HUMAN PHYSIOLOGY (normal)

LECTURE 14. The Physiology of Respiration

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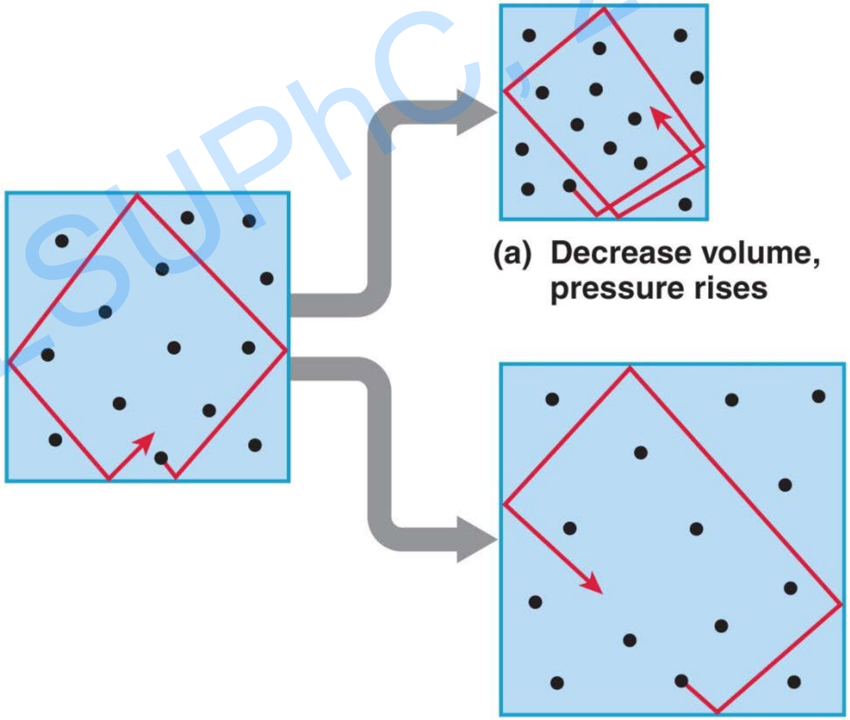
Types and Phases of the Respiration

- Respiration is the process by which **oxygen is taken in** and **carbon dioxide is given out** of the organism
- **External Respiration** - all processes involved in exchanging O_2 and CO_2 with the environment
- **Internal Respiration** - the utilization of O_2 and production of CO_2 by cells and exchange of gases between blood and tissues
- **Phases of the Respiration**:
  - **pulmonary ventilation** - inflow and outflow of air between the atmosphere and the lung alveoli
  - **diffusion of gases** between the alveoli and the blood
  - **transport of oxygen and carbon dioxide** in the blood
  - **diffusion of gases** in the tissues
  - **utilization of O_2 and production of CO_2** by cells

Pulmonary Ventilation

- Is the **physical movement** of air in and out of respiratory tract
- Provides **alveolar ventilation**
- Air flows from area of **higher pressure to area of lower pressure**
- Volume of thoracic cavity changes create changes in pressure with accordance of **Boyle's Law**
- Defines the **relationship between gas pressure and volume**:
  - **P = 1/V**
- **Respiratory Cycle** consists of
  - **Inspiration** (inhalation)
  - **Expiration** (exhalation)



(a) Decrease volume, pressure rises

(b) Increase volume, pressure falls

Pressure Changes in Respiratory Cycle

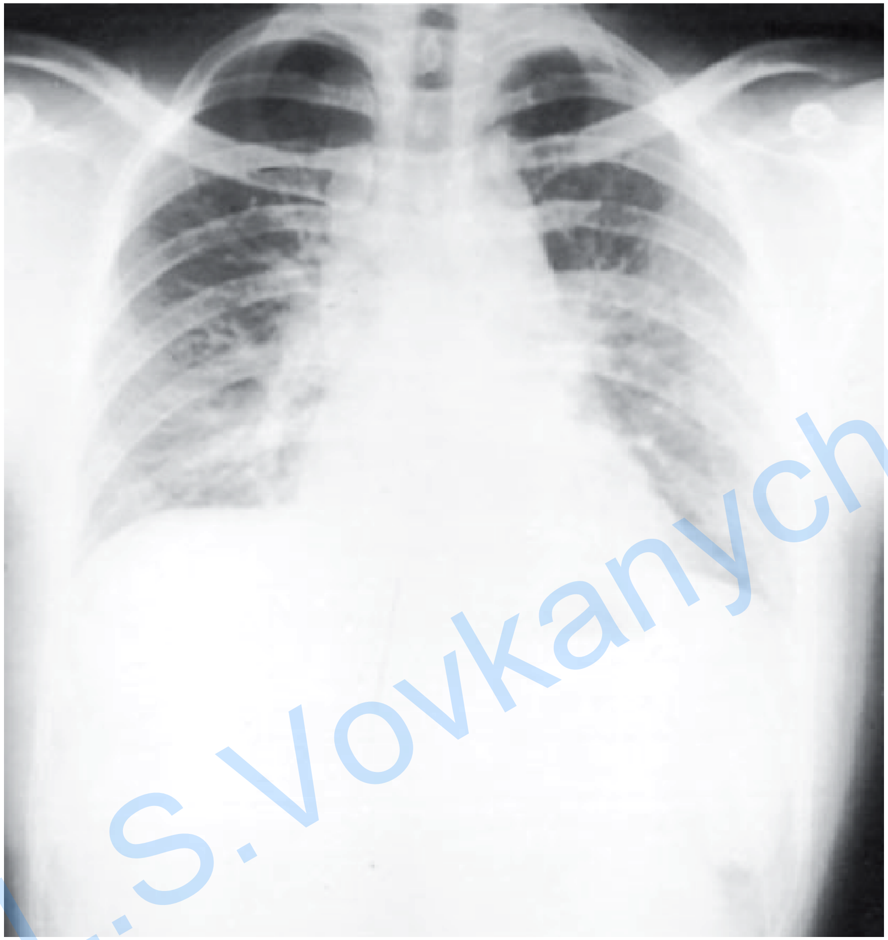
The **Intrapulmonary Pressure** (Intra-alveolar pressure)

- In **relaxed breathing**, the difference between atmospheric and intrapulmonary pressure is small:
- About **-1 mm Hg** on inhalation or **+1 mm Hg** on exhalation
- In case of maximal activity can increase:
- From -30 mm Hg to +50 mm Hg (+100 mm Hg in case of forced expiration with closed glottis)

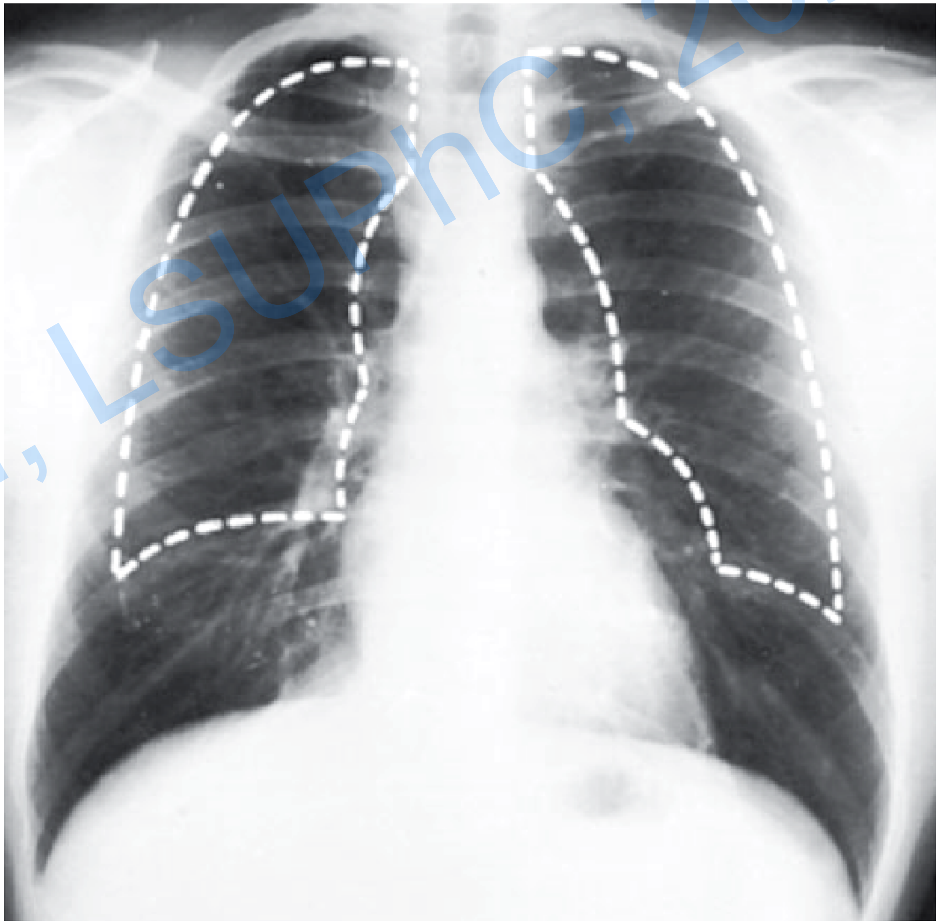
The **Intrapleural Pressure**

- Pressure **in space between parietal and visceral pleura**
- Averages **-4 mm Hg** (normal inspiration: –6 mm Hg; normal expiration: –2 mm Hg)
- Maximum of -18 mm Hg (forced inspiration: –30 mm Hg)
- Remains below atmospheric pressure throughout respiratory cycle

Respiratory Cycle. Volume of Thoracic Cavity

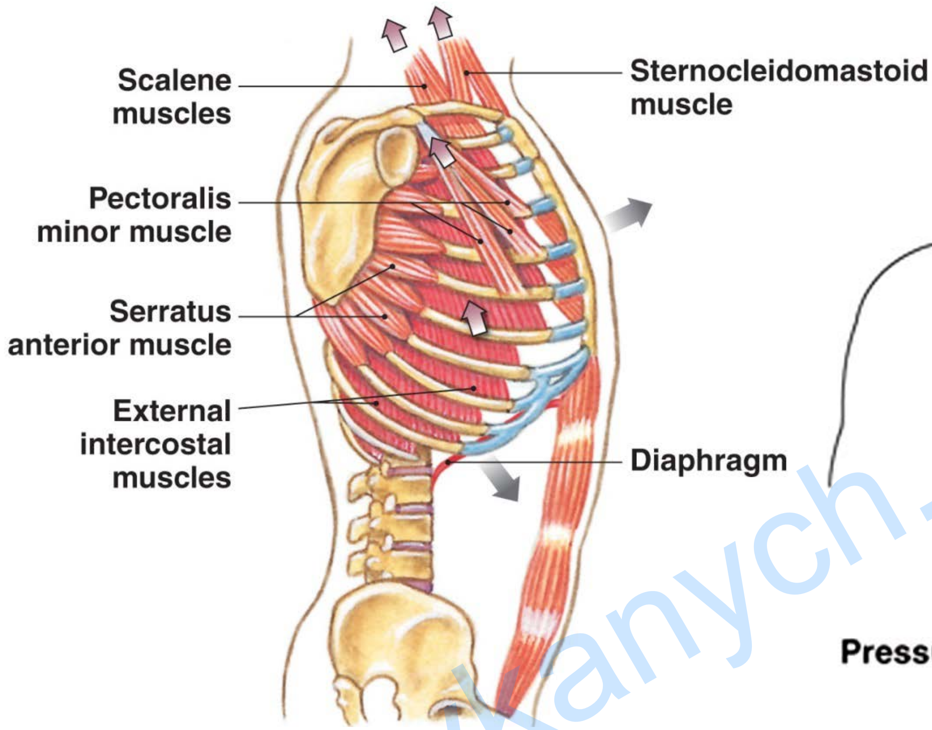


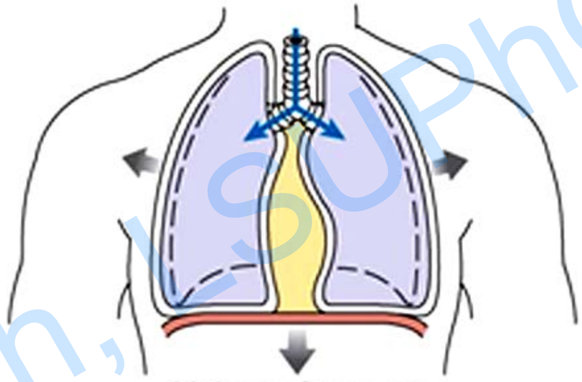
Expiration

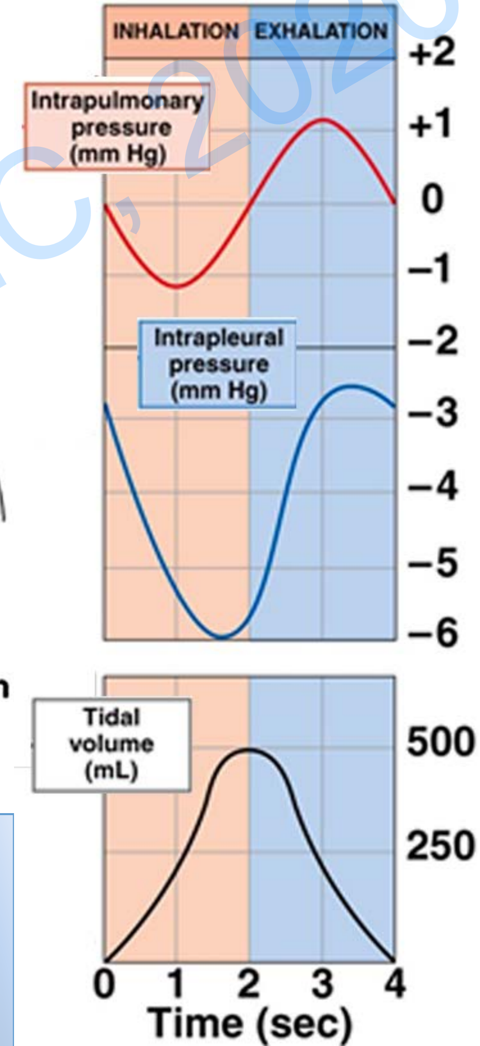


Inspiration
(volume at expiration is marked by dashed lines)

Respiratory Cycle. Inspiration



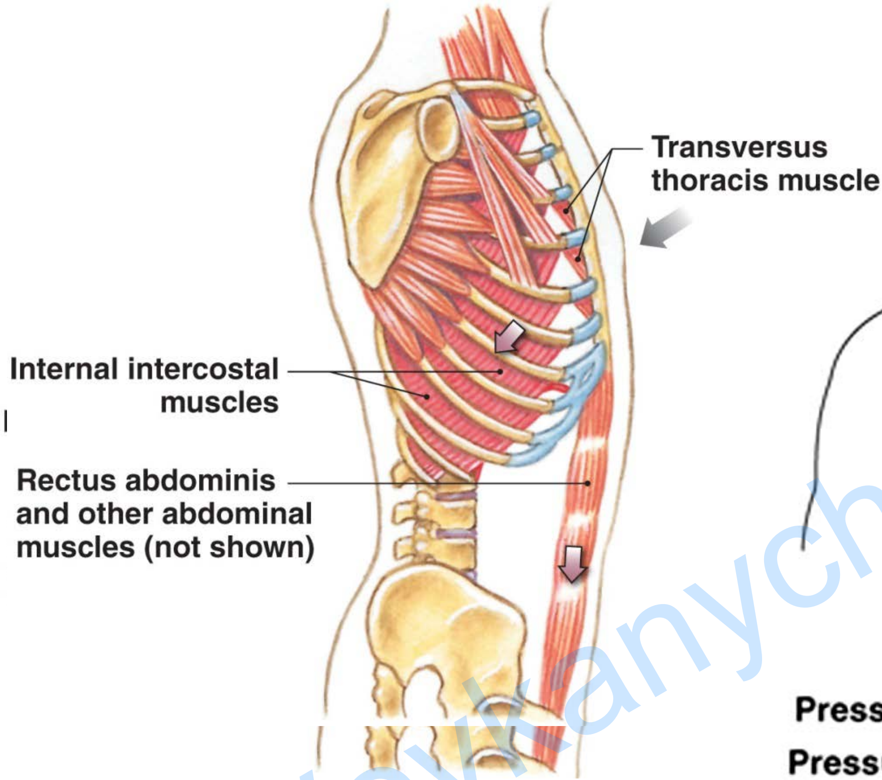


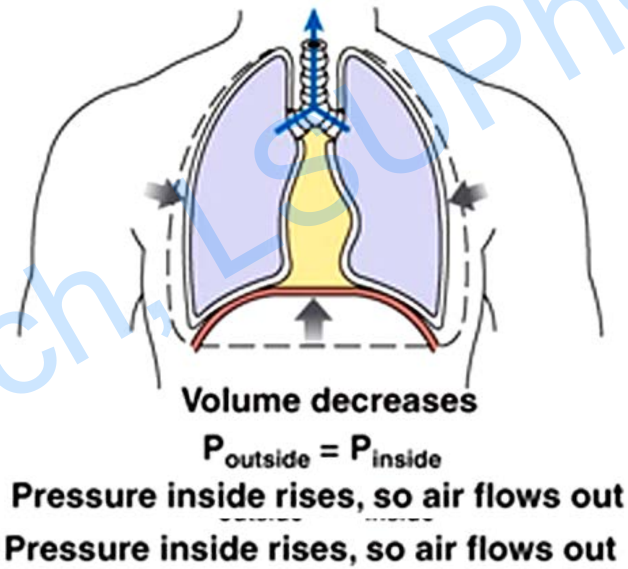


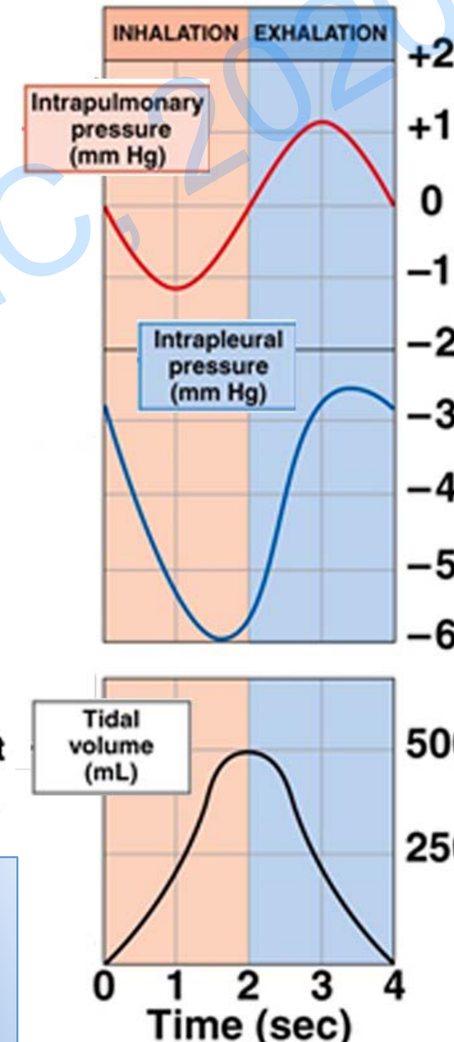
Most important **Inspiratory muscles** are

- The **diaphragm** (phrenic nerve - C3 to C5)
- **External intercostal muscles** (intercostal nerves - T1 to T11)

Respiratory Cycle. Expiration







Resting Exhalation – passive (**relaxation** of inspiration muscles)

Forced Exhalation – active, with main muscles:

- **Internal intercostal** and transversus thoracis muscles
- **Abdominal** muscles

Pulmonary Ventilation

Quiet Breathing (eupnea)

- Involves **active inhalation** and **passive exhalation**
  - Elastic rebound
  - When inhalation muscles relax
  - Elastic components of muscles and lungs recoil
  - Returning lungs and alveoli to original position

Forced Breathing (hyperpnea)

- Involves **active inhalation and exhalation**
- Assisted by accessory muscles

Age	Resting respiratory rate (per minute)
Newborn	30-60
Early childhood	20-30
Late childhood	15-25
Adult	12-16

Work of Breathing and Compliance

- **Compliance** is the ability of the lungs and thorax to expand or it is the expansibility of lungs and thorax
- Compliance **increases** due to **loss of elastic property** of lung tissues, which occurs both in physiological and pathological conditions:
  - Physiological condition: **Old age**
  - Pathological condition: **Emphysema**
- **Work of breathing** is the work done by respiratory muscles during breathing to overcome the resistance in thorax and respiratory tract
- Takes up to the **3% of total energy demands** even during exercise

Pulmonary Ventilation

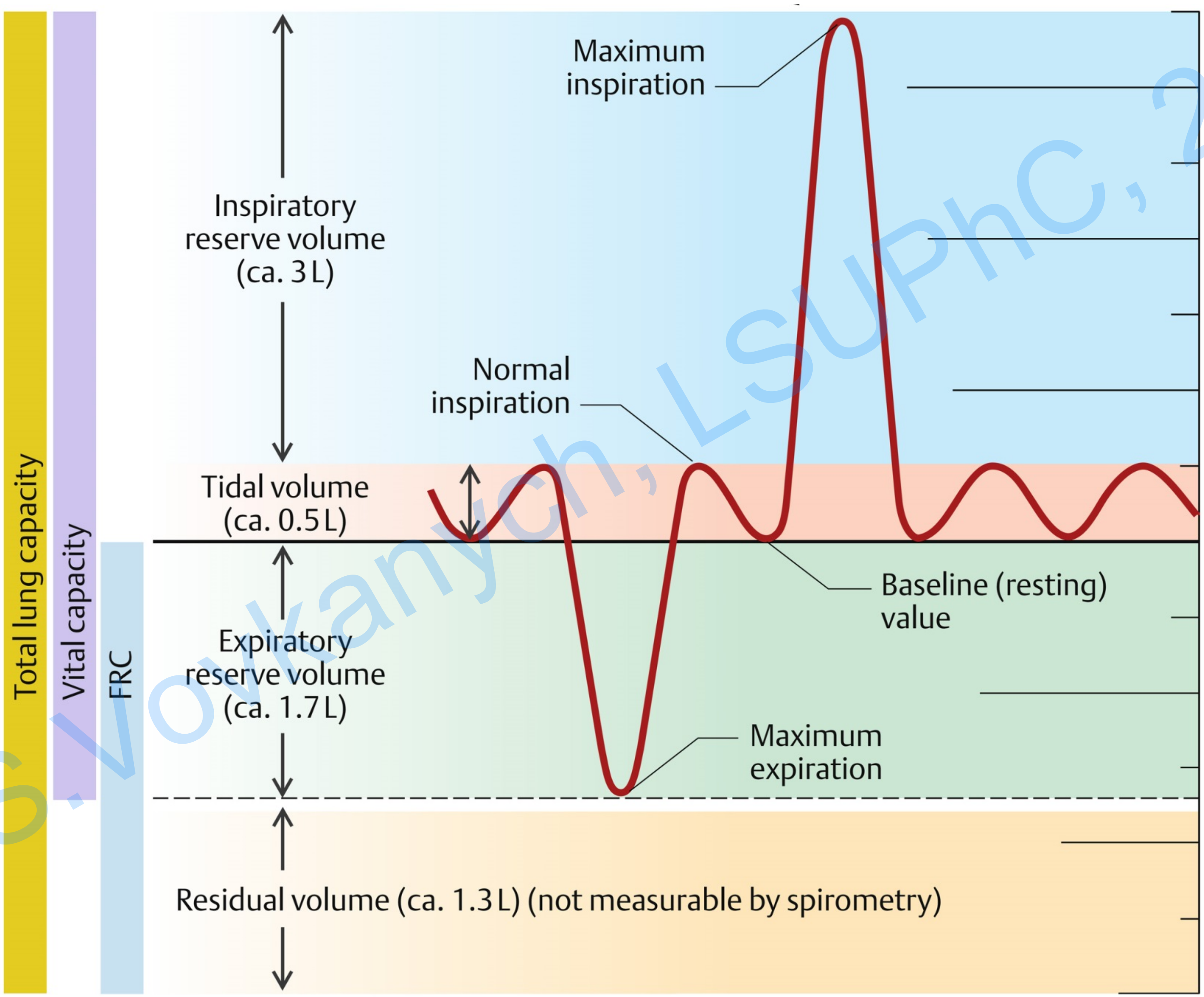
Respiratory system **adapts** to changing oxygen demands by varying

- **Respiratory Rate** - number of breaths per minute
- **Tidal Volume** - volume of air moved per breath (at rest – 0,5 L)

- **Pulmonary ventilation** is measured by the **Respiratory Minute Volume** - amount of air moved per minute
  RMV = respiratory rate x tidal volume (at rest – 5-6 L/min)
- But only a part of respiratory minute volume reaches alveolar exchange surfaces
- Volume of air remaining in conducting passages is **anatomic dead space**

- **Alveolar Ventilation** - amount of air reaching alveoli each minute
  AV = (tidal volume - anatomic dead space) x respiratory rate

Pulmonary Volumes and Capacities



Pulmonary Volumes

Resting **tidal volume** (V_T)

- volume of air breathed in and out of lungs in a normal respiratory cycle

Expiratory reserve volume (ERV)

- additional volume of air that can be expired out forcefully, after normal expiration

Inspiratory reserve volume (IRV)

- additional volume of air that can be inspired forcefully after the end of normal inspiration

Residual volume (RV)

- volume of air remaining in lungs even after forced expiration

Dead space

- part of the respiratory tract, where gaseous exchange does not take place.

Respiratory Capacities

Inspiratory capacity

- Tidal volume + inspiratory reserve volume

Functional residual capacity (FRC)

- Expiratory reserve volume + residual volume

Vital capacity

- Expiratory reserve volume + tidal volume + inspiratory reserve volume

Total lung capacity

- Vital capacity + residual volume

Volumes and Capacities

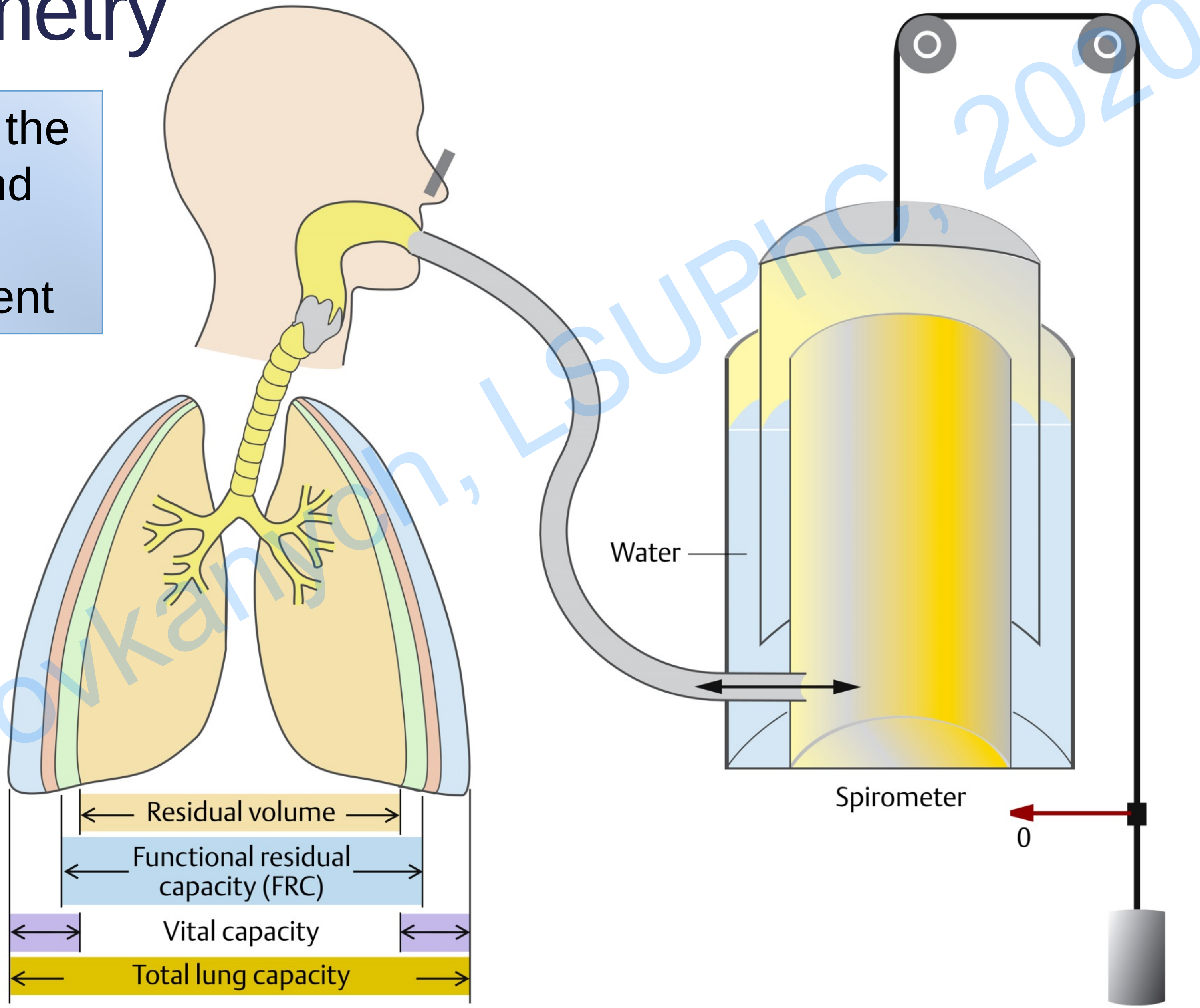
Normal values depends on:

- Age (increase up to adulthood, then – gradual decrease)
- Sex (larger in males)
- Height (directly proportional)

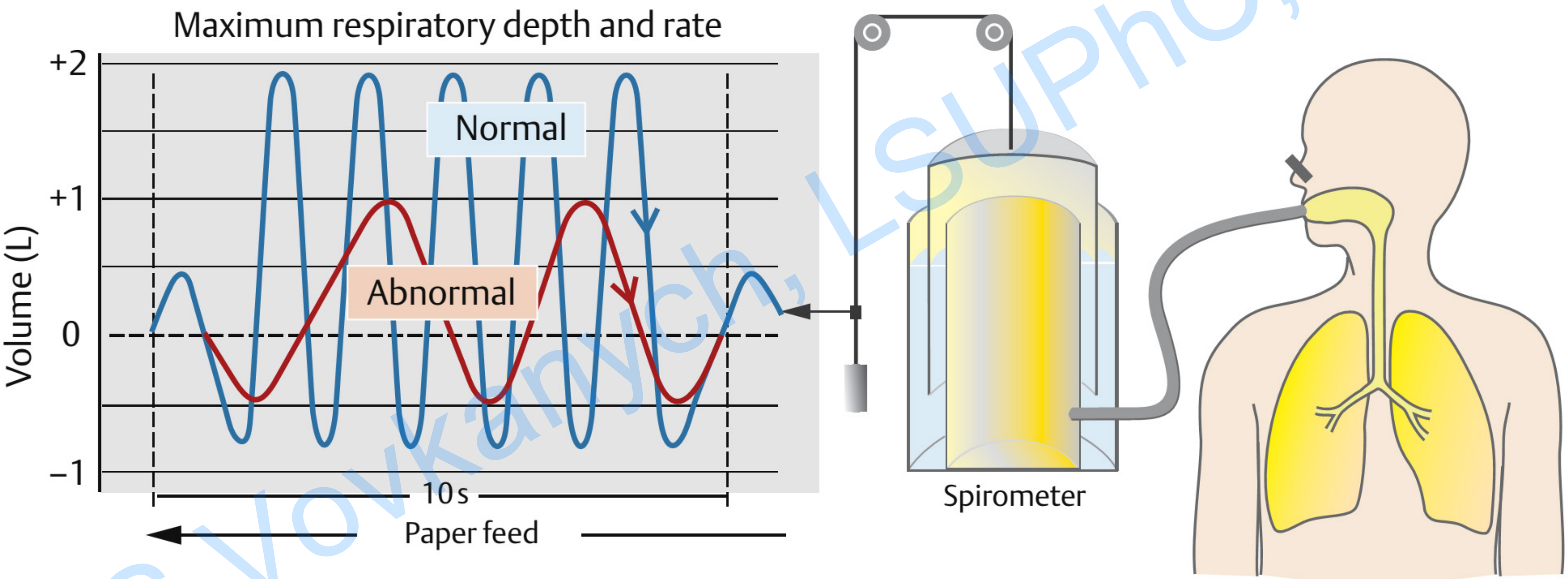
Value (for adults)	Males	Females
Tidal volume (V_T), mL	500	300
IRV, mL	2500	1900
ERV, mL	1500	1000
VC, mL	4500	3200
RV, mL	1200	1100
Total lung capacity	5700	4300

Spirometry

Method for the volumes and capacities measurement



Spirography



Method of the graphical registration and analysis of breathing

Forced Expiratory Volume

Forced expiratory volume (FEV) is the volume of air, which can be expired forcefully in a given unit of time

- **FEV_1** - volume of air expired forcefully in 1 second (83%)
- **FEV_2** - volume of air expired forcefully in 2 seconds (94%)
- **FEV_3** - volume of air expired forcefully in 3 seconds (97%)

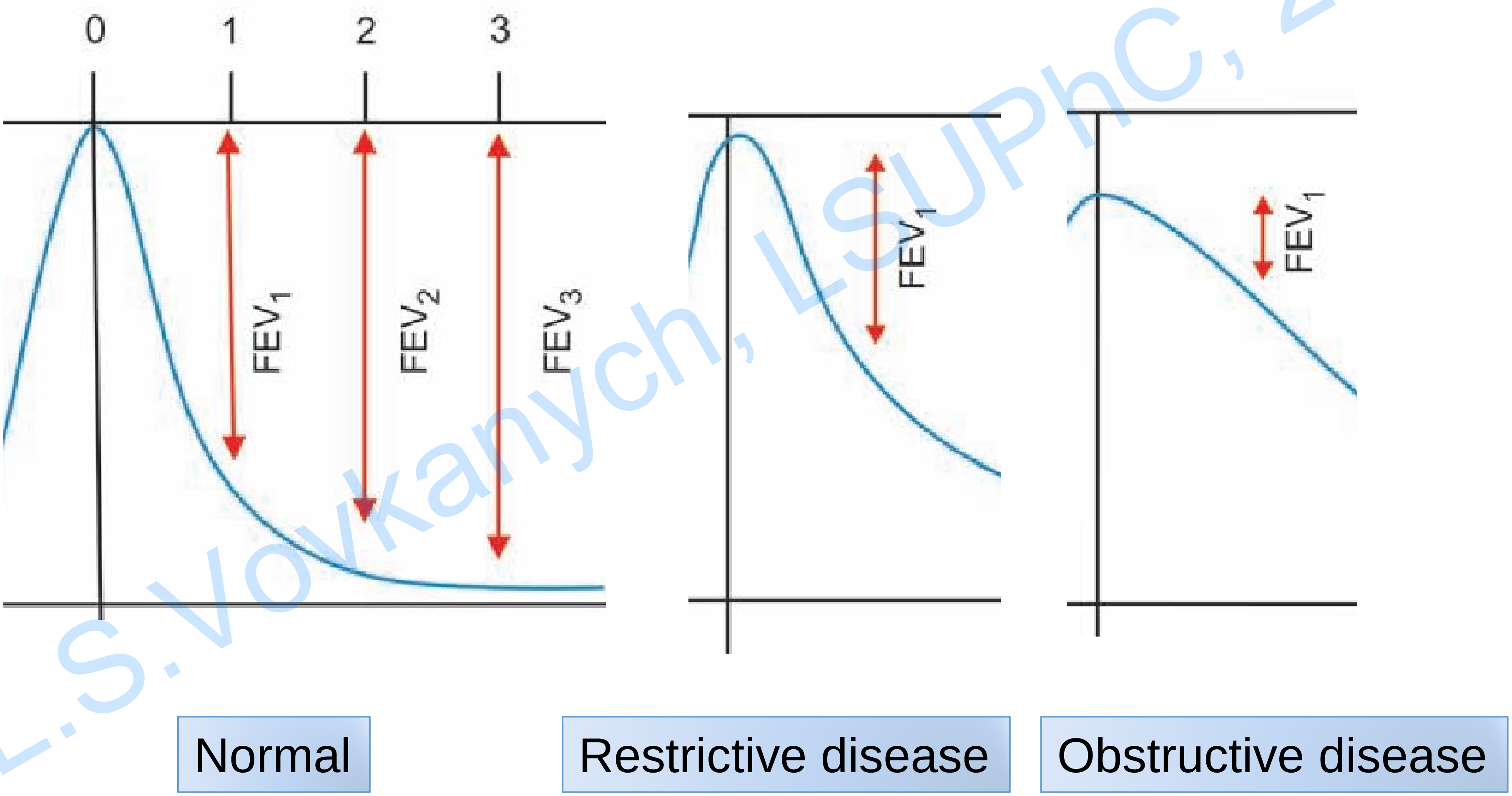
FEV **is decreased** significantly in some respiratory diseases

Peak expiratory flow rate (PEFR) is the maximum rate at which the air can be expired after a deep inspiration

PEFR rate is useful for **assessing the respiratory diseases** especially to differentiate the

- **obstructive** (difficulty in expiration) and
- **restrictive** (difficulty in inspiration) diseases

Forced Expiratory Vital Capacity



Gas Exchange

Diffusion is the passive transport along the concentration gradient and is described by **Fick law** of diffusion

- Amount of a substance crossing a given area is directly proportional to the
- **area** available for diffusion,
- **gradient** of the **partial pressure**
- **diffusion coefficient**

- **Partial pressure** is the pressure of particular gas in the gas mixture. It is proportional to its number of molecules (**Dalton's law**) or to the percent of gas and total pressure.
- The total pressure of the atmospheric air is 760 mm Hg, and the Composition of Air (percent and partial pressure)
  - Nitrogen (N_2) is about 78.6% (597 mm Hg)
  - Oxygen (O_2) is about 20.9% (159 mm Hg)
  - Water vapor (H_2O) is about 0.5% (3.7 mm Hg)
  - Carbon dioxide (CO_2) is about 0.04% (0.3 mm Hg)

Partial Pressures and Gas Concentration

Sample	N_2, mm Hg/%	O_2, mm Hg/%	CO_2, mm Hg/%	Water vapour, mm Hg/%
Inhailed air	597 (78,6%)	159 (20,9%)	0,3 (0,04%)	3,7 (0,5%)
Alveolar air	573 (75,4%)	100 (13,2%)	40 (5,2%)	47 (6,2%)
Exhailed air	569 (74,8%)	116 (15,3%)	28 (3,7%)	47 (6,2%)

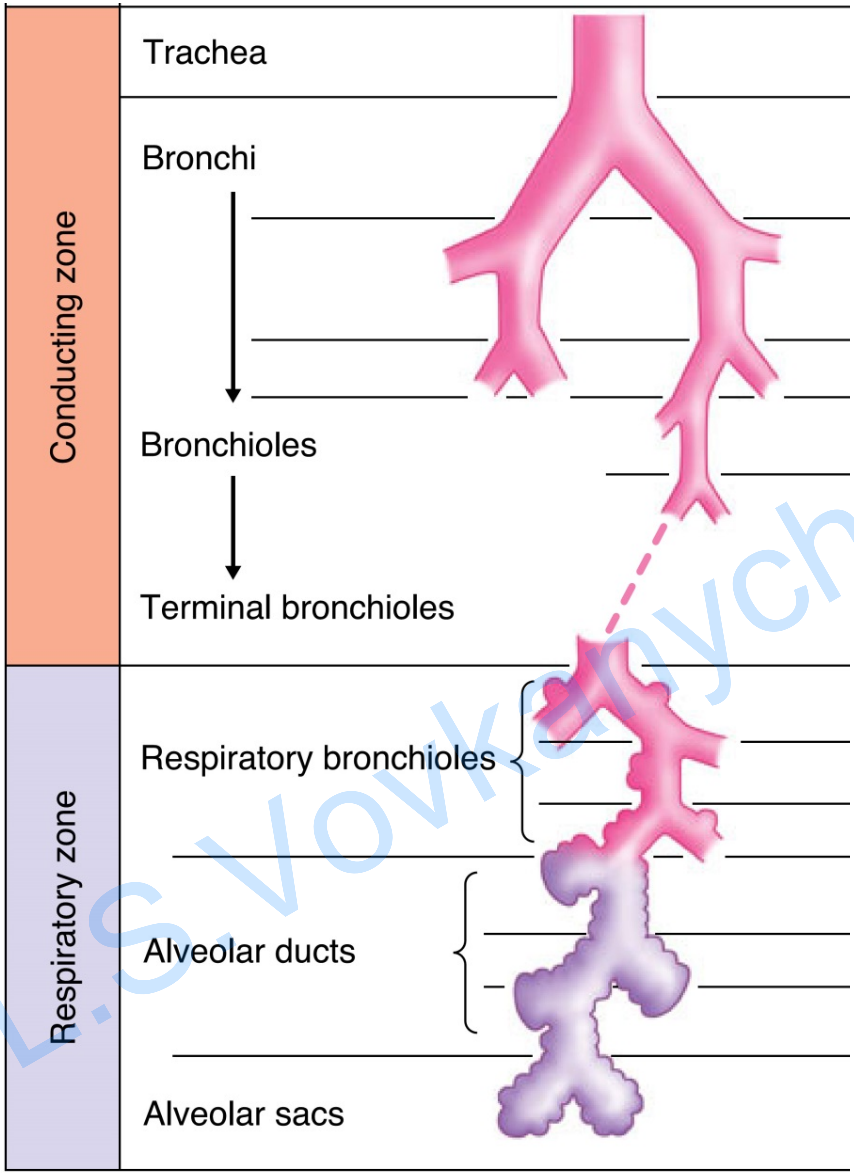
Diffusion and the Respiratory Membrane

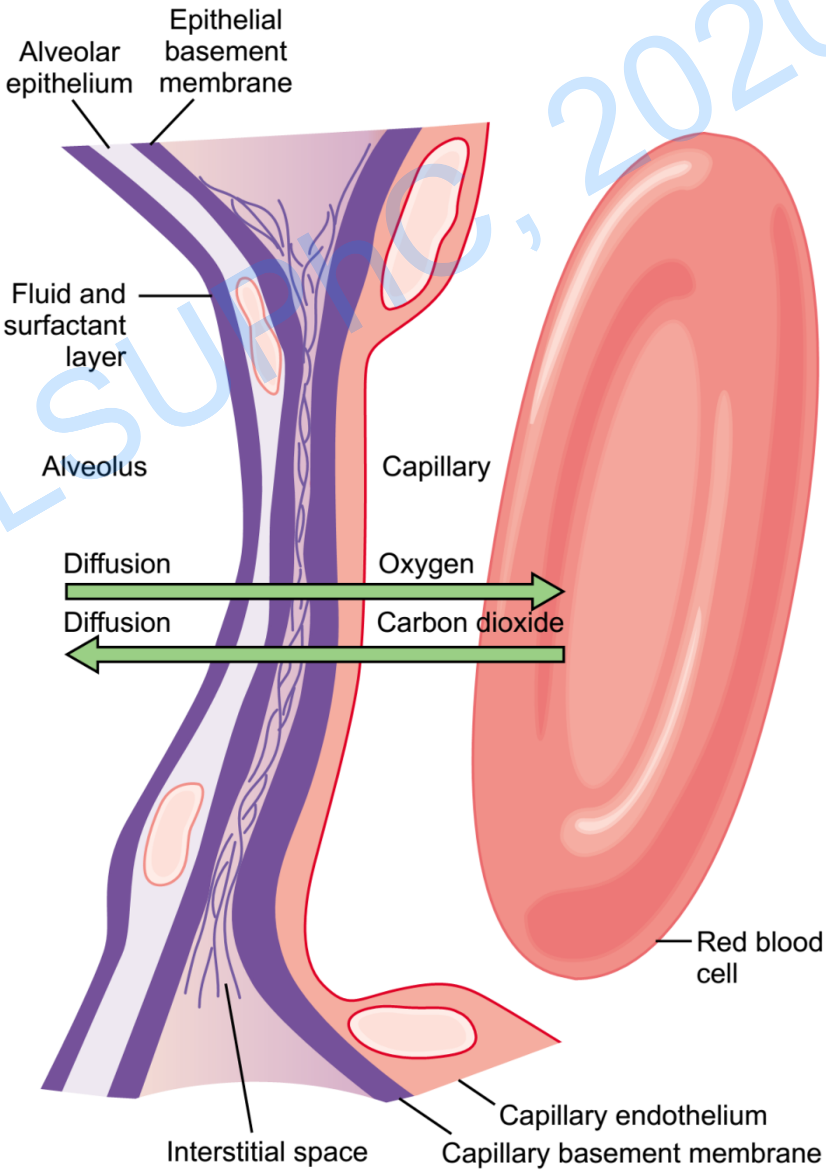
- **Direction and rate** of diffusion is determined by **gradient of partial pressures**
- **Rate of diffusion** is determined by
  - **solubility** of gases
  - **distances** of diffusion
  - **total surface area**

Gas Exchange

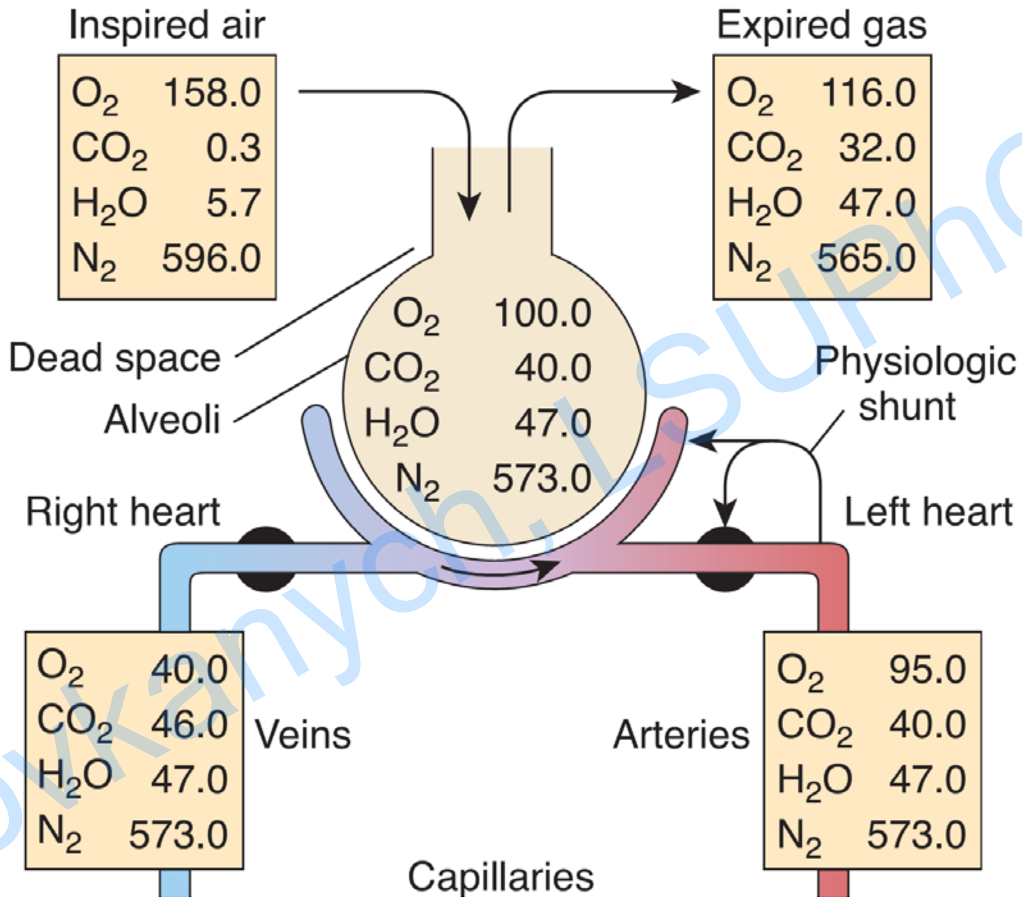
- Each gas in the mixture **dissolves in the liquid** to an extent determined by its **partial pressure** and its **solubility** in the fluid
- The actual amount of a gas in solution (at given partial pressure and temperature) depends on the solubility of that gas in that particular liquid
- **Solubility** in Body Fluids
  - CO_2 is very soluble
  - O_2 is less soluble
  - N_2 has very low solubility
- **Normal Partial Pressures** in pulmonary vein plasma
  - pCO_2 = 40 mm Hg
  - pO_2 = 100 mm Hg
  - pN_2 = 573 mm Hg

Gas Exchange





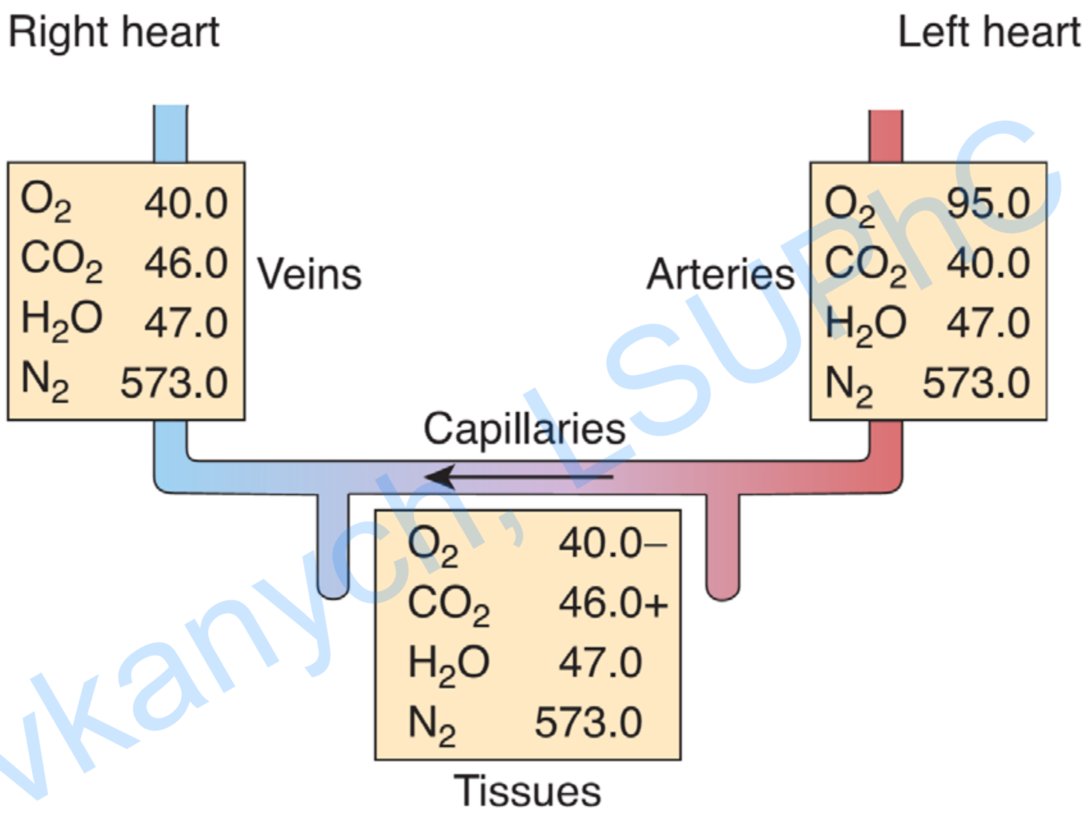
Gas Exchange in the Lungs



The gradient of partial pressure causes

- O_2 to enter blood
- CO_2 to leave blood

Gas Exchange in the Tissues



Concentration gradient in peripheral capillaries is opposite of lungs

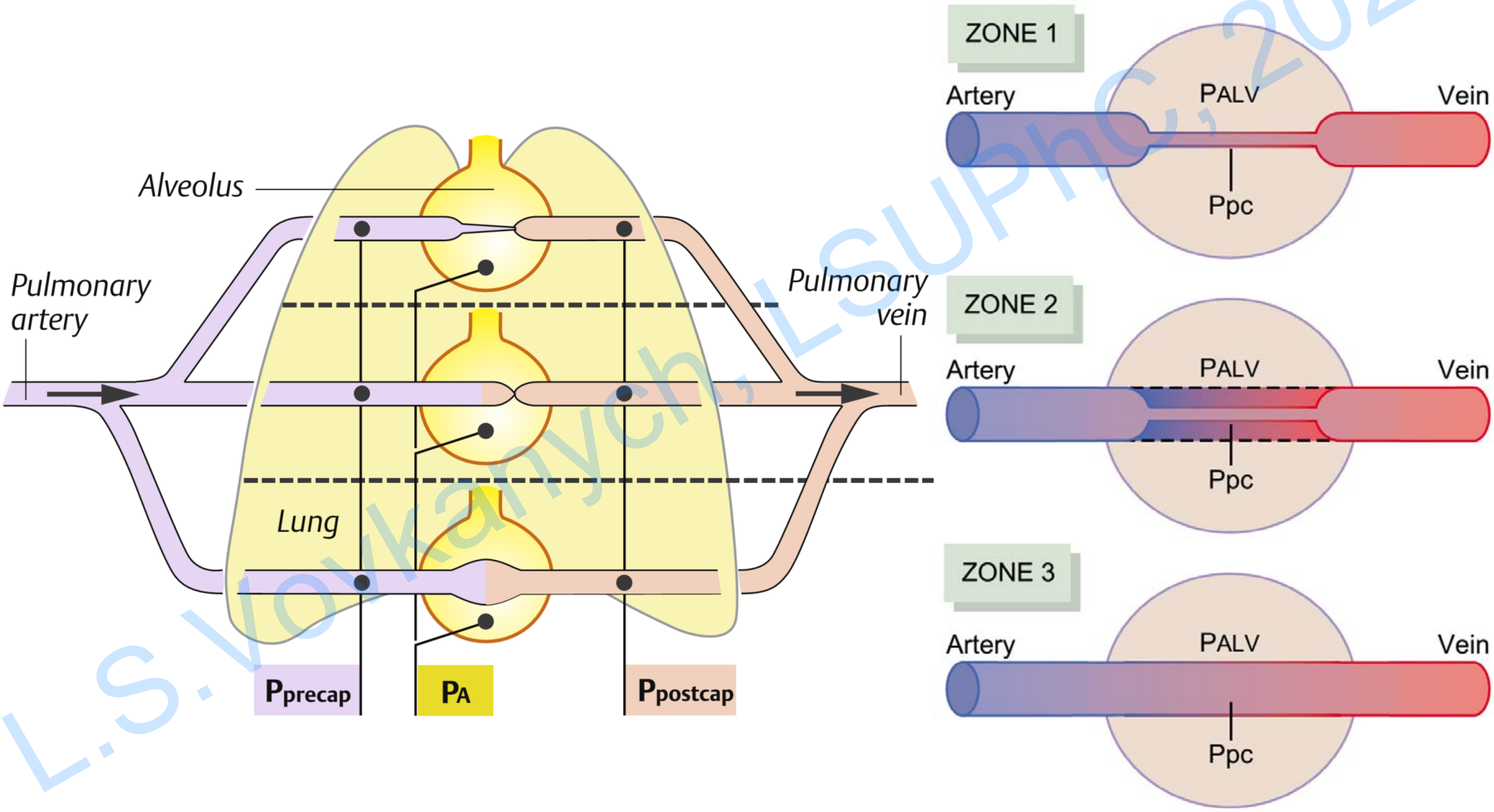
- CO_2 diffuses into blood
- O_2 diffuses out of blood

Pulmonary Circulation

- Lungs receive the whole amount of blood that is pumped out from right ventricle (the same in both right and left ventricle)
- The **blood pressure is less** in pulmonary blood vessels
  - Systolic Arterial pressure : 25 mm Hg
  - Diastolic Arterial pressure : 10 mm Hg
  - Pulmonary capillary pressure is about 7 mm Hg

- Pulmonary blood flow **is regulated** by the following factors:
  - **Cardiac output** (directly proportional)
  - **Vascular resistance** (low resistance, inversely proportional)
  - **Chemical factors** (excess of carbon dioxide or lack of oxygen causes vasoconstriction)
  - **Gravity** and **hydrostatic** pressure

Pulmonary Circulation



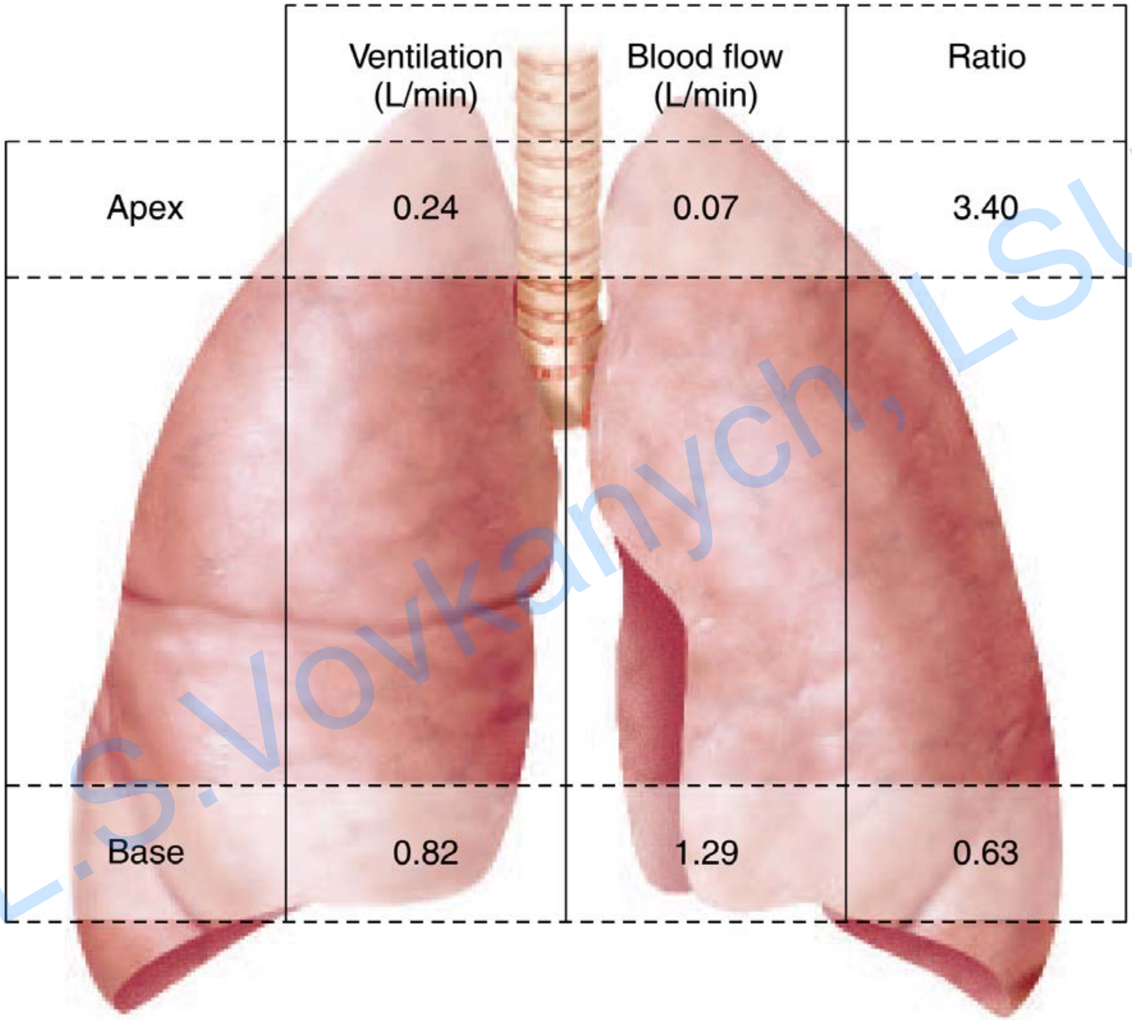
Pulmonary Circulation

Pulmonary vascular pressure and blood flow varies in different parts of the lungs:

- **area of zero blood flow** - in the **apical** portion of lungs, if pulmonary arterial pressure decreases or if alveolar pressure increases, the capillaries are collapsed
- **area of intermittent flow** - in the **midportion** of lungs, the ressure in alveoli is less than pulmonary systolic pressure and more than the pulmonary diastolic pressure, blood flow depends on the stage of cardiac cycle
- **area of continuous blood flow** - in the **lower** portion of lungs, the pulmonary arterial pressure is high and it is more than alveolar pressure both during systole and diastole

Ventilation-perfusion ratio

Ventilation-perfusion ratio is the ratio of alveolar ventilation and the amount of blood that perfuse the alveoli



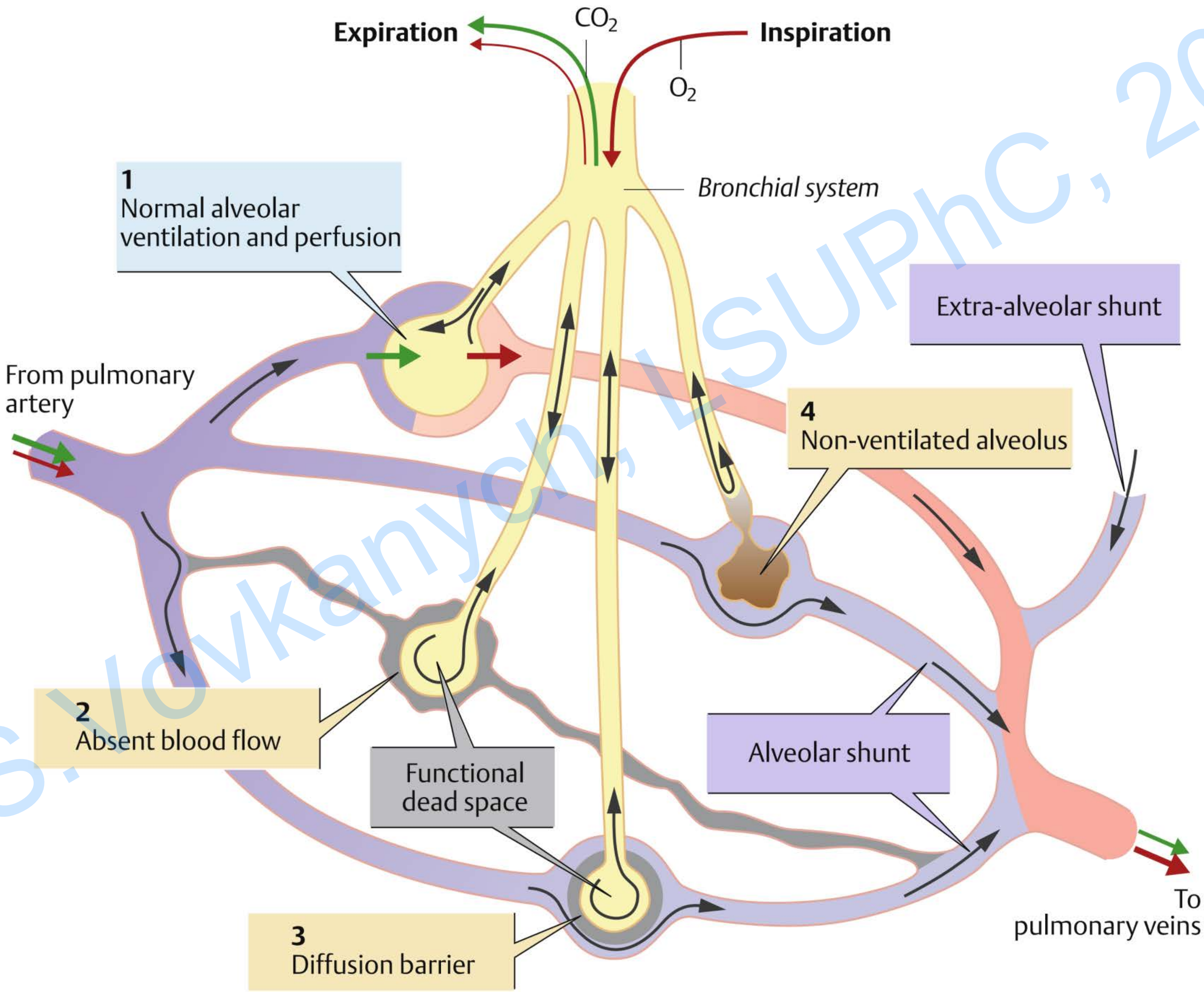
	Ventilation (L/min)	Blood flow (L/min)	Ratio
Apex	0.24	0.07	3.40
Base	0.82	1.29	0.63

Ventilation-perfusion ratio is **high** (decreased blood flow)

Ventilation-perfusion ratio is **normal** (near about 0,9)

Ventilation-perfusion ratio is **low** (increased blood flow)

Limitations of Alveolar Gas Exchange

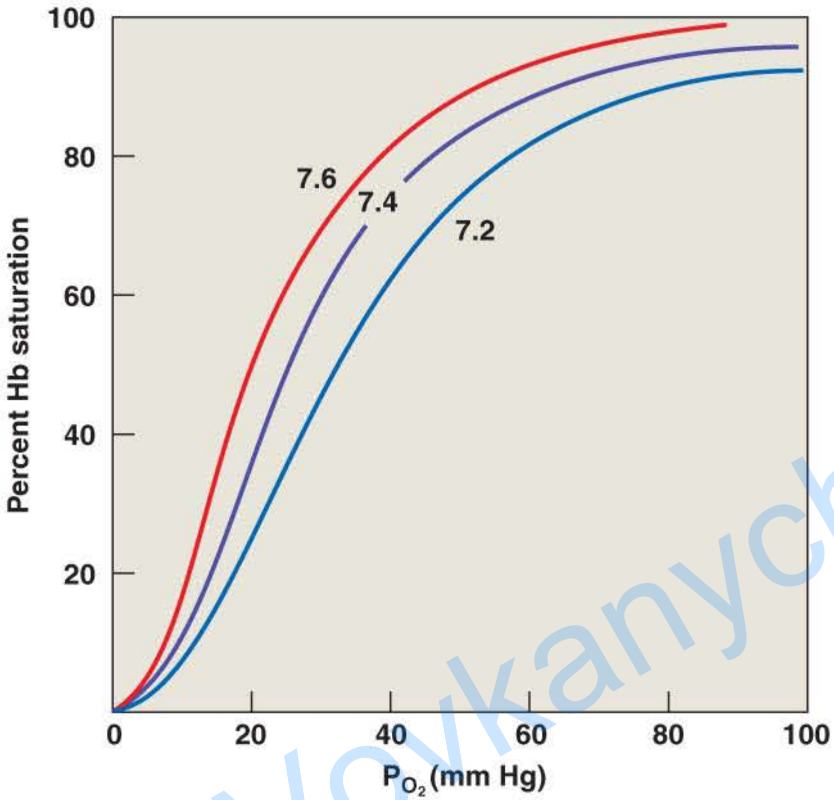


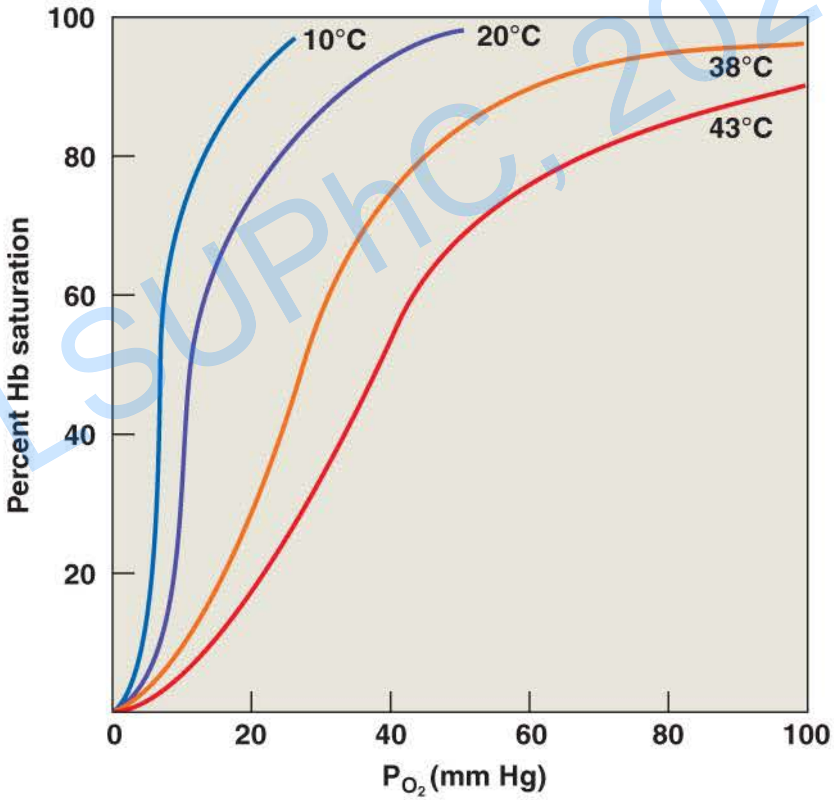
Gas Transport by Blood. Oxygen

- O_2 binds to iron ions in **hemoglobin** (Hb) molecules (98% of transport)
- **Oxygen–Hemoglobin** Saturation Curve - graph relating the saturation of hemoglobin to partial pressure of oxygen
- Higher pO_2 results in greater Hb saturation
- Hb changes shape each time a molecule of O_2 is bound, each O_2 bound makes next O_2 binding easier
- Allows Hb to bind O_2 when O_2 levels are low

- **Carbon Monoxide**
  - CO generates from burning fuels
  - Binds strongly to hemoglobin
  - Takes the place of O_2
  - Can result in carbon monoxide poisoning

The Oxygen–Hemoglobin Saturation Curve

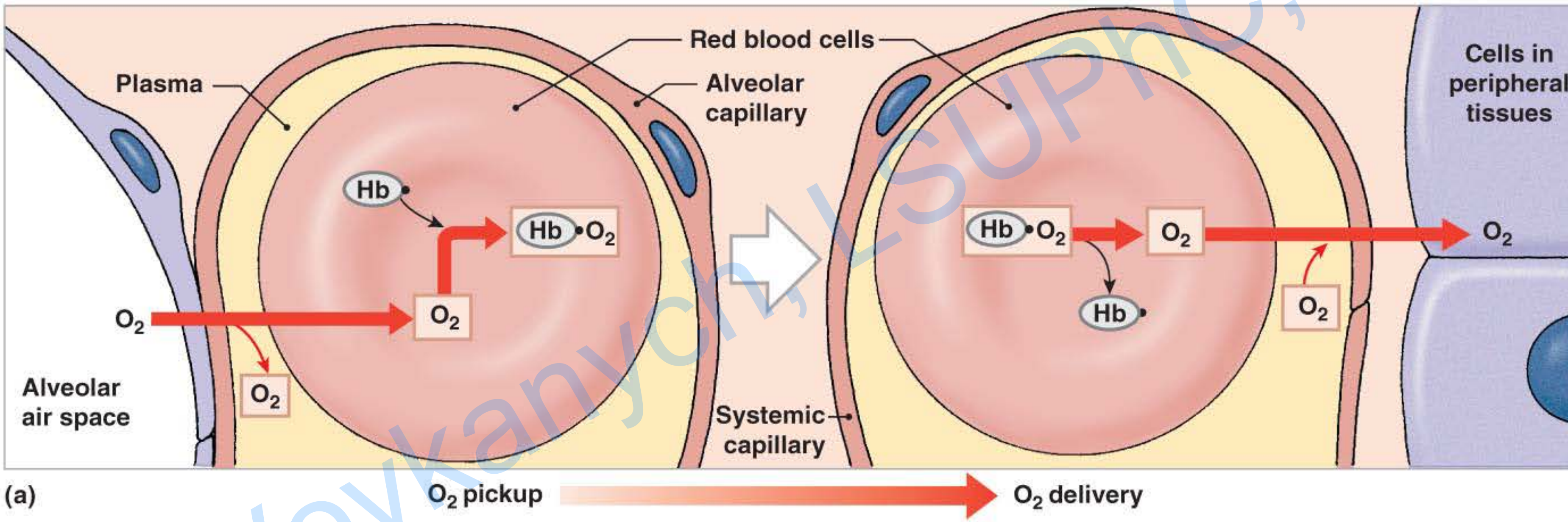




When pH drops or temperature rises curve shifts to right and more oxygen is released

The Bohr Effect Is the effect of pH on hemoglobin-saturation curve, caused by CO_2

A Summary of Oxygen Transport

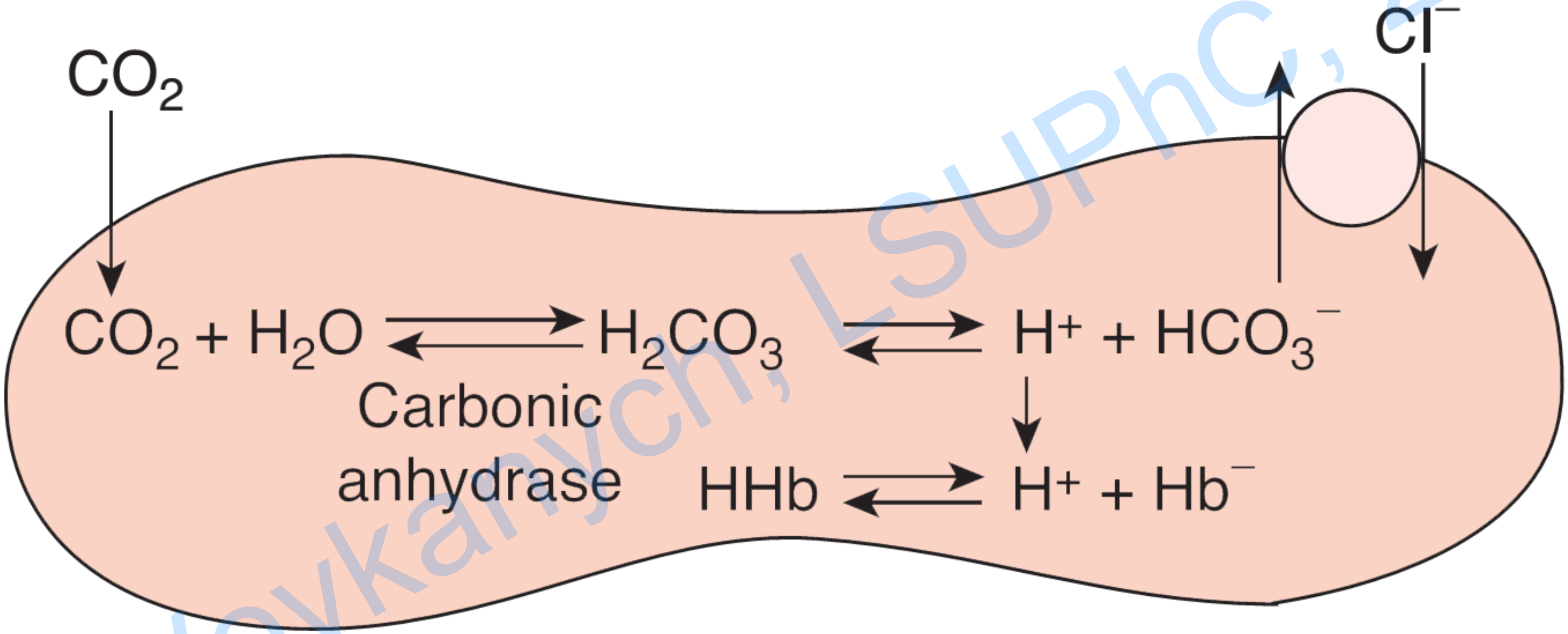


Gas Transport by Blood. Carbon Dioxide

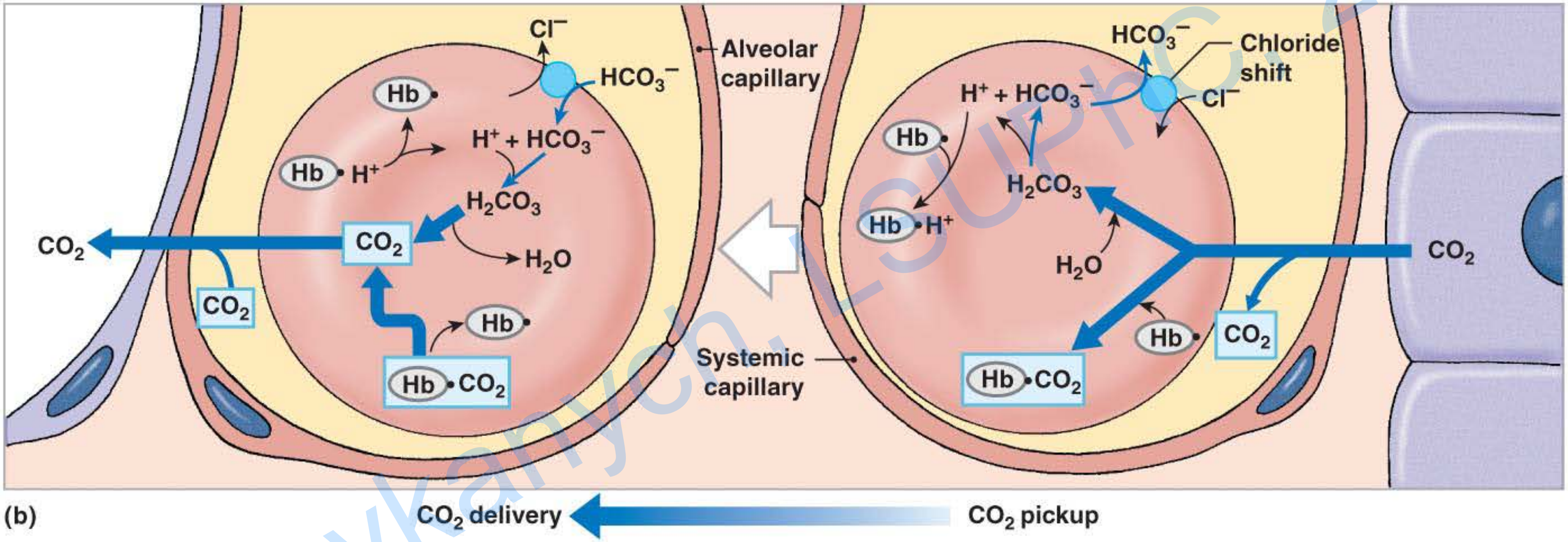
- 70% is transported as **carbonic acid** (H_2CO_3) which dissociates into H^+ and bicarbonate (HCO_3^-)
- 23% is **bound to amino groups** of globular proteins in Hb molecule forming **carbaminohemoglobin**
- 7% is transported as CO_2 **dissolved in plasma**

- **Stages** of transport:
  - CO_2 **diffuses into RBC** and **carbonic anhydrase** catalyzes reaction with H_2O produces **carbonic acid** (H_2CO_3)
  - Carbonic acid (H_2CO_3) **dissociates** into hydrogen ion (H^+) and bicarbonate ion (HCO_3^-)
  - Bicarbonate Ions move **into plasma** by an exchange mechanism (the chloride shift) that takes in Cl^- ions without using ATP

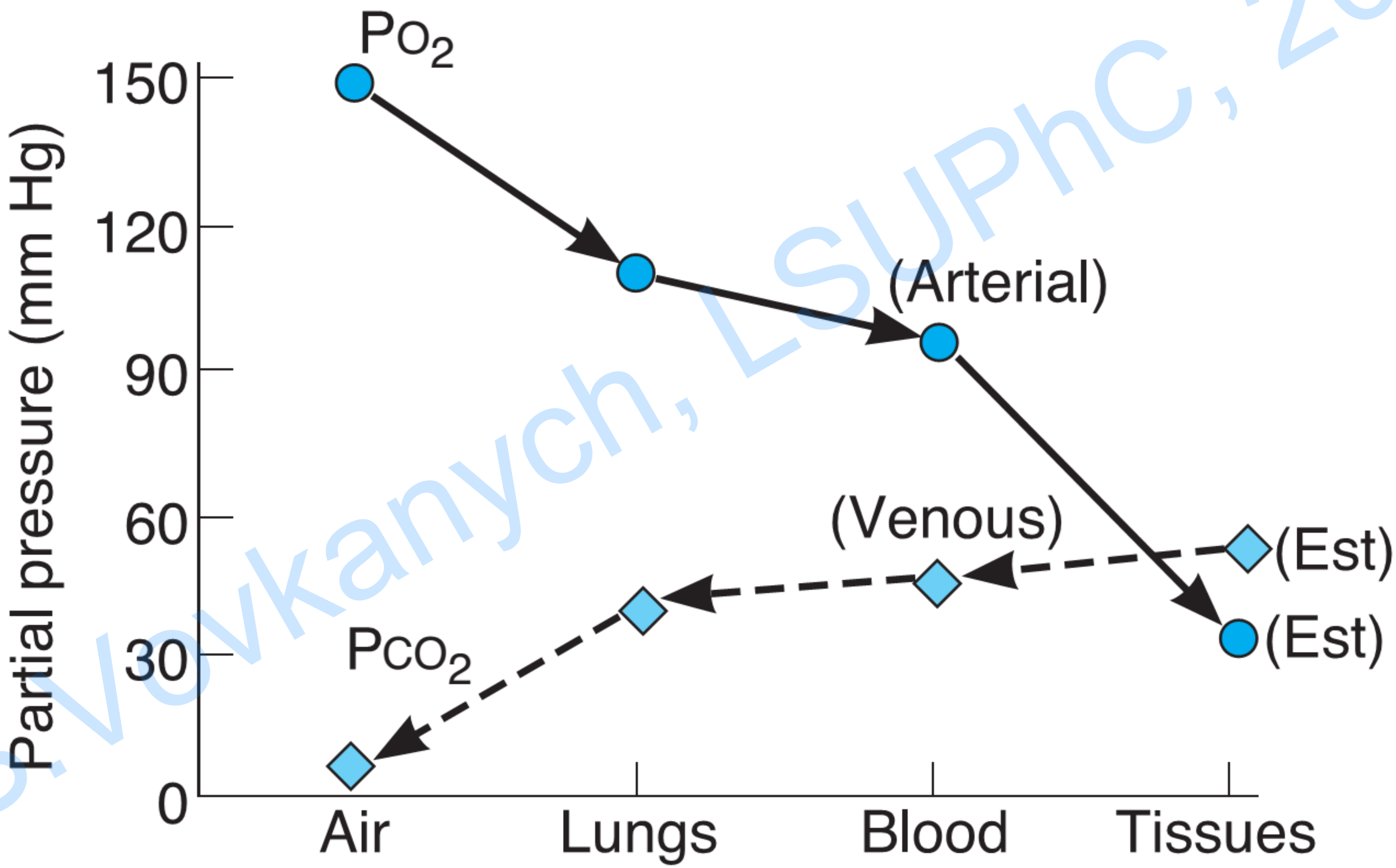
Carbon Dioxide Transport in Blood



A Summary of Carbon Dioxide Transport



Summary of the Gas Transport by Blood



Control of Respiration by CNS

The **Respiratory Centers of the Brain**

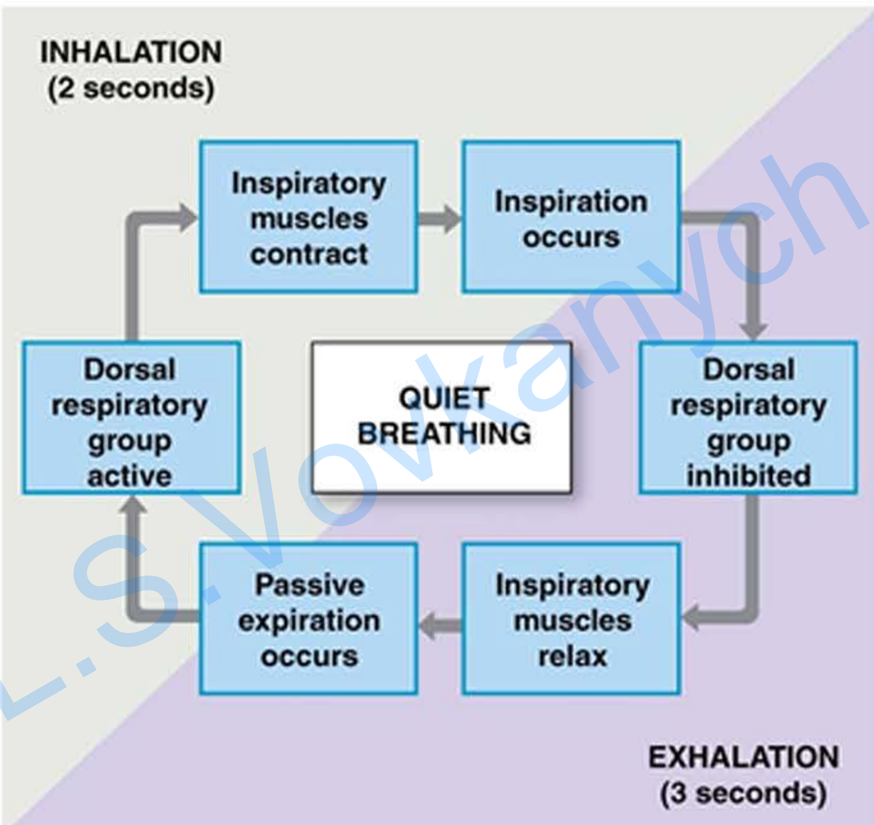
- Respiratory centers of **pons** and **medulla oblongata**
- **Motor neurons** that control respiratory muscles

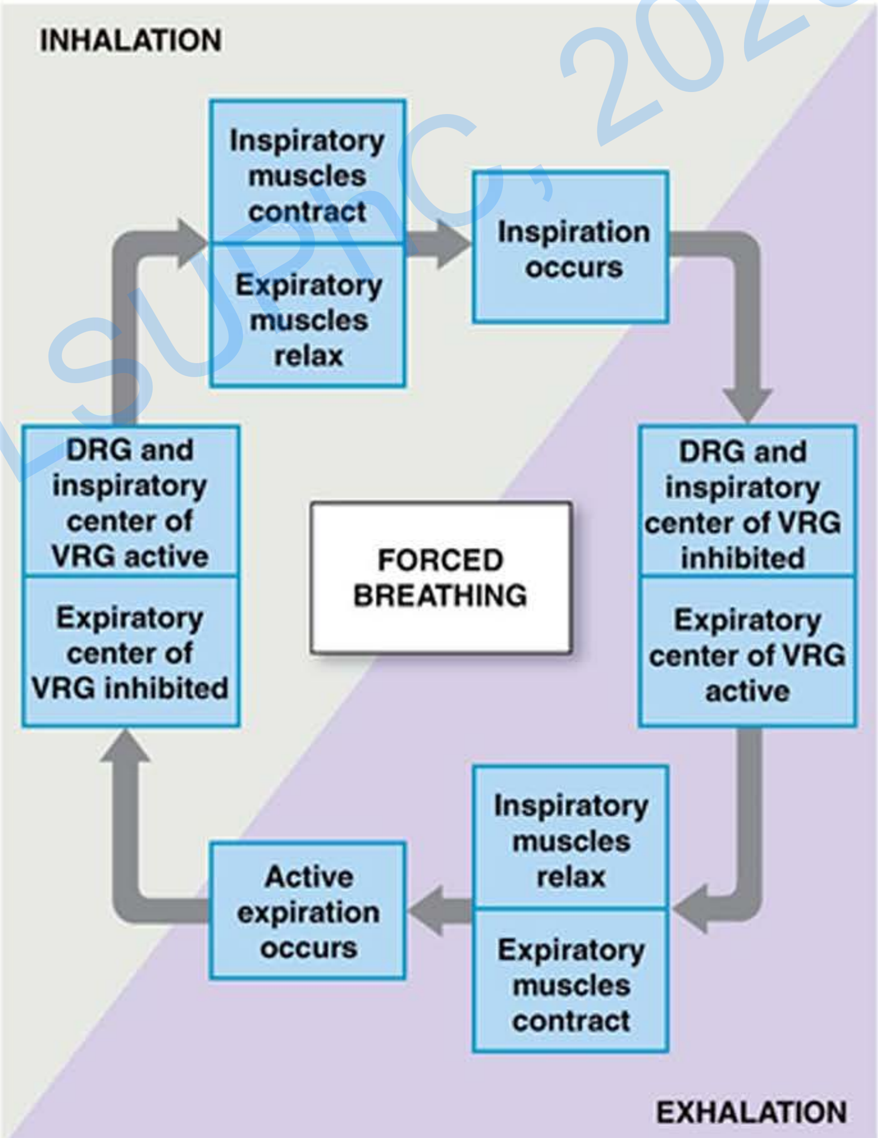
Respiratory **Rhythmicity Centers** of the **Medulla Oblongata** set the pace of respiration

- Can be divided into **two groups**
- **Dorsal respiratory group** (DRG) – the **Inspiratory** center, functions in **quiet** and **forced** breathing
- **Ventral respiratory group** (VRG) - **Inspiratory** and **expiratory** center, functions **only in forced** breathing

Quiet Breathing	Forced Breathing
Brief DRG activity (stimulating inspiratory muscles)	Increased activity in DRG **stimulation of VRG** (activation of accessory inspiratory muscles)
DRG inactivates (inspiratory muscles relax)	Expiratory center neurons in **VRG stimulate active exhalation**

Control of Respiration by CNS





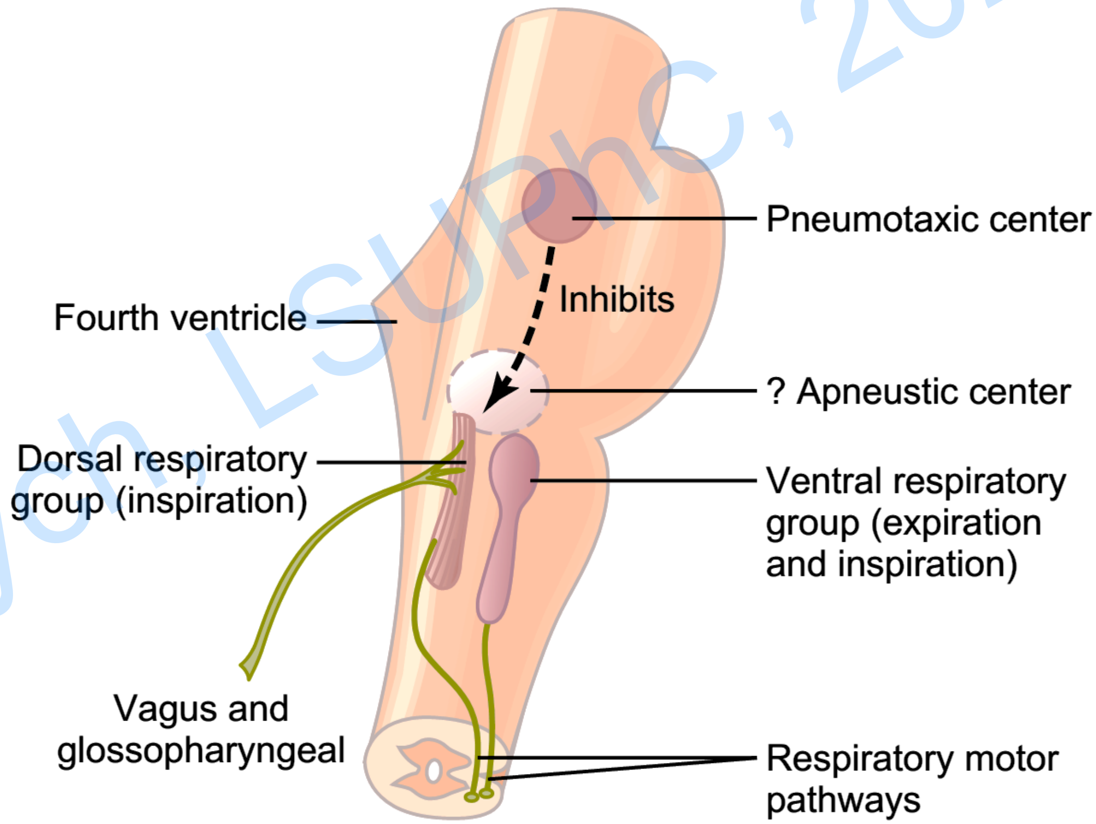
Control of Respiration by CNS

The **Apneustic** and **Pneumotaxic Centers** of the **Pons**

- Paired nuclei that **adjust** output of respiratory rhythmicity centers
- **Regulating respiratory rate and depth** of respiration

Respiratory Reflexes

- Changes in patterns of respiration induced by sensory input



Control of Respiration

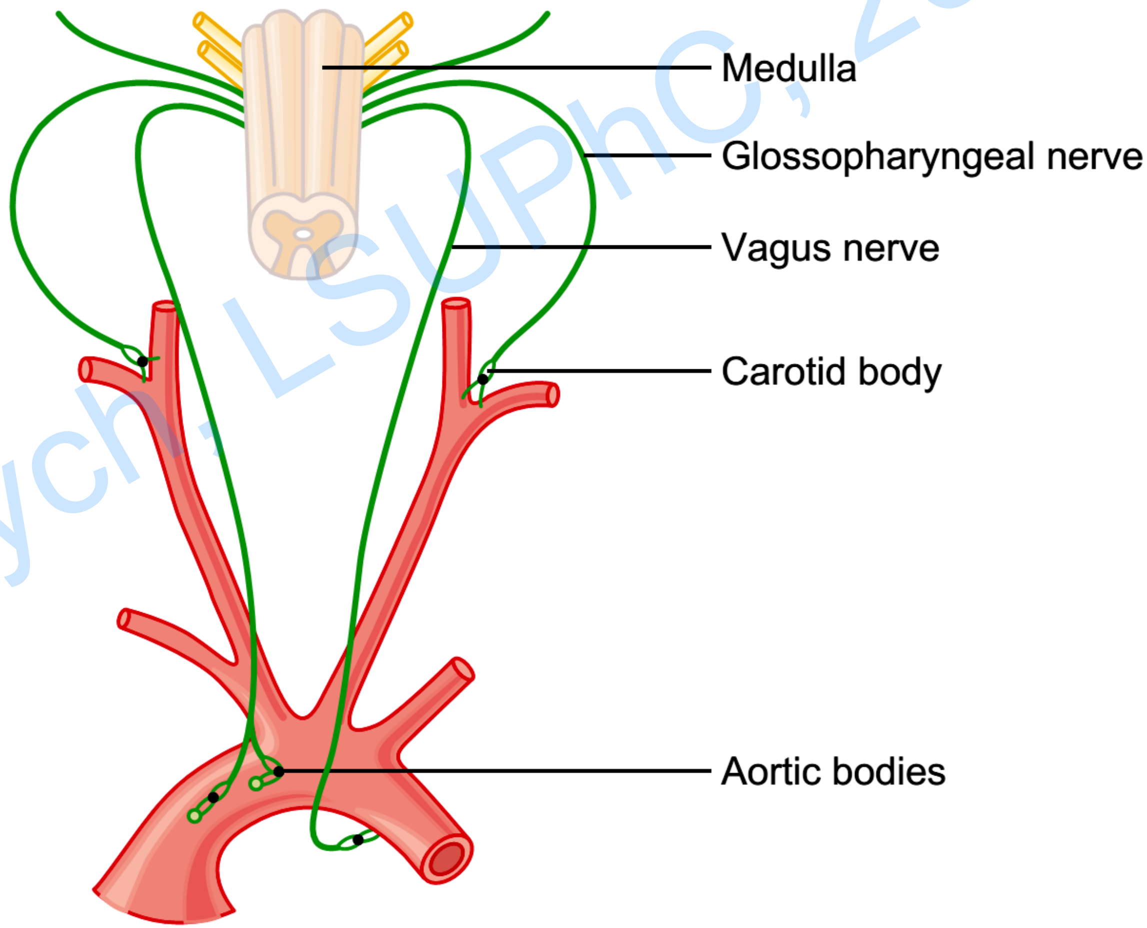
Sensory inputs that Modifiers of Respiratory Center Activities

- **Chemoreceptors** are sensitive to pCO_2, pO_2, or pH of blood or cerebrospinal fluid
- **Baroreceptors** in aortic or carotid sinuses are sensitive to changes in blood pressure
- **Stretch receptors** respond to changes in lung volume
- **Irritating physical or chemical stimuli** in nasal cavity, larynx, or bronchial tree
- **Other sensations** including pain, changes in body temperature, abnormal visceral sensations

Chemoreceptors Localization

Carotid bodies
Stimulated by changes in blood **pH** or **pO_2**
Sends output by **glossopharyngeal** (IX) nerve

Aortic bodies
Stimulated by changes in blood **pH** or **pO_2**
Sends output by **vagus** (X) nerve

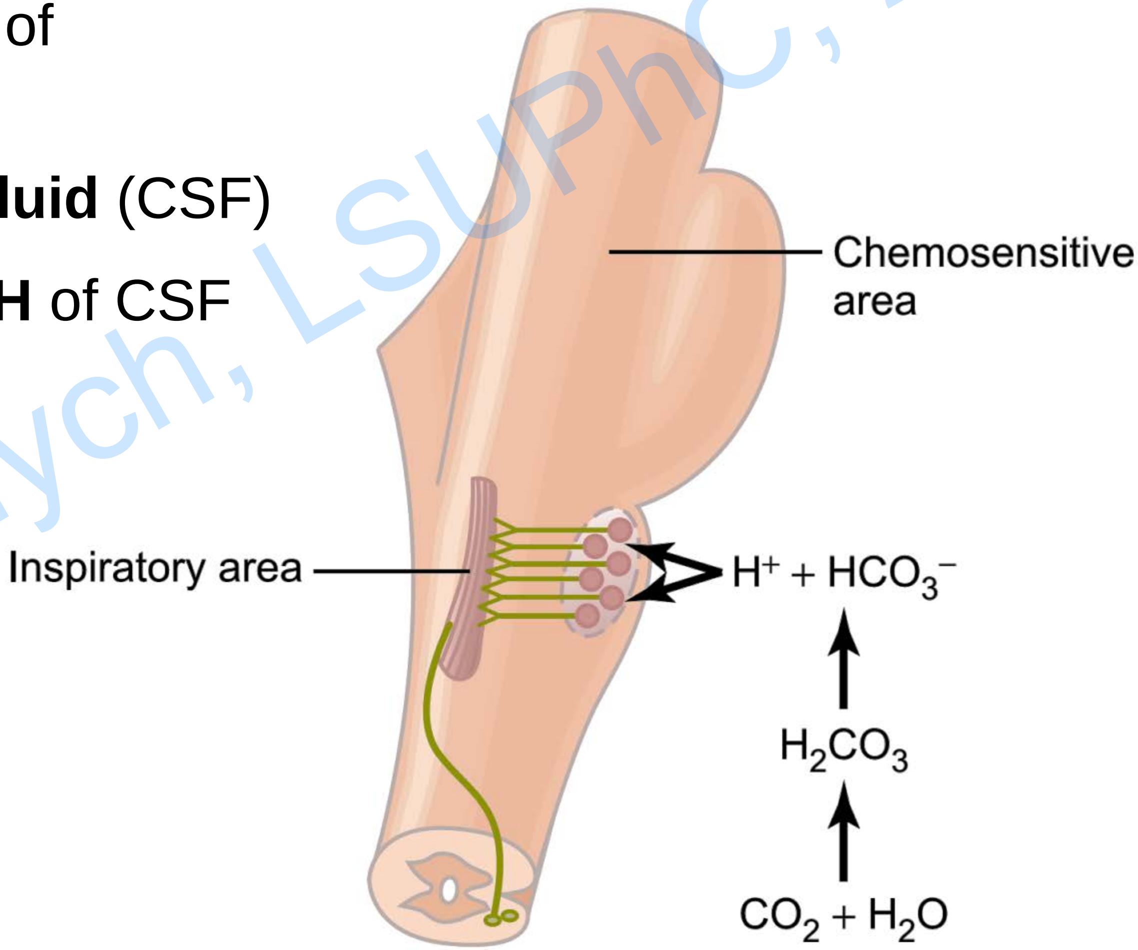


Chemoreceptors Localization

On ventrolateral surface of **medulla oblongata**

Monitor **cerebrospinal fluid** (CSF)

Respond to **pCO_2** and **pH** of CSF



Chemoreceptors Reflexes

- Respiratory centers are strongly influenced by chemoreceptor input
- Chemoreceptor stimulation leads to increased depth and rate of respiration

Hypercapnia	Acidosis	Hypoxemia
An increase in arterial pCO_2	The decrease in arterial pH	The decrease in arterial pO_2
Stimulates chemoreceptors in the **medulla oblongata**	Stimulates **all chemoreceptors**	Stimulates chemoreceptors **in aortic bodies** and **carotid bodies**
Stimulate respiration	Stimulate respiration	Stimulate respiration
* **Hypocapnia** – causes decrease in respiratory rate		

Mechanoreceptors Reflexes

Baroreceptor of blood vessels

- When blood pressure falls - respiration increases
- When blood pressure increases - respiration decreases

Stretch receptors of lungs

- **Hering-Breuer Reflexes**
- Inflation reflex: prevents overexpansion of lungs
- Deflation reflex: inhibits expiratory centers, stimulates inspiratory centers during lung deflation

Protective Reflexes

- Triggered by receptors in epithelium of respiratory tract when lungs are exposed to
- Toxic vapors
- Chemical irritants
- Mechanical stimulation
- Cause sneezing, coughing, and laryngeal spasm

Other Reflexes

- **Temperature** receptors of skin – stimulation (in cold)
- **Mechanoreceptors** of muscles – stimulation
- **Pain** receptors - stimulation

- **Strong emotions**: can stimulate respiratory centers in hypothalamus
- **Emotional stress**: can activate sympathetic division of ANS causing bronchodilation and increase in respiration rate
- **Anticipation of physical exercise**: can increase respiratory rate and cardiac output by sympathetic stimulation

Control by Dissolved Substances (Autoregulation in Tissues and Lungs)

Oxygen delivery **in tissues** and **pickup at lungs** are regulated by **rising pCO_2 levels**:

- relaxes smooth muscle in arterioles
- increases blood flow

Coordination of lung perfusion and alveolar ventilation, caused shifting of **blood flow** and **air flow** in **lungs**:

- pCO_2 levels: control bronchoconstriction and bronchodilation
- pO_2 levels: control vasodilation and vasoconstriction in lungs, increase blood flow to the alveoli with high pO_2

Effects of Exercise on Respiration

During exercise **hyperventilation** occurs (due to increase in rate and force of respiration) and **diffusing capacity** of lungs increase

- In moderate exercise, respiratory rate increases to about 30/minute and tidal volume increases to about 2,000 mL, the pulmonary ventilation increases to about 60 L/minute
- Diffusing capacity for oxygen is about 21 mL/minute at resting condition. It rises to 45 to 50 mL/minute during moderate exercise

Factors increasing pulmonary ventilation during exercise

- Higher centers
- Chemoreceptors (hypoxia and hypercapnea)
- Proprioceptors (from contracted muscles)
- Acidosis (lactate and other acids accumilation)

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