Pathophysiology of hypercapnic and hypoxic respiratory failure and V/Q relationships

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Respiratory Failure
inadequate blood oxygenation or CO₂ removal
A syndrome rather than a disease

Hypoxemic
PaO₂ < 60 mmHg

Hypercapnic
PaCO₂ > 45 mmHg

These two types of respiratory failure always coexist

Acute
Chronic
Respiratory function

Two main categories

Ventilation

Removal of waste CO₂

Oxygenation

Transfer of O₂ from air in blood
Ventilation

Dysfunction of any of the component leads to ventilatory failure
Chemical Stimuli

- **Peripheral chemoreceptors**
  - Carotid bodies, Aortic bodies
  - Stimulus: $\text{PaO}_2$, Acidemia (pH), $\text{PaCO}_2$

- **Central chemoreceptors**
  - Near the ventrolateral surface of the medulla
  - Stimulus: $\text{H}^+ \text{ of brain ECF (pH)}, \text{PaCO}_2$
Chemical Stimuli

- **Hypoxia** → peripheral receptors
- **Hypercapnia** → central receptors

- Response to respiratory acidosis is always greater than metabolic acidosis
Hypercapnic Respiratory Failure

Partial pressures of CO₂ in blood depends on:
- Co₂ production
- Dead space
- Minute ventilation

\[ VA = \frac{VCO₂}{PACO₂} \times K \]

↑CO₂ Production
↑Dead Space Ratio
↓Minute Ventilation
Hypercapnic respiratory failure

**Decreased minute ventilation**

\[ V_T = V_D + V_A \] (multiplying by respiratory frequency)

\[ V_E = V_D + V_A \quad \text{OR} \quad V_A = V_E - V_D \]

According to alveolar ventilation equation:

\[ V_A \times F_aCO_2 = V_A \]

So \[ V_{CO2} = V_A \times P_ACO_2 \times K \]

**Now, \( V_A = V_{CO2} / P_ACO_2 \times K \)**

Paco\(_2\) is inversely proportional to minute ventilation
Hypercapnic respiratory failure

**Decreased minute ventilation**

- CNS disorders
  - Stroke, brain tumor, spinal cord lesions, drug overdose
- Peripheral nerve disease
  - Guillain-Barre syndrome, botulism, myasthenia gravis
- Muscle disorders
  - Muscular dystrophy, respiratory muscles fatigue
Hypercapnic respiratory failure

- Chest wall abnormalities
  - Scoliosis, kyphosis, obesity
- Metabolic abnormalities
  - Myxedema, hypokalemia
- Airway obstruction
  - Upper airway obstruction, Asthma, COPD

Pathophysiology in Asthma and COPD more complex
Hypercapnic respiratory failure

Increase dead space

- Airway obstruction
  - Upper airway obstruction
  - Asthma, COPD
  - Foreign body aspiration (check-valve)

- Chest wall disorder
  - Kyphoscliosis, thoracoplasty etc
Hypercapnic respiratory failure

Increase \( \text{CO}_2 \) production

- Fever, sepsis, seizure, obesity, anxiety
- Increase work of breathing (asthma, COPD)
- High carbohydrate diet with underlying lung disease (high RQ)
Ventilatory Demand

Ventilatory Supply

Ventilatory Demand > Ventilatory Supply \rightarrow \text{Ventilatory Failure}

Ventilatory demand depends on
- O_2 demand
- CO_2 production
- dead space and minute ventilation

Ventilatory supply depends on
- Respiratory drive
- Muscle / neuron function
- Respiratory mechanics

This is responsible for MSV
CAUSES OF VENTILATORY FAILURE

A. Respiratory centre
B. UMN
C. Ant.horn cell
D. LMN
E. NMJ
F. Respiratory muscles
G. Altered elasticity
H. Loss of structural integrity
I. Small airway resistance
Respiratory Failure in a patient with Asthma

Ventilatory Demand
- Work of breathing
- Increased dead space
- Hyperventilation

Ventilatory Supply
- Airway obstruction
- Decreased FEV₁
- Altered pulmonary mechanics

Ventilatory Demand > Ventilatory Supply → Ventilatory Failure
Respiratory failure in COPD

- Decreased FEV$_1$
  - Relationship is curvilinear; CO$_2$ retention does not occur unless FEV$_1$ < 20 – 30 % of normal

- Altered lung mechanics

- Increased dead space ventilation

- Expiratory air trapping due to obstructive physiology

- Respiratory muscle fatigue

- Decreased muscle blood flow

- Increased CO$_2$ production
Hypoxic Respiratory Failure

\[ \text{PaO}_2 = \left( \text{FiO}_2 (\text{P}_{\text{ATM}} - \text{P}_{\text{H}_2\text{O}}) - \text{PaCO}_2/R \right) - \left[ \text{A-a gradient} \right] \]

- Low Inspired Oxygen
- Shunt
  - V-Q mismatch
  - Diffusion impairment

Hypoxemic Respiratory Failure
Hypoxic Respiratory Failure

- **Shunt:**
  Blood pathway which does not allow contact between alveolar gas and red cells

- **Physiological**
  - Pulmonary
  - Non-pulmonary

- **Pathological**
Hypoxic Respiratory Failure

- Normal shunting: (2~3% of C.O.)
  - Some of the bronchial arterial blood
  - Some of the coronary venous blood

- Abnormal shunting:
  - Congenital defects in the heart or vessels
    - ASD, VSD(with reversal), Pulmonary AVM
  - Lung atelectasis or consolidation
    - Pneumonia, Cardiogenic or Non-cardiogenic pulmonary edema
Hypoxic Respiratory Failure

- Shunt (right-to-left shunt)
  Resistant to $O_2$ supplementation when shunt fraction of CO $> 30\%$
Hypoxic Respiratory Failure

- Etiologies of Shunt physiology
  - Diffuse alveolar filling
  - Collapse / Consolidation
  - Abnormal arteriovenous channels
  - Intracardiac shunts

Hallmark of shunt is poor or no response to O2 therapy

Usually causes hypoxemic respiratory failure
Hypoxic Respiratory Failure

- Shunt can lead to hypercapnia when more than 60% of the cardiac output
  - Ventilatory compensation fails
  - ↑RR → Increased dead space
  - ↓ total alveolar ventilation
  - Respiratory muscle fatigue
Hypoxic Respiratory Failure

- Ventilation-Perfusion mismatch
  - Gas exchange depends on
    - V/Q ratio
    - Composition of inspired gas
    - Slopes and position of relevant blood gas dissociation curves
Hypoxic Respiratory Failure

CO₂ lost in alveolar gas from capillary:

\[ V_{CO2} = Q(C_{vco2} - C_{cco2}) \]

CO₂ lost from exhaled gas into air

\[ V_{CO2} = V_A \times P_{ACO2} \times K \]

In steady state CO₂ lost from capillary and alveoli is same

So \[ V_a \times P_a \cdot CO2 \times K = Q(C_{vco2} - C_{cco2}) \]

i.e. \[ V_A/Q = (C_{vco2} - C_{cco2}/ P_A \cdot CO2) \times K \ldots \ldots (1) \]
Hypoxic Respiratory Failure

Similarly for O$_2$:

$$V_{O2} = V_I \times F_{iO2} - V_a \times F_{AO2}$$

And..

$$V_{O2} = Q( Cc_{O2} - Cv_{O2})$$

Now, as Inspired $V_A = \text{Expired } V_A$

So,

$$V_A/Q = Cc_{O2} - Cv_{O2} / F_{iO2} - F_{AO2} \ldots(2)$$
Hypoxic Respiratory Failure

- In normal lungs 5-10 mm difference in alveolar and arterial blood is due to physiological inequality
  - Gravitationally based inequality
  - Fractally based inequality
  - Longitudinally based inequality
  - Collateral ventilation
  - Reactive vaso- and broncho-constriction
Hypoxic Respiratory Failure

Ventilation-Perfusion Mismatch

- Vascular obstruction
  - Pulmonary embolism
- Air-space consolidation
  - Pneumonia, Pulmonary edema
- Airway obstruction
  - Asthma, COPD etc.
- Diffuse parenchymal lung diseases
  - ILDs, DAD etc
Models for V/Q relationship

- Both the obstructive models result in hypoxemia and hypercapnia
- But the effects on $O_2$ and alveolar arterial gradient exceed greatly those for $CO_2$
- Airway obstruction cause more hypoxemia and less hypercapnia than identical degrees of vascular obstruction
Hypoxic Respiratory Failure

- Principal effects of V/Q inequality on $O_2$ and $CO_2$ exchange are:
  - Affects both gases no matter what the pathological basis of inequality
  - Causes hypoxia and hypercapnia
  - Causes more severe hypoxia than hypercapnia
  - Impairs total $O_2$ and $CO_2$ exchange by lungs
Hypoxic Respiratory Failure

- Affects $O_2$ more than $CO_2$ in very low V/Q areas
- Affects $CO_2$ more than $O_2$ in very high V/Q areas
- Creates alveolar arterial difference for both the gases
Response to V/Q mismatch

Physiologically the response to V/Q mismatch is primarily by:
- Changes in mixed venous saturation
- Increase in ventilation
- Changes in cardiac output

In low V/Q areas
- ↑ in ventilation leads to significant drop in CO$_2$
- But O$_2$ is barely affected if at all
Response to V/Q mismatch

- In high V/Q areas:
  - Both $O_2$ and $CO_2$ usually come to nearly normal levels

- Changes in cardiac output have starkly contrast effects
  - In low V/Q areas $O_2$ improves to some extent but,
  - In high V/Q areas there is no significant effect
Hypoxic Respiratory Failure

- Diffusion Impairment
  - Interstitial lung disease
  - Pulmonary fibrosis, Connective tissue disease, Interstitial pneumonia, interstitial pulmonary edema
  - ARDS
  - Obstructive lung disease
    - Emphysema, Asthma
Diffusion capacity of a gas depends on:
- Thickness of the alveolar basement membrane.
- Avidity of the gas to bind to hemoglobin
- Hemoglobin concentration
- Alveolar partial pressures of $O_2$
- Capillary transit time
- Lung volumes
The capillary transit time of RBC is 0.75 seconds.

With normal DL, it takes < 0.25 seconds to equilibration.

Only when the DL is severely limited (<0.25 normal) or the transit time is markedly shorten (<0.25 seconds) is it possible to have a PaO2 less than PAO2.
Hypoxic respiratory failure

- Acute lung injury:
  - Maldistribution of ventilation
  - Shunt physiology
  - Alveolar hypoventilation
  - Diffusion limitation

Predominantly hypoxic respiratory failure

Hypercapnia may appear in late phases
Mechanisms of hypercapnia in acute lung injury

- Increased O2 consumption by lungs
- Increased dead space
- Decreased total alveolar ventilation
- Increased lung compliance
- Decreased FRC
- Increased air flow resistance
- Respiratory muscle fatigue

Ventilatory Demand

Ventilatory Supply
Thank You