DEBRE MARKOS UNIVERSTY SCHOOL OF MEDICINE

Human Respiratory Physiology

For Pharmacy students

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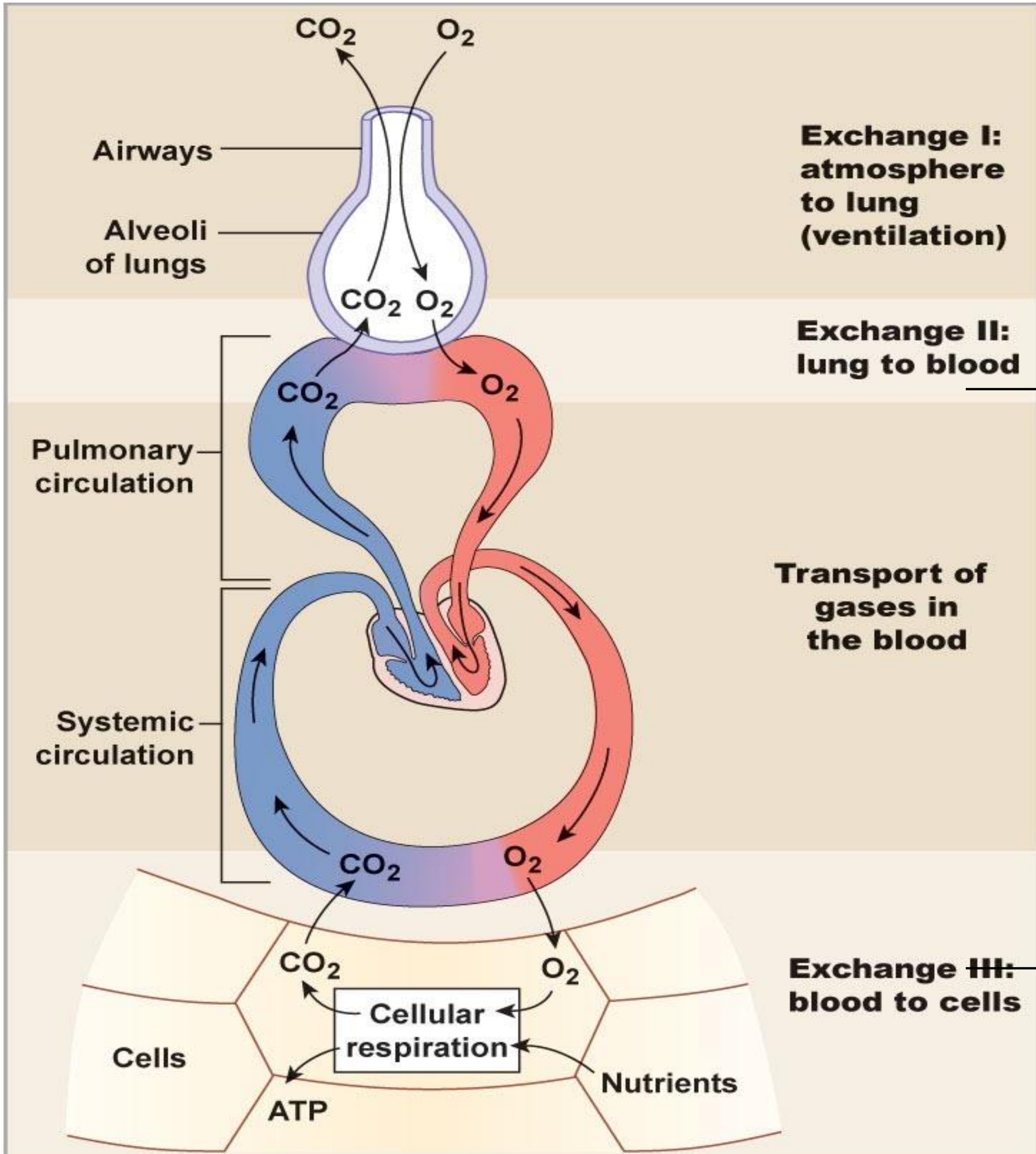
INTRODUCTION

- What is respiration?
  - Far from self-sustaining, trillions of cells making up the body require a continuous supply of oxygen to carry out their vital functions. We cannot do without oxygen for even as little as we can without food or water.
  - Respiration = the series of gas exchanges that leads to the uptake of oxygen by the cells, and the release of carbon dioxide to the lungs.

Major respiratory organs and surrounding structure

1. Pulmonary ventilation: gas exchange between the atmosphere and lungs
2. External respiration -gas exchange between the lungs and blood (O_2 loading and CO_2 unloading).
3. Transport of respiratory gases –via movement of blood O_2 from the lungs is transported to the cell and tissues.
4. Internal respiration –gas exchange between the capillaries and the tissues (O_2 unloading and CO_2 loading).

Schematic View of Respiration



External Respiration

Internal Respiration

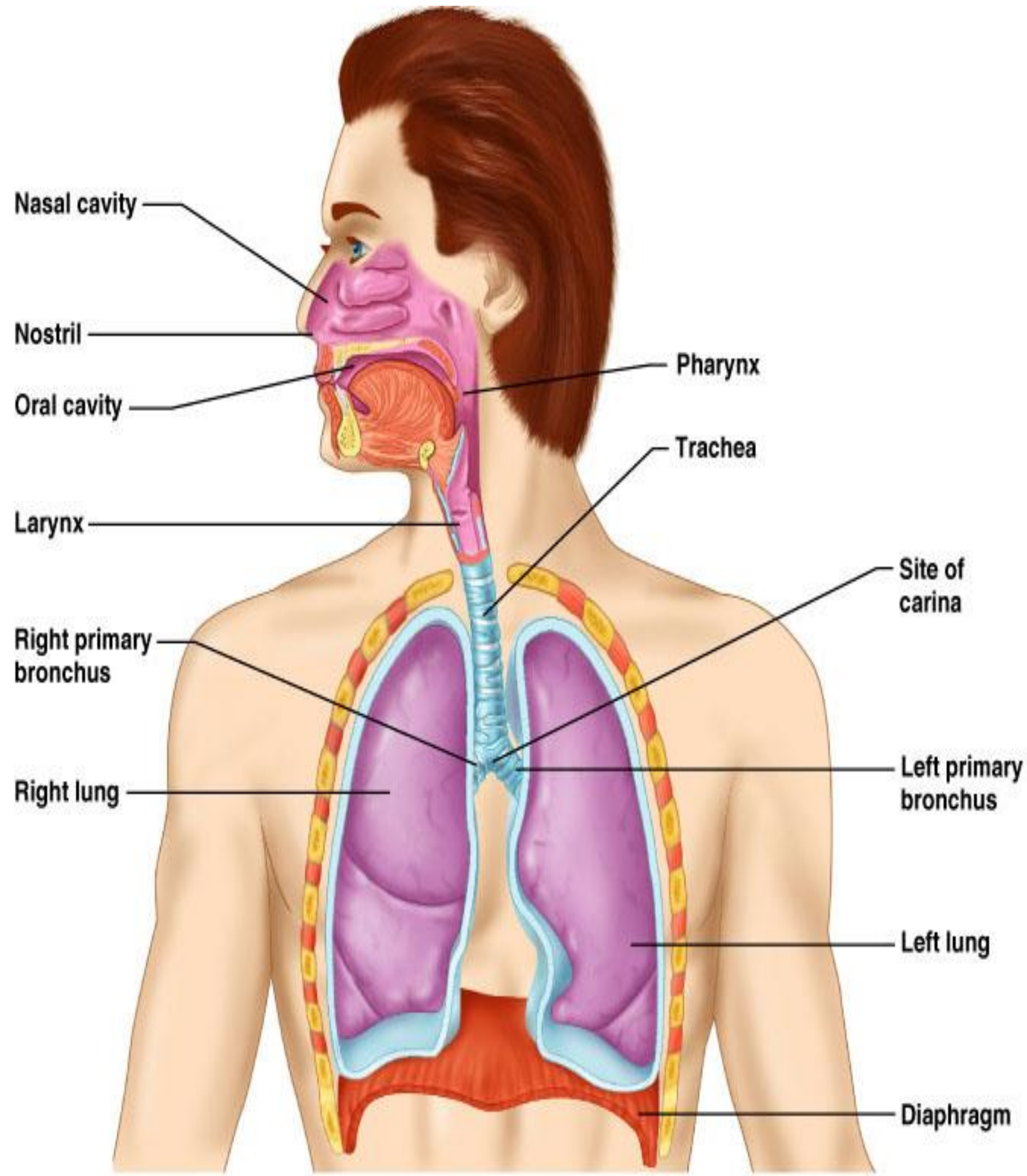
Physiological classification of the respiratory tract

1. Conducting Zone

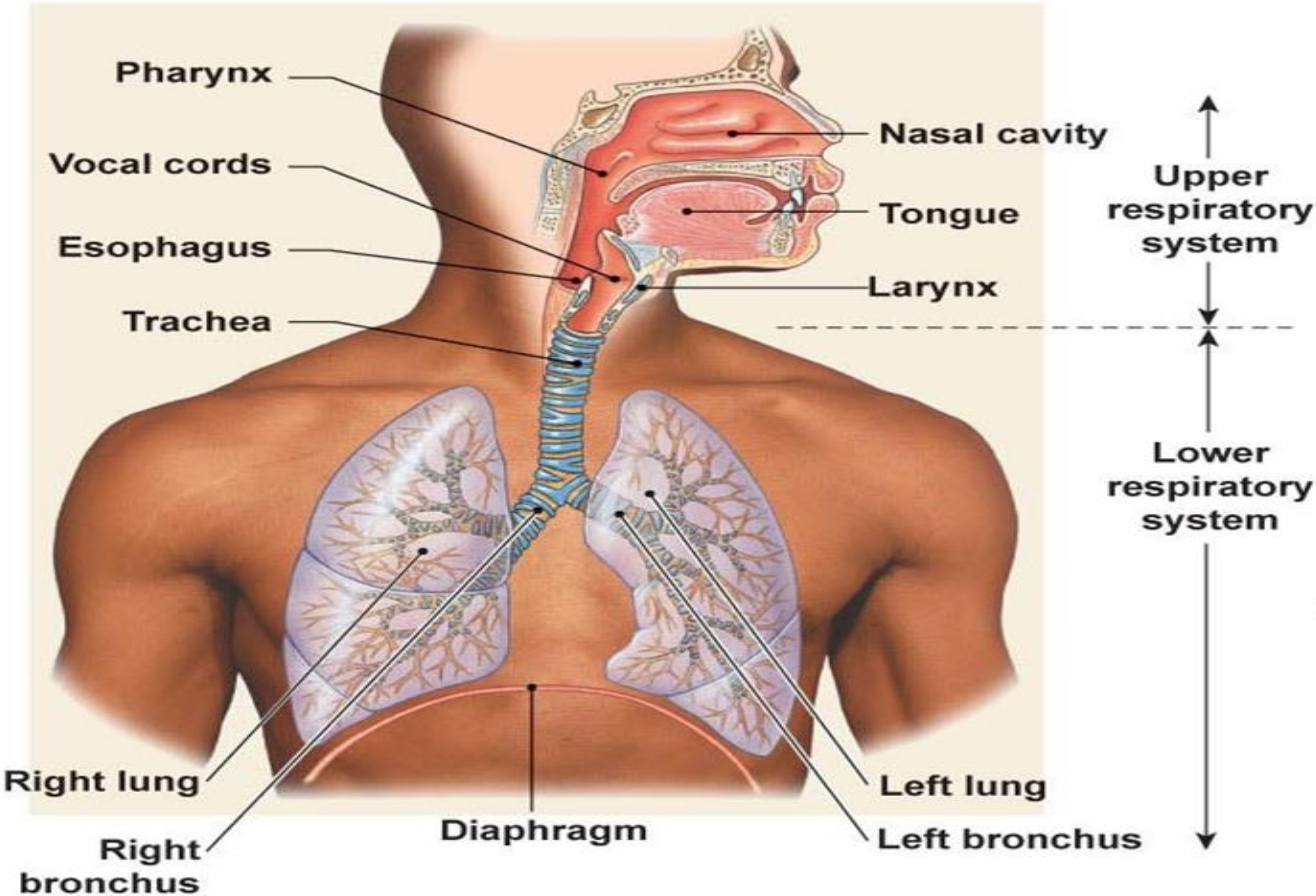
➢Rigid conduits for air to reach site of gas exchange
- -nose/mouth
- -nasal cavity
- -pharynx
- -larynx
- -trachea
- -bronchi
- -Terminal bronchioles

2. Respiratory Zone/exchange portion

➢Site of gas exchange
- -respiratory bronchioles
- -alveolar ducts



Functional Anatomy



Conducting Zone

Nose

- Produces mucus; filters, warms, and moistens incoming air; resonance chamber for speech

Pharynx

- Passageway for air and food
- Facilitates exposure of immune system to inhaled antigens

Larynx

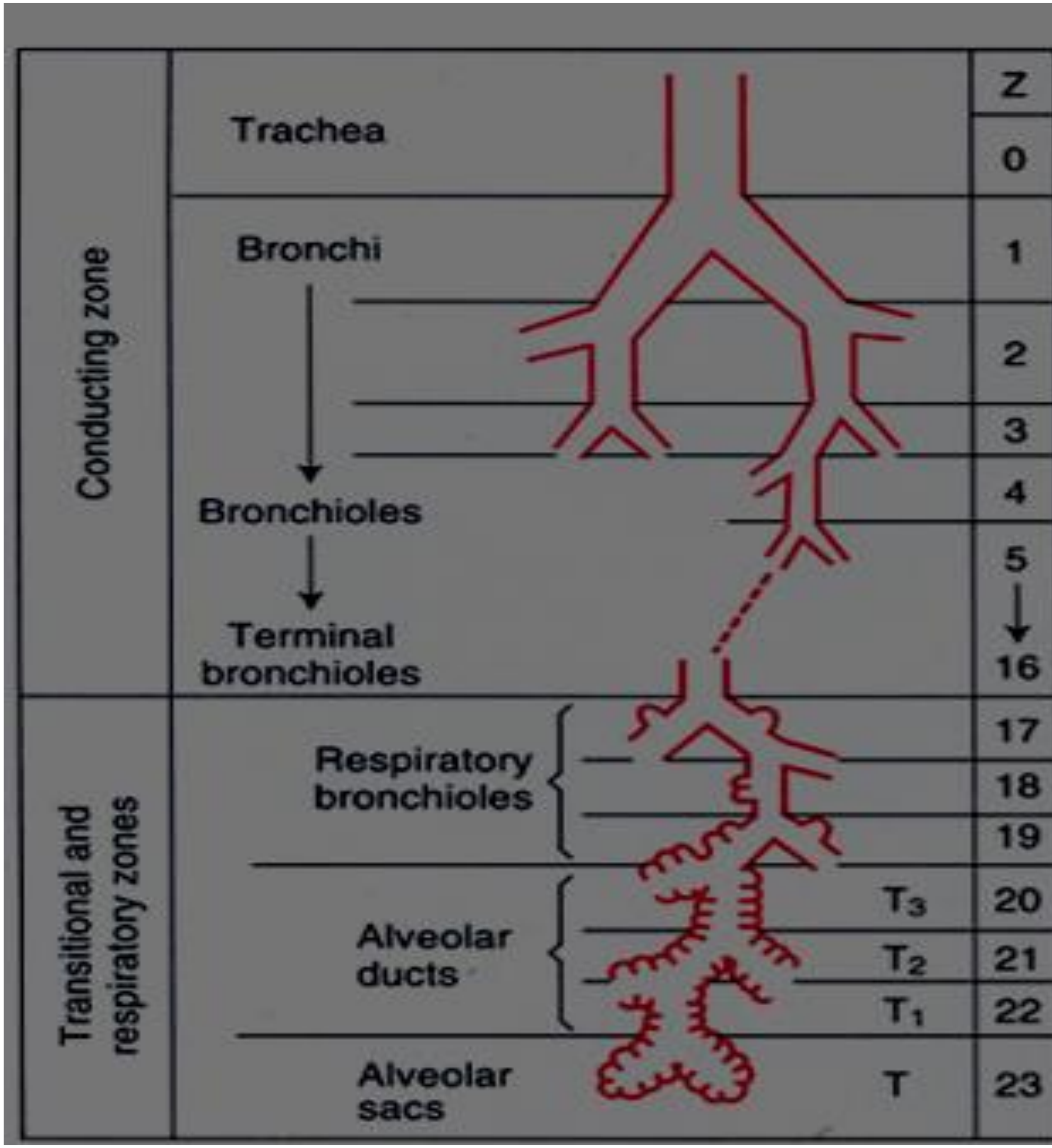
- Provide a patent airway and switching route air and food into the proper channel
- Voice production
- Sphincter Functions

Trachea and Bronchial tree

- Air passageway; cleans, warms, and moisten

Respiratory Zone/Exchanging zone

- Site of exchanging of respiratory gas includes
  - ✓ **Respiratory bronchioles** with alveoli in their walls, make up the 17^{th}-20^{th} generations;
  - ✓ **Alveolar ducts** making up the 21^{st}-23^{rd} generations terminate in alveolar sacs
  - ✓ **Alveoli**
    - Approximately there are 300 million alveoli:
    - Account for most of the lungs' volume
    - Provide tremendous surface area for gas exchange



Diameter (mm)	How many?	Cross-sectional area (cm^2)
15-22	1	2.5
10-15	2	↓
1-10	4 ↓ 1×10^4	
0.5-1	2×10^4 ↓ 8×10^7	100 ↓ 5×10^3
0.3	$3\text{-}6 \times 10^8$	$>1 \times 10^6$

Alveoli

- The functional units of the respiratory system
- About 300 million alveoli in the lung → ↑surface area for exchange (60–80 m2, 40x surface area of the body)
- Each alveolus is 1 cell layer thick → ↑rate of diffusion
- Do not contain muscle because muscle fibers would block rapid gas exchange. However, it contains elastin and collagen fibers that create elastic recoil when lung tissue is stretched
- Contain open pores that:
  - Connect adjacent alveoli
  - Allow air pressure throughout the lung to be equalized

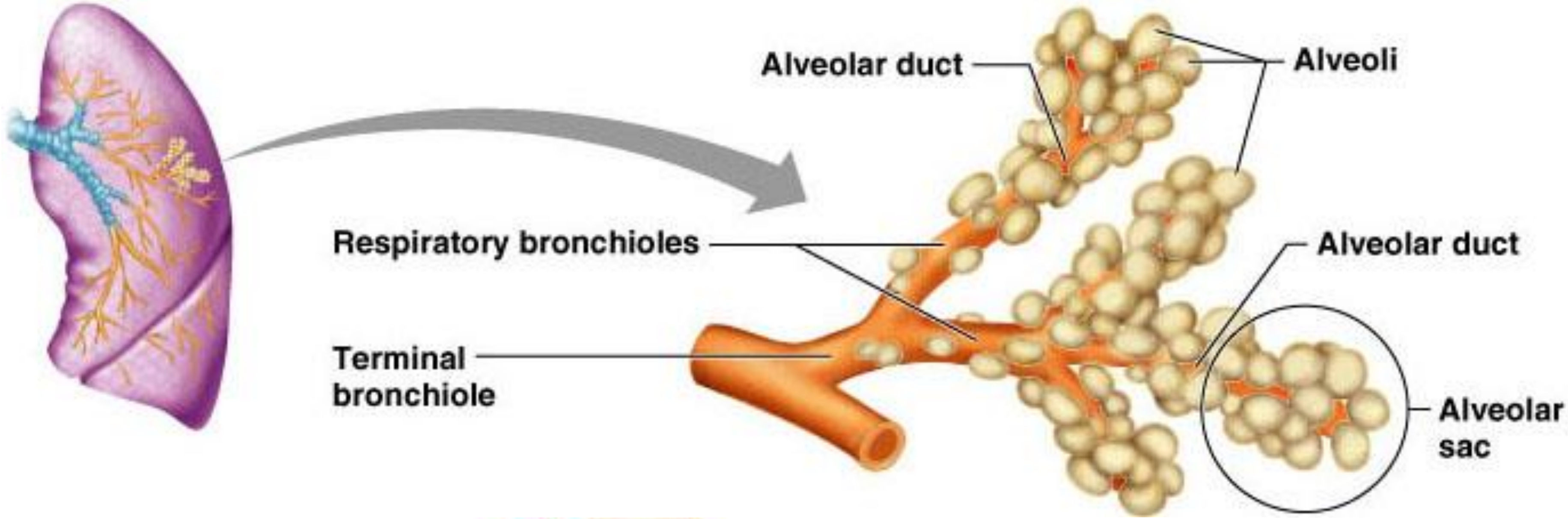
Structural specialization of the Alveoli

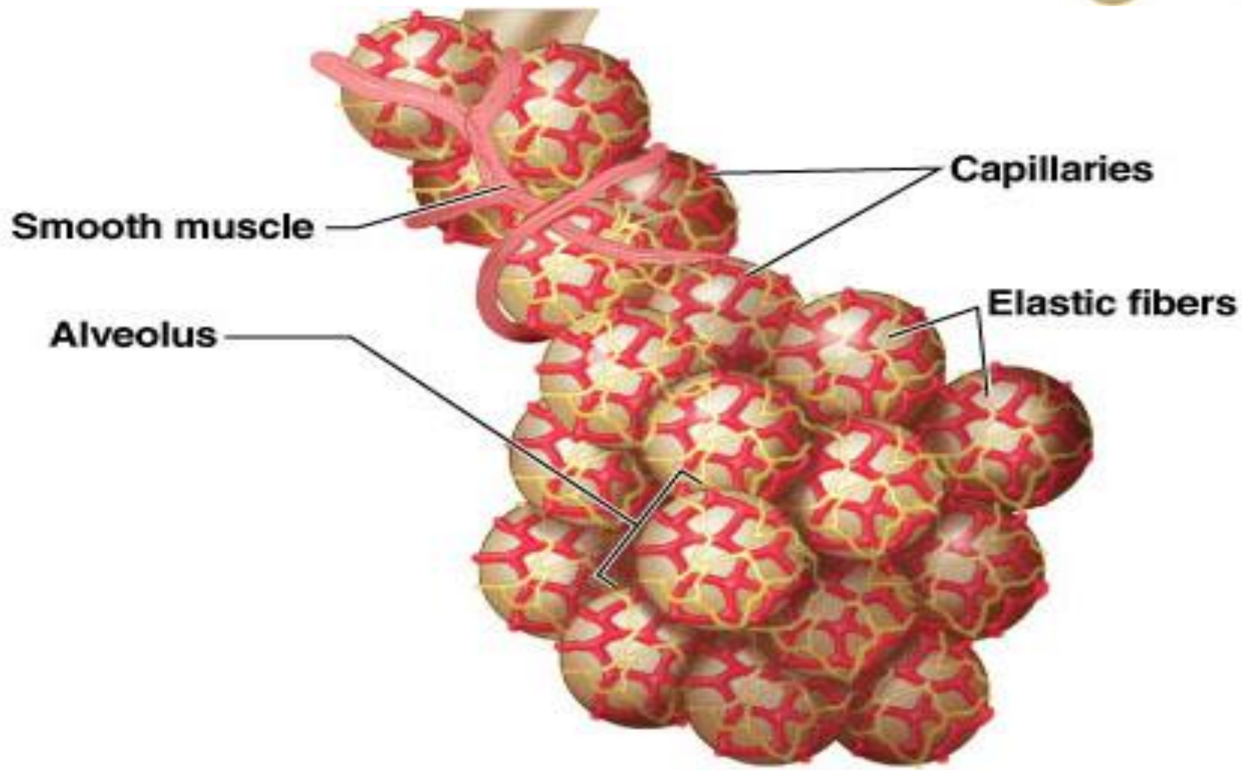
1) **Type I pneumocytes - O**ccupy 95% of the alveolar surface area, so that gases can diffuse rapidly through them.

2) **Type II pneumocytes -** are less in number and constitute thick granulocytes that are responsible for the production of **surfactants**.

3) **Type III pneumocytes -** are large phagocytic macrophage cells found in alveolar cavities.

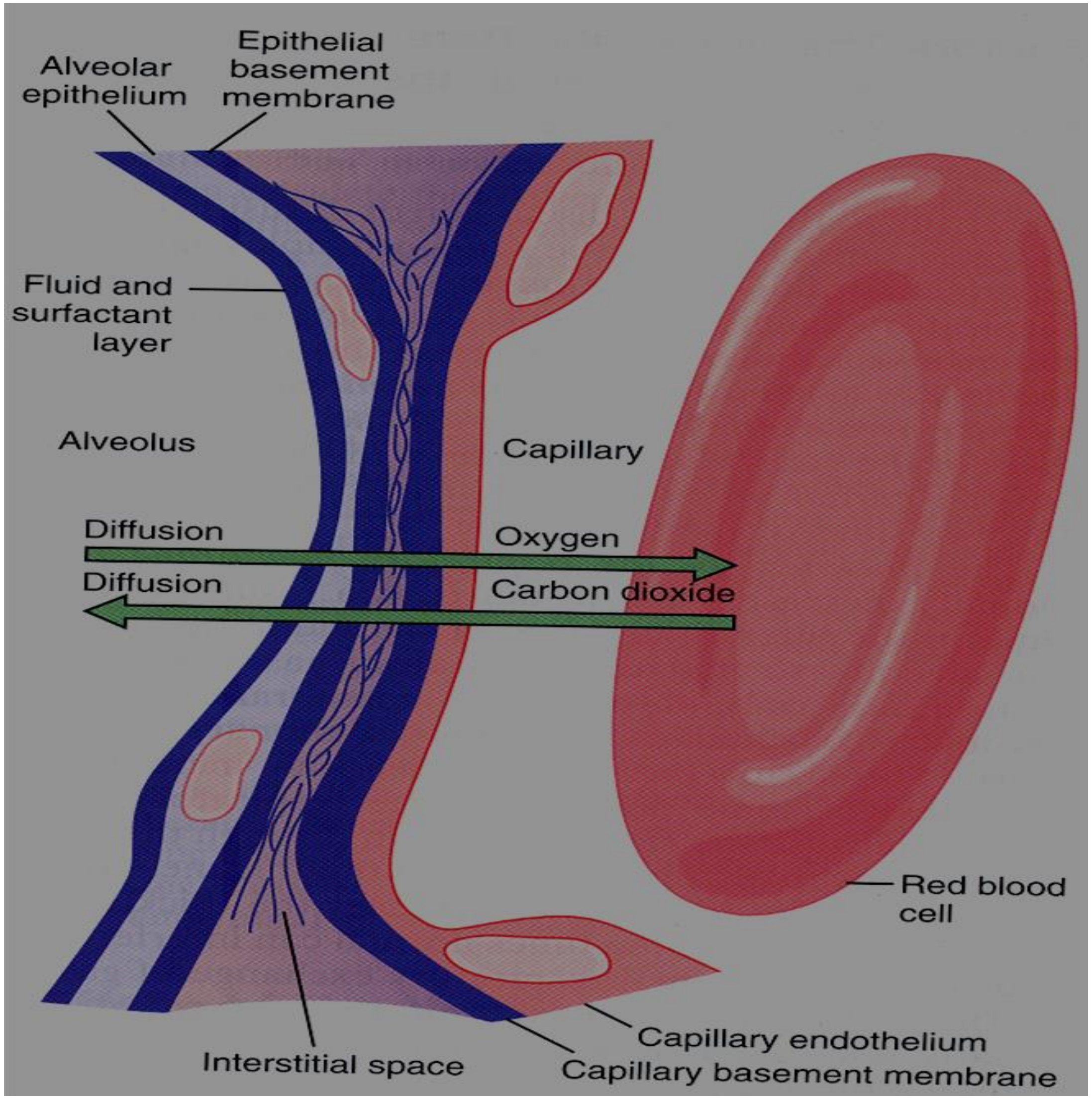
   - ✓ These cells keep alveolar surfaces sterile by removing debris and microbes.


Alveolar duct
Alveoli
Respiratory bronchioles
Alveolar duct
Terminal
bronchiole
Alveolar
sac

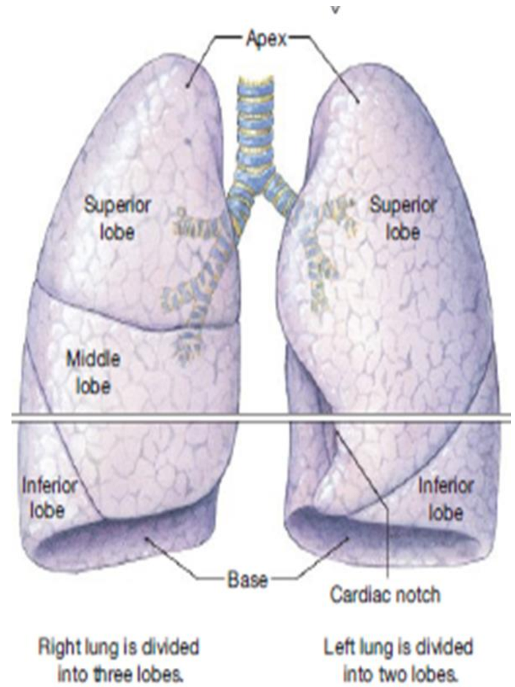

Capillaries
Smooth muscle
Elastic fibers
Alveolus

Respiratory Membrane

- Respiratory Membrane is composed of alveolar and capillary walls
- Alveolar walls:
  - Are a single layer of type I epithelial cells
  - Permit gas exchange by simple diffusion



Physical Properties of the Lungs



- Compliance:
  - Distensibility (stretch ability):
    - Ease with which the lungs can expand.
  - 100 x more distensible than a balloon.
- Elasticity:
  - Tendency to return to initial size after distension.
  - High content of elastin proteins.
    - Very elastic and resist distension.
      - Recoil ability

General Functions of the Respiratory System

- **Primary Functions**
  - Extra-cellular respiration:
    - Conduction of air to and from the terminal air spaces.
  - Intracellular respiration: utilization of O_2 & production of CO_2
- **Secondary Functions**
  - Deglutition and modification of inspired air,
  - Defense of body against noxious stimuli like inhaled particles,
  - Olfaction, phonation, conduction of air.
  - Acid-base balance,
  - Regulation of various humoural concentrations(ACE)

Mechanism of Ventilation/ Breathing

- **Terminology**
  - Inspiration = the movement of air into the respiratory tracts.
  - Expiration = movement of air out of the respiratory tracts.
  - Respiratory cycle = is one inspiration followed by an expiration.
  - Ventilation = Mechanical process that moves air in (Inspiration) and out (Expiration) of the lungs.

Mechanism of Ventilation/ Breathing….cont'd

- Ventilation is mainly a result of pressure differences between the lung and the environment.
- Respiratory pressure is always described relative to atmospheric pressure (P_{atm})
- Atmospheric pressure:
  - ✓Pressure exerted by the air surrounding the body
  - ✓Negative respiratory pressure is less than P_{atm}
  - ✓Positive respiratory pressure is greater than P_{atm}

Mechanism of Ventilation/ Breathing….cont'd

- There are four important pressure compartments that dictate ventilation.
  - Atmosphere pressure
  - Intrapulmonary /intra-alveolar pressure (-1 - +1cm H_2O)
    - pressure in the alveoli or pressure of the air inside the lung alveoli
  - Intrapleural pressure (-3 cm H_2O – +10 cm H_2O)
    - Pressure in the intrapleural space due to the fluid in the pleural cavity.
    - is negative, due to lack of air in the intrapleural space

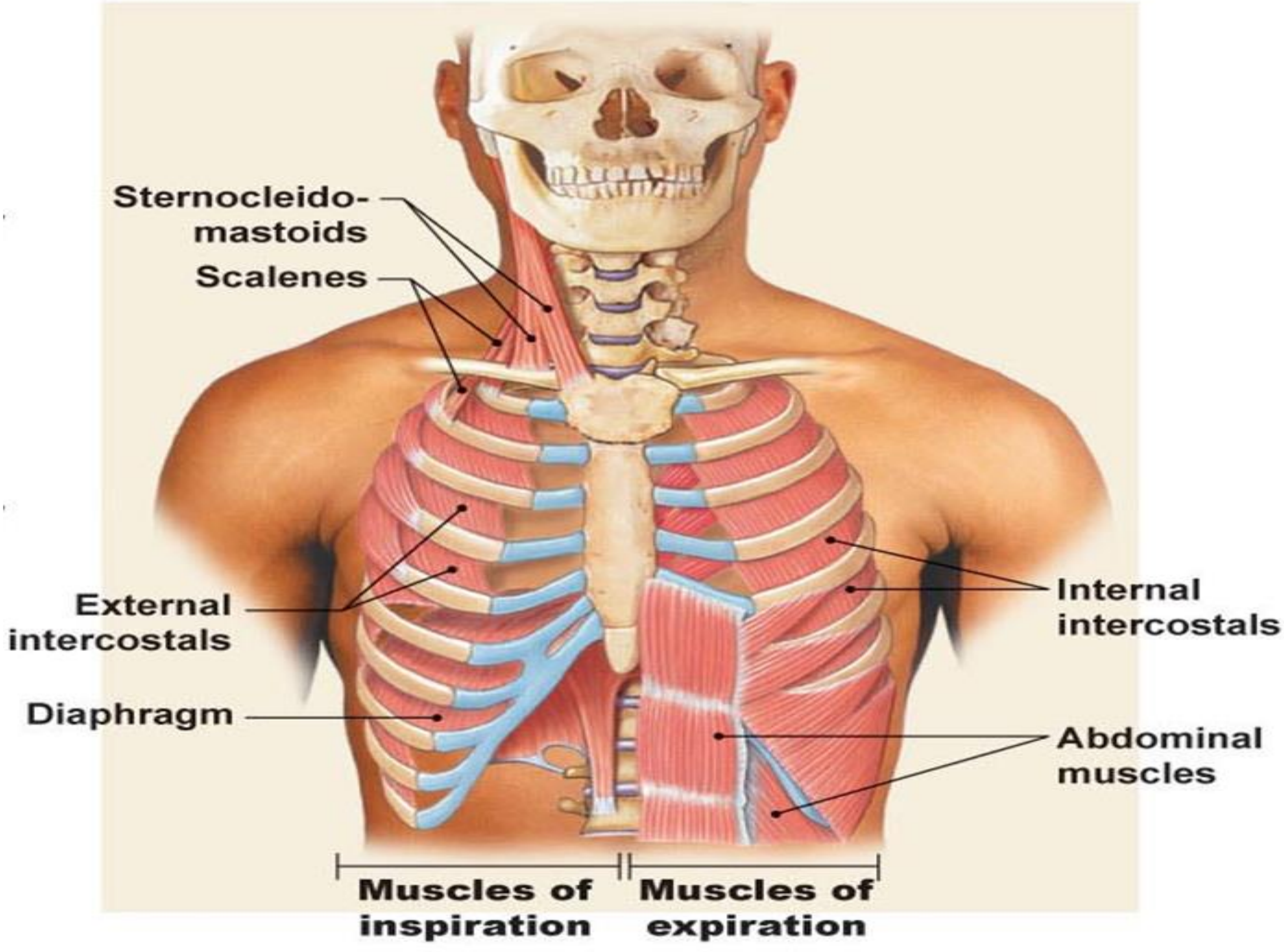
- (NB: 1 mm Hg=1.36 cm H2O)

  - Transpulmonary pressure=Pressure difference across the wall of the lung

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

  - The force acting across the wall of the lung to expand it

Structure involved during ventilation

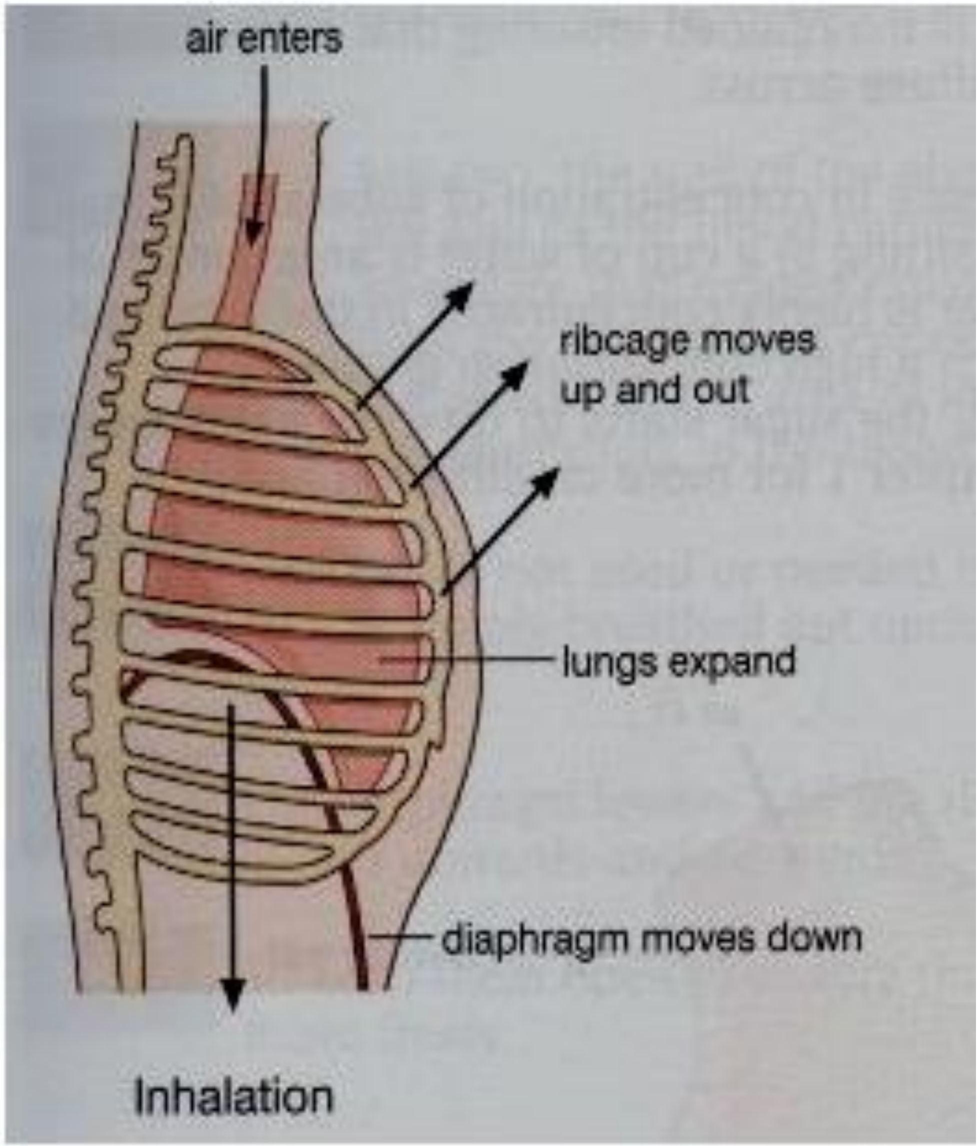


Muscle Forces→ Movement of lungs and chest wall

↑ ↑

Groups of muscles	Resistances to be overcome during inspiration (-)
1. Diaphragm 2. Intercostals 3. Auxiliary muscles: . Sternocleidomastoid . Scalenes . Pectoralis . Latismus dorsi . etc…	Elastic resistance (65%) -elastic recoil of lungs -elastic recoil of thorax Non-elastic resistance (35%) - airway resistance (20%) -tissue resistance of lungs & thorax (15%)

- INSPIRATION→ enlargement of chest cavity→↑ volume of thorax→↑-ve Ppl→↑Lung expansion



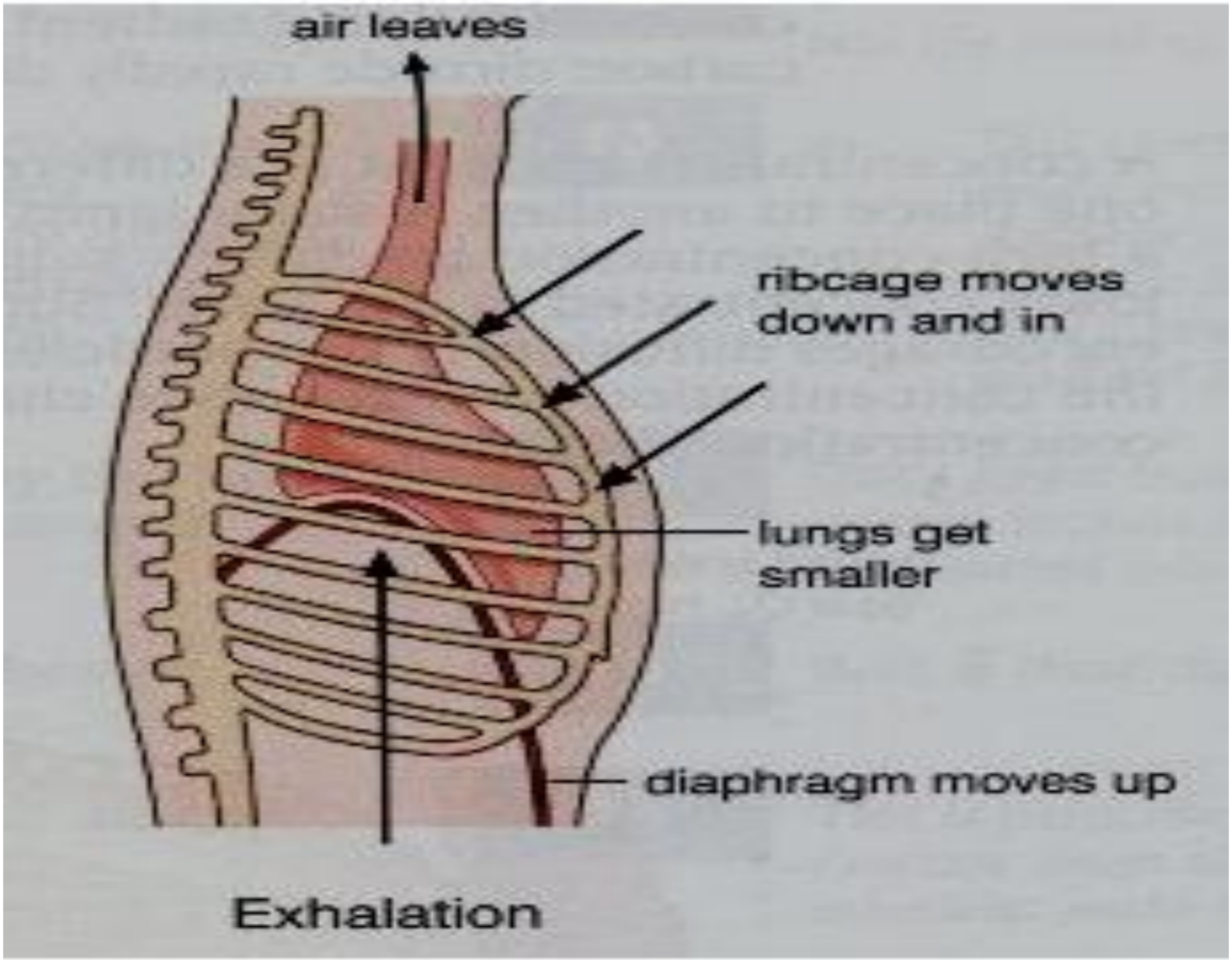
During Inspiration, at rest

Active ↓ **Nerve impulse** ↓ **Contraction of:** **-diaphragm** **-external intercostals** **-accessory muscles (scalene, sterno- cleidomastoid, pectoralis, latismus dorsi)** NB: Accessory muscles are involved when TV is very large during inspiration.	**Contraction of:** Diaphragm(1.5-7cm) ↓ -↑vertical diam. of thorax ↓ Contributes 70% of TV	**Contraction of:** External intercostals ↓ -↑antero-posterior diam. of thorax ↓ Contributes 30% of TV

Inspiration…

- **Inspiration(quit normal breathing)**
  - Intra alveolar pressure falls from 0 to -1 mmH2O
  - Intrapleural pressure falls further to -7.5 mmH2O
  - Transpulmonary pressure raises to +6 mmH2O
- **Net= 0.5(500ml) of air gushs to the lungs in 2-3 seconds**.

EXPIRATION: Reduction in chest cavity→↓volume of thorax→↓-ve Ppl →↓lung vol.



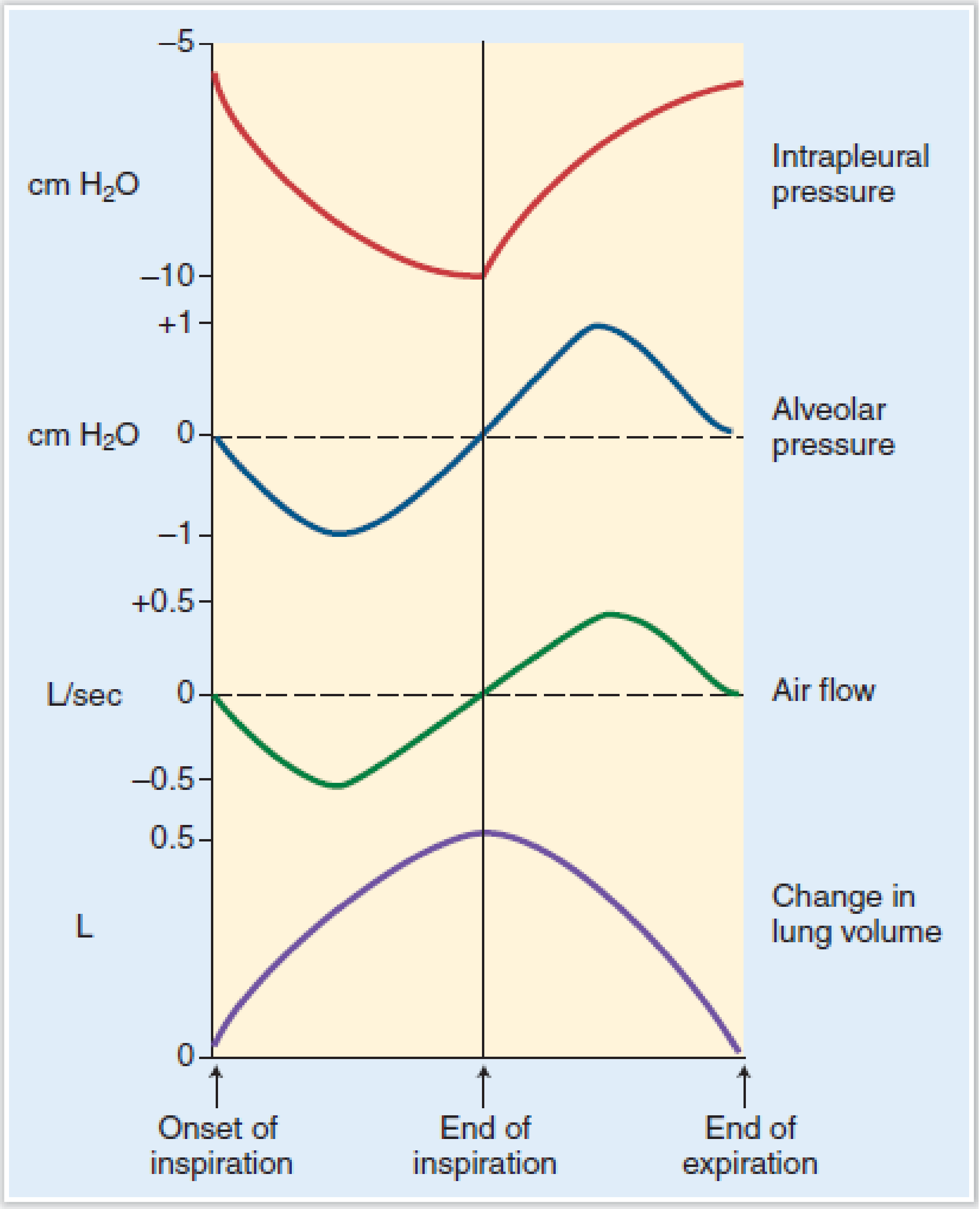
During Expiration

Passive at rest		Active during exercise
Elastic recoil of:	**Surface tension effect of:**	**Nerve impulses** ↓ **Contraction of :**
Stretched tissues in thorax, lungs and abdominal muscles ↓ **30% of TV**	**Fluid lining alveoli and respiratory bronchioles** ↓ **70%TV**	**• expiratory muscles (internal intercostals)** **•ant. abdominal muscles including pelvic floor muscles** ↓ **Upward movement of diaph.**

Expiration …

- Expiration:(quit normal breathing)
  - Intra alveolar pressure raise from -1 to +1 mmH2O
  - Intrapleural pressure raise from -7.5 to -4 mmH2O
  - Transpulmonary pressure falls to +5 mmH2O
- **Net= 500ml of air is expehaled from the lungs.**

Ventilation cvcle



Surfactant

- Surfactant is a complex mixture of several phospholipids, proteins, and ions
  - Important components are the phospholipid dipalmitoylphosphatidylcholine, surfactant apoproteins, and calcium ions.
- Surfactant is a surface active agent in water, which means that it greatly reduces the surface tension of water.
  - Reduces attractive forces of hydrogen bonding by becoming interspersed between water molecules.

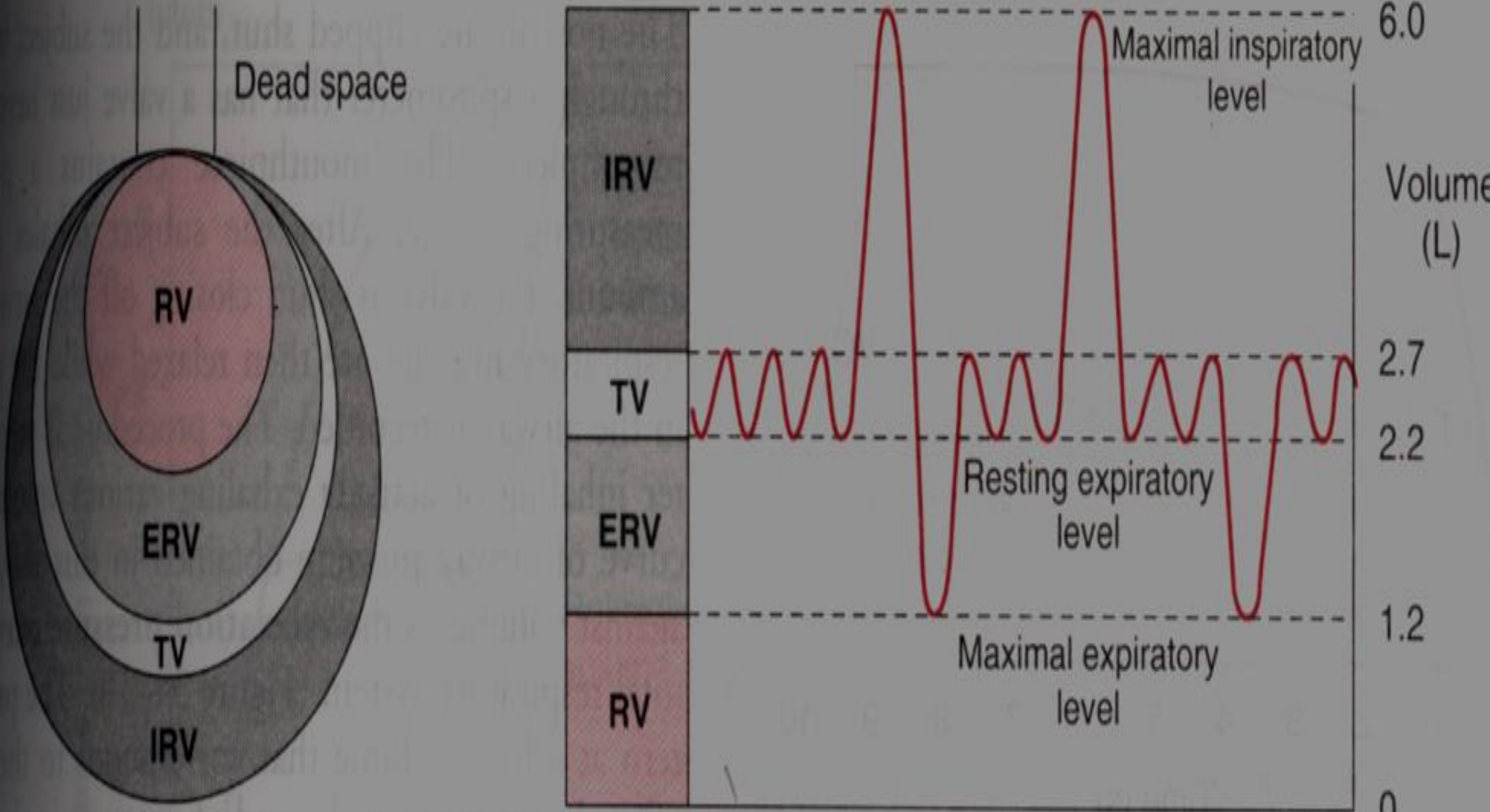
Respiratory Volume and Capacity

- The process of recording the volume of air moving into and out of the lungs, with different phases of respiration is a called spirometry.
- The equipment used in the process is called spirometer.
- There are about four lung volume and four lung capacity.

Respiratory Volume and Capacity….

Lung volumes

- **Tidal volume (TV)** – air that moves into and out of the lungs with each breath (approximately 500 ml)
- **Inspiratory reserve volume (IRV)** – air that can be inspired forcefully beyond the tidal volume (3000 ml)
- **Expiratory reserve volume (ERV)-** volume maximum expiration (1200ml)
- **Residual volume (RV)** – air left in the lungs after maximal expiration (1300 ml)



IRV = Inspiratory reserve volume
ERV = Expiratory reserve volume
TV = Tidal volume
RV = Residual volume

Respiratory Volume and Capacity….

Lung Capacities

- **Vital Capacity (VC)** – the total amount of exchangeable air (TV + IRV + ERV)
- **Inspiratory Capacity (IC) -** the sum of TV and IRV
- **Functional Residual Capacity (FRC) -**the sum of RV& ERV
- **Total Lung Capacity (TLC)** – sum of all lung volumes (approximately 6000 ml in males)

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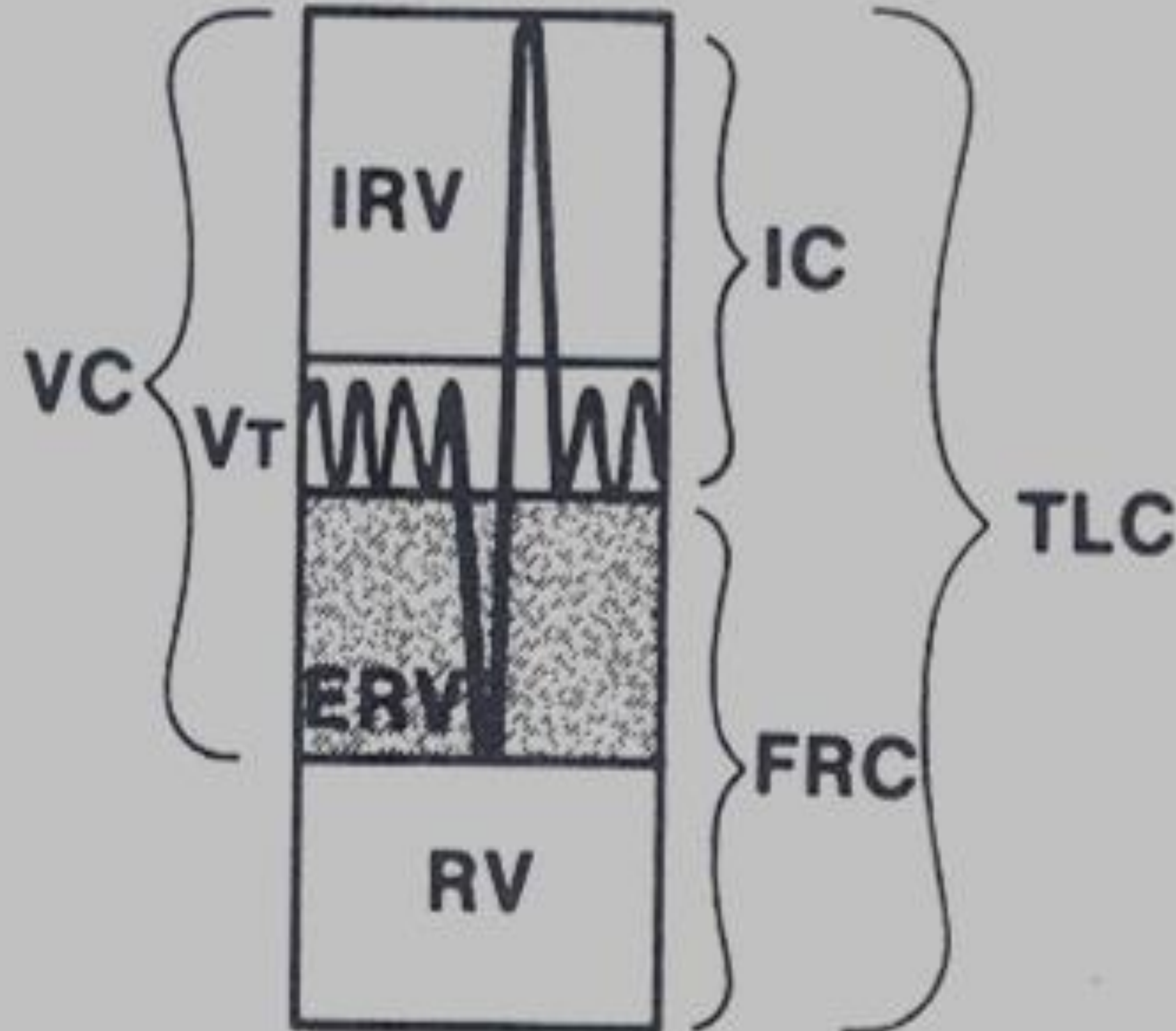

VC
VT
IRV
ERV
RV
IC
FRC
TLC

Restrictive Disease:

- Makes it more difficult to get air in to the lungs.
- They “restrict” inspiration.
- Decreased VC, TLC, RV, FRC
- Includes:
  - Fibrosis
  - Sarcoidosis
  - Muscular diseases
  - Chest wall deformities

Obstructive Disease

- Make it more difficult to get air out of the lungs.
- Decrease VC; Increased TLC, RV, and FRC
- Includes:
  - Emphysema
  - Chronic bronchitis
  - Asthma

COMPARISON OF VOLUME-TIME AND FLOW-VOLUME CURVES

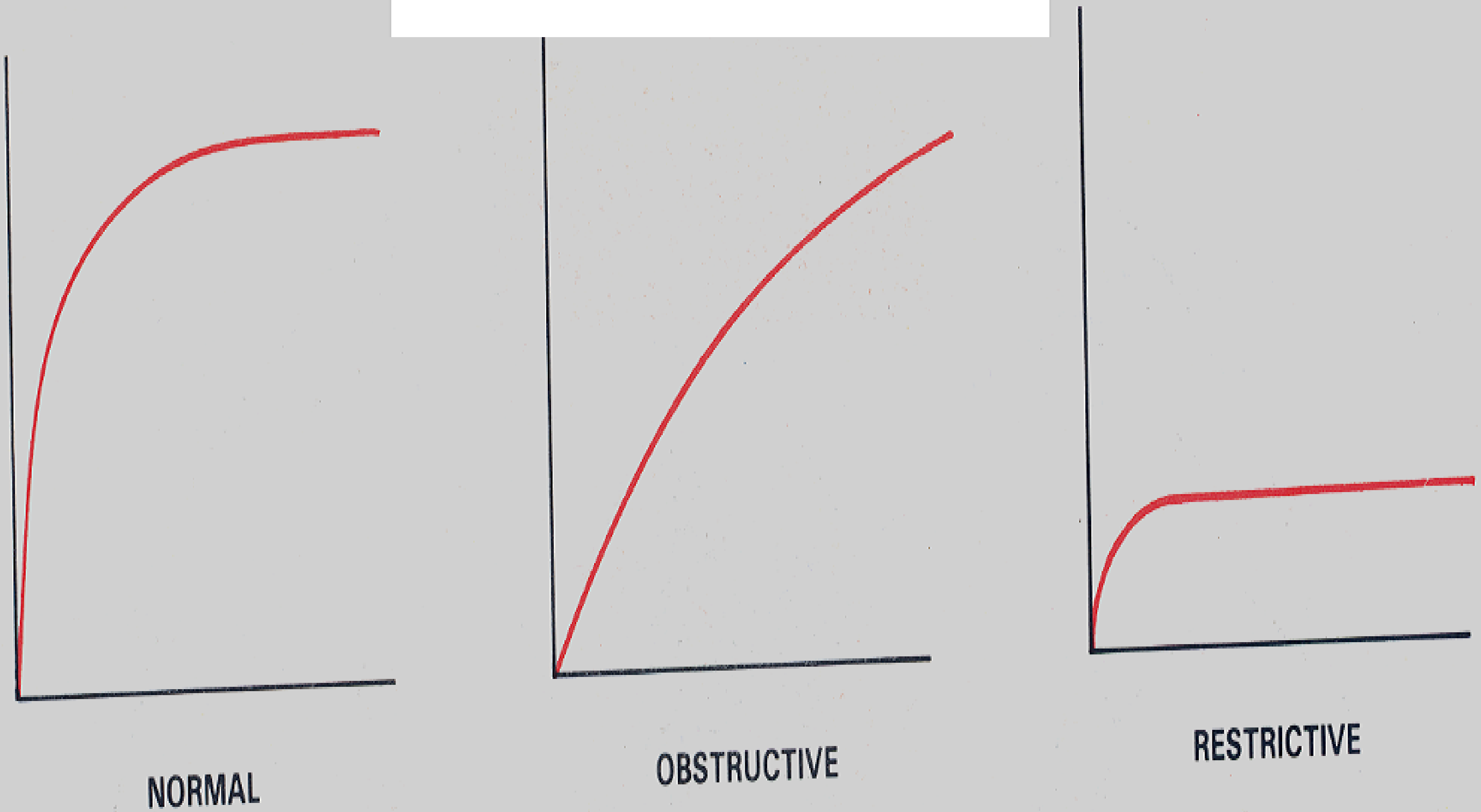


Fig. Normal, Obstructive and Restrictive patterns of airways condition recorded by a dry spirometer (vitalograph).

Minute Ventilation and Alveolar Ventilation

➢ Minute Ventilation

- It is the product of breathing rate and tidal volume

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

$\dot{V}_E$ = Expired minute ventilation rate

V_T = Tidal volume

f = Breathing frequency

- This is dived into dead space ventilation and alveolar ventilation, so that

$$\dot{V}_E = \dot{V}_A + \dot{V}_D$$

$\dot{V}_E$ = Expired minute ventilation rate

$\dot{V}_A$ = Alveolar ventilation rate

$\dot{V}_D$ = Dead space ventilation rate

Dead Space

➢ The part of the respiratory system where gas exchange does not take place is called the dead space.

1. Anatomic dead space
   - Conduction air ways are fixed dead space
   - Its volume is 150 ml
2. Alveolar dead space
   - Unperfused but ventilated alveoli
   - Pulmonary embolism increases
3. Physiologic dead space
   - Sum of anatomic and alveolar dead space
   - In diseases this becomes large resulting in hypercapnea and hypoxemia

Gas Exchange and Transport

- Air is a mixture of gases, each of which contributes a share, called its partial pressure, to the total atmospheric pressure.
- That is, $P_{N2}+ P_{O2}+P_{H2O} +P_{CO2}$=597.0 +159.0 +3.7 + 0.3= 760.0 mmHg.
- These partial pressures are important because they determine the rate of diffusion of a gas and therefore strongly affect the rate of gas exchange between the blood and alveolar air.
- Greater P_{O2} in the alveolar air more O_2 picks up to the blood and blood arriving at an alveolus has a higher P_{CO2} than air, the blood releases CO_2 into the air. At the alveolus, the blood is said to *unload CO_2 and load O_2*.
- Each gas in a mixture behaves independently; the diffusion of one gas does not influence the diffusion of another.

Alveolar Gas Exchange

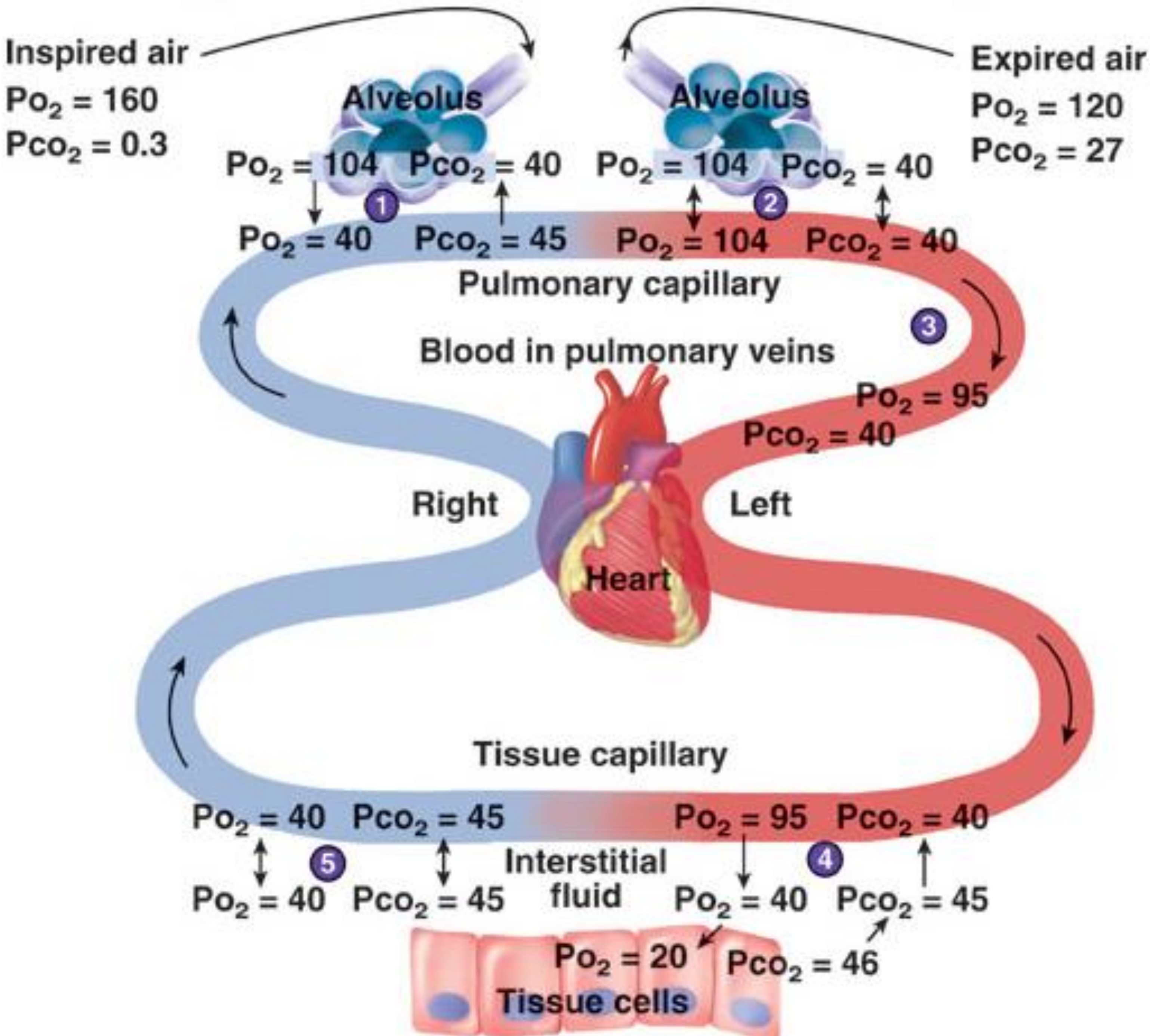
- Alveolar gas exchange is the process of O_2 loading and CO_2 unloading in the lungs through simple diffusion
- Since both processes depend on erythrocytes (RBCs), their efficiency depends on how long an RBC spends in an alveolar capillary compared to how long it takes for O_2 and CO_2 to reach equilibrium concentrations in the capillary blood.

- A RBC passes through an alveolar capillary in about 0.75 second at rest and 0.3 second during vigorous exercise, when the blood is flowing faster. But it takes only 0.25 second for the gases to equilibrate, so even at the fastest blood flow, a RBC spends enough time in a capillary to load as much O_2 and unload as much CO_2 .

- The following factors especially affect the efficiency of alveolar gas exchange:
  - Concentration gradients of the gases.
  - Solubility of the gases.
  - Square root of molecular wt of the gas($\sqrt{mw}$)
  - Membrane thickness (0.5 nm)
  - Membrane area (70 m^2).
  - Absolute temperature of fluid
  - Permeability of membrane
  - Fluid viscosity in lung (η)
  - Contact or transit time of gas
  - Ventilation-perfusion coupling.
  - Exercise or change in metabolic rate
    - Opening of more capillaries→↑3-4 folds due to dilatation of existing capillaries.

- The PO_2 is about 104 mmHg in the alveolar air and 40 mmHg in the blood arriving at an alveolus.
- Oxygen therefore diffuses from the air into the blood, where it reaches a PO_2 of 104 mmHg.

- Before the blood leaves the lung, however, this drops to about 95 mmHg because blood in the pulmonary veins receives some oxygen-poor blood from the bronchial veins by way of anastomoses.
- The PCO_2 is about 46 mmHg in the blood arriving at the alveolus and 40 mmHg in the alveolar air.
- Carbon dioxide therefore diffuses from the blood to the alveoli.



Inspired air
$Po_2 = 160$
$Pco_2 = 0.3$
Alveolus
$Po_2 = 104$
$Pco_2 = 40$
1
$Po_2 = 40$
$Pco_2 = 45$
Alveolus
$Po_2 = 104$
$Pco_2 = 40$
2
$Po_2 = 104$
$Pco_2 = 40$
Expired air
$Po_2 = 120$
$Pco_2 = 27$
Pulmonary capillary
3
Blood in pulmonary veins
$Po_2 = 95$
$Pco_2 = 40$
Right
Left
Heart
Tissue capillary
$Po_2 = 40$
$Pco_2 = 45$
5
$Po_2 = 40$
$Pco_2 = 45$
Interstitial fluid
$Po_2 = 95$
$Pco_2 = 40$
4
$Po_2 = 40$
$Pco_2 = 45$
$Po_2 = 20$
$Pco_2 = 46$
Tissue cells

Solubility of the gases

- Gases differ in their ability to dissolve in water.
- CO_2 is about 20 times as soluble as O_2, and oxygen is about twice as soluble as N_2.
- Even though the conc. gradient of O_2 is much greater than that of CO_2 across the respiratory membrane, equal amounts of the two gases are exchanged because CO_2 is so much more soluble and diffuses more rapidly.

Gas Transport

- It is the process of carrying gases from the alveoli to the systemic tissues and vice versa.

1) Transport of O_2

- The conc. of O_2 in arterial blood is about 20 mL/dL.

✍Mode of Transport

i. Solution (1.5%)

ii. chemical combination with Hb (98.5%)

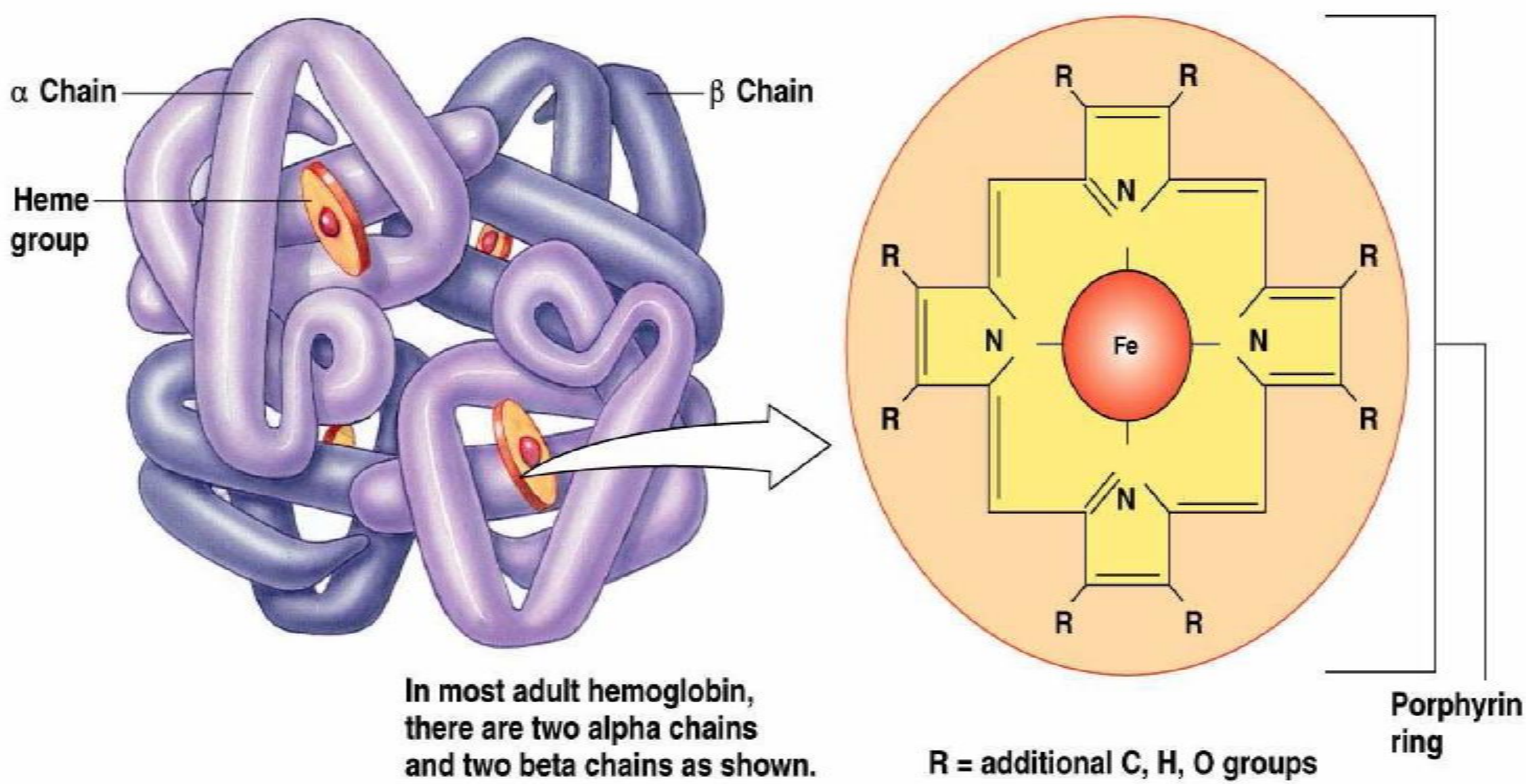
Transport of O_2 …..

i. Transport of O_2 in dissolved form :

- Henry's Law of solubility states that the amount of gas that dissolves in a liquid is directly proportional to:
    - a) partial pressure of the gas,
    - b) solubility of the gas.
- For each mm Hg of P_{O2} there is 0.003 ml O_2 / 100 ml of blood (0.003 vol %).
- Thus, normal arterial blood with a P_{O2} of 100 mm Hg contains 0.31 ml O_2 /100 ml (0.31 vol %).
- Dissolved O_2 transport accounts for only about 1.5% of the O_2 transported which is insufficient for tissue need.

Transport of O_2 …..

ii. Chemical combination with Hb



(a) A hemoglobin molecule is composed of four protein globin chains, each surrounding a central heme group.

(b) Each heme group consists of a porphyrin ring with an iron atom in the center.

Transport of O_2 …..

- Each heme group can bind 1 O_2 to the ferrous ion at its center; thus, one hemoglobin molecule can carry up to 4 O_2

- If O_2 is bound to hemoglobin, the compound is called oxyhemoglobin (HbO_2), whereas hemoglobin with no oxygen bound to it is deoxyhemoglobin (HHb).

- When hemoglobin is 100% saturated, every molecule of it carries 4 O_2; if it is 75% saturated, there is an average of 3 O_2 per hemoglobin molecule; if it is 50% saturated, there is an average of 2 O_2 per hemoglobin; and so forth.

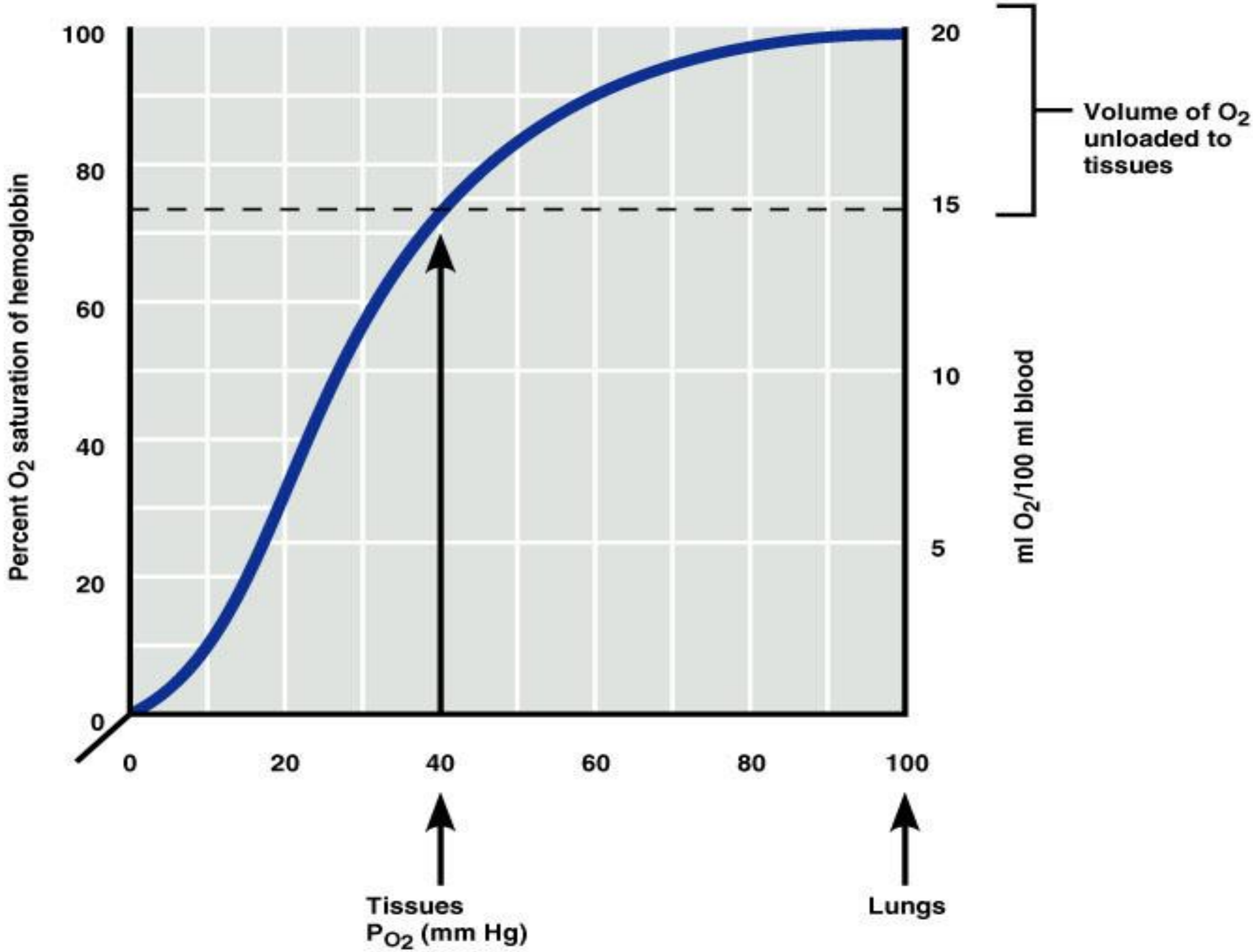
- The poisonous effect of CO is from its competition for the O_2 binding site.

Transport of O_2 …..

- Amount of O_2 combining with 1gm of Hb
  - Adult =1.306 ml
  - Foetus = 1.312 ml
- At PO_2 95mmHg in adult:
  - dissolved O_2= 0.31ml/dl of blood,
  - chemically bound O_2=19.6 ml/dl of blood
- 100 ml of arterial blood carrying 20ml of O_2 has Hb saturated with 97-98% of O_2.

Oxygen dissociation (Delivery) Curve

- O_2 forms easily reversible combination with Hb to give oxyhaemoglobin: O_2 +Hb ←→ HbO_2



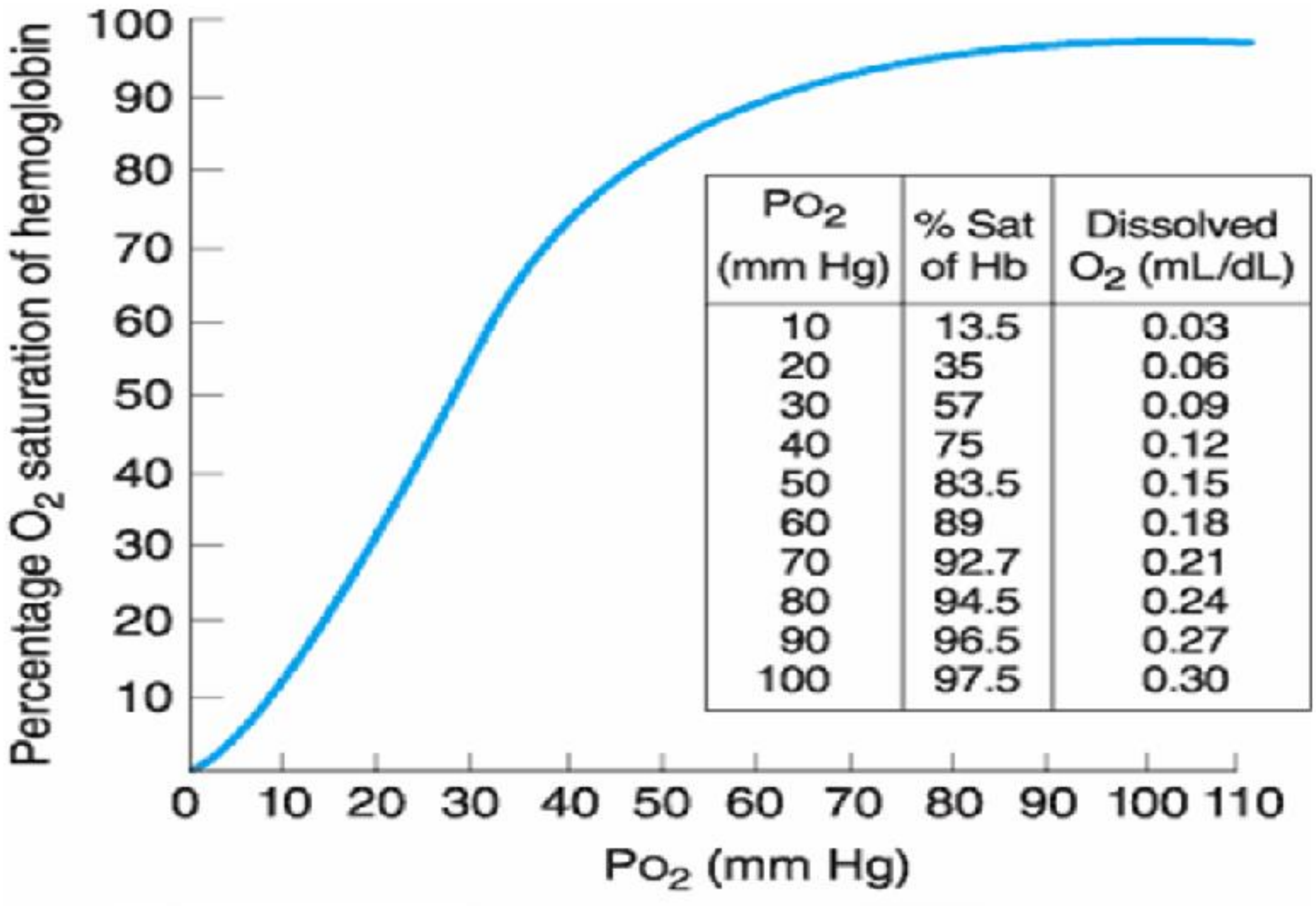
Percent O_2 saturation of hemoglobin
100
80
60
40
20
0
0
20
40
60
80
100
20
15
10
5
ml O_2/100 ml blood
Volume of O_2 unloaded to tissues
Tissues
P_{O_2} (mm Hg)
Lungs

Oxygen dissociation (Delivery) Curve…

- The amount of O_2 carried by Hb increases rapidly as a result of progressively increasing affinity until a PO_2 of about 50 mmHg is reached as shown by the pattern of combination of HbO_2-PO_2 curve (Fig. below).
- Hb is said to be fully saturated when all four hemes of its molecule are bound to oxygen and partially saturated when only one to three of its hemes are bound to oxygen.

NB: There are about 250 million Hb molecules in each RBC and 15 g/dl of blood.

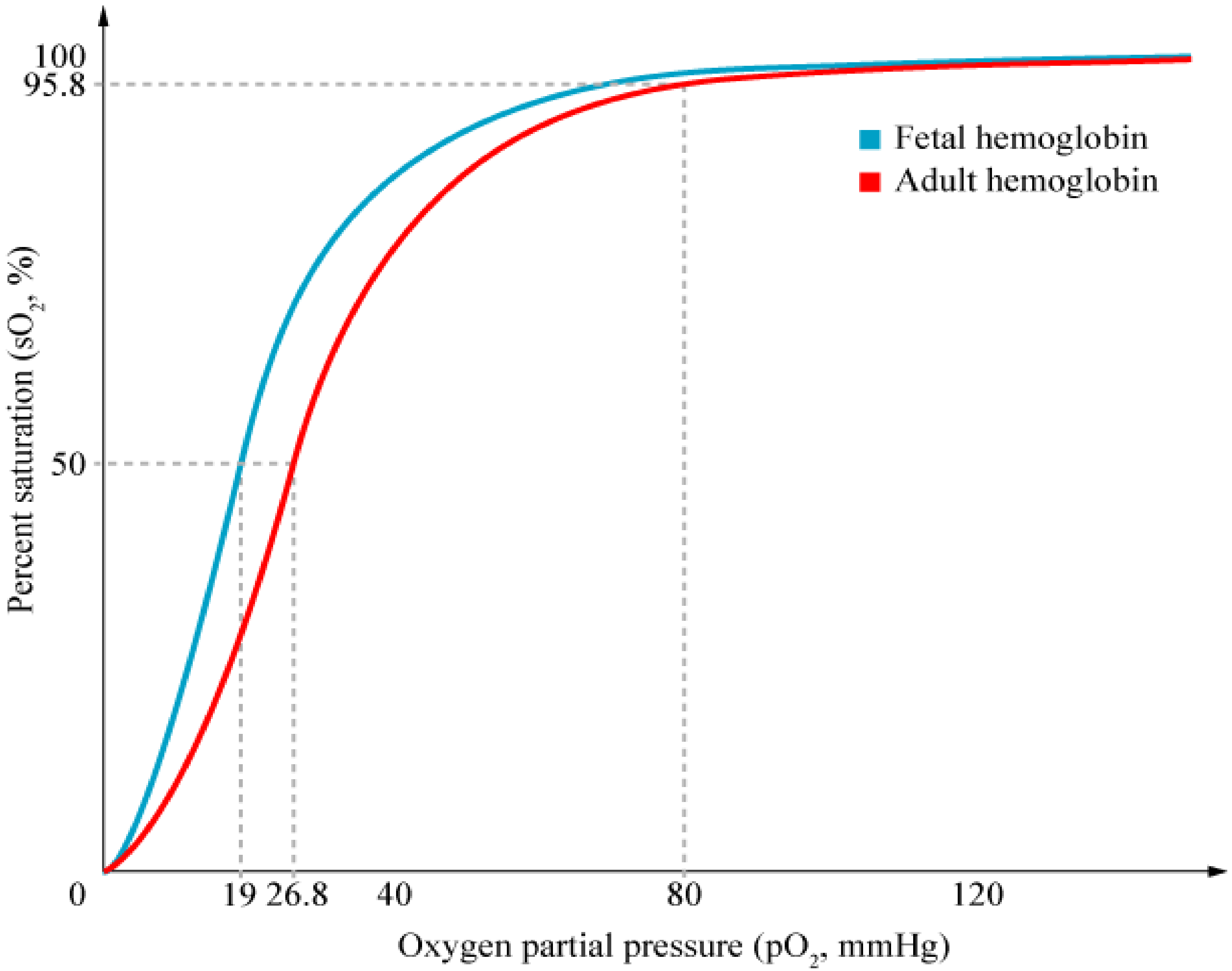
Oxygen dissociation (Delivery) Curve…



Po_2 (mm Hg)	% Sat of Hb	Dissolved O_2 (mL/dL)
10	13.5	0.03
20	35	0.06
30	57	0.09
40	75	0.12
50	83.5	0.15
60	89	0.18
70	92.7	0.21
80	94.5	0.24
90	96.5	0.27
100	97.5	0.30

Oxygen dissociation (Delivery) Curve…

- Foetal Hb(Hb F) has greater affinity for O_2 than adult Hb(HbA).
- Two of its protein globin chains are gamma chains instead of beta chains, 2,3-DPG cannot shift the dissociation curve to the right.
- Functionally, Hb F differs from HbA in that it is able to bind oxygen with greater affinity than the adult form, giving the developing fetus better access to oxygen from the mother's blood stream.
- HbF is 20-50% more saturated with O_2 than HbA at low PO_2 levels


100
95.8
50
0
19
26.8
40
80
120
Percent saturation (sO_2, %)
Oxygen partial pressure (pO_2, mmHg)
Fetal hemoglobin
Adult hemoglobin

Factors affecting O_2 dissociation

Factors	Right shift of curve	Left shift of curve
PH +/-	-	+
Temperature +/-	+	-
PCO2 +/-	+	-
2, 3-DPG +/-	+	-

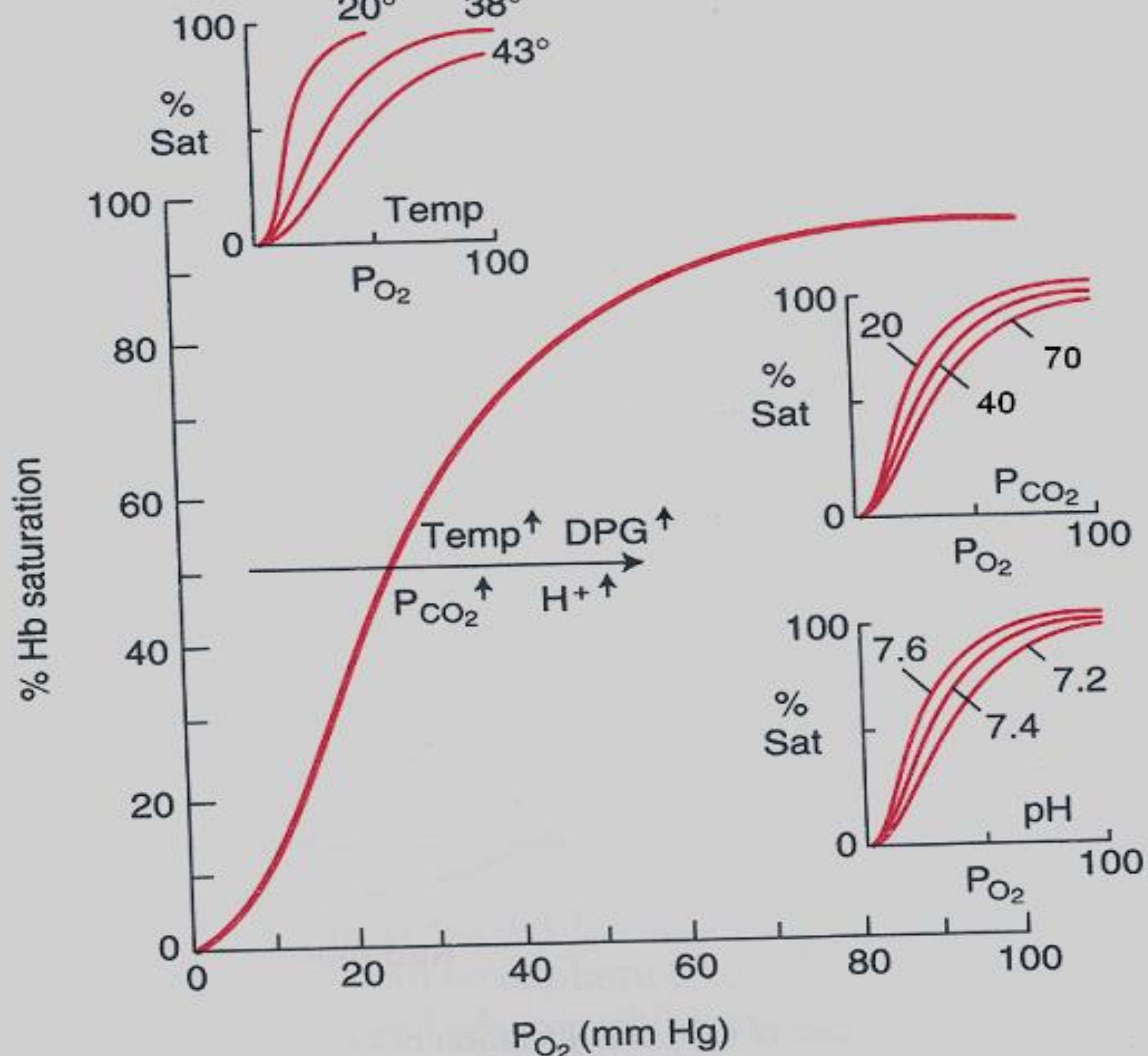
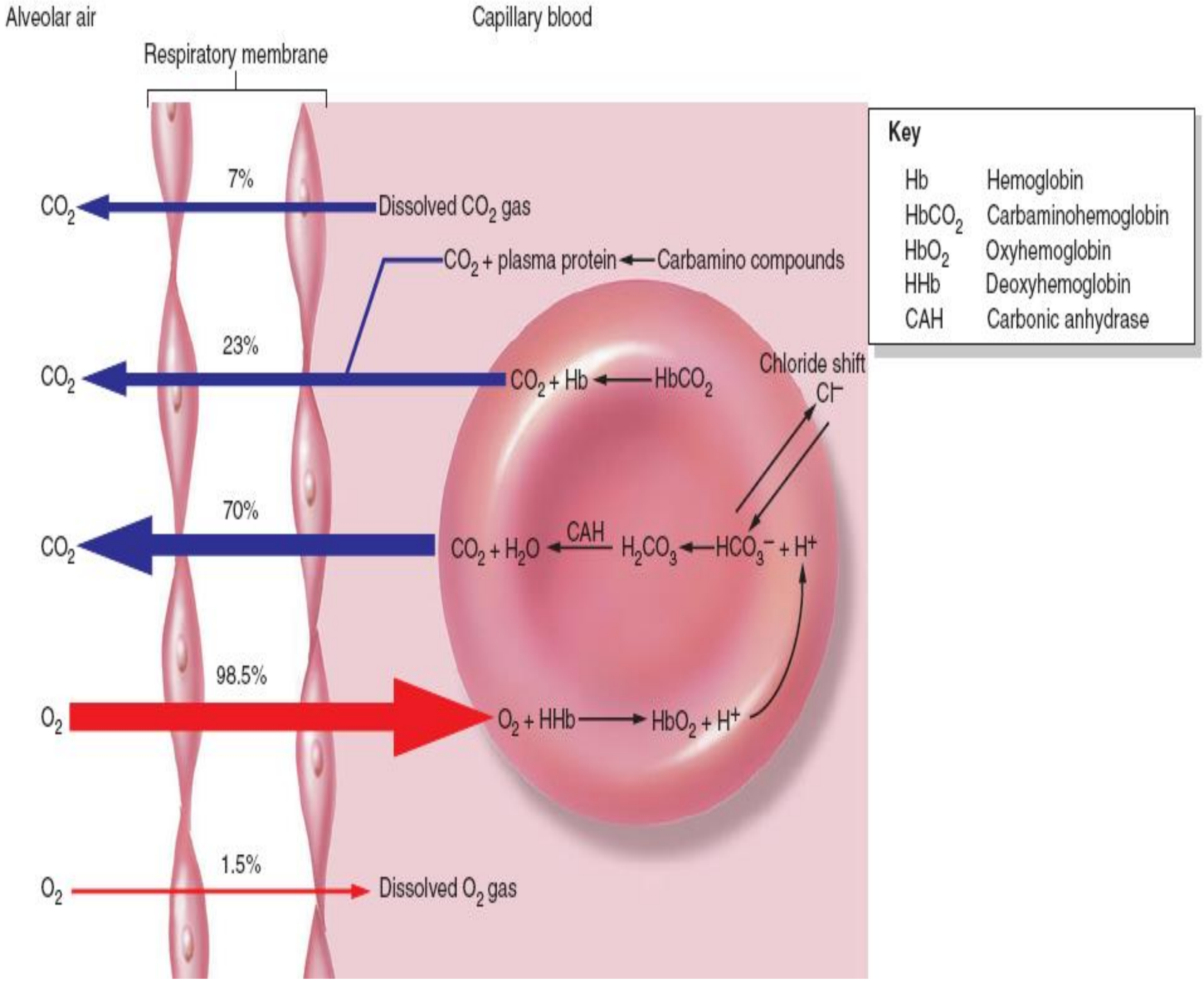


Fig. . Rightward shift of the O_2 dissociation curve by increase of H^+, P_{CO_2}, temperature, and 2,3-diphosphoglycerate (DPG).


Alveolar air
Capillary blood
Respiratory membrane
7%
CO2
Dissolved CO2 gas
CO2 + plasma protein ← Carbamino compounds
23%
CO2
CO2 + Hb ← HbCO2
Chloride shift
Cl−
70%
CO2
CO2 + H2O ← CAH H2CO3 ← HCO3− + H+
98.5%
O2
O2 + HHb → HbO2 + H+
1.5%
O2
Dissolved O2 gas
Key
Hb Hemoglobin
HbCO2 Carbaminohemoglobin
HbO2 Oxyhemoglobin
HHb Deoxyhemoglobin
CAH Carbonic anhydrase

NB:

- CO_2 does not compete with O_2 because CO_2 and O_2 bind to different sites on the hemoglobin molecule.
- Hb can therefore transport both O_2 and CO_2 simultaneously.

- Where as, CO interferes with the O_2 transport by combining with Hb to form carboxyhemoglobin (COHb).
- CO has about 240 times the affinity of O_2 for Hb.

Some clinical correlates

1. Hypoxia: induced when
   a. PaO_2 is decreased
   b. Cardiac output is not optimal
   c. Tissue uptake and utilization of O_2 is impaired

Types of hypoxia:

a. Hypoxic hypoxia: low PO_2
b. Hypoemic or anaemic hypoxia: low Hb
c. Stagnant (ischaemic) hypoxia: stagnant blood flow
d. Histotoxic hypoxia: failure of cell to utilize O_2

- **Cyanosis**:
  - ✍ A bluish discoloration of the skin, lips, nails, etc. due to excessive arterial deoxy-haemoglobin (>50g/L).
  - ✍ A sign of hypoxia with normal or moderately reduced Hb

2. Use of 100% oxygen

- Indicated for a limited period of time in:

✍ CO poisoning

✍ RDS

✍ Mediastinal emphysema

✍ Myocardial infarction

✍ Reduced CBF and dizziness

✍ Convulsions and coma, etc.

3. Hyperoxia and O_2 toxicity

- Use of 100% O2 for a prolonged period of time →

✍ Irritation of respiratory passages

✍ Coughing

✍ Airway hemorrhage

✍ Nasal congestion

✍ sub-sternal distress

✍ O_2 toxicity occurs when inspired O_2 is >165 mmHg

✍ O_2 toxicity depends on the level (300mmHg) and duration of hyperoxia.

Transport of CO_2

- The total **CO_2** content of arterial blood is about 48 mL/dL of blood.
- Mixed venous blood contains about 52 mL/dL of blood.

- Carbon dioxide is transported mainly in three forms:
  - as bicarbonate
  - as carbamino compounds and
  - as dissolved gas.

Transport of CO_2 ….

1. About 90% of the CO_2 is hydrated (reacts with water) to form H_2CO3, which then dissociates into HCO_3^- and H^+ inside RBC.

- The reaction of CO_2 and H_2O occurs slowly in the blood plasma but much faster in the RBCs (c*arbonic anhydrase).*

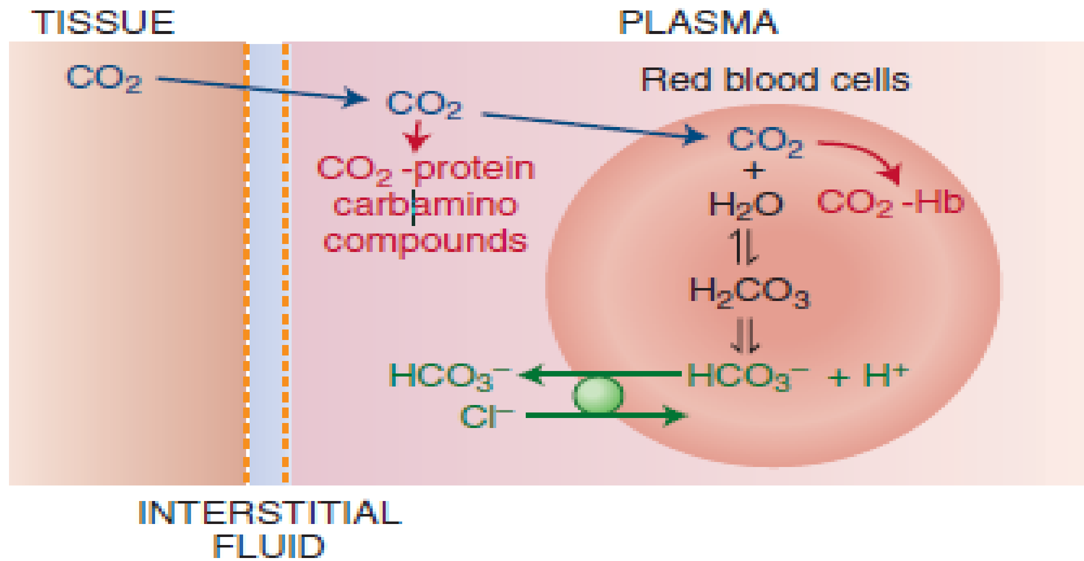
$$CO_2 + H_2O \overset{CA}{\leftrightarrows} H_2CO_3 \leftrightarrows HCO_3^- + H^+$$

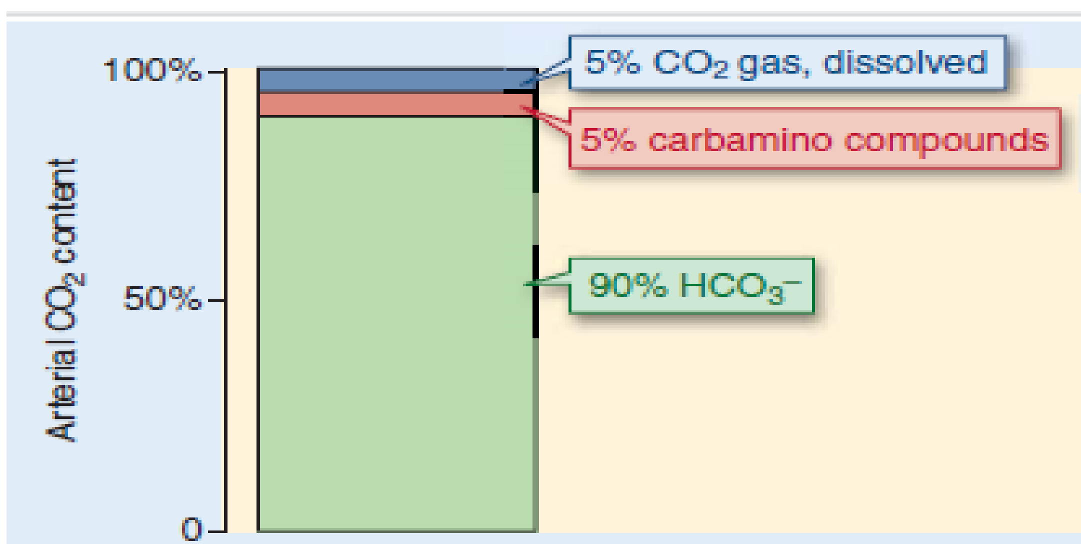
- HCO_3^- is delivered into plasma via the Cl^-/HCO_3^- exchange (known as the "chloride shift").

2. About 5% binds to the amino groups of plasma proteins and Hb within RBC to form carbamino compounds.

Transport of CO_2 ….

3. The remaining 5% of the CO2 is carried in the blood as dissolved gas.



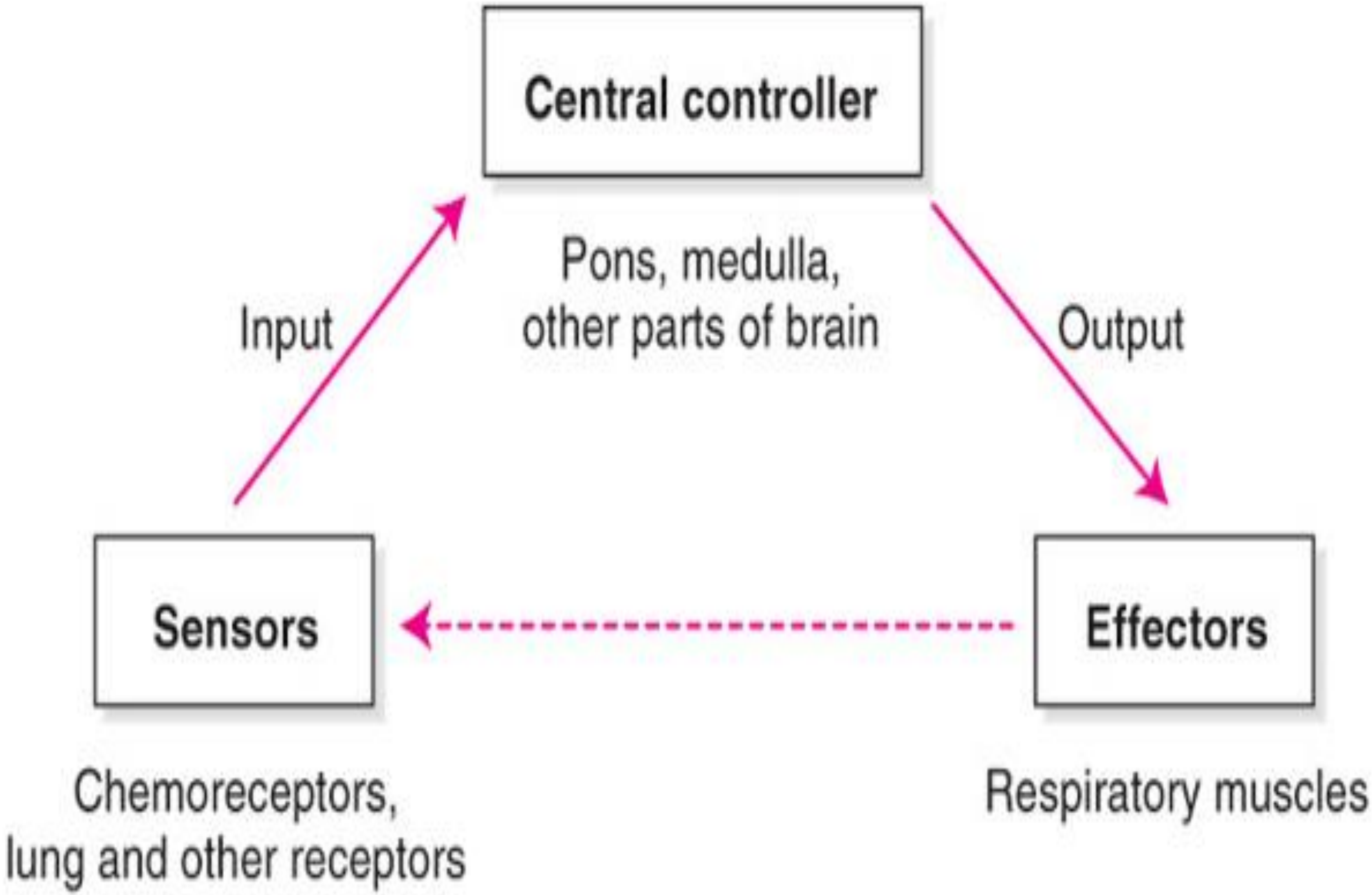


Some clinical correlates

1. Hypocapnia : PCO_2=15mmHg → apnoea

   PO_2=120-140mmHg

2. Hypercapnia: PCO_2>46mmHg→respiratory acidosis, confusion, decreased sensory activity, comma and death
3. Acid-base disturbance :: acidemia, alkalemia
4. Effects of CO_2 on the body:
   - Narcotic effect (Unconsciousness)
   - ↓Excitability of neurones
   - ↓intracellular pH
   - ↑BF in brain


Central controller
Pons, medulla,
other parts of brain
Input
Output
Sensors
Effectors
Chemoreceptors,
lung and other receptors
Respiratory muscles

Role of respiratory system in acid base regulation

- Lungs help to regulate pH through carbonic acid bicarbonate buffer system
  - ✓Changing respiratory rates changes P_{CO2}
- Respiratory compensation is a change in the respiratory rate to stabilize the pH of the ECF.
- **Respiratory compensation** is activated within minutes.

1. **Chemoreceptors** in carotid and aortic sinuses sense changes in pH of blood; receptors on **ventrolateral** surfaces of the medulla oblongata sense changes in pH of the CSF.

2. Receptors are stimulated by a fall in pH (rise in PCO_2) and inhibited by a rise in pH (fall in PCO_2).

3. Stimulation increases respiration rate ⇒ more CO_2 expired; PCO_2 returns to normal➔ ↑pH.

4. When PCO_2 falls, respiration rate decreases and PCO_2 rises ➔ ↓pH.

Respiratory acidosis (↓pH, ↑PCO_2)

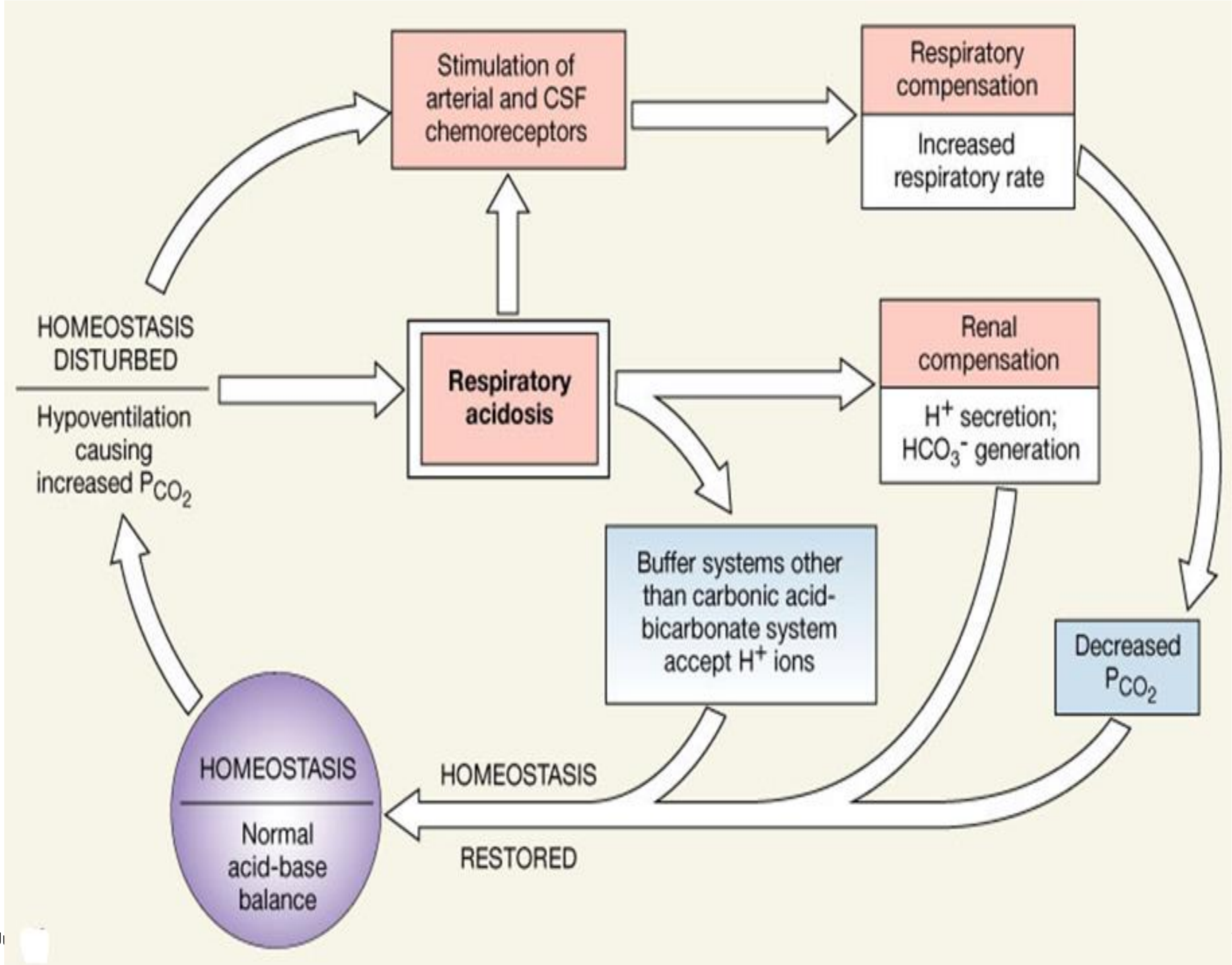
- Respiratory acidosis occurs when the respiratory system is unable to eliminate CO_2 produced from cellular metabolism
- An increase in CO_2 increases H+ ion concentration and the body's pH starts falling below 7.40
- The increase in PCO_2 stimulates chemoreceptors to increase respiratory rate.
- When ventilation is increased above the normal rate, excessive amounts of CO_2 are excreted in expired air.

- In this situation CO_2 is washed out of the body leading to a hypocapnia, the pH rises.
- A rise in pH is again sensed by central chemoreceptors in the medulla and CSF???.
- Both CO_2 and H+ concentration reduction resulting in a decrease in ventilation➔↑Pco2➔ ↓pH.

Causes of respiratory acidosis

- Caused by **hypercapnia** due to **hypoventilation**
- Any condition that impairs gas exchange or lung ventilation (chronic bronchitis, cystic fibrosis, emphysema, pulmonary oedema)
- Rapid shallow breathing, hypoventilation
- Narcotic or barbiturate overdose or injury to brain stem
- Airway obstruction
- Chest or head injury
- **Effects:** muscle weakness, fatigue, drowsiness and coma

Compensation:



Respiratory alkalosis (↑pH, ↓PCO2)

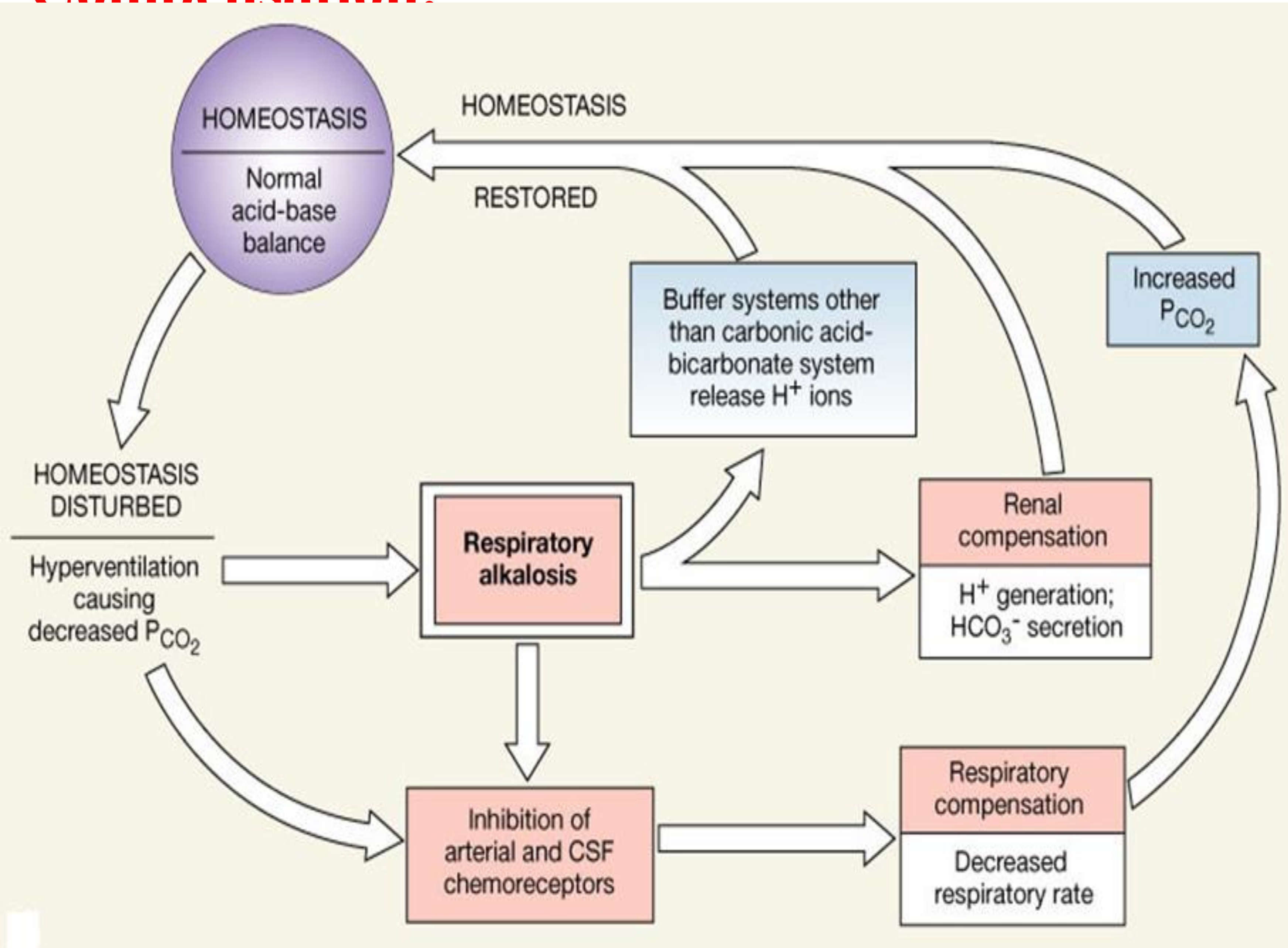
- Cause: <u>**Hyperventilation,**</u> Leads to eliminating excessive amounts of **CO_2.**
- This reduction of PCO_2 below the range of 4.5-5.6 kPa (30—35 mmHg) causes a reduction in H+ generation.
- The decreasing H+ concentration raises the blood pH above the normal range of **7.45**
- Any condition that causes hyperventilation can cause a **respiratory alkalosis**.

Causes:

- Direct cause is always hyperventilation (e.g. too much mechanical ventilation, pulmonary lesions)
- Brain tumor or injury
- Acute anxiety
- Asthma

Effects: Muscle pain, twitching , loss of appetite, headache, irritability, nausea and vomiting

Compensation:



The end!

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