Physiological Responses to Oxygen and Carbon Dioxide in the Breathing Environment

W. Jon Williams, Ph.D.

National Institute for Occupational Safety and Health, USA

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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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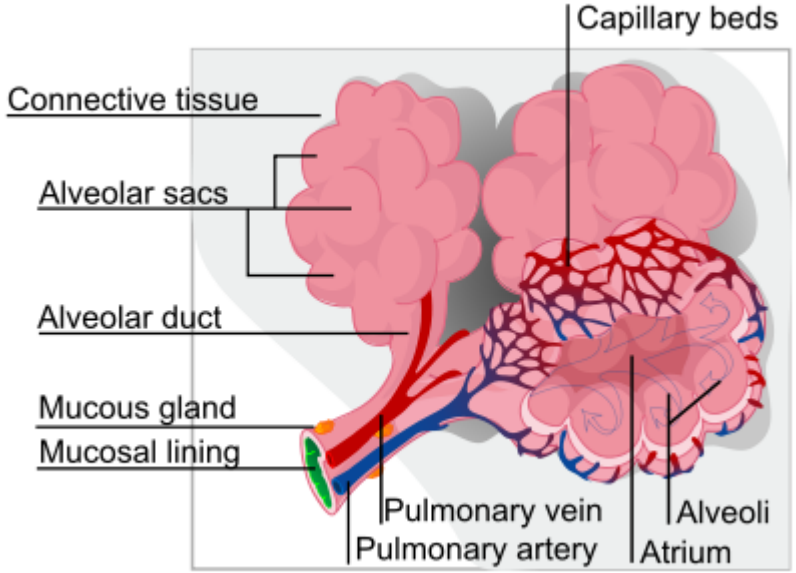
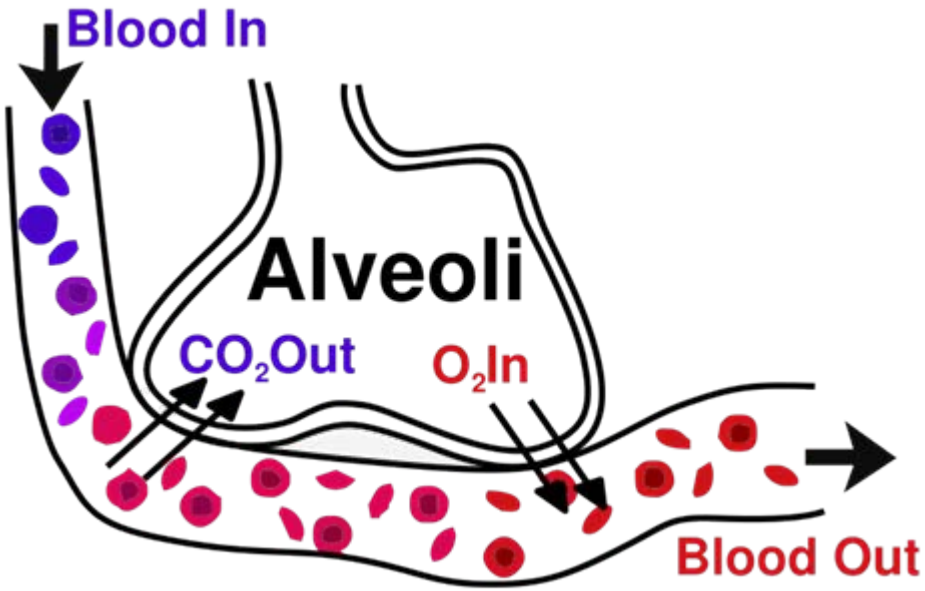
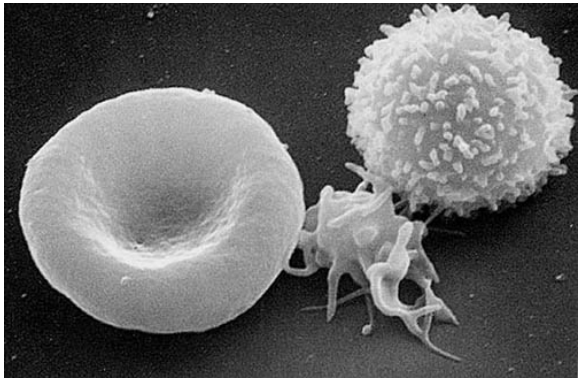
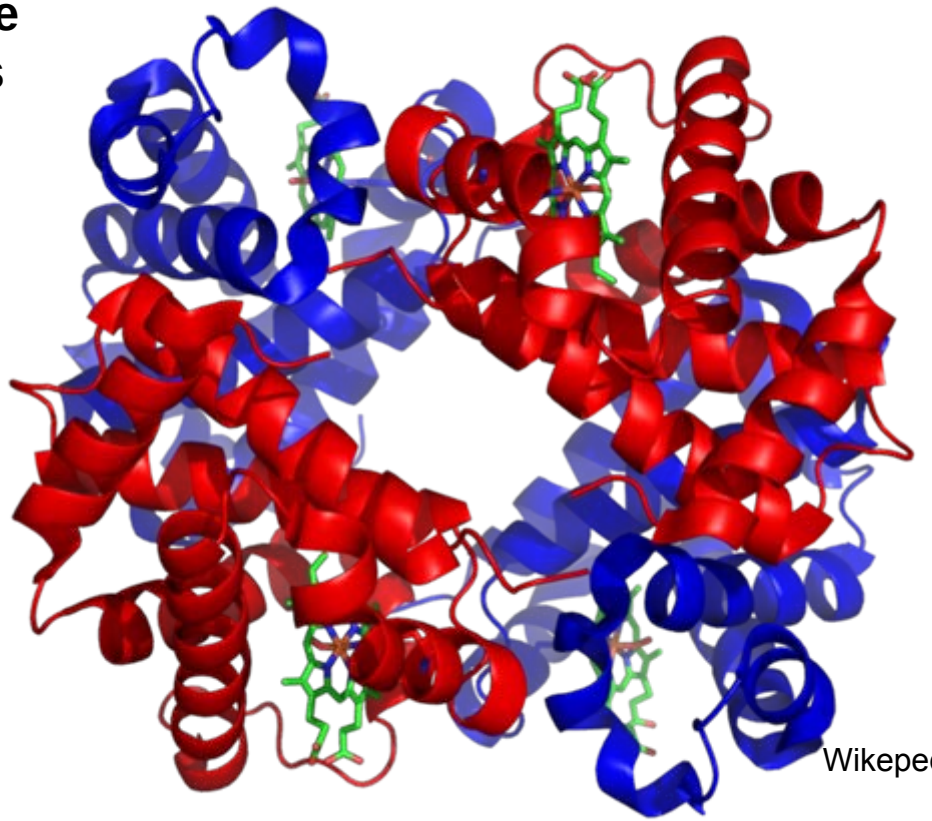






Oxygen Transport

Fe^{+} containing heme molecule that binds oxygen shown in green



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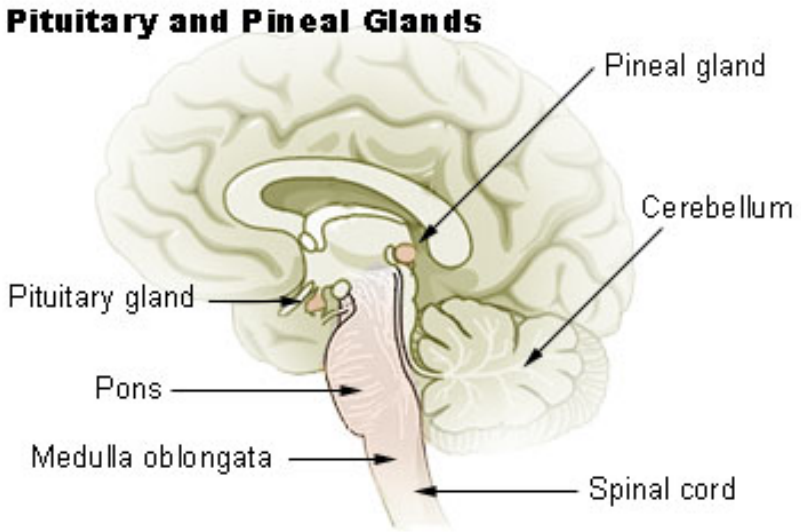
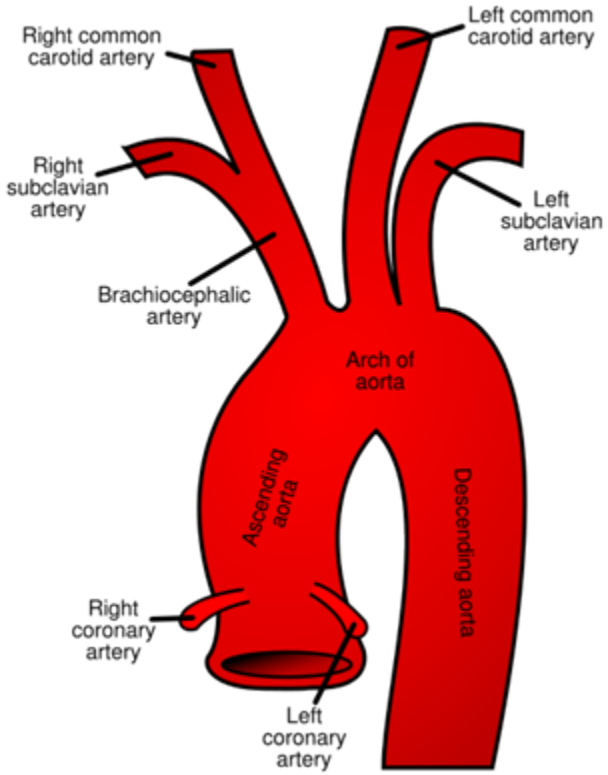
There are approximately 280 million hemoglobin molecules per RBC – 400 billion RBCs are produced daily. RBC production can increase 20-fold in response to hypoxemia.

Central and Peripheral Chemreceptors

Detect changes in pH, PaO_2, and $PaCO_2$ in the blood resulting in a ventilatory response





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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% O_2
  - Increased ventilation due to paradoxical increase in CO_2 (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% O_2, 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% O_2
  - Cardiovascular: Decreased HR, Q, SV, and total peripheral resistance of vascular beds

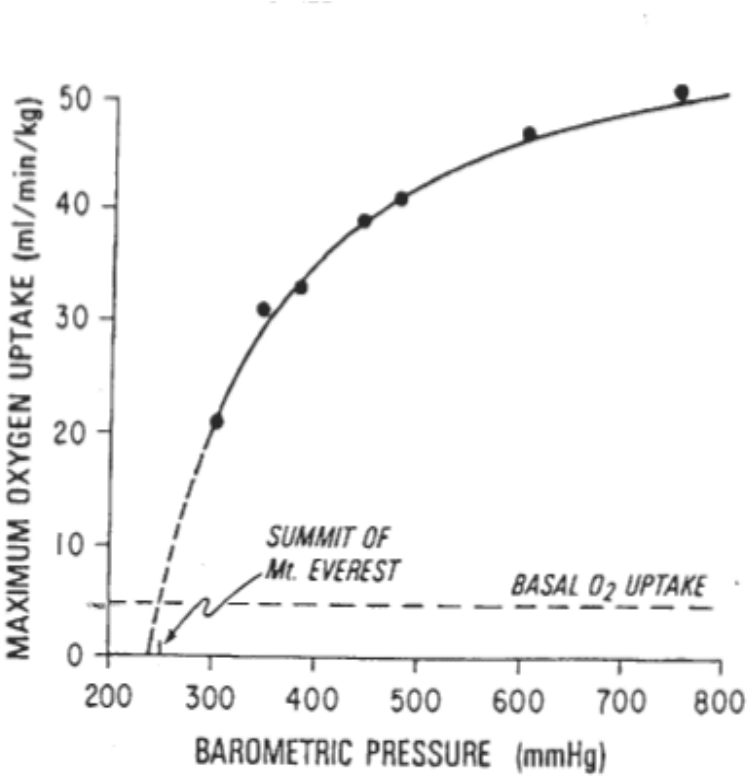
Hyperoxia – Physiological effects:

- **Opposite response in special vascular beds:**
  - Increased cerebral vasoconstriction and decreased cerebral blood flow
  - General vasoconstriction of renal and splancnic (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

VO_2max at the summit of Mt. Everest



Sun et al., Aviat Space Environ Med 1996 67(1):34-39
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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 $PO_2 \leq 3.9\text{-}5.3$ 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

- **CO_2 is a normal by-product of aerobic metabolism**
- **Increased CO_2 in the body results in important physiological responses throughout the body**
- **CO_2 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 CO_2 production keeps alveolar PCO_2 in dynamic equilibrium with metabolically produced CO_2
- **CO_2 is also a potent stimulus of cerebral vasodilation and blood flow**

Hypercarbia

- **Hypercarbia can result from:**
  - Hypoventilation: low breathing rate allows build-up of CO_2 (e.g., deliberate “skip-breathing” by SCUBA divers)
  - Malfunctioning respirator can lead to increased re-breathing of CO_2
  - 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

- **CO_2 can induce:**
  - Visual disturbances
  - Headache
  - Reduction in reasoning ability
  - A sense of “air hunger” or dyspnea
- **CO_2 can act as an anesthetic and can cause unconsciousness**
  - Can induce inert gas narcosis similar to nitrous oxide
- **CO_2 can alter the intracellular pH thus having effects on metabolism (also probable mechanism for inert gas narcotic effect)**

Hypercarbia – Summary of Exposure/Activity Limits

	At Rest (65 W·m^2)		Very, very high work rate (400 W·m^2)	
Average %CO_2 (Displacement of Oxygen in air)		**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

Wikepedia:Image
From: Imagery from the History of Medicine

21st Century Surgeons in a Modern Operating Room

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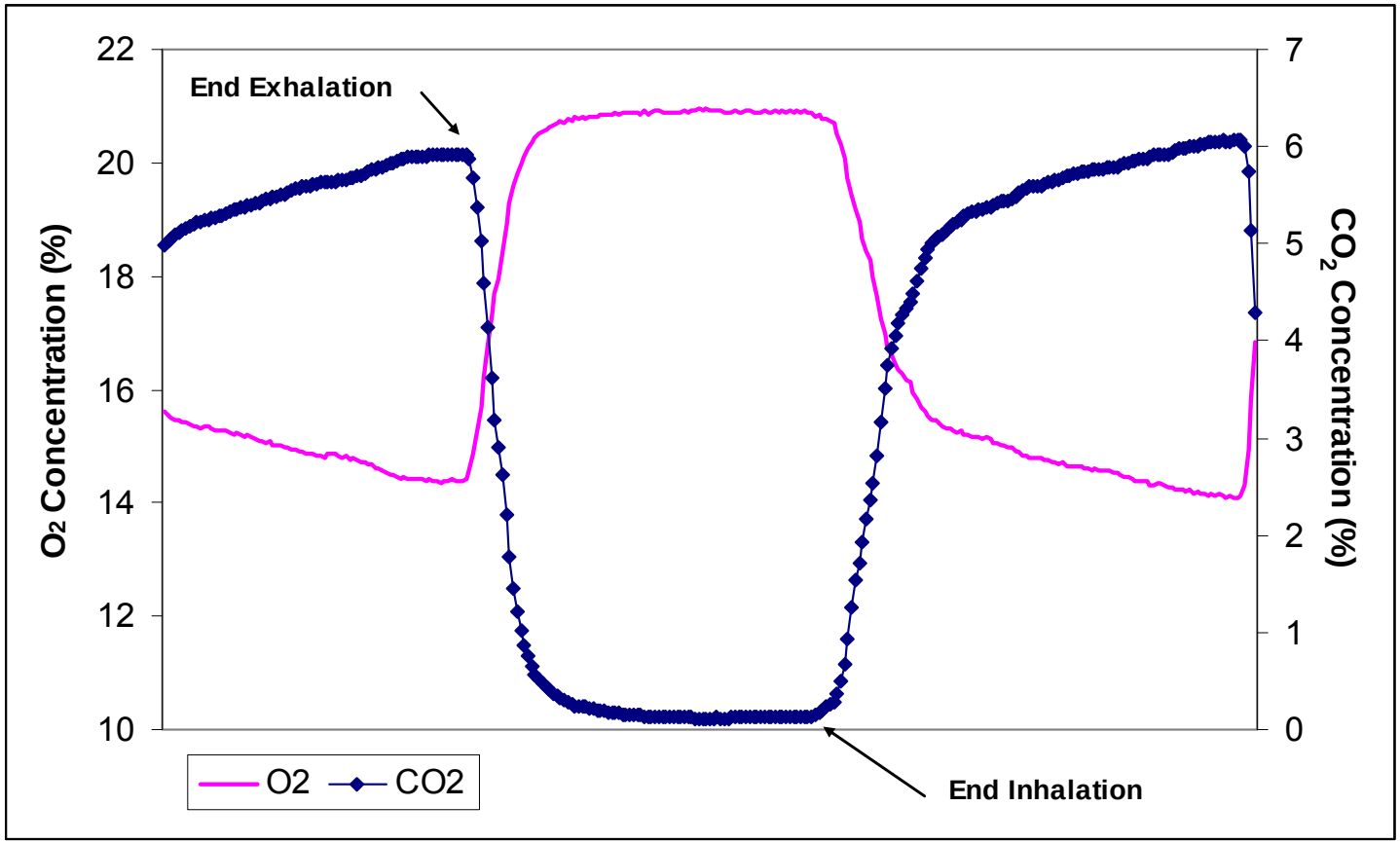
Versions of Respiratory Protection

NIOSH Photos

Relevance to Respiratory Protective Devices

- **At rest:**
  - Oxygen consumption is ~250 $mL \cdot min^{-1}$
  - Carbon dioxide production is ~200 $mL \cdot min^{-1}$
- **At maximal exercise:**
  - Oxygen consumption is can exceed 3.5 $L \cdot min^{-1}$
  - Carbon dioxide production can exceed 4.0 $L \cdot min^{-1}$

Single Breathing Cycle in Respirator
O_2 and CO_2 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 CO_2

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

Contact Information:

W. Jon Williams, Ph.D.

Technology Research Branch
NPPTL/NIOSH/CDC
626 Cochrans Mill Road
Pittsburgh, PA 15236
412-386-4002
412-386-6864 (fax)
aun7@cdc.gov

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National Personal Protective Technology Laboratory
626 Cochrans Mill Road
P.O. Box 18070
Pittsburgh PA 15236
(412) 386-6111

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