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

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, 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 [O₂] or PO₂ 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 [O₂] or PO₂ 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 PO₂ maintained at 4.7 kPa (35 mmHg) only by extreme hyperventilation
Mt. Everest is 8848 m (29,029 ft) high

VO_2max at the summit of Mt. Everest

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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

<table>
<thead>
<tr>
<th>At Rest (65 W·m⁻²)</th>
<th>Exposure Limit (time)</th>
<th>Potential effects and/or Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No restrictions on activity</td>
<td>No restrictions within the exposure limit</td>
<td>No restrictions on collapse / unconsciousness</td>
</tr>
<tr>
<td>Indefinite exposure</td>
<td>15 hours</td>
<td>Increase in ventilation</td>
</tr>
<tr>
<td>Increase in ventilation</td>
<td>8 hours</td>
<td>Collapse / unconsciousness</td>
</tr>
<tr>
<td>Increase in ventilation</td>
<td>&lt;30 min</td>
<td>Collapse / unconsciousness</td>
</tr>
<tr>
<td>Increase in ventilation</td>
<td>&lt;2.0 min</td>
<td>Collapse / unconsciousness</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure Limit (time)</th>
<th>Average %CO₂ (Displacement of Oxygen in air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours</td>
<td>1.5</td>
</tr>
<tr>
<td>30 min</td>
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Respiratory Protection – Not New

17th Century Physician Visiting a Plague House
"Doktor Schnabel von Rom" ("Doctor Beak from Rome")
engraving, Rome 1656

21st Century Surgeons in a Modern Operating Room

Wikipedia: Image - public domain

From: Imagery from the History of Medicine
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 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

End Exhalation

End Inhalation

Graph kindly provided by D. Caretti

CDC Workplace Safety and Health
NIOSH
NPPTL Research to Practice through Partnerships
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”

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