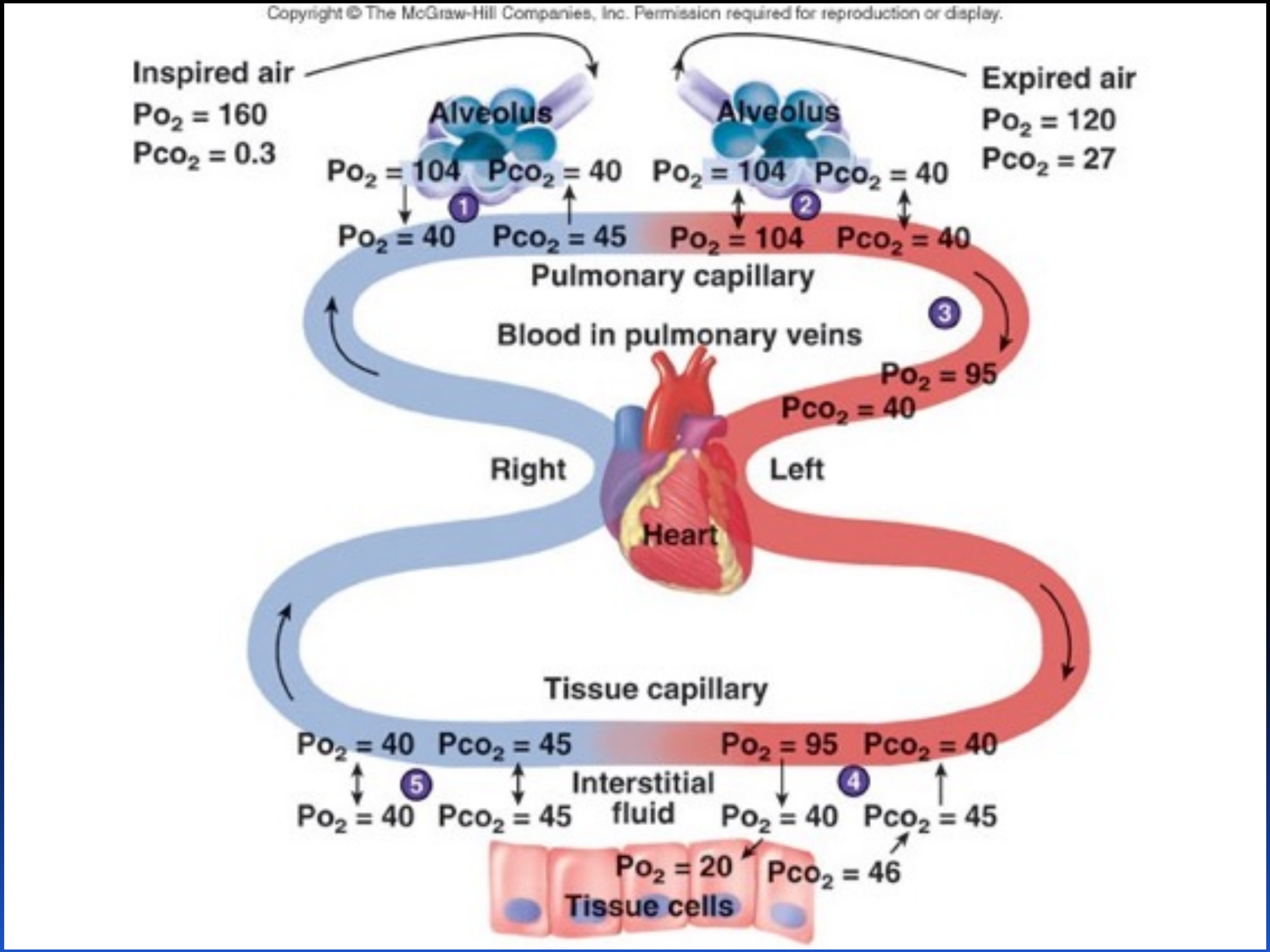
- Diffusion of gases through the respiratory membrane
  - Depends on membrane's thickness, the diffusion coefficient of gas, surface areas of membrane, partial pressure of gases in alveoli and blood
- Relationship between ventilation and pulmonary capillary flow
  - Increased ventilation or increased pulmonary capillary blood flow increases gas exchange
  - Physiologic shunt is deoxygenated blood returning from lungs

Oxygen and Carbon Dioxide Diffusion Gradients

- Oxygen
  - Moves from alveoli into blood.
  - $P0_2$ in blood decreases because of mixing with deoxygenated blood
  - Oxygen moves from tissue capillaries into the tissues
- Carbon dioxide
  - Moves from tissues into tissue capillaries
  - Moves from pulmonary capillaries into the alveoli

- Oxygen:
  - Diffusion capacity(Transfer factor)
    - 20ml/min/mmHg diff in PO2
  - If alveolar 'block' eg alveolar fibrosis
    - Less diffusion
- Carbondioxide
  - 20 x more diffusable
  - Alveolar block usually does not affect the diffusion

Changes in Partial Pressures



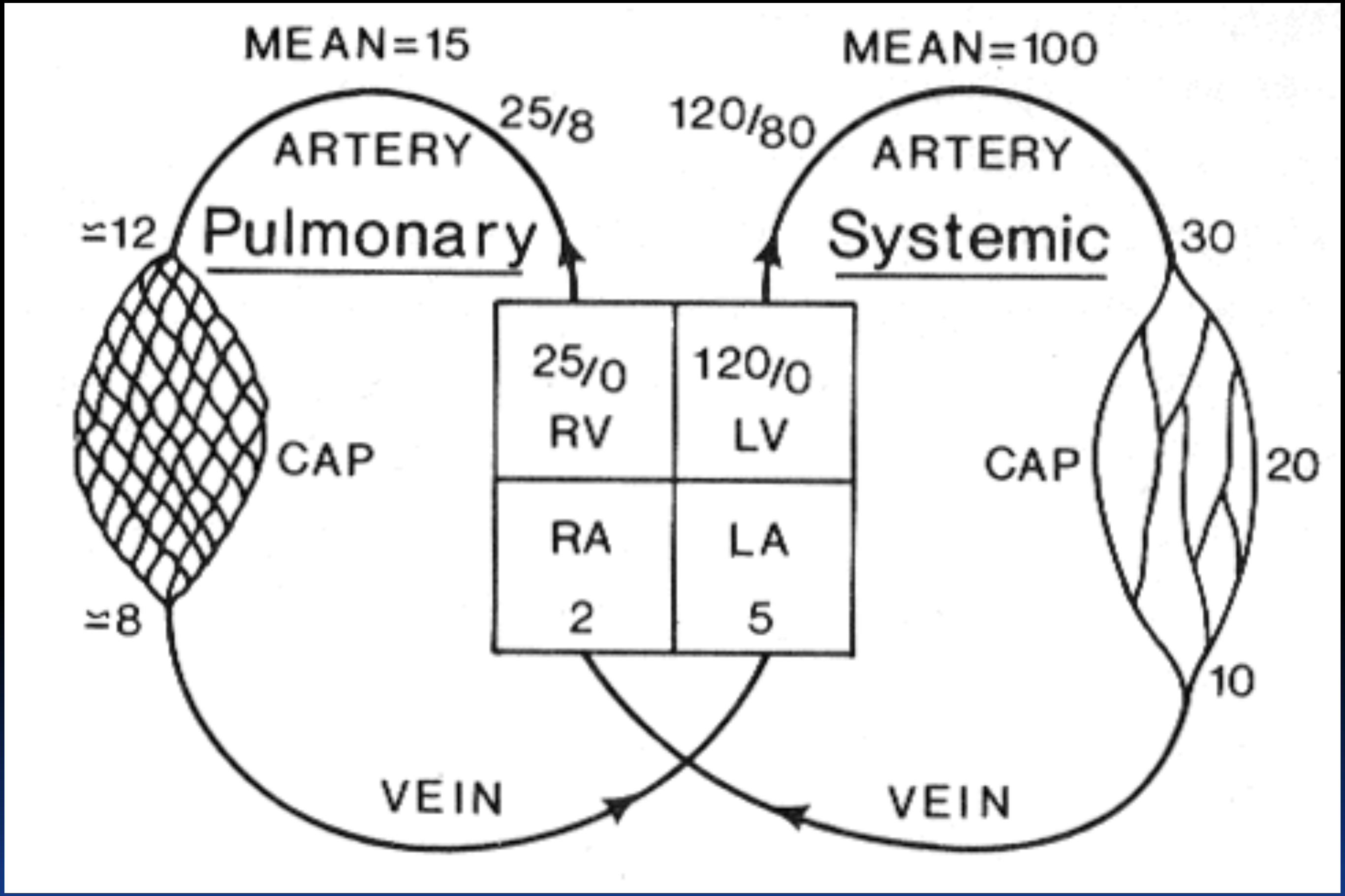
‘Alveolar air’

- This is the air in contact with alveoli
- Volume: 2L
- Each breath adds and takes away 350ml
- The composition remains relatively constant
- Can be sampled by the last 10ml of expired air.

- Exchange completed in 0.25 seconds
- Oxygen diffusion is ‘ Perfusion limited’
- Carbondioxide diffusion is
‘Diffusion limited’

Pulmonary circulation

Characteristics of the Pulmonary Circulation



Pulmonary circulation

- Pulm. art: is thin walled and has little musculature
- Receive total cardiac output
- Cf.
  - Bronchial circulation is like systemic circulation, but bronchial veins cause Physiological shunt

Pulmonary Capillaries

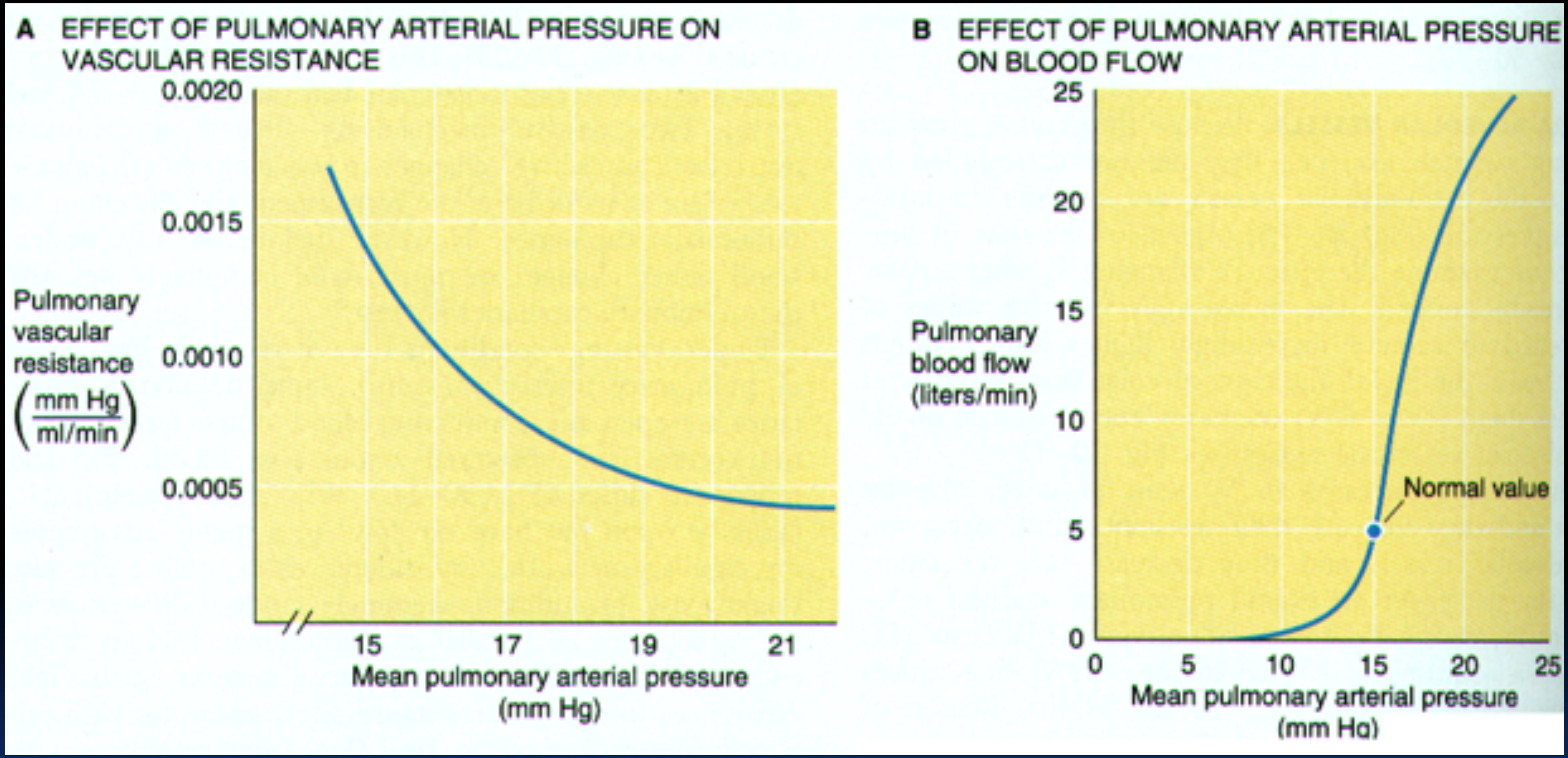
- Vast bed
- Pressure is evenly distributed
- 'Alveolar vessels':
  - affected by the alveolar distention:
  - If large pressure rise- capillaries may collapse
  - If fall in pressure – capillaries may distend
- Extra-alveolar vessels
  - These have connections with the elastic fibres
  - As lung distended these distend also
- Each RBC spends 0.75s, traverses 2-3 alveoli, has to squeeze through

“Special” Characteristics of the Pulmonary Circulation

	Systemic Circ.		Pulmonary Circ.
C.O. (L/min)	6.0	≈	5.9
Arterial B.P. (mm Hg)	100	>>	15
Venous B.P. (mm Hg)	2	“≈”	5
Vascular resistance (ΔP/flow)	100-2/6=16.3	>	15-5/5.9=1.7
Vascular compliance (ΔV/ΔP)	$C_{systemic}$	<<	C_{pulm}

Special Characteristics of the Pulmonary Circulation: high compliance

Ability to promote a decrease in resistance as blood pressure rises



Remember that resistance to Flow = $R = \dfrac{8\eta l}{\pi r^4}$

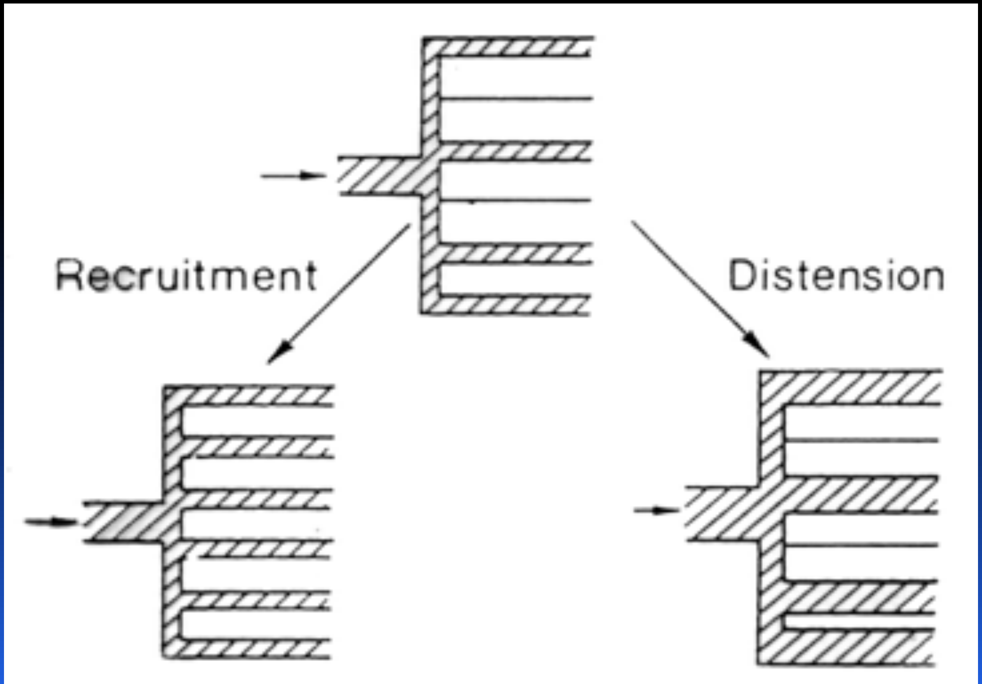
viscosity (η), length (l), radius (r)

Pulmonary blood vessels are much more compliant than systemic blood vessels. Also the system has a remarkable ability to promote a <u>decrease in resistance</u> as the blood pressure rises.

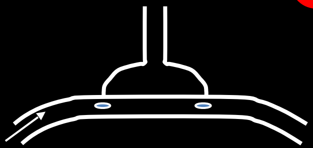
Two reasons are responsible:

Recruitment: opening up of previously closed vessels

Distension: increase in caliber of vessels



Capillary Dynamics



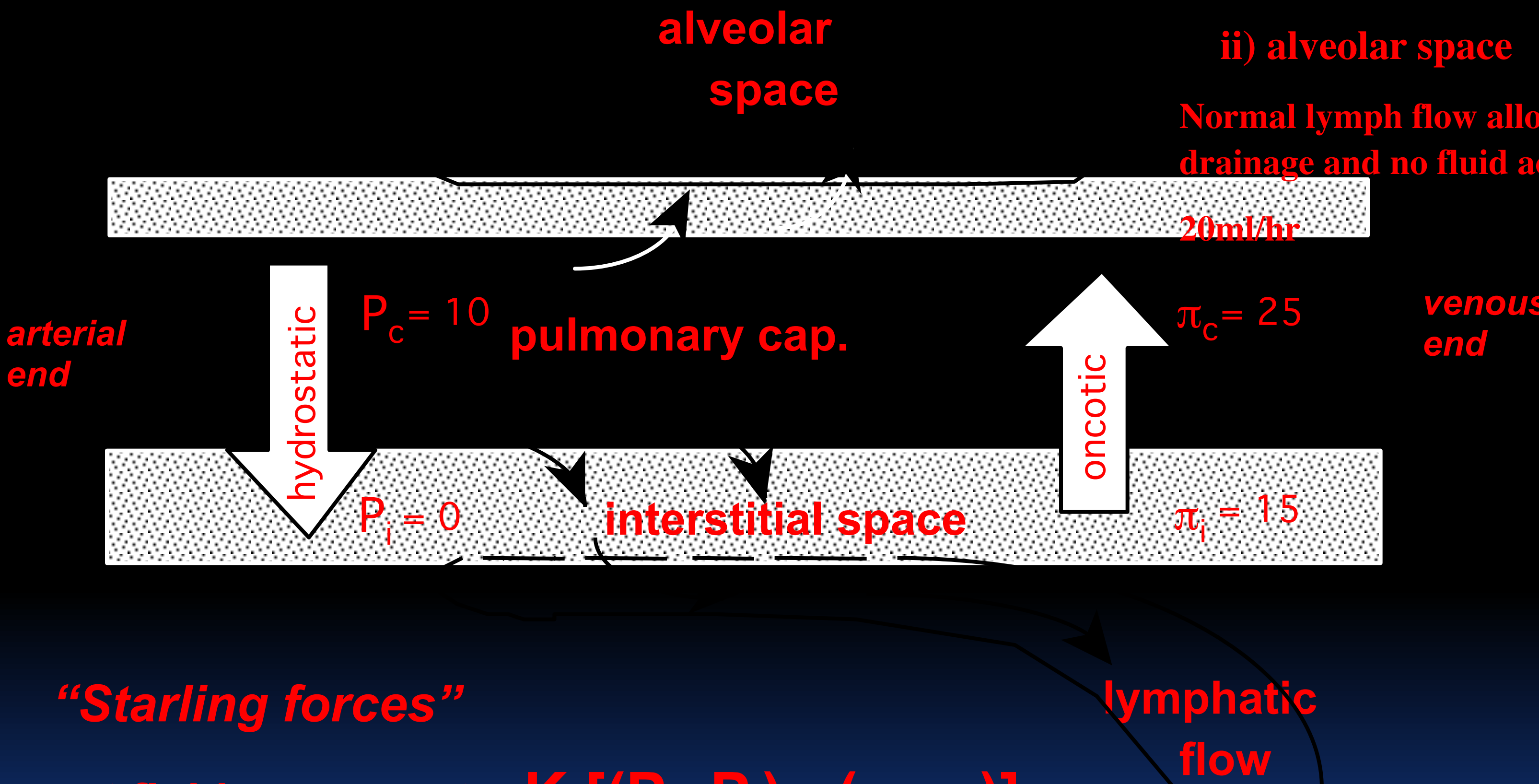
Two routes for possible fluid loss from pulmonary capillary:

i) interstitium

ii) alveolar space

Normal lymph flow allows adequate drainage and no fluid accumulation.

20ml/hr

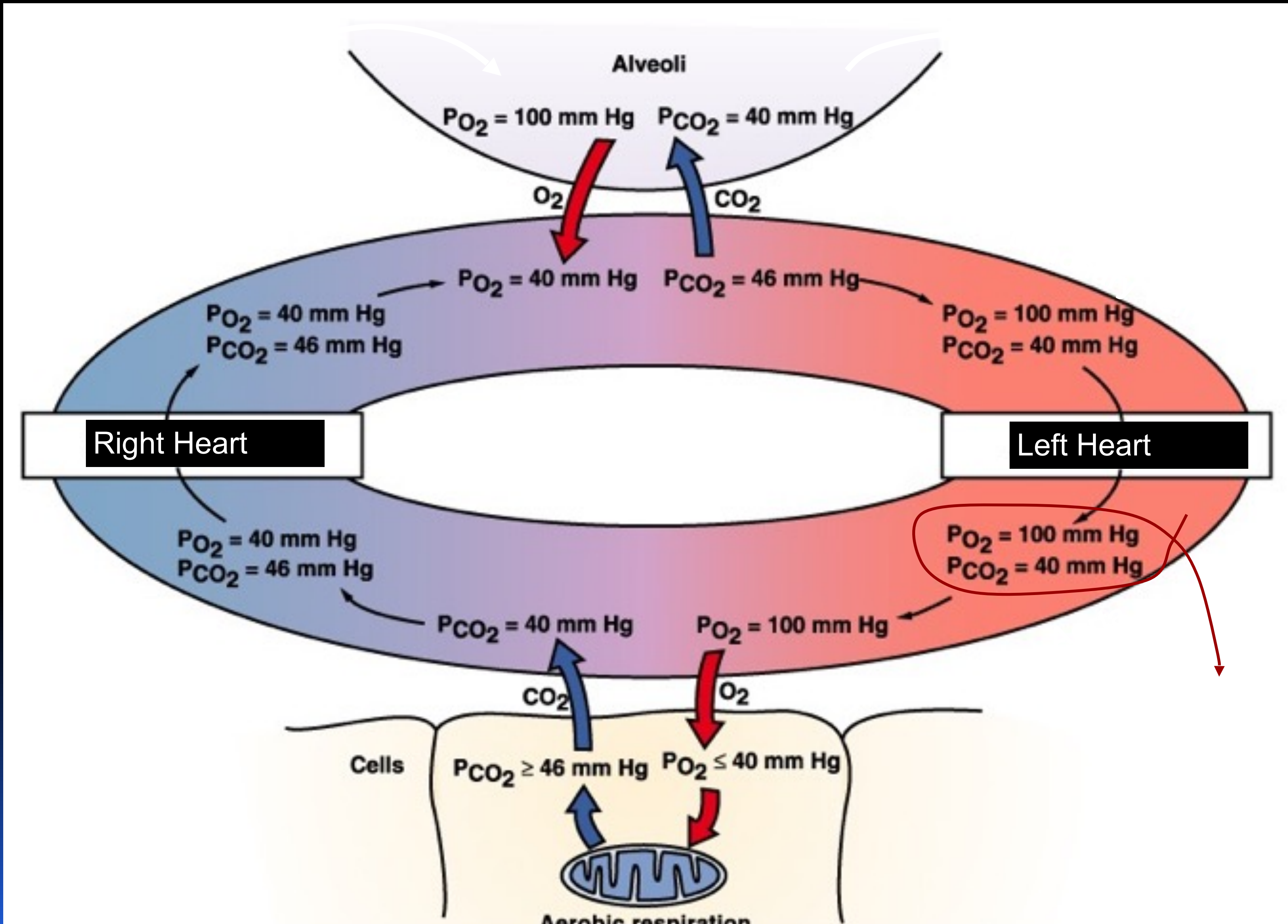


"Starling forces"

net fluid movement = $K\,[(P_c - P_i) - (\pi_c - \pi_i)]$

Fluid movement out of cap. $= K \times \Delta P = K\,[(10-0) - (\underline{25-15})] = K[\sim 0 \text{ mm Hg}]$

Gas exchange at alveolar and systemic capillaries



Regional circulation

- Apex(Upper)
  - Less perfusion
- Bases(Lower)
  - More perfusion

This is simply due to gravity.

c.f. in supine position

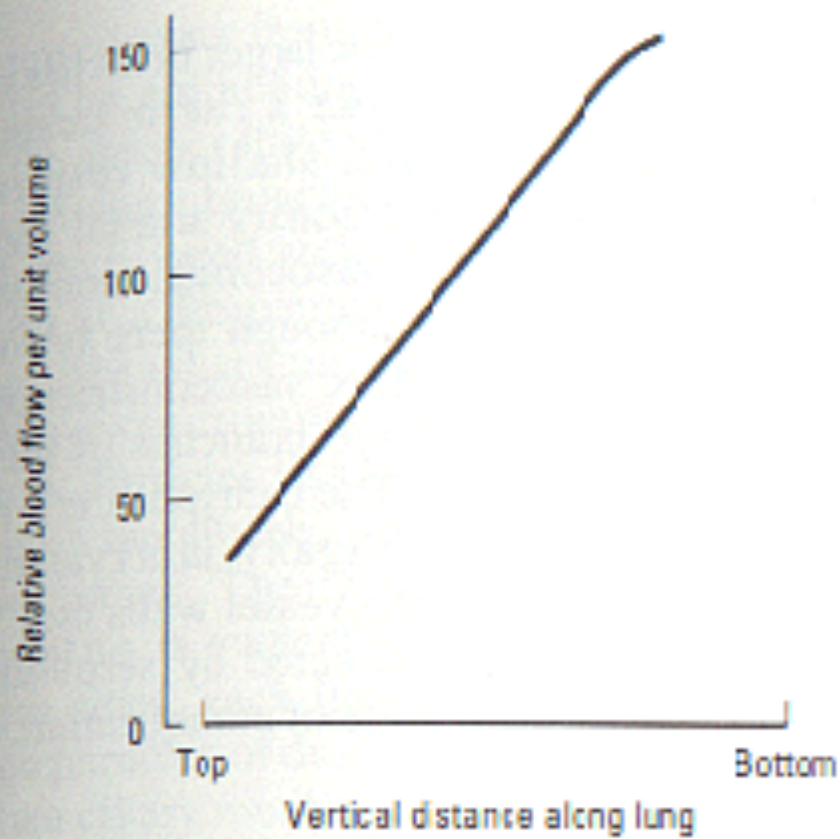


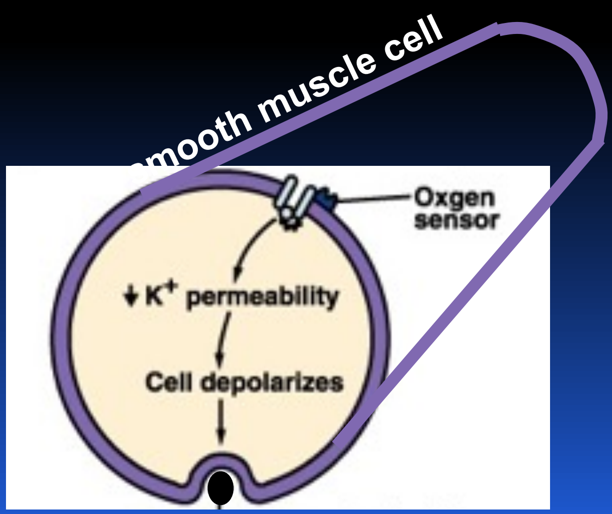
Figure 34–17. Relative blood flow from the top to the bottom of the lung in the upright position. The values for lung blood flow are scaled so that if flow were uniform, the value would be 100 throughout.

Special characteristic of blood vessels surrounding alveoli:
hypoxic vasoconstriction

When PO_2 within the alveoli decreases there is a decrease in blood flow to that alveolus(is more when pO2 is less than 70mmHg)

This is called hypoxic vasoconstriction

Thought to be the result of O_2-sensitive K^+ channels in the smooth muscle membrane. At low O_2 the K^+ channels close, the E_m rises, and the cell reaches threshold and depolarizes and contracts.



This phenomenon is just the opposite the response to hypoxia you get with arteriole smooth muscle in the systemic circulation, but it is an important feature of the pulmonary circulation that helps to match perfusion with ventilation

Hypoxic vasoconstriction

- This directs blood away from under-ventilated areas
- Directs blood to well ventilated areas
- In fetal life result in high pulm vasc resistance therefore less flow
- In high altitude may cause pulmonary hypertension

Other factors influencing the pulmonary circulation

- Autonomic nervous system
  - Sympathetic
    - Constriction
  - Parasympsthetic
    - Vasodilation
- Catecholamines
  - Constriction
- Cardiac output
  - If rises-capillary dilation, recruitment, more apical perfusion, less transition time
- pH- fall causes vasoconstriction

Ventilation-Perfusion matching

Matching respiration & blood flow: the Ventilation-Perfusion Ratio

Ventilation

Alveolar ventilation, $\dot{V}_A$

$\dot{V}_A = (V_T - V_D)$ x resp. rate

$= (0.5 - 0.15) \times 12 = 4.2$ L/min

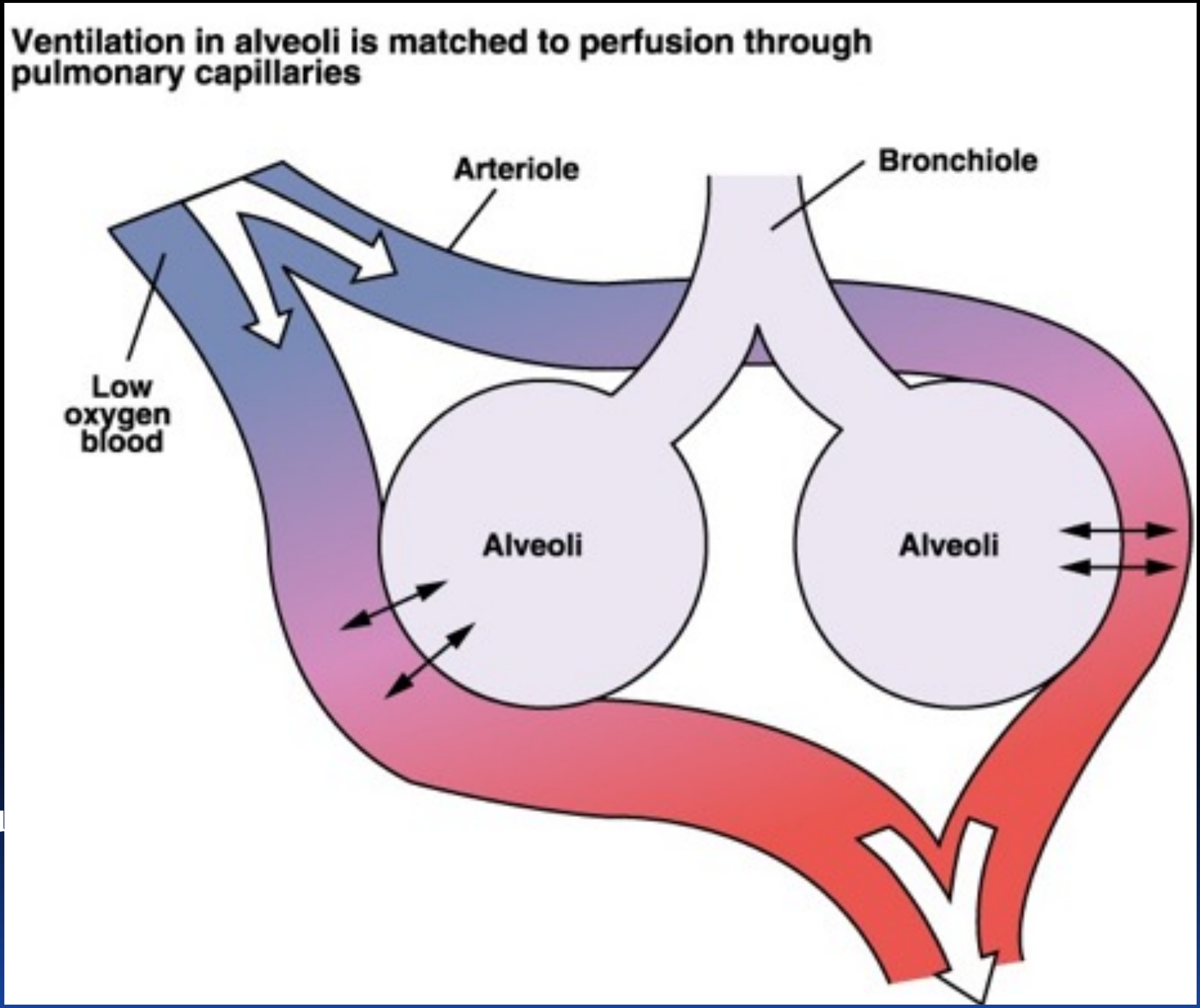
Perfusion

Cardiac output = C.O. = $\dot{Q}$

$\dot{Q}$ = stroke vol. x heart rate

$= (0.086) \times 70 = 6.0$ L/min

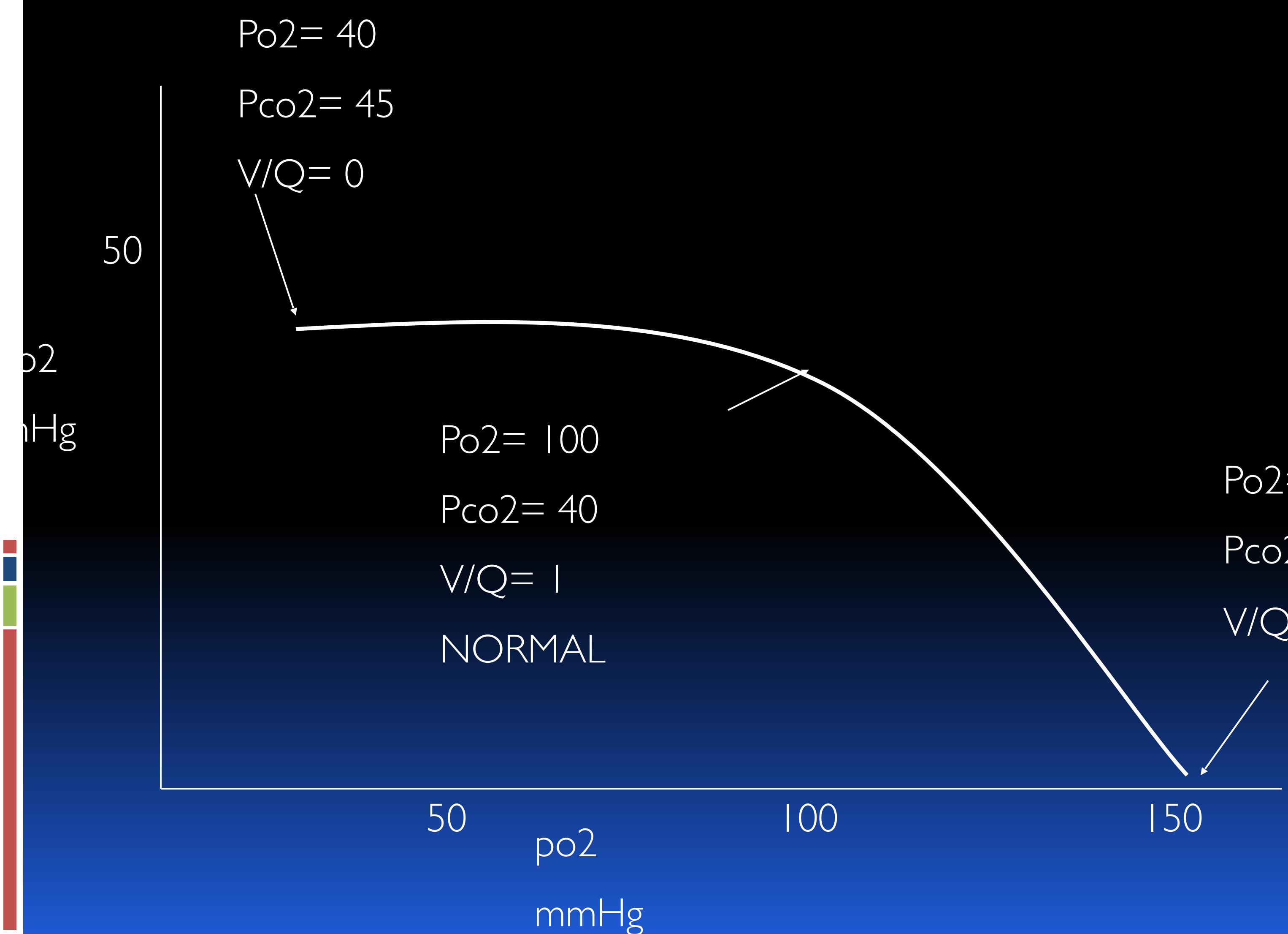
$$\frac{\dot{V}_A}{\dot{Q}} = \textbf{ventilation/perfu}$$



V/Q ratio

- Ideally should be 1:1
- Normal range:
  - 0.63- 3.3
- Theoretical range:
  - If NO ventilation, normal perfusion
    - V/Q ratio= 0
  - If normal ventilation, NO perfusion
    - V/Q ratio= ∞

V/Q ratio line



Effect of V/Q ratio on Gas exchange

- When 1:1, ideal exchange
- When <1, then
  - Fall in O_2
  - Slight rise in CO_2
- If >1
  - Not much rise in O_2

Regional differences in V/Q ratio

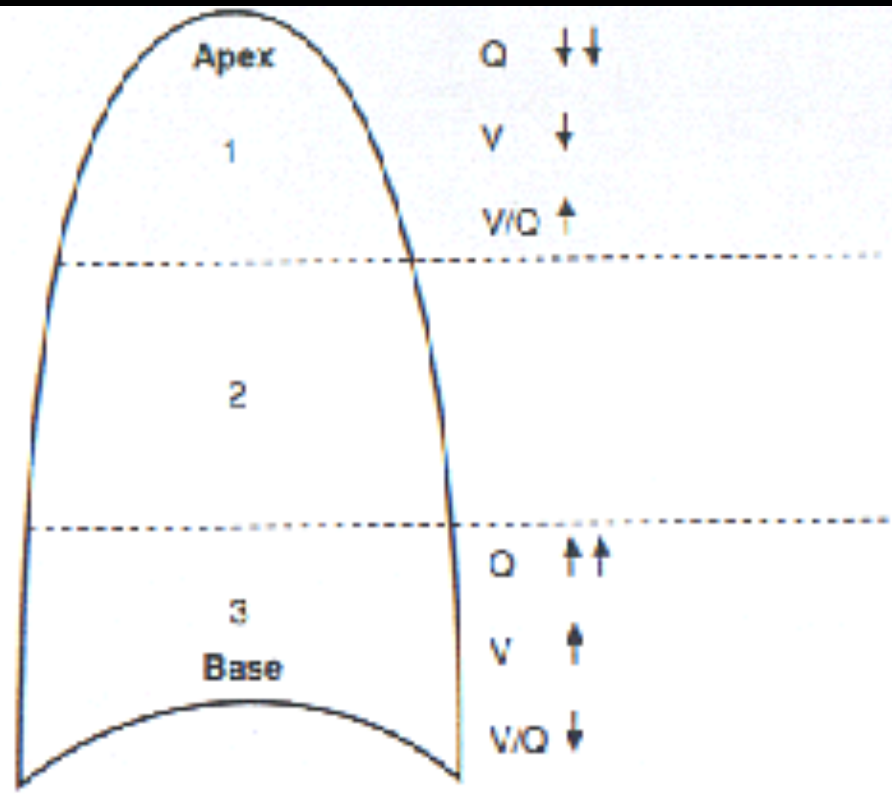
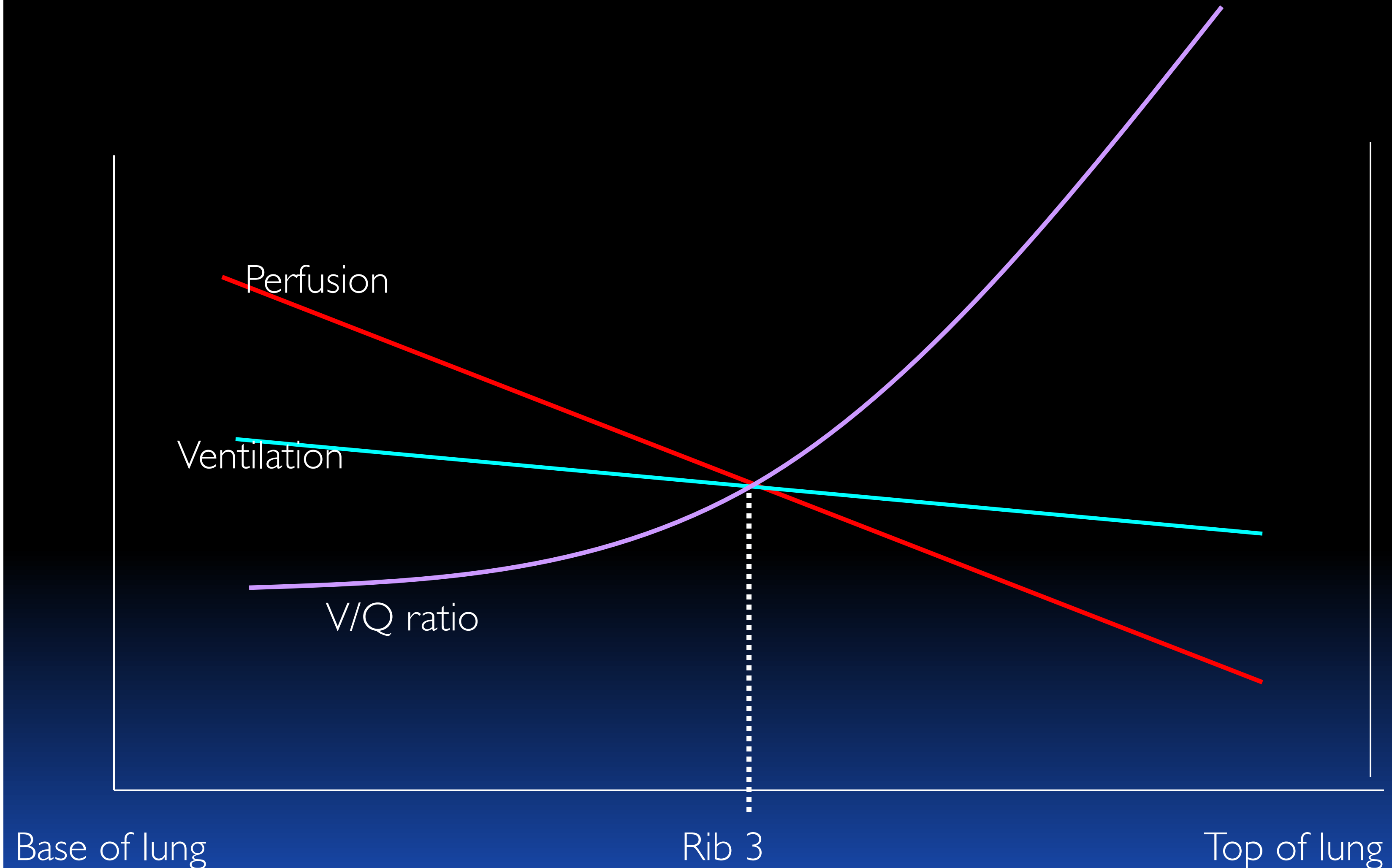


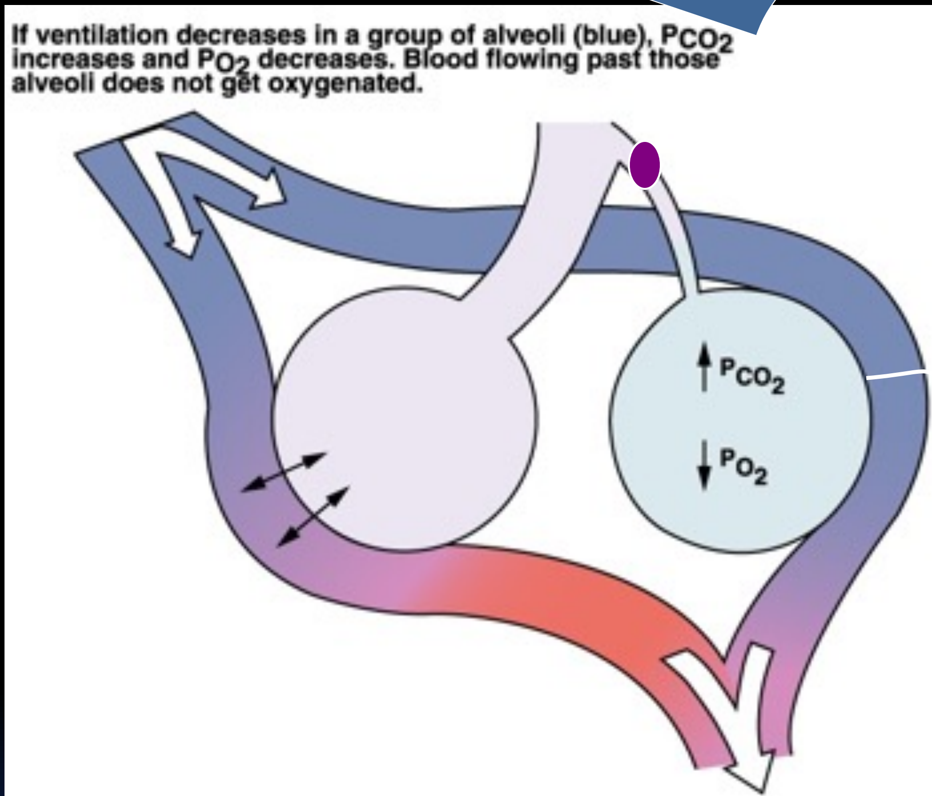
Figure 4-10. Variation of ventilation and blood flow (perfusion) in different regions of the lung.

Regional V/Q ratio

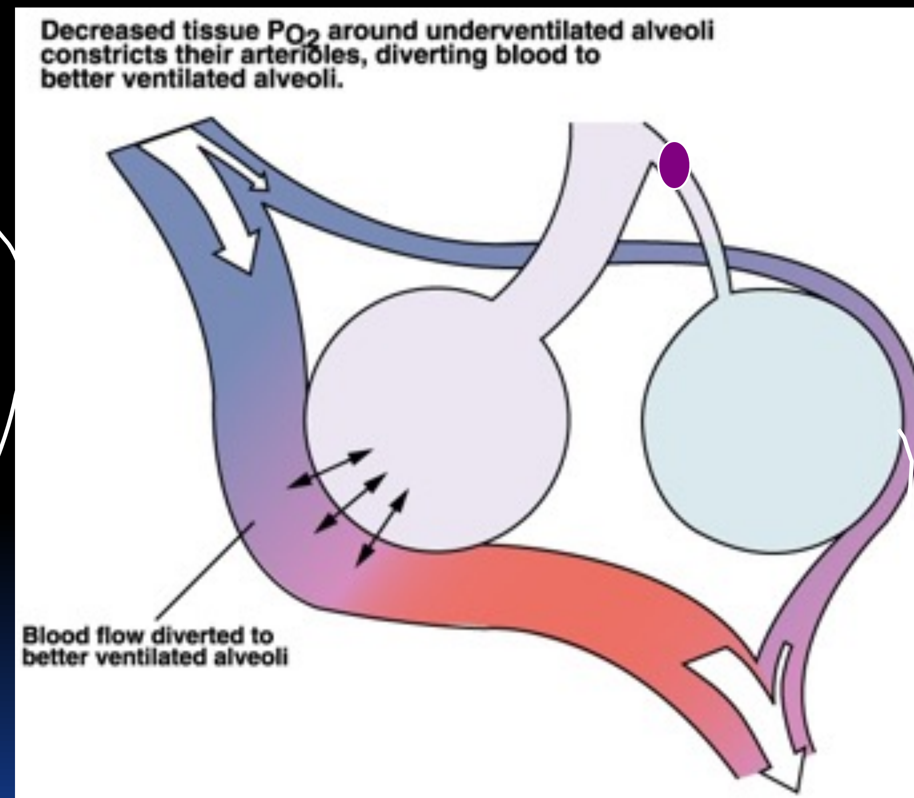


	Apex	Base
PO2	132	89
PCO2	28	42
Ventilation	↓	↑
Perfusion	↓↓	↑↑
V/Q Ratio	3.3	0.63

Let's assume that there is a blockage of one alveolar region



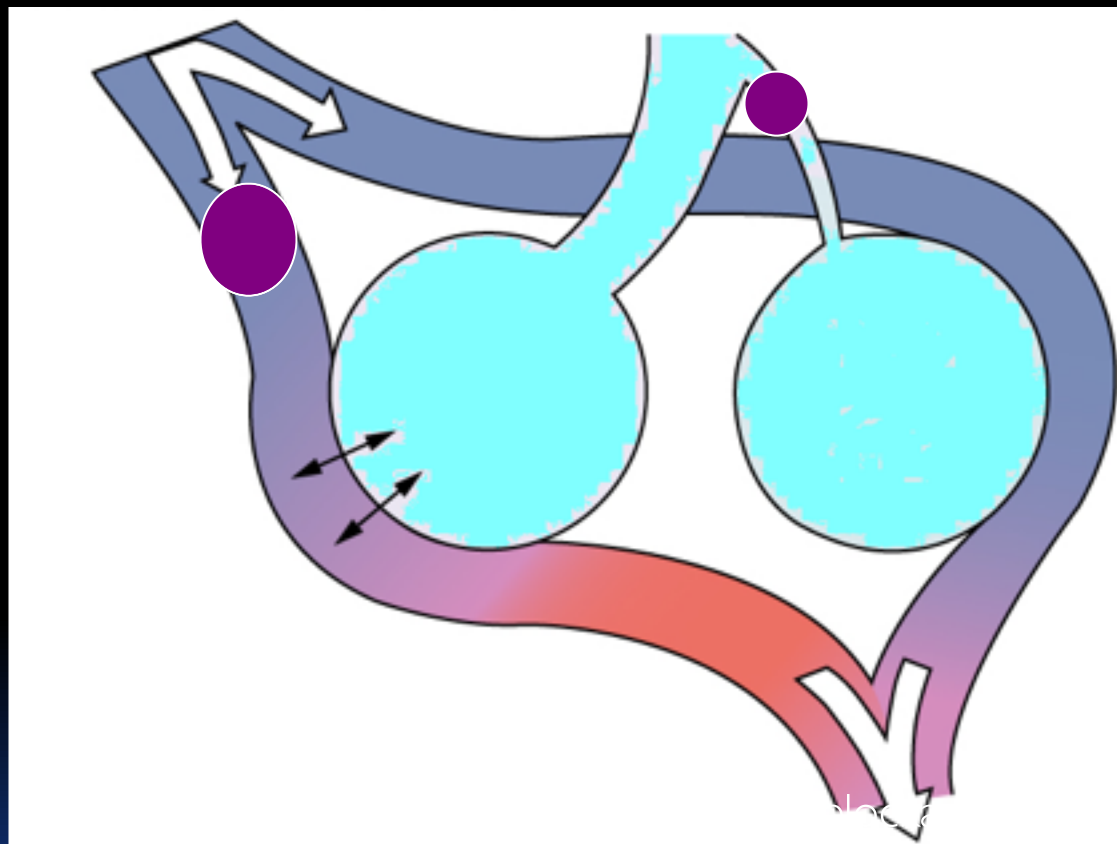
Response



$$\frac{\dot{V}_A}{\dot{Q}} << 0.8$$

$$\frac{}{\dot{Q}} \approx 0.8$$

It is regional V/Q, not overall V/Q ratio that is important:



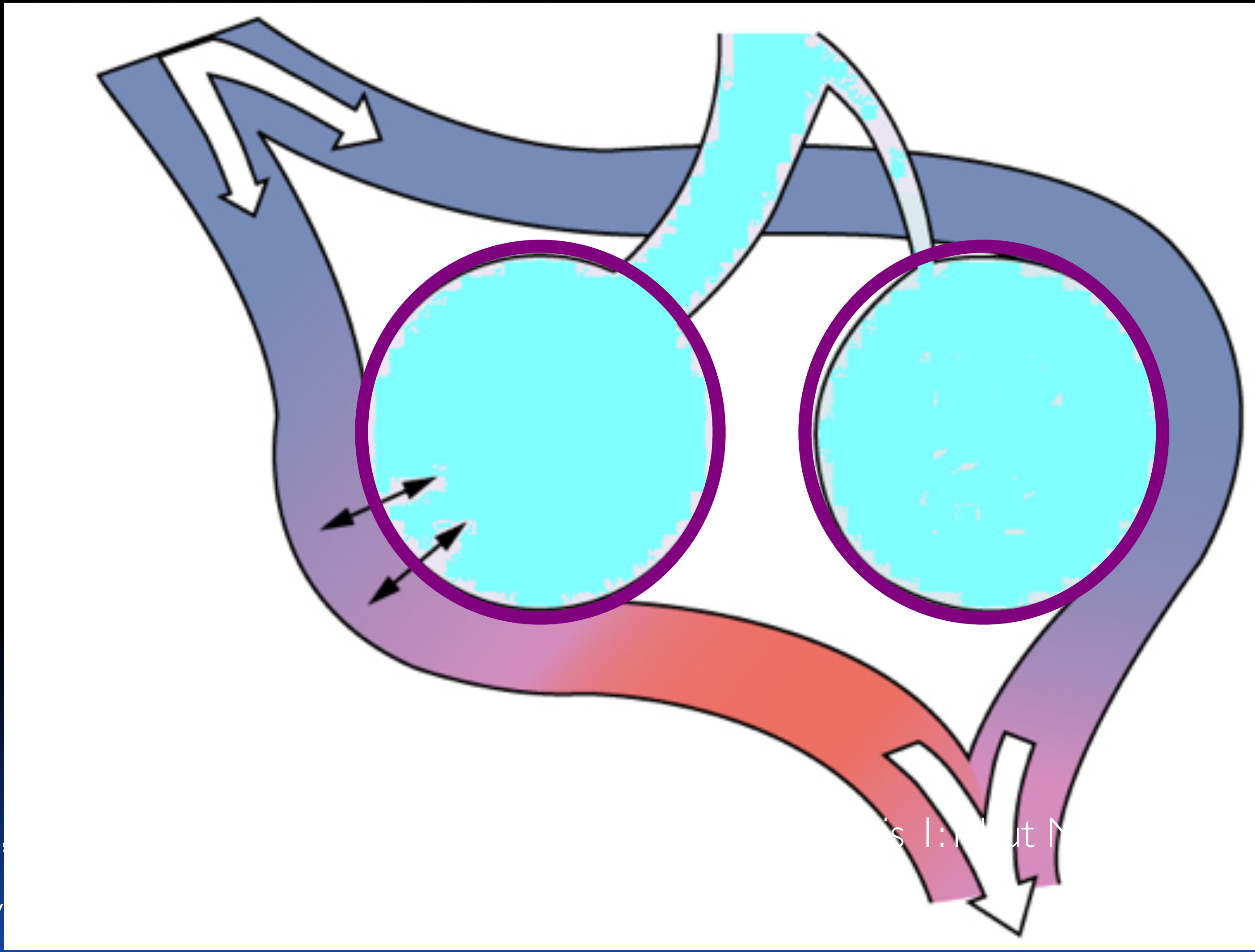
If total right

Then, overall V/Q ratio= 1:1

But for right side: ∞

And for left side: 0

If complete alveolar block



Then, [illegible] is 1:1 [illegible] ut N[illegible] ge,

for v[illegible]

and for perfusion, NO ventilation V/Q= 0

- Measurement of the effectiveness of V/Q matching is by:
  - Arterial O2 measurement in comparison with the alveolar O2

- If V/Q < 1 then
  - O_2 falls
  - Rise in CO_2 will cause it to be flushed away, with no change in O_2, this is 'wasted ventilation'

- If V/Q ratio > 1
  - This implies a rise in Physiological dead space

- If V/Q ratio < 1
  - Implies a rise in ‘Shunt’

Blood Gas transport

Carriage of blood gases

all values are in ml of gas/100 ml solution

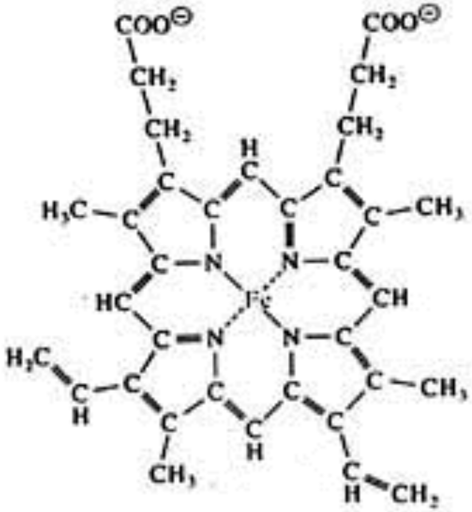
	H_2O or plasma (pH = 7.4)		Whole blood (Hct = 0.45)	
	dissolved	combined	dissolved	combined
(at a PO_2 = 100 mm Hg)	0.3	0	0.3	19.5
$_2$ (at a PCO_2 = 40 mm Hg)	2.6	43.8	2.6	46.4

S_{CO_2} = 30.0 µmol/L / mm Hg = 0.65 ml/L / mm Hg
S_{O_2} = 1.37 µmol/L / mm Hg = 0.03 ml/L / mm Hg

Oxygen transport

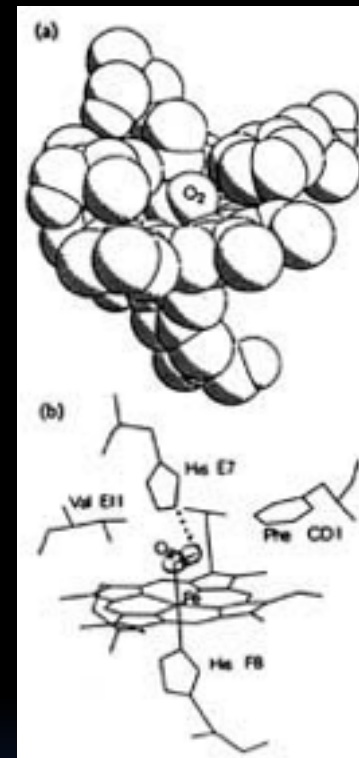
- Minor
  - Dissoved- 3% of total
  - In arteries- 0.3ml/100ml of blood
  - Not sufficient for body requirement
- MAJOR
  - In combination with haemoglobin
  - 97%

6.1.B. A Heme Prosthetic Group Binds Oxygen

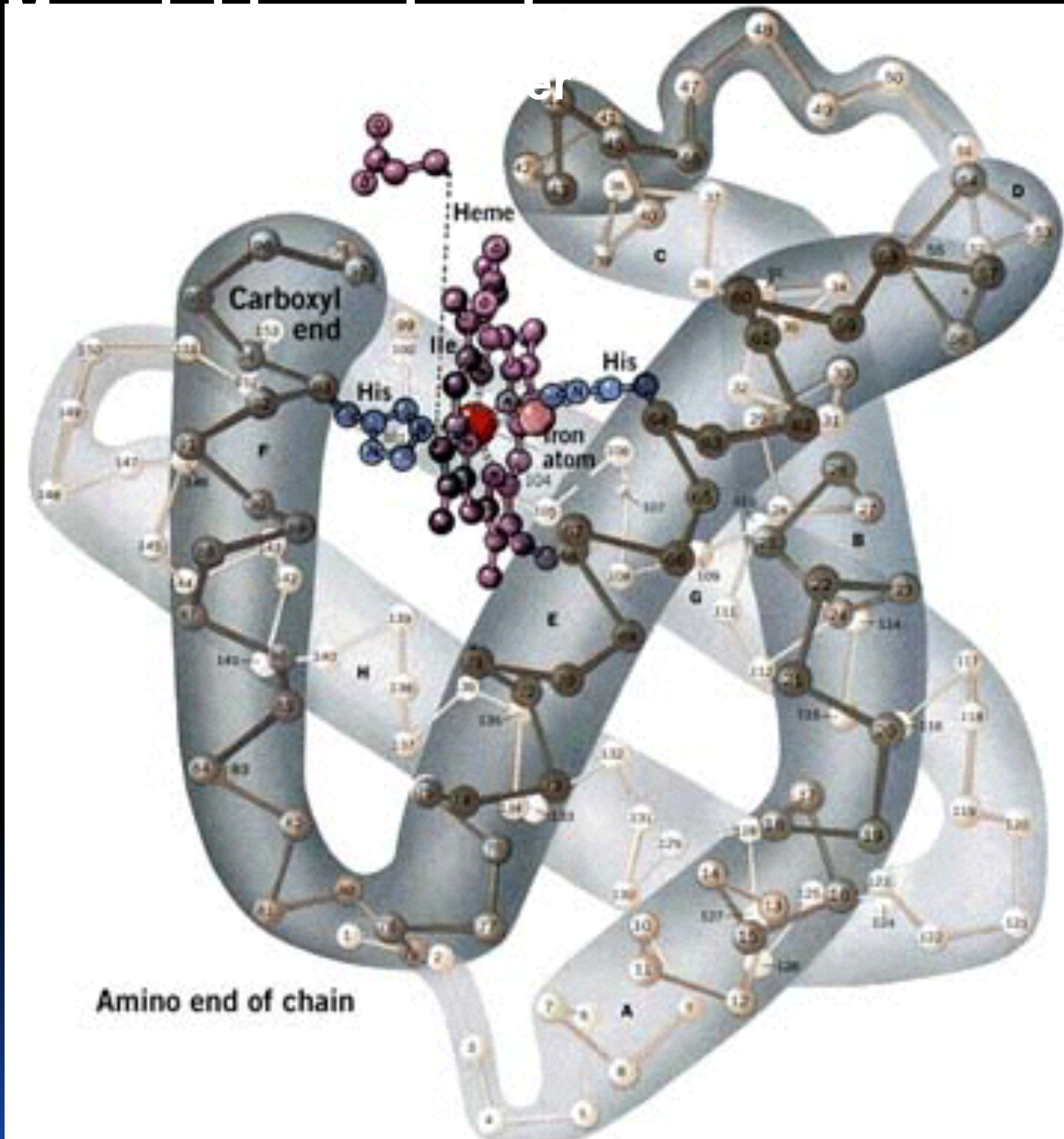


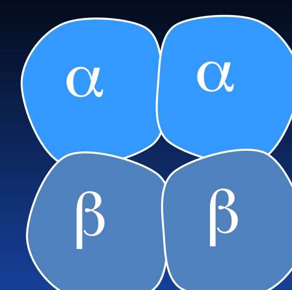
Heme
(Fe-protoporphyrin IX)

Figure 6·3
Structure of heme (Fe-protoporphyrin IX). The iron atom is in the ferrous oxidation state.



The oxygen-binding site of oxyhemoglobin, space filling model (a) and stick model (b). The Fe^{2+} ion is bound to oxygen. The Fe^{2+} ion lies almost in the heme plane. Valine E11 and phenylalanine CD1 provide a hydrophobic environment at the oxygen-binding site.





Hemoglobin molecule
tetramer, $2\alpha 2\beta$

Spectral characteristics of Hemoglobin:

color changes with reaction of iron heme

Oxygenation:

Hb (deep red to bluish) **+ O_2 ⟵⟶ HbO_2** (oxyhemoglobin; red)
(deoxyhemoglobin)

readily reversible

in fact, since Hb is a tetramer the reaction is really

$$Hb + 4O_2 \longleftrightarrow Hb(O_2)_4$$

Oxidation:

$Hb(Fe^{2+}) \rightarrow\rightarrow Hb(Fe^{3+})$ (methemoglobin; brownish)

difficult to reduce

CO reaction:

Hb + CO →→→→→→→→ HbCO (carboxyhemoglobin; bright red, pink)

very high affinity (230X greater than for O_2)

Oxygen carrying capacity

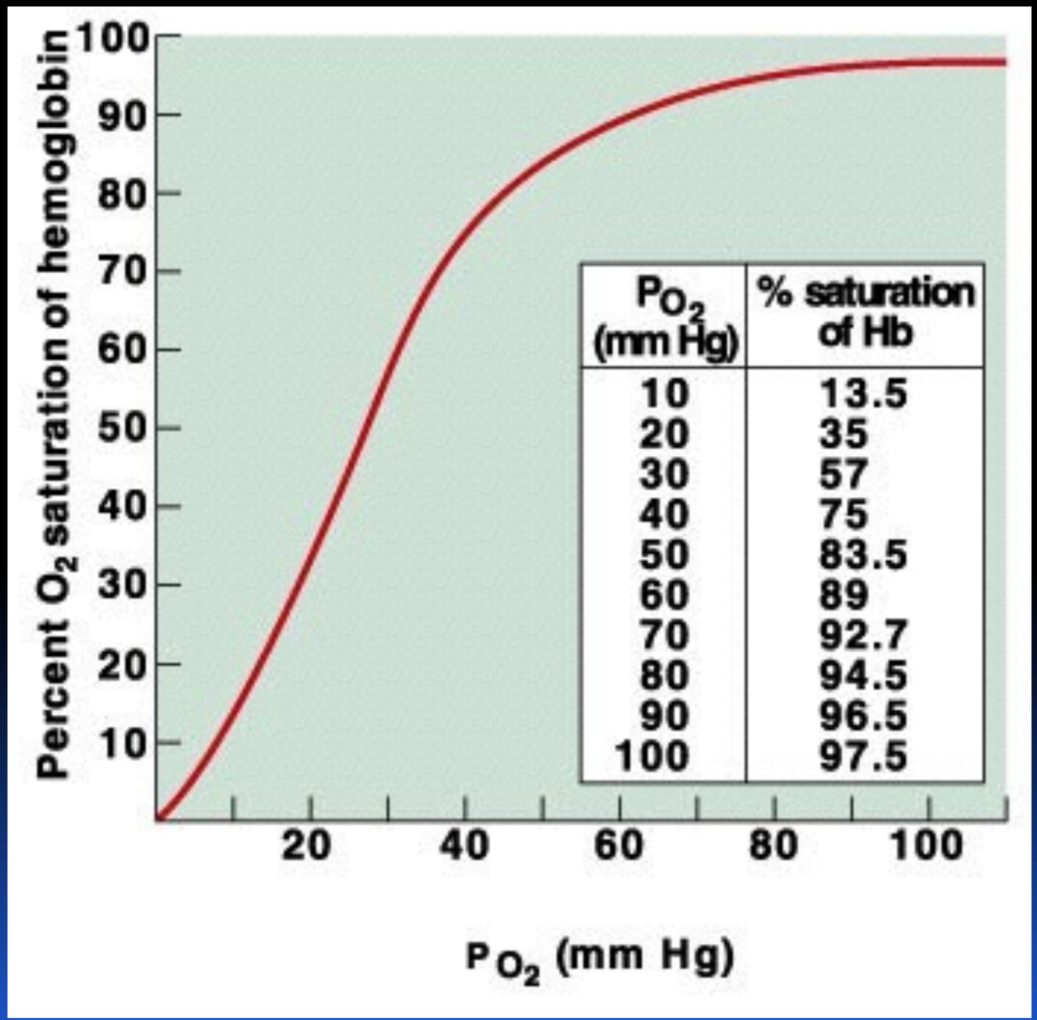
- 1g of Hb- 1.39ml of O2
- Normal O2 carrying capacity
  - 20.8ml/100ml of blood
- O2 saturation

= actual O2 carried/O2 carrying capacity X 100%

Oxygen carrying capacity

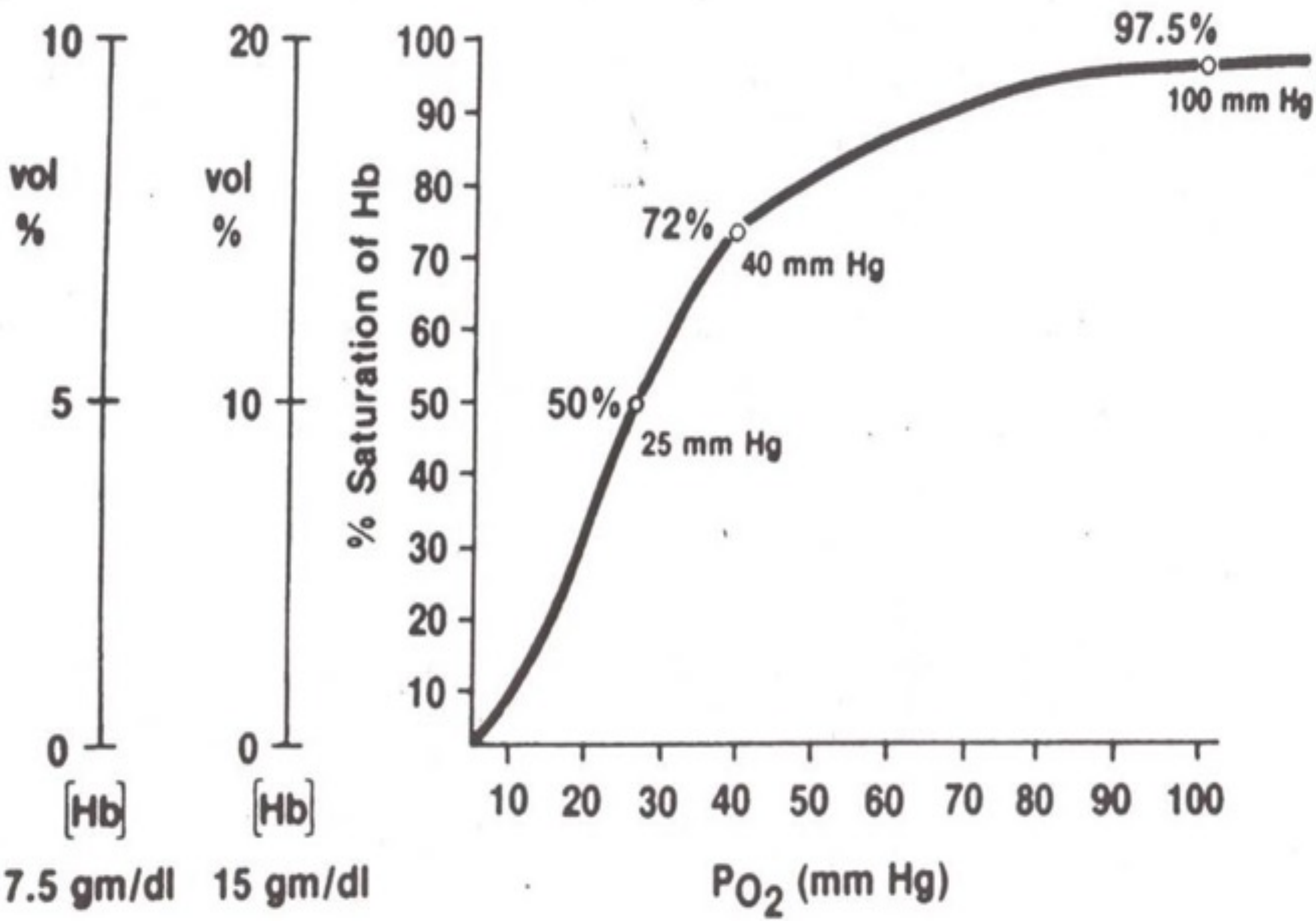
- Arterial:
  - 97.5% (PO_2= 100mmHg)
- Venous:
  - 75% (PO_2= 40mmHg)

Oxygen-Hemoglobin Dissociation Curve



P_{O_2} (mm Hg)	% saturation of Hb
10	13.5
20	35
30	57
40	75
50	83.5
60	89
70	92.7
80	94.5
90	96.5
100	97.5

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



Why is Hb-O_2 association "S-shaped"?

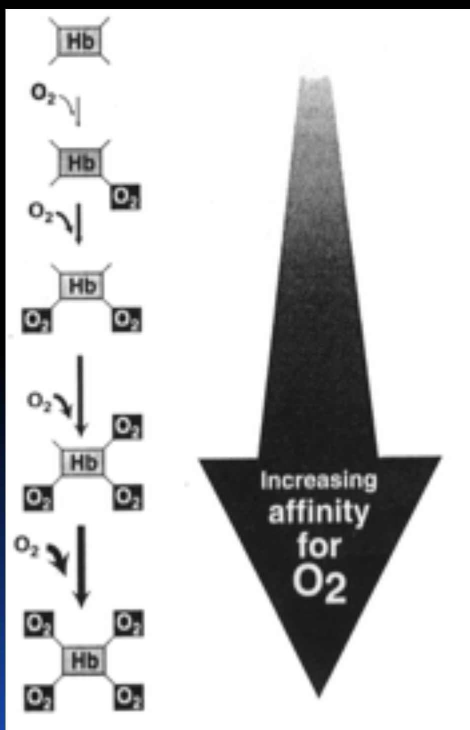
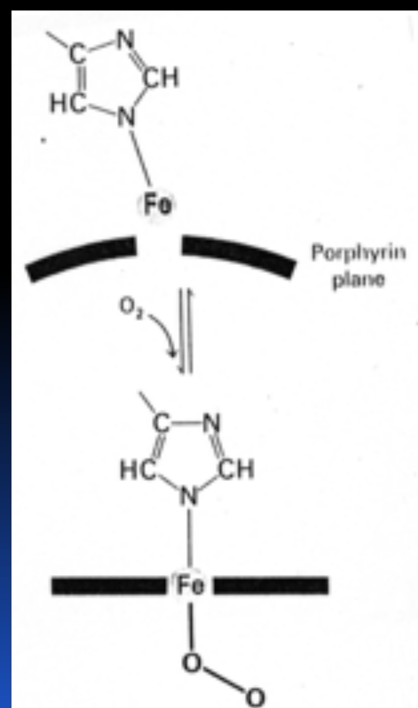
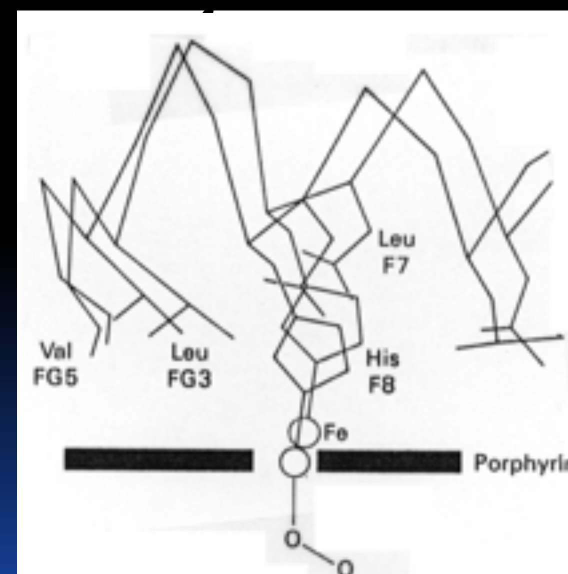


Figure 3.7
Hemoglobin binds oxygen with increasing affinity.



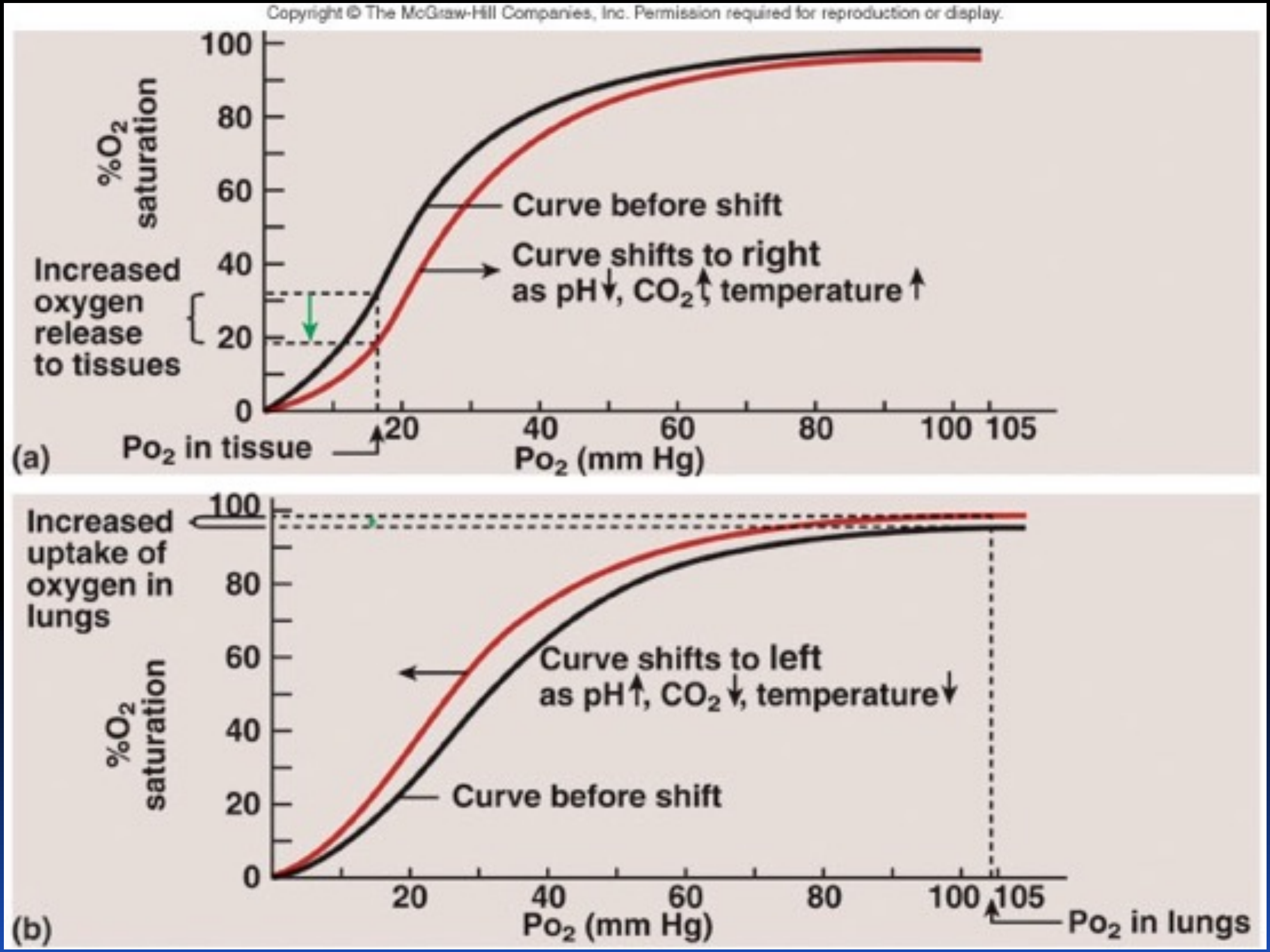


…rmational change induced by the movement of …n atom on oxygenation are transmitted to parts of the molecule that are far away

O_2/Hg dissociation curve

- Plateau part: >60mmHg close to 100% saturation
  - So even if alveolar O_2 falls, not much effect on saturation
- Steep part- this is important at tissue level
  - A small drop of O_2 will cause a large change in the saturation enabling O_2 release

Shifting the Curve



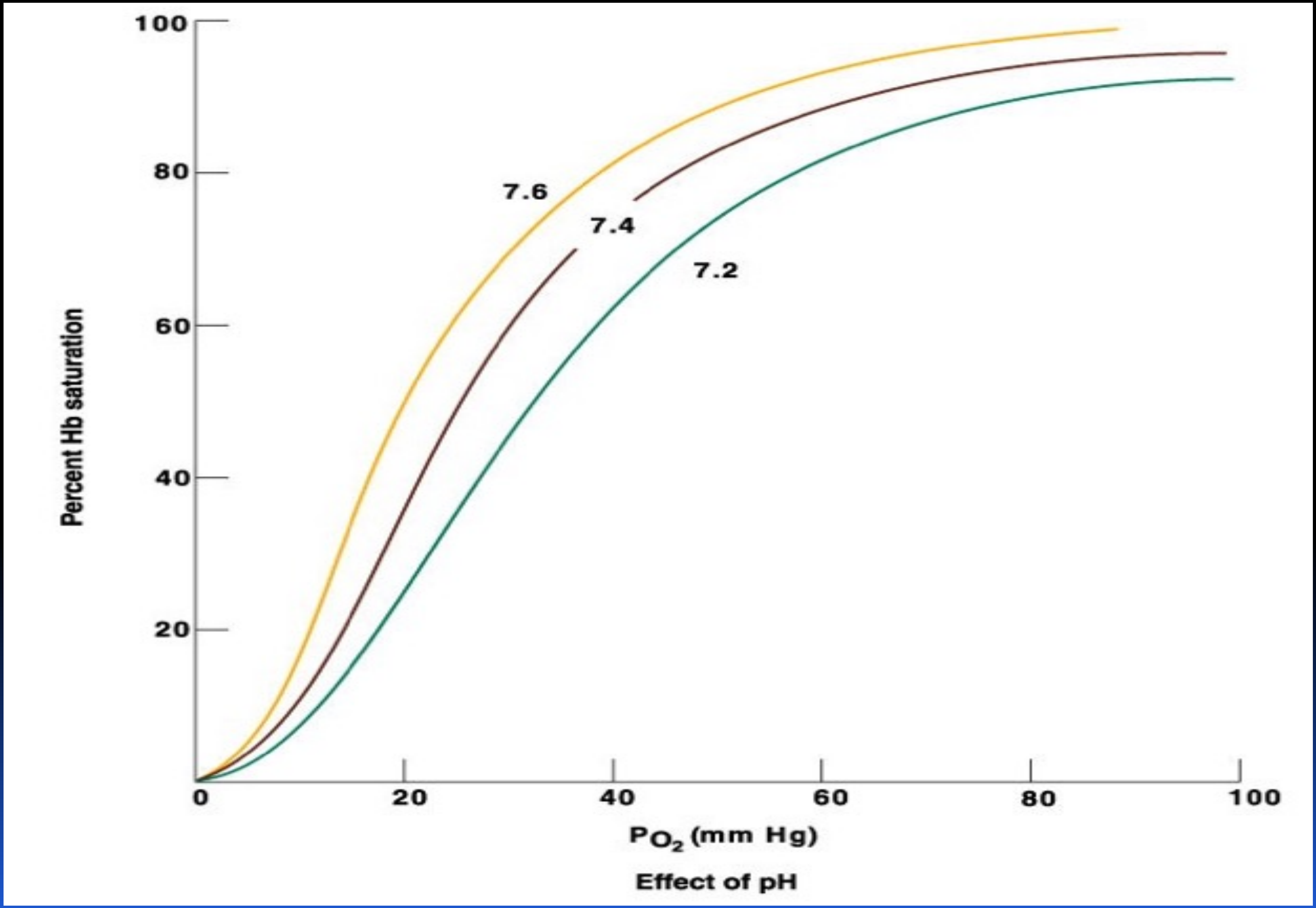
Hemoglobin and Oxygen Transport

- A shift of the curve to the right because of a decrease in pH, an increase in carbon dioxide, or an increase in temperature results in a decrease in the ability of hemoglobin to hold oxygen
- The substance 2.3-bisphosphoglycerate increases the ability of hemoglobin to release oxygen
- Fetal hemoglobin has a higher affinity for oxygen than does maternal

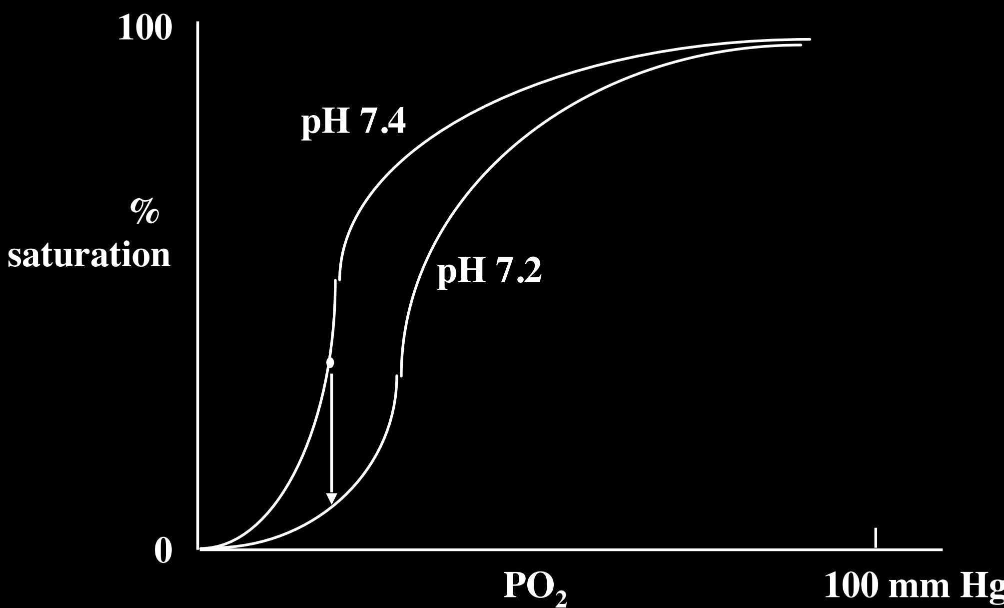
Curve shift

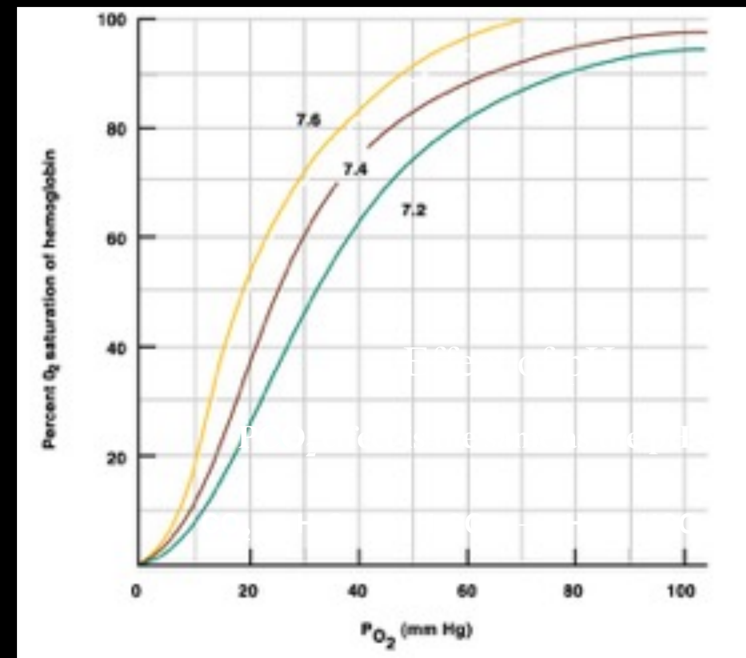
- Right shift:
  - This enables O_2 to be given up more easily
- Left shift
  - This results in O_2 NOT been given up easily

Bohr effect: fall in pH, right shift

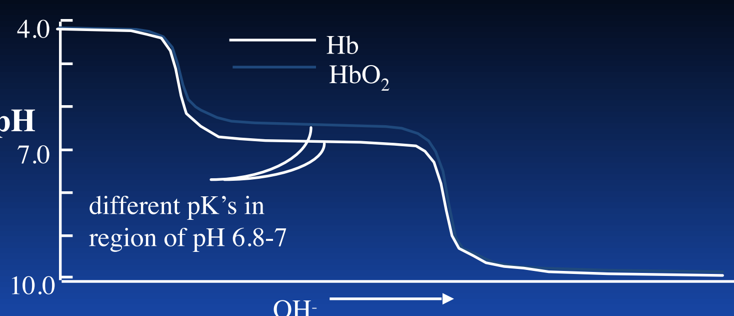


Advantages & Mechanistic Basis of the Bohr effect (change in pH or PCO_2)

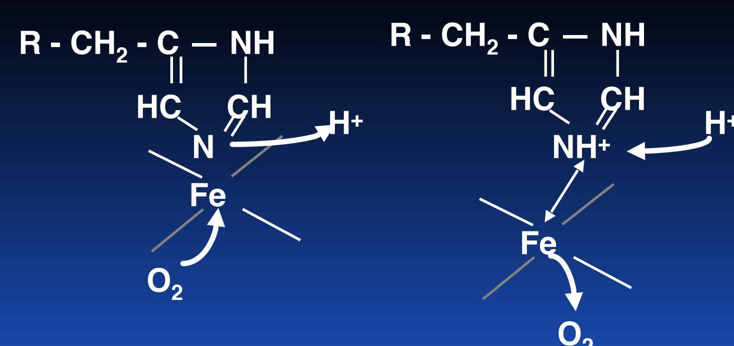




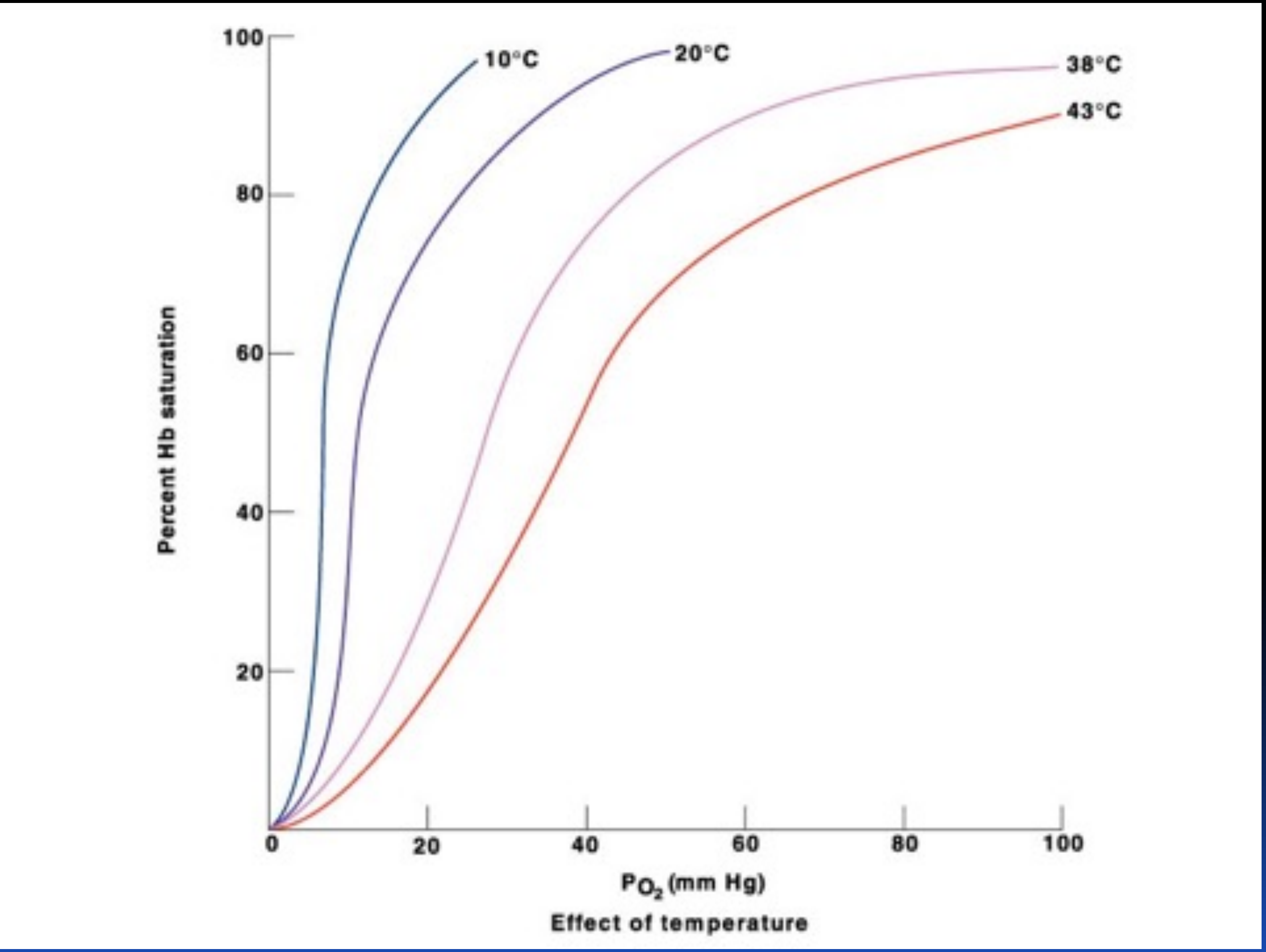
Titration of Hb & HbO_2

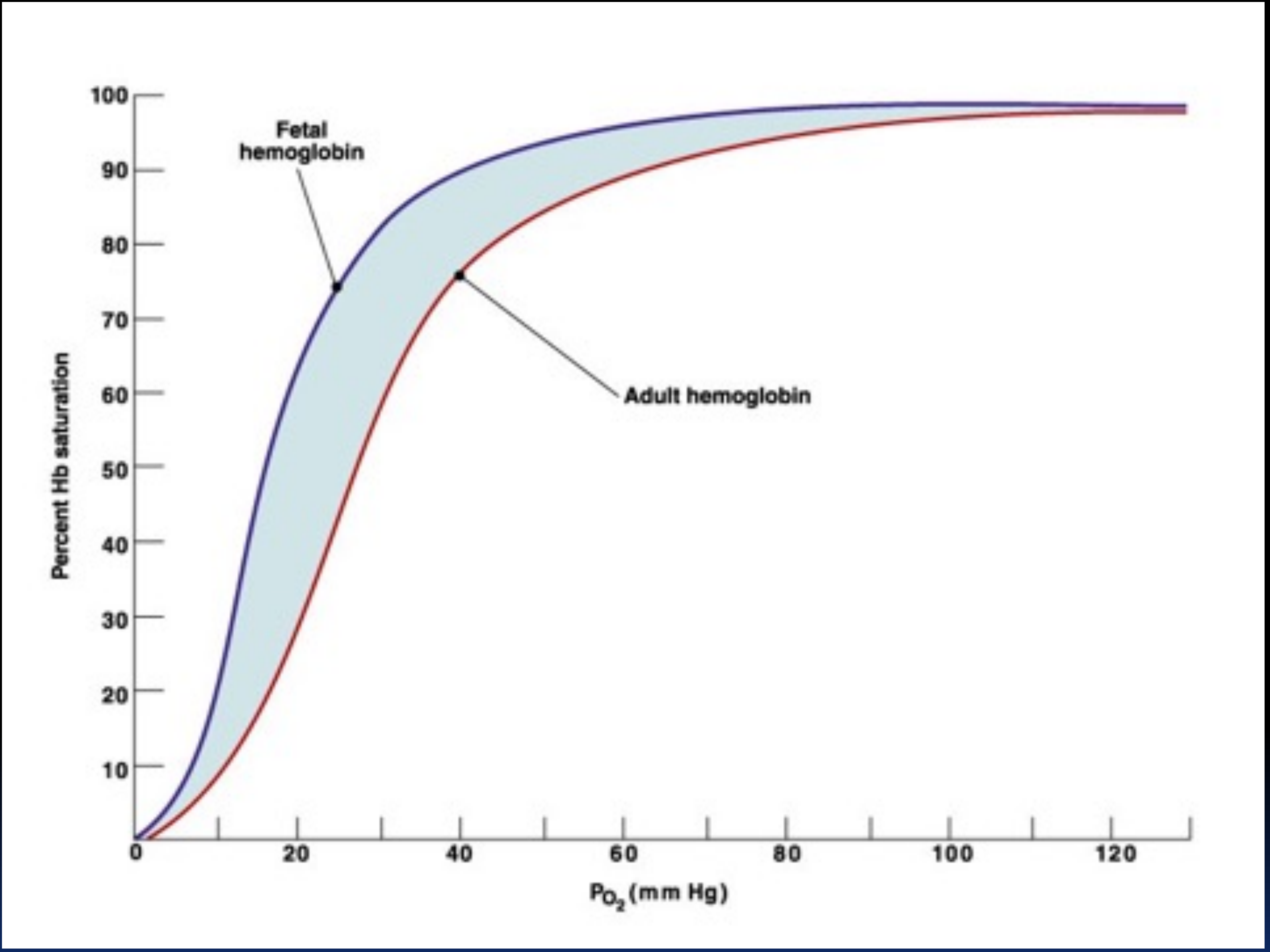


Protonic association alters O_2 affinity



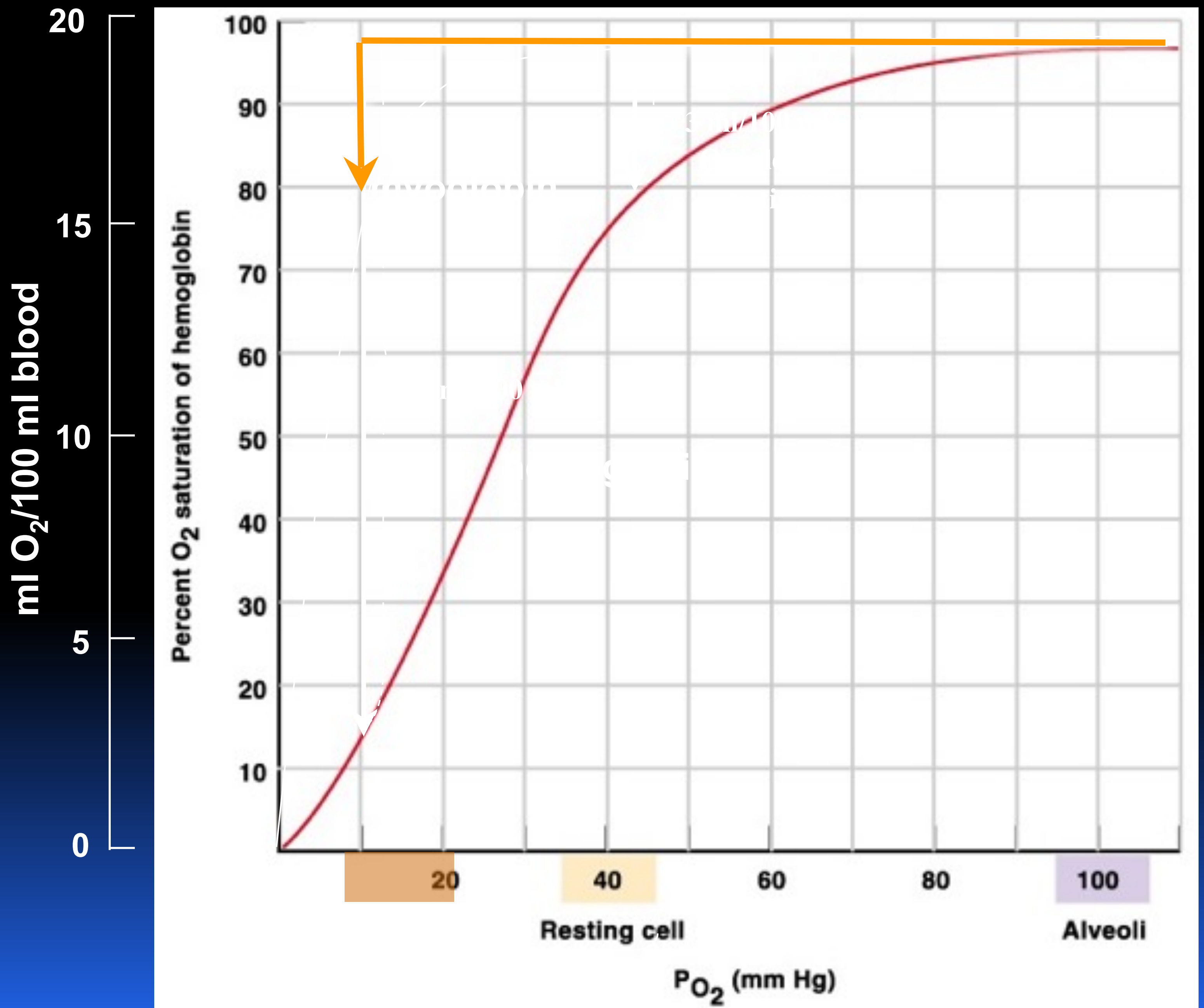
Temperature effects:



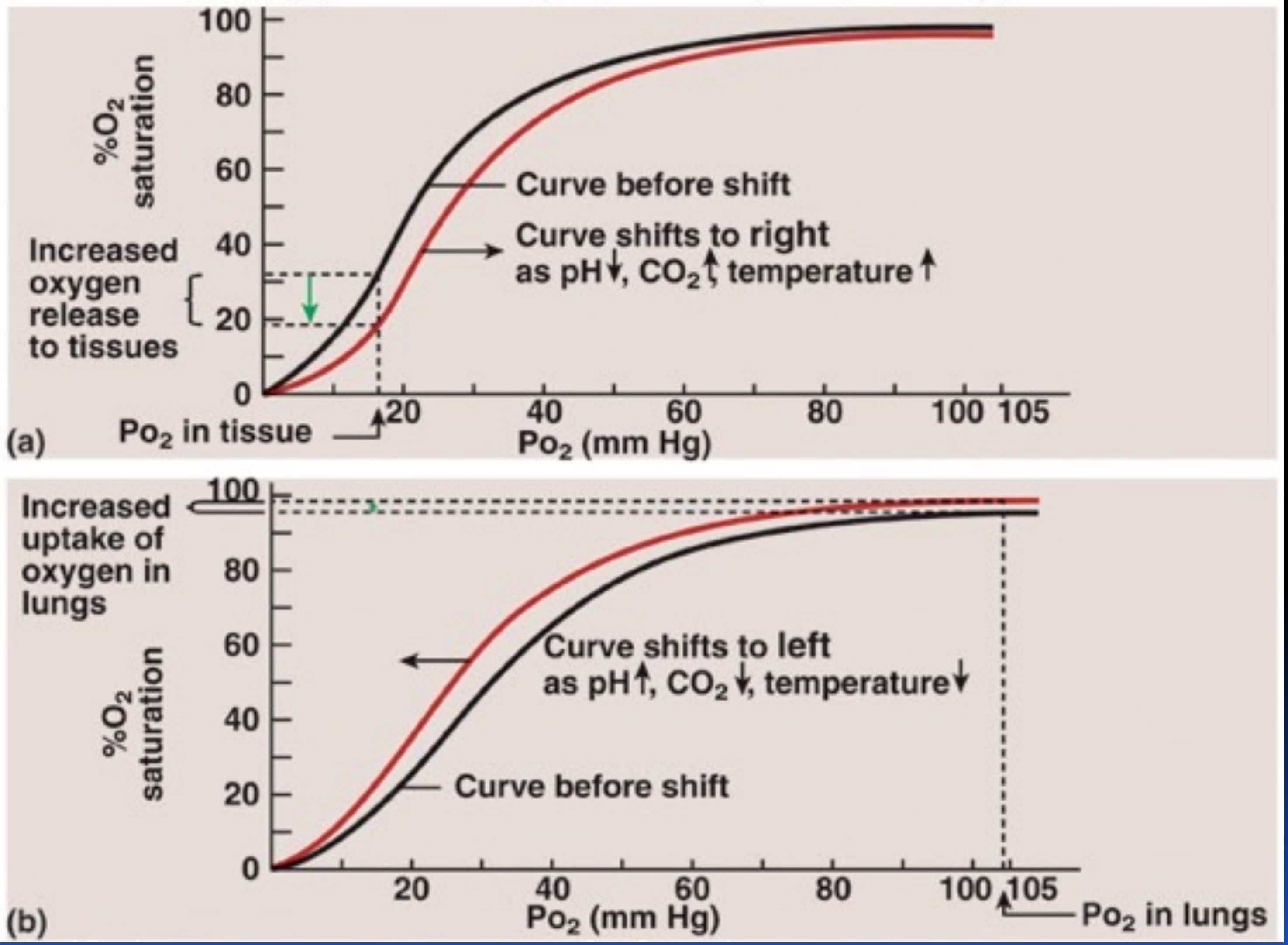


Fetal hemoglobin
Adult hemoglobin
Percent Hb saturation
100
90
80
70
60
50
40
30
20
10
0
20
40
60
80
100
120
P_{O_2} (mm Hg)

Compare Hemoglobin and Myoglobin

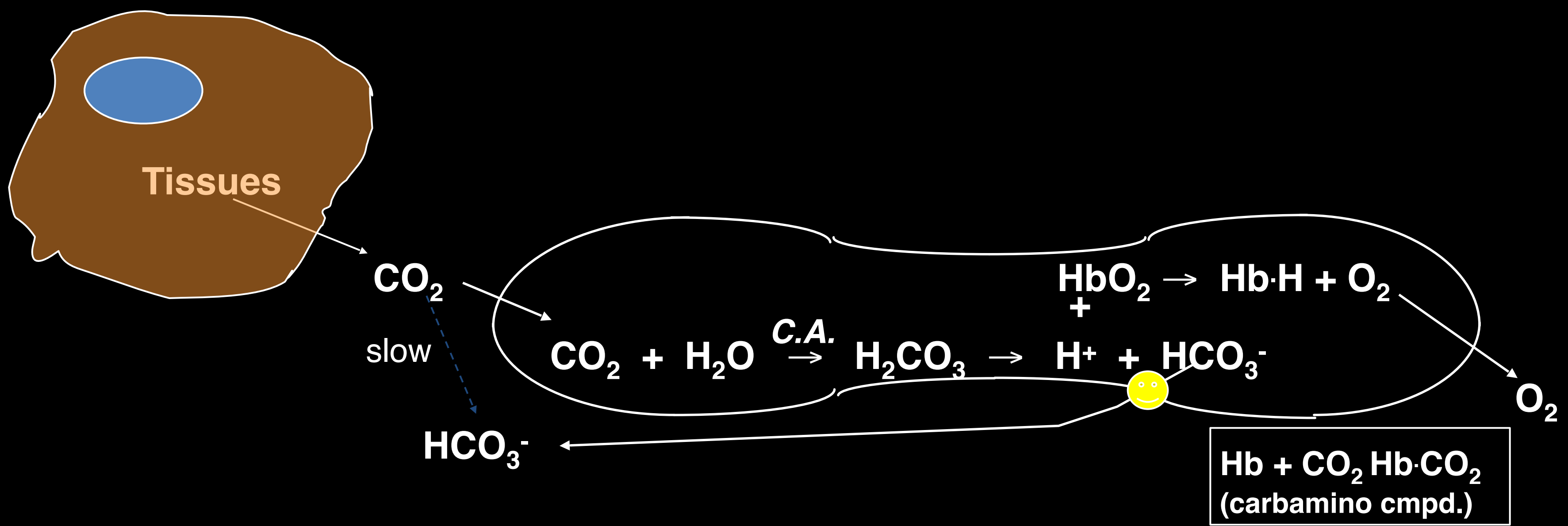


Shifting the Curve



Carbondioxide transport

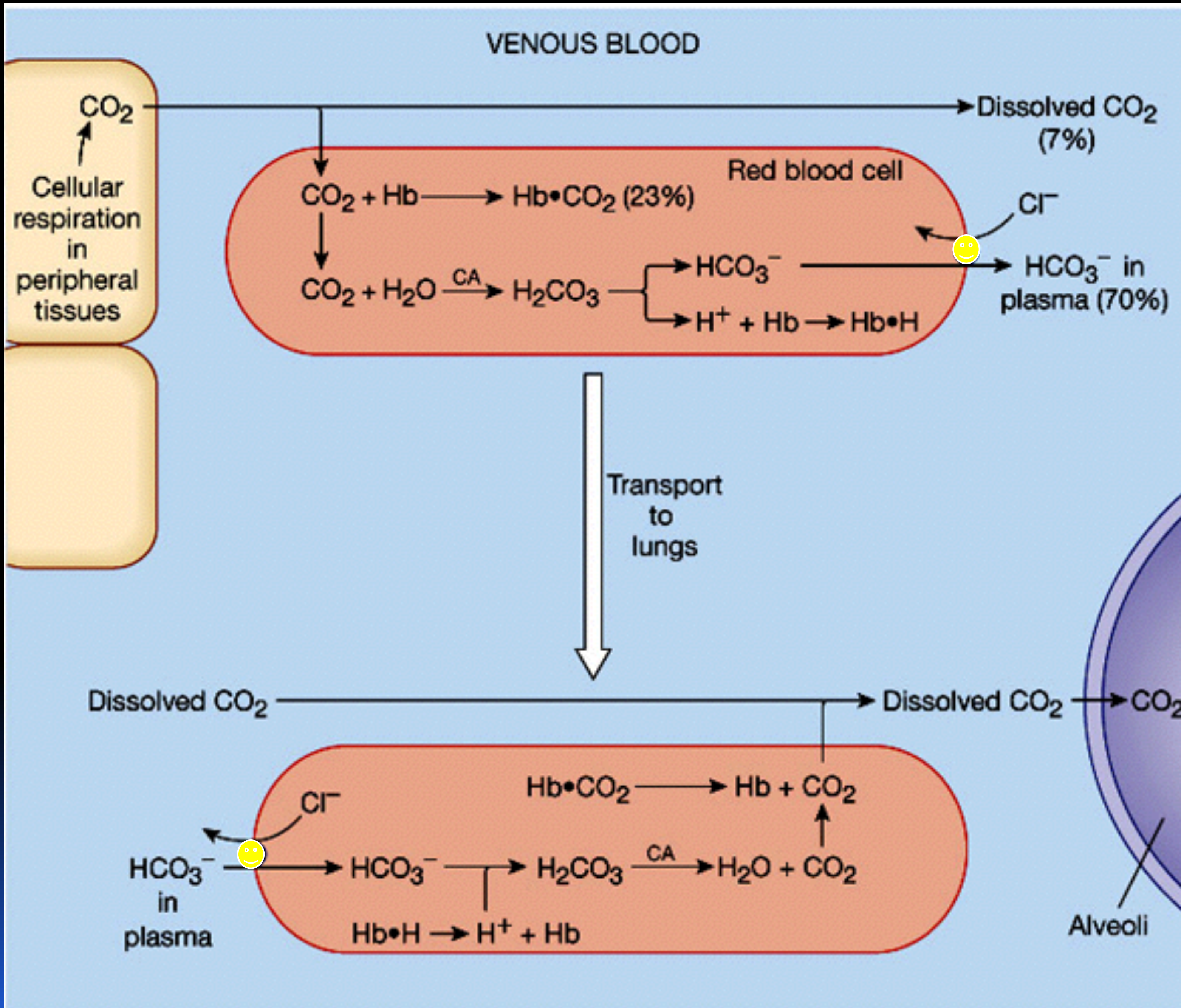
- Dissolved- 10%
- As Bicarbonate- 70%
- As Carbamino compounds- 20%



How is CO_2 carried by the blood??

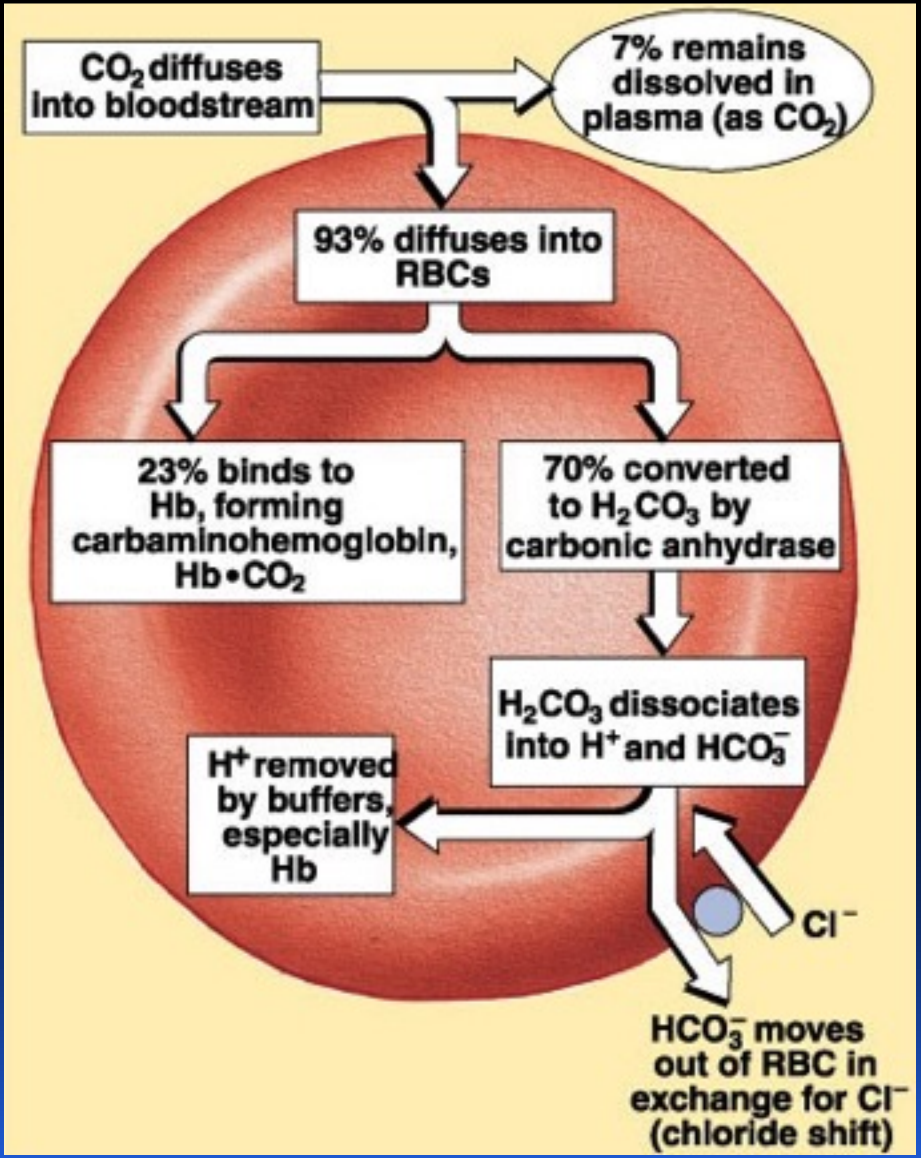
	Arterial blood	Venous blood	CO_2(%)
Total CO_2	49	52.7	100
CO_2 in solution	2.6	3.0	11
H_2CO_3	negligible	negligible	0
HCO_3^-	43.8	46.3	67
Carbamino compounds	2.6	3.4	21

Tissues



Lungs

CO_2 Transport and Cl^- Movement

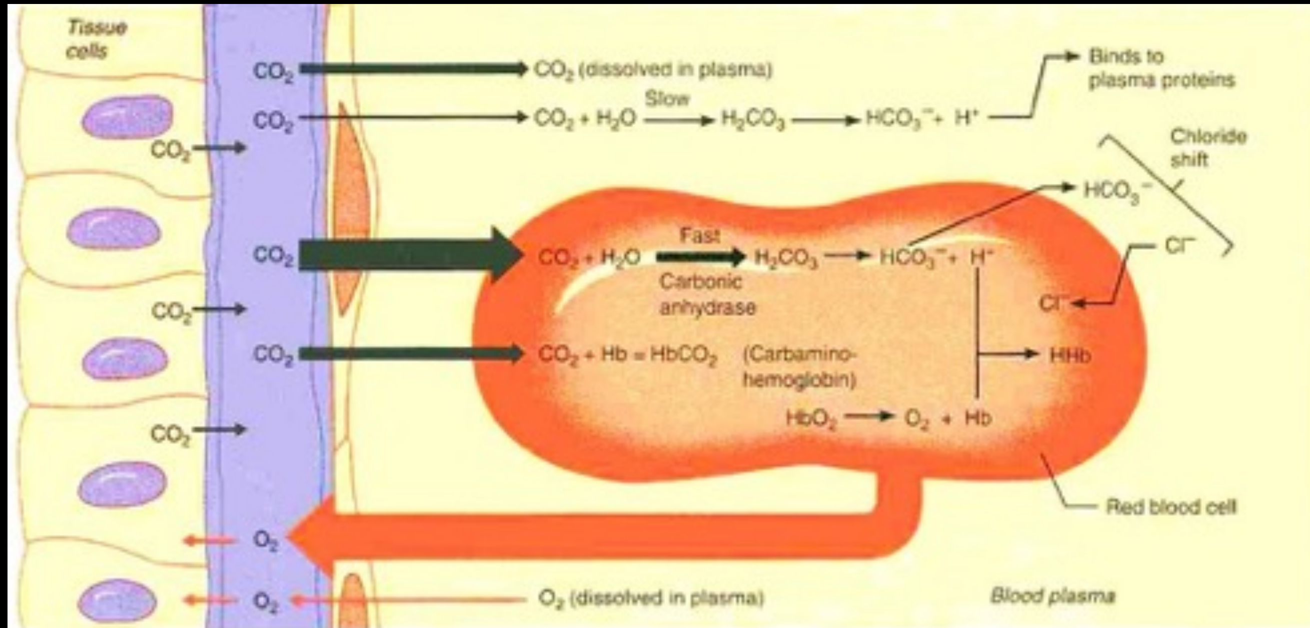


Chloride shift (Hamberger's shift)

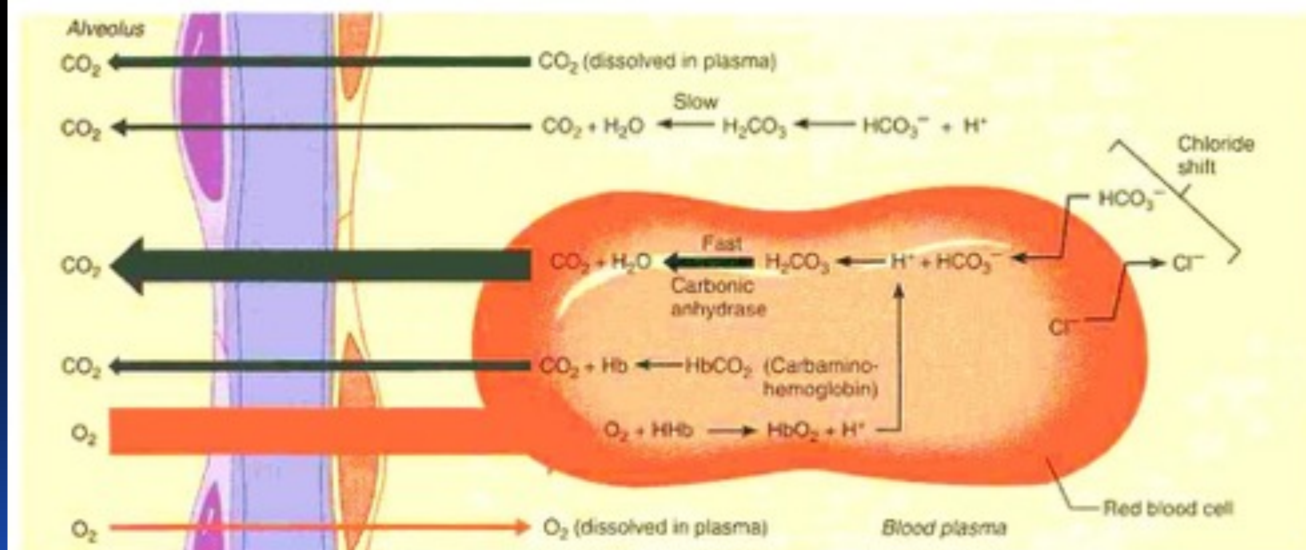
- Exchange of CL^- with HCO_3^-
- Results in more HCO_3^- in blood
- Fall in pH in the RBC
- More O_2 released
- More Cl^- in RBC's, causes them to swell up due to osmosis

Haldane effect

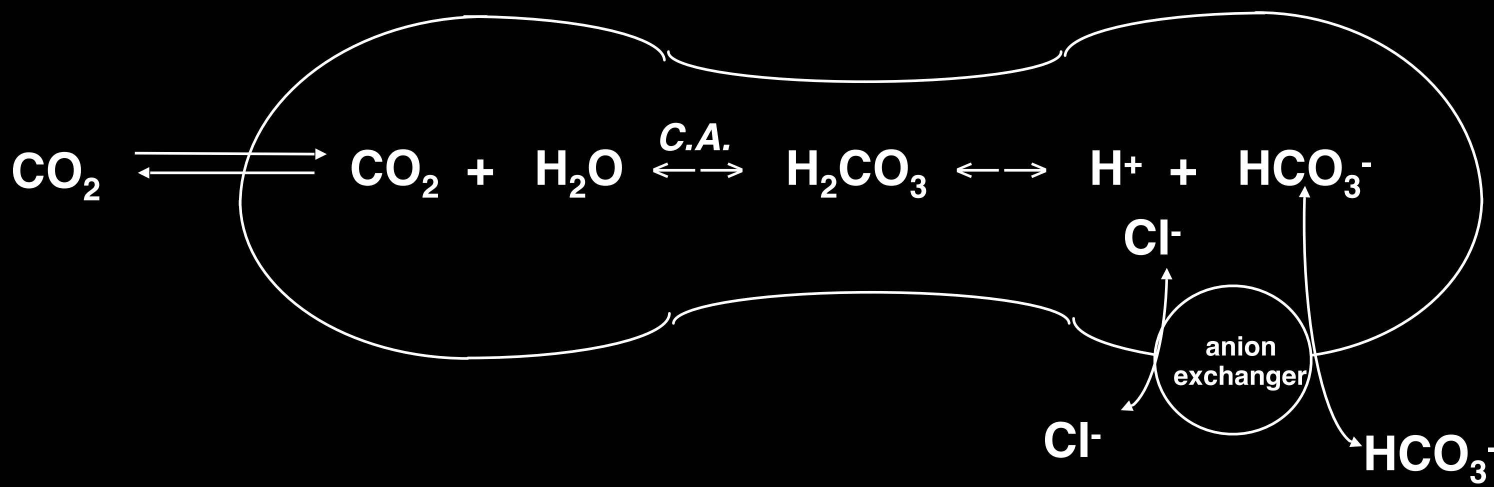
- As oxygen rises in RBC, more HbO_2 formed, this causes less affinity for CO_2. This occurs in lungs
- The reverse occurs in tissues
  - This is due to HbO_2 being a stronger acid which drives the equation towards release of CO_2

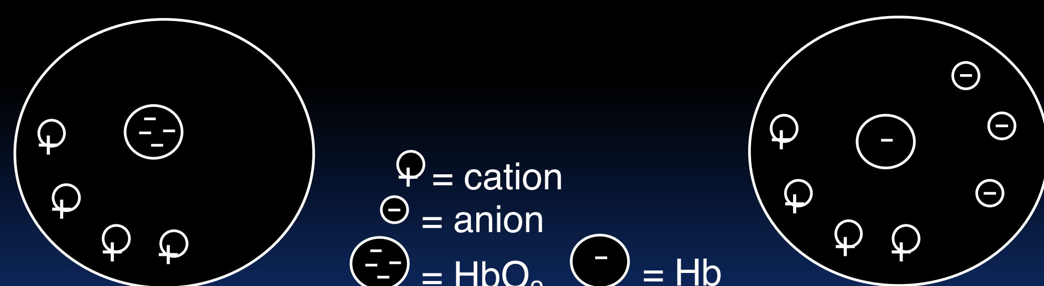


(a) Oxygen release and carbon dioxide pickup at the tissues



(b) Oxygen pickup and carbon dioxide release in the lungs



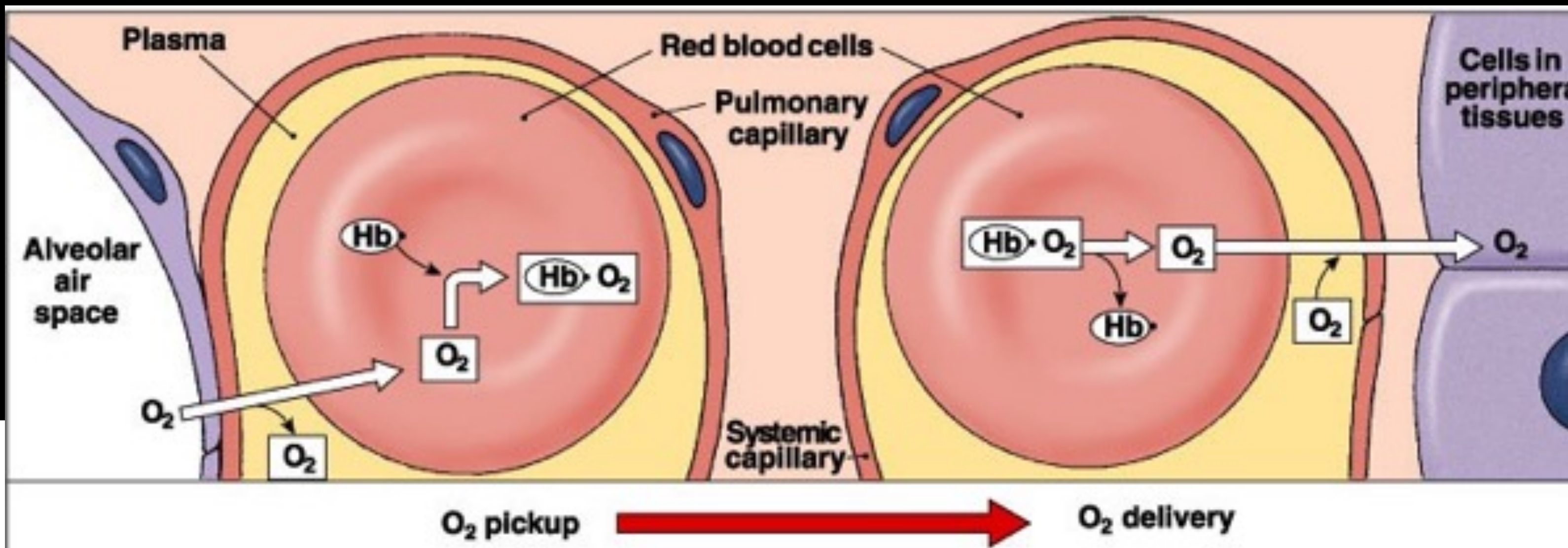


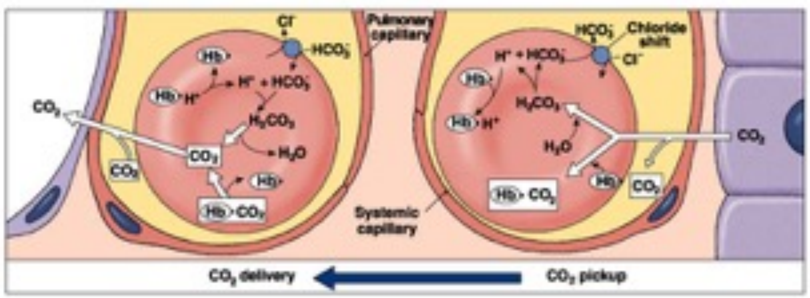
Arterial blood

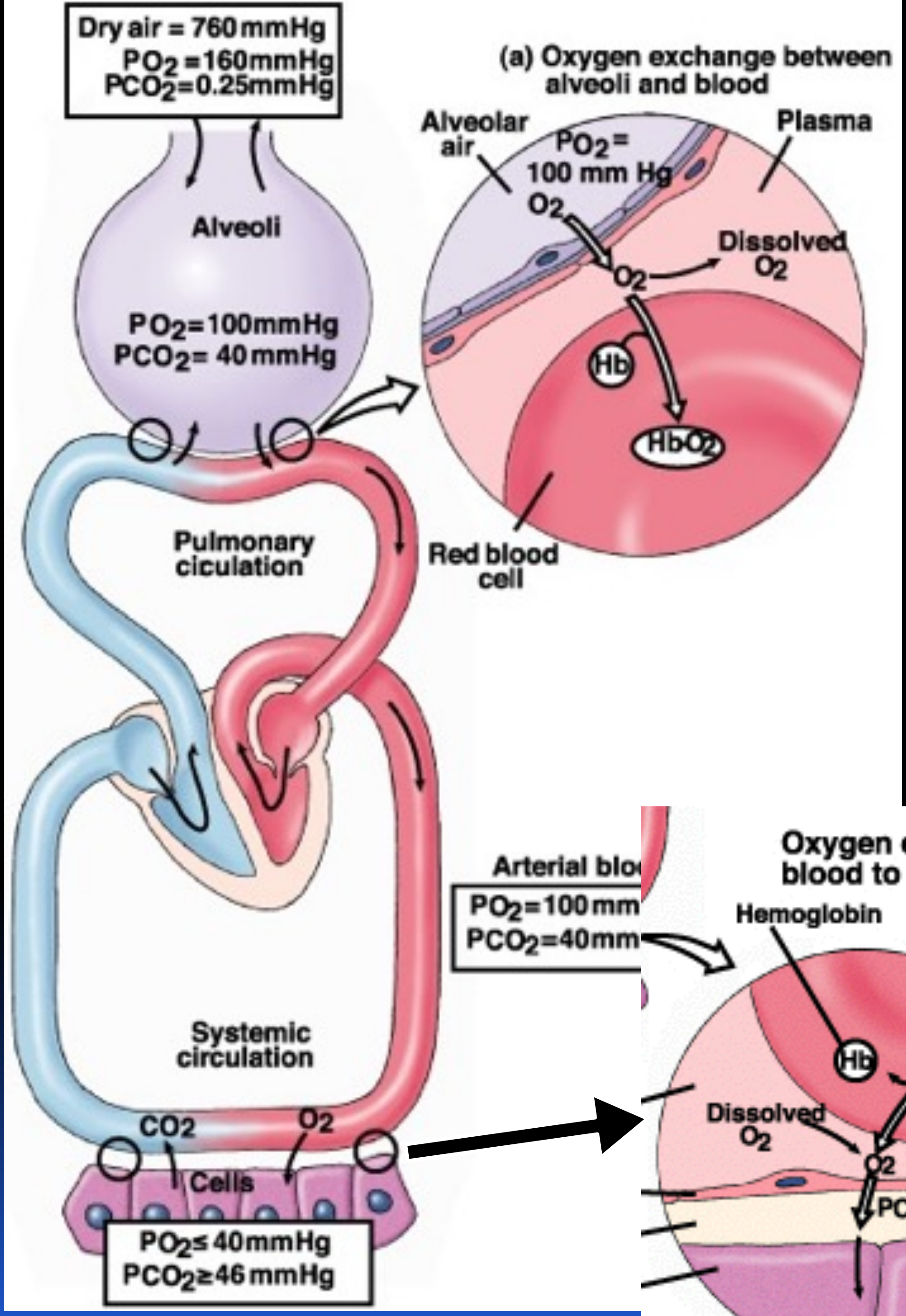
Venous blood

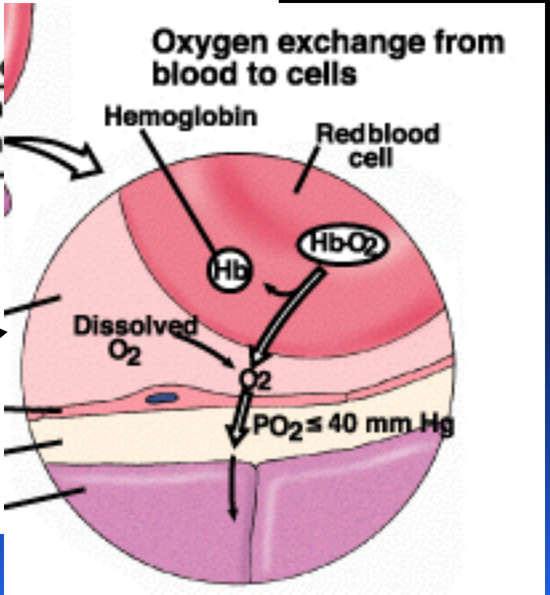
(more osmoles associated with O_2 removal)

Blood tissue gas exchange


Plasma
Red blood cells
Pulmonary capillary
Cells in peripheral tissues
Alveolar air space
Hb
Hb · O2
O2
Systemic capillary
O2 pickup
O2 delivery


Pulmonary capillary
Systemic capillary
Chloride shift
Cl⁻
HCO3⁻
H⁺ + HCO3⁻
H2CO3
H2O
CO2
Hb · CO2
Hb · H⁺
CO2 delivery
CO2 pickup


Dry air = 760 mmHg
PO2 = 160mmHg
PCO2 = 0.25mmHg
(a) Oxygen exchange between alveoli and blood
Alveolar air
PO2 = 100 mm Hg
Plasma
O2
O2
Dissolved O2
Hb
Hb-O2
Red blood cell
Alveoli
PO2 = 100mmHg
PCO2 = 40 mmHg
Pulmonary ciculation
Systemic circulation
Arterial blo
PO2 = 100 mm
PCO2 = 40mm
CO2
O2
Cells
PO2 ≤ 40 mmHg
PCO2 ≥ 46 mmHg


Oxygen exchange from blood to cells
Hemoglobin
Red blood cell
Hb
Hb-O2
Dissolved O2
O2
PO2 ≤ 40 mm Hg

Blood-tissue gas exchange

- Passive
- By diffusion
- Barrier is thin
  - 50 microns
- Large surface area

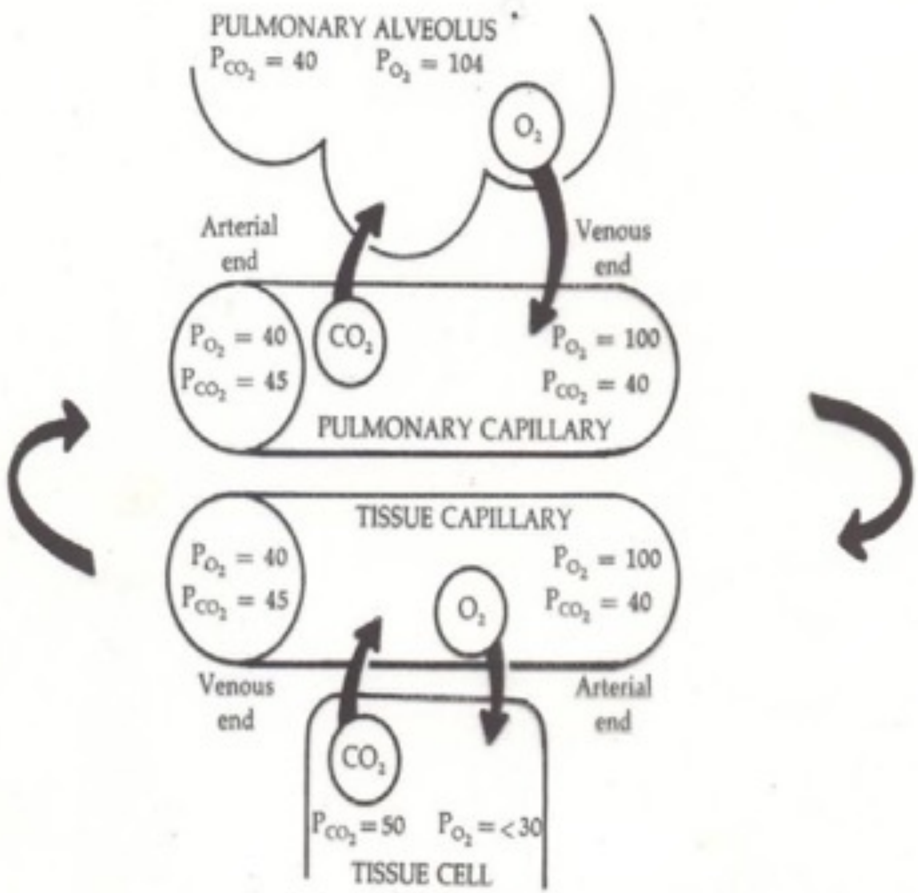
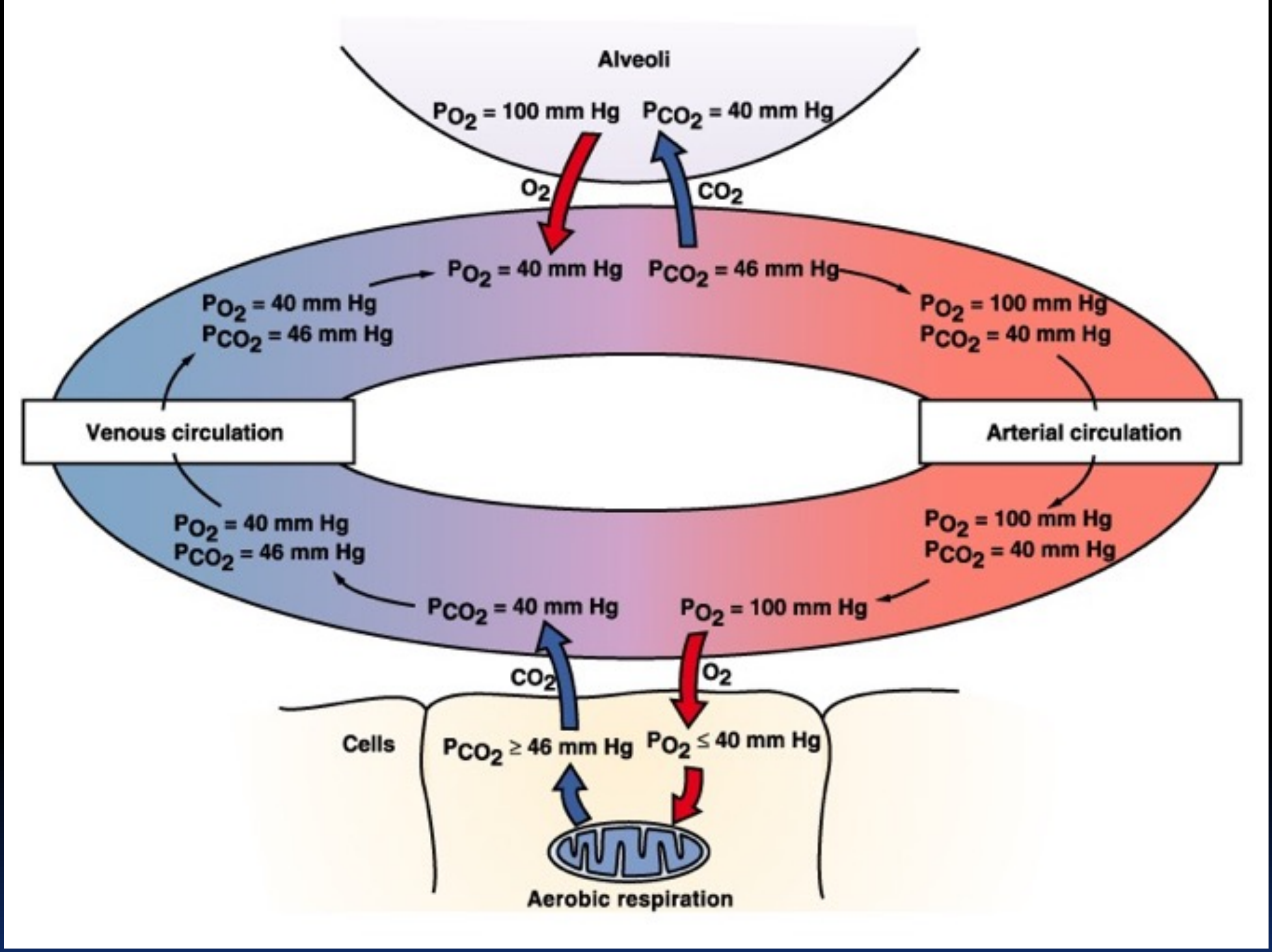
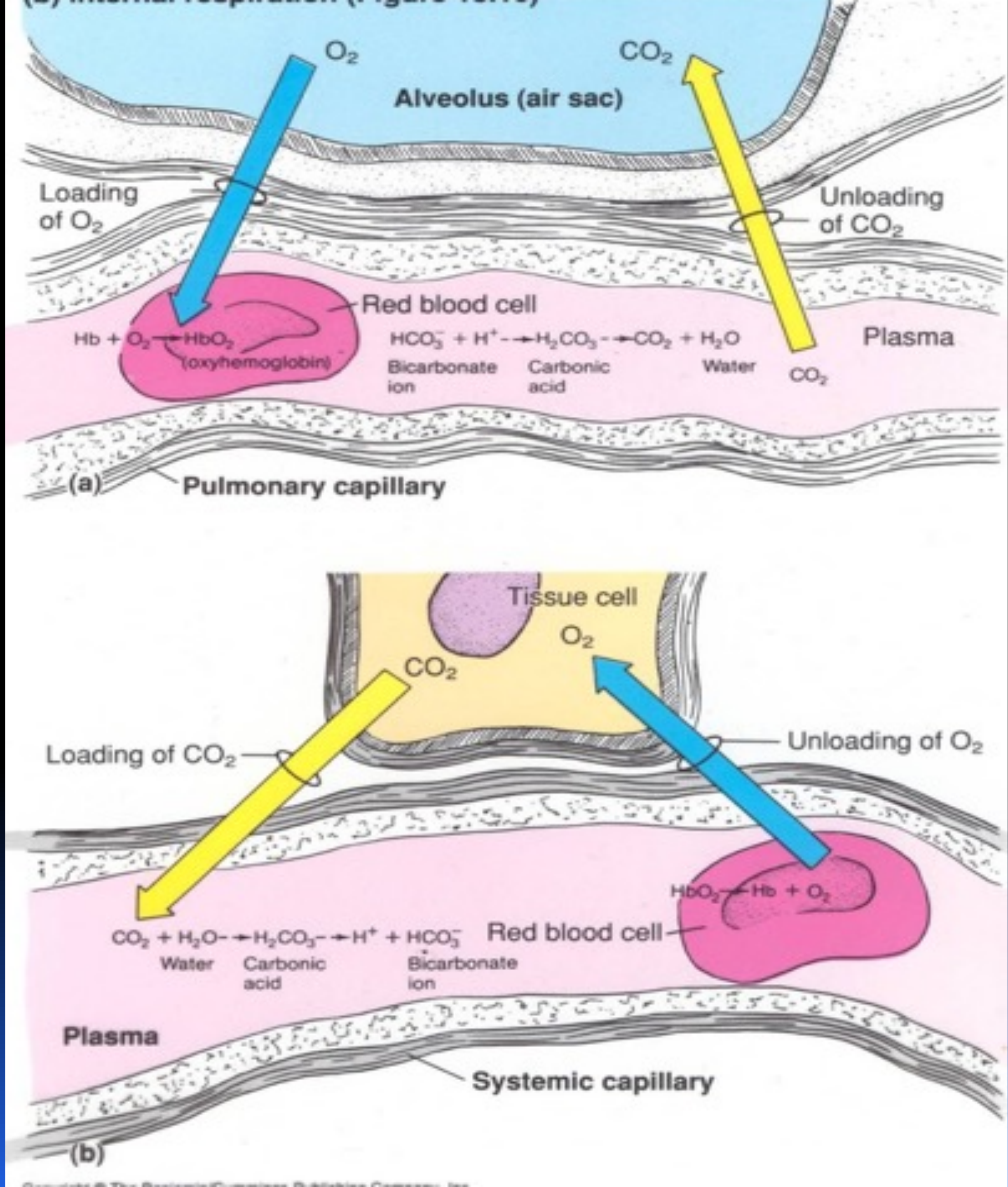


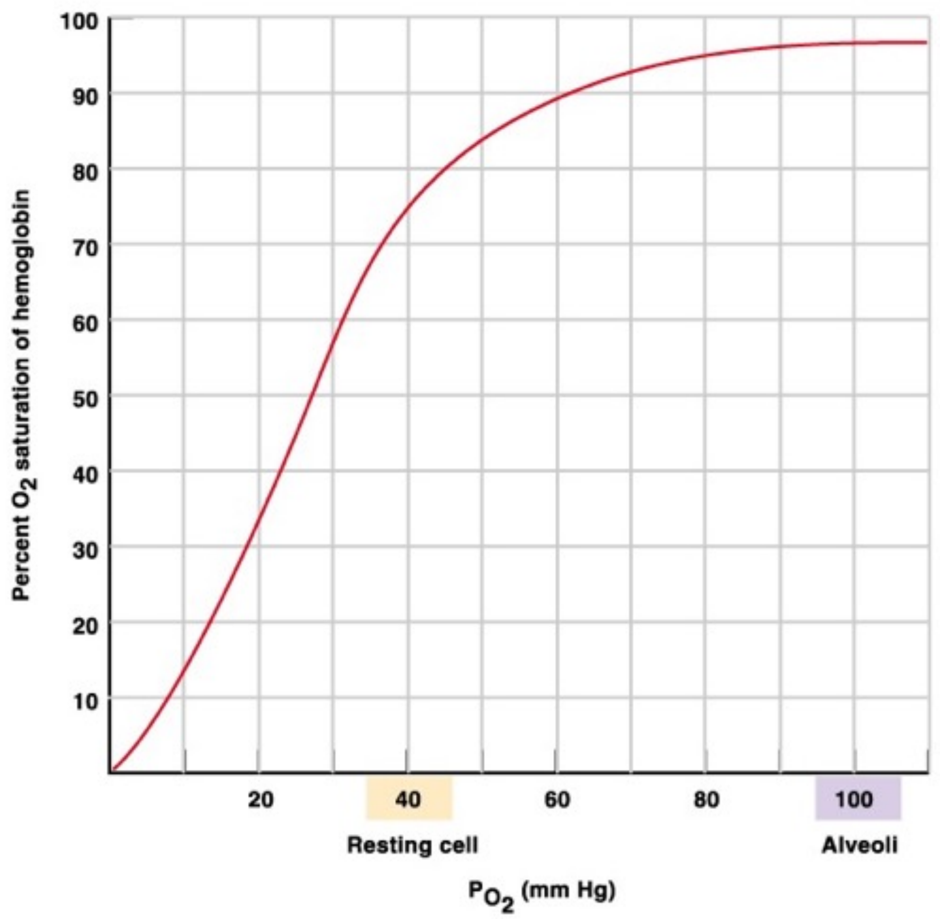
Figure 8.12. Direction of diffusion for oxygen (O_2), and carbon dioxide (CO_2), as shown by arrows. In the pulmonary alveolus the P_{CO_2} is 40 mm Hg and the P_{O_2} is 104 mm Hg; at the arterial end of the pulmonary capillary the P_{O_2} is 40 mm Hg and the P_{CO_2} is 45 mm Hg, whereas at the venous end the P_{O_2} is 100 mm Hg and the P_{CO_2} is 40 mm Hg; at the venous end of the tissue capillary the P_{O_2} is 40 mm Hg and the P_{CO_2} is 45 mm Hg, whereas at the arterial end the P_{O_2} is 100 mm Hg and the P_{CO_2} is 40 mm Hg; and in the tissue cell the P_{CO_2} is 50 mm Hg and the P_{O_2} is <30 mm Hg.



Alveoli
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
O_2
CO_2
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
Venous circulation
Arterial circulation
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
P_{CO_2} = 40 mm Hg
P_{O_2} = 100 mm Hg
CO_2
O_2
Cells
$P_{CO_2} \geq$ 46 mm Hg
$P_{O_2} \leq$ 40 mm Hg
Aerobic respiration

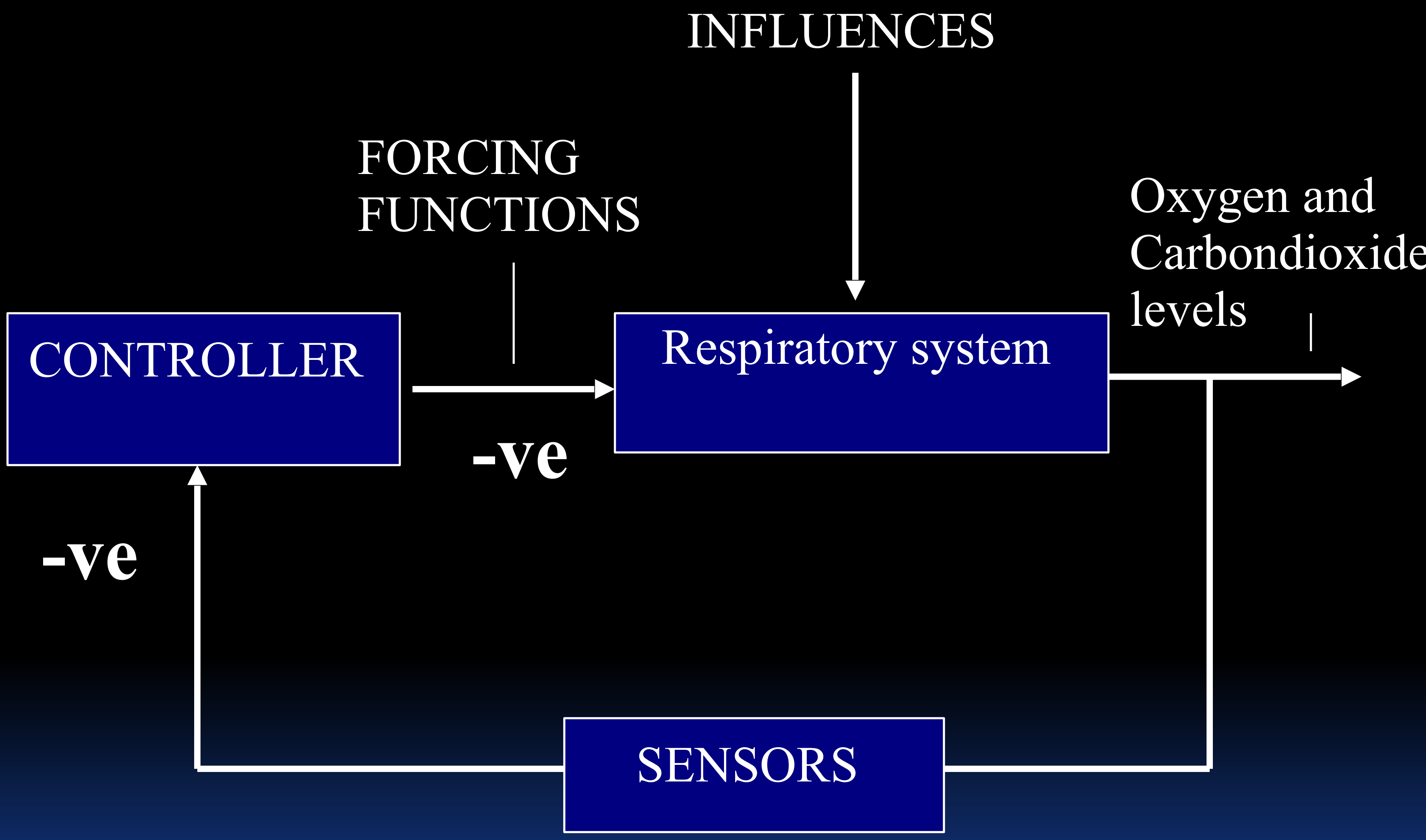


O2
CO2
Alveolus (air sac)
Loading of O2
Unloading of CO2
Red blood cell
Hb + O2 → HbO2 (oxyhemoglobin)
HCO3- + H+ → H2CO3 → CO2 + H2O
Bicarbonate ion
Carbonic acid
Water
CO2
Plasma
(a)
Pulmonary capillary
Tissue cell
O2
CO2
Loading of CO2
Unloading of O2
HbO2 → Hb + O2
CO2 + H2O → H2CO3 → H+ + HCO3-
Water
Carbonic acid
Bicarbonate ion
Red blood cell
Plasma
Systemic capillary
(b)


100
90
80
70
60
50
40
30
20
10
Percent O2 saturation of hemoglobin
20
40
60
80
100
Resting cell
Alveoli
PO2 (mm Hg)

Control of respiration

- Aim is to maintain physiological levels of
  - Pa O2
  - Pa CO2
  - pH



CONTROL MODEL

A. Respiratory Centers

1. Medullary Respiratory Centers

a. Inspiratory Area - DRG - dorsal respiratory group neurons

b. Expiratory Area - VRG - ventral respiratory group neurons

2. Pontine Centers:

a. Pneumotaxic Center - located in upper pons (“off switch”)

b. Apneustic Center - located in lower pons (prevents turn-off)

B. Receptors

a.Pulmonary Receptors: pulmonary stretch receptors (Hering-Breuer reflex)

b. other receptors??

c. **Central or Medullary Chemoreceptors**

d. **Peripheral Chemoreceptors**

C. Effectors: the Ventilatory system

D. Other influences:

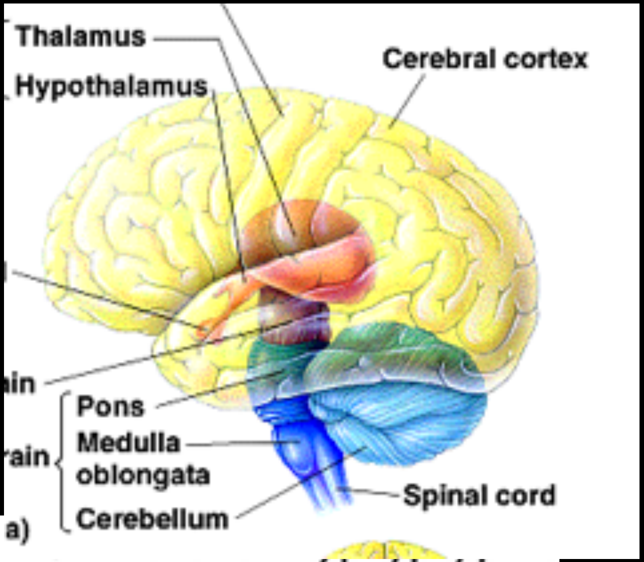
Cortical & other higher centres

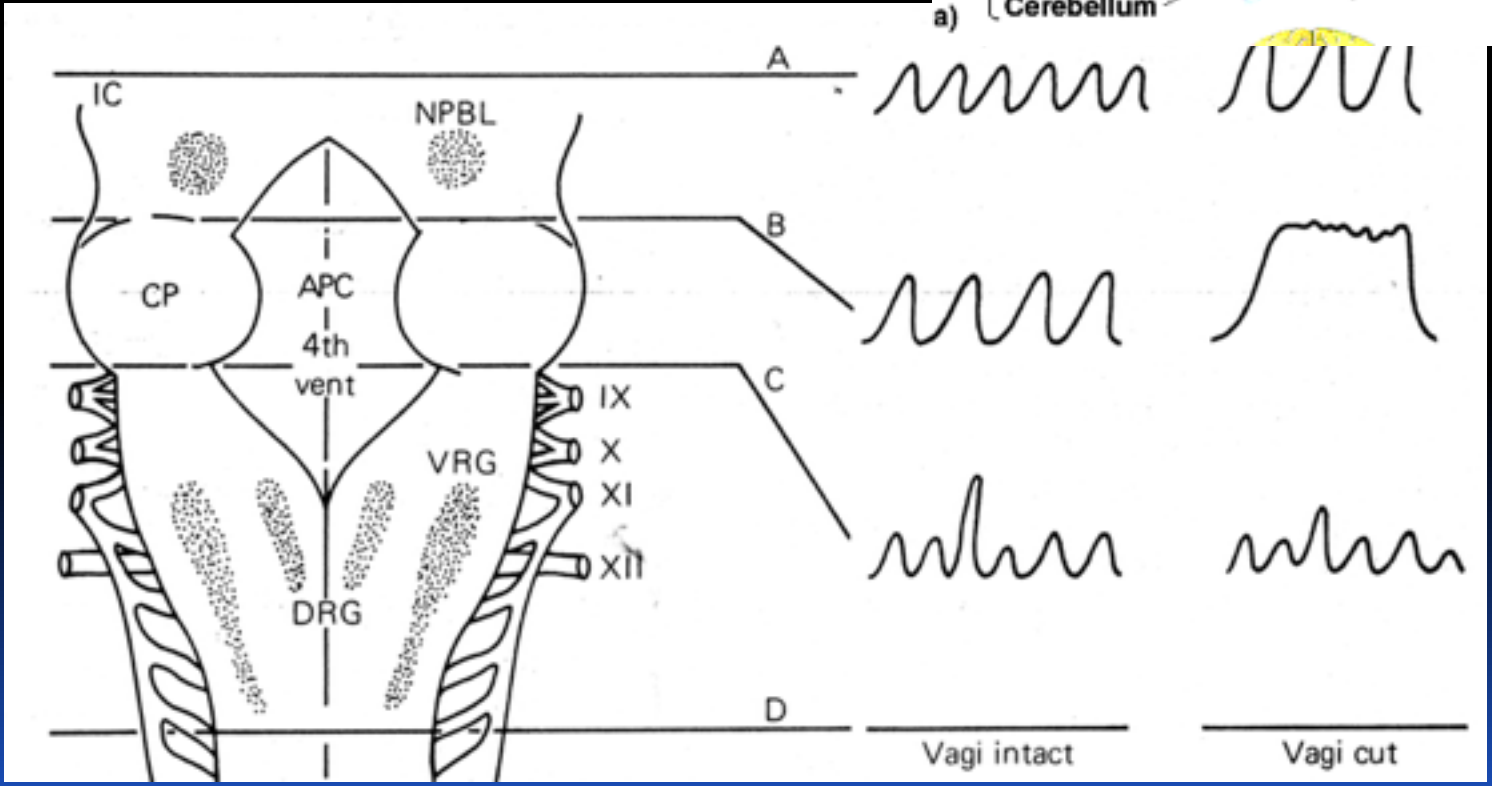
Respiratory Areas in Brainstem

- Medullary respiratory center
  - Dorsal groups stimulate the diaphragm- Inspiratory
  - Ventral groups stimulate the intercostal and abdominal muscles- Expiratory
- Pontine (pneumotaxic) respiratory group
  - Involved with switching between inspiration and expiration
  - May 'fine-tune' resp rhythm

- Apneustic centre- In lower pons
  - Prolongs inspiratory potential

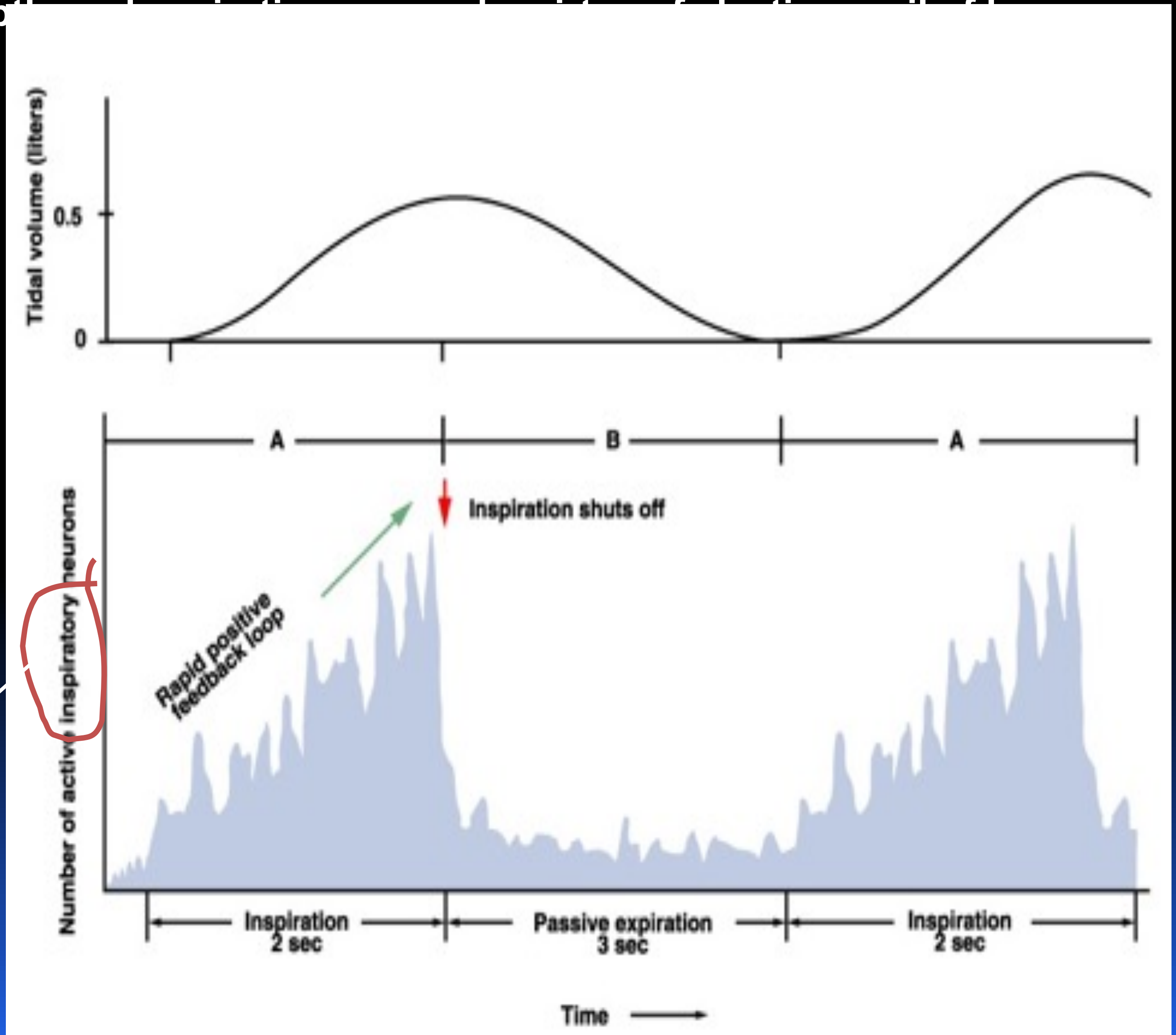
Control of Respiration





Basic rhythmic breathing and Inspiratory Neuronal Activity

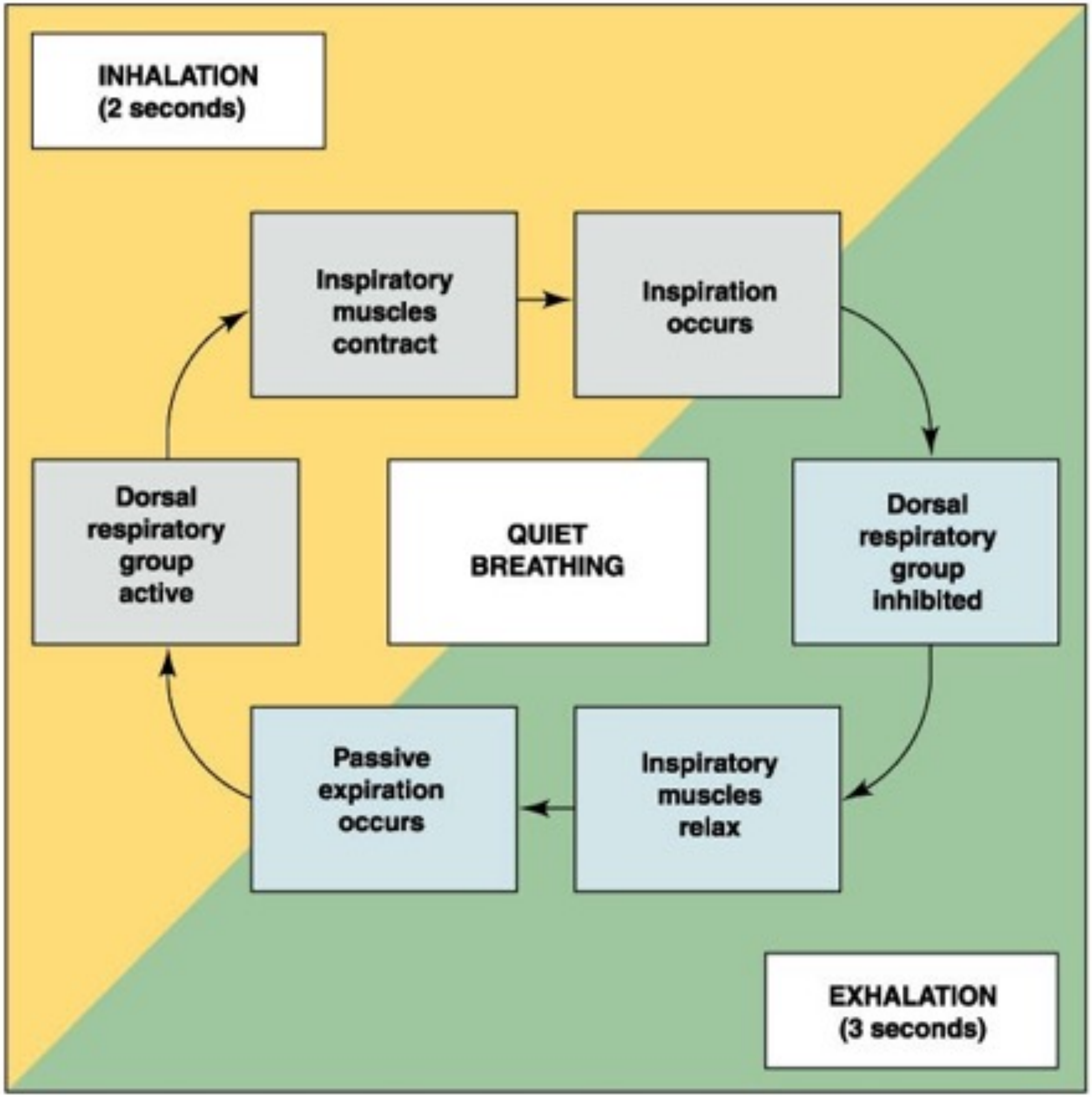
The basis of rhythmic breathing. During inspiration the activity of inspiratory neurons increases steadily (ramps up). At the end of inspiration, the activity shuts off abrup

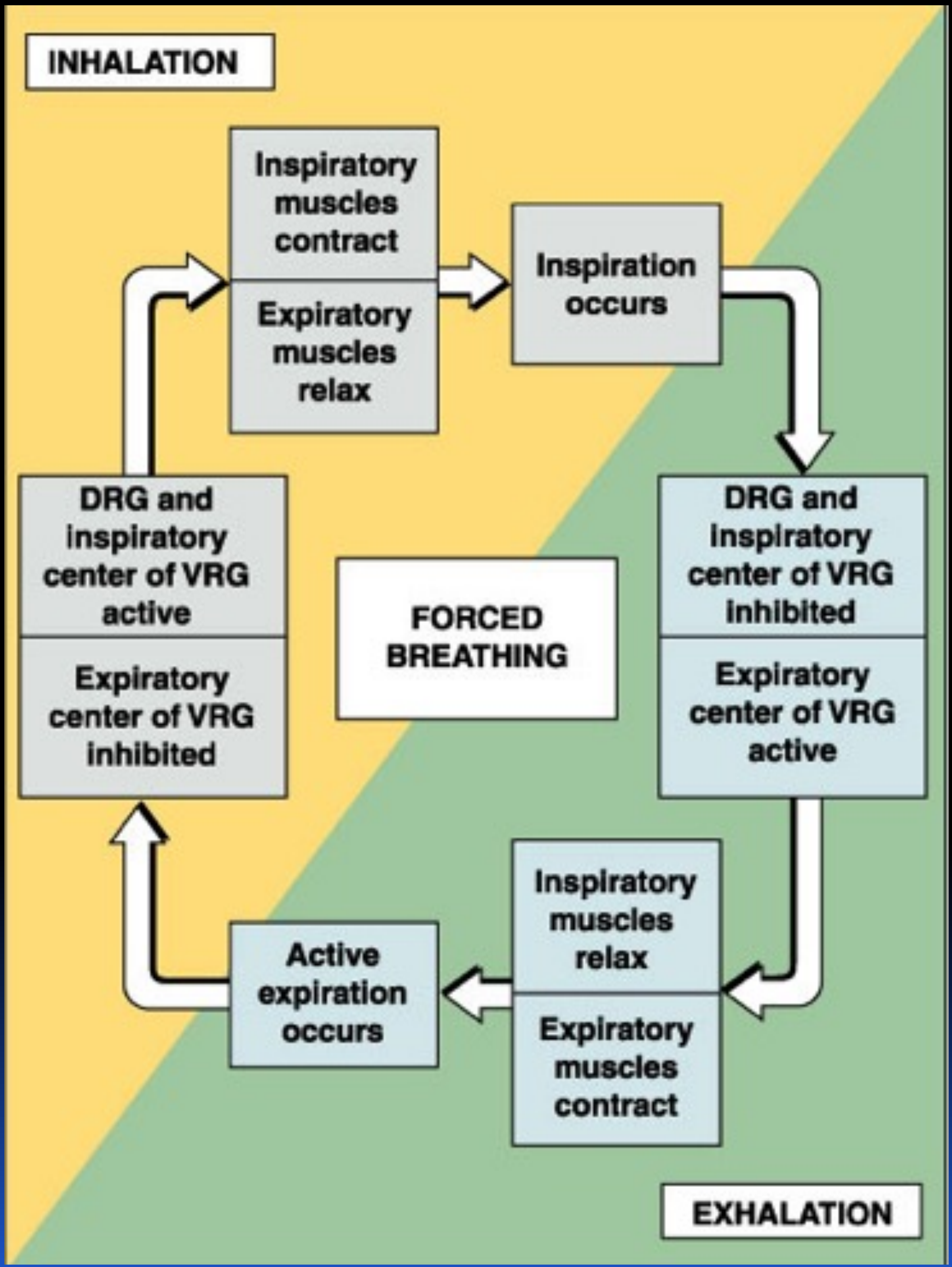


Recorded from DRG neurons

Rhythmic Ventilation

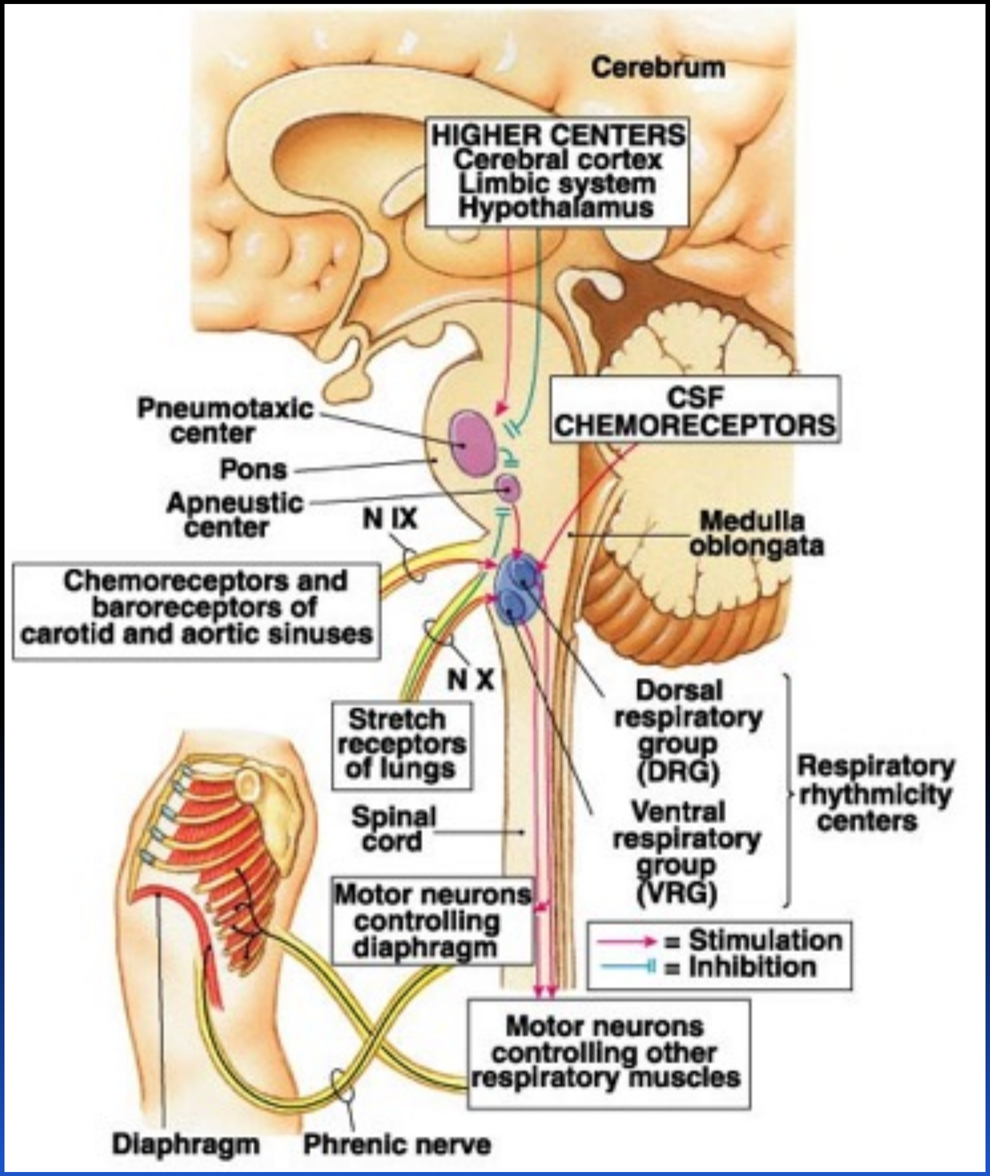
- Starting inspiration
  - Medullary respiratory center neurons are continuously active
  - Center receives stimulation from receptors and simulation from parts of brain concerned with voluntary respiratory movements and emotion
  - Combined input from all sources causes action potentials to stimulate respiratory muscles
- Increasing inspiration
  - More and more neurons are activated
- Stopping inspiration
  - Neurons stimulating also responsible for stopping inspiration and receive input from pontine group and stretch receptors in lungs. Inhibitory neurons activated and relaxation of respiratory muscles results in expiration.


INHALATION
(2 seconds)
Inspiratory muscles contract
Inspiration occurs
QUIET BREATHING
Dorsal respiratory group active
Dorsal respiratory group inhibited
Passive expiration occurs
Inspiratory muscles relax
EXHALATION
(3 seconds)



INHALATION
Inspiratory muscles contract
Expiratory muscles relax
Inspiration occurs
DRG and inspiratory center of VRG active
Expiratory center of VRG inhibited
FORCED BREATHING
DRG and inspiratory center of VRG inhibited
Expiratory center of VRG active
Inspiratory muscles relax
Expiratory muscles contract
Active expiration occurs
EXHALATION

Respiratory Structures in Brainstem

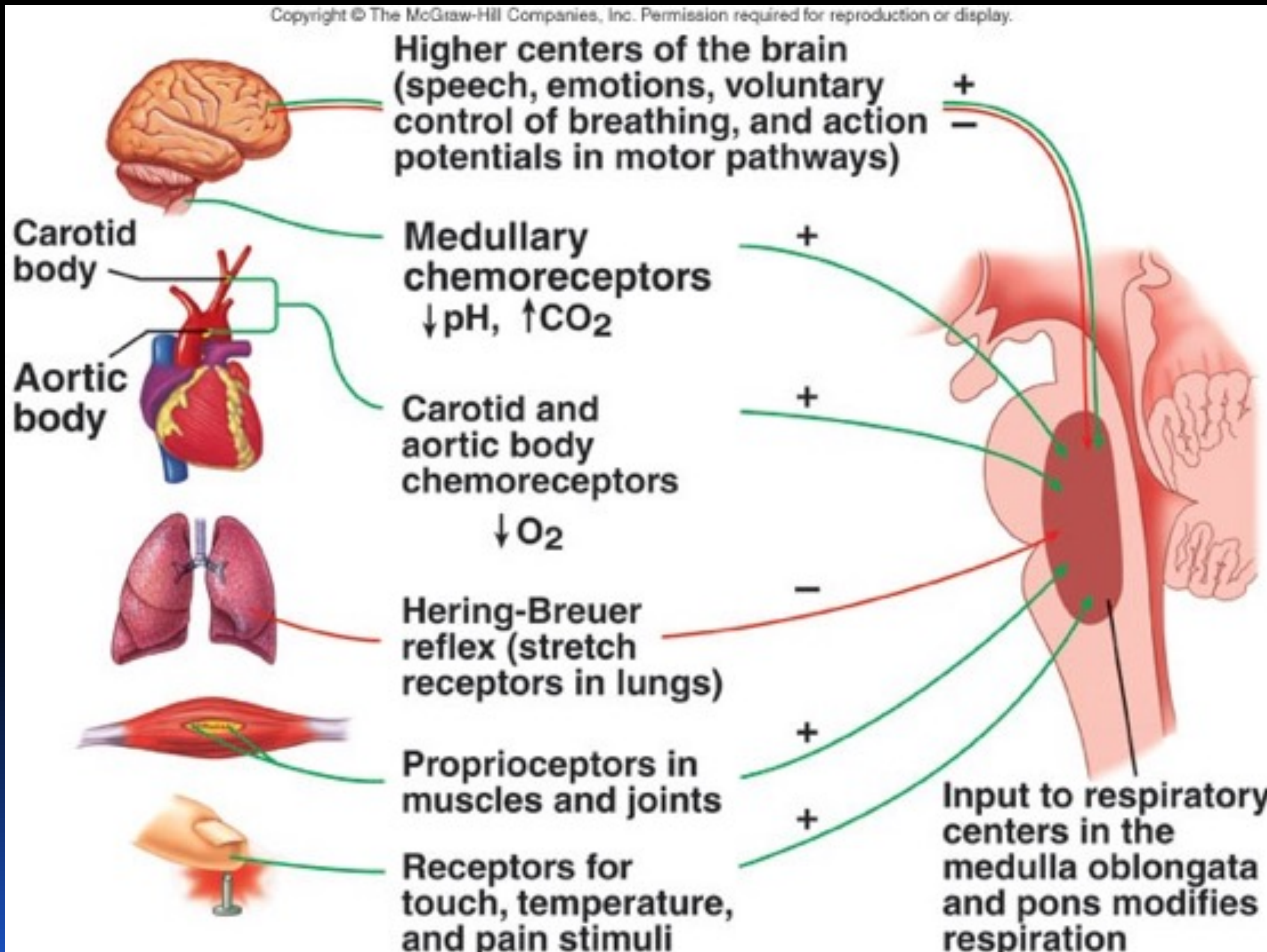


Modification of Ventilation

- Cerebral and limbic system
  - Respiration can be voluntarily controlled eg speech, instruments and modified by emotions eg anger, fear
  - Hyper/hypoventilation
  - Breath holding and breaking point

- Chemical control
  - Carbon dioxide is major regulator
    - Increase or decrease in pH can stimulate chemo- sensitive area, causing a greater rate and depth of respiration
  - Oxygen levels in blood affect respiration when a 50% or greater decrease from normal levels exists

Input to Resp. centres



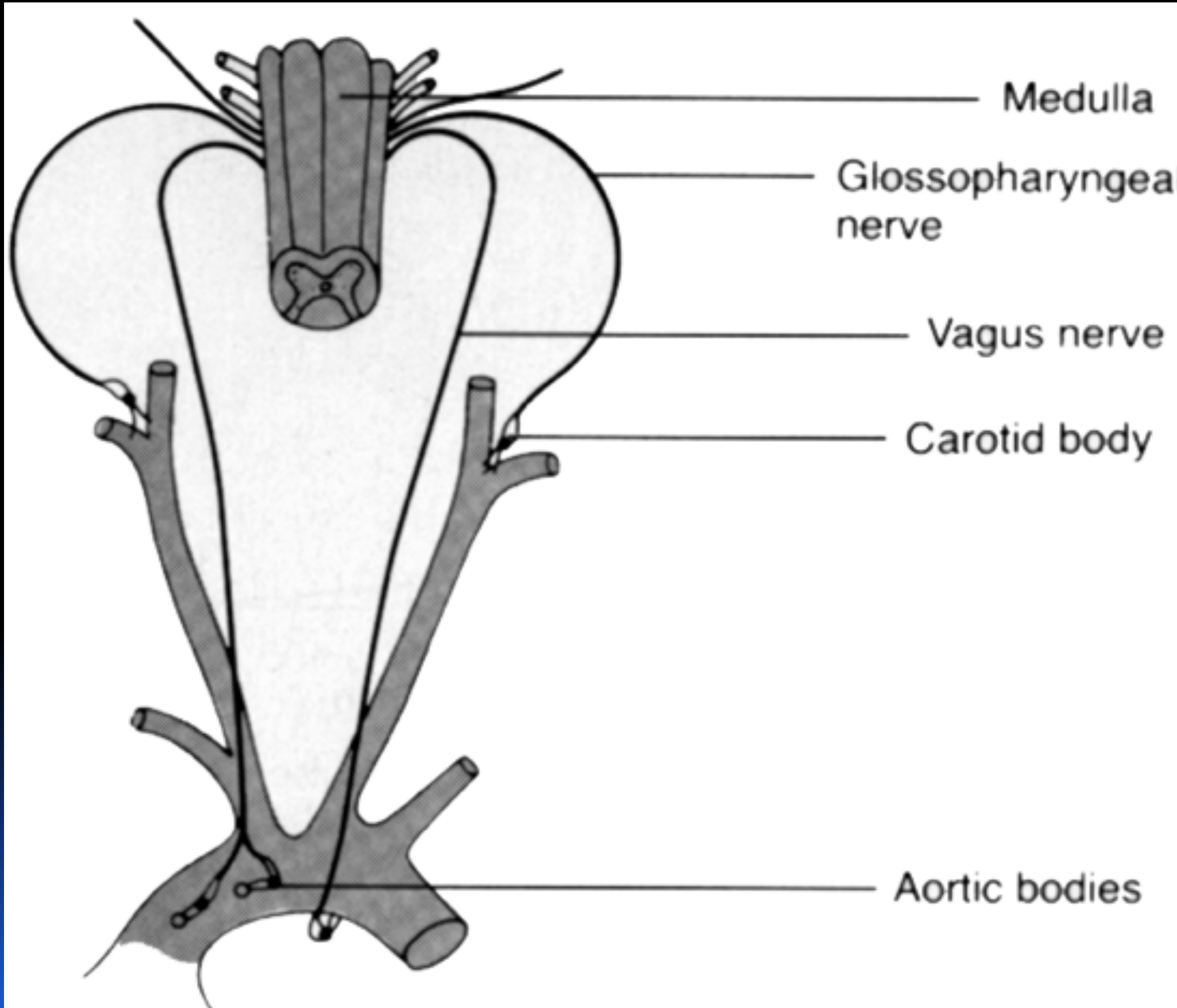
Receptors

- Chemoreceptors
  - Detect: oxygen, carbondioxide and pH
  - Central
  - Peripheral
    - Carotid and aortic bodies
- Other receptors
  - Pulmonary stretch receptors
  - Proprioceptors
  - Airway irritant receptors
    - Detect eg smoke, temperature
  - 'J'receptors (juxta capillary receptors)
    - Respond to chemicals in pulm. circulation

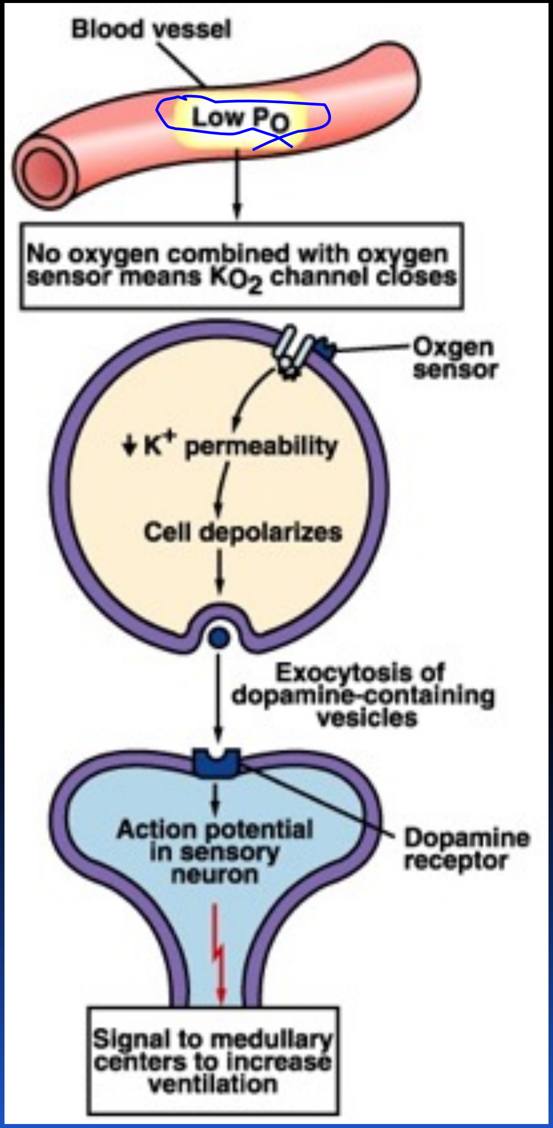
Other receptors

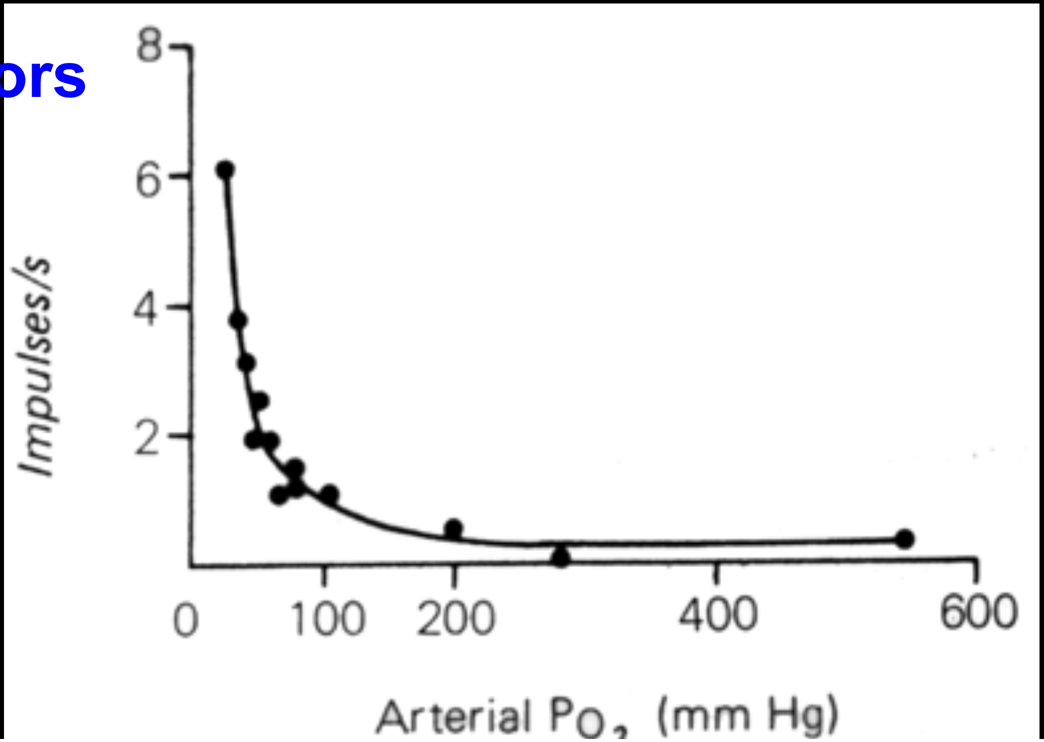
- Nose & upper airway
  - Mechanical, chemical irritation
- Baroreceptors
  - Rise in BP causes fall in vent.
- Pain & temperature receptors
- Atrial stretch receptors

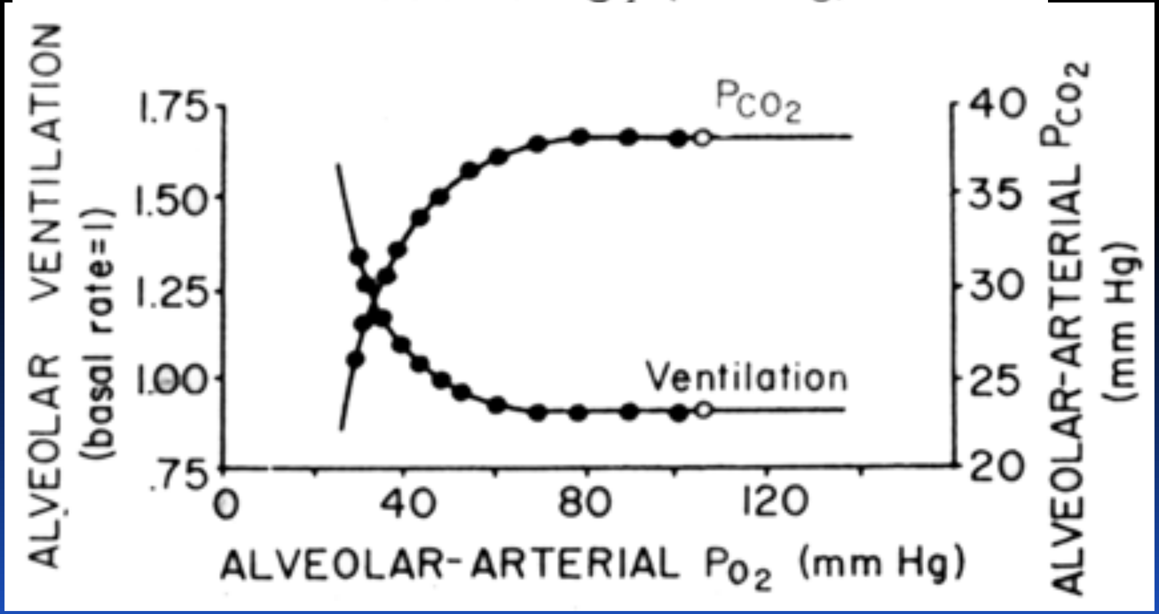
The chemical sensors



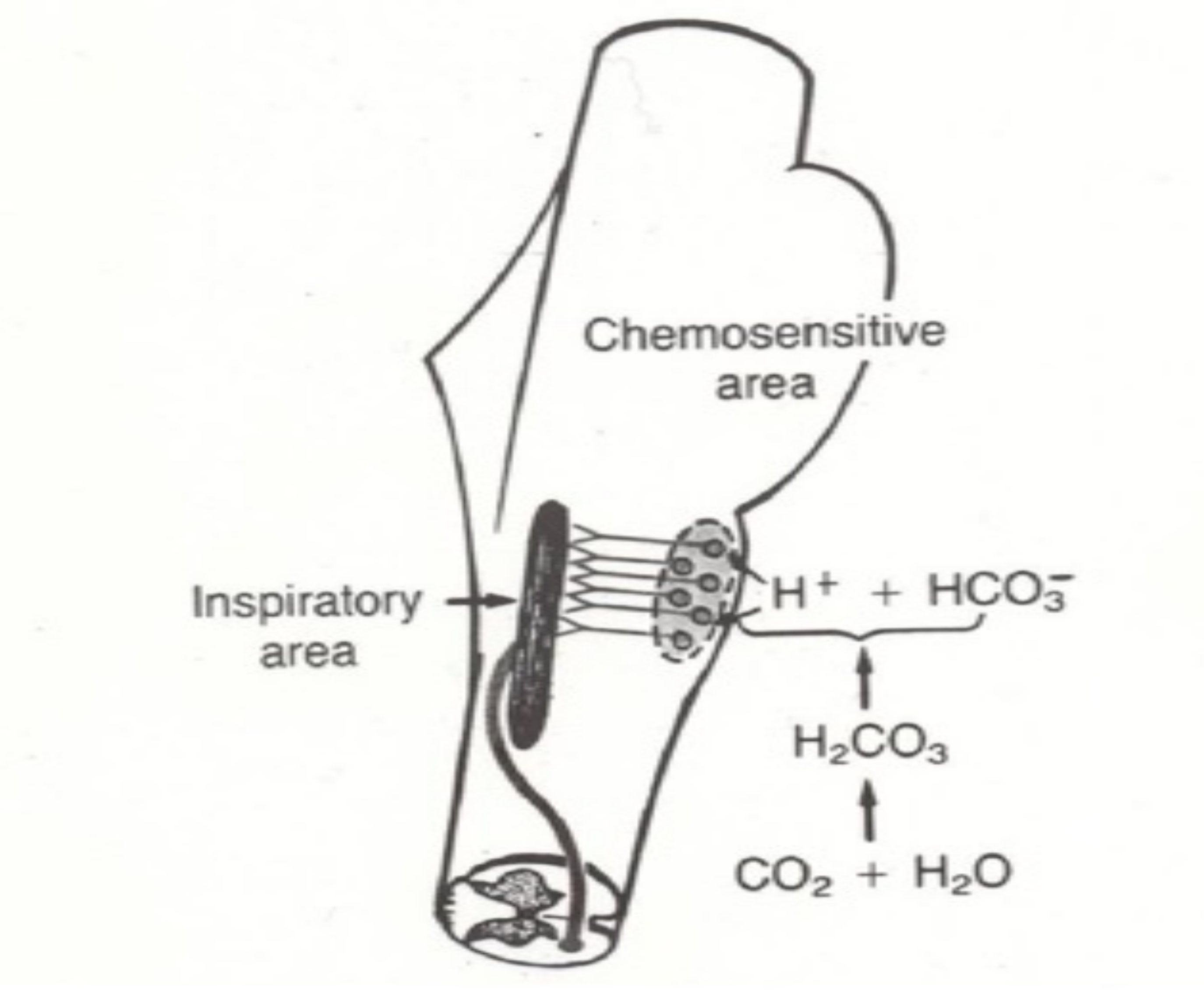
The Chemical Sensors







Central Chemoreceptors

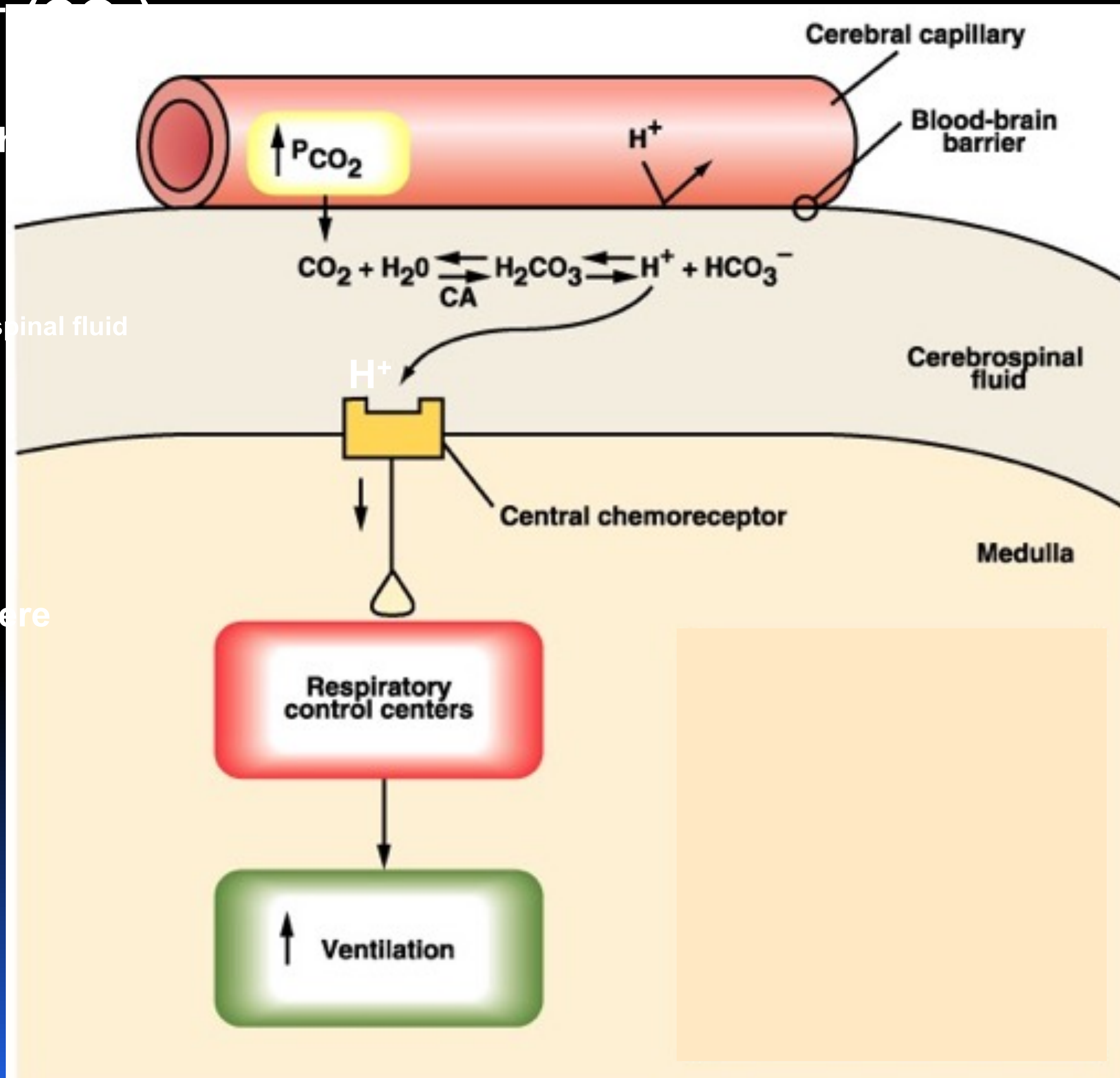


Central (medullary) Chemoreceptors (mechanisms)

the H^{+}

blood h

cerebrospinal fluid
between



brain here

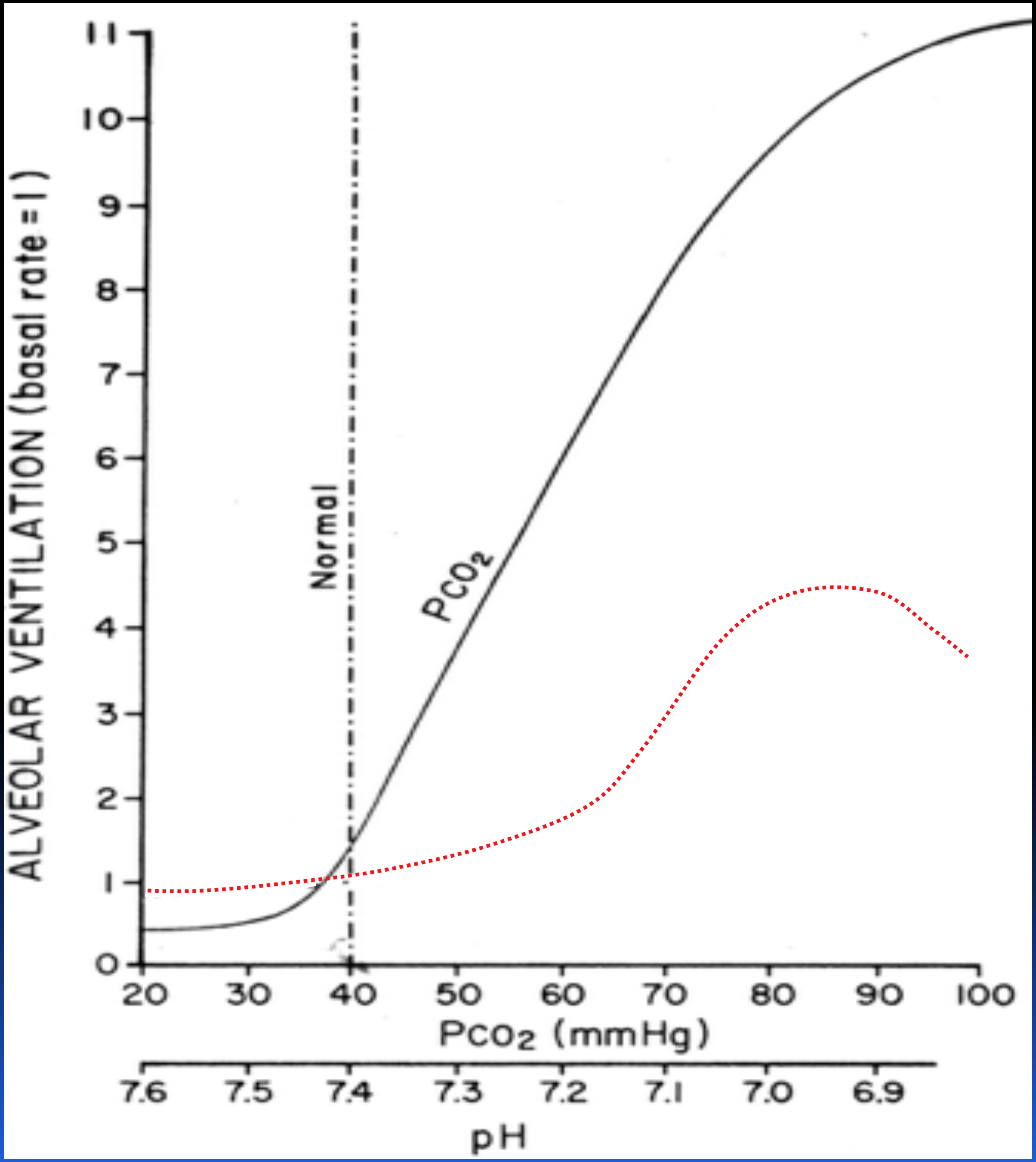
Herring-Breuer Reflex

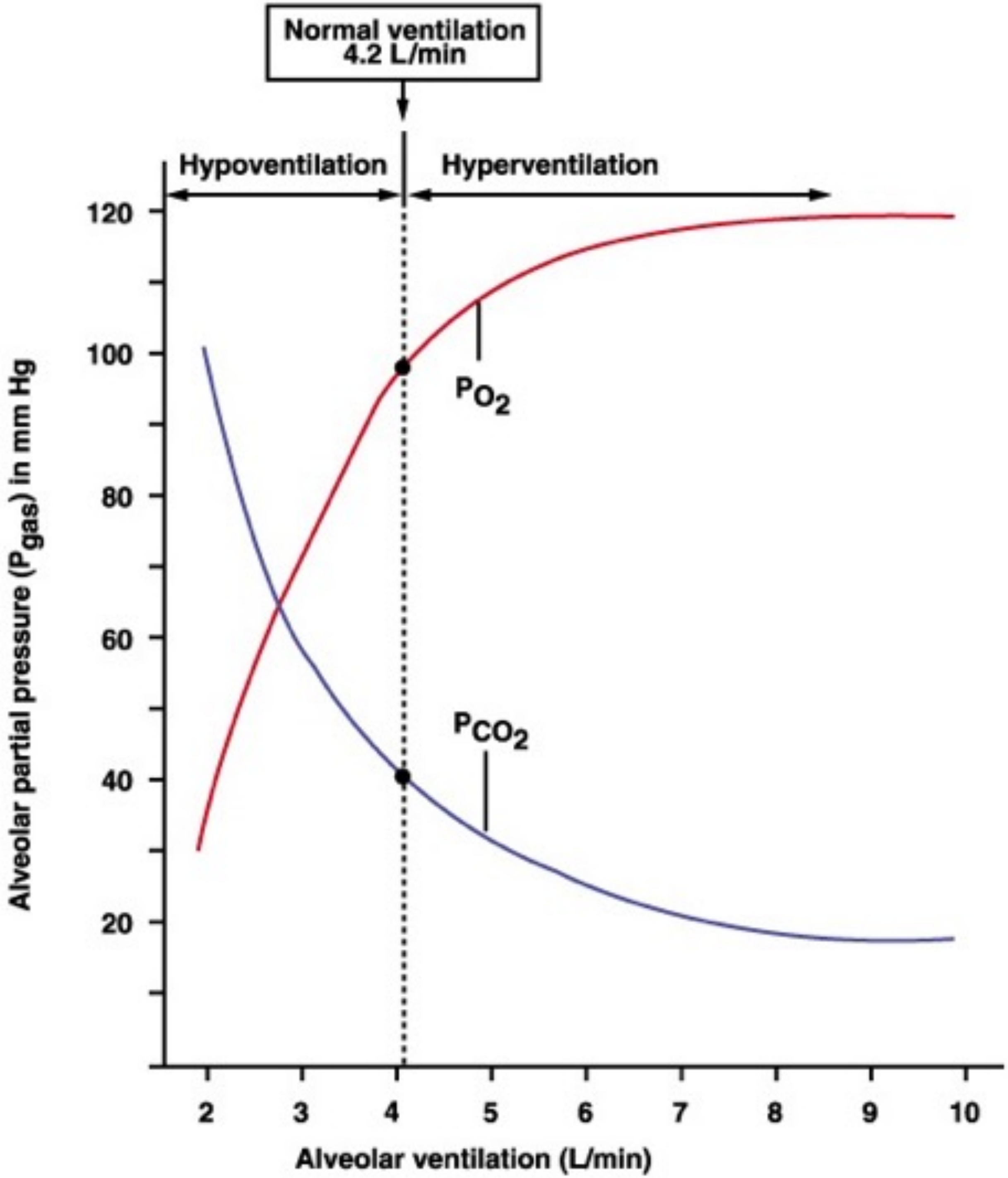
- Limits the degree of inspiration and prevents overinflation of the lungs
  - Infants
    - Reflex plays a role in regulating basic rhythm of breathing and preventing overinflation of lungs
  - Adults
    - Reflex important only when tidal volume large as in exercise, > 1L

Integrated responses

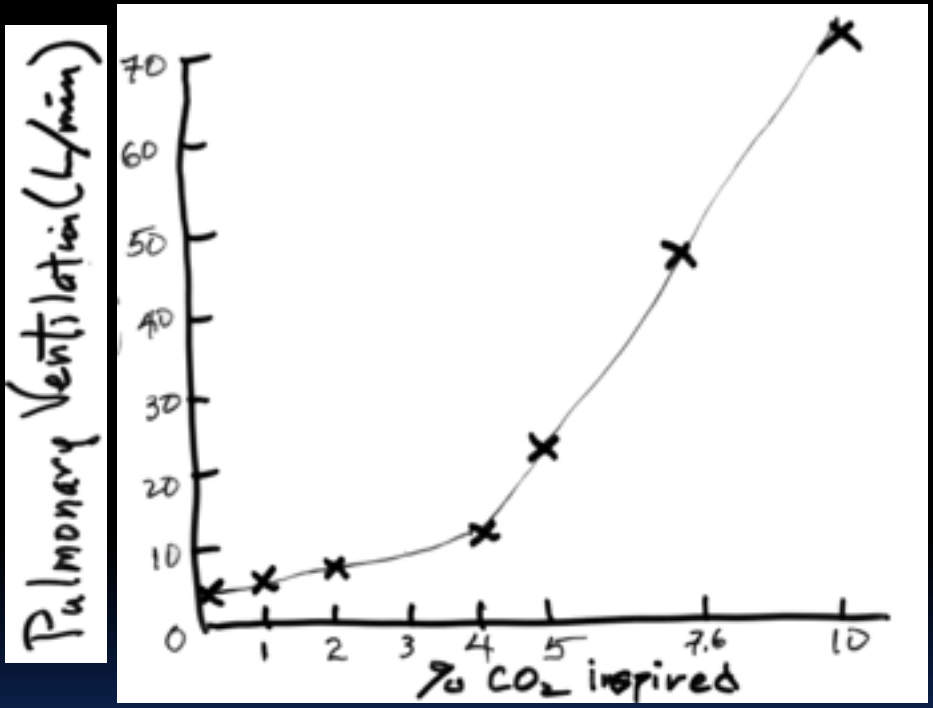
How is respiration regulated as a function of blood gases?

[PCO_2 and pH]

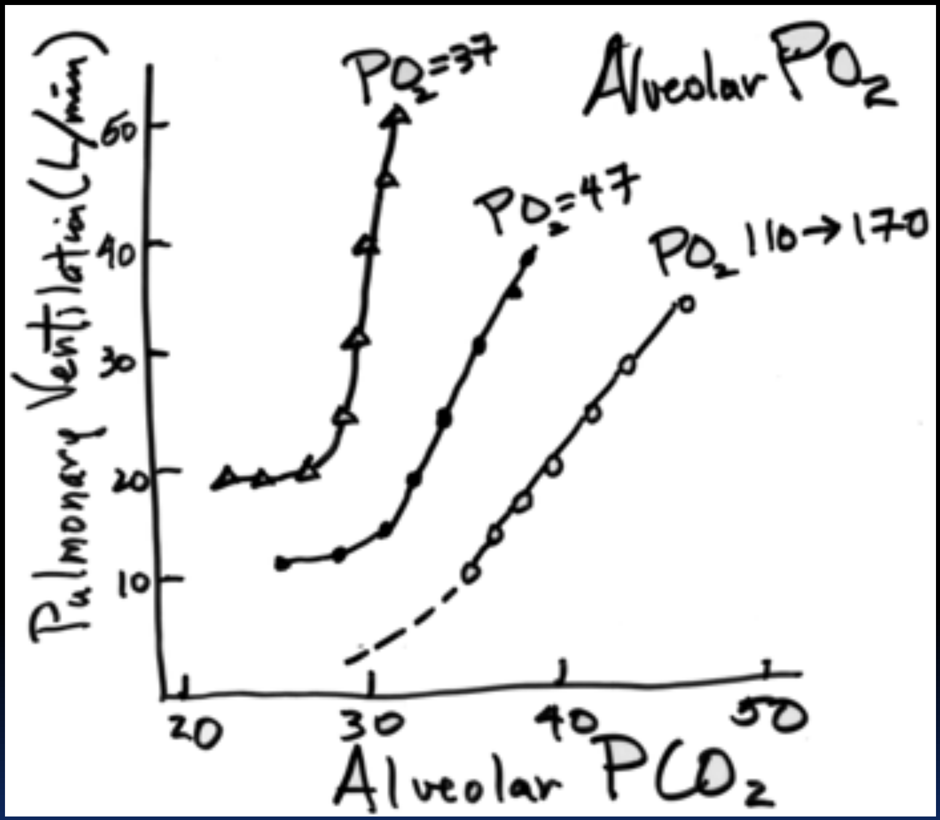



Normal ventilation
4.2 L/min
Hypoventilation
Hyperventilation
120
100
80
60
40
20
P_{O_2}
P_{CO_2}
Alveolar partial pressure (P_{gas}) in mm Hg
2
3
4
5
6
7
8
9
10
Alveolar ventilation (L/min)

CO_2 effects are influenced by variation in PO_2



low O_2 potentiates the CO_2 effect



The effects of O_2 are influenced by variation in PCO_2

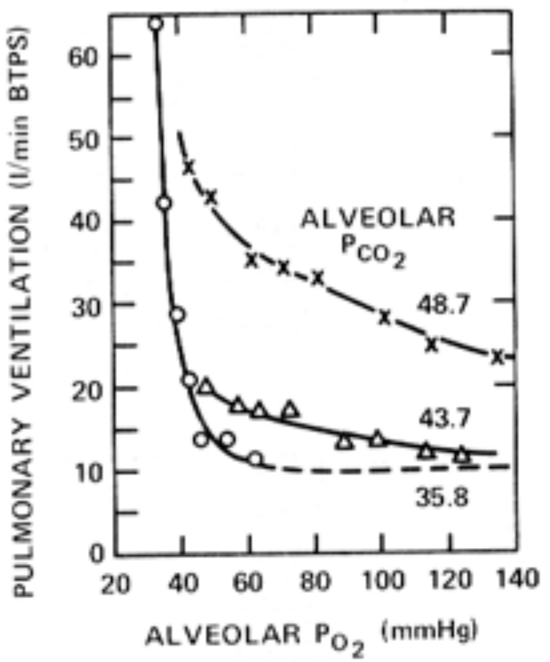
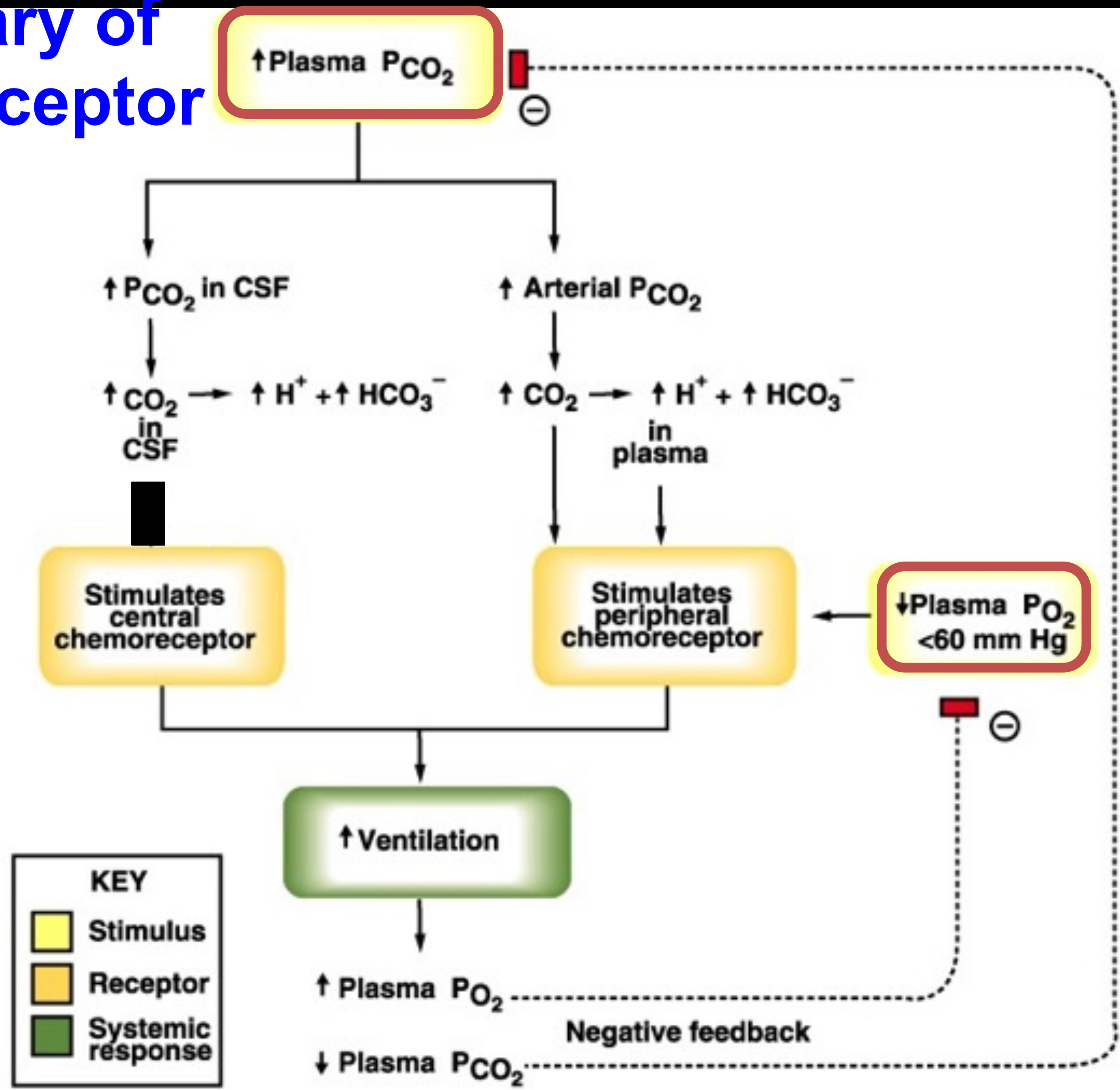


Figure 78. Hypoxic response curves. Note that when the P_{CO_2} is 36 mm Hg, almost no increase in ventilation occurs until the P_{O_2} is reduced to about 50 mm Hg. (Modified from Loeschke, H. H., and K. H. Gertz. *Arch. Ges. Physiol*. 267: 460, 1958.)

A Summary of Chemoreceptor Reflexes



- Hypercapneic ventilatory drive
  - Important in short term, in the long term the pH changes in CSF are buffered so becomes ineffective.
  - Is the one driving resp in most physiological instances
- Hypoxic ventilatory drive
  - Very powerful, more important when low oxygen levels

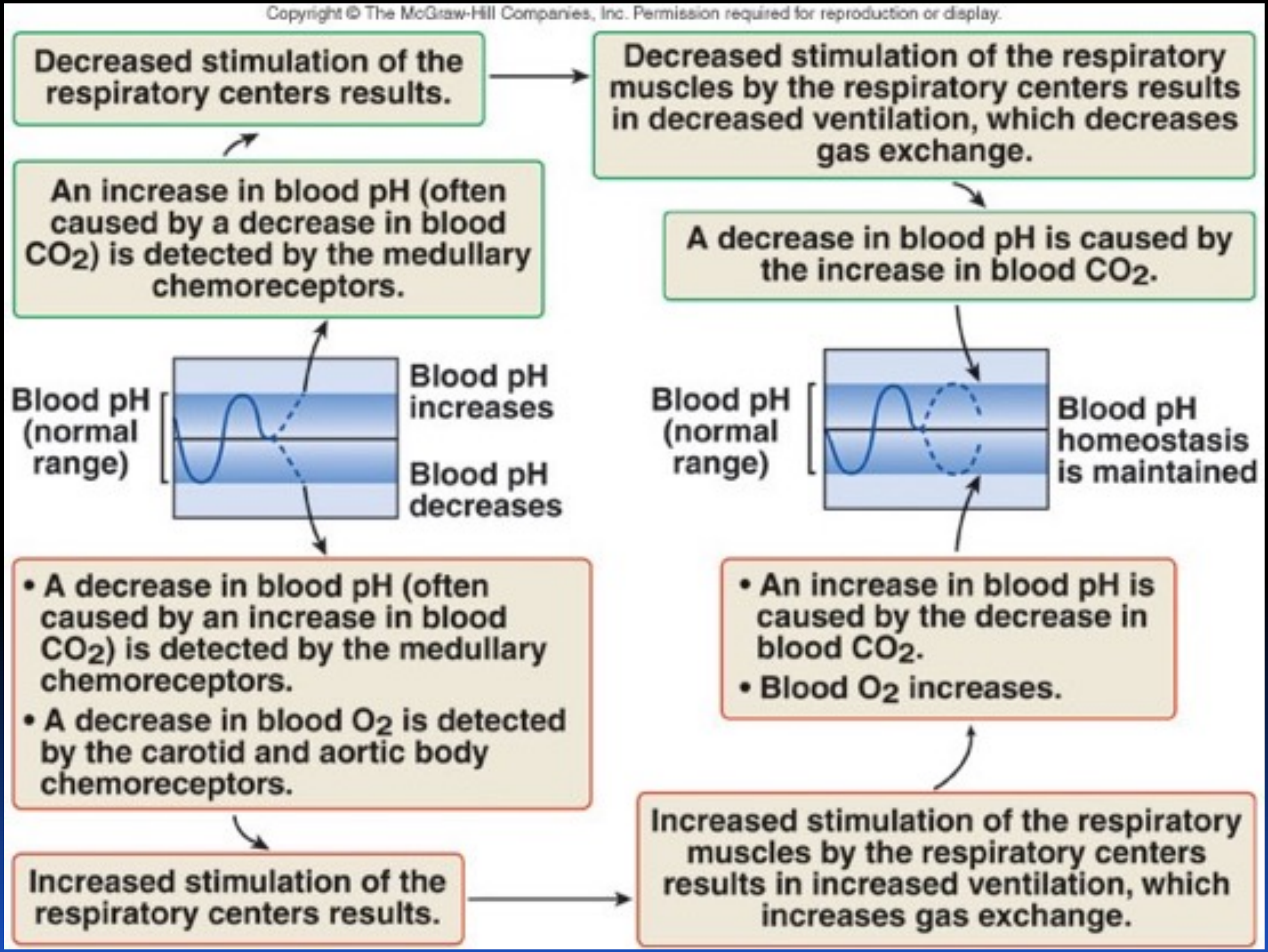
- In chronic airway obstructve disease: there is chronic hypercapnoea so no hypercapnoeic drive
- In this hypoxic vent drive very important.

  Caution about gining 100% oxygen

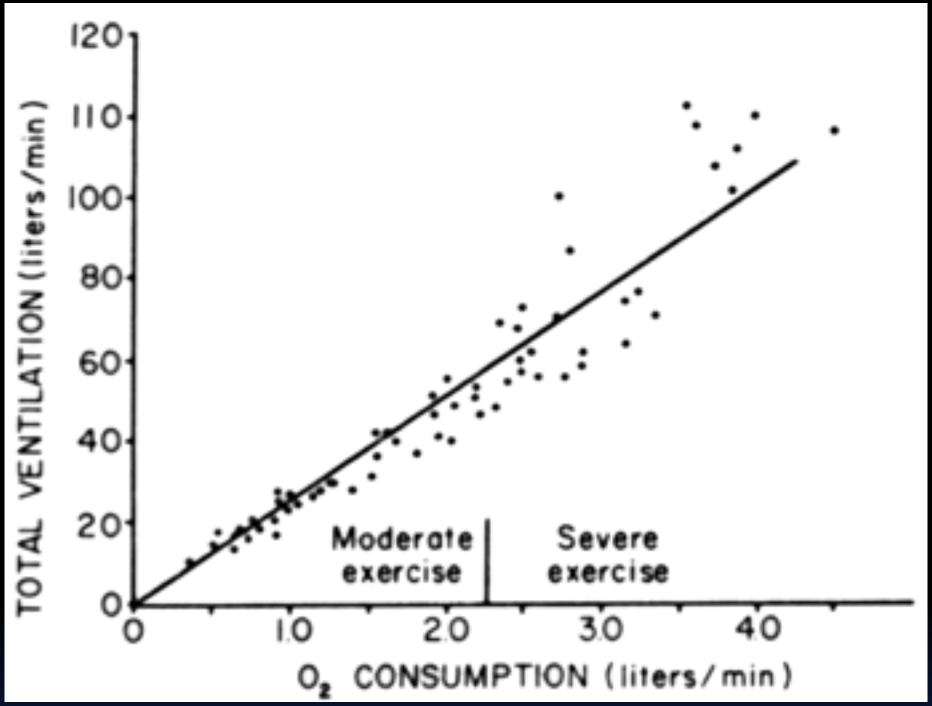
pH

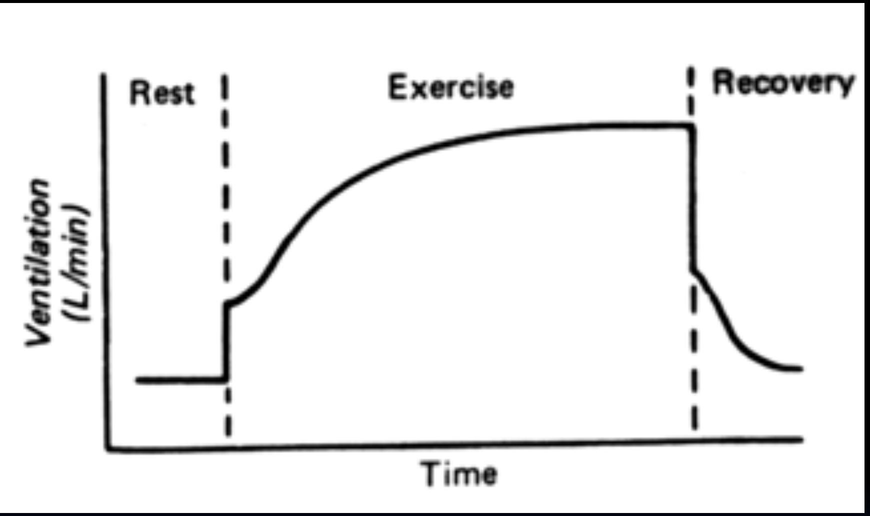
- Fall in pH- causes rise in ventilation
  - Via peripheral chemoreceptors
  - May occur in diseases that result in acidosis eg Diabetic ketoacidosis
- Rise in ventilation causes rise in pH
  - Due to blowing off of carbondioxide
  - Hyperventilation may cause ' respiratory alkalosis'

Regulation of Blood pH and Gases

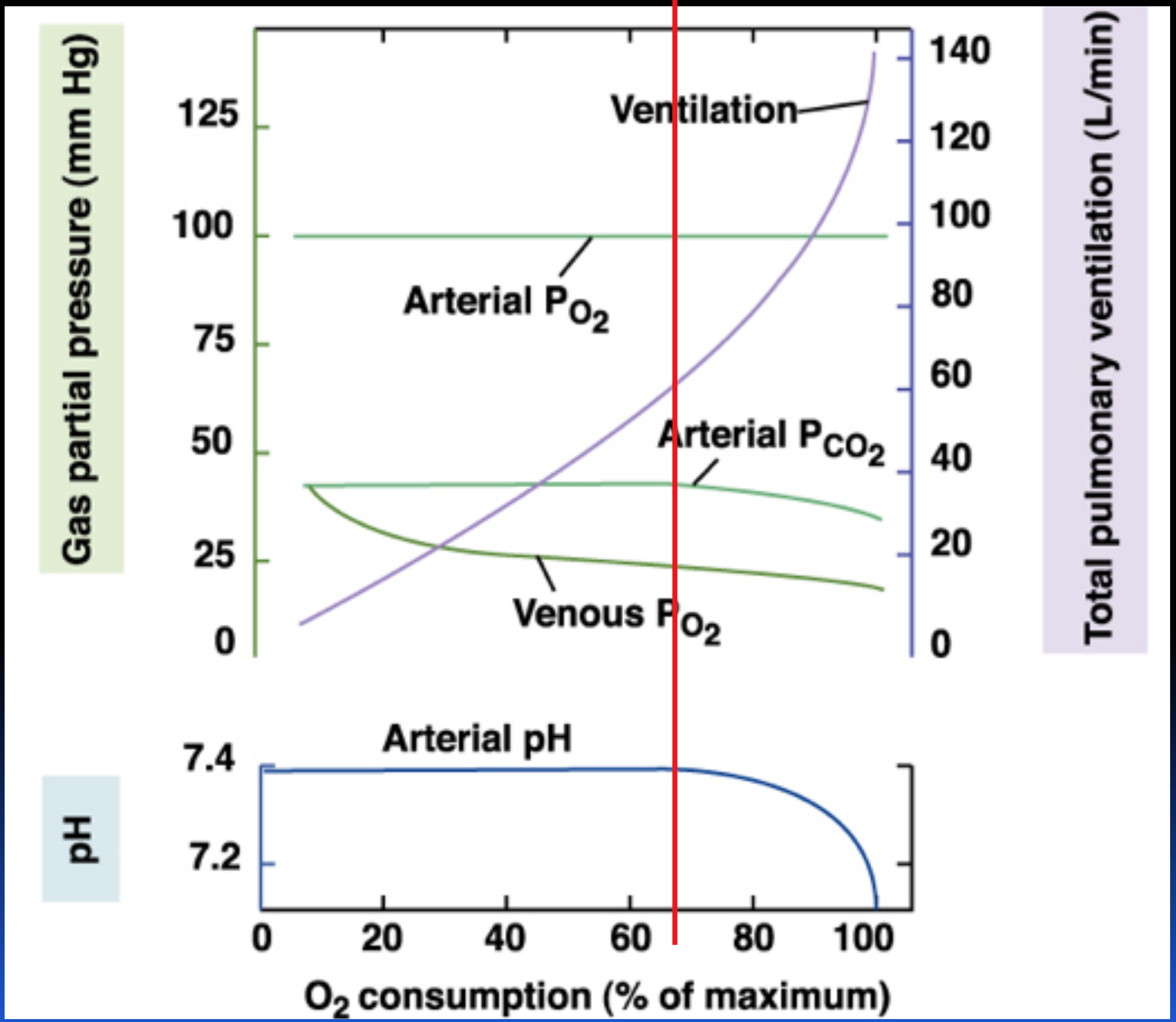


Responses of the Respiratory System to Exercise

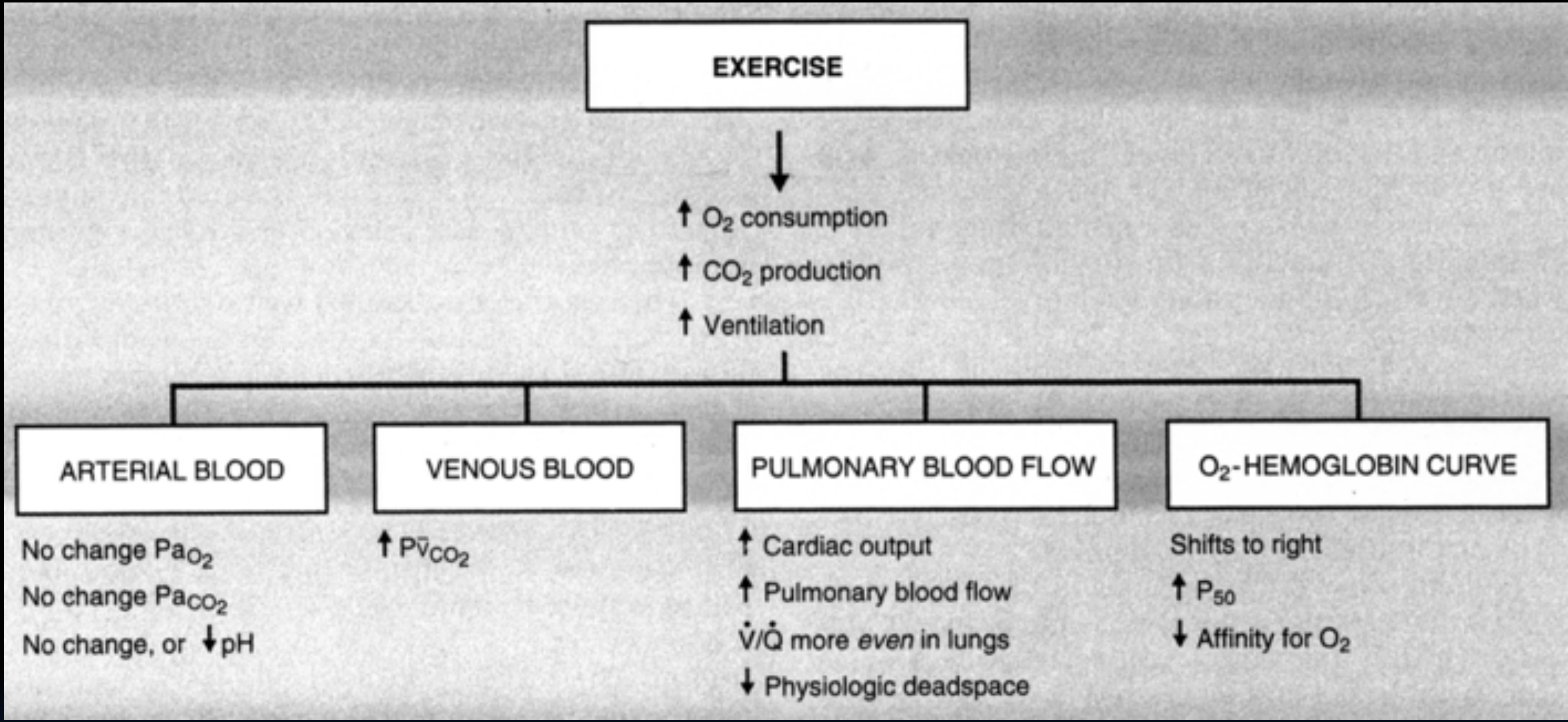




CHANGES IN BLOOD GASES WITH EXERCISE



Responses of the Respiratory System to Exercise



Influencing factors and theories to account for respiration response to exercise.

1. Cerebral cortical influences.
2. Limb movements - proprioceptors
3. Increase body temp. may play modulating role on activities of controlling centers.
4. Small oscillations in arterial PO2 & PCO2 may occur,.
5. "Set-point" may be reset so that system is driven to a different control level.

RESPONSES TO CHANGE IN RESPIRATORY GASES

Hypoxia - O_2 deficiency at the tissue level.

There could be several causes.

1. **Hypoxic-hypoxia** (PO_2 of arterial blood is reduced). e.g., breathing O_2-poor gas or at reduced atmospheric pressures.

With altitude, composition of air remains about same but there are pressure changes.

2. Anemic-hypoxia

Essentially low Hb content.

Also in CO poisoning, effective Hb content is reduced by HbCO complexing.

3. Stagnant-hypoxia

Hypoxia due to circulation that is so slow that tissue does not receive its necessary "flow" of O_2. Shock, congestive heart failure (or localized restriction) can lead to damage of important organs.

4. Histotoxic-hypoxia

Inhibition of tissue oxidative processes by poisons. e.g., Cyanide poisoning - combines with cytochrome oxidase preventing O_2 from serving as the ultimate electron

Abnormal patterns of breathing

- Cheyne-Stokes
  - 10-20s of apnoea, followed by a period of hyperventilation with a gradually increasing tidal volume
  - In severe hypoxaemia
  - Severe circulatory disorders
  - Brain damage
- Ondine's curse
  - No involuntary breathing

Pathological Examples of Altered Respiratory Mechanics