MARROW

2024 NEET-SS

UPDATED PEDIATRICS NOTES

CRITICAL CARE

RESPIRATORY PHYSIOLOGY PART - I

Active space

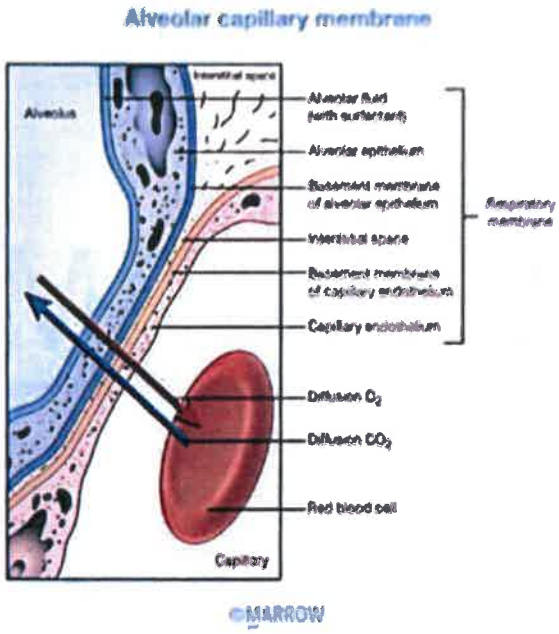
Physiology of gas exchange

00.01:15

Diffusion of pulmonary gases :

Alveolar capillary membrane is made up of alveolar epithelium, interstitial space, basement membrane, capillary endothelium and red blood cell.

- Ventilation merely moves gas into and out of the lungs.
- The process that moves gas across the A-C membrane is passive diffusion.
- Diffusion is the movement of gas molecules from an area of high concentration to an area of low concentration.



Atmospheric gas :

- Barometric pressure is the sum of all gases exerting pressure on the earths surface.
- At sea level atmospheric pressure is 760 mmHg.
- The primary components of this pressure is nitrogen, oxygen, argon and carbon dioxide.

Components of atmosphere :

Composition of dry air :

Substance.	% by volume.
Nitrogen (N_2)	78.08
Oxygen (O_2)	20.95
Argon (Ar)	0.93
Carbondioxide (Co_2)	0.033
Neon (Ne)	0.0018
Helium (He)	0.00052
methane (CH_4)	0.0002
Krypton (Kr)	0.00011
Nitrogen oxide (N_2O)	0.00005
Hydrogen (H_2)	0.00005

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Partial pressure :

- The pressure exerted by an individual gas in a mixture of gases.
- Designated by PGAS.
- To determine the partial pressure of any gas, multiply the percentage of that gas by the total pressure.

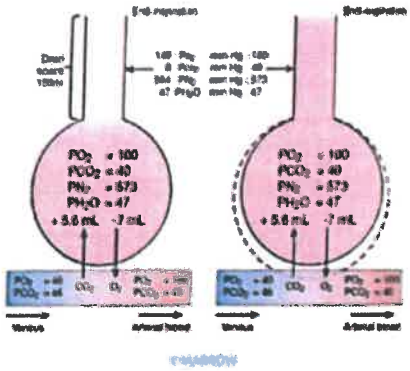
  Example : Oxygen occupies 21% of the atmosphere. If the total pressure of the atmosphere (i.e. Barometric Pressure) is 760 mmHg, the PO2 of the atmosphere is 159.6 mmHg (760 x .21).

Partial pressure of key gases :

Oxygen partial pressure is reduced as it goes from the atmosphere to the alveoli secondary to "competition" with carbon dioxide and water vapor.

Partial pressure of O2 and CO2 :

- The partial pressure of O2 is significantly lower in the alveoli than in the atmosphere.
- If you imagine the alveoli as a micro-environment the CO2 level and water vapor content are much higher.
- By the time the atmospheric gas reaches the alveoli they are diluted by CO2 and H2O.



Partial pressure of key gases.

Water vapour pressure :

- When water vapor is present in a volume of gas it exerts its own partial pressure in accordance with Daltons Law.
- Alveolar gas is 100% humidified at body temp.
- It is assumed to have an absolute humidity of 44mg/l and a partial pressure of (PH2O) of 47 mmHg.

Temperature.	Absolute (maximum) Humidity.	Water vapour pressure.
37°C.	44.0 mg/L.	47.0 mmHg.
35°C.	39.6 mg/L.	42.2 mmHg.
30°C.	30.4 mg/L.	31.8 mmHg.
27°C.	25.8 mg/L.	26.7 mmHg.
25°C.	23.0 mg/L.	23.8 mmHg.
20°C.	17.3 mg/L.	17.5 mmHg.

Feedback

Alveolar gas equation :

Active space

- Thus, alveolar oxygen (PAO2) is calculated using the "ideal alveolar gas equation" or " the alveolar gas equation".

  $$PAO_2 = [P_B - PH_2O]FIO_2 - PaCO_2 / R$$

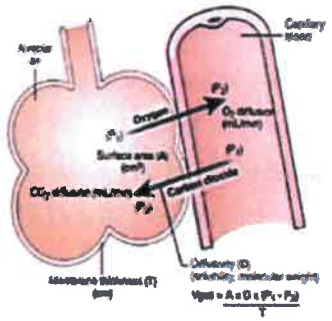
- This equation computes the total PIO2 available for oxygen transfer.

Factors affecting gas exchange 00:08:08

These factors affect the gas exchange at the alveolo capillary level.

Fick's law :

- Adolph Fick (1831 – 1879).
- The law states that the rate of gas transfer across a sheet of tissue is directly proportional to
  i. Surface area of the tissue.
  ii. Diffusion constant.
  iii. Difference in partial pressure of the gas between the two sides of the tissue.
  iv. Inversely proportional to the thickness of the tissue.



Diffusion of gas across alveolar capillary membrane.

- $V = [A * D * (P_1 - P_2)] / T$.
- Gas moves from alveoli to capillary because of a pressure gradient.

Henry's law :

The amount of gas that can be dissolved by 1 ml of a given liquid at standard pressure (760 mm Hg) and at a specified temperature is called the solubility coefficient.

- The solubility coefficient varies inversely with temperature.
- For oxygen at 37° C the coefficient is 0.0244 ml/mm Hg/mL H2O.
- For carbon dioxide it is 0.592 ml/mm Hg/mL H2O.
- In a liquid medium (like the blood and interstitial space), carbon dioxide is 24 times more soluble.

Henry's law states that the amount of a gas that dissolves in a liquid at a given temperature is proportional to the partial pressure of the gas.

Feedback

Active space

Partial pressure = Concentration of dissolved gas

Solubility coefficient

Gas.	Solubility coefficient.
Oxygen.	0.024
Carbon dioxide.	0.57.
Carbon monoxide.	0.018
Nitrogen.	0.012
Helium.	0.008

Graham's law :

- Graham's law states that the rate of diffusion of a gas through a liquid is :
  i. Directly proportional to the solubility coefficient of the gas.
  ii. Inversely proportional to the square root of the gram-molecular weight of the gas.
- The diffusion rate of CO2 is 20 times greater than that of O2.

Summary :

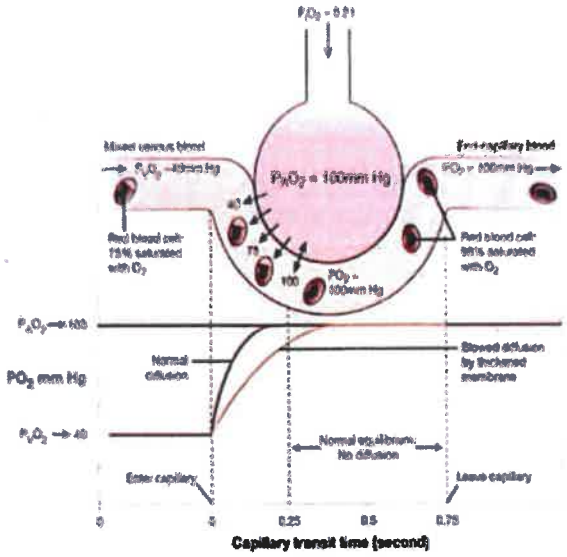
- The greater the solubility of the gas, the greater the number of molecules available to diffuse for any given partial pressure difference.
- The greater the cross-sectional area of the diffusion pathway, the greater the total number of molecules that diffuse.
- Conversely, the greater the distance the molecules must diffuse, the longer it will take the molecules to diffuse the entire distance.
- Finally, the greater the velocity of kinetic movement of the molecules, which is inversely proportional to the square root of the molecular weight, the greater the rate of diffusion of the gas.

Time interval of diffusion :

- Diffusion of oxygen and carbon dioxide occurs because of a pressure gradient.
- The diffusion of O2 and CO2 will continue until equilibrium is reached between the two gases; this is usually accomplished in about .25 second out of .75 sec total.
- Under normal resting conditions, the total transit time for blood to move through the A/C system is about 0.75 second.

Feedback

Active space



Perfusion limited gas transport.

Exercise and diffusion :

- During exercise, the transit time can be reduced to as low as .40 seconds. Increased cardiac output, decreased transit time (less time spent in the capillary in front of a alveolus).
- Since only 0.25 seconds required for complete diffusion – normal patient can maintain oxygenation during exercise.

Diffusion during exercise :

- In the presence of certain pulmonary diseases, the time required to achieve oxygen equilibrium in the A-C system may not be adequate.
- Such diseases include alveolar fibrosis, alveolar consolidation, and pulmonary edema.

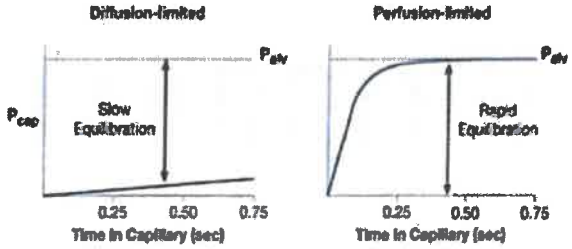
Clinical application of Fick's law :

- A decreased alveolar surface area (ie. Atelectasis) decreases the ability of O2 to enter the pulmonary capillary blood.
- A decreased alveolar O2 pressure (ie. High altitudes) reduces the diffusion of O2 into the pulmonary capillary blood.
- An increased alveolar tissue thickness (ie. Pulmonary fibrosis, pulmonary edema) reduces the movement of O2 across the A-C system.

Feedback

Active space

Diffusion of gases

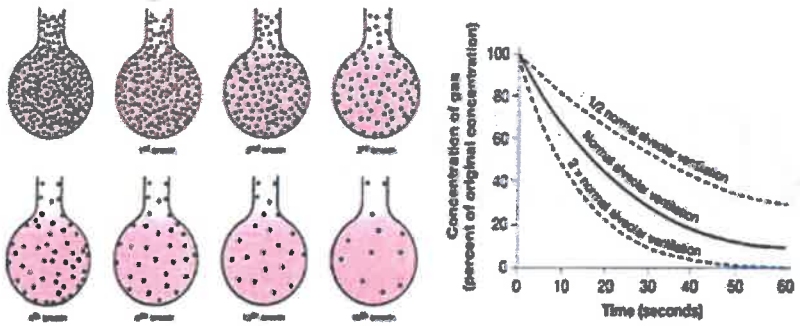


Alveolar ventilation and gas diffusion :

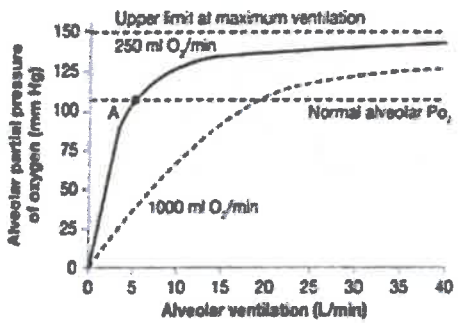
Concentration of oxygen in the alveoli is more during initial ventilation.

As the ventilation increases the oxygen in the alveoli gets diluted.

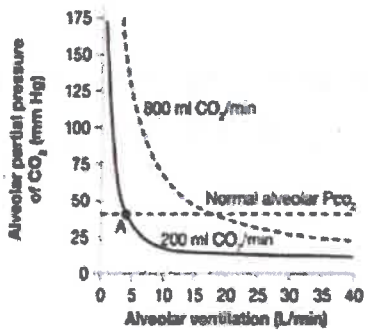
When the demand of oxygen increases in case of hypoxia, burns the respiratory rate increases to maintain the oxygen levels inside the alveoli.



Alveolar ventilation.



Alveolar ventilation according to demand of oxygen.



Alveolar ventilation in increased CO_2 levels.

Feedback

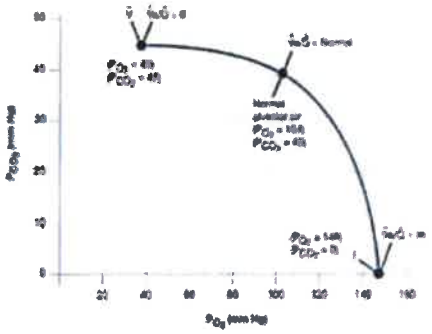
In case of increased carbondioxide levels the alveolar ventilation increases to maintain the required oxygen levels.

Perfusion of gas

00:28:48

Effect of perfusion on alveolar gas transfer across A – C membrane :

Ventilation is zero :
V/Q = 0.
Ventilation is zero while perfusion is present.
Partial pressures will mimic that of venous gas because the venous capillaries by-passes and directly ends in arterial end.
There is no gas exchange.
Arterial partial pressure is similar to gases in venous end.
This is called shunt.



Ventilation perfusion ratio.

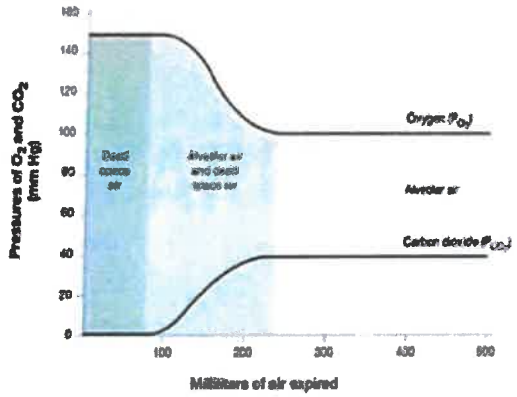
Normal lung :
Ventilation and perfusion is present.
There is $\uparrow PO_2$ $\downarrow PCO_2$.
Gas exchange takes place.
Takes place in normal lung.

Ventilation is present but no perfusion :
Ventilation is positive but perfusion is zero.
V/Q is infinity.
Venous end is not communicating with alveoli , so the alveoli is having arterial oxygenation.
Arterial oxygen concentration is equivalent to PH49.
There is no carbondioxide transfer.
This is called dead space.

Concept of dead space :
Two types :
Anatomical dead space : Does not take part in gas exchange.
Physiological dead space : Gas in the alveoli that does not have perfusion contributes to physiological dead space.

Active space

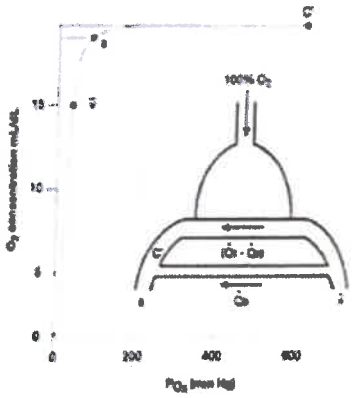
Initial breath will have gas present in anatomical dead space and the breath between 100 to 200 milliseconds will have gas combined with alveolar air and dead space air.
After reaching a plateau it will have air from alveolar ventilation.



Dead space.

Shunt:

- Some part of pulmonary capillary blood is not oxygenated and a part of cardiac output goes to bronchial vessels.
- Some of the alveoli are not ventilated.
- ↑ in Physiological shunt → Deoxygenated blood leaving the lungs is ↑ (Base of lung).
- ↑ in Physiological dead space → Wasted ventilation proportion is ↑ (Apex of lung).



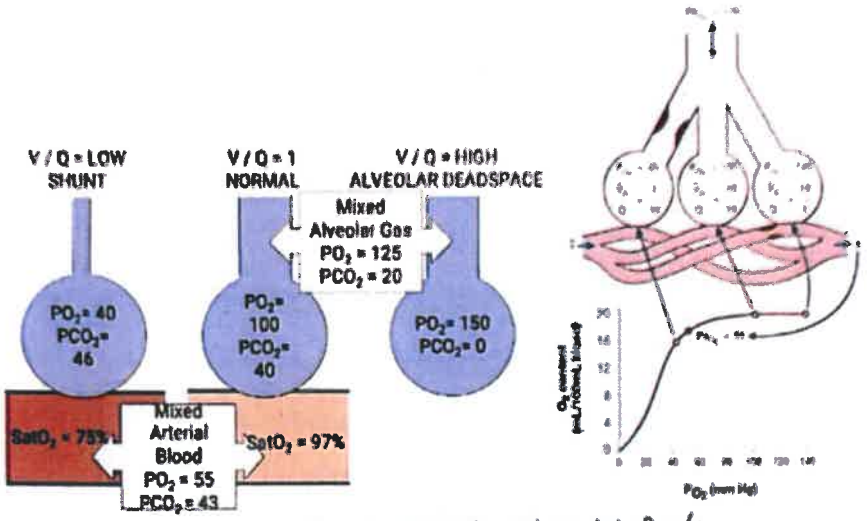
Shunt.

$$\frac{Q_{PS}}{Q_T} = \frac{Ci_{O_2} - Ca_{O_2}}{Ci_{O_2} - Cv_{O_2}}$$

This formula is derived from Fick's principle.
Dead space is calculated by the formula:

$$\frac{V_{D phys}}{V_T} = \frac{Pa_{CO_2} - PE_{CO_2}}{Pa_{CO_2}}$$

Active space



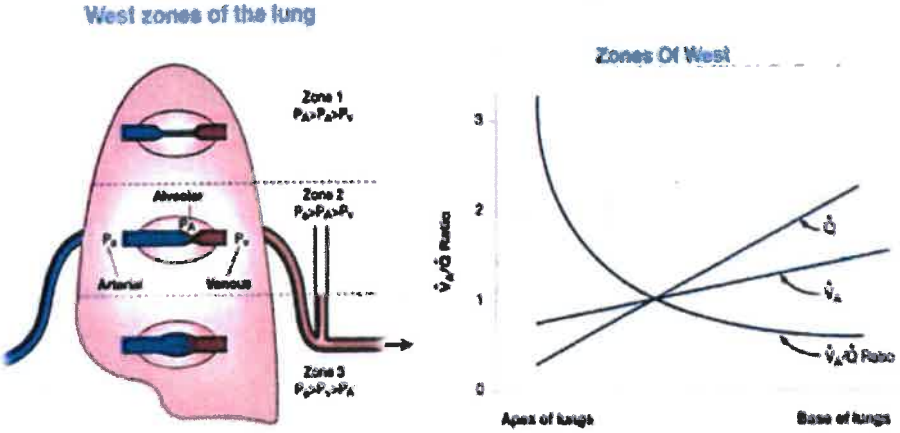
Three compartment model of V/Q.

more shunt → more hypoxia (↓PO_2).
more dead space → more carbondioxide retention.

Inspite 100% oxygenation if there is no increase in saturation it indicates that tehre is increased shunting. It is also seen in severe diffusion restriction.

Zones of west :

Zone I : Apex of the lung ($P_A > P_a > P_v$) → Increased dead space.
Zone II : $P_a > P_A > P_v$ → Normal oxygenation.
Zone III : $P_a > P_v > P_A$.



west zone of lung.

Active space

Fourth zone :

- In this zone the interstitial pressure is higher than the alveolar and pulmonary arterial pressures.
- Eg: Pulmonary edema, Interstitial pneumonia.
- Interstitial pressure is determined by the oncotic pressure.

Pinterstitial >Ppa>Ppv>Palv.

Oxygen transport :

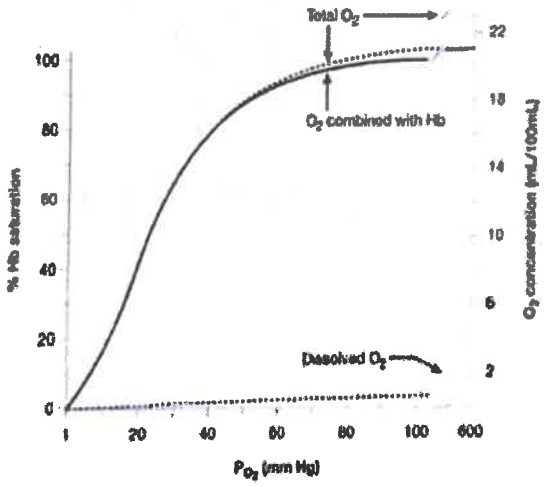
- Linear relation of dissolved Oa in blood with PaOa.
- ↑ PaOa → ↑ in Oa content.
- Oa content ↑ 0.003 ml/100ml blood for 1mm ↑ in PaOa.
- At 21% Oa, dissolved Oa content is 2%, at 100 %----10%.
- Hb binding of Oa is Non-Linear.
- Binding to Hb increases at low Poa...levels at PaOa>40mm hg.....flattens at Paoa>100mmhg.
- Oa binds reversibly to Hb.
- Each Hb molecule binds to 4 Oa molecule, carrying 1.34 ml Oa/gm Hb.
- Total CaOa = CaHb + Ca dissolved in blood.

Blood oxygen equilibrium curve 00:54:10

The curve is sigmoid in shape.

P50 is the POa at 50% saturation.

The P50 quantifies the affinity of Hb for Oa.



Oxygen hemoglobin dissociation curve.

Active space

Shift to left :

(↑ O2 affinity to Hb)

- ↑ in Fetal Hb.
- Alkalotic Ph > 7.45 ; Soda bicarb infusion.
- ↓ in body temp.; heart surgery.
- ↓ in 2-3 DPG (PT and RDS).
- ↓ in Pco2 ; hyperventilation.
- Same level of Spo2 can be obtained at lower Pao2.

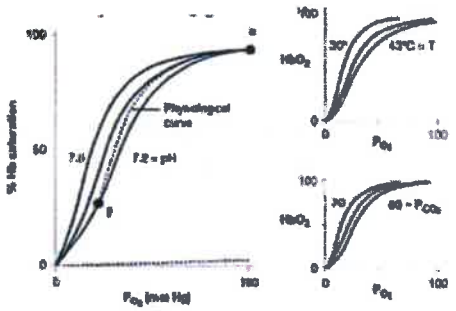
Shift to right :

(↓ O2 affinity to Hb)

- ↓ Fetal Hb; transfusion of adult bld.
- Acidic pH <7.35.
- ↑ in body temp.; Fever.
- ↑ in 2-3 DPG; high altitude, after birth.
- ↑ in Pco2; Co2 retention (Bohr effect).
- Higher level of Pao2 needed to achieve a particular Spo2 level.

Bohr effect :

- ↓ in pH/ ↑ in pCo2 /both ,shifts curve to Rt, in adult & fetus both.
- -Δ log P50/- Δ pH = Bohr effect, -0.48 in adult , -0.44 in newborn.
- Larger at a varying Pco2 than, at fixed Pco2 with varying met acidosis
- (-0.48 vs -0.44).
- Acute change in pH by 01, Changes P50 by 3mm hg.
- Effect is most pronounced in 2-3 DPG depleted blood and as Spo2 ↓.



Bohr effect.

Haldane's effect :

- Pul Arterial blood has low O2 and high Co2 → Passes through lung capillary, releases Co2 → Local pH is raised, O2 binds to Hb at low Pao2 → Conc gradient for O2 diffusion , alveoli to capillary bld is maximized.
- Syst art bld has high O2 and low Co2 → Enters tissue capillary where Co2 is high, pick up Co2 → pH and hence O2 affinity lowers → Allows Hb to release O2, without decrease in Pao2.

Feedback

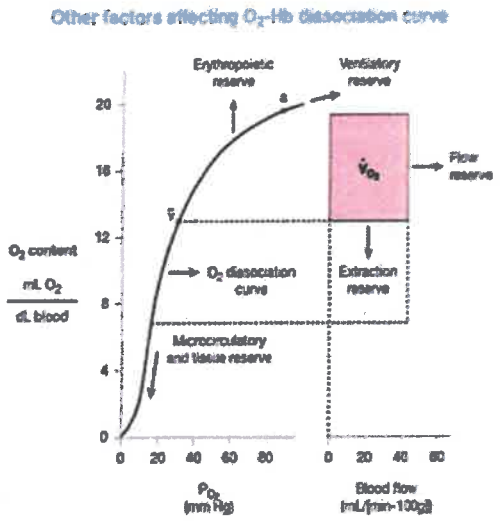
Active space

Effect of 2,3 DPG on Hb -O2 curve :

- Competes at O2 binding site on β globin chain.
- Most important phosphate in RBC (4.5 micromol/ml).
- On oxygenation , it is extruded .
- It altering pH in Erythrocytes, reducing O2 affinity via Bohr effect.
- Level depends on Gest. age, postnatal age, pH, Hb level, oxygenation and RBC enzyme pyruvate ⅌ hexokinase.
- Effect of 2,3 DPG on fetal Hb is 40% of adults, functioning fraction is low (binding constant is low).

Other factors affecting O2- Hb dissociation curve :

- metabolic rate of peripheral tissue activate local regulatory mechanism.
- Arterial blood flow and venous return are modulated.
- Neuro-humoral factors affect cardiac contractility.
- Blood viscosity and volume of blood also determines CO.
- A normal load of 4ml of O2/ Kg body mass increase 15 folds in response to carotid, aortic and brainstem chemo-receptors.



Carbondioxide exchange :

	Difference between CO_2 and O_2
Partial pressure	PCO_2 difference btw arterial and venous is much lower, because CO_2 more soluble in blood
Hypoventilation	$PAO_2 = PIO_2 - (PACO_2/R) + F$ A normal R = 0.8 magnifies PaO_2 changes for a given $PaCO_2$ change.
Membrane diffusion capacity	$CO_2 > O_2$, because CO_2 solubility is much greater $D=[solubility/MW]_{gas} * [area/thickness]_{membrane}$
Equilibrium	Similar for both, CO_2 slower than expected because slow chemical rxns
Shunt and V/Q mismatch	Small for CO_2, due to: (a) CO_2-blood equilibrium curve is steep (b) ventilatory control will increase overall V* to restore $PaCO_2$

Feedback

Alveolar gas equation

01:07:29 Active space

$PAO_2 = PIO_2 - 1.2\ (PaCO_2)$

where $PIO_2 = FIO_2\ (PB - 47\ mm\ Hg)$

Except in a temporary unsteady state, alveolar PO_2 (PAO_2) is always higher than arterial PO_2 (PaO_2). As a result, whenever PAO_2 decreases, PaO_2 also decreases. Thus, from the AG equation:

- If FIO_2 and PB are constant, then as $PaCO_2$ increases both PAO_2 and PaO_2 will decrease (hypercapnia causes hypoxemia).
- If FIO_2 decreases and PB and $PaCO_2$ are constant, both PAO_2 and PaO_2 will decrease (suffocation causes hypoxemia).
- If PB decreases (e.g., with altitude), and $PaCO_2$ and FIO_2 are constant, both PAO_2 and PaO_2 will decrease (mountain climbing leads to hypoxemia).

$P(A-a)O_2$:

- $P(A-a)O_2$ is the alveolar-arterial difference in partial pressure of oxygen. It results from gravity-related blood flow changes within the lungs (normal ventilation-perfusion imbalance).
- PAO_2 → Calculated based on FIO_2, $PaCO_2$, and barometric pressure.
- PaO_2 → measured on an arterial blood sample in a blood gas machine.
- Normal $P(A-a)O_2$ ranges from at 5 to 25 mm Hg breathing room air.
- A higher than normal $P(A-a)O_2$ means the lungs are not transferring oxygen properly from alveoli into the pulmonary capillaries.
- Except for right to left cardiac shunts, an elevated $P(A-a)O_2$ signifies some sort of problem within the lungs.

Physiological causes of low PaO_2:

Non respiratory.	$P(A-a)O_2$
Cardiac right to left shunt.	↑.
Decreased PIO_2.	Normal.
Low mixed venous oxygen content.	↑
Respiratory.	**$P(A-a)O_2$.**
Pulmonary right to left shunt.	↑
Ventilation perfusion imbalance.	↑
Diffusion barrier.	↑
Hypoventilation(Increased $PaCO_2$).	Normal.

Feedback

RESPIRATORY PHYSIOLOGY PART II

Active space

Introduction 00:00:21

Chest wall mechanics :

Muscles involved :

- Diaphragm.
- External intercostal.

Inspiration mechanics :

- Diaphragm goes down.
- Chest wall moves (Outward & upward).
- Increase in AP & transverse diameter.
  - Outward movement : Pump Handle.
  - Upward movement : Bucket handle.

Respiratory regulation 00:02:23

Respiratory centers :

1. medullary center :

Dorsal respiratory group :

- Responsible for inspiration.
- Input : Peripheral chemoreceptors & mechanoreceptors (Via the vagus & glossopharyngeal nerve).
- Output : Phrenic nerve.

Ventral respiratory group :

Responsible for expiration.

2. Pontine center :

Apneustic center :

- Role : Controls the intensity of breathing.
- mechanism : Promotes deep gasping inspiration by ⊕ of the dorsal respiratory group and ⊖ of the pneumotaxic center.

Feedback

Active space

Pneumotaxic center :

- Role : Smooth transition from INS to EXP.
- Mechanism : Vagus → ⊕ Pneumotaxic center → ⊖ DRG.

Receptors :

- Central chemoreceptors in the medulla oblongata.
- Peripheral chemoreceptors in aorta & carotids (Carotid body) via CN IX & CN X.
- Mechanoreceptors in the airways & respiratory muscles.

Peripheral chemoreceptors :

- Peripheral chemoreceptors present in aorta & carotids (Carotid body).
- Cell type : Type II glomus cells.
- Type II glomus cells when PO2 normal : Constant K efflux.
- Type II glomus cells when PO2 low : ↓ K efflux → ↑L-Type Calcium influx → Dopamine NT → ⊕ CN IX & CN X.

Central chemoreceptors CO2 :

Blood.	$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
BBB.	↓↑
CSF.	$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$

Sensitivity of peripheral chemoreceptors to oxygen :
Location : Carotid body and aortic body.
Function : measure PaO2 (< 60 mm Hg), CO2 and pH.
Mechanisms of action :
↑ CO2, ↓ O2, and ↓ pH → ↑ sympathetic innervation.
modulate breathing via the respiratory center in the medulla.

Regulation :
Deep inspiration :
DRG → ⊕ Inspiratory group of neurons in VRG (VRG has both INS & EXP group of neurons which are ⇌) = Deep inspiration.

Expiration :
Once inspiration is maximum → Stretch receptors → CN IX & CN X → ⊖ DRG → ⊕ Stimulation of expiratory group of neurons from VRG = Expiration.

Feedback

Inspiration stimulus :

- Prebotzinger complex ¶ cortex.
- Prebotzinger complex : Involuntary respiratory control.
- Cortex : Voluntary respiratory control.
- Prebotzinger : Rhythmic firing of neurons → ⊕ inspiratory center in DRG.

Reflex :

- Cough reflex.
- Sneeze reflex.
- J receptors :
  - Sense pulmonary edema.
  - Cause shallow breathing.

Injury :

At the level of cortex :

- Cortical control of breathing lost.
- Regular pattern of breathing present (Due to Prebotzinger complex).
- Vagus intact : Regular respiration.
- Vagus not intact : RR ¶ TV decreased.

Lesion between pneumotaxic ¶ apneustic center :

- Vagus intact : Regular respiration (Not as smooth as in cortical injury).
- Vagus not intact : Apneustic breathing.

Lesion at apneustic center :

- Vagus intact : Irregular respiration.
- Vagus not intact : Ataxic breathing (Slow and irregular respiration).

Lesion below medulla : Apnea.

Concepts of respiratory control :

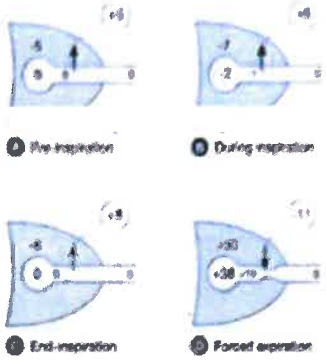
- Respiration is controlled via a negative feedback system in (CNS).
- Central neuronal processing and integration in the brainstem is hierarchical.
- Brainstem neurons have cellular ¶ membrane properties that allow them to beat (cycle) spontaneously. These properties play a role in generating rhythmic respiratory neuronal behavior.
- Respiratory rhythm generation in central neurons is most likely a result of integration between network, synaptic, cellular ¶ molecular characteristics.
- Afferent information is not essential for generation of breathing, but modulates respiration.

Active space

Terminologies and lung volumes 00:22:53

Terminologies :

- Paw : Airway pressure.
- Patm : Atmospheric pressure.
- Ppl : Pleural pressure.
- Pes : Esophageal pressure.
- Transpulmonary pressure : Palv-Ppl.
- Transthoracic pressure : Ppl-Patm.
- Trans-respiratory pressure : Paw-Patm.



movement of gas in lungs.

Boyle's law : $P_1V_1 = P_2V_2$

Boyle's law states that pressure and volume are inversely related within a closed system. This means that as volume increases, pressure decreases, and vice versa.

Expiration happens because of 2 properties : Elasticity of the lungs and the chest wall.

Physiological lung volumes :

Tidal volume (TV) : Volume of air inhaled & exhaled in a normal breath at rest. ~ 500 mL or 7 mL/kg.

Inspiratory reserve volume (IRV) : maximum volume of air that can still be forcibly inhaled following the inhalation of a normal TV.

Expiratory reserve volume (ERV) : maximum volume of air that can still be forcibly exhaled after the exhalation of a normal TV.

Residual volume (RV) : Volume of air that remains after maximum exhalation.

Total lung capacity (TC, TLC) : TC = VC + RV (Volume of air in the lungs after maximal inhalation).

Vital capacity (VC) : VC = TV + IRV + ERV (Difference in lung volume between maximal exhalation and maximal inhalation).

Functional residual capacity (FRC) : FRC = RV + ERV (Volume of air that remains in the lungs after the exhalation of a normal TV).

Feedback

Flow relations

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Flow relation with resistance :

Poiseuille equation = (8 × viscosity × length)/(π × radius⁴).

Laminar flow. Turbulent flow.

Viscosity :

- Viscosity creates friction.
- The higher the viscosity, the higher the resistance.

Laminar flow :

- Viscous force > inertial force.
- Lesser heat production.
- Peripheral airways.
- Reynolds number : <2300.

Turbulent flow :

- Inertial force > viscous force.
- More heat production.
- Poiseuille equation = (8 × viscosity × length)/(π × radius⁴).
- Larger airways.
- Reynolds number : >2300.

$$Re = \frac{\rho v d}{\eta}$$

Note :

- Reynolds number : Flow rate × length × density.
- Heliox helps in reducing resistance.

Flow volume relationship (Dynamic flow limitation) :

Flow = Volume/Time.

Velocity = Distance/Time.

Velocity = Flow/Area.

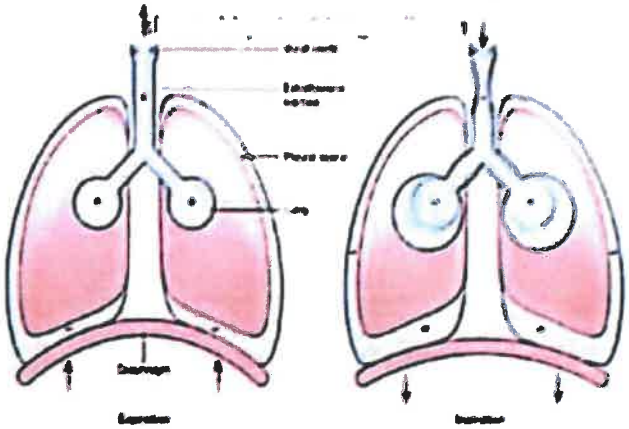
Expiratory flow has a limit after which there wont be any increase in the flow called as dynamic flow limitation.

TAP : Paw-Palv. Keeps the airway open.

Feedback

Active space

Normal Inspiration and Expiration :



Inspiration and expiration

Obstruction in extra thoracic airway :
Atmospheric pressure in the extra thoracic airway = (+).
Trans airway pressure = (-).
Peribronchial pressure = (-).
Extra thoracic airway gets compressed = Stridor.

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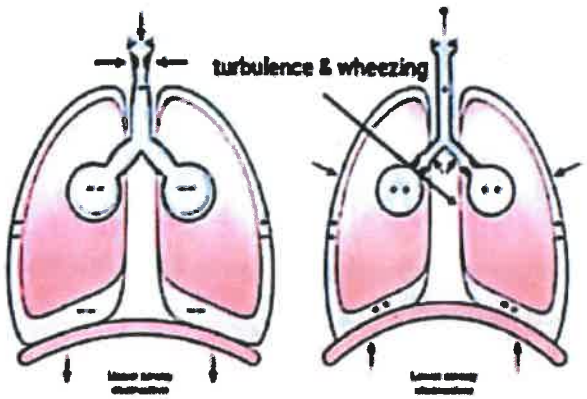

Extra & intra thoracic upper airway obstruction

In intra thoracic obstructive diseases : Limitation of expiratory flow
In extra thoracic obstructive diseases : Limitation of inspiratory flow

Feedback