Pulmonary Physiology

Pulmonary Physiology

- Control of Breathing
- Mechanics/Work of Breathing
- Ventilation
- Gas transport (including pulmonary circulation)
- Gas Exchange (including diffusion of gas/gas transfer)

- “When you can’t breathe, nothing else matters.”

Control of Breathing

- Keep PCO_2 40 mmHg awake
- Neural Control
- Chemical Control

Neural Control

- Inspiratory inhibition reflex (Hering Breuer); irritant, mechano, j receptors: stimulation in patients with, e.g., interstitial fibrosis, pulmonary embolism, atelectasis
- Stimulation of mechanoreceptors in airways: can cause tachypnea, bronchoconstriction

Chemical control

- CO_2 stimulation
- Hypoxemic stimulation
- H^+ stimulation

Chemical Control: CO_2 stimulation

- Rise in $PaCO_2$ = increase in $[H^+]$ concentration in ECF and ventrolateral surface of the medulla, stimulating ventilation (hyperventilation)
- In turn, dilation of CNS blood vessels by increased CO_2 leads to increased removal of CO_2 and decrease in central CO_2 stimulation; also, the hyperventilation results in lower CO_2 to stimulate. Then, lower CO_2 = brain vessel constriction =buildup in ECF CO_2 again
- **Chronically elevated $PaCO_2$ = increased ECF $[HCO3^-]$ so acute increase in $PaCO_2$ will induce less of a change in $[H^+]$ and therefore less stimulus to ventilation

Chemical Control: Hypoxemic Stimulation

- Peripheral chemoreceptors (carotid body, aorta) respond primarily to low PaO_2; also can respond to PCO_2 and $[H^+]$ as well as decreased blood flow and increased temperature
- Low PaO_2=increased V_E,then decreased arterial and CNS CO_2 and $[H^+]$ = less central stimulus to breathe
- Hypoxic ventilatory depression may be seen early after initial stimulation (10-30 minutes) at altitude

Chemical Control: Hydrogen ion stimulation

- Metabolic acidosis stimulates; alkalosis inhibits breathing primarily through peripheral chemoreceptors, ~7.30 to 7.50
- Acute metabolic acidemia = increased ventilation; then decreased $PaCO_2$ and CNS PCO_2, decreased $[H^+]$, decreased $[HCO3^-]$, and after 24 hours normalization of CNS [H+].
- So, chronically low $[HCO3^{-}]$ = easier to stimulate by CO_2. Conversely, met alkalosis = low VE; eventual increase in CNS $[HCO3^-]$ = more difficult to stimulate by CO_2

Chemical Control of Breathing

- When WOB elevated, PCO_2 not as potent a stimulus to breathe
- Sleep depresses ventilatory stimulation; $PaCO_2$ rises by several mmHg in sleep (most in REM sleep)

Mechanics of breathing

- Total mechanical work of breathing=overcoming elastic-resistive work+ flow-resistive work; in normal individual this applies to INSPIRATION.
- Severe airway obstruction:, may need expiratory work to overcome EXPIRATORY flow resistance
- Asthma= normal elastic resistance, high flow resistance
- Pulmonary fibrosis/stiff lungs (eg ARDS)= normal flow resistance, high elastic resistance and need for work to overcome this.

Mechanics of breathing

- Elastic forces: recoil of lungs and recoil of chest wall =equilibrium at FRC (functional residual capacity)
- *Elastance*= Δ P/ Δ V; this is the distensibility of the respiratory system (lungs, chest wall)
- *Compliance*= Δ V/ Δ P
- Lung volume dependent
- Healthy: Lung compliance~0.2 L/cmH20: eg, change inspiratory pressure 5 cmH20, 1.0 L air is inspired,=1 L/5 cmH20=0.2 L/cmH20

Mechanics of breathing

- Emphysema: increased compliance due to loss of elastic recoil pressure: e.g., change in inspiratory pressure 5 cmH20/2.0 L inspired air, or 0.4 L/cmH20 compliance
- (Sounds like a good thing for inspiration, but less efficient expiration..)
- Pulmonary fibrosis: increased elastic recoil pressure (stiff lungs): 5 cmH20 inspiratory pressure change with 0.5 L air inspired; compliance=0.1 L/cmH20

Mechanics of Breathing

- Transpulmonary pressure: difference between pleural pressure (usually measured as esophageal pressure) and mouth pressure static=no airflow
- Static compliance: relationship of transpulmonary pressure under static conditions (no airflow) to different degrees of lung inflation (volumes)
- Static inspiratory compliance=V_T/Pplateau-PEEP

Mechanics of Breathing

- Dynamic compliance: compliance determined during breathing
- Dynamic compliance=V_T/Pdynamic (peak)-PEEP (recall that static inspiratory compliance=V_T/Pplateau-PEEP)

Mechanics of Breathing

- Inspiratory airway resistance=pressure difference across airways between mouth and alveoli=Pdynamic-Pplateau/flow (normal=<4 cmH20/L/sec)
- Maximal inspiratory flow rate depends primarily upon muscular effort
- Expiration: higher volumes=higher flow rates, but once ~50% TLC, rate declines with greater effort because of dynamic airway compression
- Dynamic airway compression=more collapse of airways in expiration in emphysema (loss of elastance/increased compliance) as effort increases=gas trapping

Mechanics/Work of Breathing

- Note that low and high respiratory rates cause increased mechanical work of breathing:
- High rates=low lung volumes=need to increase total ventilation (by increasing flow rate) to maintain alveolar ventilation, since there is increased wasted (dead space) ventilation, so increased work necessary to overcome flow resistance
- Slow rates=little flow resistive work because of low flow rates but must increase VT to maintain alveolar ventilation; thus must use increased work to overcome elastic resistance

Mechanics/Work of Breathing

- Elastic resistance high (low compliance) = increased respiratory frequency; V_T usually low, so rapid, shallow breathing=least work
- eg, pulmonary fibrosis = low lung compliance; obesity, kyphoscoliosis = low chest wall compliance
- Flow resistance high= decreased respiratory frequency ; generally deeper and slower breathing (eg, chronic airflow limitation)
- Note, however: with lung hyperinflation, volume pressure curve changes with decreasing compliance and the patient may breathe more rapidly and shallowly as well

Mechanics/Work of Breathing

- Metabolic work:
- Oxygen consumption (VO_2) in normals~1.0 ml/liter of ventilation; O_2 cost of breathing increases in patients with respiratory disorders due to the increased work required

Ventilation

- $PACO_2 = VCO_2/VA \times K$ (the constant is actually 863 mmHg, derived from ideal gas laws).
- The ratio of VCO_2/VA for normal people at rest, at sea level, is about 1/21.6; thus, normal $PACO_2$ = 1/21.6 x 863 mmHg = ~40 mmHg.

Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Conduction of blood coming from the tissues through the alveolar capillaries so that O_2 can be added and CO_2 removed.
- Pulmonary vessels=low pressures and low resistance to flow (thin walled)
- Resistance=driving pressure/flow (Q)
- Most resistance in the arterioles and capillaries
- Driving pressure=pressure at the beginning of the pulmonary circulation (the pulmonary artery) and other end (left atrium); normally, eg, blood flow 6 L/min and mean driving pressure of 9 mmHg, resistance is 9mmHg/6 L/min, or 1.5 mmHg/L/min (~10% of systemic pressure).

Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Pulmonary capillary blood volume increases during inspiration and exercise
- Reduced when patients receive mechanical ventilation (intrathoracic pressure is raised, thus impeding venous return to the heart)
- Patients with increased pulmonary pressure (eg pulmonary hypertension, pulmonary embolism)=cardiodynamic consequences as well as disturbance of gas transfer

Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Transfer of O_2 and CO_2 between alveolar gas and pulmonary capillary blood is entirely passive, with the *rate of diffusion* of gas across alveolar-capillary barrier determined by (1) solubility of gas in liquid, (2) density of gas, (3) partial pressure difference between alveolar air and pulmonary capillary blood, and (4) surface area available for diffusion
- CO_2 diffusion not a clinical problem because CO_2 much more soluble and diffusible than oxygen between air and blood
- Total diffusing capacity includes uptake by hemoglobin and rate of flow

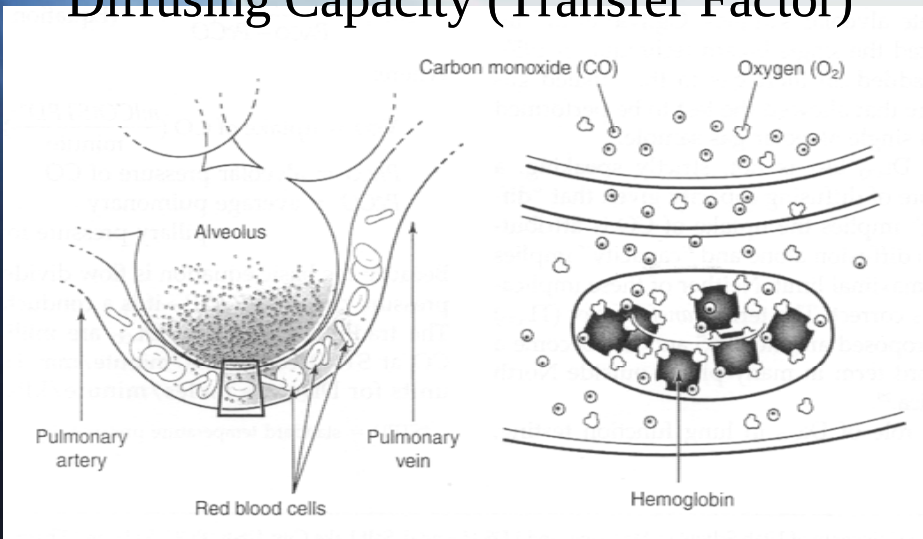
Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Low diffusion capacity not necessarily low PaO_2, since so much redundancy:
- Complete exposure of alveolar PO_2 to capillary blood=no decrease in end capillary PO_2, even if there is less volume, or Hgb), and no change in $AaDO_2$ (
- But incomplete transfer = decrease in end capillary PO_2 and widened $AaDO_2$

"Diffusion Capacity" vs Diffusion

- Note that: decreased diffusing capacity/gas transfer abnormality can result from numerous abnormalities not having anything to do with diffusion block itself

Diffusing Capacity (Transfer Factor)



"Diffusion Capacity" vs Diffusion

- So when we say diffusion abnormality=cause of hypoxemia, we mean those abnormalities which involve some form of diffusion block, or other inability to transfer gas completely (eg, low PIO_2+ ***decreased*** circulatory time) so that insufficient transfer of alveolar PO_2 occur
- Low alveolar volume, low Hgb, may result in low diffusing capacity as measured by transfer of CO, and low O_2 content, but not low PaO_2

Gas Transport: CO_2

- CO_2 in physical solution: most carried in RBCs either as bicarbonate, or bound to Hgb (carbaminoHgb)
- Some is dissolved in plasma

Gas Transport:Oxygen

- O_2 combined with Hgb in RBCs, and dissolved O_2 in physical solution in the plasma
- Normal: 1 gm of Hgb able to combine chemically with 1.34 ml O_2
- Thus: O_2 capacity=1.34 ml O_2 /gmHgb
- If 15 gm Hgb/100 ml blood, O_2 capacity=20 ml O_2 /100 ml blood=200 ml O_2 /liter blood
- Dissolved O_2 = .003 ml O_2 /100 ml blood/mmHg PaO_2
- **CaO_2 =SaO_2 x [O_2 capacity] + dissolved O_2**
- If PaO_2 =100 mmHg, and Hgb=15, then O_2 content = 200 ml O_2 /liter blood + 3 mlO_2/liter blood=~203 mlO_2/liter blood x SaO_2

Hypoxemia

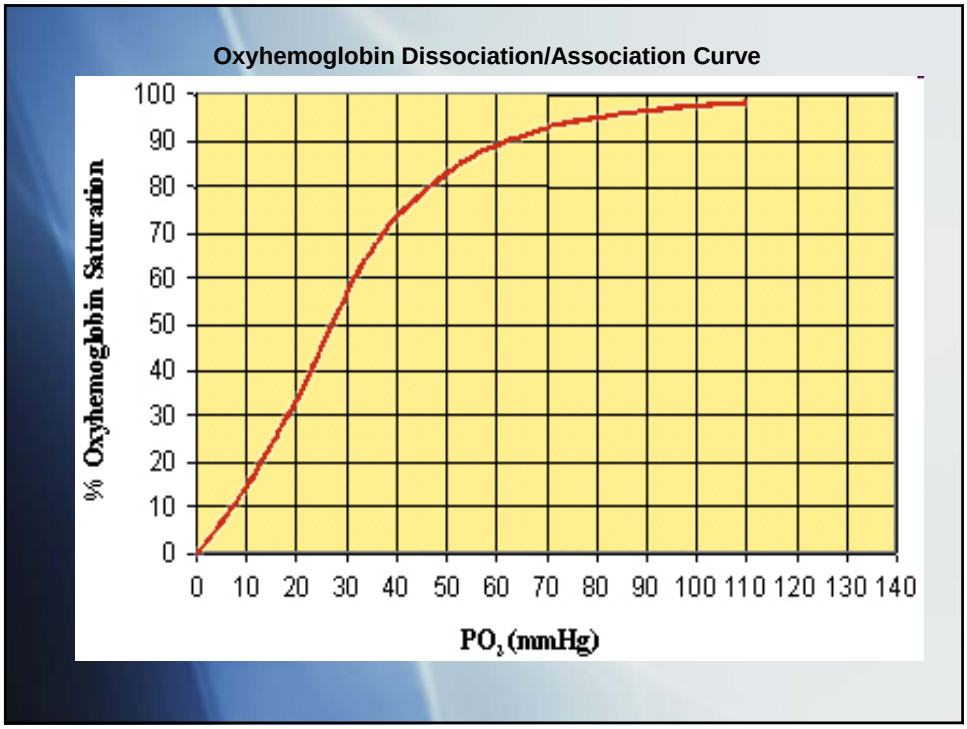
- Low partial pressure of O_2 in blood (PaO_2) OR low O_2 content

Hypoxia

- Metabolic O_2 deficiency Unable to meet tissue demands)
- Hypoxia causes are:
  - "stagnant", as with impaired blood flow; normal PaO_2 and SaO_2
  - "histocytoxic",as with metabolic impairment using O_2, such as cyanide poisoning; normal PaO_2 and SaO_2
  - "anemic", as with low Hgb or carbon monoxide poisoning; normal PaO_2 and SaO_2
  - "hypoxic" or "hypoxemic", as with impaired oxygenation such as low V/Q, shunt, diffusion block, or low PIO_2 such as high altitude; PaO_2 and SaO_2 decreased

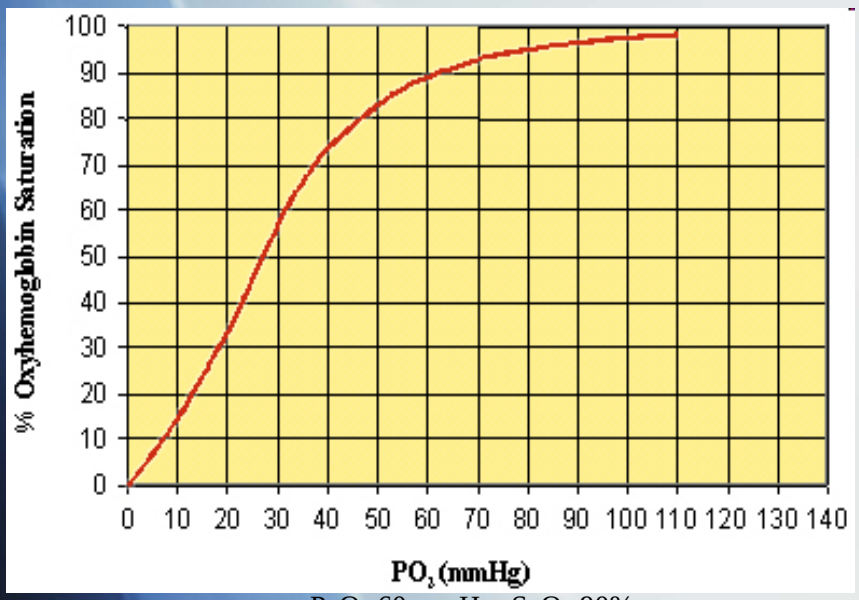
Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Hypoxemia: hypoventilation, low PIO_2, diffusion abnormality (must be severe if at rest), V/Q mismatch, shunt (note that shunt and diffusion block manifest similarly in corresponding areas of lung; but diffusion abnormality (if not block) does NOT equal shunt)
- Note that low V/Q does not=shunt
- Degree of O_2 saturation depends on O_2 tension

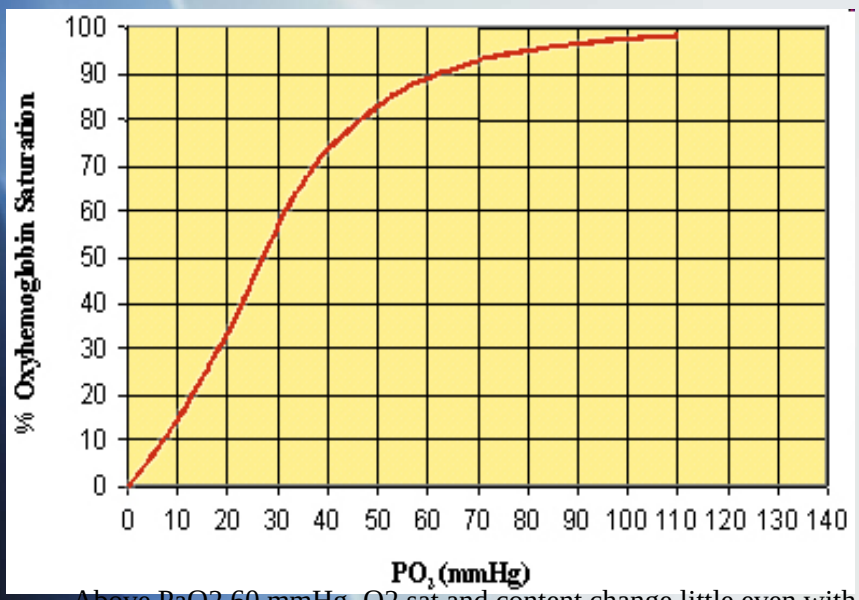


Oxyhemoglobin Dissociation/Association Curve: Key Points

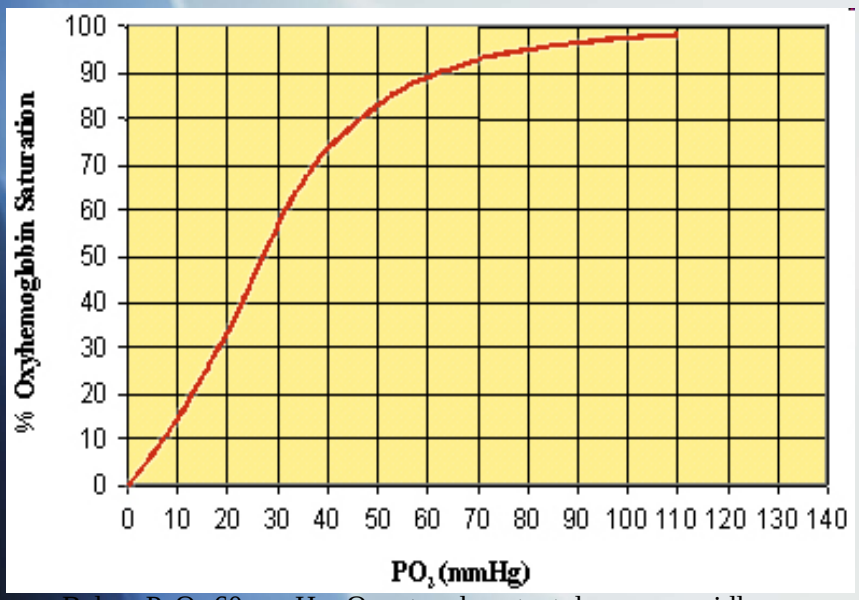
- O_2 saturation=O_2 bound to Hgb/O_2 carrying capacity; degree of O_2 bound depends upon PO_2 Hgb is exposed to



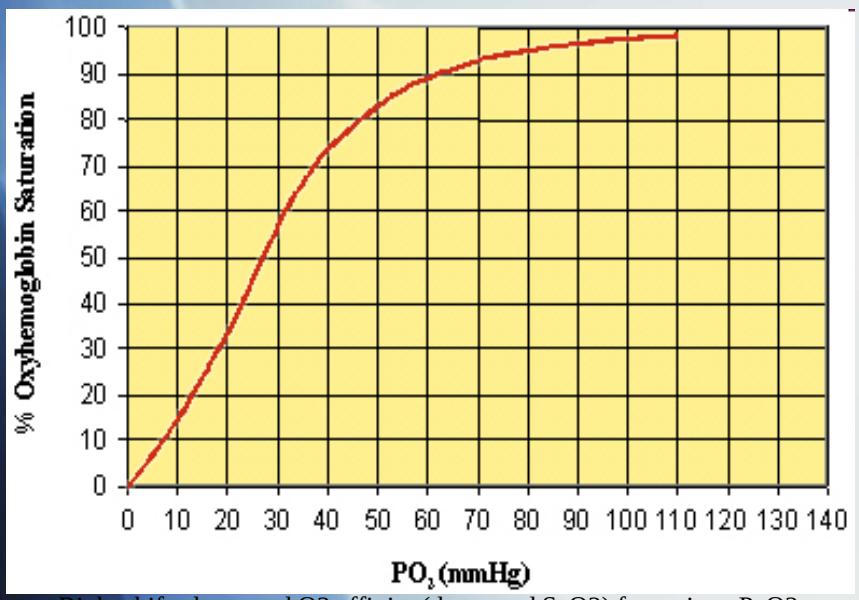
- PaO_2 60 mmHg=SaO_2 90%



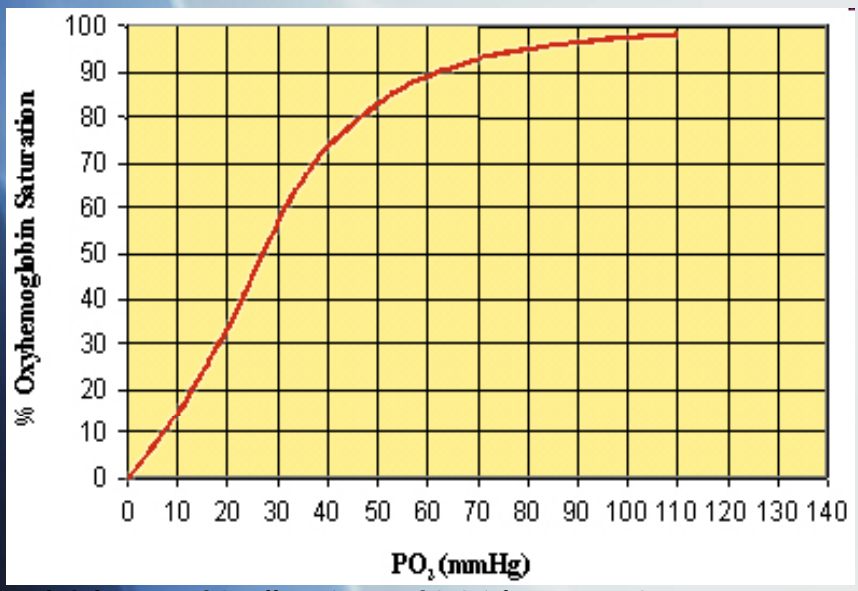
Above PaO2 60 mmHg, O2 sat and content change little even with large PaO2 increase



- Below PaO_2 60 mmHg, O_2 sat and content decrease rapidly
- (ie, rapid dissociation and tissue unloading)



- Right shift=decreased O2 affinity (decreased SaO2) for a given PaO2
- (ie, more tissue unloading: increased temp, 2,3 DPG, PCO2, low pH)



- Left shift=increased O2 affinity (increased SaO2) for a given PaO2
- (ie, less tissue unloading: low 2,3 DPG, high CO, low temp, methHgb, fetal Hgb)

Physiologic Causes of Hypoxemia

Alveolar Hypoventilation

Decreased PIO_2

Diffusion Abnormality

V/Q mismatch

Shunt

Physiologic Causes of Hypoxemia

Widening of $AaDO_2$:
Diffusion Abnormality
V/Q mismatch
Shunt

No widening of $AaDO_2$:
Hypoventilation
Low PIO_2 (may contribute to widenening if impaired diffusion)

Gas Exchange

- Alveolar Gas Equation:
- $PAO_2 = FIO_2 x (PB-PH20) – PCO_2/R + [PACO_2 x FIO_2 x 1-R/R]$ (full)
- $PAO_2 = FIO_2 x (PB-PH20) – PCO_2/R$ (simplified)
- R=Respiratory Exchange Ratio: (gas R=CO_2 added to alveolar gas by blood/amount of O_2 removed from alveolar gas by blood; low V/Q=low R); normal=0.8

Two patients breathing room air at sea level:

1. PaO_2=40 mmHg, $PaCO_2$=90 mmHg:

2. PaO_2=40 mmHg, $PaCO_2$=22 mmHg:

Abnormal Ventilation, Abnormal Gas Exchange

Ventilation and Gas Exchange

- Objective: to achieve adequate tissue oxygenation and remove metabolically produced CO_2.
- Ventilation: concerned with delivery of fresh volume of air to gas exchanging units, and the removal of a sufficient volume of mixed gas out
- Gas Exchange: the ability to move gas across the alveolar-capillary membrane

Ventilation and Gas Exchange

- The failure of either or both results in impaired arterial blood gases and ultimately *respiratory failure.*
- Ventilatory failure: *Hypercapnic respiratory failure*
- Gas exchange failure: *Hypoxemic respiratory failure*
- *Hypoxemia is the inevitable result of both*

Hypoxemia

- Low partial pressure of O_2 in blood (PaO_2) OR low O_2 content (CaO_2:SaO_2 x O_2 carrying capacity+.03 ml O_2/l/mmHg PaO_2)

Hypoxemia

- Hypoxemia is not synonymous with:

Hypoxemia

- Hypoxemia is not synonymous with:
  - Hypoxia, which is metabolic O_2 deficiency
  - Hypoxia causes are:
  - “stagnant”, as with impaired blood flow;
  - “histocytoxic”,as with metabolic impairment using O2, such as cyanide poisoning;
  - “hypoxic”, as with impaired oxygenation such as low V/Q, or low PIO2 such as high altitude;
  - “anemic”, as with low Hgb or carbon monoxide poisoning

Hypoxemia

- Hypoxemia is not synonymous with:
  - Low O_2 carrying capacity (1.34 ml O_2 /gm Hgb; if 15 gmHgb/100ml blood, then 20 ml O_2 /100ml blood, or 200 ml O_2 /liter of blood)

Hypoxemia

- Hypoxemia is not synonymous with:
  - Low O_2 delivery (Ca O_2 x C.O.)

Physiologic Causes of Hypoxemia

Alveolar Hypoventilation

Decreased PIO_2

Diffusion Abnormality

V/Q mismatch

Shunt

Ventilation

- Minute Ventilation (V_E)=tidal volume (V_T) x respiratory frequency (“dead space” volume not accounted for)
- Alveolar ventilation (V_A)=that part of minute ventilation which participates in gas exchange (that volume of fresh gas entering the respiratory exchange zone each minute)
- Alveolar ventilation=alveolar volume (tidal volume-dead space volume) x respiratory frequency

Ventilation

- Alveolar PCO_2 ($PACO_2$)=VCO_2/V_A x K
- VCO_2=CO_2 production
- V_A=alveolar ventilation
- Normal: VCO_2/V_A=1/21.6; K=863 mmHg, so $PACO_2$=~40mmHg))
- Alveolar PCO_2=CO_2 leaving lungs after gas exchange; directly reflects arterial PCO_2
- e.g., halving alveolar ventilation with constant CO_2 production will double the alveolar PCO_2
- e.g., doubling the alveolar PCO_2 reflects halved alveolar ventilation

Hypoventilation

- Inability to inspire and expire a volume of air/gas sufficient to meet metabolic demands
- Inabilty to bring a fresh volume of O_2 with each breath to the gas exchanging unit, and inability to remove CO_2 produced by metabolism.
- *Sine qua non:* Increased arterial PCO_2 ($PaCO_2$); decreased arterial PO_2 (PaO_2) breathing room air *(parallel changes!!)*

Hypoventilation/ Alveolar hypoventilation

- All hypoventilation concerns either :
- increased dead space/tidal volume ratio (anatomic or physiologic), ie “wasted” ventilation; or
- Decreased MINUTE ventilation (decreased tidal volume, and/or decreased respiratory rate)
- Each may result in alveolar hypoventilation ($PaCO_2$ elevated)

Alveolar Hypoventilation: 2 Clinical Pearls

- Does not widen the $AaDO_2$
- The hypoxemia may be readily ameliorated with supplemental O_2
- Challenge: Write a proof for this latter statement

Alveolar Gas Equation

- $PAO_2 = PIO_2 - PACO_2/R$
- $PAO_2 = PIO_2 - PACO_2/R + [PCO_2 \times FIO_2 \times 1\text{-}R/R]$

Alveolar Gas Equation

- PAO2=PIO2 – PACO2/R
- PIO2: FIO2 (Patm-PH20)

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- PAO2=PIO2 – PACO2/R
- PIO2: FIO2 (Patm-PH20)
- PACO2=PaCO2

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- R=Respiratory Exchange Ratio: (gas R=CO2 added to alveolar gas by blood/amount of O2 removed from alveolar gas by blood; low V/Q=low R); normal=0.8

Case History

- Room air: PaO_2=30 mmHg, $PaCO_2$=90 mmHg, pH=7.08
- PAO_2= 0.21 (760-47) –90/0.8

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- PAO_2= 0.21 (760-47) –90/0.8
- PAO_2=150-112.5=37.5

Case History

- PaO2=30 mmHg, PaCO2=90 mmHg, pH=7.08
- PAO2= 0.21 (760-47) –90/0.8
- PAO2=150-112.5=37.5
- AaDO2=7.5 mmHg

Alveolar Hypoventilation

- CNS: central hypoventilation; infectious, traumatic, vascular damage to medullary centers; pharmacologic and sleep suppression of ventilatory drive

Alveolar Hypoventilation

- CNS: central hypoventilation; infectious, traumatic, vascular damage to medullary centers; pharmacologic and sleep suppression of ventilatory drive
- Peripheral nervous system/myoneural junction: poliomyelitis, Guillain-Barre, myasthenia gravis

Alveolar Hypoventilation

Respiratory muscles: muscular dystrophy, ALS, increased inspiratory loading (eg emphysema)

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- Chest wall/mechanical restriction: kyphoscoliosis, trauma, splinting, obesity

Alveolar Hypoventilation

- Respiratory muscles: muscular dystrophy,increased inspiratory loading (eg emphysema)
- Chest wall/mechanical restriction: kyphoscoliosis, trauma, splinting, obesity
- Airway obstruction: upper airway, lower airway

Hypercapnic Respiratory Failure

- Primary deficit=hypoventilation without gas exchange abnormality
- Hypoxemia MUST result if patient breathing room air
- $AaDO_2$ not widened if no supervening gas exchange abnormality

$AaDO_2$ and Hypoxemia

- Widened in diffusion disorder, V/Q mismatch, and shunt
- Not widened in alveolar hypoventilation and decreased PIO_2
- Normal $AaDO_2$ ~10-15 mmHg in young adult at sea level breathing RA

Climbing Everest (Decreased PIO2)

- P atm= 250 mmHg
- PaCO2=18 mmHg; R=1
- PAO2=PIO2-PCO2/R
- PAO2=.21 (250-47)-18/1=24.6 mmHg
- Recent data: altitude 8400m, mean PaO2=30 mmHg, Mean AaDO2 5.4 mmHg (wider than expected): Grocott et al, NEJM 2009, 360;2: 141

Case History

- RA: PaO2=70, PaCO2=30 mmHg

Case History

- RA: PaO2=70, PaCO2=30 mmHg
- No treatment: RA PaO2=50 mmHg, PaCO2=28 mmHg
- What happened? Did $AaDO_2$ change?

What happened?

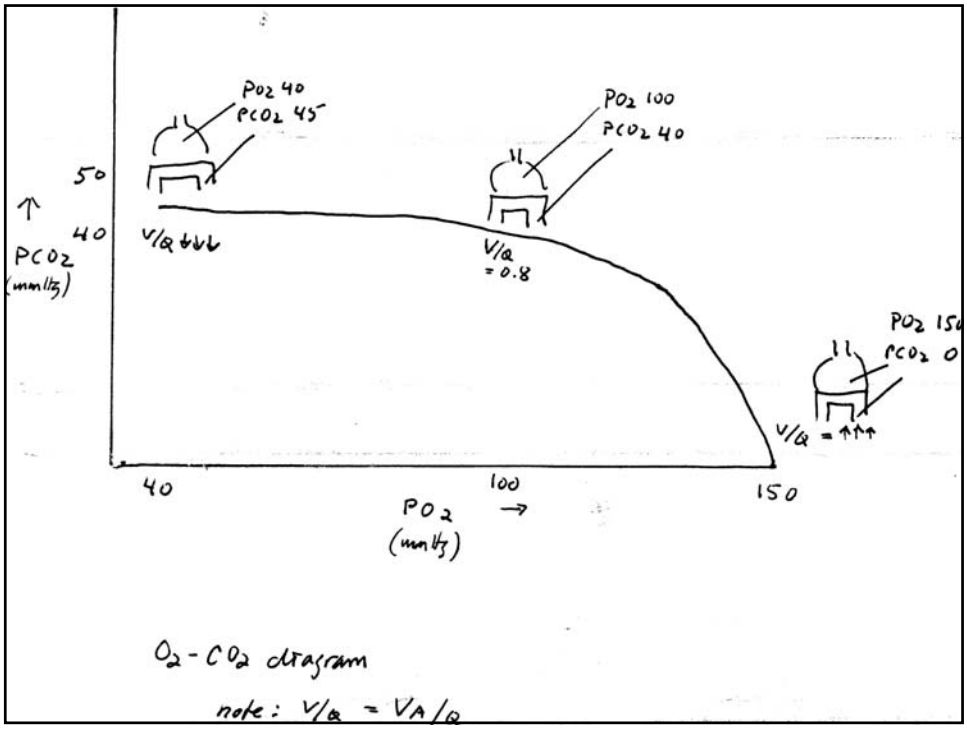
- $PAO_2=PIO_2 – PACO_2/R$
- 0.21 FIO_2, PaO_2=50 mmHg, $PaCO_2$=28 mmHg
- PAO_2=0.21(713)-28/0.8=150-35= 115 mmHg
- $AaDO_2$=115-50= 65 mmHg

Hypoxemia

- No widening of $AaDO_2$: hypoventilation, low PIO_2.
- Widened $AaDO_2$: shunt, low V/Q, low diffusing capacity
- Hypoxemia of each may be overcome with supplemental O_2 *except: shunt.*
- Note: no gas exchange=no amelioration of hypoxemia with O_2, whether dead space, shunt, or no diffusion.

Low V/Q

- "Venous admixture"
- Alveolar filling: pneumonia, pulmonary edema (cardiogenic/non-cardiogenic)
- COPD a common situation of low V/Q
- Usually will involve some infinitely low V/Q (shunt) and decreased diffusion.



Low V/Q

- Low relationship of V to Q; NOT low ventilation in all alveolar capillary units
- That is, Low V/Q is NOT hypoventilation (unless all units see the same lowering of V/Q)

Diffusion Abnormality

- Alveolar-capillary membrane thickening (pulmonary hypertension, pulmonary vasculitis, pulmonary embolism)
- Alveolar-capillary membrane destruction (emphysema)
- Pulmonary interstitial thickening (pulmonary fibrosis)
- Alveolar filling (pulmonary edema, pneumonitis)

Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

- Low gas transfer and measured diffusing capacity may also result from processes not clearly blocking diffusion, such as low Hgb, or increased rate of flow disallowing adequate gas transfer
- All diffusion abnormalities do not typically =low PaO_2, or low O_2 content, since so much redundancy

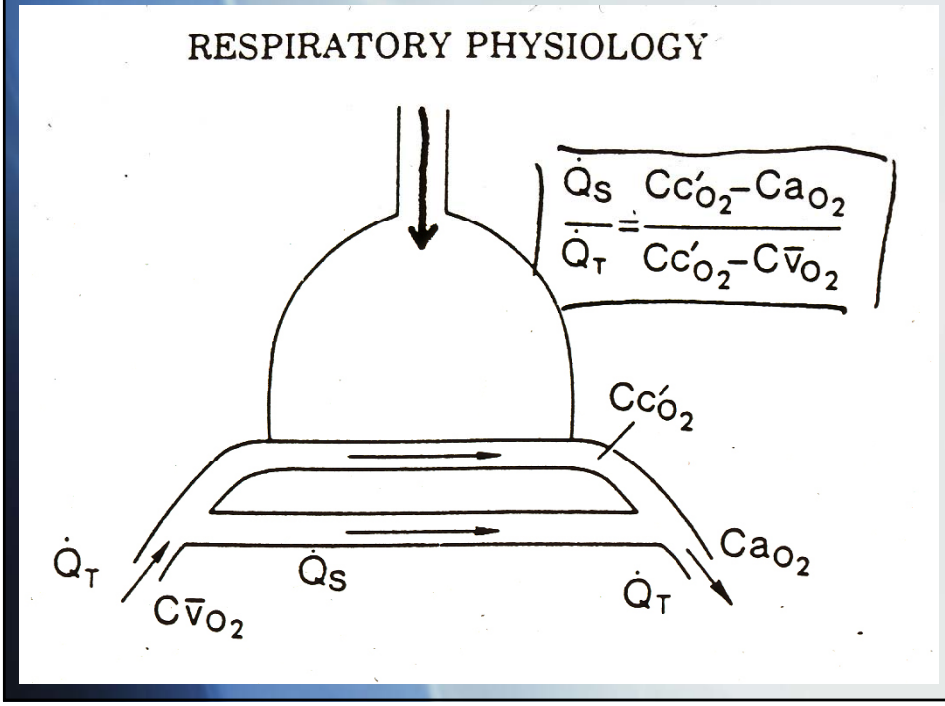
Gas Transport: Pulmonary Circulation and Diffusion of Gas (Gas Transfer)

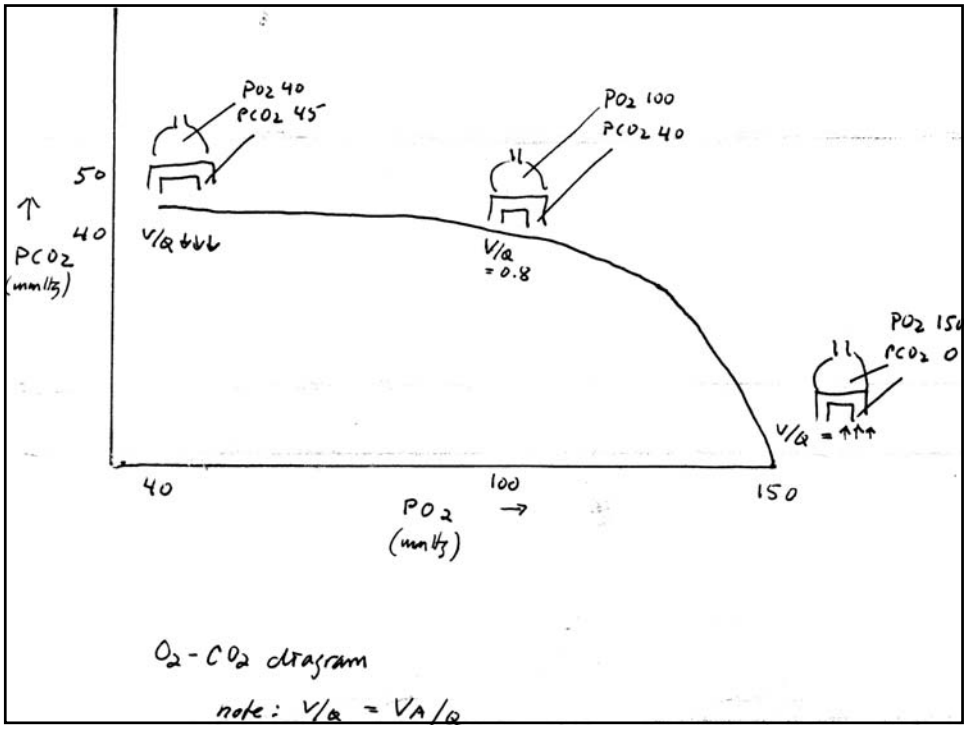
- Diffusing capacity, measured diffusing capacity (DLCO), and diffusion of gases differ
- Low diffusion will cause low measured diffusing capacity, possibly low PaO2, and widened AaDO2, low diffusing capability because of non-diffusion reasons (eg low Hgb, low volumes) will cause low measured diffusing capacity and low O2 content but not necessarily decreased PaO2 or widened AaDO2

Shunt

- Infinitely low V/Q (but NOT low V/Q)
- Supplemental O_2 will not raise PaO_2 with large shunt
- Clinical examples: ARDS, other severe pneumonia, cardiogenic pulmonary edema
- May also be cardiogenic R-L shunt

- Shunt Fraction (Qs/Qt): Cc'O2-CaO2/Cc'O2-CvO2 (normal <5%)
- Where CaO2 is arterial O2 content;
- Cc'O2 is end capillary oxygen content;
- CvO2 is mixed venous (pulmonary artery) O2 content





Hypoxemic Respiratory Failure

- Primary deficit=hypoxemia without hypoventilation, until late (?)
- Gas exchange abnormality: shunt, low V/Q, low diffusing capacity, all…
- Widened $AaDO_2$

SUMMARY

- Hypoventilation: High $PaCO_2$, Low PaO_2, no widening of $AaDO_2$
- Gas exchange abnormality: Low PaO_2, normal or low $PaCO_2$, widened $AaDO_2$
- Hypoxemia of all hypoventilation and gas exchange abnormalities may be sufficiently overcome by supplemental O_2 unless gas exchange abnormality is *absolute (eg shunt)*

Two patients breathing room air at sea level:

PaO_2=40 mmHg, $PaCO_2$=90 mmHg:

Severe alveolar hypoventilation; no gas exchange abnormality: ventilate, give oxygen if necessary to prevent severe hypoxemia; find and treat cause (s) of hypoventilation

PaO_2=40 mmHg, $PaCO_2$=22 mmHg:

Severe gas exchange abnormality: oxygenate; find and treat cause (s) of gas exchange problem (or low PIO2)