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

Dr.Alok Nath
Department of Pulmonary Medicine
PGIMER
Chandigarh

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Respiratory Failure

inadequate blood oxygenation or CO_2 removal

A syndrome rather than a disease

Hypoxemic	Hypercapnic
$PaO2 < 60$ mmHg	$PaCO2 > 45$ mmHg

These two types of respiratory failure always coexist

Acute

Chronic

Respiratory function

Two main categories

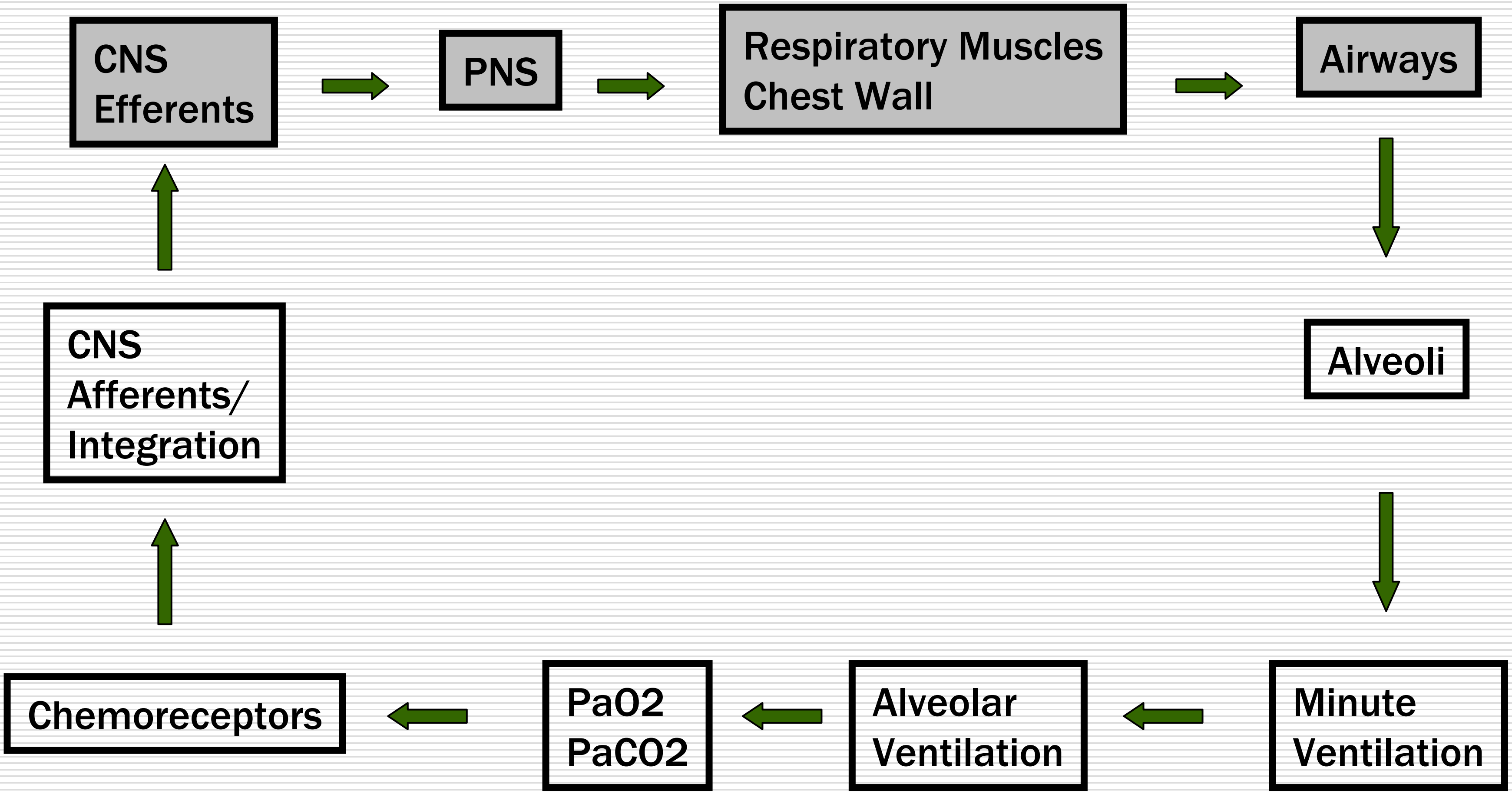
Ventilation

Oxygenation

Removal of waste CO_2

Transfer of O_2 from air in blood

Ventilation



Dysfunction of any of the component leads to ventilatory failure

Chemical Stimuli

- **Peripheral chemoreceptors**
  - Carotid bodies, Aortic bodies
  - Stimulus: **PaO2, Acidemia (pH), PaCO2**

- **Central chemoreceptors**
  - Near the ventrolateral surface of the medulla
  - Stimulus: **H^+ of brain ECF (pH), PaCO2**

Chemical Stimuli

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

- Response to respiratory acidosis is always greater than metabolic acidosis

Hypercapnic Respiratory Failure

Partial pressures of CO_2 in blood depends on:
Co_2 production
Dead space
Minute ventilation

VA = VCO2 / PACO2 x K

↑CO2 Production
↑Dead Space Ratio
↓Minute Ventilation

➡ **Hypercapnic Respiratory Failure**

Hypercapnic respiratory failure

Decreased minute ventilation

$V_T = V_D + V_A$ (multiplying by respiratory frequency)

$V_E = V_D + V_A$ OR $V_A = V_E – V_D$

Acc. 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

Pathophsiology in Asthma and COPD more complex

Hypercapnic respiratory failure

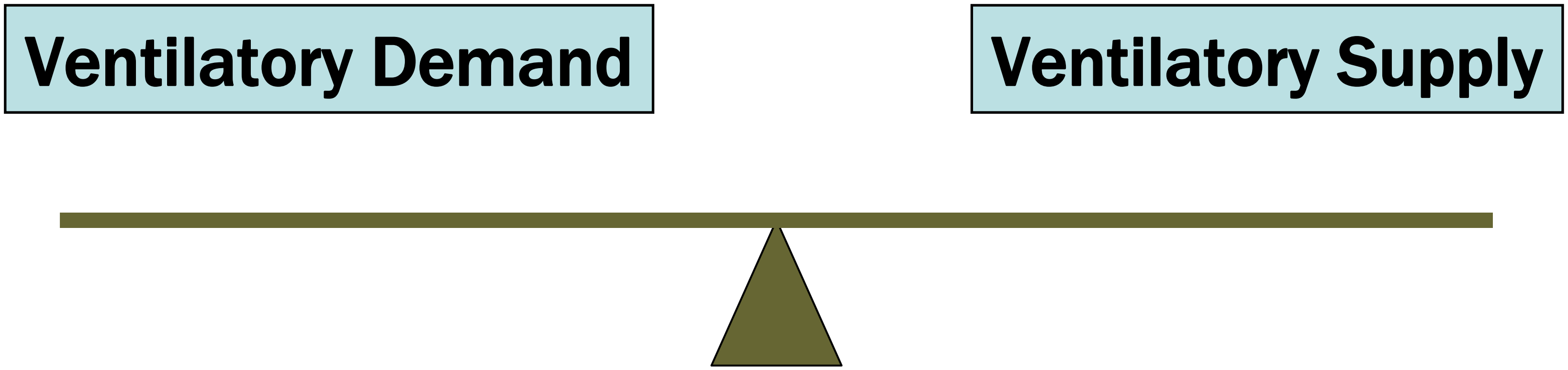
Increase dead space

- Airway obstruction
  - Upper airway obstruction
  - Asthma, COPD
  - Foreign body aspiration (check-valve)
- Chest wall disorder
  - Kyphoscliosis, thoracoplasty etc

Hypercapnic respiratory failure

Increase 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 Failure

Ventilatory demand depends on

- O_2 demand
- CO_2 production
- dead space and minute ventilation

Ventilatory supply depends on

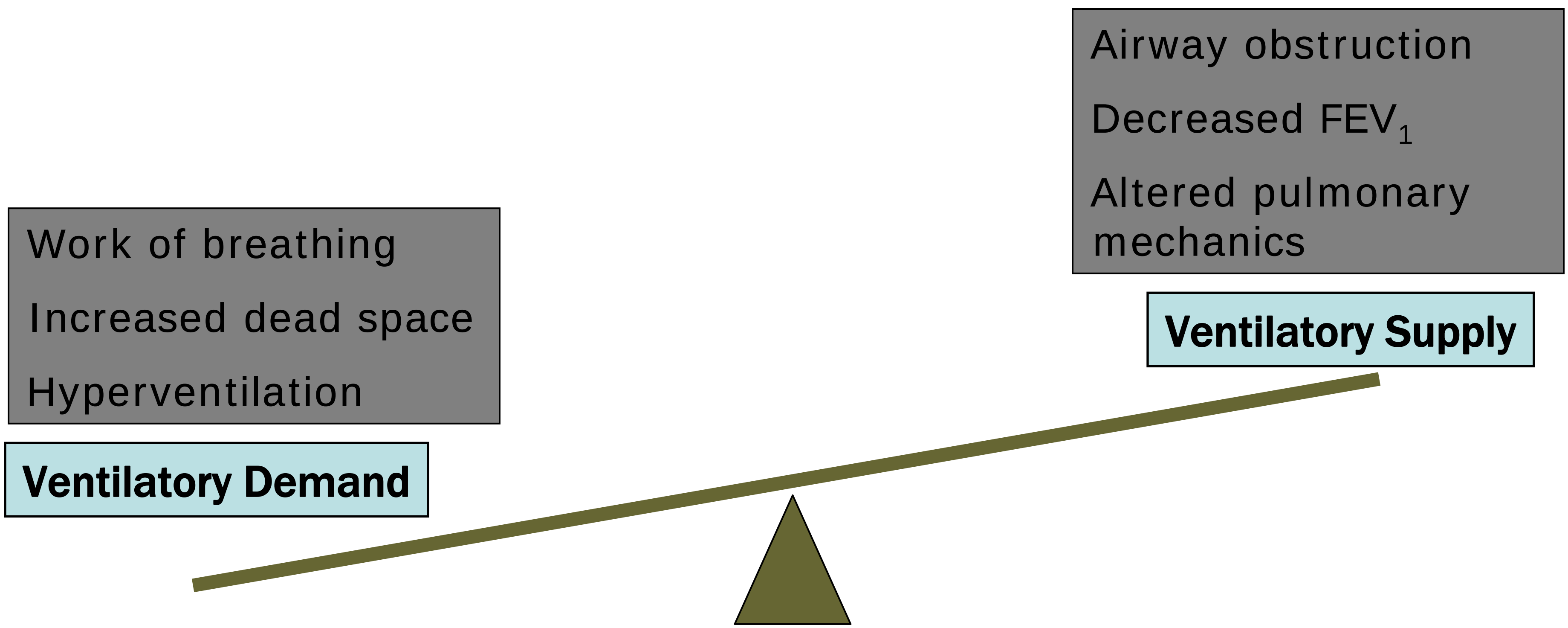
- Respiratory drive
- Muscle /neuron function
- Respiratory mechanics

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 > 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

$$PaO_2 = [\ FiO_2\,(P_{ATM} - P_{H2O}) - PaCO_2/R\ ] - [\ \text{A-a gradient}\ ]$$

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

PATHOLOGICAL

Pulmonary

Non-pulmonary

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

CO_2 lost in alveolar gas from capillary:

$$V_{CO2} = Q(C_{vco2}-C_{cco2})$$

CO_2 lost from exhaled gas into air

$$V_{CO2} = V_A \times P_{ACO2} \times K$$

In steady state CO_2 lost from capillary and alveoli is same

So $V_a x\ P_a co2\ xK = Q(C_{vco2}-C_{cco2})$

i.e. $V_A / Q = (C_{vco2}-c_{cco2} / P_A co_2) x\ K$…….(1)

Hypoxic Respiratory Failure

Similarly for O_2:

$$V_{O2} = V_I \times Fi_{o2} - V_a \times F_{AO2}$$

And.. $V_{O2} = Q(Cc_{o2} - Cv_{O2})$

Now,as Inspired V_A = Expired V_A

So, $\mathbf{V_A / Q = Cc_{O2} - Cv_{O2} / F_{IO2} - F_{AO2}}$**.....(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

Hypoxic Respiratory Failure

- 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.

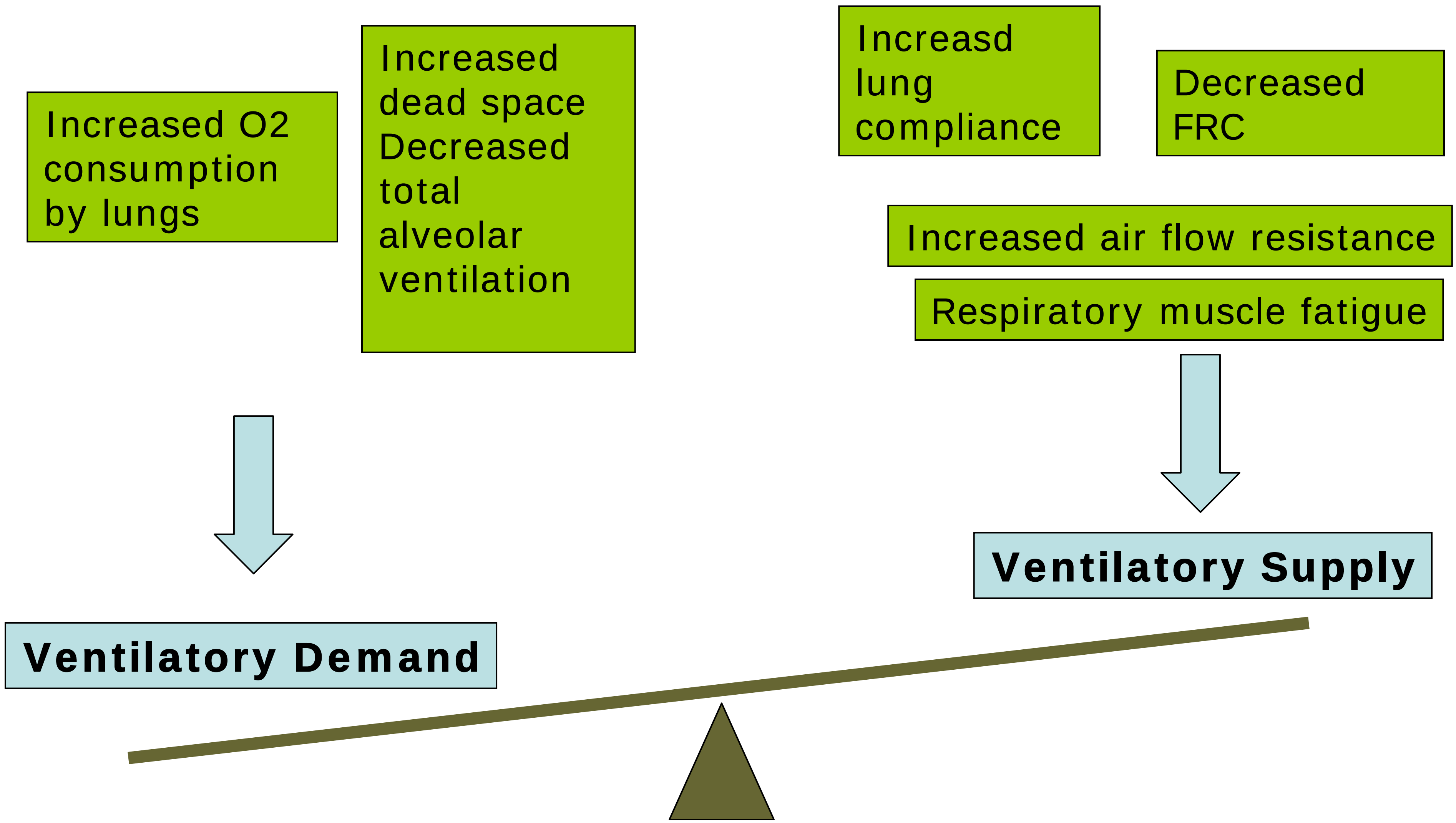
Hypoxic respiratory failure

- 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



Thank You