Physiological response to alterations in [O_2] and [CO_2]: relevance to respiratory protective devices

W. Jon Williams

National Institute for Occupational Safety and Health, National Personal Protective Technology Laboratory, 626 Cochrans Mill Road, P.O.Box 18070, Pittsburgh, PA 15236, USA
E-mail: aun7@cdc.gov

ABSTRACT

Millions of workers rely on respiratory protective devices (RPD) because of workplace inhalation hazards. Many workers also engage in increased physical activity while wearing RPDs. Demand is placed on the RPD to supply oxygen, purge carbon dioxide produced from the breathing space, and still provide respiratory protection. Moreover, changes in the composition of the breathing atmosphere result in significant physiological responses, mostly affecting the cardiopulmonary systems, which permit short term survival or may result in long term adaptation to the changed atmospheric composition. However, these changes can have a significant impact on the ability to perform occupational tasks and can potentially result in injury and death. This article provides a review of the origin of the earth's atmosphere, the physiology of respiration and responses to changes in environmental concentrations of oxygen and carbon dioxide, impact of exercise, and their relevance to respiratory protection in various occupational settings. In addition, O_2 and CO_2 concentration limit values verses time have also been identified which, if not exceeded, would not be expected to impose physiological distress. However, since changes in the concentrations of these gases in the breathing atmosphere can strongly influence ventilation, RPD function and the physical performance of an individual during respirator wear may be affected. Increased ventilation will place demands on respirators that could result in increased breathing resistance or impact the performance of filter elements. Increased concentration of CO_2 in the breathing space of an RPD may result in a sensation of dyspnea to the degree that the wearer may remove the RPD. Hypoxia may occur unnoticed by the wearer of RPD and the individual may lose consciousness with no warning. This could result in injury or fatality if the loss of consciousness occurred in a dangerous situation (e.g., firefighting, underwater diving, search and rescue activities). Therefore, "scrubbing" or clearing CO_2 from the breathing space, as well as careful monitoring of the atmosphere, is as critical to wearer safety as selection of the proper RPD for the complete protection of the user.

Keywords: carbon dioxide, oxygen, hypoxia, hyperoxia, hypercapnia, respiratory protective devices

INTRODUCTION

Due to the nature of their occupations, millions of workers worldwide are required to wear respiratory protective devices (RPDs) (Roberge et al., 2009, Roberge et al., 2010; US Dept Labor, 2001; NIOSH, 2001). RPDs vary considerably, from air purifying respirators (APRs) or powered air purifying respirators (PAPRs), self-contained breathing apparatus (SCBAs), and underwater breathing apparatus (UBAs), to escape respirators used in emergency situations, such as self-contained self-rescuers (SCSRs). Many of

these devices protect against airborne contaminants without supplying air or other breathing gas mixtures to the user. Therefore, the user may be protected from particulates or other airborne toxins, but still be exposed to an ambient gas mixture that differs significantly from that which is normally found at sea level. RPDs that supply breathing air to the user (SCBAs, UBAs, SCSRs) can malfunction or not adequately remove carbon dioxide from the breathing space, thus exposing the user to an altered breathing gas environment. In special cases, RPDs intentionally expose the user to breathing gas mixtures that significantly differ from the normal atmospheric gas mixture of approximately 79% nitrogen and 21% oxygen with additional trace gases. These special circumstances occur in aviation, underwater diving, and in clinical settings (APRs).

Breathing gas mixtures that differ from normal atmospheric levels can have significant effects on most physiological systems. Many of the physiological responses to exposure to high or low levels of either oxygen or carbon dioxide can have a profound effect on the ability to work safely, to escape from a dangerous situation, and/or on the ability to make clear judgments about the environmental dangers. In addition, alteration of the breathing gas environment can, if severe enough, be deleterious to health or even life-threatening. Therefore, monitoring and control of the breathing gas and limiting user exposure to significant variations in the concentration or partial pressure of oxygen and carbon dioxide is crucial to the safety and health of the worker.

This review briefly discusses the origin of oxygen (O_2) and carbon dioxide (CO_2) in the Earth's atmosphere, the basic physiology of metabolism as the origin of CO_2 in the body, respiratory physiology and the transport of O_2 to the cells and tissues of the body and the subsequent transport of CO_2 from the tissues to the lungs for removal from the body. Following the basic physiology of respiration, the discussion turns to the physiological responses to altered breathing environments (hyperoxia, hypoxia) and to the effects of excess CO_2 in the blood (hypercapnia). Finally, the discussion turns to the physiological responses to altered partial pressures/concentrations of O_2 and CO_2 during respirator use.

METHODS

The literature surveyed in this review were obtained through internet searches (PubMed®) using key words, electronic database search by a National Institute for Occupational Safety and Health (NIOSH) professional librarian (Index Medicus, OVID), and information contained in contemporary textbooks on physiology and medicine. A list of key word included the following: carbon dioxide, oxygen, physiological exposure limits, high altitude, hypoxia, medical oxygen, hyperoxia, hypercapnia, underwater diving, submarine atmospheres, and confined spaces atmospheres. The search was conducted in order to review the literature published in this topic over the last 25 years. References older than 25 years were also used when the reference was considered relevant to the discussion. A total of 350 general articles out of 1231 were obtained that proved relevant to the present topic. Of the 350 articles on the general topic, the author selected those cited in the present work as the most relevant to a focused review of the literature on the physiological responses to CO_2 and O_2 and the importance to respiratory protection.

RESULTS

The Earth's Atmosphere

Over the last ~ 4 billion years, many physicochemical and later biological processes have occurred that have contributed to the present composition of the Earth's atmosphere (Nunn, 1998; Oró, 1994; Nisbet and Sleep, 2001; Lumb, 2005). The early atmosphere of the Earth began with the cooling of the Earth's crust approximately 3.8 billion years ago. The resulting off-gassing of CO_2 and water vapor eventually comprised the major components of the early atmosphere and, upon the condensation of water, the planet's oceans. The high concentration of atmospheric CO_2 slowly reacted with surface silicates to form

carbonates trapped in the Earth's crust thus greatly reducing the atmospheric partial pressure of CO_2. The gravitational force of the Earth (g = 9.8 m·s^2) was sufficient to allow the retention of heavier gases (CO_2, O_2, nitrogen [N_2]), but not the lighter gases such as hydrogen and helium, thus leading to the loss of these lighter elements to space and leaving a largely N_2 atmosphere.

The development of photosynthetic organisms in the early oceans produced large amounts of atmospheric O_2 as a result of the metabolic process of photosynthesis. Although atmospheric CO_2 now occurs in very low concentrations (~0.03%), its presence is important for photosynthesis as described in the following equation:

$$6CO_2 + 6H_2O + \text{light} + \text{chlorophyll} \rightarrow C_6H_{12}O_6 + 6O_2 \qquad \text{Eq. 1}$$

This reaction occurs only in the presence of light (and the appropriate chlorophyll molecules) and produces both O_2 and carbohydrates (Stryer, 1981). Essentially all aerobic life on Earth relies on the photosynthetic reaction that supplies not only O_2 to the atmosphere but carbohydrates to the food chain. Over time, the Earth's atmosphere reached its contemporary status composed primarily of 78.8 % N_2 and 20.94% O_2 along with some trace gases with an average sea level barometric pressure of 101.3 kPa (760 mmHg).

Humans have, of necessity, evolved strong physiological defenses (e.g., enzymes such as superoxide dismutase and catalase) against toxic reactive oxygen species (ROS) in order to survive in the oxidizing atmosphere of Earth. This has allowed humans to utilize oxygen and carbohydrates as primary components in the production of energy during aerobic cellular metabolism (Lumb, 2005). This adaptive process has resulted in the physiological responses to CO_2 and O_2 that will be discussed in detail in the following pages.

Oxygen and Carbon Dioxide Gas Exchange in the Lungs

Pulmonary minute ventilation ($\dot{V}_E$ in L·min^{-1}) is generally controlled by neural activity in the respiratory control centers located in areas of the brainstem known as the medulla oblongata and the pons. Gas exchange does not occur in all regions of the pulmonary system. Anatomical dead space (regions where gas diffusion to the blood does not occur) comprises of about 1 ml for each 0.454 kg of lean body mass (~150 ml for a 68 kg person) within the pulmonary system. Physiological dead space is the sum of all parts of the tidal volume (the volume of air inhaled or exhaled in a single breath) that does not participate in gas exchange. In addition, alveolar dead space comprises the volume of air that passes the anatomical dead space and mixes with gas at the alveolar level but does not participate in gas exchange (Lumb, 2005).

Inhaled gas must pass through the regions of dead space to the pulmonary alveoli. Gas exchange occurs in the alveoli (the terminal air sacs of the lung) that are in contact with blood capillaries. The exchange of O_2 into the blood stream and CO_2 out of the blood stream into the alveoli is driven by simple diffusion down a concentration gradient. The partial pressure of O_2 in the alveoli (P_AO_2) is approximately 13.3 kPa (100 mmHg) whereas the partial pressure of O_2 in the venous blood (P_VO_2) is approximately 5.3 kPa (40 mmHg). Therefore, O_2 will move from the alveoli to the venous blood. O_2 will also be transported into the red blood cells along a similar concentration gradient to be bound to hemoglobin. Conversely, the partial pressure of CO_2 (P_VCO_2) in the venous blood is roughly 6.1 kPa (46 mmHg) and is only 5.3 kPa (40 mmHg) in the alveoli. Therefore, CO_2 will move from the venous blood to the alveoli to be exhaled to the atmosphere. After this gas exchange has taken place, arterial blood contains an O_2 partial pressure (P_aO_2) of 13.3 kPa (100 mmHg) and a CO_2 partial pressure (P_aCO_2) of 5.3 kPa (40 mmHg). The arterial blood arriving at the cells will release O_2 and take up CO_2 based on a similar process of diffusion along a concentration gradient. After O_2 delivery to the cells takes place, the red blood cells have a PO_2 of 5.3 kPa (40 mmHg) and a PCO_2 of 6.1 kPa (46 mmHg). Upon return to the lungs for another round of gas exchange the process is repeated. Proper O_2 delivery to the cells and CO_2 removal from the body will occur as long as a match exists between $\dot{V}_E$ of the lungs and blood perfusion driven by a robust circulatory system.

Oxygen and Carbon Dioxide Transport in the Blood

Oxygen has a very low solubility in the blood and must be transported to the vital organs, working muscles, and brain by a special transport mechanism in the blood. When O_2 diffuses from the alveoli to the circulation, about 98% of the O_2 present in the alveoli is rapidly transported into the red blood cells where it binds to hemoglobin (Hb) to form oxyhemoglobin (HbO_2). Oxygen affinity for Hb is very high in the venous blood returning from the general circulation. Oxyhemoglobin in the red blood cells is carried through the arterial circulation to the capillaries where the O_2 is released from Hb and diffuses from the red blood cells to the cells of the target tissues. The O_2 is then utilized in aerobic metabolic energy production. Several factors affect the affinity of O_2 for Hb. For any given PO_2, an increase in body temperature, blood lactate (↓ pH), increased PCO_2, or an increase in 2, 3-diphosphoglycerate (DPG - a product of anaerobic metabolism in red blood cells), can decrease the affinity of O_2 for Hb (Berne and Levy, 1988). The decreased affinity of O_2 for Hb under these circumstances is beneficial insofar as that it increases the availability of O_2 to tissues under conditions of increased O_2 demand. The effect of CO_2 on the affinity of O_2 for Hb is a phenomenon known as the Bohr Shift (Figure 1).

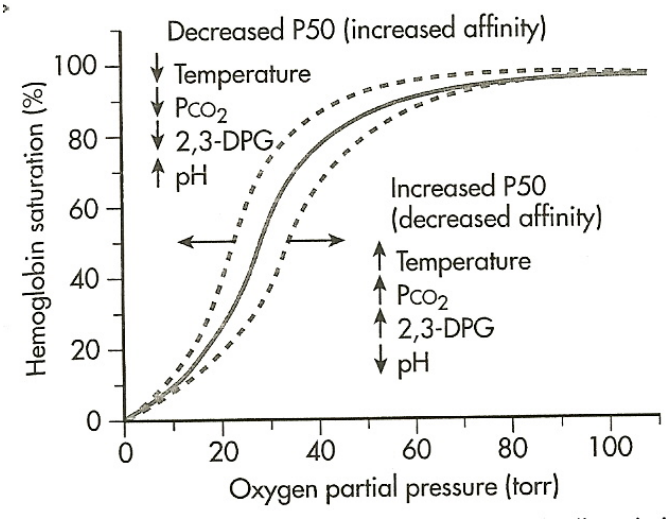

Figure 1. Shift of the oxyhemoglobin (HbO_2) dissociation curve by pH, CO_2 temperature, and 2,3-diphosphoglycerate (2,3 -DPG). Reproduced with permission (Berne and Levy, 1988).

By contrast, CO_2 is about 20-25 times more soluble in blood than O_2. Carbon dioxide produced as a by-product of aerobic metabolism diffuses from the cells of the tissue to the red blood cells in the circulation along a concentration gradient. In addition, CO_2 combines with Hb to form carbaminohemoglobin ($HbCO_2$). The affinity of Hb for CO_2 increases as O_2 dissociates from Hb during delivery of O_2 to the tissues (Haldane effect). Approximately 5% (arterial) to 30% (arterio-venous difference) of the CO_2 in the blood is transported to the lungs in the form of $HbCO_2$. Some of the CO_2 (~5-10%) is carried to the lungs in solution in the blood plasma. Another portion of the CO_2 combines with water to form carbonic acid according to the equation:

$$CO_2 + H_2O \leftrightarrows H_2CO_3 \qquad \text{Eq. 2}$$

This reaction occurs slowly and most of the CO_2 remains in solution in the plasma. However, a small amount of carbonic acid in the plasma dissociates to bicarbonate following the equation:

$$H_2CO_3 \leftrightarrows H^+ + HCO_3^- \qquad \text{Eq. 3}$$

Whereas the reaction in Eq. 2 occurs in very small amounts in the plasma, it occurs to a very large extent in red blood cells. Red blood cells contain the enzyme *carbonic anhydrase* (CA) which catalyzes the reversible reaction between CO_2 and H_2O extremely rapidly (approximately 10^6 reactions per second) (Berg et al., 2002) in the following manner:

$$CO_2 + H_2O \xrightleftharpoons{CA} H_2CO_3 \leftrightarrows H^+ + HCO_3^- \qquad \text{Eq. 4}$$

Approximately 60% (arterio-venous difference) to 90% (arterial) of the CO_2 is transported to the lungs in the form of bicarbonate (West, 1985).

The reaction in Eq. 4 significantly affects respiratory physiology. CO_2, as a product of aerobic metabolism occurring in cellular mitochondria, increases with an increase in metabolic activity (as with muscular exercise). Although $\dot{V}_E$ increases linearly with increased O_2 consumption and increased CO_2 production during mild to moderate exercise (e.g., up to ~55% maximal aerobic capacity or $\dot{V}O_2$ max), the relative P_aO_2 and P_aCO_2 do not vary significantly. It is thought that the change in blood pH, and not an increase in molecular CO_2 per se, that stimulates ventilation by action on peripheral chemoreceptors. However, during exercise, the arterial change in pH varies directly with CO_2 content. $\dot{V}_E$ increases nonlinearly and disproportionately to the exercise effort once the anaerobic threshold is exceeded. The physiological basis for exercise hyperventilation is not completely understood but appears to be related to a decrease in arterial pH that is related to bicarbonate buffering of the increase in metabolic CO_2 production (McArdle et al., 1996).

Oxygen and Carbon Dioxide and the Control of Respiration

Human life is entirely dependent on an adequate supply of O_2 to support the metabolic processes that produce energy. Because of this, the ability to sense changes in PO_2 has evolved. In addition, although atmospheric CO_2 concentrations are almost negligible, CO_2 is produced as a by-product of metabolism and has a profound effect on the respiratory system. Thus, mechanisms for sensing PCO_2 in the blood have also evolved. Indeed, changes in PCO_2 are more powerful stimulators of respiration than changes in PO_2. A brief overview of the process is presented in the following pages.

Chemoreceptors exist in both the central nervous system (medulla oblongata in the brain stem) and the peripheral nervous system integrated with the vascular system (i.e., carotid bodies in the carotid artery in the neck and chemoreceptors in the aorta) that sense changes in P_aO_2 and P_aCO_2. When these areas detect changes in P_aO_2 and P_aCO_2, neural signals are integrated into a respiratory response that usually results in a normalization of the P_aO_2 and/or P_aCO_2. Under conditions of hypoxia, the decreased P_aO_2 is sensed primarily by peripheral chemoreceptors in the carotid bodies and the aortic bodies within the vasculature. The respiratory response is an increase in ventilation in order to increase the O_2 uptake to maintain metabolic energy production. However, if the carotid and aortic bodies are removed or damaged, a decrease in P_aO_2 can result in a decrease in ventilation because a reduction in brain P_aO_2 can act directly to depress respiratory cells in the brain. Low P_aO_2 also increases brain blood flow thereby lowering P_aCO_2 and $[H^+]$ and decreasing ventilation. Complete loss of ventilatory drive due to hypoxia has been shown in patients with bilateral resection of the carotid bodies.

Inhalation of supra-atmospheric concentrations of CO_2 also increases pulmonary ventilation. However, the increased P_aCO_2 stimulates ventilation largely in central chemoreceptors located in the medulla oblongata and pons area of the brainstem and, to a much lesser extent, in the peripheral carotid bodies. The increase in ventilation with increased P_aCO_2 is exaggerated in the presence of hypoxia. From a functional standpoint, ventilation is stimulated either in the presence of a decreased P_aO_2 (hypoxia) or an increased P_aCO_2 (hypercapnia). This results in a ventilatory response that ensures appropriate oxygenation of the blood and elimination of CO_2.

Hyperoxia – Physiological Effects

Hyperoxia is defined as an excess of O_2 in the body due to exposure to an O_2 concentration above 21% in the breathing environment or to a normoxic gas concentration under hyperbaric conditions. One does not normally encounter an elevated O_2 level in the atmosphere. Hyperoxia is normally encountered in a clinical setting (breathing 21% - 100% O_2) or during the use of special gas mixtures for underwater diving or aviation. Hyperoxia has known effects on pulmonary ventilation under normal atmospheric pressures of 1 ATM. Donoghue et al. (2005) have shown that even mild changes in O_2 concentration can effect ventilation.

Exposure to mild hyperoxia can decrease pulmonary ventilation and a small increase can result in an increase in $\dot{V}_E$ in humans. Breathing mild hyperoxic gas mixtures for a limited period of time is usually not harmful and involves an acclimation process to compensate for the initial increase in ventilation (Donoghue et al., 2005). At sea level, breathing a hyperoxic gas mixture over many hours can result in pulmonary injury through a direct effect of oxidative stress on alveolar cells. Breathing 100% O_2 can result in an initial mild respiratory depression followed by an increase in ventilation due to a paradoxical increase in PCO_2 (Eckenhoff and Longnecker, 1996). The increase in PCO_2 is due to an increase in oxyhemoglobin resulting in a less efficient transport of CO_2 to the lungs for elimination. In contrast, breathing mild hyperoxic gas mixtures under hyperbaric conditions above 1 atmosphere (ATM) can be harmful. Oxygen toxicity can occur when the partial pressure of inspired O_2 reaches a point where neurological or pulmonary changes become pathological. Under greater than 1 ATM (101.3 kPa or 760 mmHg) of pressure, such as occurs during underwater diving, hyperoxic exposure can have effects on the nervous system as manifested by seizures. Seizures will not occur while breathing 100% O_2 at sea level (1 ATM). However, seizures are a potential risk while breathing 100% O_2 at 2 or more ATM (≥ 202.6 kPa or 1520 mmHg) of pressure and, in the US Navy, the threshold for O_2 toxicity which poses a risk for seizures is considered to be between 1.3-1.5 ATM (131.7 – 151.9 kPa or 988 – 1140 mmHg). Although seizures are the most dramatic consequence of O_2 toxicity, other symptoms such as hallucinations, involuntary movements, paresthesias, psychological changes (dysphoria), and vegetative disturbances have been reported (Spigno et al., 2008).

Much of the research on hyperoxia has been performed on the professional underwater diving community. Professional underwater divers are often required to breathe special gas mixtures during deep or "saturation" diving. For instance, hyperoxic gas mixtures can be administered to promote nitrogen washout (i.e., reducing the amount of dissolved N_2 in the body) thereby limiting the potential for decompression sickness ("bends") and inert gas narcosis ("rapture of the deep"). However, breathing hyperoxic gas mixtures carries the risk of O_2 toxicity since the partial pressure of O_2 increases with depth. The potentially heavy exercise performed by professional divers and an increase in hypercapnia can accelerate the effects of O_2 toxicity (Eckenhoff and Longnecker, 1996). Central nervous system toxicity secondary to hyperoxia is rapidly reversed by a decrease in P_aO_2 and, in general, no sequelae have been observed assuming, should O_2 toxicity occur, that the diver survives the seizures while still underwater. However, a case report on two recreational underwater divers breathing Nitrox, a hyperoxic breathing gas mixture used for underwater diving, experienced transient global amnesia immediately after surfacing (Spigno et al., 2008). Although the mechanism involved in the induction of transient global amnesia after breathing hyperoxic gas mixtures under hyperbaric conditions is not understood, both divers revealed upon magnetic resonance brain imaging, clinically silent cerebrovascular ischemia. Spigno et al. (2008) suggested that the cerebrovascular ischemia may have been a predisposing feature in these unusual episodes of amnesia after breathing hyperoxic gases mixtures under hyperbaric conditions. The issue remains unresolved.

While at least one study has reported an improvement in maximal exercise during exposure to hyperoxia while wearing an SCBA (Evest et al., 2002), hyperoxia has also been shown to have a negative impact on the cardiovascular system. Recent studies in hyperbaric chambers found reductions in key cardiovascular parameters (heart rate, cardiac output, stroke volume, ejection fraction, total arterial compliance) in military divers subjected to hyperoxic gas mixtures at 1.6-3.0 ATM. These cardiovascular changes are possibly due to a decrease in the force of contraction of the heart as an effect of hyperoxia

or an increase in parasympathetic nervous system activity secondary to hyperoxia (Molénat et al., 2004; Lund et al., 2000). It also appears plausible that the heart is capable of regulating the ratio of O_2 delivery to O_2 consumption to limit hyperoxic damage to cardiomyocytes (Winegrad et al., 1999). General vasoconstriction of the central and peripheral circulation as well as vasoconstriction of the renal and splanchnic regions also results from hyperoxia and the effect appears to be independent of sympathetic neural input (Rousseau et al., 2005; Dean et al., 2003). General, but non-uniform, cerebral vasoconstriction, as evidenced by decreased cerebral blood flow during exposure to hyperbaric hyperoxia, has also been described (Di Piero et al., 2002).

In normoxic emergency clinical settings, sudden retinal artery occlusion is treated by having the patient breath into a paper bag to increase $PaCO_2$ to induce retinal artery dilation to relieve the occlusion (Mitchell, 2004). However, retinal blood flow is also affected by breathing hyperoxic gas mixtures at 1 ATM (101.3 kPa or 760 mmHg). The decreased blood flow appears to be the result of vasoconstriction that is not mediated by changes in arterial pH (acidosis) and is not counteracted by increased arterial PCO_2 in the systemic circulation (Luksch et al., 2002). Refractive changes can also occur when breathing hyperoxic gas mixtures at >1 ATM. Professional deep sea divers using hyperoxic gas mixtures repetitively over a prolonged period of time (i.e. multiple dives each lasting several hours) have experienced myopia (loss of distance vision) that resolved only after more than one month (Butler et al., 1999).

Hypoxia – Physiological Effects

Hypoxia occurs when there is insufficient O_2 available for aerobic energy production. Some types of hypoxia can occur when: 1) the atmospheric oxygen concentration or partial pressure is low (such as at altitude), 2) anemic hypoxia where the oxygen transport mechanism in the blood is impaired, and 3) circulatory hypoxia where a stagnant blood supply fails to deliver oxygen to an organ. Much of the physiological research on hypoxia has been performed during high altitude studies (mountain climbing or aviation). In extreme hypoxia, there is not enough O_2 available to maintain basal metabolism and the person dies from asphyxiation.

Predictions regarding reaching the summit of Mt. Everest (altitude at the summit is 8848 m or 29,028 ft) suggested that the PO_2 at that altitude was lower than that needed to sustain basal metabolic needs and, therefore, ascent to the summit could not be performed without supplemental O_2 (West, 2000). Calculations indicated that the maximal O_2 uptake was equal to that required for basal metabolism at the summit of Mt. Everest. Therefore, there was not enough “extra” O_2 available to perform physical work. However, the air density (and therefore the PO_2) at the summit of Mt. Everest varies seasonally and the first successful ascent to the summit without supplemental O_2 occurred in 1978 (West, 2000). Refined calculations based on data collected indicated that, during the months of May to October, the PO_2 was enough to perform the physical work required to reach the summit whereas during the winter months the PO_2 was not enough. The PO_2 at the summit of Mt. Everest is 6.6 kPa (49.3 mm Hg) (PO_2 at sea level is 21.2 kPa or 159 mm Hg) and is approximately the same as breathing a gas mixture containing only 5-6% (PO_2 = 5.1 – 6.0 kPa or 38 – 45 mmHg) O_2 at sea level (Figure 2).

At the summit of Mt. Everest, alveolar PO_2 is 4.7 kPa (35 mmHg) in spite of the low atmospheric PO_2 (Figure 2). This level of alveolar PO_2 is maintained primarily by extreme hyperventilation which results in a decrease in PCO_2 leading to respiratory alkalosis (West, 1993). Nevertheless, the ventilatory suppression normally associated with respiratory alkalosis is overcome by the hypoxic stimulation of ventilation. Whereas measurable adaptive changes in the cerebrovascular response to mild hypoxia occurs over days to weeks (Xu et al., 2006), as the PO_2 falls below a critical value, there is not enough O_2 being transported to the vital organs and the central nervous system to sustain life and health. With atmospheric O_2 concentrations below about 4-5% (PO_2 = 3.9-5.3 kPa or 30-40 mmHg), a loss of consciousness and death will ensue within minutes. The victim is often unaware of the progression to loss of consciousness (Eckenhoff and Longnecker, 1996).

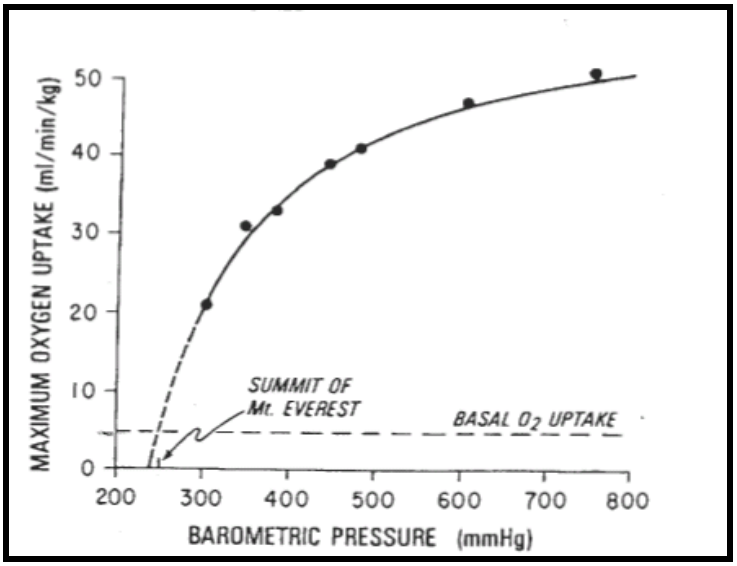

Figure 2: Maximal O_2 uptake in acclimatized subjects plotted against barometric pressure using the data from Silver Hut expedition. Note that the maximum O_2 uptake at the summit was predicted to be the same as the basal O_2 uptake indicating that no work would be possible. Also note that $VO_{2\ max}$ near the summit is exquisitely sensitive to barometric pressure. Reproduced with permission from Blackwell Publishers (West 2000).

Exposure to hypoxia results in several significant physiological adjustments. Acute hypoxia results in an increased ventilatory response (Crosby et al., 2003) and if the hypoxia is sustained, the peripheral chemoreceptors become hypersensitized and the ventilatory response to hypoxia increases. The increased ventilatory response serves to increase the O_2 content of the blood and eliminate the increased PCO_2 in the lungs (Berne and Levy, 1988) and is accompanied by a concomitant increase in cardiac output as a result of central nervous system stimulation (Eckenhoff and Longnecker, 1996). Although maximal O_2 uptake ($\dot{V}O_{2max}$) is reduced during exposure to hypoxia (especially for those with a higher $\dot{V}O_{2max}$), the increase in peripheral chemoreceptor sensitivity during hypoxia results in a smaller drop in $\dot{V}O_{2max}$ under hypoxic conditions (Ogawa et al., 2007).

Inhalation of supra-atmospheric concentrations of CO_2 also increases pulmonary ventilation (Berne and Levy, 1988). The increased P_aCO_2 stimulates ventilation largely in central chemoreceptors located in the medulla oblongata and pons area of the brainstem and, to a much lesser extent, in the peripheral carotid bodies. Interestingly, the increase in ventilation with increased PCO_2 is exaggerated in the presence of hypoxia (Figure 3). Thus, from a functional standpoint, ventilation is stimulated either in the presence of a decreased PO_2 (hypoxia) or an increased PCO_2 (hypercapnia) thus ensuring appropriate oxygenation of the blood and elimination of CO_2.

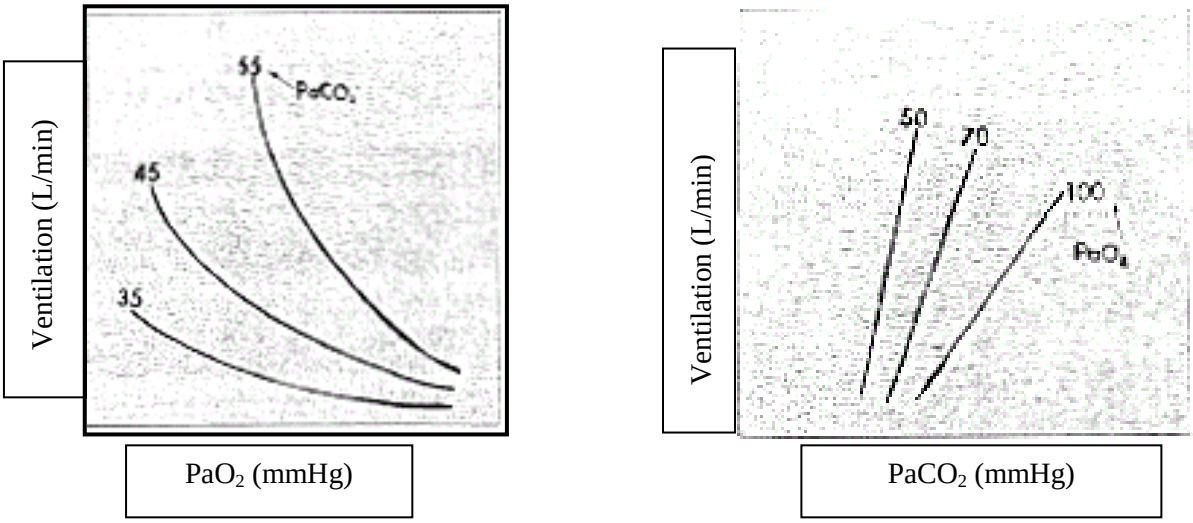

Figure 3. The effects of hypoxia and hypercapnia on ventilation. A, At a given $PaCO_2$, ventilation increases in a hyperbolic fashion as the PaO_2 is reduced. The vetilatory response to hypoxia is greater the higher the $PaCO_2$. B, The ventilatory response to hypercapnia is accentuated by hypoxia. Reproduced with permission (Berne and Levy, 1988).

Humans can adapt to chronic hypoxia. Some 40 million people live and work at altitudes between 3048 and 5486 m (10,000 - 18,000 ft). Although there are some immediate adaptive responses to exposure to hypoxia (e.g., an increase in ventilation), full adaptation to chronic hypoxia may take months to years. Native populations in the Peruvian Andes and Himalayan mountains reside at altitudes as high as 5486 m (18,000 ft) (McArdle et al., 1996). The barometric pressure at this altitude is approximately 50.6 kPa (380 mmHg) - about one half of that measured at sea level. At this altitude, ambient PO_2 is roughly 10.5 kPa (79 mmHg). The physiological adaptations to this low PO_2 from living at high altitude include increases in the number of pulmonary alveoli at birth, increased blood concentration of Hb and myoglobin (Mb) in the muscle, increased pulmonary ventilation, and a decreased ventilatory response to hypoxia (Eckenhoff and Longnecker, 1996). In spite of an atmospheric PO_2 of 10.5 kPa (79 mmHg), and an arterial PO_2 of 5.1 kPa (38 mmHg), the blood Hb is still 73% saturated. And yet, because the HbO_2 dissociation curve is sigmoidal, even a small decrease in atmospheric PO_2 at this altitude can result in a rapid O_2 desaturation of Hb down to about 50%. Although the great majority of high altitude acclimatized individuals show little or no adverse effects under these circumstances, a small minority of those acclimatized individuals develop Monge's disease (chronic mountain sickness) over time characterized by a poor ventilatory response to hypoxia, low P_aO_2 and high P_aCO_2, high hematocrit, pulmonary hypertension, right heart failure, dyspnea, and lethargy (Lumb, 2005). It should be remembered that the unacclimatized individual rapidly exposed to high altitude would rapidly become incapacitated and probably die from hypoxia.

In acclimation studies conducted by Angerer and Norwak (2003) designed to determine if human subjects could tolerate short-term intermittent exposure to hypoxia, it was revealed that humans could tolerate daily occupational exposure to an atmosphere composed of 13-15% (PO_2 = 13.2 – 15.2 kPa or 99 – 114 mmHg) O_2 (balance nitrogen) for periods of approximately 8 hours without significant physiological or health consequence. The results of this study have been used to support the suggestion that *healthy* workers could function in a hypoxic atmosphere designed for fire suppression with no significant ill-effects. However, the authors cautioned that workers with cardiovascular or pulmonary disease may not tolerate a hypoxic work environment. Moreover, endurance and peripheral limb fatigue have been reported in subjects exposed to acute severe hypoxia (13% O_2 or a PO_2 = 91.7 mmHg). Thus physical activity in the healthy worker would be reduced in a severely hypoxic environment (Romer et al.,

2007). A summary of the effects of hyperoxia and hypoxia at rest and at a high workrate (400 $W \cdot m^2$) appear in Table I.

Table I. The Potential Effects and Limitations on Human Tolerance Imposed by Exposure to Decreased [O_2] or PO_2 in the Inspired Air at Rest and at High Work Rates (Table constructed from data in Harabin and Survanshi, 1993)

		Rest ($65\ W \cdot m^2$; $\dot{V}_E$=13 $L \cdot min^{-1}$)		High workrate ($400\ W \cdot m^2$; $\dot{V}_E$=77 $L \cdot min^{-1}$)	
Average atmospheric %O_2	**Average PO_2 in mmHg**	**Potential effects and/or Limitations**	**Exposure Limit (time)**	**Potential effects and/or Limitations**	**Exposure Limit (time)**
20.9%	**79 (Altitude - 5486 m) Andes Mtns**	Large increase in ventilation, severe limitations on activity	<30 min	n/a Collapse / unconsciousness	<30 min
20.9%	**49 (altitude – 8848 m) Mt. Everest**	Large increase in ventilation, severe limitations on activity	<30 min	Collapse / unconsciousness	<30 min
19.5%	**148 (1 ATM)**	Well tolerated, no symptoms	indefinite	Well tolerated, no symptoms	indefinite
13-15%	**99-114 (1 ATM)**	Tolerated in the healthy individual, symptoms in the cardiopulmonary patient	hours	Decrease in exercise tolerance, symptoms in the cardiopulmonary patient	<60 min

There is also evidence that hypoxia can affect the thermoregulatory response to cold stressors. Exposure to intermittent hypobaric hypoxia sufficient to cause acclimation resulted in a blunted thermoregulatory response to a standard cold air exposure test at sea level (1 ATM). Much of the response was through peripheral vasoconstriction that may have been driven by hypocapnia due to the increase in the ventilatory response to hypoxia (Launay et al., 2006).

Hypercapnia - Physiological Effects

The term hypercapnia refers to the presence of excess CO_2 in the blood. The physiological effect of increasing the PCO_2 in the breathing atmosphere has been studied extensively for decades. Hypercapnia actually serves a protective role due to its stimulatory effect on ventilation. As previously noted, alveolar and arterial PO_2 can be maintained by hyperventilation through direct stimulation of the chemoreceptors in the carotid bodies as well as stimulation of the respiratory centers in the brain and brainstem (Berne and Levy, 1988). In addition, studies have demonstrated that increased PCO_2 increases cerebral blood flow and increased regional cerebral oxygenation (Imray et al., 2000). Hypercapnia also is a potent stimulus of peripheral vasculature, but the effect is not as great as on the cerebral vasculature probably due to the critical importance of defending full oxygenation to the brain (Vantanajal et al., 2007). This effect of CO_2 seems, therefore, to increase both the O_2 uptake by stimulating ventilation, but also O_2 delivery through increased cerebral blood flow (probably due to vasodilation of cerebral blood vessels). In fact, when atmospheric CO_2 was chemically scrubbed while human subjects were exposed to simulated high altitude in a hypobaric chamber, both regional cerebral O_2 and peripheral O_2 levels decreased (Imray

et al., 2001). Indeed, breathing gas mixtures containing 3% CO_2 and 35% O_2 have been used at altitude to increase both pulmonary ventilation and cerebral O_2 delivery by increasing cerebral vasodilation and peripheral O_2 delivery to skeletal muscle, thereby increasing human performance (Imray et al., 2003).

In spite of the use of supplemental CO_2 in both clinical and high altitude settings, there are some drawbacks to breathing elevated concentrations of CO_2. Stereoacuity and perception of coherent motion are reduced at atmospheric concentrations of only 2.5% CO_2 (Sun et al., 1996; Yang et al., 1997). Breathing CO_2 concentrations ranging from 2.5-8% (balance O_2) has been shown to reduce retinal blood flow (Luksch et al., 2005), and increase the rate of body core temperature heat loss during snow burial (Grissom et al., 2004). Nevertheless, there appear to be no pronounced disabling physiological effects or clinical symptoms associated with exposures of up to 5% CO_2 (Vercruyssen and Kamon, 1984). Breathing gas mixtures containing >6.5% CO_2 decreased performance on reasoning tasks and subjectively increased both irritability and discomfort (Sayers et al., 1987). Subjects participating in a simulated emergency Space Shuttle egress while wearing the launch and entry suit experienced a build-up of >6% CO_2 in the non-conformal helmet during a 5 minute walk on a treadmill at 3.5 mph. This CO_2 concentration limited the ability of most subjects to complete the simulated egress (Bishop et al., 1999). Breathing 10% CO_2 can result in a resting $\dot{V}_E$ of 75 $L \cdot min^{-1}$ which is maximal for many healthy middle-aged untrained individuals (Simon et al., 2006). Thus, while breathing increased CO_2 concentrations may seem beneficial by increasing cerebral blood flow which serves to protect brain oxygenation during exposure to reduced PO_2 at high altitude this strategy must be tempered with the consideration that CO_2 can also impede performance in a crucial way at sea level. Inhalation of CO_2 is known to induce anesthesia in animals and inhalation of 30% CO_2 can induce anesthesia in humans. However, the administration of CO_2 to achieve anesthesia in humans is complicated by the frequent incidence of seizures during the exposure (Lumb, 2005). Carbon dioxide can induce inert gas narcosis in patients with ventilatory failure probably through changes in intracellular pH that alters the metabolic processes that underlie the narcosis (Lumb, 2005).

Increased concentrations of CO_2 in the breathing environment can limit human performance. Elevated concentrations of CO_2 or increased PCO_2 affects pulmonary minute ventilation disproportionate to the level of exercise, thus increasing the metabolic cost of breathing as well as inducing a sense of “air hunger” (dyspnea) that limits exercise tolerance (Bishop et al., 1999). In addition, higher concentrations of CO_2 in the breathing space may increase the displacement of O_2 from hemoglobin, resulting in shifting the O_2 dissociation curve to the right and reducing the O_2 carrying capacity of the blood (Lumb, 2005). This could exacerbate the effects of concurrent hypoxia. A major concern is the potential of elevated levels of CO_2 to induce cardiac arrhythmias (Lumb, 2005). Usually, these arrhythmias are seldom serious but, in the presence of ischemic heart disease, could be life threatening.

A NIOSH report (PB 266 597 August 1976) summarized 19 studies on the effects of CO_2 on human subjects. Both the physiological responses to acute and longer term exposure were described. For high work rates (exercise on a treadmill at 7 km/hr, 10% grade to simulate escape), exposure to 5% CO_2 during this level of work represented the upper limit of tolerance. Exposure to 3% CO_2 posed no strict limitation on activity. It must be noted, however, that breathing concentrations consistently above 3% reduced the time to exhaustion during high intensity running on a treadmill (Craig et al., 1970). Absolute duration of exposure to CO_2 was also summarized (resting state). Human exposure to 10% CO_2 could only be tolerated for a few minutes before loss of consciousness and exposure to 7% CO_2 was only tolerable for <30 min and usually resulted in a CO_2 induced headache. Exposure to 5% CO_2 was tolerable for up to 8 h and 3% CO_2 could be tolerated for up to 15 h. Exposure to 1.5% CO_2 could be tolerated essentially indefinitely.

The summarized NIOSH data indicate that increasing the environmental (inhaled) concentration of CO_2 significantly attenuates the duration of exercise on a treadmill at a constant rate. This effect has also been corroborated by the aforementioned NASA study which reported that the increase in CO_2 concentration in the breathing space of the non-conformal helmet of the Launch Entry Suit significantly reduced the ability to complete a simulated emergency egress. The effects of 5-6% CO_2 in the breathing space of the non-conformal helmet resulted in only one-third of the subjects wearing the Launch Entry Suit being able to complete the 5 minute walk. The effect was clearly dose-related and exacerbated by

increasing the pressure in the antigravity suit bladders, situated in the lower extremities and abdominal region, to > 6.9 kPa (1.0 psi) (Bishop et al., 1999).

The published literature suggests that the reduction of the duration of exercise with increasing concentrations of CO_2 in the breathing atmosphere could be predicted from the increase in metabolic acidosis as evidenced by a decrease in blood pH, the increase in blood PCO_2, and the increase in blood potassium and phosphorus (Åstrand et al., 2003; Craig et al., 1970; Menn et al., 1968; Sinclair et al., 1971; Luft et al., 1974). In any case, it is apparent that increased PCO_2 in the breathing space or a hypercapnic physiologic state will result in a decrease in overall physical performance.

Increased CO_2 levels can have psychological effects as well. Carbon dioxide levels of >6.5% affect reasoning time (Sayers et al., 1987). Graded increases in CO_2 can induce anxiety and even panic attacks in the susceptible individual. Indeed, and single breath exposures to 30% CO_2 have been safely used as a provocative test (trigger) to assist in the diagnosis of anxiety disorder (Kaye et al., 2004). All of these effects will impact the ability of an individual to perform tasks while exposed to elevated levels of CO_2 in the breathing atmosphere.

Nevertheless, as in the case of hypoxia, human beings have a remarkable capacity to adapt to long term, low level (1.2%) atmospheric CO_2 exposure leading to hypercapnia (Elliott et al., 1998). Experience in submarine crews, astronauts, and cosmonauts exposed for weeks or months to mild hypercapnia during submarine cruises or in space stations during orbital flight have indicated that metabolic adjustments to hypercapnia can occur within days (Lumb, 2005). One of the most visible physiological responses to hypercapnia is an increase in pulmonary ventilation. Yet, after several days of exposure to elevated CO_2 in the breathing atmosphere, the ventilatory frequency returned to near baseline. The mechanism of this adaptive response appears to be an attenuation in the central chemoreceptor response to CO_2 since the compensatory response to hypercapnia is too rapid to be the result of a blood acid-base buffering system that involves the renal resorption of bicarbonate (Elliott et al., 1998). However, long-term hypercapnia tends to reduce the resorption of bicarbonate in spite of the fact that arterial pH returns toward baseline (Lumb, 2005). The increase in brachial blood flow in response to hypercapnia also gradually decreases to baseline (this effect is not observed in the cerebral vasculature) indicating an adaptive process to hypercapnia (Vantanajal et al., 2007). Unexpectedly, humans can survive exposure to extreme hypercapnia (termed “supercarbia” by the authors) as long as the subject (patient) is well oxygenated with a blood $PO_2 \geq 7.3$ kPa (55 mmHg). In the clinical cases in which “supercarbia” in the absence of hypoxia was reported, all patients recovered completely with no evidence of short- or long-term sequelae (e.g., no neurological deficit) (Goldstein et al., 1990; Potkin and Swenson, 1992). The critical fact to bear in mind is the adequate oxygenation of the subject during exposure to the episodes of supercarbia. Should the blood PO_2 have fallen below 7.3 kPa (55 mmHg) (hypoxia), a far more negative clinical outcome would have almost certainly been the result.

Relevance to the Use of RPDs

General Comments

Although the use of RPDs in the young, fit population is not associated with significant cardiovascular stress (Johnson et al., 2003), breathing high CO_2 while wearing an RPD can have a significant effect on the cardiovascular system in the susceptible individual. Hypercapnia can induce the release of enough catecholamines (epinephrine and norepinephrine) from the sympathetic nervous system to cause cardiac arrhythmias, and reduce cardiac contractility. Hypercapnia can also result in a decrease in cerebral cortex excitability, and can increase the pain threshold through its effects on the central nervous system. All of the above can promote problems with the ability to think clearly, potentially have a negative impact on the cardiovascular system, and reduce the ability to feel pain.

A sufficient increase in CO_2 or a decrease in O_2 can stimulate the respiratory system and increase ventilation thereby placing an increased physical demand on the wearer of the RPD. A sufficient build up of CO_2 in the breathing space of the RPD can negatively impact the ability to perform tasks. Similarly, a decrease in the O_2 level in the breathing space of a respirator can result in a stimulation of

ventilation and a loss of consciousness if the O_2 level is <5% (PO_2 of 3.9-5.3 kPa or 30-40 mmHg). For O_2 concentrations below about 15% (at 1 ATM), the ability to work is seriously diminished and may induce early symptoms such as chest pain/discomfort in persons with coronary artery disease. However, the duration of exposure is important because it usually influences the severity of the clinical symptoms observed. High levels of O_2 (even up to 100% O_2) can potentially be toxic, but are generally well tolerated at normal atmospheric pressures for several hours. Breathing increased PO_2 while exposed to greater than 2 ATM also can result in O_2 toxicity and should be avoided (Table I).

It should be noted that the CO_2 and O_2 limitations for respirators stated herein reflect maximal allowable average concentrations in the inspired air. During normal respiration, concentrations of CO_2 in the breathing zone at the end of exhalation can be as high as 8%, particularly during exercise. Then, at the start of the following inhalation, concentrations quickly decrease as the breathing zone is flooded with CO_2-deficient, O_2-enriched air. As such, CO_2 levels decrease to near atmospheric conditions in the early stages of inhalation and remain at such levels until inhalation ends and another exhalation begins (Figure 4). As long as this occurs, CO_2 concentration averaged for the complete inhalation phase of a breath is unlikely to exceed maximal allowable concentrations. The example presented in Figure 4 illustrates that with an end exhalation CO_2 concentration in the breathing zone of an APR of roughly 6%, the average concentration for all data of the inspired air was approximately 0.7%. Therefore, it is important to understand that average inspired CO_2 concentrations are not the same as single maximal values normally found at the end of an exhaled breath (end-tidal CO_2, as the terminal portion of exhalation that has a CO_2 concentration almost equal to that of arterial blood).

Based on respirator CO_2 limitations set forth in US standards (United States Code 42 CFR pt. 84, 2004) and international standards documents (e.g., Japanese Industrial Standard, JIS M 7651, 1996), it is evident that most requirements are below concentrations known to impair physiological or psychological performance, possibly as a built-in margin of error for individuals who may exhibit greater CO_2 sensitivity than others (Roberge, 2009). The 42 CFR pt. 84 is based on a time weighted average of CO_2 exposure ranging from 2.5% for ≤ 30 minutes to 1.0% for 240 minutes. This range has been adopted by the JIS and European standards organizations (BS EN 12941:1998+A2:2008). In the UK, maximal permissible limit for CO_2 is significantly less than in the US, i.e. 1.5% for 15 minutes (BS EN 12941:1998+A2:2008). Although the JIS sets upper limits of exposure to a maximum of 3% CO_2 (JIS M 7651, 1996, in Japanese) for all exposure regardless of time, the practical limit for the JIS is 1% CO_2 exposure. Both the Mine Safety and Health Administration (MSHA) and the Occupational Safety and Health Administration (OSHA) (29 CFR pt. 1910.1000) consider exposure to 5000 ppm CO_2 (0.5%) in the breathable atmosphere to be tolerable over a time weighted average of 8 hours. These limits have been adopted by several European countries (Austria, Belgium, Denmark, Finland, Germany, and Hungary), Australia, the UK, and Japan. NIOSH (30 CFR 11.3(t)) considers that an atmosphere containing 40,000 ppm CO_2 (4% CO_2) to be immediately dangerous to life and health (IDLH). Nevertheless, the differences between maximal allowable concentrations and concentrations known to significantly impair performance suggest that somewhat higher concentrations of CO_2 could be inhaled without harm for certain respirators and for certain periods of time. For example, a NIOSH respirator certification procedure (Procedure No. CET – APRS-STP-CBRN-0454) allows for up to 2.5% CO_2 V_{Dresp} for 15-30 min and 2.0% V_{Dresp} for 45-60 min for chemical, biological, radiological, and nuclear (CBRN) APRs used for escape. Further, NIOSH Procedure No. RCT-APR-STP-0063 and 0064 allow for a V_{Dresp} of 1.0% CO_2 with the PAPR blower on and 2.0% CO_2 with the blower off, respectively.

NIOSH also sets the minimum permissible O_2 level in the breathable air is 19.5% at 1 ATA (hypoxia at sea level – 29 CFR 1910.94) for any duration of time. However, NIOSH does not consider hyperoxia an immediate hazard at 1 ATM absolute (barometric pressure at sea level). The JIS regards 18% O_2 (hypoxia) as the lowest acceptable atmospheric concentration for filtering respirators but also does not consider hyperoxia to be a significant hazard at 1 ATM (JIS M 7651, 1996, in Japanese).

At high workloads, the demand for O_2 increases to meet the metabolic demands of working muscles. This increased $\dot{V}O_2$ is accompanied by increases in heart rate and cardiac output. The increase in O_2 consumption is directly related to workload as shown in Table II. This table is modified from ISO/TS 16976-1 Respiratory Protective Devices – Human Factors – Part 1: Metabolic Rates and Respiratory Flow Rates (ISO/TS 16976-1:2007 [E]).

Individuals engaging in activities within the range of metabolic rates (workloads) outlined in Table II must be able to increase their O_2 uptake to meet the increase in metabolic demand. If that person is wearing a RPD, the RPD must allow for this increase in O_2 consumption. If the person is wearing an APR in a "normal" atmosphere at sea level, then the partial pressure of O_2 is sufficient to allow the person to increase his/her $\dot{V}O_2$ to meet an increase in metabolic demand. Should a person be using an APR in an "abnormal" atmosphere (e.g., the partial pressure of O_2 is sub-atmospheric) then the person may be protected from particulates by the filter but may not be able to increase his/her $\dot{V}O_2$ to meet the metabolic demand because the amount of available O_2 in the atmosphere is too low (hypoxia). In a hyperoxic or hypoxic environment, there is no significant physiological difference between wearing an APR and not wearing an APR at all. If the person is wearing an SCBA, and as long as the device is functioning correctly, the wearer should be able to increase his/her $\dot{V}O_2$ regardless of the atmospheric concentration or partial pressure of O_2. However, since the air supply is limited, an increased $\dot{V}O_2$ will deplete the air cylinder supply more rapidly than at a lower $\dot{V}O_2$.

Table II: **Metabolic Rates and O_2 Consumption ($\dot{V}O_2$) Associated with 8 Levels of Work Likely to Be Encountered in a Variety of Occupations (Assuming a 1.75 m Body Height, 70 kg Body Weight and a Body Surface Area = 1.84 m^2; The CO_2 Values ($\dot{V}CO_2$), which Represent the Amount of CO_2 Being Exhaled into the Atmosphere or Respirator Breathing Space, Are Calculated from the Estimated Respiratory Exchange Ratio (RER) at each Exercise Level)**

Metabolic Rate W/m^2	$\dot{V}O_2$ ($mL \cdot kg \cdot min^{-1}$)	$\dot{V}CO_2$ ($mL \cdot kg \cdot min^{-1}$)
65	~4.91	~4.03
100	~7.54	~6.40
165	~12.46	~11.20
230	~17.36	~16.49
290	~21.90	~21.14
400	~30.20	~30.20
475	~35.86	~37.57
600	~45.30	~52.09

As the O_2 consumption increases in response to increased workload, so will the metabolically produced CO_2. The increased production of CO_2 ($\dot{V}CO_2$) will be exhaled to either the atmosphere or into the breathing (dead) space of the RPD. If exhaled into the dead space of the respirator, there is the possibility that the CO_2 will not be completely removed from the RPD breathing space and, therefore, will be re-breathed by the user. Whether none, some, or all of the CO_2 is re-inhaled by the wearer depends on such factors as respirator design (e.g., fit of the oral-nasal cavity inside a full-facepiece APR), and internal flow dynamics. In any case, should CO_2 continually increase in the RPD breathing space, re-breathing this accumulated CO_2 will result in hypercapnia and the stimulation of ventilation. Studies using unmanned assessments of respirator CO_2 levels in various RPD and with human subjects wearing various RPD for underwater diving have shown that, depending on the dead space characteristics of the RPD, the greater the workload, the greater the end-tidal CO_2 in the dead space that was being re-

breathed and the greater the stimulation of ventilation (Caretti and Coyne, 2008; Warkander and Lundgren, 1995). If ventilation increases against a RPD-imposed resistance to breathing, the resulting dyspnea could be difficult if not intolerable to the RPD wearer and reduce the time to exhaustion for a given task (see previous discussion). Indeed, increased ventilation while wearing an RPD with specific different inhalation and exhalation resistances has been shown to result in decreases in work performance times, peak flow rates, and O_2 consumption (Caretti et al., 2006).

In any case, whether wearing an APR, a PAPR, or an SCBA, the levels of O_2 within the breathing space must be sufficient to meet the metabolic demands of the user. This will be defined by the physiological responses to hyperoxia, hypoxia, or hypercapnia discussed previously. If the breathing atmosphere contains less than 5% O_2, regardless of whether it is an environmental (high altitude) or a RPD equipment malfunction, the physiological effect is the same. If the level of CO_2 increases to 10% within the breathing atmosphere, regardless of the cause, the physiological response is the same. Thus, air-supply RPD must be designed to deliver the appropriate amount of O_2 and control the level of CO_2 within the physiological limits discussed above. Should the breathing atmosphere change, the physiological responses will change accordingly. In addition, APRs must be used in an atmosphere that contains sufficient O_2 and a low enough CO_2 level to be compatible with normal respiratory function since the APR does not affect atmospheric concentrations of the breathing gases.

Machine Tests

RPD CO_2 Levels Established Using Automatic Breathing and Metabolic Simulator (ABMS) – Turner et al. (2003), using an ABMS capable of simulating human metabolism, $\dot{V}_E$, and breathing waveforms, developed a protocol to characterize the average inhaled CO_2 in the breathing space of a variety of NIOSH certified respirators at six simulated $\dot{V}_E$ rates. A total of 11 PAPRs, 20 supplied air respirators (SARs), six gas masks, 27 P-100 APRs, and 26 N95 particulate filtering facepiece respirators (FFRs) were tested using the protocol. The results indicated that over the range of $\dot{V}_E$, PAPRs CO_2 concentrations averaged between 0.2-0.8%, SARs averaged 0.4-0.5% CO_2, gas masks averaged 0.9-2.6% CO_2, P-100 APRs averaged 0.6-2.6% CO_2, and N95 FFRs averaged 2.3-3.6% CO_2. This study indicated that inhaled CO_2 levels for all the RPDs, with the exception of the N95 FFRs, were within NIOSH (42 CFR pt. 84) limits for RPD breathing space (V_{Dresp}) for use for at least 30 minutes (and up to 4 hours for PAPRs and SARs). N95 FFRs could exceed NIOSH (42 CFR pt. 84) V_{Dresp} limits for 30 minute exposure for CO_2. However, as noted in the text, these levels of CO_2 are not regarded as dangerous to healthy individuals but could result in increased $\dot{V}_E$ and an increase in the possibility of symptoms such as headache. It is important to note, however, that in many machine tests, mean inhaled CO_2 levels were, without exception, greater in tests using human subjects. In one example, in a machine test, the "inhaled" CO_2 level was measured at 0.5% whereas in the human subject tests, the value obtained was 1.2%. Thus, a machine test is likely to underestimate the level of inhaled CO_2 that will be experienced under similar conditions by a human wearer (Morris, 1991).

RPD Issues for the Human Wearer

The physiological responses to O_2 and CO_2 are important for similar and differing reasons depending on the type of RPD being worn and under what circumstances. Therefore, the relevance of the physiological responses to O_2 and CO_2 will be discussed for each RPD type listed as follows.

APRs – The use of respirators while at rest or during exercise have a significant effect on the concentration of inhaled CO_2. One study has shown that, in subjects wearing military M17 full facepiece APRs and exercising at 80-85% $\dot{V}O_2max$, subjects experienced an average of a 19% decrease in physical performance and an 18% decrease in user comfort for each 350 ml (6 dead volumes ranging from 280-1160 ml) increase in external (RPD) dead space (Johnson et al., 2000). In addition, all APRs offer some degree of breathing resistance. Other studies have shown that breathing elevated levels of CO_2 (~3%) against a resistance stimulated ventilation and increased the level of discomfort and distress

in the wearer (Takahashi et al., 1998). Indeed, resistance to breathing while wearing an APR can result in hypoventilation during exercise and the build-up of blood lactate. The buffering of the blood lactate results in increased blood CO_2 and reduced blood O_2. The increased CO_2 in the APR dead space as a consequence of breathing resistance may contribute more to RPD CO_2 than mask dead space alone depending on the style of the mask (e.g., full facepiece respirator vs. half mask FFR) (Johnson et al., 1996).

Figure 4 is illustrative of the problem of incomplete removal of CO_2 from the APR breathing space discussed previously. In the figure, it is apparent that, with a single breath recording cycle (exhalation followed by inhalation followed by exhalation), the concentration of CO_2 in the breathing space of the APR decreases to nearly zero because of the influx of fresh air during the inspiratory phase of breathing (with a concurrent increase in O_2). However, for this pattern to continue, essentially all of the CO_2 in the breathing space at the end of expiration must be eliminated to the extent that what remains is similar to atmospheric concentrations. Should any CO_2 remain in the breathing space, it may be re-inhaled with the next breath. Repetition of this pattern could result in a gradual increase in the concentration of CO_2 being re-inhaled into the lungs slowly resulting in hypercapnia. Work in the author's laboratory with subjects wearing N95 FFRs with and without a surgical mask overlay while engaging in treadmill exercise at a low work rate (2.72 km·hr^{-1} and 4.0 km·hr^{-1}) that the mixed inhalation/exhalation O_2 and CO_2 levels in the $V_{D\ resp}$ microenvironment exceed the OSHA standards for workplace ambient atmospheres over the course of one hour (Roberge et al., 2010). Although the absolute increase in transcutaneous CO_2 was not significantly different from control levels over the course of one hour, this finding suggests that exhaled CO_2 is not completely removed from the breathing space of a FFR. More research in this area is warranted in order to demonstrate this in a more definitive fashion.

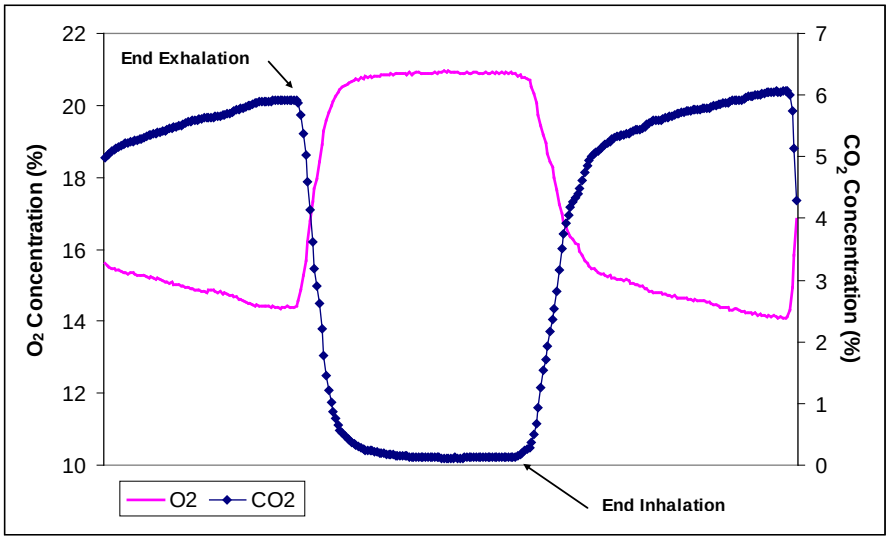

Figure 4: A typical single breath cycle recording of O_2 and CO_2 concentrations in the breathing zone of an APR during exhalation followed by inhalation while exercising at sea level. The end of exhalation and end of inhalation markings are approximate for the breath. The x-axis is relative time (Caretti, personal communication, reproduced with permission).

Exercise compounds the effects of respirator CO_2 accumulation due to increased metabolic CO_2 production. At rest, $\dot{V}CO_2$ is approximately 2.86 mL·kg^{-1}·min^{-1}. During moderate to heavy exercise, $\dot{V}CO_2$ can increase to 23.6-28.6 mL·kg^{-1}·min^{-1} while during maximal exercise $\dot{V}CO_2$ may exceed 50.0 mL·kg^{-1}·min^{-1} (Table II). Breathing an atmosphere containing 10% CO_2 can stimulate $\dot{V}_E$ to approximately 75 L·min^{-1} (Simon et al., 2006). At this level of $\dot{V}_E$ (induced entirely by breathing CO_2 and not due to exercise), issues such as work of breathing and respirator breathing resistance may become significant

dependent upon the type of respirator that is being worn (Johnson et al., 1996; Takahashi et al., 1998). Withdrawal of the CO_2 leads to a rapid reversal of these effects (Eckenhoff and Longnecker, 1996).

Whereas resistance to breathing at rest and low workloads is negligible while wearing an FFR or APR, assuming that the pressure drop across the breathing media does not exceed 17 cm H_2O (Bentley et al., 1973), wearing an APR inevitably decreases exercise performance during higher workloads because of the resistance to air flow across the filter media (Caretti et al., 2004; Caretti and Whitley, 1998). The degree of breathing resistance depends on the type of respirator being worn and the level of workload. The increased breathing resistance will have three potential results: 1) decrease in exercise performance, 2) hypoventilation, and 3) increased production of CO_2 (Caretti et al., 2004, Craig, et al., 1970). Hypoventilation is one of the most important causes of hypercapnia (Babb et al., 1989). The increased resistance to breathing at any given workload will, in turn, increase CO_2 production and end-tidal CO_2 (ET-CO_2), heart rate, and a reduced tolerance for work (Craig et al., 1970; Raven et al., 1979; Caretti et al., 1998). Paradoxically, the greatest percent change in the decreased workload tolerance occurred at the lighter workloads. Many occupations that do not involve heavy workloads but require the use of APR are also affected significantly by increased breathing resistances imposed by the APR. Indeed, should the resistance to breathing involve a decrease in breathing frequency concurrent with a decrease in tidal volume the result will be hypercapnia (Raven et al., 1979). Nevertheless, other significant factors such as a requirement for long-duration APR use, level of discomfort imposed by the APR, individual susceptibility to sensations of claustrophobia, individual sensitivity to CO_2 exposure, and the increased awareness of each of these factors also significantly affect the wearer. As the metabolic CO_2 increases (i.e., increased $\dot{V}CO_2$), ventilation will be stimulated but may not increase in the presence of an increased breathing resistance imposed by the respirator. Thus, a negative cycle is initiated by the increased breathing resistance which induces hypoventilation leading to increased hypercapnia. The resulting hypercapnia stimulates ventilation and increased re-breathing of CO_2 which further exacerbates the hypercapnia. Eventually, dyspnea caused by hypercapnia may be so great as to be intolerable. Further research in this area is required to determine the degree to which this putative cycle influences respirator wearers in dangerous environments. In any case, Babb et al., (1989) demonstrated that an increased respirator breathing resistance in conjunction with an increased level of CO_2 (3%) in the breathing space resulted in a decrease in physical performance. Further, attempts to maintain a certain level of ventilation against a breathing resistance could lead to a sense of dyspnea and physical and psychological stress (anxiety or panic) in the susceptible individual (Kaye et al., 2004).

Thus, these combined factors will increase the amount of CO_2 exposure to the APR wearer. Some investigators have shown that breathing comfort and performance time did not differ significantly between resistances below 0.39 kPa (3.9 cm H_2O) but did decrease by 35% at the highest resistance (0.49 kPa or 4.9 cm H_2O) (Caretti and Whitley, 1998). Other investigators maintain that there does not seem to be a threshold APR resistance below which there is no effect on metabolic measures (e.g., CO_2 or O_2 levels) or exercise performance during exercise (Johnson et al., 1999). The differences in these findings may be due to the use of half masks by Caretti and Whitley (1998) and the use of a full military facepiece by Johnson et al. (1999). However, the effect of CO_2 on the physiology will be the same whether or not the person is wearing an APR or breathing an atmosphere that contains an elevated concentration or partial pressure of CO_2. In any case, it is clear that the resistance to breathing offered by FFRs and other types of APRs clearly impact the metabolic response to exercise and the level of comfort experienced by the wearer.

From the previous discussion, it is apparent that the breathing resistance characteristics of an APR during inhalation or exhalation, is an extremely important factor in the user comfort and acceptance (Bentley et al., 1973; Raven et al., 1979). Therefore, APR design changes have been implemented to reduce the breathing resistances inherent in wearing APR. FFRs have demonstrated a low breathing resistance (9-12 mm H_2O – inhalation and 7-11 mm H_2O exhalation) (Jones, 1991). In addition, the development of the “electret” (electrostatically-charged) filter has resulted in an ultra-low breathing resistance in APRs (Barrett and Rouseau, 1998). As mentioned previously, it has been estimated that 90% of the users could wear an APR without experiencing distressing symptoms as long as the breathing resistances were below 17 cm H_2O (Bentley et al., 1973). Although there does not seem to be a way to completely eliminate breathing resistances in APRs, the advent of electret filters have significantly

reduced the resistances for wearers engaged in most low to medium levels of activity. Moreover, the decrease in breathing resistances will reduce the potential for hypoventilation which is a significant factor in increased P_ACO_2 and increased ET-CO_2 exhaled into the breathing space of the respirator. This will reduce the potential for CO_2 stimulation of ventilation during APR use. The addition of exhalation valves in respirators to increase the elimination of CO_2 from the breathing space have met with limited success.
APRs are designed to protect the wearer against particulates or vapors in the atmosphere. These RPDs are worn typically in an atmosphere containing the normal partial pressures of O_2, N_2, and CO_2. Because APRs do not provide an independent air supply to the wearer, they cannot be safely worn in a hypoxic atmosphere or an atmosphere containing high (>10%) concentrations or partial pressures of CO_2. For instance, workers have died of asphyxiation after environmental gas displacement by vaporization of liquid nitrogen into a confined space creating a hypoxic atmosphere. N_2 is an inert gas and is, by itself, not toxic. The death of the worker was caused by displacement of atmospheric O_2 by N_2 thus creating a hypoxic environment leading to asphyxiation (Gill et al., 2002). The worker would not have been protected against this hypoxic hazard while wearing an APR. Similarly, a research scientist died after entering a cold room with no working ventilation in which workers had stored dry ice which subsequently sublimated into CO_2 gas. The resulting high concentration of CO_2 in this confined space not only displaced the atmospheric O_2, but had an immediate toxic effect on the scientist that entered the chamber. Again, wearing an APR will not protect against the resulting hypoxic state or against the direct toxic effects of breathing high concentrations of CO_2 (Gill et al., 2002).

PAPRs – A PAPR is an APR that uses a blower to force the ambient air through air-purifying elements to the inlet covering. The blower sends air to the facepiece or hood from the external atmosphere. The PAPR air blower may limit the problems of breathing resistance over most exercise intensities, purge exhaled CO_2 from the breathing space, as well as the flow of air offers some level of cooling to the wearer. However, the PAPR only purifies the atmosphere of particulates or toxic vapor in a manner similar to FFRs and APRs. Thus, a PAPR will not protect the wearer in a hypoxic environment or an O_2 or CO_2 enriched atmosphere.

RPDs with Independent Air Supply – There are several classes of RPDs that utilize an air supply that is independent of the ambient atmosphere. These RPDs are generalized under the categories of Supplied Air Respirators (SARs) or an atmosphere-supplying respirator for which the source of breathing air is not designed to be carried by the user. These RPDs are connected by an airline connected to a compressed air cylinder or other source of compressed air. Other RPDs that fall into this category are SCSRs, SCBAs, and other UBA. These RPDs have a supply of air or oxygen that is carried on the wearer, can be used in hypoxic, toxic, or underwater environments, and thus do not rely on atmospheric oxygen to sustain the life of the wearer.

SARs can have several configurations: half-mask, full facepiece, helmet, hood, and full supplied-air suit (level “A” protection). The SAR is used in hazardous or immediately dangerous to life and health (IDLH) environments. Assuming the air source supplies clean air to the breathing space of the halfmask or full facepiece SAR, the issue of hypoxia or high levels of CO_2 (or other inhalation hazards) in the external atmosphere is irrelevant. With each breath, the SAR provides fresh air from the compressed source and each exhalation will eliminate the metabolically produced CO_2 from the breathing space. However, in SAR hoods, helmets, or air-fed suits, the increased dead space created by the hood, helmet, or suit can allow for the accumulation of exhaled CO_2. Studies have shown that in SAR hoods and helmets during light workload (48W external work) and airline flow rates of 100-200 $L \cdot min^{-1}$, re-inhaled CO_2 concentrations remained below 0.3% but increased to 0.4-0.53% at external workloads of 96 W resulting in a marginal increase of P_aCO_2 to 47 mmHg (normal range of 35-45 mmHg) (Comte and Koradecka, 1981). It should be noted that for any RPD, the CO_2 level increasing to 0.3% begins to create an unfavorable diffusion gradient from the blood to alveoli making the elimination of metabolically produced CO_2 more difficult and is initially compensated for by an increase in $\dot{V}_E$ (Morris, 1991). When inhaled CO_2 increases above 1-2%, increased ventilation is ineffective in removal of excess CO_2 and arterial hypercapnia results (Morris, 1991). In any event, the failure of the air supply will allow for the increase in the concentration of CO_2 within the SAR dead space or a state of hypoxia within the SAR.

SCSRs are designed with a canister containing the chemical compound potassium superoxide (KO_2) that will generate oxygen in the presence of water (H_2O) in the exhaled breath through the following reaction:

$$4KO_2 + 2H_2O \rightarrow 4KOH + 3O_2 \quad \text{Eq. 5}$$

The generation of O_2 in the presence of H_2O will continue until the KO_2 reactant is exhausted. According the federal regulations, the SCSRs must provide a supply of O_2 to the user for at least 60 minutes under escape conditions but the O_2 supply may last up to four hours under resting conditions (30 CFR 75.1714). Thus, the duration of the supply of O_2 to the user beyond 60 minutes will depend on the rate of O_2 consumption at a specific activity level (escape), body weight and physical fitness. The dependence on water makes a second equation equally important and critically dependent on CO_2. The following reaction is dependent on CO_2 to form water:

$$2KOH + CO_2 \rightarrow K_2CO_3 + H_2O \quad \text{Eq. 6}$$

The water formed in the above reaction is dependent on the presence of CO_2 and makes water available for the reaction in Eq. 5 which is, again, critical for the production of oxygen. Since metabolically produced CO_2 will be transported in solution in the blood to be exhaled by the lungs, then the CO_2 exhaled by the lungs will be involved in Eq. 6 in the formation of water, which in turn will be involved in the formation of oxygen by reacting in Eq. 5.

The SCSR is carried on the person and O_2 is transported from the chemical reactant canister through an air hose to a mouthpiece. The SCSR KO_2 evolves O_2 continuously, cannot be regulated, and will expose the wearer to hyperoxic conditions. However, exposure to hyperoxia for a short period of time (60 min) usually does not present a significant physiological threat. In fact, the hyperoxia may improve physical performance (Evest et al., 2002) which, however, may be offset by a negative influence on the cardiovascular system and a mild depression in $\dot{V}_E$ and decreased retinal blood flow (Luksch et al., 2002). These physiological effects could have a negative impact on the wearer during a mine emergency escape scenario. Hyperoxia may also result in the displacement of carbon monoxide on the Hb molecule thereby limiting the toxic effects of this gas (Simon et al., 2006).

Metabolically produced CO_2 is scrubbed by soda lime placed in series with the air flow of the SCSR. Under normal operating conditions, the wearer of an SCSR should not experience any adverse effects from the hyperoxic state or from re-breathing metabolically produced CO_2. However, a malfunction of the system or exhaustion of the soda lime could expose the wearer to elevated levels of CO_2 fairly quickly since large amounts of CO_2 are produced metabolically during the high intensity of exercise experienced under conditions of emergency escape (Table II). Should the wearer be exposed to high levels of CO_2, the stimulation of $\dot{V}_E$ may result in the premature exhaustion of the O_2 supply before the wearer completed the escape from the mine as well as the reduction of the physical work capacity of the wearer.

SCBAs are typically worn by firefighters but can also be worn under HAZMAT suits. The SCBA consists of a wearable compressed air cylinder that supplies breathable air through a hose to a full facepiece respirator. These RPDs can be worn in very hazardous environments characterized by hypoxia, high atmospheric CO_2 concentrations, or toxic gases. Because the supply of air contains normal atmospheric concentrations of O_2, N_2, and CO_2, the ventilatory response will not be affected by breathing these gases. In addition, under low to moderate workloads, breathing resistance offered by the SCBA facepiece will not be an issue. However, at high rates of $\dot{V}_E$ (112 $L \cdot min^{-1}$) SCBA regulators present an increased inhalation and exhalation breathing resistance and increased work of breathing (Butcher et al., 2006). Thus, it is possible that increased breathing resistance and work of breathing will result in an increase in ET-CO_2 that may be available to be re-inhaled. If symptoms become severe enough, the wearer may be motivated to remove the SCBA even in a dangerous environment. However, an interesting strategy has been used to reduce the effects of the breathing resistance and work of breathing at high workloads using an SCBA. Butcher et al. (2007) have employed a low density heliox gas mixture

(21% O_2 and 79% He) to reduce the breathing resistances and work of breathing at high breathing rates and workloads.

UBAs are worn during underwater diving and are a unique form of RPD. The apparatus, like an SCBA, consists of a compressed air cylinder that supplies air to the diver via pressure regulator/air hose/mouthpiece assembly. The UBA usually supplies normal atmospheric air to the wearer during underwater diving excursions. This is true for most "sport diving" in which the depth attained on any given dive is less than 30 m (4 ATM). However, the use of "normal" air can be toxic at depth. Increasing PO_2 in a "normal" atmosphere that occurs with increasing pressure at depth can result in O_2 toxicity and inert gas narcosis (due to a concomitant increase in the PN_2). To offset this problem, special breathing gas mixtures are used by the commercial diving community, in sport "technical" diving (SCUBA dives deeper than 40 m), and by military divers. However, military divers have used oxygen re-breathers in which the diver is breathing a hyperoxic gas mixture. Because of the potential for O_2 toxicity with these devices, military O_2 re-breathers can only be used at depths no greater than 10 m (1 ATM of sea water). The issue of CO_2 toxicity usually does not appear since the partial pressure of CO_2 in a "normal" atmosphere is so low that increasing depth will not substantially increase the partial pressure of CO_2 to pose a significant physiological problem for the diver. Should an equipment malfunction occur, thus delivering a hyperoxic mixture to the diver at depth, the toxic effects of O_2 may result in a fatal outcome for the diver. An equipment malfunction could also result in a hypoxic exposure to the diver. At depth, the increased partial pressure may relieve the effects of hypoxia but as soon as the pressure is reduced, hypoxia could become significant.

One cause of an increase in CO_2 exposure in the breathing space while using UBA is related to increased breathing resistance. Studies have shown that increased breathing resistance, particularly during inspiration, can result in hypoventilation and increased CO_2 retention (Warkander et al., 2001). Therefore, significant increases (0.8-1.2 $kPa \cdot L^{-1} \cdot sec^{-1}$; 8-12 cm $H_2O \cdot L^{-1} \cdot sec^{-1}$) in inspiratory resistance, especially during deep dives (690 kPa; 190 fsw), represents an unacceptable level of breathing resistance. Moreover, under these conditions of breathing resistance and depth, some divers have experienced sudden reactions to the resulting high end-tidal PCO_2 (P_{ET}-CO_2; ~70 mmHg) that could prove fatal. In at least two cases, divers under conditions of high resistance, depth, and high P_{ET}-CO_2 experienced sudden onset of loss of motor skills, inability to respond to commands, and sudden loss of consciousness. These divers apparently did not have the usual onset of dyspnea associated with increasing hypercpania and experienced no other warning signs of impending physiological distress (Warkander et al., 1990). Research has indicated that increased breathing resistance increases the work (power) of breathing (Warkander et al., 1992). These investigators demonstrated that the P_{ET}-CO_2 could be minimized when breathing resistance was low enough in the UBA to keep the power of breathing below 1.5-2.0 $J \cdot min^{-1}$ within a ventilation range of 30-75 $L \cdot min^{-1}$ (Warkander et al., 1992).

RPDs and the Pregnant Female

Millions of women serve in occupations that require the use of RPDs. Since pregnancy does not generally preclude women from working throughout most of gestation, it is likely that a significant number of women will continue to work in the health care field after becoming pregnant. It is fairly well documented that pregnancy results in an increased metabolism both at rest and during exercise and an increased ventilatory sensitivity to CO_2 (Roberge, 2009; Jensen et al., 2005; Jaque-Fortunato et al., 1996; Garcia-Rio et al., 1996). The increased ventilatory sensitivity to CO_2 is probably due to the changes in estrogen-dependent progesterone receptors in the hypothalamus which then, in turn, stimulate the respiratory centers in the medulla oblongata (Jensen et al., 2005; Jaque-Fortunato et al., 1996). The altered $\dot{V}_E$ is also due to some of the anatomical changes that occur in the thoracic cage during pregnancy (Jaque-Fortunato et al., 1996) as well as to changes in chemosensitivity to CO_2 during pregnancy (Garcia-Rio et al., 1996). These anatomical and physiological changes will have a significant impact on the use of FFRs and APRs in the pregnant worker.

The pregnant female also demonstrates hypersensitivity to hypoxia that appears to be linked to an increased level of progesterone. The increase in progesterone appears to increase the carotid body

neural output resulting in an increased ventilatory response to hypoxia (Jensen et al., 2005). In addition, the decrease in expiratory reserve volume and the resulting decrease in O_2 reserves secondary to an elevated diaphragm during pregnancy render the pregnant woman more susceptible to the development of hypoxia (Roberge, 2009). The increased metabolic O_2 utilization by the pregnant female also contributes to the sensitivity to hypoxia (Steinbrook, 2002).

The physiological and anatomical changes that occur in pregnancy are, therefore, problematic for the pregnant female who is required to wear an RPD occupationally or voluntarily. Hypersensitivity to both hypercapnia and hypoxia may cause an adverse response to the pregnant worker exposed to an RPD induced increase in CO_2 exposure or a hypoxic breathing atmosphere. At the minimum, the hypersensitivity to elevated CO_2 or decreased O_2 may limit the tolerance to wearing the RPD and, therefore, limit the amount of time spent on the job. A greater concern is that if the tolerability of the RPD is so low, the pregnant worker may remove the RPD to obtain relief and inadvertently become exposed to an inhalation hazard. These issues must be taken into consideration when the pregnant worker is required to wear an RPD for occupational safety (or any other) reasons.

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Disclaimer

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Ziqing Zhuang, Ph.D.
Editor, JISRP
105 Eaglebrook Court
Venetia, PA 15367 USA
Phone: 412-848-0409
JISRP-Editor@att.net

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The Americas
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Asia
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Andy.capon@avonrubber.co.uk
george@robinsg.fsnet.co.uk

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