Abnormal Ventilation, Abnormal Gas Exchange

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Ventilation and Gas Exchange

• Objective: to achieve adequate tissue oxygenation and remove metabolically produced CO₂.
• 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 Ventilation

\[ V_T = V_D + V_A \]

\[ V_T \times RR = (V_D \times RR) + (V_A \times RR) \]

\[ \dot{V}_E = \dot{V}_D + \dot{V}_A \]
Volumes and flows

**Volumes**
- Tidal volume: 500 ml
- Anatomic dead space: 150 ml
- Alveolar gas: 3000 ml
- Pulmonary capillary blood: 70 ml

**Flows**
- Total ventilation: 7500 ml/min
- Frequency: 15/min
- Alveolar ventilation: 5250 ml/min
- Pulmonary blood flow: 5000 ml/min
Total and Alveolar Ventilation

\[ \dot{V}_{CO_2} = \dot{V}_A \times F_A CO_2 \]
Total and Alveolar Ventilation

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

\[ P_a CO_2 \propto \frac{\dot{V}_{CO_2}}{V_A} \]

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
  – Inability 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 $P_{A}O_2$ (hypercapnia) indicates the presence of alveolar hypoventilation
Some Causes of Hypoventilation
1. Depression of the respiratory center by drugs, injury, tumor, etc.
2. Abnormalities of the spinal cord (e.g., following high dislocation)
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 O₂ in blood (PaO₂)
  OR
- Low O₂ content (CaO₂)

\[ CaO_2 = (1.39 \times Hb \times S_{a}O_2) + (0.003 \times P_{a}O_2) \]
Hypoxemia ≠ Hypoxia

- Hypoxia is **metabolic** $\text{O}_2$ **deficiency**
- Hypoxia causes are:
  - “stagnant”, as with impaired blood flow;
  - “histocytic”, 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 O₂ Delivery

• O₂ delivery depends on
  – O₂ content
  – cardiac output

\[ \dot{DO}_2 = C_a O_2 \times CO \]
The Alveolar Gas Equation is used to Characterize the Mechanisms and Severity of Hypoxemia

\[ P_{I}O_{2} = F_{i}O_{2} \times (P_{B} - P_{H_{2}O}) \]

\[ P_{A}O_{2} = P_{I}O_{2} - \frac{P_{A}CO_{2}}{R} + \left[ P_{A}CO_{2} \times F_{i}O_{2}x \frac{(1-R)}{R} \right] \]

\[ P_{A}O_{2} \approx P_{I}O_{2} - \frac{P_{A}CO_{2}}{R} \]
Alveolar Gas Equation

\[ P_{AO_2} \approx P_I O_2 - \frac{P_{ACO_2}}{R} \approx P_I O_2 - \frac{P_{aCO_2}}{R} \]

- \( P_{ACO_2} = P_{aCO_2} \)
- \( R = \text{Respiratory Exchange Ratio: (gas R=CO2 added to alveolar gas by blood/amount of O2 removed from alveolar gas by blood; low V/Q=low R); normal=0.8} \)
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 $AaDO_2$

\[ P_A O_2 = 100 \]

\[ P_a O_2 = 90 \]

\[ AaDO_2 = 100 - 90 = 10 \]

Normal $AaDO_2 = 10-15$ mmHg in young adults at sea level breathing RA
Normal AaDO$_2$

- Room air:
  - $P_a$O$_2$=90 mmHg
  - $P_a$CO$_2$=40 mmHg
  - pH=7.40

\[
P_{I}O_2 = F_iO_2 \times (P_B - P_{H2O})
\]

\[
P_{I}O_2 = 0.21 \times (760 - 47) = 150
\]

\[
P_{A}O_2 \approx P_{I}O_2 - \frac{P_aCO_2}{R}
\]

\[
P_{A}O_2 \approx 150 - \frac{40}{0.8} = 100
\]
Physiologic Causes of Hypoxemia

• No widening of AaDO$_2$
  – Hypoventilation
  – Low P$_1$O$_2$
    • may contribute to widening if impaired diffusion

• Widening of AaDO$_2$
  – V/Q mismatch
  – Shunt
  – Diffusion Abnormality
Alveolar Hypoventilation

• Increased $P_A O_2$ (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

- Room air:
  - $P_aO_2=30 \text{ mmHg}$
  - $P_aCO_2=90 \text{ mmHg}$
  - pH=7.08

\[
P_AO_2 \approx P_I O_2 - \frac{P_aCO_2}{R}
\]

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

\[
P_I O_2 = 0.21 \times (760 - 47) = 150
\]

\[
P_AO_2 \approx 150 - \frac{90}{0.8} = 37.5
\]
Case History

\[ P_A O_2 = 37.5 \]

\[ P_a O_2 = 30 \]

\[ AaDO_2 = 37.5 - 30 = 7.5 \]

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

\[
P_{I}O_2 = F_iO_2 \times (P_B - P_{H_2O})
\]
\[
P_{I}O_2 = 0.21 \times (250 - 47) = 43
\]

\[
P_{A}O_2 \approx P_{I}O_2 - \frac{P_{a}CO_2}{R}
\]
\[
P_{A}O_2 \approx 43 - \frac{18}{1} = 25
\]
Case History

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

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

- Room air
  - \( \text{PaO}_2 = 70 \text{ mm Hg} \)
  - \( \text{PaCO}_2 = 30 \text{ mmHg} \)
- No treatment (RA)
  - \( \text{PaO}_2 = 50 \text{ mm Hg} \)
  - \( \text{PaCO}_2 = 28 \text{ mmHg} \)
- What happened?

\[ P_A O_2 \approx 150 - \frac{30}{0.8} = 112.5 \]

\[ AaDO_2 = 112.5 - 70 = 42.5 \]
Case History

- Room air
  - $\text{PaO}_2 = 70 \text{ mm Hg}$
  - $\text{PaCO}_2 = 30 \text{ mmHg}$
- No treatment (RA)
  - $\text{PaO}_2 = 50 \text{ mmHg}$
  - $\text{PaCO}_2 = 28 \text{ mmHg}$
- What happened?

$$P_A O_2 \approx 150 - \frac{30}{0.8} = 112.5$$

$$AaDO_2 = 112.5 - 70 = 42.5$$

$$P_A O_2 \approx 150 - \frac{28}{0.8} = 115$$

$$AaDO_2 = 115 - 50 = 65$$
Physiologic Causes of Hypoxemia

• No widening of AaDO$_2$
  – Hypoventilation
  – Low P$_1$O$_2$
    • 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 **NOT** low ventilation of all alveoli
  - That would be alveolar hypoventilation
Alveolar $\text{PO}_2$ and $\text{PCO}_2$ across various V/Q relationships

\[
\begin{align*}
O_2 &= 150 \text{ mm Hg} \\
CO_2 &= 0
\end{align*}
\]

Diagram:
- **B**: $O_2 = 40$, $CO_2 = 45$
- **A**: $O_2 = 100$, $CO_2 = 40$
- **C**: $O_2 = 150$, $CO_2 = 0$

Decreasing $\dot{V}_A/\dot{Q}$

Increasing $\dot{V}_A/\dot{Q}$
O$_2$-CO$_2$ diagram showing a V/Q ratio line

- PAO$_2$ = 40
- PACO$_2$ = 45
- V/Q = 0
  (dead space)

- PAO$_2$ = 100
- PACO$_2$ = 40
- V/Q = 0.8

- PAO$_2$ = 150
- PACO$_2$ = 0
- V/Q = $\infty$
  (shunt)
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 (e.g., low PIO2+ increased circulatory time) so that insufficient transfer of alveolar PO₂ 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 \((Q_s/Q_t)\): \(Cc’O2-CaO2/Cc’O2-CvO2\) (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

\[
\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{Cc'O_2 - CaO_2}{Cc'O_2 - C\bar{V}O_2}
\]

Symbols:
- \( \dot{Q}_S \): Blood flow to the systemic circulation
- \( Cc'O_2 \): Oxygen content in the central circulation
- \( CaO_2 \): Oxygen content in arterial blood
- \( C\bar{V}O_2 \): Oxygen content in venous blood
- \( \dot{Q}_T \): Total blood flow
$O_2-CO_2$ diagram showing a V/Q ratio line

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

- $P_AO_2 = 100$
- $P_ACO_2 = 40$
- $V/Q = 0.8$

- $P_AO_2 = 150$
- $P_ACO_2 = 0$
- $V/Q = \infty$
  (shunt)

Decreasing $\dot{V}_A/\dot{Q}$

Increasing $\dot{V}_A/\dot{Q}$
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 PaCO₂, Low PaO₂, no widening of AaDO₂
• Gas exchange abnormality: Low PaO₂, normal or low PaCO₂, widened AaDO₂
• Hypoxemia of all hypoventilation and gas exchange abnormalities may be sufficiently overcome by supplemental O₂ 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)