**GAS TRANSPORT**

Oxygen

Oxygen is transported in the blood in 2 forms

1. Dissolved in plasma and 2. reversibly bound to hemoglobin

Dissolved Oxygen

Henry's law: The amount of a gas which dissolves in unit volume of a liquid of a given temperature is directly proportional to the partial pressure of the gas in the equilibrium phase.

Ostwald solubility co-efficient for $0_2$ at $37^0$C = 0.003ml/100ml blood/mm Hg

Therefore $P0_2$ of 100mmHg ⟶ dissolved $0_2$ = 0.3m/100ml blood

Total content of $0_2$ in arterial blood is 20 ml $0_2$/100ml blood

The tissue $0_2$ consumption is 250ml/min at rest, there is thus a need for extra way to transport $0_2$.

Oxygen carriage by Hemoglobin

Each hemoglobin molecule has 4 Fe combining with $40_2$ molecules. When it is carrying $40_2$ it is said to be fully saturated. One gram of Hb binds reversibly with 1.34ml $0_2$ .

$P0_2$ determines Hb saturation. Percent Hb saturation is a measure of the extent to which the Hb present is combined with oxygen and can vary from 0 to 100%.

The saturation of the Hb with oxygen depends on the $P0_2$ of the blood: $0_2$ already bound to Hb does not contribute to $P0_2$.

Relationship between $P0_2$ and percentage saturation is complex

$0_2$ – Hb dissociation curve is S shaped and not linear

At $P0_2$ = 100mg, Hb is 97.5% saturated. A large change is $P0_2$ here results in only a small change in percentage Hb saturation, therefore $P0_2$ can fall nearly 40% in the lungs. even at $P0_2$ =

60mmHg, hemoglobin is 90% saturated. From 60-760mmHg $P0_2$, Hb saturation only changes 10%, this provides margin of safety in $0_2$ carrying capacity of blood.

At $P0_2$ = 40mmHg Hb is 75% saturated. From 0-60mmHg, a small drop leads to a steep drop in the Hb saturation, Hence, when $P0_2$ falls even a little in systemic capillaries, a large amount of $0_2$ dissociates from Hb. This facilitates unloading of $0_2$ from Hb in tissues. Pulse oximeter can non invasively measure oxygen saturation.

**Modification of 0xyhemoglobin dissociation curve**

Affinity of Hb for $0_2$ is measured by the $P_{50}$ which is the $P0_2$ when Hb is 50% saturated.

At a pH = 7.4 T = $37^0$C and BE = 0 $P_{50}$ = 26.3mmHg. Decreased affinity of hemoglobin for oxygen leads to a shift of the curve to the right (Bohr effect), and an increased $P_{50.}$ Increased affinity of hemoglobin for oxygen leads to a left shift of the curve and a decreased $P_{50.}$

Increased metabolism leads to increase in tissue temperature, acidity and $C0_2$. An increase in all these, right shifts the $0_2$ – Hb curve.

Carbon monoxide left shifts the $0_2$ – Hb curve so that less $0_2$ is delivered to tissues for a given level of $P0_2$

**$C0_2$ TRANSPORT**

$C0_2$ is transported in the blood in 3 ways

a. 10% is dissolved in plasma. Dissolved $C0_2$ depends on $PC0_2$. It also gives obeys henry's law. $C0_2$ is 24 times more soluble than oxygen .b. 30% is bound to Hb

$C0_2$ bound to the globin portion of hemoglobin not heme portion as carbaminohemoglobin. unoxygenated Hb binds tighter to $C0_2$ than does oxygenated Hb.

Dissolved $C0_2$ depends on $PC0_2$. It also gives obeys henry's law. $C0_2$ is 24 times more soluble than oxygen

c. 60% of $C0_2$ is transported as $HC0_3^-$.

$C0_2 + H_20 \longleftrightarrow H_2C0^-_3 \longleftrightarrow H^+ + HC0^-_3 \longleftrightarrow 2H^+ + C0^{2-}_3$

Carbonic anhydrase catalyses the 1st reaction in the RBC. $HC0_3$ then diffuses out of the RBC. Erythrocyte membrane is relatively impermeable to $H^+$ so $HC0_3^-$ diffuses alone. $HC0_3^-$ diffuses out into plasma and chloride diffuses into RBC – chloride shift. Most $H^+$ that is left binds to Hb (reduced Hb has a greater affinity for Hydrogen ion than $HbO_2$

These reactions are reversed once the blood reaches the pulmonary capillaries and $CO_2$ leaves the blood and enters the alveoli.

**Haldane effect**: removing $0_2$ from the Hb increases its ability to pick up $C0_2$, $H^+$. Bohr effect and Haldane effect feeds into one another. Increased $CO_2$ and Hydrogen ion lead to an increased oxygen release. The increased release of oxygen increases the $CO_2$ and Hydrogen ion binding capacity of hemoglobin.

$C0_2$ dissociation curve depicts relationship between $PC0_2$ and total content of $C0_2$ in the blood. In the physiological range, the curve is almost linear.

Therefore changes in $PC0_2$ are accompanied by corresponding changes in $C_{c02}$.

- The position of the dissociation curve is the dependent upon $Hb0_2$ saturation – Haldane effect
- The slope of the $C0_2$ curve is much steeper in the physiological range than for $0_2$.

**Control of Respiration**

Quite unlike the heart where the role of CNS is modulatory. The CNS input is required for breathing to occur at all.

Various part of the brain stem are involved in control of rhythmic breathing.

Neural control of respiration includes

1. factors responsible for alternating inspiration/expiration rhythm
2. factors that regulate magnitude (rate, depth) of ventilation
3. factors that modify respiratory activity to serve other purposes.

**Medullary respiratory center**

**DRG** originates from NTS. It lies within the reticular formation of the brain stem. They are mostly inspiratory neurons. Cells within the DRG are thought to possess inherent rhythmicity generating bursts of neuronal activity to the diaphragm and inspiratory muscles.

**VRG** – nucleus retroambiguus. both inspiratory and expiratory neurons, both remain inactive during quiet breathing. Important in active expiration. Only during active expiration do impulses travel to expiratory muscle. The neurons of the expiratory VRG are quiescent during tidal respiration.

Generation of respiratory rhythm comes from the rostral ventromedial medulla. It drives the rate at which inspiratory neurons fire.

**Apneustic Centre**

Situated in the lower pms in the floor of the $4^{th}$ ventricle near the middle cerebellar peduncle. impulses from these neurons inspiratory DRG and increased ramp AP's.

Section of the brainstem immediately above this group ⟶ apneusis.

Prolonged inspiratory gasps interrupted by transient expiratory efforts. Apneustic center prevents inspiratory neurons from being turned off.

**Pneumotaxic Centre**

Located in the upper pons. Acts to limit the activity of the inspiratory DRG. Without pneumotoxic brakes, apneusis : pronlonged inspiratory gasps with very brief interrupting expirations.It regulates inspired volume and rate of inspiration.It acts only as a modulator, as normal respiratory rhythm can exists in its absence.

Cortex – involved in voluntary control of respiration. the hypothalamus and the limbic system can alter pattern of breathing i.e. affective states like fear, rage.

The brain stem respiratory centers are influenced by

(a) carotid and aortic chemoreceptors

(b) central chemoreceptors

(c) cerebral blood flow

(d) reflexes from lungs, inflation reflex

(e) carotid, aortic baroreceptors

(f) muscle spindles in respiratory muscle

(g) thoracic chemo-receptors

(h) peripheral/somatic receptors (1) temperature

(2) Pain receptors

(3) Mechanoreceptors

(i) cerebral cortex – emotion, breath holding

**Central chemoreceptors**

These are located near the ventral surface of medulla in the vicinity of exist of $9^{th}$ and $10^{th}$ cranial nerves. They monitor $PC0_2$. An increase in $PC0_2$ results in more $C0_2$ crossing blood-brain barrier. The $C0_2$ reacts with water to form bicarbonate and $H^+$. The increase in $H^+$ is detected by the central chemoreceptors.

The central chemoreceptors are bathed in the brain ECF. The composition of ECF is determined by CSF, local blood flow and local metabolism. CSF contain less protein than blood = poorer buffering capacity. Change in $PC0_2$ will change pH of CSF more than it changes pH of blood.

**Peripheral Chemoreceptors**

These receptors are very sensitive to change in blood pH and cause changes in ventilation. They respond primarily to decrease $P0_2$. They are responsible for all the ventilatory response to hypoxia. The peripheral responses to increased $PC0_2$ are lesser than those of the central chemoreceptors.

**Respiratory Cycle**

Respiration works by changing the volume of the chest cavity. Before the start of inspiration, respiratory muscle is relaxed. Intravascular pressure = atmospheric pressure and so no air is flowing.

- Atmospheric pressure and so no air is flowing
- At the onset of inspiration, inspiration muscle (diaphragm) contract, which results in enlargement of the thoracic cavity
- As the thoracic cavity enlarges, the lungs are forced to expand to fill the larger cavity

- Because the intra-alveolar pressure is less than atmospheric pressure air follows its pressure gradient and flows into the lungs until no further gradient exists.
- Deeper inspirations are accomplished by contracting inspiration muscle more forcefully and by using accessory inspiratory muscle to enlarge the chest cavity.
- At the end of inspirations the inspiratory muscles relax, the chest cavity returns to the original size and the lungs return to the original size.

Respiratory cycles are generally continuous, however during anaesthesia there may be intervals between cycles.

The inspiratory and expiratory phases of the cycles are generally smooth and symmetrical. The horse is however an exception it had two phases each during inspiration and expiration.

**LUNG VOLUMES**

1. Tidal Volume (TV): The amount of air inspired or expired during normal quiet respiratory cycle.
2. Inspiratory Reserve Volume (IRV): The amount of air which can be inspired above and beyond that which is inspired during normal quiet inspiration.

3. Expiratory Reserve Volume (ERV): The maximal amount of air which may be expired following a normal quiet expiration.
4. Residual volume (RV) : the amount of air remaining in the lungs after a maximal expiratory effort.

In addition to the four volumes which do not overlap, there are four capacities which are made up of two or more of the volumes.

1. Total lung capacities: the amount of air contained in the lungs at the end of maximal inspiration.
2. Vital capacity: the maximal amount of air which can be expired after a maximal inspiration.
3. Functional residual capacity: The amount of air remaining in the lungs after a normal expiration. FRC = ERV+ RV
4. Inspiratory capacity (IC): The maximal amount of air which can be inspired after a normal expiration.
5. Forced vital capacity (FVC): Total volume expired from maximum inspiration to maximum expiration.
6. Forced expiratory volume in one second ($FEV_1$): The maximum volume that can be expired in one second. $FEV_1$= 80% of VC.

**VENTILATION.**

This is the process whereby gas in a closed place is renewed or exchanged. It is the process of exchanging the gas in the airways and alveoli with gas from the environment.

Total Ventilation: is the volume of air moved into or out of the airways and alveoli over a certain period of time.

Minute Ventilation: is the total volume of air moved into or out of the alveoli and airways in one minute. $V_E=Fv_{T.}$ Where $V_E$ = minute volume of ventilation (expired), f= respiratory frequency in cycles per minute. $V_T$ = average tidal volume in milliliters.

Dead space ventilation: is the volume of air that does not take part in gas exchange over a certain period of time.

Alveolar Ventilation: is determined by subtracting dead space ventilation from total ventilation.

Alveolar ventilation per minute $V_A$ is the volume of air that contributes to diffusional exchange of gas each minute. $V_A= f( V_T-V_D) = Fv_A$. Where f = respiratory frequency, $V_T$ = tidal volume, $V_D$= dead space volume, $V_A$= Alveolar volume

**VENTILATION AND PERFUSION RELATIONSHIP**

The amount of alveolar ventilation in relation to pulmonary capillary blood flow i.e the V/Q ratio determines the adequacy of pulmonary gas exchange. There is no perfect matching of ventilation to perfusion in most alveoli. Non uniform distribution results in alveolar units with varying ratios of ventilation to perfusion. V/Q.

Alveoli at the apex are overall poorly ventilated and perfused but relatively better ventilated than perfused. i.e high V/Q ratio. This results in increased $PAO_2$ and decreased $PACO_{2.}$

Alveoli at the base are well ventilated but better perfused than ventilated i.e low V/Q ratio. $PAO_2$ will be low and $PACO_2$ will be high.

Alveoli at the centre is ideal, it receives ventilation and blood flow with a V/Q ratio of 0.8.

Units with low V/Q ratios have a greater effect on overall gas exchange since they receive greater proportion of total pulmonary blood flow. A high V/Q unit cannot compensate for the impact of low V/Q unit. It raises $PO_2$ which result in more dissolved oxygen but not $HbO_2$.