Abnormal Ventilation, Abnormal Gas Exchange

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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

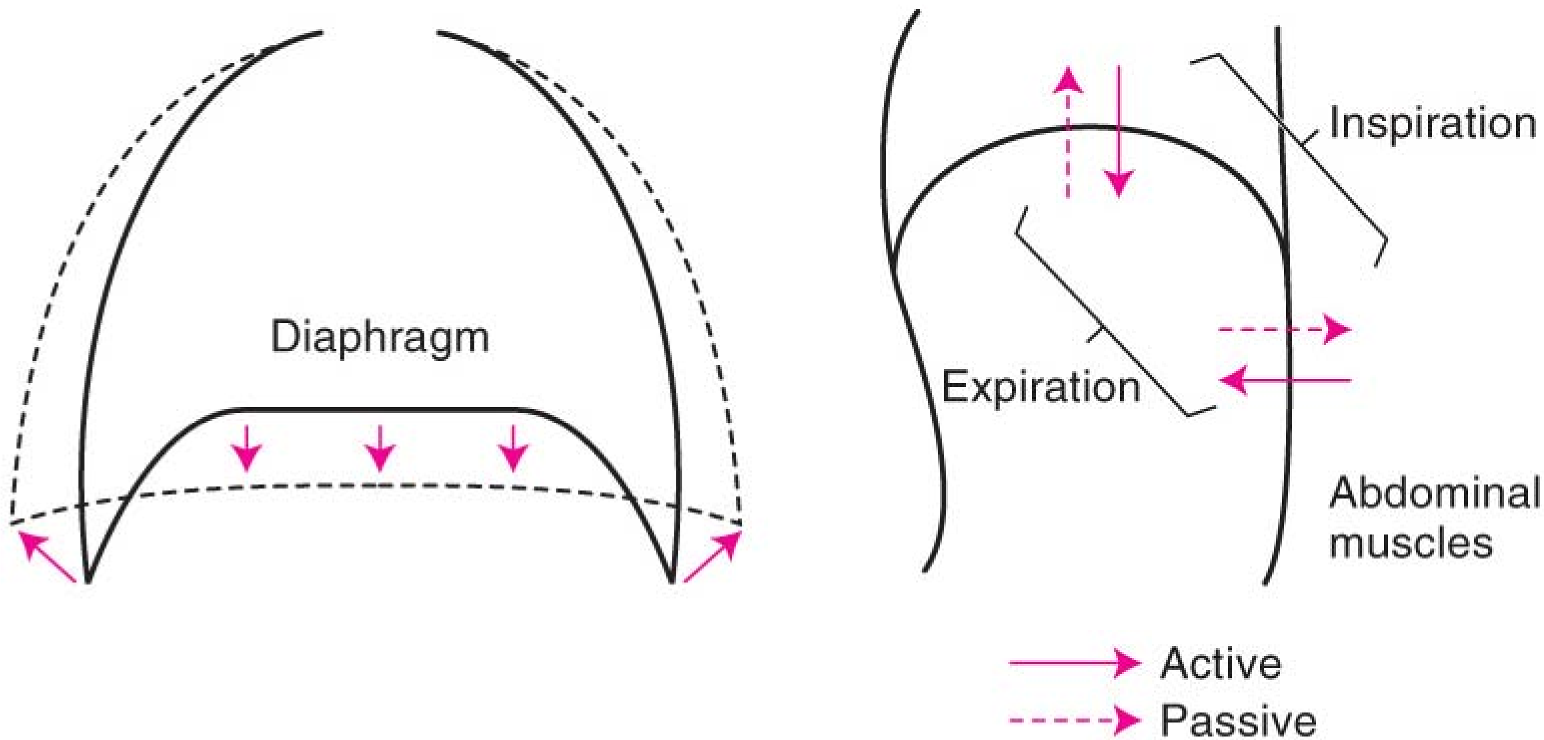
Ventilation and Gas Exchange

- 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*

Ventilation

Ventilation = Breathing

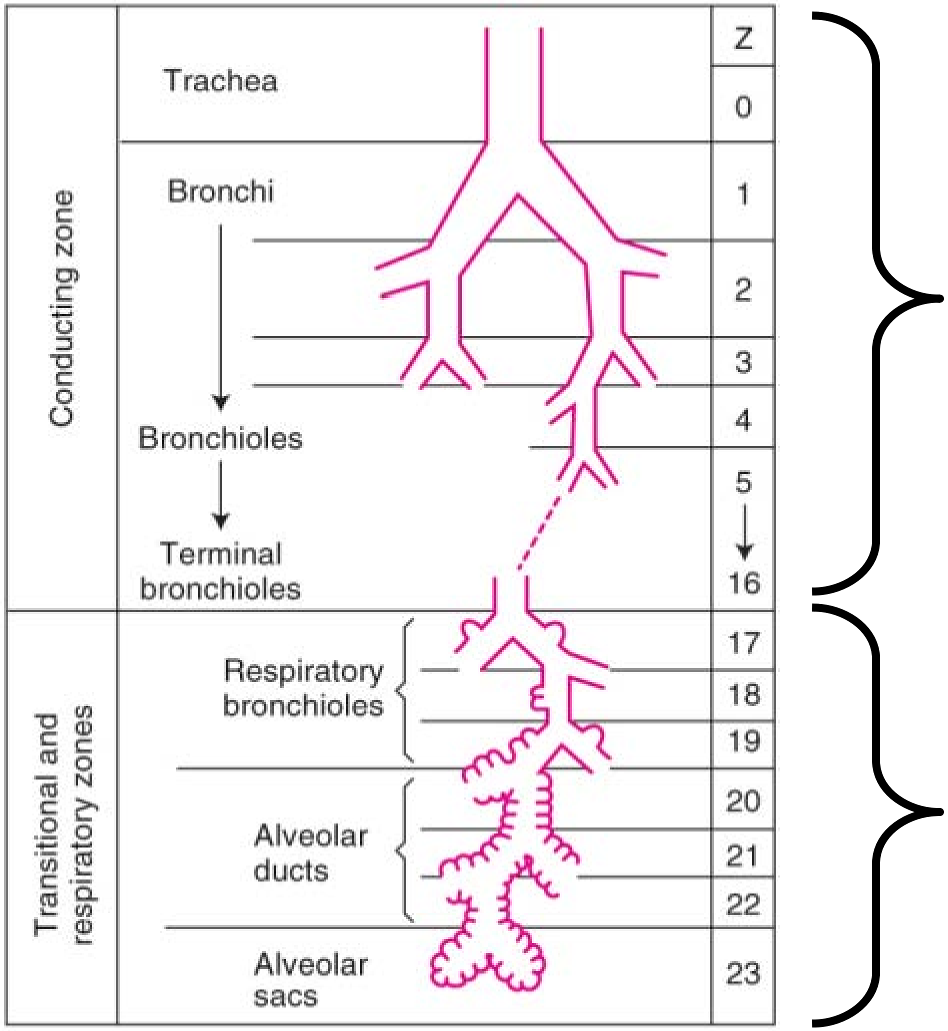
- Ventilation is the process of moving gases between the atmosphere and the alveoli



Normal breathing

- **Respiratory rate** = the number of breaths per minute
  - About 12 to 15 per minute
  - Abbreviated RR
- **Tidal volume** = volume of gas inspired in a single breath
  - About 0.5 liters
  - Abbreviated VT
- **Minute ventilation** = volume of gas inspired per minute = RR x VT
  - About 6 liters per minute
  - Abbreviate V_E

Only Some of the Tidal Volume Reaches Alveoli



“Anatomic Dead Space”

“Alveolar Space”

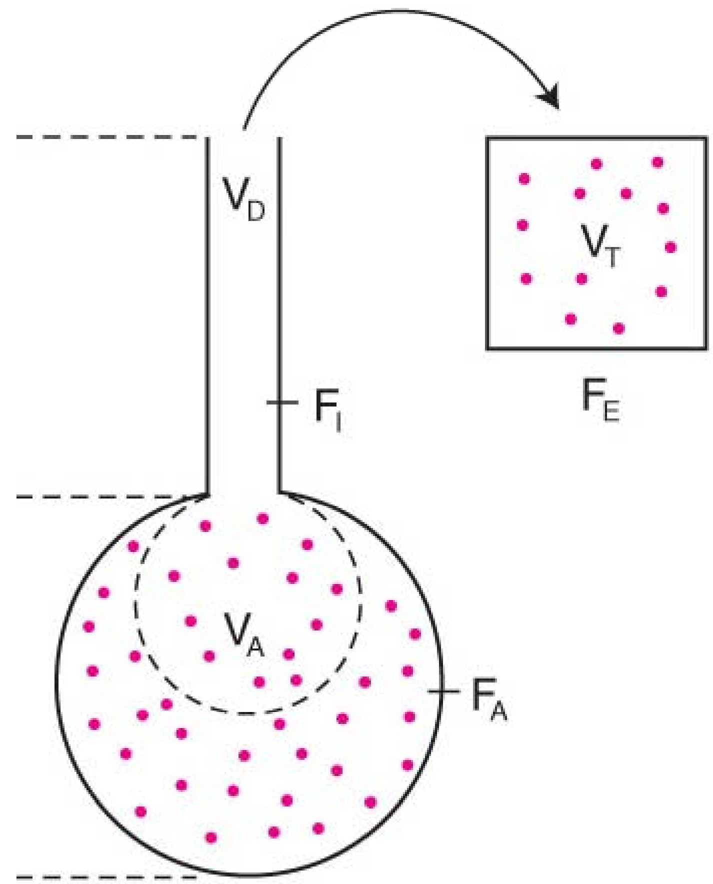
Dead Space

- **Anatomic Dead Space**
  - Normal
  - About 1ml per lb. body weight (~150 ml)
- **Physiologic Dead Space**
  - Abnormal
  - Areas not participating in gas exchange (more later)

Dead Space

$$V_T = V_D + V_A$$

500 ml = 150 ml + 350 ml



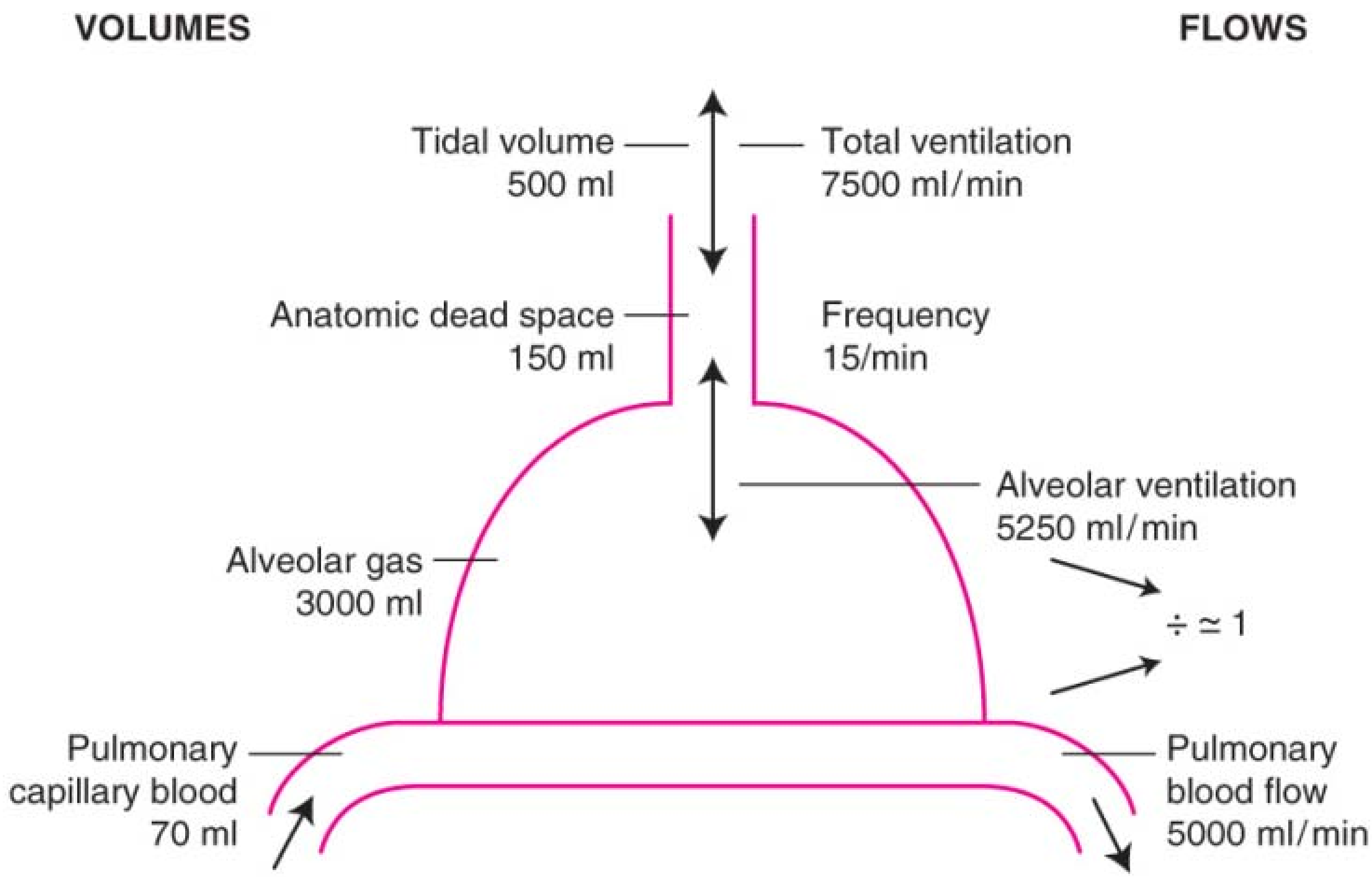
Alveolar and Dead Space <u>Ventilation</u>

$$\mathbf{V}_T = \mathbf{V}_D + \mathbf{V}_A$$

$$V_T \times RR = \left(V_D \times RR\right) + \left(V_A \times RR\right)$$

$$\dot{\mathbf{V}}_E = \dot{\mathbf{V}}_D + \dot{\mathbf{V}}_A$$

Volumes and flows



Total and Alveolar Ventilation

$$\dot{V}_{CO_2} = \dot{V}_A \times F_A CO_2$$

Total and Alveolar Ventilation

$$\dot{V}_{CO_2} = \dot{V}_A \times F_ACO_2 = \dot{V}_A \times \frac{P_ACO_2}{K}$$

Total and Alveolar Ventilation

$$\dot{V}_{CO_2} = \dot{V}_A \times F_A CO_2 = \dot{V}_A \times \frac{P_A CO_2}{K}$$

$$\dot{V}_A = \frac{\dot{V}_{CO_2}}{P_A CO_2} \times K$$

Total and Alveolar Ventilation

$$\dot{V}_{CO_2} = \dot{V}_A \times F_A CO_2 = \dot{V}_A \times \frac{P_A CO_2}{K}$$

$$\dot{V}_A = \frac{\dot{V}_{CO_2}}{P_A CO_2} \times K \approx \frac{\dot{V}_{CO_2}}{P_a CO_2} \times K$$

Application of the Alveolar Ventilation Equation

$$P_aCO_2 \propto \frac{\dot{V}_{CO_2}}{\dot{V}_A}$$

What happens if…

1. Dead space increases (minute ventilation held constant)
2. Minute ventilation increases (V_D is constant)
3. CO_2 production increases

PaCO2 is used to determine alveolar ventilation

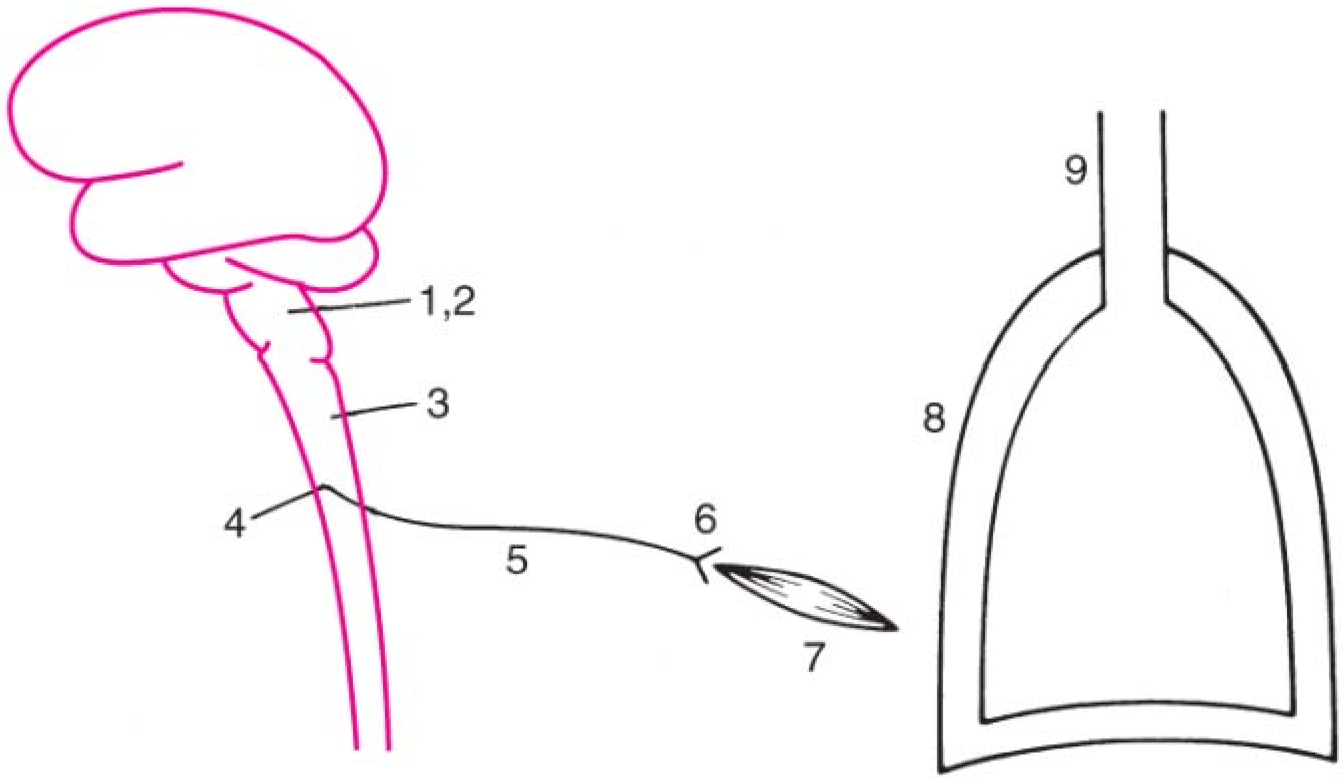
- Normal PaCO2 = 37 to 42 mm Hg
- PaCO2 > 42 mm Hg = alveolar hypoventilation
- PaCO2 < 37 mm HG = alveolar hyperventilation

Hypoventilation

- Hypoventilation
  - Decreased minute ventilation (decreased RR and/or VT)
- Alveolar 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
  - Alveolar hypoventilation can only result from one or both of the following:
    - Hypoventilation
    - Increased dead space fraction (dead space/tidal volume ratio)
- Increased P_AO_2 (hypercapnia) indicates the presence of alveolar hypoventilation

Some Causes of Hypoventilation

1,2 Depression of the respiratory center by drugs, injury, tumor, etc.
3. Abnormalities of the spinal cord (e.g., following high dislocation)
4. Anterior horn cell disease (e.g., poliomyelitis)
5. Diseases of the nerves to the respiratory muscles (e.g., Guillain-Barré)
6. Diseases of the myoneural junction (e.g., myasthenia gravis)
7. Diseases of the respiratory muscles (e.g.,muscular dystrophy)
8. Thoracic cage abnormalities (e.g., crushed chest)
9. Upper airway obstruction (e.g., tracheal compression by the thymoma)



Causes of Alveolar Hypoventilation

- Neuromuscular insufficiency (previous slide)
- Respiratory muscle fatigue
  - A prolonged increase in the work of breathing will lead to respiratory muscle fatigue
  - Common cause of *hypercapneic respiratory failure*

- *We will come back to alveolar hypoventilation during our discussion of hypoxemia*

Hypoxemia

Definition of Hypoxemia

- Low partial pressure of O_2 in blood (PaO_2)

OR

- Low O_2 content (CaO_2)

$$C_aO_2 = (1.39 \times \mathrm{Hb} \times S_aO_2) + (0.003 \times P_aO_2)$$

Hypoxemia ≠ Hypoxia

- Hypoxia is <u>metabolic O_2 deficiency</u>
- 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 ≠ Anemia

- Anemia is low hemoglobin
- Low hemoglobin decreases the
  - O_2 carrying capacity of the blood
  - CaO_2

Hypoxemia ≠ Low O_2 Delivery

- O_2 delivery depends on
  - O_2 content
  - cardiac output

$$\dot{D}O_2 = C_aO_2 \times CO$$

The Alveolar Gas Equation is used to Characterize the Mechanisms and Severity of Hypoxemia

$$P_I O_2 = F_i O_2 \times (P_B - P_{H_2O})$$

$$P_A O_2 = P_I O_2 - \frac{P_A CO_2}{R} + \left[P_A CO_2 \times F_I O_2 x \frac{(1-R)}{R} \right]$$

$$\boxed{P_A O_2 \approx P_I O_2 - \frac{P_A CO_2}{R}}$$

Alveolar Gas Equation

$$\boxed{P_A O_2 \approx P_I O_2 - \frac{P_A CO_2}{R} \approx P_I O_2 - \frac{P_a CO_2}{R}}$$

- $P_A CO_2 = P_a CO_2$
- 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

$AaDO_2$ and Hypoxemia

- The difference between predicted P_AO_2 and measured P_aO_2 is called the “alveolar-arterial oxygen gradient” or “A-a gradient”, abbreviated $AaDO_2$
- Normal $AaDO_2$ ~ 10-15 mmHg in young adult at sea level breathing room air (RA)

Normal $AaDO_2$

$$P_AO_2 = 100$$

$$P_aO_2 = 90$$

$$AaDO_2 = 100 - 90 = 10$$

Normal $AaDO_2$ = 10-15 mmHg in young adults at sea level breathing RA

Normal $AaDO_2$

- Room air:
  - P_aO_2=90 mmHg
  - P_aCO_2=40 mmHg
  - pH=7.40

$$P_IO_2 = F_iO_2 \times (P_B - P_{H_2O})$$

$$P_IO_2 = 0.21 \times (760 - 47) = 150$$

$$P_AO_2 \approx P_IO_2 - \frac{P_aCO_2}{R}$$

$$P_AO_2 \approx 150 - \frac{40}{0.8} = 100$$

Physiologic Causes of Hypoxemia

- **No widening of $AaDO_2$**
  - Hypoventilation
  - Low P_IO_2
    - may contribute to widening if impaired diffusion
- **Widening of $AaDO_2$**
  - V/Q mismatch
  - Shunt
  - Diffusion Abnormality

Alveolar Hypoventilation

- Increased P_AO_2 (hypercapnia) indicates the presence of alveolar hypoventilation
- 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

Case History

$$P_AO_2 \approx P_IO_2 - \frac{P_aCO_2}{R}$$

- Room air:
  - P_aO_2=30 mmHg
  - P_aCO_2=90 mmHg
  - pH=7.08

$$P_IO_2 = F_iO_2 \times (P_B - P_{H_2O})$$

$$P_IO_2 = 0.21 \times (760 - 47) = 150$$

$$P_AO_2 \approx P_IO_2 - \frac{P_aCO_2}{R}$$

$$P_AO_2 \approx 150 - \frac{90}{0.8} = 37.5$$

Case History

$$P_AO_2 = 37.5$$

$$P_aO_2 = 30$$

$$\mathrm{AaDO_2} = 37.5 - 30 = 7.5$$

Normal $AaDO_2$ = 10-15 mmHg in young adults at sea level breathing RA

PaO_2 and $AaDO_2$ at altitude

- Patm = 250 mm Hg
- PaCO2 = 18 mm Hg
- R = 1
- Recent data
  - altitude 8400m
  - PaO2=30 mmHg
  - AaDO2 5.4 mmHg
  - wider than expected

Grocott et al, NEJM 2009, 360;2: 141

$$P_I O_2 = F_i O_2 \times (P_B - P_{H_2O})$$

$$P_I O_2 = 0.21 \times (250 - 47) = 43$$

$$P_A O_2 \approx P_I O_2 - \frac{P_a CO_2}{R}$$

$$P_A O_2 \approx 43 - \frac{18}{1} = 25$$

Case History

- Room air
  - PaO2=70 mm Hg
  - PaCO2=30 mmHg
- No treatment (RA)
  - PaO2=50 mmHg
  - PaCO2=28 mmHg
- What happened?

Case History

$$\boxed{P_AO_2 \approx P_IO_2 - \frac{P_aCO_2}{R}}$$

- Room air
  - PaO2=70 mm Hg
  - PaCO2=30 mmHg
- No treatment (RA)
  - PaO2=50 mmHg
  - PaCO2=28 mmHg
- What happened?

$$P_AO_2 \approx 150 - \frac{30}{0.8} = 112.5$$

$$AaDO_2 = 112.5 - 70 = 42.5$$

Case History

$$\boxed{P_AO_2 \approx P_IO_2 - \frac{P_aCO_2}{R}}$$

- Room air
  - PaO2=70 mm Hg
  - PaCO2=30 mmHg
- No treatment (RA)
  - PaO2=50 mmHg
  - PaCO2=28 mmHg
- What happened?

$$P_AO_2 \approx 150 - \frac{30}{0.8} = 112.5$$

$$AaDO_2 = 112.5 - 70 = 42.5$$

$$P_AO_2 \approx 150 - \frac{28}{0.8} = 115$$

$$AaDO_2 = 115 - 50 = 65$$

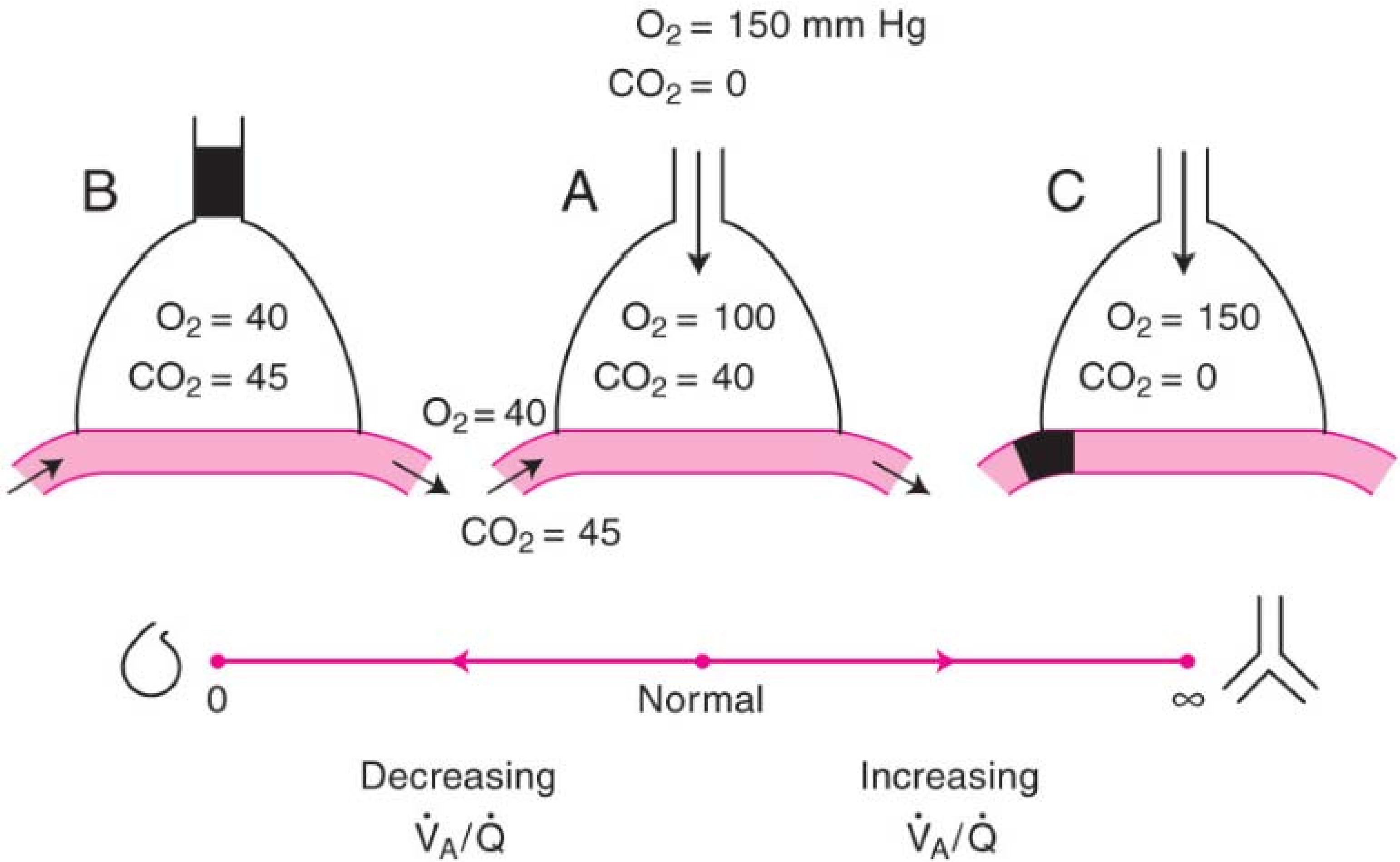
Physiologic Causes of Hypoxemia

- **No widening of $AaDO_2$**
  - Hypoventilation
  - Low P_IO_2
    - may contribute to widening if impaired diffusion
- **Widening of $AaDO_2$**
  - V/Q mismatch
  - Shunt
  - Diffusion Abnormality

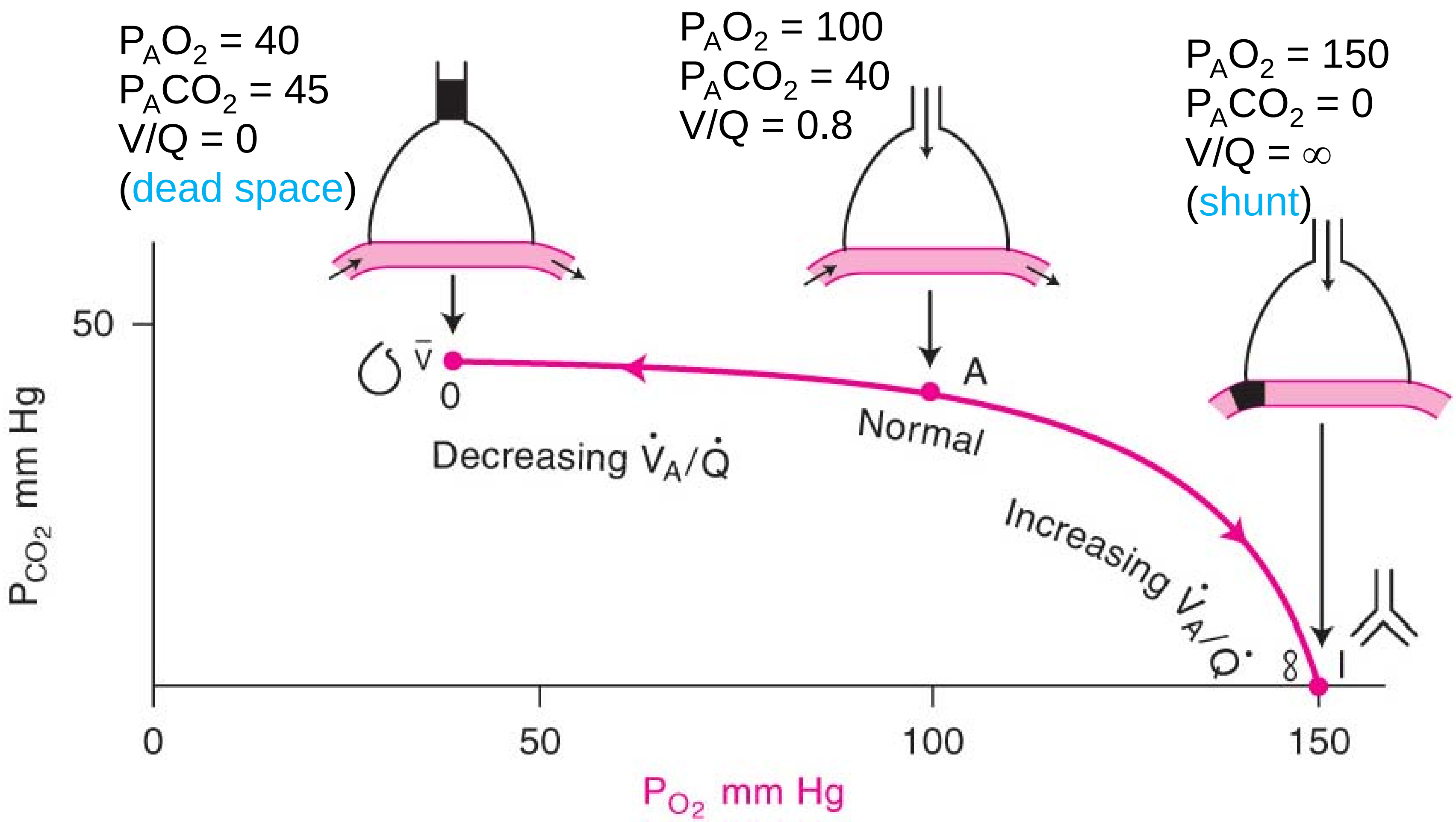
Low V/Q

- Low relationship of V to Q
  - Some alveoli are "underventilated"
- Low V/Q is <u>NOT</u> low ventilation of <u>all</u> alveoli
  - That would be alveolar hypoventilation

Alveolar PO_2 and PCO_2 across various V/Q relationships



O_2-CO_2 diagram showing a V/Q ratio line



Examples of V/Q mismatch

- Most parenchymal lung diseases cause hypoxemia by altering V/Q matching
- Examples
  - Asthma
  - COPD
  - Pulmonary Fibrosis
  - Pulmonary Edema

Diffusion Abnormality

- Alveolar capillary thickening
  - pulmonary hypertension
  - pulmonary vasculitis
  - pulmonary embolism
- Alveolar destruction (emphysema)
- Alveolar wall thickening
  - pulmonary fibrosis
- Alveolar filling
  - pulmonary edema
  - pneumonia

"Diffusion Capacity" vs Diffusion

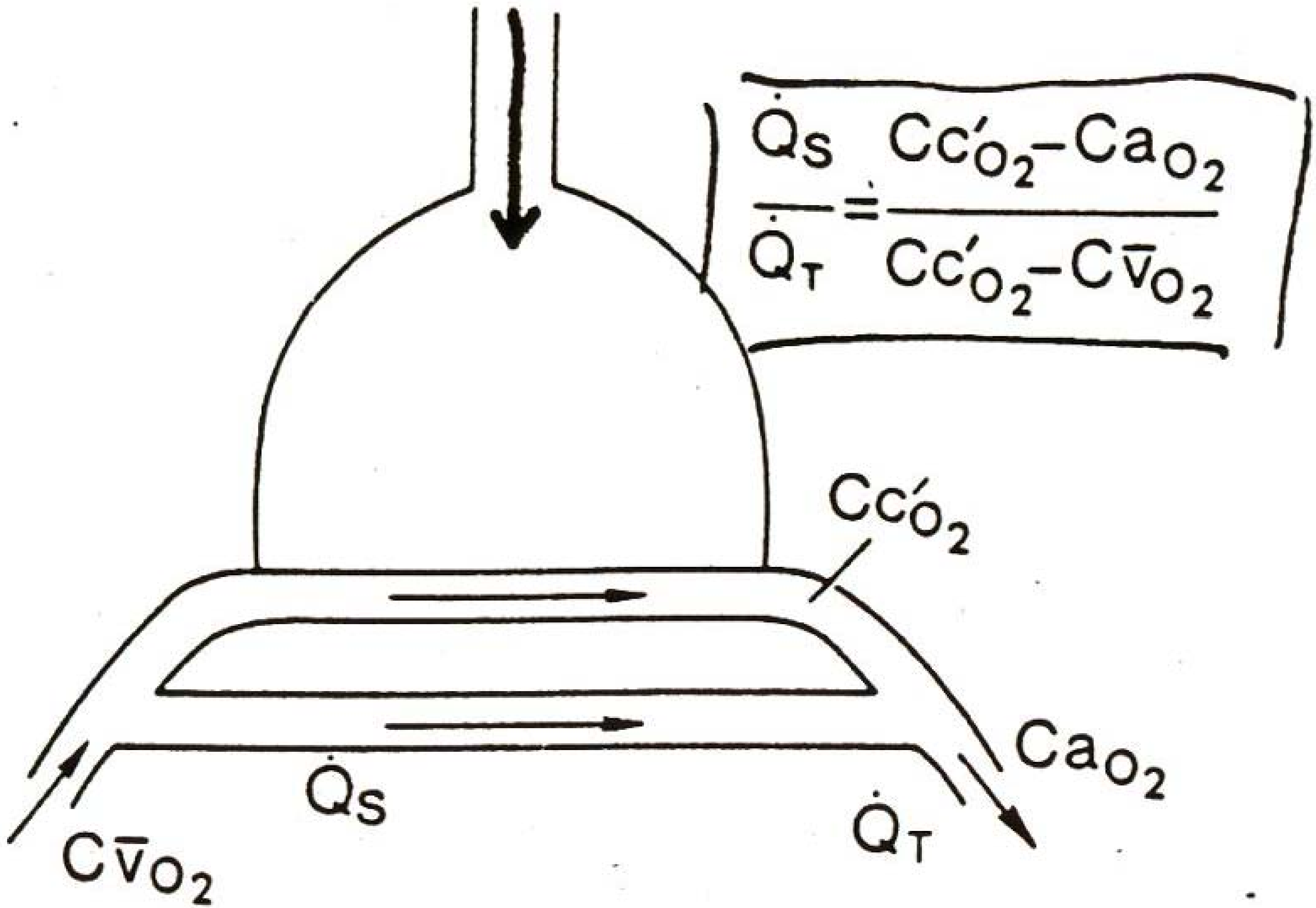
- Decreased diffusing capacity can result from numerous abnormalities unrelated to diffusion block itself
- Diffusion abnormality as a cause of hypoxemia
  - Diffusion block or other inability to transfer gas completely (eg, low PIO2+ increased circulatory time) so that insufficient transfer of alveolar PO_2 occur
- Decreased diffusing capacity without diffusion block
  - low alveolar volume,
  - low Hgb

Right to Left Shunt

- V/Q =0
  - NOT low V/Q
- Supplemental O_2 will not raise PaO_2 with large shunt
  - Can be diagnostic at the bedside!
- Clinical examples
  - ARDS
  - Severe pneumonia
  - Cardiogenic pulmonary edema
- May also be cardiogenic R-L shunt
  - ASD, VSD, PDA

- 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

RESPIRATORY PHYSIOLOGY

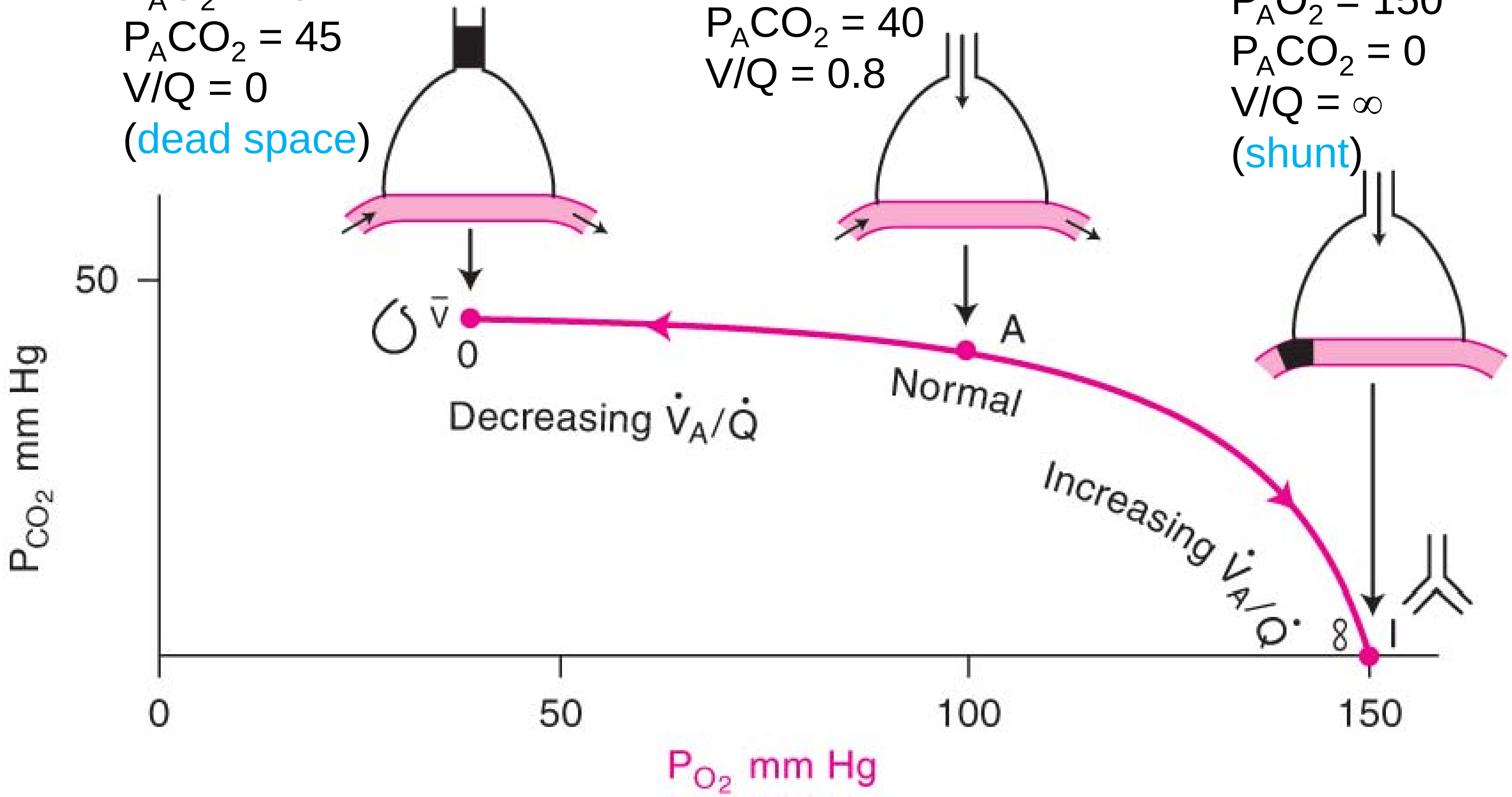


O_2-CO_2 diagram showing a V/Q ratio line

P_AO_2 = 40
P_ACO_2 = 45
V/Q = 0
(dead space)

P_AO_2 = 100
P_ACO_2 = 40
V/Q = 0.8

P_AO_2 = 150
P_ACO_2 = 0
V/Q = ∞
(shunt)



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)