Physiological Responses to Oxygen and Carbon Dioxide in the Breathing Environment

W. Jon Williams, Ph.D.
National Institute for Occupational Safety and Health, USA

NIOSH Public Meeting
September 17, 2009, Pittsburgh, PA
“All things are poison and nothing is without poison, only the dose makes something not a poison”

- Paracelsus (1493-1541)

Swiss physician and alchemist
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

Wikipedia:Images – public domain
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.
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% O\textsubscript{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\textsubscript{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$_2$max at the summit of Mt. Everest

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

reproduced with permission

Wikipedia:Image – public domain
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

- $\text{CO}_2$ is a normal by-product of aerobic metabolism
- Increased $\text{CO}_2$ in the body results in important physiological responses throughout the body
- $\text{CO}_2$ 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 $\text{CO}_2$ production keeps alveolar $\text{PCO}_2$ in dynamic equilibrium with metabolically produced $\text{CO}_2$
- $\text{CO}_2$ is also a potent stimulus of cerebral vasodilation and blood flow
Hypercarbia

Hypercarbia can result from:

- Hypoventilation: low breathing rate allows build-up of 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>Average %CO₂ (Displacement of Oxygen in air)</th>
<th>At Rest (65 W·m²)</th>
<th>Very, very high work rate (400 W·m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure Limit (time)</td>
<td>Potential effects and/or Limitations</td>
</tr>
<tr>
<td>1.5</td>
<td>No restrictions on activity</td>
<td>Indefinite exposure</td>
</tr>
<tr>
<td>2.5</td>
<td>Increase in ventilation</td>
<td>unknown</td>
</tr>
<tr>
<td>3.0</td>
<td>Increase in ventilation</td>
<td>15 hours</td>
</tr>
<tr>
<td>5.0</td>
<td>Increase in ventilation</td>
<td>8 hours</td>
</tr>
<tr>
<td>7.0</td>
<td>Increase in ventilation</td>
<td>&lt;30 min</td>
</tr>
<tr>
<td>10.0</td>
<td>Increased heart rate Collapse / unconsciousness</td>
<td>&lt;2.0 min</td>
</tr>
</tbody>
</table>
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

Wikipedia:Image
From: Imagery from the History of Medicine
Versions of Respiratory Protection

NIOSH Photos
Relevance to Respiratory Protective Devices

- **At rest:**
  - Oxygen consumption is ~250 mL·min$^{-1}$
  - Carbon dioxide production is ~200 mL·min$^{-1}$

- **At maximal exercise:**
  - Oxygen consumption is can exceed 3.5 L·min$^{-1}$
  - Carbon dioxide production can exceed 4.0 L·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 \( \text{CO}_2 \)
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

This presentation is a summary of ISO Technical Specification 16976-3 developed by the author for the ISO TC94SC15WG1PG5 Human Factors Committee.
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
Disclaimer:
The findings and conclusions in this presentation have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

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

www.cdc.gov/niosh/nppltl