وَقُل رَّبِّ زِدْنِي عِلْمًا

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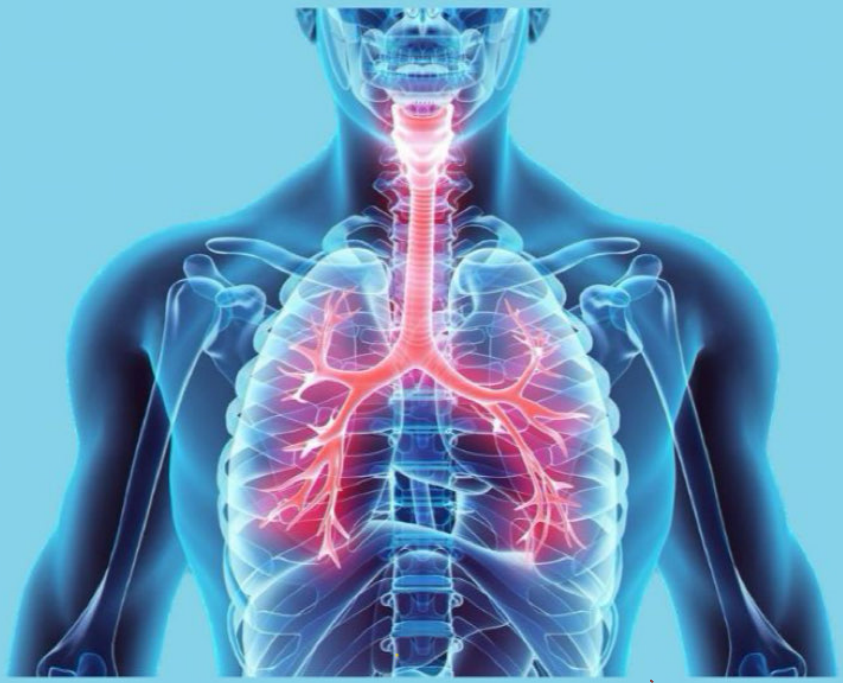
RESPIRATORY SYSTEM

HAYAT BATCH



SUBJECT : Summary for physiology

LEC NO. : 7-9

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ventilation - prefusion relationship lecture (7)

* apex → low ventilation & low prefusion → so not all oxygen is being used → where infection occur so → 2.5 V/Q
* base of the lung has higher rate of ventilation
* prefusion is higher due to gravity but prefusion is higher than ventilation leading that some blood wont be oxygenated → 0.6 → V/Q

(4.5-5 / 5-5.5) = 0.8 → normal V/Q in Rest

so now lets discus what happen in case of

1) shunt : when there is local hypoxia it will cause vasoconstriction so partial blockage of ciradation and the blood will go to the surrounding blood vessels insted why? → due to obstruction in the alveoli so zero ventilation rating the V/Q = 0
so no ventilation the air in the alveoli would be = to the venous blood so
PAO_2 = 40 $PACO_2$ = 45 or 46

2) alveolar dead space : when there is complete cut in circulation leading the prefusion to be around zero
why? → emboli is the most common cause
→ making the alveolar / prefusion = ∞
PAO_2 = 150 $PACO_2$ = 0
why not 100 → lack of CO_2

* the previous situations are called ventilation / prefusion mismatch

in some disease both of these effects might occur, alveolar dead space & shunt like emphysema in COPD

shunted blood is : the venous blood that remains unchanged (passing unfunctional alveoli) → shunted blood / minute called physiological shunt.
↳ decreased amount of PO_2 in arterial will increase in P_{CO_2}

in case of alveolar dead space → CO_2 retention → hypercapnia → hypoxia
→ hyperventilation → correct the CO_2 retention

* during excercise the ventilation & prefusion increase leading to decrease the inequality in the ratio → more uniform topographical distribution of blood flow

oxygen content is : the amount of blood dissolved in 100 ml in blood

so during excercise the content in arterial stay the same due to increase of ventilation while the O_2 content in venous blood is reduced due to the increase dissaccation of O_2 to the cell during excercise due to increase in demand

Pathophysiology

mismatch of this ratio is caused by

① Reduced prefusion of the lungs
typically embolism → higher ratio
$PACO_2$ ↓ PAO_2 ↓ PaO_2 ↓ leading
to dyspnea and tachypenea

② Reduce ventilation
pneumonia → exudate
COPD & asthma → less air out
respiratory distress syndrome → collapse
↳ lead to hypoxemia but the rest of the lung can remove the CO_2
so hypercapnia doesn't occur

③ both
emphysema
→ bronchial obstruction → ↓ ventilation V/Q = 0
Shunt
→ enlargment of air sacs → No prefusion

limitation of movment of gases due to diffusion co-efficient $CO_2 > O_2$
notice that O_2 is transported by Hb instead of plasma 230 ml/min

the PO_2 in LV is less than PaO_2 why is that?

1) deoxygenated blood from the base
2) venous drainage to the pulmonary vein from the bronchial arteries
3) coronary circulation microarteries drain directly to the left ventrical

O_2 is transported by Hb (97%) & plasma (3%)

Hb is 4 proteins subunit with heme group attached to each protein
when no O_2 in it it is harder to bind with oxygen T state
while when it's bind with O_2 it increase its affinity to O_2
called R state

Functions of hemoglobin

1) O_2 transport
2) CO_2 transport
3) buffer
4) transport NO vasodilator

transport of O_2 by Hb
it gives sigmoid shaped due to the T & R state
the saturation of O_2 in arterial blood = 97%
while in venous is 75%, blood content 20 → 15

it can buffer oxygen concentration changed in atmosphere
so even when $PaO_2 = 60$ about 40% is the saturation of Hb preventing hypoxemia
we need, in exercise the saturation of venous blood is reduced due to ↑ in O_2 consumption so its about 40% while the saturation of arterial blood is not changed

factor affecting the saturation of Hb (decrease it) → shift to the right

1) bohr's effect → ↑CO_2 ↑H^+ ↓Hb lead to decrease O_2 affinity to Hb → this cause shif to the right around the tissue (systematic) while in pulmonary circulation → not so much → ↑ affinity to O_2

2) increase temperature

3) increase BPG or DPG
diphosphoglycerate a product of glycolysis → how RBCs produce ATP this bind to the deoxygenated Hb making it in T state → less affinity to O_2 it's useful to prevent tissue hypoxia, 1) DPG increase 30% during pregnancy so the mother Hb would have less afinity allowing the O_2 to pass from uterine arteries to the fetal umbilical arteries → HbF → in the fetus has higher affinity & not effected by DPG so even $\downarrow O_2$ in uterine it will take the blood
2) Thyroid hormone, growth hormone
3) high altitude
4) anemia
5) diseases associated with hypoxia such as in congestive heart failure & congestive heart failure
in these situation it help to increase O_2 & the tissue

4) exercise
in exercise DPG, CO_2 & temperature increased
also the myoglobin get excreted to the blood
a protein found in skeletal & heart muscle that have high affinity to O_2 even higher than HbF which bind to one O_2 → dissacciation curve was rectangular hyperbolic rather than sigmoid

now let's talk about CO_2
CO_2 need very little difference in gradiant due to the high solubility, 1 between blood & tissue & 5 between blood and alveoli, hyperventilation should cause increase in peripheral tissue P_{CO_2}

only 4 ml/dcl of blood is transfered to the lung

methods of co transport:
1) transport CO_2 in dissolved state 7% carbaminohemoglobin
2) transport CO_2 in combination with hemoglobin being attached to the a.a of globulin not the heme group
* it also decrease the Hb affinity to O_2
3) transport CO_2 in the form of bicarbonate ion (70%) in dissolved form
* CO_2 blood concentration in veins = 2.7
* CO_2 blood concentration in arteries = 2.4
so 0.3 ml/dc is transported

how is the CO_2 is being transported as bicarbonate

1) enter the RBCs bind with water forming carbonic acid
2) carbonic anhydrase convert it to bicarbonate & H^+ ions
3) HCO_3^- leave to the plasma & Cl enter to combasenate the loss of HCO_3^- while H^+ bind to the hemoglobin

CO_2 saturation is 52% in the blood passing through the tissue and 48% blood passing the lung only 4% is being transported

binding of O_2 to Hb reduce it's ability to bind with CO_2 & displace CO_2 in carboaminohemoglobin from the blood
release H^+ ions bind with bicarbonate then dissolve to CO_2 & water result & release CO_2 to alveoli

↳ Haldane effect
↳ double the amount of CO_2 released from the blood to the lungs
double the pick up of CO_2 to tissue.

now lets learn about the neurons that control how much we breath and how deep our breaths

we have pacemaker in the brain to control our breathing cycle it generat action potential & then it transfer it to the phrenic nerve & contract diaphragm

Respiratory centers are located

in the brain steam → medulla oblinganta + Pons (above)
» the higher in location the higher in power «
The groups of neuron are :.
① Dorsal respiratory group → inspiration
② ventral respiratory group → expiration
③ Pneumotaxic center → control the rate & depth of breathing
④ Apneustic center → unknown function in human

* there is other neuron that can control the DRG & VRG hypothalamus, Reticular activating system, cerebral cortex & efferent from the vagus glossopharyngeal & somatic nerves

① DRG
located within → nucleus of tractus sorlitarius
they are also the terminal sensation station of vagus & glossopharyngeal nerves (Receive input from receptors)

* they are the pace maker of the basic respiratory rythem → latent period exhilation → no action potential and we need to know that the action potential is in Ramp or crescendo manner → gradual action potential which mean not all of the sudden we take a turn breath we do it in gradual way ↑Ramp ↑ inspired air verce virsa

② Pneumotaxic center
located in the parabrachialis of the upper pons so it can control and overide the DRG so it stop it so it allow this center to control the deepth (tidal volume) & number of breaths
so when it stop the ramp causing decrease in tidal volume while increase the respiration rate
* activating Pneumotaxic center lead to shallow & rapid inspiration
* without it we can still have normal rhythm

③ventral respiratory group VRG
they aren't pace maker & work only in some cases such as in exercise it's located in nucleus ambiguss & nucleus retroambigual, so it works by orders from DRG to assist in when greater ventilation is needed which pass signals to abdominal muscle

④ apneustic centers
in animal it prolonged inspiration by inhibt the switch off of the inspiratory ramp signals but in human it's unknown

· vegal signal → inspiratory inhibitory reflex
how it works? by stimulation of bronchial & bronchilar stretch receptors → afferent signal to the vegus nerve → inhibition of DRG → it is stimulated when tidal volume exceed 1.5 L (protective mechanism)

⑤ Reticular activating system
it's responsible to increase the respiratory drive when we are awake
* it's inhibited while we are sleeping slight ↑ in CO_2
effort of the respiratory muscles which control the intensity of the output

now we are going to study the receptors which provide the respiratory centers with information so they decide how to work according to different situations :.
① chemical receptors ② non-chemical receptors
P_{CO_2} & P_{O_2}

① chemical receptors are
Ⓐ central chemoreceptors :.
they are located in medulla beneth the ventral surface around the IX & X cranial nerves
they are facing the CSF so they could measure the change in CO_2 & H^+ ions in the brain the can't sense any chang in O_2 or H^+ in the blood

②peripheral chemoreceptors :.
they are located in the carotid & aortic bodies → detect change in P_{O_2} & slightly the change in P_{CO_2} & H^+ in the arterial blood how?
Ⓐ aortic bodies → vagus → DRG
Ⓑ carotid bodies → glossopharyngeal → DRG

* central chemoreceptors accately can only sense the change of H^+ ions in the CSF but H^+ cant cross the BBB how it sense it?
→ Co_2 can cross the BBB easily & then it react with H_2O in CSF → H_2CO_3 → $H^+ + HCO_3^-$ so the change in Co_2 change the H^+ then it stimulate the central chemoreceptors

what happen in case of increasing of PCO_2
central chemoreceptors get activated which is going to increase the inspiration & excpiration strength of muscle causing hyperventilation, 85% chang in the respiratory mouthing caused by changed in CO_2 which is sensed by CCR so PCO_2 is the major controller of respiration.

what happen when PO_2 is below 70 mmHg?
Peripheral chemoreceptors sense the change of PO_2 then stimulation of DRG → increase rate & depth of respiration.

* stimulation of respiration is 5 times faster by the peripheral chemo receptors than central chemical receptors

what happen in high altitudes
accumalization which is
PO_2 drops at HA leading to stimulation of peripheral chemical receptors leading to hyperventilation then $\downarrow CO_2$ decrease the $\downarrow H^+$ so central chemical receptors are induced leading to hypoventilation (lower rate the peripheral) but with time the kidney take ove the respiration to correct the alkalosis caused by $\downarrow CO_2$ so central receptor loss their sensitivity

why in anemia doesn't induce hyperventilation?
because peripheral receptors only sense O_2

what happen during excercise?
no body actually know because PO_2 & PCO_2 in arterial blood are the same
theories regarding excercise
1) stimulatory impulses from higher centers of the brain to both respiratory muscle & respiratory centers
2) propriceptive stimulatory reflex to respiratory center

Non-chem receptors
1) voluntery respiration by the cortex
2) limbic system → emotional changes such as fear & rage cause changes in breathing
3) coughing sneezing & even breath holding due to stimulation of pulmonary irritant receptors
4) pulmonary edema & heart failure cause stimulation of J receptor causing dyspnea & tachypnea
5) anesthesia causing respiratory depression
6) Hering Breuer effect (reflex)

Respiratory failure

1) hypoxemic failure: $\downarrow PO_2$ or $\downarrow PCO_2$ → most common <60
2) hypercapnia failure: $\uparrow PCO_2$ >50

Respiratory acidosis

1) Generalized hypoventilation → no respond to change in CO_2
2) obstructive lung disease → reduce alveolar ventilation