APPENDIX B – Overview of Acute Health Effects

Appendix B presents an overview of the acute health effects associated with carbon dioxide. Part I discusses the dangerous, lethal effects of carbon dioxide at high exposure concentrations. The minimum design concentration of carbon dioxide for a total flooding system is 34 percent (340,000 ppm). When used at this design concentration, carbon dioxide is lethal. Part II discusses the potentially beneficial effects of carbon dioxide at low exposure concentrations and the use of added carbon dioxide in specialized flooding systems using inert gases.

PART I: Acute Health Effects of Carbon Dioxide

Carbon dioxide acts as both a stimulant and depressant on the central nervous system (OSHA 1989, Wong 1992). Table B-1 summarizes the acute health effects that are seen following exposure to high concentrations of carbon dioxide. Exposure of humans to carbon dioxide concentrations ranging from 17 percent to 30 percent quickly (within 1 minute) leads to loss of controlled and purposeful activity, unconsciousness, coma, convulsions, and death (OSHA 1989, CCOHS 1990, Dalgaard et al. 1972, CATAMA 1953, Lambertsen 1971). Exposure to concentrations from greater than 10 percent to 15 percent carbon dioxide leads to dizziness, drowsiness, severe muscle twitching, and unconsciousness within a minute to several minutes (Wong 1992, CATAMA 1953, Sechzer et al. 1960).

Exposure to 7 to 10 percent carbon dioxide can produce unconsciousness or near unconsciousness within a few minutes (Schulte 1964, CATAMA 1953, Dripps and Comroe 1947). Other symptoms associated with the inhalation of carbon dioxide in this range include headache, increased heart rate, shortness of breath, dizziness, sweating, rapid breathing, mental depression, shaking, and visual and hearing dysfunction that were seen following exposure periods of 1.5 minutes to 1 hour (Wong 1992, Sechzer et al. 1960, OSHA 1989). In a study of 42 human volunteers, following inhalation of 7.6 and 10.4 percent carbon dioxide for short periods of time (2.5 to 10 minutes), it was reported that only about 30 percent of the subjects complained of difficult breathing (dyspnea), although respiration was vigorously stimulated (Lambertsen 1971, Dripps and Comroe 1947). In this study, the most common symptoms were headache and dizziness (Lambertsen 1971, Dripps and Comroe 1947). Other symptoms described included mental clouding or depression, muscle tremors or twitching, tingling or cold extremities, and exhaustion (Lambertsen 1971, Dripps and Comroe 1947). Confusion to the point of unconsciousness was reported in several subjects at both concentrations (Lambertsen 1971). Increasing concentrations of carbon dioxide up to 7.5 percent for a period of 20 minutes had no significant effects on accuracy of reasoning and short-term memory, although speed of performance of reasoning tasks was significantly slowed at the higher levels (Sayers et al. 1987). Exposure to a concentration of 6 percent carbon dioxide can produce hearing and visual disturbances within 1 to 2 minutes (Gellhorn 1936, Gellhorn and Spiesman 1935). Acute exposures (minutes) to 6 percent carbon dioxide affected vision by decreasing visual intensity discrimination in 1 to 2 minutes (Gellhorn 1936) and resulted in a 3 to 8 percent decrease in hearing.

Table B-1. Acute Health Effects of High Concentrations of Carbon Dioxide

Carbon Dioxide Concentration (Percent)	Time	Effects
17 - 30	Within 1 minute	Loss of controlled and purposeful activity, unconsciousness, convulsions, coma, death
>10 – 15	1 minute to several minutes	Dizziness, drowsiness, severe muscle twitching, unconsciousness
7 – 10	Few minutes	Unconsciousness, near unconsciousness
	1.5 minutes to 1 hour	Headache, increased heart rate, shortness of breath, dizziness, sweating, rapid breathing
6	1 – 2 minutes	Hearing and visual disturbances
	≤16 minutes	Headache, dyspnea
	Several hours	Tremors
4 – 5	Within a few minutes	Headache, dizziness, increased blood pressure, uncomfortable dyspnea
3	1 hour	Mild headache, sweating, and dyspnea at rest
2	Several hours	Headache, dyspnea upon mild exertion

threshold in six human subjects (Gellhorn and Spiesman 1935). Headache and dyspnea were also seen during a 16-minute exposure to 6 percent carbon dioxide in air or oxygen (White et al. 1952, Wong 1992). Tremors were produced in human subjects exposed to 6 percent carbon dioxide for several hours (Schulte 1964). Mental depression occurred following exposures (several hours) to 5 percent carbon dioxide (Schulte 1964, Consolazio et al. 1947). Exposure to 4 to 5 percent carbon dioxide for 15 to 32 minutes can produce headache and dizziness, increased blood pressure, and can produce uncomfortable dyspnea within a few minutes (Schulte 1964, Schneider and Truesdale 1922, Patterson et al. 1955).

A concentration of 3 percent carbon dioxide produced headache, diffuse sweating, and dyspnea at complete rest after an exposure period of several hours (Schulte 1964). Sinclair et al. (1971) showed that 1-hour exposures of 4 human volunteers to 2.8 percent carbon dioxide resulted in occasional mild headaches during strenuous, steady-state exercise. Menn et al. (1970) found that in 30-minute exposures to 2.8 percent carbon dioxide, dyspnea was detected in 3 out of 8 human volunteers during maximal exercise, but not during half-maximal or two-thirds maximal exercise. After several hours exposure to atmospheres containing 2 percent carbon dioxide, headache and dyspnea can occur with mild exertion (Schulte 1964). Table B-2 shows the physiological tolerance time for various carbon dioxide concentrations in healthy males under exercising conditions. Short-term exposures (5 to 22 minutes) to carbon dioxide-air mixtures (2 percent to 8.4 percent carbon dioxide) also caused a distinct hearing loss at 3 percent carbon dioxide (Gellhorn and Spiesman 1934, 1935). No effect on the hearing threshold was observed at 2.5 percent (Gellhorn and Spiesman 1935).

Table B-2. Physiological Tolerance Time for Various Carbon Dioxide Concentrations

Concentration of Carbon Dioxide in Air (percent by Volume)	Maximum Exposure Limit (Minutes)
0.5	***indefinite***
1.0	***indefinite***
1.5	***480***
2.0	***60***
3.0	***20***
4.0	***10***
5.0	***7***
6.0	***5***
7.0	***Less than 3***

Source: Compressed Gas Association 1990.

Carbon dioxide is normally present in the atmosphere at a concentration of 0.03 percent (NFPA 12, Wong 1992). It is also a natural end product of human and animal metabolism. As a result, carbon dioxide dramatically influences the function of major vital processes, including control of breathing, vascular dilation or constriction (particularly in certain brain tissues), and body fluid pH.

The most familiar effect of inhaled carbon dioxide is its stimulant action upon respiration (Lambertsen 1971). The respiratory system acts as a physiologic buffer system (Jensen 1980). It is controlled by a typical feedback mechanism where the respiratory center responds directly to alterations in blood pH (i.e., changes in blood H^+ concentrations), and the alveolar ventilation rate in turn can regulate H^+ concentration. When blood H^+ concentrations rise above normal levels, alveolar ventilation is stimulated, and the concentration of carbon dioxide in the blood is reduced. The H^+ concentration falls toward normal level, eliminating the stimulus to an increased ventilatory rate. Greatly elevated carbon dioxide concentrations can lead to respiratory acidosis if the capacity of the blood buffering system is exceeded. In response, respiratory excretion of carbon dioxide occurs rapidly through an increase in the ventilation rate.

Immediately after exposure to elevated carbon dioxide levels, the minute ventilation, tidal volume (total volume of air inhaled and exhaled during quiet breathing), alveolar carbon dioxide, and acidity of the blood are elevated (Glatte et al. 1967). Acute exposure to 1 percent and 1.5 percent carbon dioxide is tolerated quite comfortably. Very little noticeable respiratory stimulation occurs until the inspired carbon dioxide concentration exceeds about 2 percent (Glatte et al. 1967, Lambertsen 1971). At 3 percent carbon dioxide, measurable increases in pulmonary ventilation, tidal volume, and arterial P_{CO_2} occur (Glatte et al. 1967). Respiratory stimulation then increases sharply until inspired carbon dioxide concentrations of about 10 percent are reached (Lambertsen 1971). Between 10 and 30 percent inspired carbon dioxide, the increase in respiratory minute volume (the product of tidal volume and respiratory rate) is less per unit of rise in inspired carbon dioxide than with the lower concentrations (Lambertsen 1971). Within 1.5 minutes of inhalation of 30 percent carbon dioxide in oxygen, ventilation suddenly declines, and convulsions occur (Lambertsen 1971).

Carbon dioxide also affects the circulatory system. If the concentration of carbon dioxide in the inspired air increases, the body will compensate by increasing the respiratory depth and rate with an accompanying increase in cardiac output (Schulte 1964). If the carbon dioxide in the breathing atmosphere continues to increase, the increases in cardiac and respiratory rates cannot effectively compensate (i.e., eliminate carbon dioxide) and carbon dioxide will accumulate in the blood and other body tissues (Schulte 1964). A short-term exposure of 17 to 32 minutes in humans to 1 or 2 percent carbon dioxide has been shown to cause a slight increase in systolic and diastolic pressure (Schneider and Truesdale 1922). A 15 to 30 minute exposure to 5 or 7 percent carbon dioxide caused increases in blood pressure and cerebral blood flow and a decrease in cerebrovascular resistance but no change in cardiac output (Kety and Schmidt 1948). However, in another study, exposure to 7.5 percent carbon dioxide for 4 to 25 minutes showed an increase in cardiac output and blood pressure (Grollman 1930). Dripps and Comroe (1947) studied the respiratory and circulatory responses of 42 normal young men to inhalation of 7.6 and 10.4 percent carbon dioxide for 2.5 to 10 minutes. Inhalation of both 7.6 and 10.4 percent carbon dioxide increased

the average minute volume of respiration, pulse rate, and blood pressure. Acute exposures to higher concentrations of carbon dioxide (30 to 70 percent carbon dioxide for 38 seconds) may result in electrocardiogram changes (Wong 1992).

PART II: Effects of Added Carbon Dioxide at Low Concentrations

Carbon dioxide is useful for counteracting the effects of oxygen deficiency (Gibbs et al. 1943). In the presence of low oxygen, carbon dioxide is beneficial because it exerts a vasodilator effect on cerebral blood vessels (Patterson et al. 1955, Gibbs et al. 1943). Patterson et al. (1955) studied the threshold of response of the cerebral vessels in humans following exposure to 2.5 and 3.5 percent carbon dioxide for up to 30 minutes. The results showed that the threshold for cerebral vasodilator effects was greater than 2.5 percent, based on the absence of changes in cerebral blood flow, vascular resistance, and arteriovenous oxygen difference seen at this exposure concentration (Patterson et al. 1955). In the same study, inhalation of 3.5 percent carbon dioxide produced a 10 percent mean increase in cerebral blood flow, but little change in blood pressure in most subjects. Dilation of cerebral blood vessels may account for the severe headache also produced by carbon dioxide inhalation (Lambertsen 1971).

Other beneficial effects of carbon dioxide in the presence of low oxygen include the fact that it increases the ventilation of the lungs, and it shifts the hemoglobin dissociation curve so that with a given oxygen saturation more oxygen is delivered to the tissues. A study of arterial and internal jugular blood oxygen, carbon dioxide content, and brain function in eight healthy young men who breathed mixtures containing low percentages of oxygen and varying ratios of carbon dioxide indicated that normal brain function can be maintained for very short periods of time in spite of low percentages of oxygen in the inspired air (as low as 2 percent oxygen). This study can be summarized as follows: in four experiments, the subjects breathed 6 percent oxygen plus 5 percent carbon dioxide for 3 minutes and then 4 percent oxygen plus 5 percent carbon dioxide for three minutes. None of the subjects lost consciousness, response to commands and memory remained normal, and the electroencephalograms were unchanged. Two subjects were given 2 percent oxygen plus 5 percent carbon dioxide. For over 2 minutes, both were able to subtract and obey commands, and the electroencephalograms remained unchanged. Then the deep rapid breathing was interrupted by a single shallow respiration, the arterial oxygen saturation dropped, and consciousness was lost (Gibbs et al. 1943).

Lambertsen and Gelfand (1995) conducted an experiment with human volunteers to study the physiological effects of abrupt exposures to 10 percent oxygen with 4 percent carbon dioxide. Their results showed that for 3 minute exposures at 10 percent oxygen with 4 percent carbon dioxide and for 3 minute exposures at 10 percent oxygen without carbon dioxide, there were several advantages that resulted from breathing carbon dioxide in the presence of low oxygen. These included a higher end tidal oxygen partial pressure, increased ventilation, slightly lower heart rate, stable hemoglobin saturation (above 90 percent), higher middle cerebral artery blood velocity, and increased (above normal) brain oxygenation flow.

In instances where carbon dioxide is added in specialized flooding systems using inert gases, different regulatory agencies treat these agents differently. For example, in the United States, EPA does not distinguish between inert gas blends with and without added carbon dioxide. However, in the UK, inert gas blends containing added carbon dioxide are granted longer “safe exposure” times (HAG 1995).

In conclusion, uptake of oxygen into the bloodstream in low oxygen environments can be enhanced by the presence of carbon dioxide within a narrow concentration range.

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