

Physiological Responses to Oxygen and Carbon Dioxide in the Breathing Environment

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“All things are poison and nothing is without poison, only the dose makes something not a poison”

- Paracelsus (1493-1541)

Swiss physician and alchemist



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Introduction

- **Earth's Atmosphere**
 - 20.95% Oxygen
 - 78.0% Nitrogen
 - 0.038% Carbon Dioxide
 - Trace elements
- **Oxygen – produced by photolysis, photosynthesis**
- **Carbon dioxide – produced by oceans, animal respiration, plant decay, burning of fossil fuels**
- **All aerobic life is dependent on the presence of oxygen for metabolic energy**

Introduction

- **Variations in gas concentrations from that normally found in the atmosphere at sea level can have significant influences on human physiology as evidenced primarily as changes in:**
 - pulmonary function
 - metabolism
 - neurologic
- **These physiological changes have relevance to the use of respiratory protective devices (RPDs)**

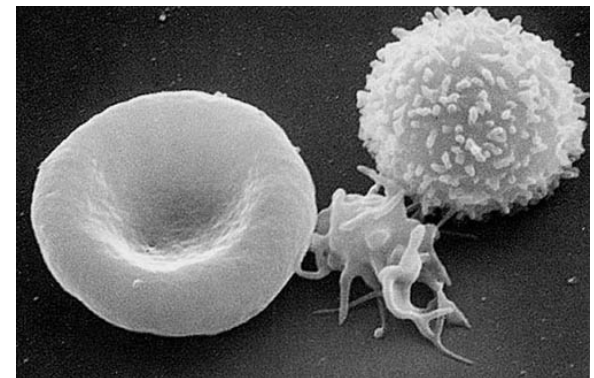
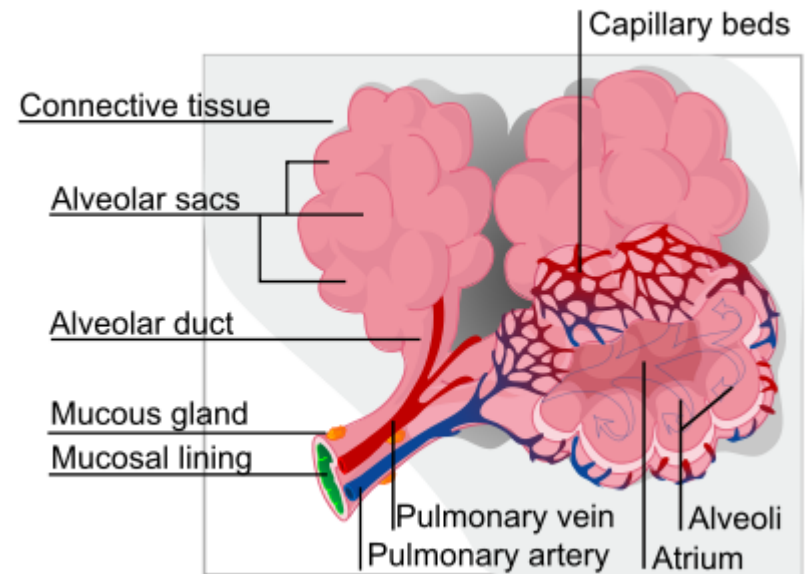
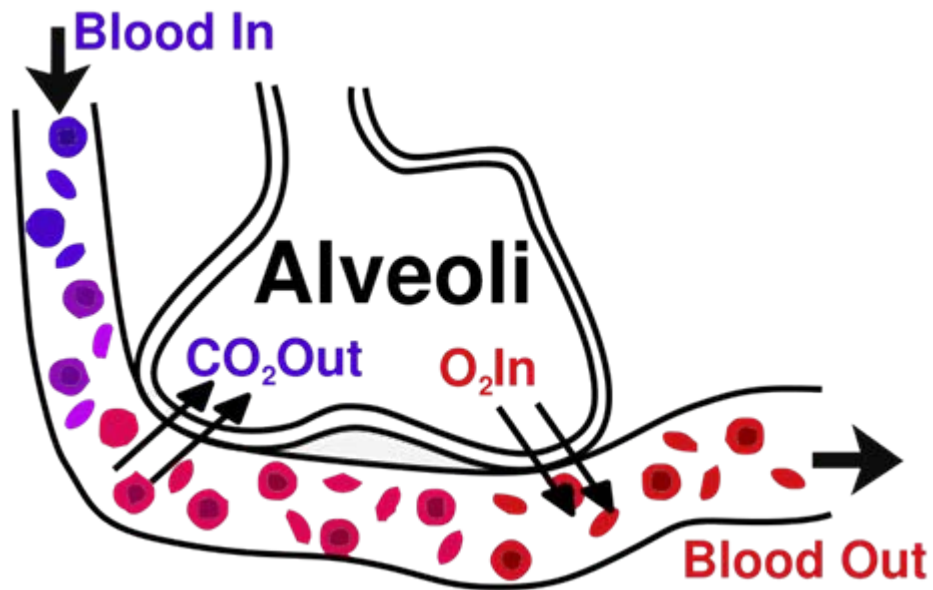
Physiological Considerations

- **Gas exchange in humans occurs in the lungs**
 - Inhaled air is conducted via the airways to the alveoli
 - Alveoli are in close proximity to blood capillaries – gas exchange between alveoli and capillaries is driven by diffusion gradients
 - Oxygen is transported by diffusion from the alveoli to the blood and is transported by the hemoglobin in red blood cells
 - Carbon Dioxide – produced metabolically – is carried from the blood to the alveoli where it is exhaled to the atmosphere
- **The exchange is rapid and normally occurs regardless of the level of physical activity**

Diagram of the Alveoli-Capillary Relationship

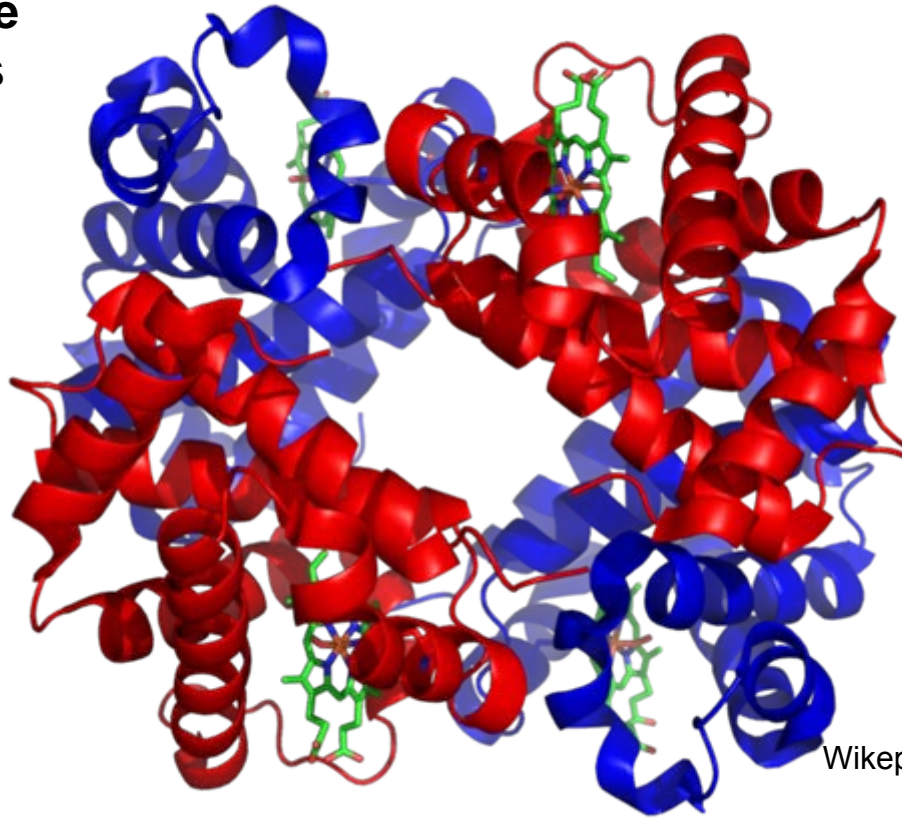
Principles of gas exchange between alveoli, capillary, red blood cells

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Oxygen Transport

Fe⁺ containing heme molecule that binds oxygen shown in green



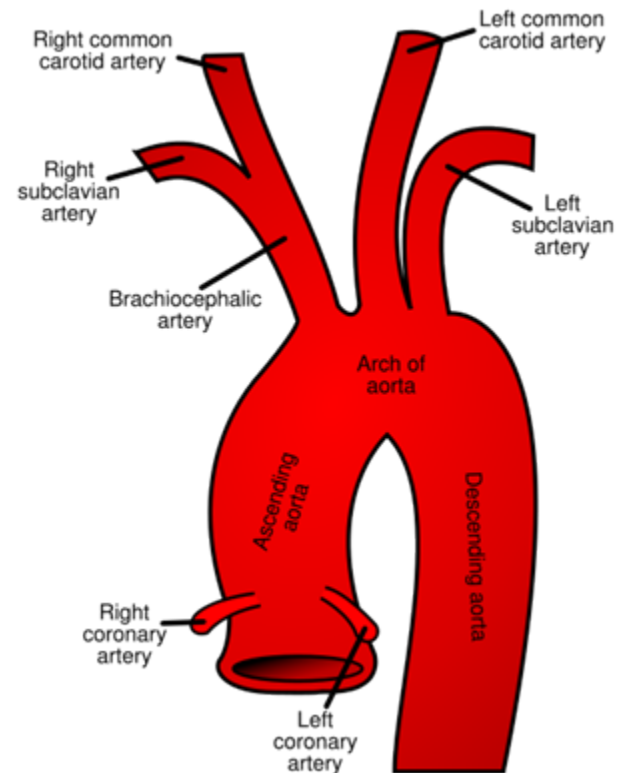
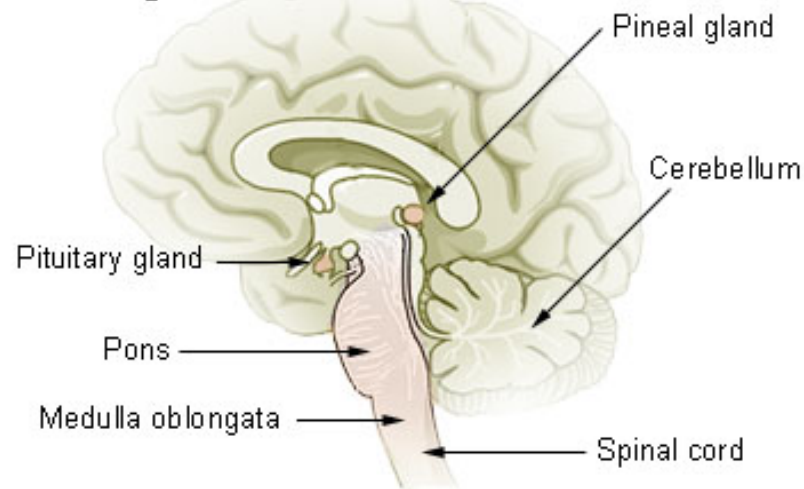
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There are approximately 280 million hemoglobin molecules per RBC – 400 billion RBCs are produced daily. RBC production can increase 20-fold in response to hypoxemia.

Central and Peripheral Chemoreceptors

Detect changes in pH, PaO₂, and PaCO₂ in the blood resulting in a ventilatory response

Pituitary and Pineal Glands



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Changes in Gas Concentration

- **Hyperoxia – a $[O_2]$ or PO_2 in the breathing environment greater than that which is found in the Earth's atmosphere at sea level**
- **Can occur in:**
 - Hyperbaric conditions (i.e., diving, caisson work)
 - Normobaric (i.e., clinical settings)
- **Contributes to an excess of oxygen in the body**
- **Mild hyperoxia is usually well tolerated – humans can acclimate to mild hyperoxia**
- **Extreme hyperoxia can cause pulmonary damage over time**

Hyperoxia – Physiological effects:

- **Normobaric:**

- Mild respiratory depression breathing 100% O₂
- Increased ventilation due to paradoxical increase in CO₂ (result of a decrease in carboxyhemoglobin)
- Pulmonary injury after 3-4 days of continuous exposure (probably due to the presence of increased oxygen free radicals) resulting in oxidative stress to alveolar cells

Hyperoxia – Physiological effects:

- **Hyperbaric**

- Breathing 100% O₂, while used therapeutically, is toxic under hyperbaric conditions over time
- Neurological: seizures can occur at 2 ATM (absolute), death
- US Navy has determined that the threshold for oxygen toxicity occurs between 1.3 – 1.5 ATM (absolute) while breathing 100% O₂
- Cardiovascular: Decreased HR, Q, SV, and total peripheral resistance of vascular beds

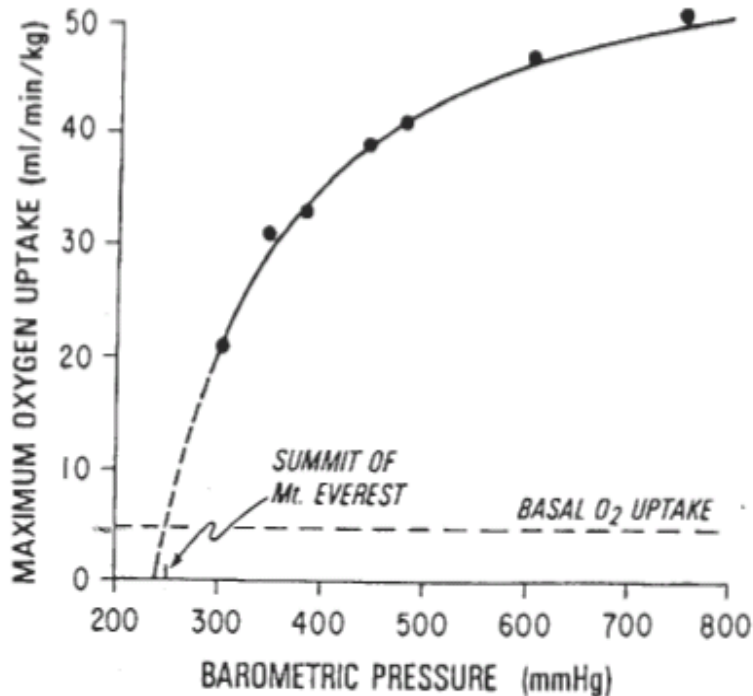
Hyperoxia – Physiological effects:

- **Opposite response in special vascular beds:**
 - Increased cerebral vasoconstriction and decreased cerebral blood flow
 - General vasoconstriction of renal and splanchnic (gut) blood vessels
 - Decrease in retinal blood flow
- **Vascular changes are not associated with altered neural activity**

Hypoxia: Physiological Effects

- **Hypoxia – an $[O_2]$ or PO_2 in the breathing environment below that which is found in the Earth's atmosphere at sea level.**
- **Acute exposure (mountain climbing or aviation) studies**
 - Increased pulmonary minute ventilation, oxygen consumption
 - At summit of Mt. Everest, minute ventilation is at maximal at rest without oxygen supplementation
 - Maximal oxygen consumption barely sufficient to maintain basal metabolism – little left for muscular exercise
 - Alveolar PO_2 maintained at 4.7 kPa (35 mmHg) only by extreme hyperventilation

VO₂max at the summit of Mt. Everest



Sun et al., *Aviat Space Environ Med* 1996 67(1):34-39
reproduced with permission

**Mt. Everest is 8848 m
(29,029 ft) high**

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Hypoxia: Physiological Effects

- **Chronic hypoxia (days to months):**
 - May hypersensitize peripheral chemoreceptors thus increasing the ventilatory response to hypoxia
 - Hypersensitivity may be protective by increasing the oxygen content in the lungs
 - Increase in cardiac output secondary to CNS stimulation
 - Metabolic alkalosis (due to hyperventilation)
 - Reduction in exercise tolerance

Hypoxia: Physiological Effects

- **Adaptation**

- Humans can adapt to chronic hypoxia - ~40 million people live and work at altitudes between 3048 and 5486 m (10000 – 18000 ft)
- Peruvians work in copper mines at 5183 m (17000 ft)
- Increased number of pulmonary alveoli (occurs with exposure to hypoxia at birth – not in adults exposed to hypoxia)
- Increased blood hemoglobin and myoglobin
- Decreased ventilatory response to hypoxia
- Increased pulmonary ventilation above baseline

Hypoxia: Physiological Effects

- **Hypoxic Limits:**

- However, when alveolar $PO_2 \leq 3.9-5.3$ kPa (30-40 mmHg) loss of consciousness occurs rapidly – insufficient oxygenation of brain, organs, and tissues.
- Person is often unaware of the progression to loss of consciousness
- Death ensues due to asphyxia shortly thereafter unless oxygen is administered
- Can occur in workers exposed to low oxygen environments while cleaning chemical storage tanks
- Displacement of oxygen by other gases in the breathing environment

Hypercarbia

- **CO₂ is a normal by-product of aerobic metabolism**
- **Increased CO₂ in the body results in important physiological responses throughout the body**
- **CO₂ is a potent stimulus of pulmonary minute ventilation**
 - Acts by stimulating chemoreceptors in the carotid bodies and respiratory control centers in the brain and brainstem
 - Changes in ventilation in response to CO₂ production keeps alveolar PCO₂ in dynamic equilibrium with metabolically produced CO₂
- **CO₂ is also a potent stimulus of cerebral vasodilation and blood flow**

Hypercarbia

- **Hypercarbia can result from:**
 - Hypoventilation: low breathing rate allows build-up of CO₂ (e.g., deliberate “skip-breathing” by SCUBA divers)
 - Malfunctioning respirator can lead to increased re-breathing of CO₂
 - Increase in the dead space of breathing apparatus or increased alveolar dead space (e.g., pulmonary embolism)
 - Increased breathing resistance of RPD leading to a reduction in breathing frequency

Hypercarbia – Summary of Physiological Effects

- **CO₂ can induce:**
 - Visual disturbances
 - Headache
 - Reduction in reasoning ability
 - A sense of “air hunger” or dyspnea
- **CO₂ can act as an anesthetic and can cause unconsciousness**
 - Can induce inert gas narcosis similar to nitrous oxide
- **CO₂ can alter the intracellular pH thus having effects on metabolism (also probable mechanism for inert gas narcotic effect)**

Hypercarbia – Summary of Exposure/Activity Limits

Average %CO ₂ (Displacement of Oxygen in air)	At Rest (65 W·m ²)		Very, very high work rate (400 W·m ²)	
		Exposure Limit (time)	Potential effects and/or Limitations	Exposure Limit (time)
1.5	No restrictions on activity	Indefinite exposure	Increase in ventilation	unknown
2.5	Increase in ventilation	unknown	Increase in ventilation	2 hours
3.0	Increase in ventilation No restrictions within the exposure limit	15 hours	Increase in ventilation	30 min
5.0	Increase in ventilation No restrictions within the exposure limit	8 hours	Increase in ventilation Collapse / unconsciousness	5 min
7.0	Increase in ventilation Severe limitations on activity	<30 min	Collapse / unconsciousness	n/a
10.0	Increased heart rate Collapse / unconsciousness	<2.0 min	Collapse / unconsciousness	n/a

Respiratory Protection – Not New

17th Century Physician Visiting a Plague House

"Doktor Schnabel von Rom" ("Doctor Beak from Rome")
engraving, Rome 1656



Wikipedia:Image

From: Imagery from the History of Medicine

21st Century Surgeons in a Modern Operating Room



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Versions of Respiratory Protection



NIOSH Photos



Relevance to Respiratory Protective Devices

- **At rest:**

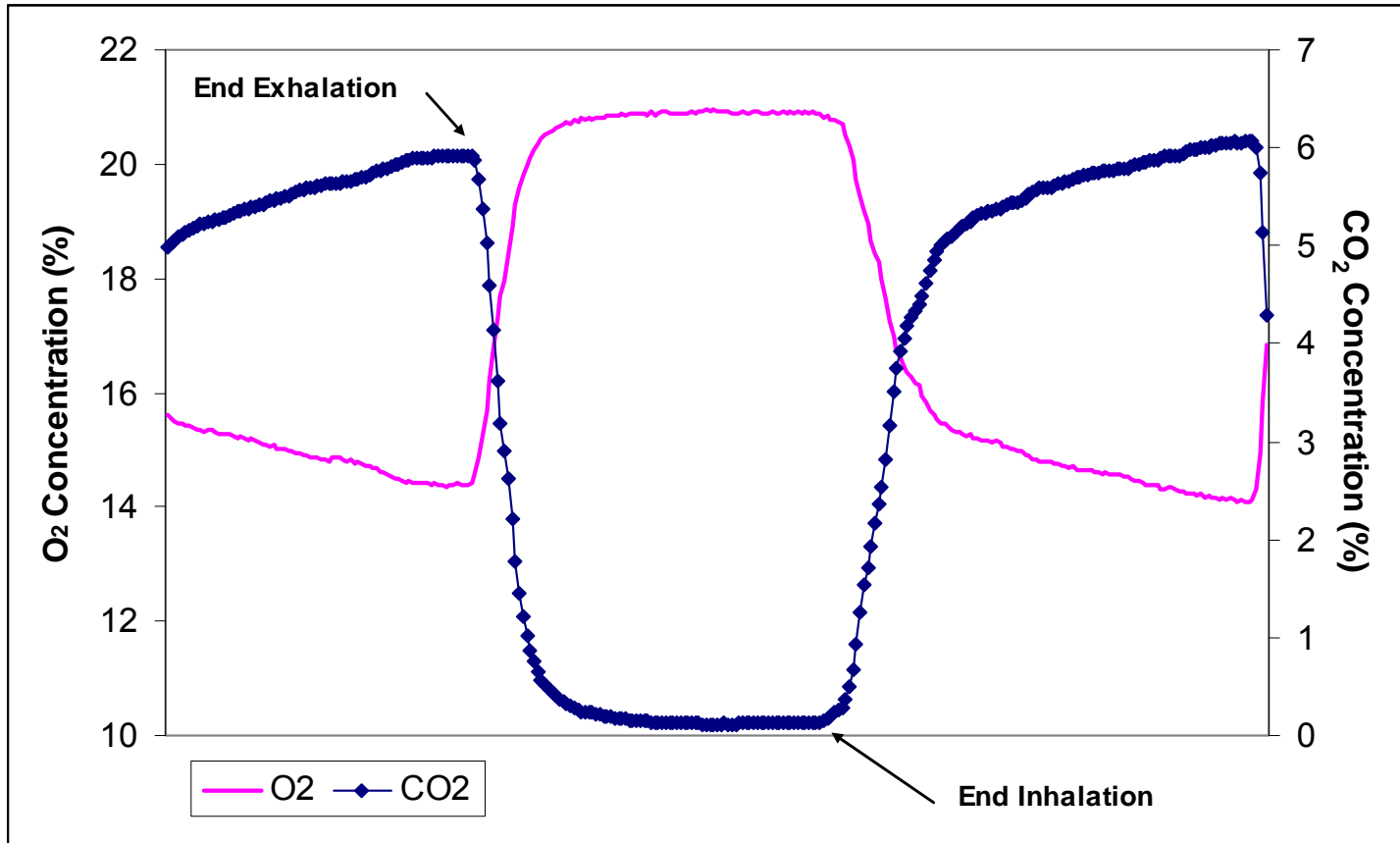
- Oxygen consumption is $\sim 250 \text{ mL}\cdot\text{min}^{-1}$
- Carbon dioxide production is $\sim 200 \text{ mL}\cdot\text{min}^{-1}$

- **At maximal exercise:**

- Oxygen consumption is can exceed $3.5 \text{ L}\cdot\text{min}^{-1}$
- Carbon dioxide production can exceed $4.0 \text{ L}\cdot\text{min}^{-1}$

Single Breathing Cycle in Respirator

O₂ and CO₂ Concentrations in the Breathing Space



Graph kindly provided by D. Caretti

Relevance to Respiratory Protective Devices

- **If a respiratory protective device (RPD):**
 - Fails to deliver enough (or delivers too much) oxygen to match demand, and/or,
 - eliminate the carbon dioxide in the breathing space
- **Then hyperoxia, hypoxia, or hypercapnia may become significant issues for the user**
- **A filtering facepiece respirator**
 - Only protects against particulates
 - Does not protect against a hyperoxic or hypoxic atmosphere or protect against an atmosphere containing high levels of CO₂

Summary

- Whereas oxygen is necessary for life and vital for aerobic metabolism, and
- carbon dioxide is a normal product of aerobic metabolism and is an important regulator of physiological function

- High levels of oxygen, especially under hyperbaric conditions is toxic and can be fatal
- Low levels of oxygen at sea level or at altitude can result in asphyxia and death
- High levels of carbon dioxide can result in asphyxia and death

Summary

Thus-

“All things are poison and nothing is without poison, only the dose makes something not a poison”

Acknowledgements

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Thank You

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