Physiology
Team 438
KSU

Respiratory block
PHYSIOLOGY 438 TEAMWORK

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PHYSIOLOGY

Summary File

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Lecture 1:
Functional organization of the respiratory system

Functions of the respiratory system include

- Gas exchange
- Pulmonary defense
- Phonation
- Converting of Angiotensin I to Angiotensin II by Angiotensin Converting Enzyme (ACE)
- Regulating the acid- base status of the body
- Secretion of important substances like surfactant.

Respiratory passages airways can be divided into:

Conductive zone:
- nose —> terminal bronchioles.
- 1- Protective function by cough and sneezing reflexes.
- 2- Air modification

Respiratory zone (unite):
- Respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli.
- Function in gas exchange.

External & Internal respiration: 3 major functional events occurs during it

- **Pulmonary ventilation**: inward and outward movement of air between lung and atmosphere.
- **Diffusion**: of oxygen and CO_2 between the alveoli and the pulmonary capillary blood.
- **Transport**: of O_2 & CO_2 in the blood and body fluids to and from the cells.

Functions of the respiratory system include

- Type I alveolar cells (type I pneumocytes): Where gas exchange takes place.
- Alveolar macrophages
- Type II alveolar cells (type II pneumocytes): Secrete surfactant.

Surface Tension: When H_2O molecules at the surface of alveoli are attracted to each other by attractive forces that resist distension.

- Surface tension tends to oppose alveoli expansion.
- Collapsing Pressure is Caused by Surface Tension and is indirectly related to the size of alveoli (law of LaPlace) . Less Radius of alveoli more surface tension

$$\text{Pressure} = \frac{2 \times \text{Surface tension}}{\text{Radius of alveolus}}$$

Surfactant phospholipids dipalmitoylphosphatidylcholine and number of Apoproteins.

Surfactant

reduces the surface tension of the fluid lining the alveoli.

Functions of surfactant:
- Prevents alveolar collapse
- Decreases airway resistance
- Decreases work of breathing.
- Keep the alveoli dry

Surfactant deficiency
- Respiratory Distress Syndrome of the newborn (RDS)
- adult Respiratory Distress Syndrome. (RDS)

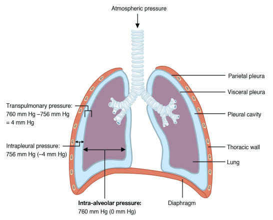
Prevention:
before delivery: Corticosteroid
After delivery: inhaled surfactant.

Lecture 2: Mechanics of breathing

Respiration is happened by expanded and contracted lungs

Inspiratory muscles	Expiratory muscles
During resting inspiration, the muscles are 1- diaphragm 2- external intercostals.	Resting expiration is a passive process that depends on the recoil tendency of the lung
During forced inspiration the Accessory muscles of inspiration participate	forced expiration is active and need contraction of the 1- Abdominal muscles . 2- internal intercostal muscles.

by elevation and depression of the ribs to increase and decrease the anteroposterior diameter of the chest cavity



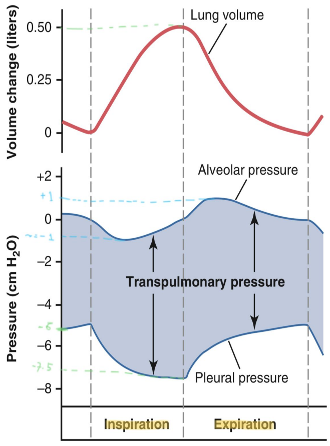
Pressure changes in the lungs during breathing

Pressure	During rest	During inspiration	During expiration
Intra-alveolar pressure	(0 mmHg) 760 mmHg	(-1 mmHg) 759 mmHg	(+1 mmHg) 761 mmHg
Intrapleural pressure	(-5 mmHg) 755 mmHg	(-7.5 mmHg) 752.5 mmHg	(just for your information) -6.5 mmHg according to Linda
Transpulmonary pressure **TPp = Palv-Ppl**	TPp= 0- (-5)= +5 mmHg	TPp= -1 - (-7.5)= +6.5 mmHg	(just for your information) TPp= +1 -(-6.5)= +7.5 mmHg

Why negative??:

1- The lung's elastic tissue causes it to recoil, while that of the chest wall causes it to expand. Because of these two opposing forces the pressure in the pleural cavity becomes negative.

2-The pleural space is a potential space,(empty) due to continuous suction of fluids by lymphatic vessels.



Compliance of the lung (CL)

The extent to which the lungs will expand for each unit increase in the transpulmonary pressure

$$CL = \frac{(\Delta V)}{(\Delta P)}$$

Lung compliance is reduced	Lung compliance is increased
-pulmonary fibrosis -pulmonary edema -diseases of the chest wall.	Emphysema it destroys the alveolar septal tissue rich with elastic fibers that normally opposes lung expansion.

For both lungs in adult = 200 ml of air/cm H_2O.

For lungs and thorax together = 110 ml/cm H_2O.

The characteristics of the compliance diagram are determined by the elastic forces of the lungs. These can divided into:

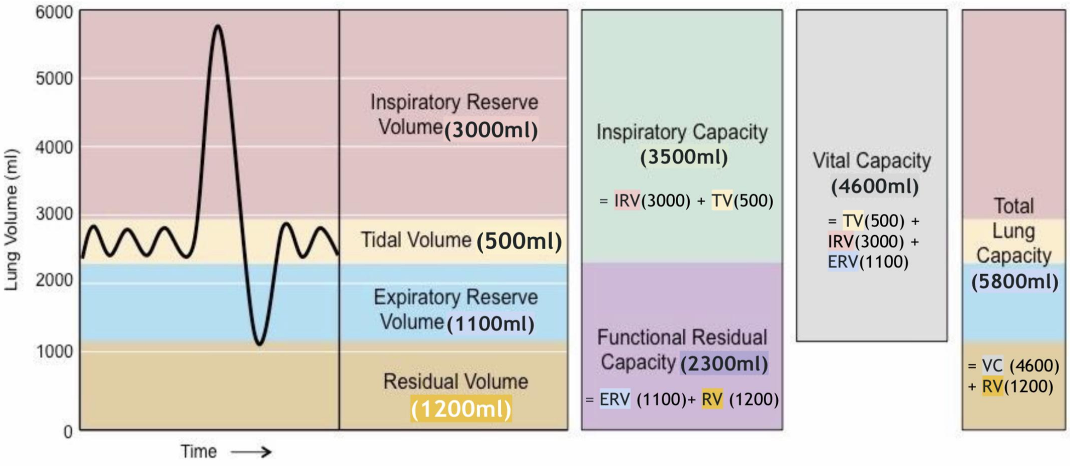
(1) 1/3 is due to elastic forces of the lung tissue itself via elastin (collagen)

(2) 2/3 of the elastic forces caused by **surface tension.**

Lecture 3: Respiratory Ventilation.

Volume	Definition	value
Tidal volume TV	is the volume of air **inspired or expired** with **each normal breath.**	500ml
Inspiratory reserve volume IRV	is the extra volume "Maximal" of air that can be **inspired over and beyond the normal tidal volume**	3000ml
Expiratory reserve volume ERV	is the extra amount "Maximal" of air that can be **expired by forceful expiration** after the end of a **normal tidal expiration**	1100ml
Residual volume RV	is the volume of air that **still remain** in the lungs after the most forceful expiration	1200ml

capacity	Definition	Equation	Volume
Functional residual capacity FRC	is the volume of air remaining in the lungs **after normal expiration.**	ERV(1100)+ RV(1200)	2300ml
Inspiratory capacity IC	is the volume of air inspired by **a maximal inspiratory effort after normal expiration.**	IRV(3000) + TV(500)	3500ml
Forced Vital Capacity FVC	is the volume of air expired by a **maximal expiratory effort** after filling the lung to **maximal inspiration** then expiring to maximum extent.	TV(500) + IRV(3000) +ERV(1100)	4600ml
Total lung capacity TLC	is the **maximum** volume of **air** that **can be accommodated** in the lungs.	it is the **sum of all** pulmonary volumes	5800ml



the volume of air expelled during the **first second** of a forced expulsion after a maximum inspiration. **Value=3680ml**

FEV1/FVC ratio

- This ratio differentiates between obstructive and restrictive lung diseases, Normally it is about 80%.

Respiratory Zone	VS	Anatomical Dead Space
- Start from the respiratory bronchioles down to the alveolar sacs.		- Start from air-conducting system down to the terminal bronchioles.
-Gas exchange takes place.		-No gas exchange.
-350 ml/min.		-150 ml.

Another important laws:

Minute Respiratory Volume (MRV):
-Total amount of air moved into and out of respiratory system **per minute.**

- *Equation*= Respiratory Rate **x** tidal volume = **6000 ml/min.**

$$FRC = \left[\frac{C_i\ HE\ (c_1)}{C_f\ HE\ (c_2)} - 1\right] V_i\ (v_1)$$

Alveolar ventilation per minute VA:
is the **total volume of new air entering the alveoli** and other adjacent gas exchange areas **each minute.**

- *Equation*= Respiratory rate X (Vt - Vd)=12 X (500 - 150) = 4200ml

Lecture 4: lung function in health and disease

Spirometry 

It is the measurement of the speed and the amount of air that can be exhaled and inhaled.

Indications of Spirometry

- Arterial Blood Gas Analysis:
  - Hypoxemia
  - Hypercapnia
- Abnormal Chest X-ray
- Symptoms:
  - Dyspnea
  - Cough
  - Sputum production
  - Chest Pain
- Signs :
  - Cyanosis
  - Clubbing of the fingers
  - Hyperinflation
  - Diminished breath sounds,
  - Prolongation of expiratory phase.

Spirometry is a simple most commonly used test to:

- Play a critical role in the diagnosis, differentiation and management of respiratory diseases
- Measure the physiological parameters.
- Assess the lung performance

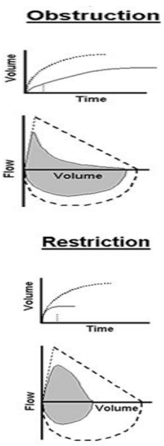
Physiological conditions affecting lung functions:
1-Age. 2- Gender.
3- height. 4-weight.
5- Ethnic group.
6-Pregnancy.

diseases affecting PFTs (Pulmonary Function Tests)

- **Neuromuscular diseases:**
  Guillain Barrè Syndrome, Myasthenia gravis
- **Pulmonary diseases:**
  Obstructive and Restrictive airway diseases, Interstitial lung diseases
- **Adverse reactions:**
  Drugs with known pulmonary toxicity [Pulmonary fibrosis]

PFTs in Obstructive and restrictive pulmonary diseases:

	Obstructive	Restrictive
FVC (Forced vital capacity)	Normal or Decreased	Decrease a lot
FEV1 (Forced Expiratory volume in one second)	Decrease a lot	Normal or Decreased
FEV1/FVC ratio	Decreased	Normal or increased
TLC (Total lung capacity)	Increased	Decreased



Effect of smoking on lung function

Non Smoker

In normal healthy non smoker subject after the age of 30 the expected decline in Lung function parameter [FEV1] is 25-30 ml/ year.

Smoker

The average rate of decline of lung function in smokers as measured by Forced Expiratory Volume in 1 sec [FEV1] is 60-70 ml / year.

Lecture 5: Gas exchange and gas transfer

★ Factors that affect the rate of gas diffusion through the respiratory membrane

$$\text{Diffusion rate} \propto \frac{\Delta P \times A \times S}{d \times \sqrt{MW}}$$

➔ directly proportional:
- P: Partial pressure differences
- A: Surface area for gas exchange
- S: Solubility of gas

➔ inversely proportional:
- d: Diffusion distance
- MW: Molecular weight

Dalton's law

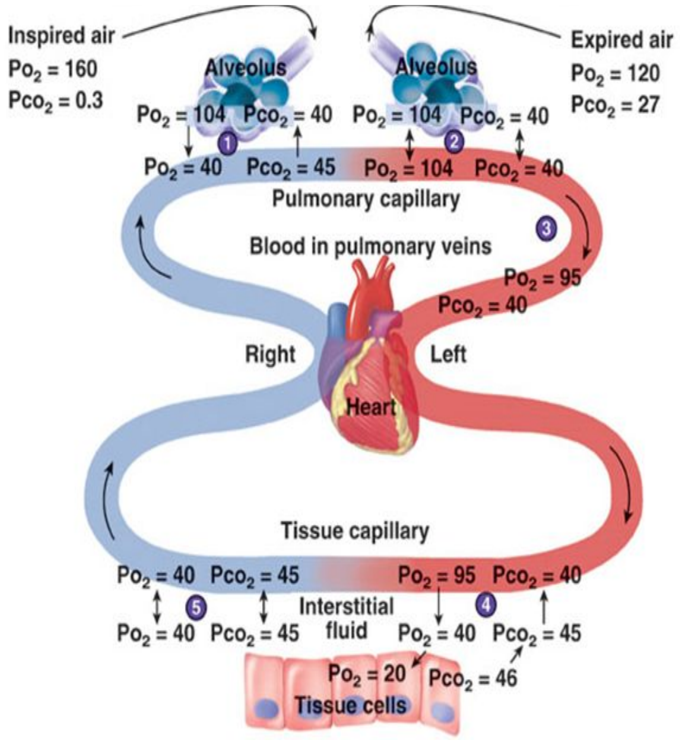
$$P_{total} = P_1 + P_2 + P_3 + \ldots$$

Henry's law

$$\text{Partial pressure} = \frac{\text{Concentration of dissolved gas}}{\text{Solubility coefficient}}$$

solubility of gas is directly proportional to the partial pressure

★ Partial pressure of gases



	PO_2	PCO_2
atmospheric air	160 mmHg	0.3 mmHg
Alveoli	104 mmHg	40 mmHg
arterial pressure	95 mmHg	40 mmHg
venous pressure	40 mmHg	45 mmHg
Interstitial fluid	40 mmHg	45 mmHg
Cells	23 mmHg	46 mmHg
expired air	120 mmHg	27 mmHg

	ventilatory rate	of O_2 consumption by tissues	CO_2 excretion from the blood
At resting condition	4.2 L/min.	250 ml/min	200ml/min
During exercise	must increase 4 times	1000 ml/min (x4 normal volume)	

Lecture 6: O_2 and CO_2 transport

Transport of O_2

➔ Oxygen can combine loosely and reversibly with hemoglobin.

Oxygen-carrying capacity of blood determined by:

1- PO_2 of environment.
- PO_2 is high (pulmonary capillaries) → O_2 binds to hemoglobin → Greater Hb saturation
- PO_2 is low (tissue capillaries) → Hb releases O_2 → Lower Hb saturation

2- Affinity between hemoglobin and O_2

Forms of Oxygen transported in blood:

1- 97% Binds to Hemoglobin
- Hb + $4O_2$ → Hb(O_2) 4"oxyhaemoglobin"
- Normal Hb in young adults = **16 gm/dl**
  Each gram binds to **1.34 ml** of O_2
  → 16 x 1.34 = **21.44 ml of O_2 /dl**
- venous blood → Hb carry **14.4 ml** of O_2 (Normal State)
  → Hb carry **4.4 ml** of O_2 (Strenuous exercise)

% saturation of Hb = $\frac{\text{Oxygen content}}{\text{Oxygen capacity}} \times 100$

2- 3% Dissolved In plasma
- Normal arterial PO_2 = 95 mmHg → 0.29 ml
- Tissue capillaries PO_2 = 40 mmHg → 0.12 ml
- **Oxygen transported = 0.17 ml**

Transport of CO_2

CO_2-carrying capacity of blood determined by:

1- PCO_2
- Higher In Tissues Than In Capillary

2- CO_2 concentration gradient

3- Distance

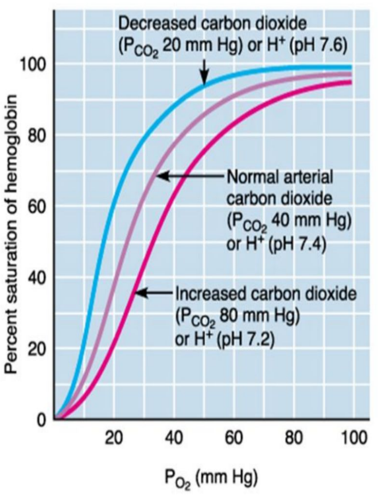
Forms of CO_2 transported in blood
(4 ml CO_2 is carried to the lung)

1- 70% Bicarbonate form
- tissues → Right shift → Cl- shift
- alveoli → Left shift → Reverse Cl- shift

2- 7% dissolved in plasma
- PCO_2 (venous blood) =45 m(m Hg → 3.15 ml of CO_2
  PCO_2 (arterial blood) =40 mmHg. → 2.8 ml of CO_2
- **0.3 ml** of CO_2 is transported

3- 23% carbamino hemoglobin form

oxygen-haemoglobin dissociation curve

	Right shift	Normal Function	left shift
Affinity	Lower affinity for O_2	Normal Affinity	Higher affinity for O_2
Meaning	Release <u>More</u> O_2 → oxygen is **<u>unloading</u>** to the tissues from Hb	Releasing 5 mL of O_2	Release <u>less</u> O_2 → **<u>loading</u>** or attachment of oxygen to Hb
pH (H^+ conc)	↓ pH (↑H^+ conc)		↑ pH (↓H^+ conc)
Temperature	↑(↑Exercise)		↓
(2,3-DPG)	↑		↓
PCO_2	↑ (Bohr effect)		↓
P50	↑		↓
Fetal haemoglobin	_____		✓

Lecture 7: hypoxia and cyanosis

Hypercapnia Excess of CO_2 in body, PCO_2 increases above **52 mmHg**, it decreases the PH.

Types of Hypoxia

Hypoxic or arterial hypoxia	Anemic hypoxia
Reduced **arterial PO_2**.	Reduction in the oxygen carrying capacity • The PO2 & %Hb-O2 is normal
Causes: •Alveolar hypoventilation, Diffusion abnormalitie, Right to left shunt, Ventilation-perfusion imbalance.	Causes: 1- Anemia 2-Abnormal Hb e.g methemoglobin, carboxyhemoglobin
Stagnant hypoxia:	**Histotoxic hypoxia**
Reduced blood flow through the tissues, due to slow circulation,leading to hypoxia.	This is **inability of the tissues to <u>use</u> oxygen** due to inhibition of the oxidative enzyme activity • e.g cyanide poisoning causing blockage of the cytochrome oxidase activity
Causes: 1-General slowing 2-Local slowing	

Effect of Hypoxia	**According to the <u>degree</u> of hypoxia** Clinical features: depend on how fast and how severely partial pressure of O_2 is decreased
Treatment	**oxygen therapy**. (Not effective for the histotoxic hypoxia)

Cyanosis

Blue discoloration due to more than 5 g/dl of **<u>reduced</u>** (deoxygenated) hemoglobin in blood, patients with anemia almost never develop cyanosis,but they can develop in polycythemia.

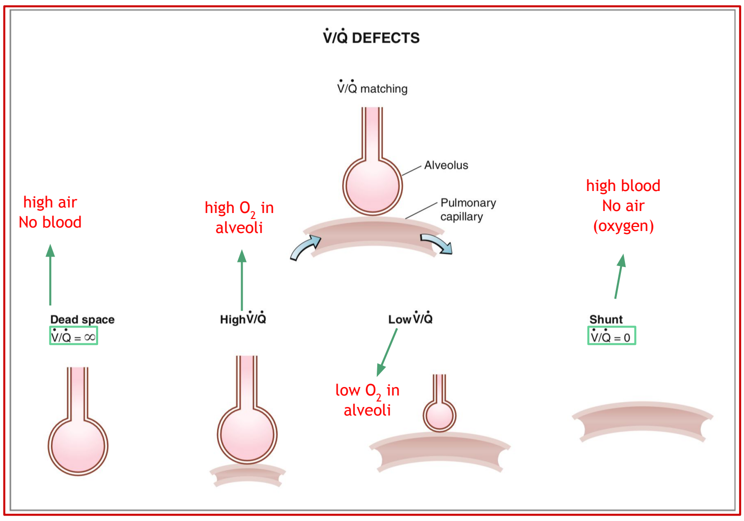
Causes of Cyanosis	Inadequate oxygenation of blood in the lungs	presence of aerated shunt between vessels	other: Moderate cold & Diminished blood flow to tissues
Types of Cyanosis	Central General impairment of circulation. Can occur in hypoxic hypoxia	Peripheral Decrease in blood flow in one body part. Ex: arterial obstruction	

Ventilation perfusion ratio

alveolar ventilation **at rest**	The pulmonary blood flow	V/Q ratio
4.2 L/min	5L/min	**4.2/5 = 0.84**

Ventilation/perfusion abnormalities

- physiologic dead space (More than normal) Ex:apex of the lung
- physiologic shunt (Less than normal) Ex: base of the lung



Lecture 8: Control Of Breathing

Controls of rate and depth of

Arterial PO_2: When PO_2 is VERY low, ventilation increases.

Arterial pH: As hydrogen ions increase (acidosis), alveolar ventilation increases.

Arterial PCO_2 : The most important regulator of ventilation is PCO_2, small increases in PCO_2, greatly increases ventilation.

Respiratory centers

Medullary Respiratory Center

- Inspiratory area (Dorsal Respiratory Group) DRG: Determines basic rhythm of breathing.
- Expiratory area (Ventral Respiratory Group) VRG: Activated by inspiratory area during forceful breathing.

Pontine Respiratory Center

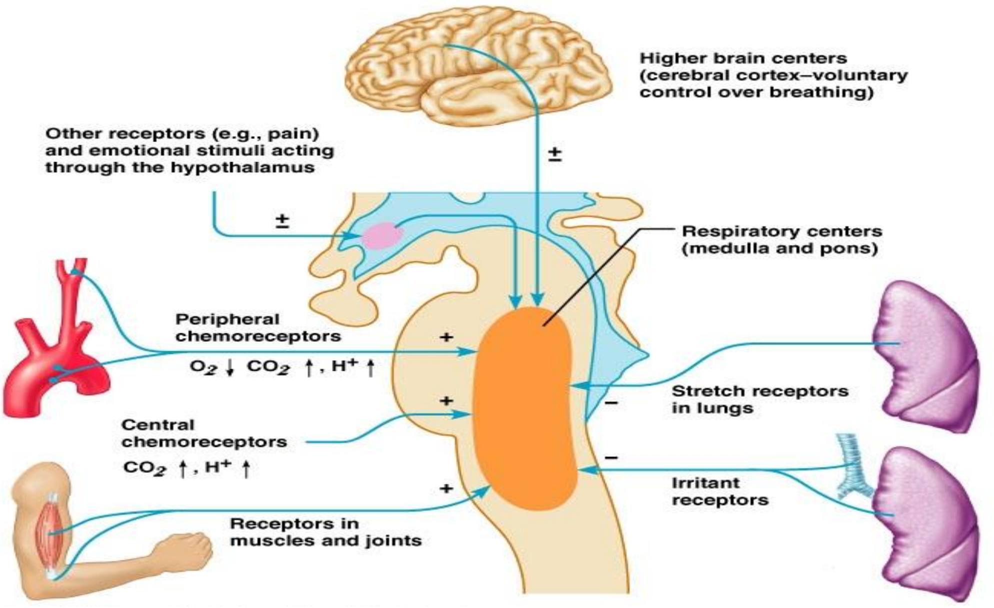
- Pneumotaxic area (in pons): Inhibits inspiratory area of medulla to stop inhalation. Therefore, breathing is more rapid.
- Apneustic area (in pons): Stimulates inspiratory area of medulla to prolong inhalation.

Other Factors Influencing Respiration

Effect of irritant receptors in the airways
are stimulated by irritants that enter the respiratory airways causing coughing, sneezing and bronchoconstriction.

Function of lung J receptors
Few receptors in the wall of the alveoli in juxtaposition to the pulmonary capillaries.

Function of stretch receptors
they are located in the wall of bronchi and bronchioles transmit signals through vagus nerve to DRG producing effect similar to pneumotaxic center stimulation.

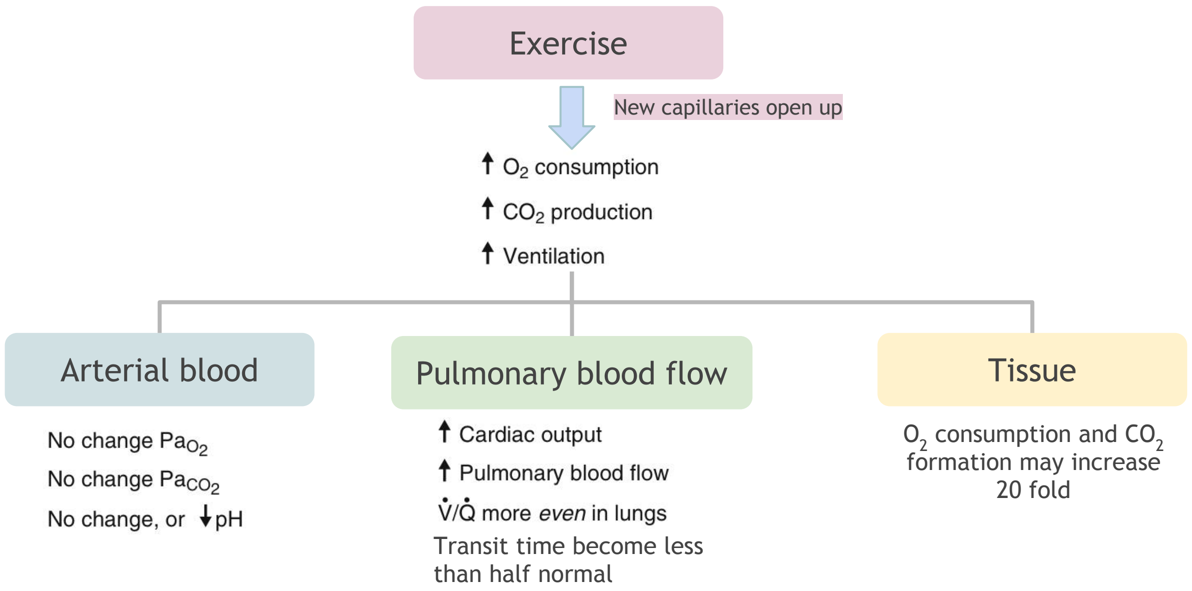


The respiratory system can compensate for metabolic acidosis or alkalosis by altering alveolar ventilation.

Lecture 9:
effect of exercise on respiratory system

What causes intense ventilation during exercise?

1. Neural signals from the motor areas of the brain (motor cortex) to the respiratory center.
2. The joint proprioceptors
3. Body temperature (hypothalamus).
4. Possibility that the neurogenic factor for control of ventilation during exercise is a **learned response** (cerebral cortex)
5. chemical factors play important role in final adjustment of respiration required



the blood is almost completely saturated with oxygen when it leaves the pulmonary capillaries despite of the changes happen during exercise ! **How ?**

1- The diffusing capacity for oxygen increases almost three fold during exercise, **because** of increase surface area (opening of new capillaries) + increase alveolar ventilation + V/Q ratio more even

2- At rest the blood normally stays in the lung capillaries about three times as long as necessary

Diffusing capacity : Is the volume of gas that diffuses through the membrane each minute for a pressure difference of 1 mmHg.

	O_2 diffusing capacity	CO_2 diffusing capacity
During rest	21 ml/min/mmHg	400ml/min/mmHg
During exercise	65 ml/min/mmHg	1300ml/min/mmHg

Trait of male :	O_2 consumption
Normal, at rest	**250 ml/min**
Untrained , during exercise	3600 ml/min
Athletically trained , during exercise	4000 ml/min
marathon runner , during exercise	5100 ml/min

Lecture 10: Low and high altitude

Effect of increased barometric pressure (Deep sea diving)

When **descending below** the sea, the pressure **INCREASES** → The surrounding pressure increases by 1 atm for every 10 meters (33 feet) of depth in sea water.(at depth of 31 meter he diver is exposed to a pressure of 4 atmospheres) → These problems confront SCUBA (self contained underwater breathing apparatus.)

Effects of depth on
- Volume of gases — compression of gases to smaller and smaller volumes
- Density of gases — Increase in the density of gas and hence increased work of breathing

Nitrogen Narcosis

Nitrogen <u>dissolve freely</u> in the fats including the membranes and other lipid structures of the neurons → alteration of the electrical conductance of the membranes → reduces their excitability + Nitrogen narcosis

Decompression Sickness (Caisson's Disease): Syndrome caused by a decrease in the ambient pressure which occur when the tissues of the body contain an excess of physically inert gas	
During descending	During fast ascent
the high partial pressure of nitrogen forces this gas into solution in body tissue particularly in fat	Bubbles of gaseous nitrogen are released in tissues and blood

Symptoms

Mild	Severe
•Fatigue or drowsiness •Local skin rash	-Bubbles in the tissues -Neurological symptoms. -Thoracic pains -Bubbles in coronary arteries → myocardial damage -Decompression sickness shock (hypovolemia) -Edema → shock

Treatment

Rapid <u>recompression</u> in a pressure chamber followed by slower <u>decompression</u>	Replacing Nitrogen by helium: - less the narcotic effect of nitrogen on CNS. -low molecular weight. -Low density → decreased airway resistances -more soluble in body fluids -High diffusion through tissue	Reduce the oxygen concentration in the gaseous mixture

Oxygen toxicity: Condition resulting from the harmful effects of breathing oxygen at increased partial pressure

the amount of oxygen in the blood <u>increases</u> → When the Po_2 in the blood rises above 100 mmHg
The oxygen is converted into its <u>active</u> form→ free radicals → then causing serious destructive

Symptoms

brain seizures → followed by coma within 30-60 minutes
Other symptoms:
-Nausea -Muscle twitching
-Dizziness -Disturbance of vision. -Irritability -Disorientation

ascend to high altitude

As the **barometric pressure** <u>decreases</u> → the **oxygen partial pressure** <u>decreases</u> **proportionally**.

Water vapor pressure and CO2 remain normal.Therefore, these two gases dilute the oxygen in the alveoli → reducing the oxygen concentration and therefore **hypoxia develops**.

<u>The decrease in barometric pressure is the cause of hypoxia in high altitude physiology.</u>

The longer the person stays at high altitudes the more acclimatized the person become to low PO_2.

➔ fewer deleterious effects + becomes possible for the person to work harder without hypoxic effects