CLEAN FIRE EXTINGUISHING AGENTS HUMAN SAFETY TESTING

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INTRODUCTION

With the demise of Halon 1301 as a clean, gaseous fire extinguishing agent for total flooding applications, two classes of replacement agents – inert gases and halocarbons – are now commonly used because of their cleanliness, effectiveness, and non-conductive nature.

In addition to these desirable properties, it is essential that the replacement agents be safe for people, and that the level of safety be documented through thorough testing using procedures that will accurately measure effects in humans. There are distinct differences in the human safety test procedures now employed for halocarbons versus the test procedures in use for inert gases. There are also distinct differences in the physiological results found for INERGEN® agent versus the other available inert gas agents. All inert gases extinguish fires by lowering the normal 21% oxygen concentration in air to a level of 10-14%. However, at its extinguishing concentration, only INERGEN agent contains the small amount of carbon dioxide (CO_2) needed to provide oxygen flow to the brain at a level equal to or greater than when breathing a normal atmosphere.

EXPOSURE SCENARIOS

Humans should not normally be exposed to design concentrations of any clean fire extinguishing agent. Common design practice in accordance with NFPA 2001: *Standard For Clean Fire Extinguishing Agents* [1] and ISO 14520: *Standard for Gaseous Fire Extinguishing Systems* [2] calls for the use of warning alarms and time delays to allow sufficient time for evacuation of the protected space before the clean agent system is discharged. However, it is not always possible for all occupants of a protected space to evacuate, either because of a critical task which cannot be abandoned (e.g. a nuclear plant operator during an emergency situation) or because of an injury that has rendered one or more people immobile or unconscious. It is also possible that personnel will attempt to re-enter the hazard space after the fire is extinguished, but before the clean agent has been purged from the area, and will thus be exposed to the resulting post-discharge atmosphere.

The key factors in evaluating any exposure scenario are **time** and **agent concentration**. The combined impact of these two factors – the highest expected concentration for the longest expected time – determines the likely adverse physiologic impact on humans. Exposure times in the order of a few minutes are most probable. NFPA 2001 [3] limits exposure scenarios based on a combination of time and concentration, using five minutes as the maximum exposure time and concentrations that are specific to each agent.

HALOCARBON CLEAN AGENTS

Toxicology testing of Halon 1301 was conducted in the 1960s[4]. The standardized test protocol involved exposing dogs to the selected concentration of Halon 1301 in air, and then monitoring the dogs' hearts for any signs of irregularity – an indication of "cardiac sensitization." Cardiac sensitization is a property of some halocarbons whereby the human heart becomes sensitized to adrenaline, a naturally occurring substance produced by the human body during times of stress, and life threatening irregular heart beats can occur [5]. This parameter was selected for testing since it was considered to be the greatest threat to humans of any of the physiologic effects that Halon 1301 might cause (such as an anesthetic effect at high concentrations). Cardiac sensitization was felt to be more severe and occurred at concentrations closer to the actual design concentrations for fire extinguishing systems.

With the advent of halon replacement agents in the early 1990s, similar testing was required by the United States Environmental Protection Agency [6] and other international agencies. The selected test protocol was based on that used for Halon 1301, namely exposure of dogs to concentrations at and above the design concentration needed for fire protection purposes. Based on these tests, the NOAEL level (No Observable Adverse Effect Level) has been set as follows for the two most common halocarbon agents [7]:

HFC-227ea	9.0%
HFC-23	50%

Permissible exposure time varies with concentration.

The major concern regarding the toxicology data for halocarbons is the need to extrapolate from animal data to the projected effects on humans. This projection is done using a computerized model to predict the rate of uptake of the halocarbon into the blood at a given exposure concentration, and compares the predicted halocarbon concentration in the blood to the concentrations found to cause sensitization in dogs [8]. No actual human measurements are made. Without data from the actual exposure of humans to the same concentrations as used for the dogs, there can be no calibrated and validated correlation between the cardiac sensitization effects in dogs and the possible cardiac sensitization effects in humans. These projections may be based on the best science available, but they remain projections only.

A second area of concern is the focus on only one possible adverse effect – cardiac sensitization. Although this effect is certainly potentially serious, without the benefit of human testing we do not know if the design concentrations for halocarbons could result in impaired physical or mental functions that could limit an individual's ability to escape the hazard area. Indeed, the design concentrations are often less than 10% below the NOAEL values, a small margin for error [9].

Some human testing has been conducted for certain halocarbon agents, but the concentrations were not in accordance with the fire protection exposure scenarios outlined above (e.g. testing for propellant agents in medical inhalers [10]). Until extensive human testing is conducted for halocarbon agents at and above the necessary design concentrations, a question will remain regarding the human safety of these agents.

INERT GAS CLEAN AGENTS

A. Historical Human Testing

In contrast to the halocarbon agents, extensive human testing of inert gas clean agents has been conducted. In fact, an entire body of data has been developed since the 1940s [11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21] because the same condition created by an inert gas fire extinguishing system (lowered oxygen level) is also found in undersea and high altitude flight environments. From submarines to the space shuttle, the effects of low oxygen (hypoxic) atmospheres on humans have been extensively tested on human volunteers in controlled, well-documented experiments.

Furthermore, the testing conducted not only has measured physiologic values such as respiration volume and blood and brain oxygenation factors, but also has included cognitive and motor skill testing that would indicate a person's ability to evacuate the hazard area.

The testing procedures and results of these forms of tests, physiologic measurements and performance measurements, are discussed in sections C and D. The effects of two types of inert gases, INERGEN agent (which contains CO_2) and all other inert gas agents (which do not contain CO_2), are analyzed to show the significant beneficial effect from the small amount of CO_2 included in INERGEN agent. Before discussing the human test results, it is important to explain the physiologic effects of exposure to hypoxia, and the mechanisms by which the CO_2 in INERGEN agent exerts its positive influence on human safety in low oxygen atmospheres.

B. The CO_2 Effect

Delivery of oxygen to the brain, even when the available oxygen concentration in the inspired air is reduced (hypoxia), is influenced primarily by several normal physiologic control mechanisms related to levels of CO_2 and oxygen partial pressures in arterial blood [14, 17, 20]. To compensate for a lowered oxygen level in the atmosphere being breathed, the body first attempts to limit the decrease of arterial blood oxygen partial pressure (PO_2) by increasing respiration. Second, the lowered arterial blood PO_2 tends to cause a slight dilation of brain blood vessels. However, each of these normal responses to hypoxic exposure is counteracted and limited to some degree by the simultaneous lowering of carbon dioxide partial pressure (PCO_2) in arterial blood, which results from exhaling more CO_2 as respiration increases.

The respiration, arterial blood oxygenation, and brain blood flow responses are all favorably affected by the normal presence of CO_2 [17] acting in part through the increased acidity of the blood as the result of additional carbonic acid. Improvement of arterial blood PCO_2 additionally produces a shift in the hemoglobin dissociation curve, which enhances the transfer of oxygen from hemoglobin to brain tissues. CO_2 is, in several of its respiratory effects, the fine control parameter for normal oxygenation and acidity of brain and other tissues.

Therefore, the presence of CO_2 in INERGEN agent brings into play these natural mechanisms, and results in increased blood oxygen, increased blood flow to the brain, and more efficient transfer of oxygen to the brain tissue. Since all of these mechanisms are natural and pre-existing in the human body, there is no potential for adverse effects.

As a result of this "CO_2 Effect," INERGEN agent allows humans to endure lower inspired oxygen levels for much longer periods of time than would be true for any inert gases without carbon dioxide.

C. Human Test Results – Physiologic Measurements

Testing the effects of low oxygen atmospheres on human subjects without and with added CO_2 has been conducted extensively over the past 60 years [14, 18, 19, 20, 21]. We will concentrate on a recent series of tests for which the measurement of control states and effects was done mostly on a second-by-second, heart-beat-by-heartbeat basis [15, 17]. The seven figures which follow represent the mean values obtained for a group of the same subjects when exposed to three different atmospheres: normal air (21% oxygen – designated the *normoxic control*), 10% oxygen without added CO_2 (*hypoxia* – the atmosphere created by other inert gas fire extinguishing systems), and 10% oxygen with 4% added CO_2 (*hypoxia/CO_2* – an INERGEN atmosphere). Both moderate exercise (50 watts – equivalent to walking at a 3 mile per hour pace) and at-rest conditions were evaluated.

End Tidal PO_2 Responses to 10% O_2 & 10% O_2/4% CO_2
At Rest and 50 Watt Exercise
Average ± SEM of 7 Subjects

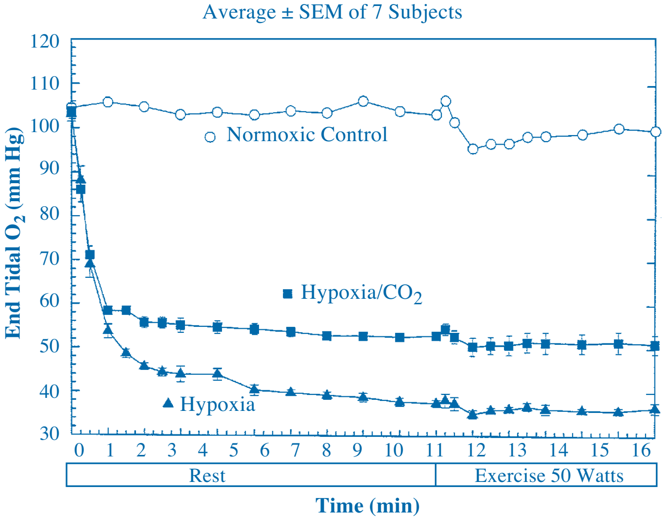

Figure 1 – End Tidal O_2 Partial Pressure

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The end tidal O_2 partial pressure is a measurement on gas samples taken inside the mouth of each subject during the last bit of each exhalation, and is a measurement of the oxygen partial pressure of the gas from deep within the lungs. Note in this graph (Figure 1) that after the first few breaths of the 10% oxygen atmosphere the end tidal partial pressure of oxygen drops rapidly due to the low oxygen content of the inspired gas. This drop is quickly attenuated in the presence of CO_2 because of its prompt and beneficial physiologic effects on respiration.

End Tidal PCO_2 Responses to 10% O_2 & 10% O_2/4% CO_2
At Rest and 50 Watt Exercise
Average ± SEM of 7 Subjects

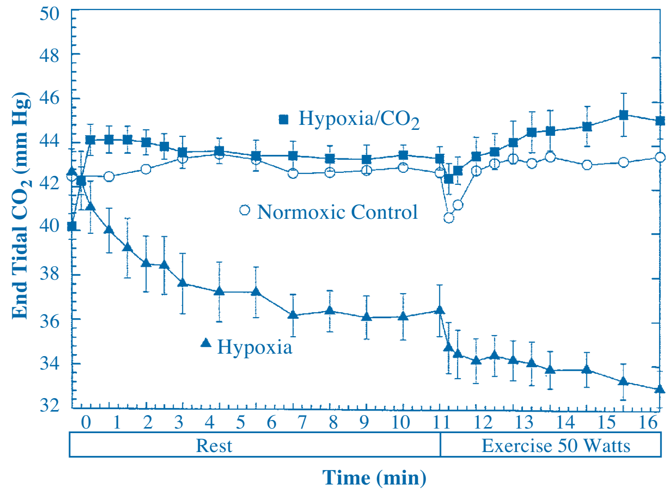

Figure 2 – End Tidal CO_2 Partial Pressure

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Here again, the end tidal CO_2 partial pressure, which reflects CO_2 partial pressure of deep lung gas and arterial blood, shows a distinct drop with hypoxia alone, due to the increased breathing caused by hypoxia. However, it actually increases due to the presence of CO_2 in INERGEN. Figure 2 shows the extremely rapid response, which will drive both respiration and brain oxygenation favorably. Recalling that the CO_2 of the blood controls the several mechanisms whereby the oxygen inhaled is delivered internally more efficiently, it is clear that the difference between 44 mm Hg and 39 mm Hg after one minute is very significant in terms of early improvement in respiration, arterial oxygenation and brain blood flow. Loss of CO_2 from the blood, as will occur in a hypoxic atmosphere without added CO_2, will have a corresponding negative effect on oxygenation of vital body tissues.

D. Human Testing – Mental Performance

In addition to repeated measurements of the amounts and partial pressures of oxygen reaching the brain as cited above, it is also critical to know whether such oxygenation levels allow individuals in an INERGEN atmosphere to perform normal mental functions that would be necessary for evacuation from the hazard area. Specifically, the ability to make decisions and to process words and numbers would be measurable critical factors.

Testing has been conducted [16], again on human subjects, using standardized cognitive performance tests administered under normal room air oxygen levels, followed by testing during inhalation of 10% oxygen without CO_2 (the hypoxic atmosphere created by inert gases without CO_2), and finally the testing was repeated while breathing 10% oxygen with 4% added CO_2 (INERGEN atmosphere).

Effects of Hypoxia (10% O_2) Without CO_2 & and with 4% CO_2 on Mental Performance Test Scores

(% of Control ± SEM, N = 8)

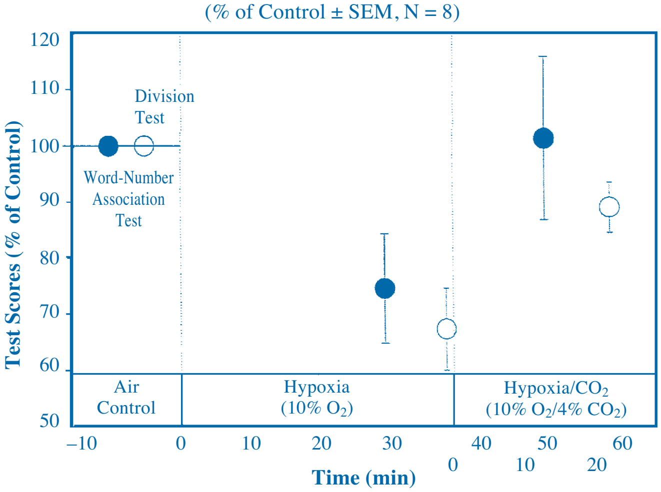

Figure 8 – Mental Performance

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The results shown in Figure 8 clearly show that a significant decrease in performance occurs when breathing the 10% oxygen atmosphere, and a return to high scores follows when breathing is shifted to the INERGEN atmosphere. This restoration of performance corresponds to the fact that more oxygen reaches the brain in an INERGEN atmosphere.

The same series of tests also indicated that the observed drop in cognitive performance with reduced oxygen levels did not begin until the inhaled oxygen level was decreased below 14% [21]. However, inert gas agents typically employ design concentrations that lower the oxygen concentration into the 10-12% range. At that degree of hypoxia, the "CO_2 effect" is considered critical for maintaining cognitive and psychomotor functions.

CONCLUSIONS

From the dynamic experimental evidences shown above, it can be concluded that the "CO_2 Effect" is real. It results in immediate responses and provides tolerance to oxygen levels at the low end of the fire suppression design range for extended periods of time – for inactive and exercising conditions – well in excess of the NFPA 2001 exposure time of five minutes. Further, the data were all gathered by testing humans, not animals, and includes both physiologic measurements and performance measurements.

Specifically, in the first few minutes, the presence of 4% CO_2 in a 10% O_2 INERGEN atmosphere:

- Maintains end tidal O_2 partial pressure more than 20% higher than without CO_2.
- Maintains end tidal CO_2 partial pressure at desirable levels at or above normal.
- Maintains arterial hemoglobin saturation at 90% and stable, versus 70-80% and falling without CO_2.
- Increases middle cerebral artery blood flow velocity 10% above normal air atmosphere exposure levels, while a 10% decrease occurs without added CO_2.
- Increases brain oxygen flow levels 10% above normal levels, while without CO_2 a 15% decrease occurs.

Cognitive testing confirms the beneficial effects of added CO_2 in hypoxia showing little, if any, decrement in the presence of an INERGEN atmosphere, but a significant decrease in the mental performance capabilities tested for the low oxygen conditions created by inert gas without CO_2. The physiologic and cognitive testing combined indicate that the negative effects on individuals at atmospheric oxygen concentrations of 10% **without added CO_2** may be severe and incapacitating relative to the ability to evacuate the hazard area. With the added CO_2 in INERGEN agent, no adverse effects will occur.

The physiologic data also confirms the rapidity of the "CO_2 Effect," resulting in beneficial influences for all measured functions within the first minute, and probably beginning within the first breath cycle. Furthermore, the beneficial effects continue for at least 10 minutes and undoubtedly well beyond.

Finally, it should again be noted that all of the data cited in this document come from actual testing on humans at the fire protection design concentration with no animal testing, extrapolations, computer models, assumptions or projections necessary.

Ventilation Volume Responses to 10% O_2 & 10% O_2/4% CO_2

At Rest and 50 Watt Exercise

Average ± SEM of 7 Subjects

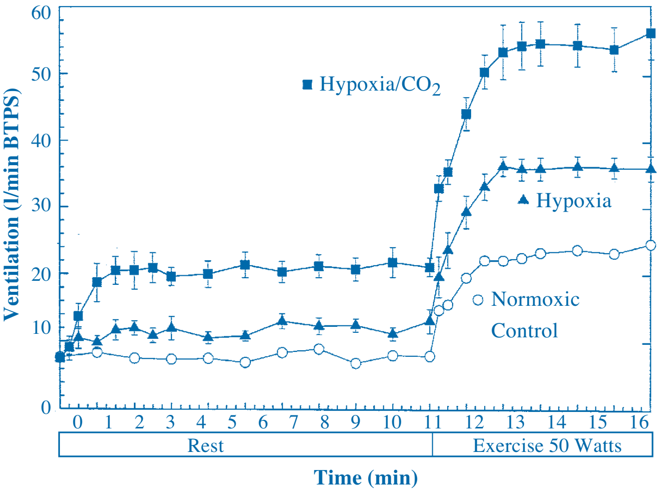

Figure 3 – Ventilation Volume

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The immediate impact on the volume of air breathed per minute when encountering a low oxygen (hypoxic) atmosphere is clearly indicated in Figure 3. Within the first minute, the inspired volume has essentially doubled when breathing an INERGEN atmosphere, but is only slightly increased without added CO_2. The increase is a normal physiologic mechanism for supplying more oxygen to the body through the lungs. The rapidity with which the body adjusts is well within the likely exposure time in any fire protection scenario, and the difference between 20 l/m and 10 l/m is often not subjectively noticeable.

Heart Rate Responses to 10% O_2 & 10% O_2/4% CO_2

At Rest and 50 Watt Exercise

Average ± SEM of 7 Subjects

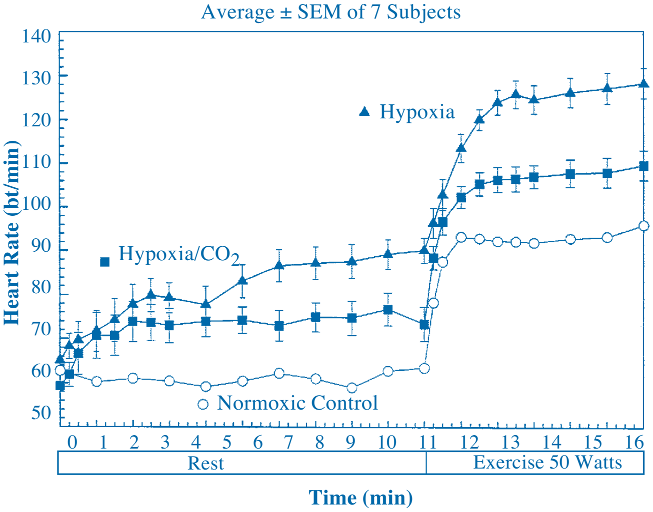

Figure 4 – Heart Rate

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Figure 4 demonstrates that heart rate in fact is subject to a separate control system within the body from that used to regulate respiration. The effect of hypoxia on heart rate at rest is minor, but does show that the presence of CO_2 results in smaller increases than for hypoxia alone, both at rest and in exercise.

Hemoglobin O_2 Saturation Responses to 10% O_2 & 10% O_2/4% CO_2

At Rest and 50 Watt Exercise

Average ± SEM of 7 Subjects

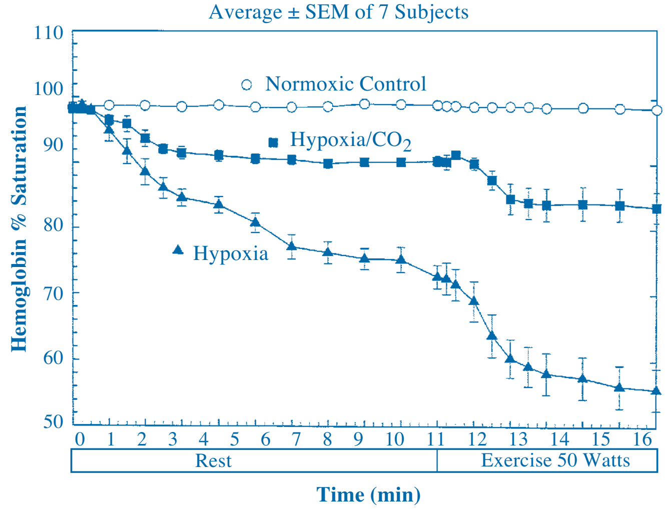

Figure 5 – Hemoglobin Saturation

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Normal hemoglobin oxygen capacity is around 19 ml of oxygen per 100 ml of blood. Using this value as 100%, Figure 5 shows the maintaining of a significantly higher hemoglobin oxygen saturation level when breathing an INERGEN atmosphere versus 10% oxygen with no added CO_2. Again, effects can be seen during the first several minutes. After 10 minutes, the INERGEN atmosphere still maintains over 90% saturation, while the non-INERGEN atmosphere has decreased to 75% and is still falling.

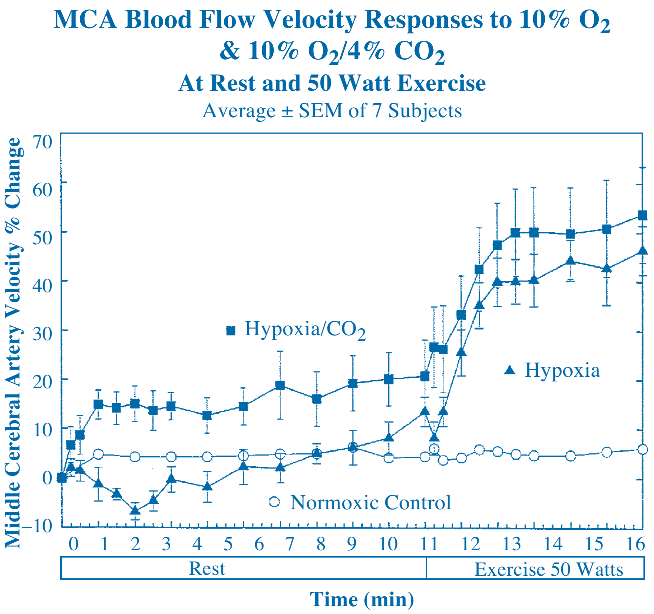

Figure 6 – Middle Cerebral Artery Blood Velocity

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The amount of oxygen reaching the brain is the product of the quantity of blood flow reaching the brain and the oxygen available in the blood itself (Figure 6). In addition to maintaining a high level of oxygen in the blood hemoglobin, the blood flow to the brain is in fact increased, again as a natural physiologic adjustment when breathing an INERGEN atmosphere. Note again that this effect occurs within the first minute of exposure. Without the benefit of the added CO_2, the blood flow initially drops and then only slowly rises as oxygenation of arterial blood decreases. This is extremely serious since without the effects of added CO_2, there is a lower partial pressure of oxygen and lower amount of oxygen carried by hemoglobin, and a lower flow of blood to the brain. Together, these result in a lower partial pressure of oxygen in brain tissues [14, 20].

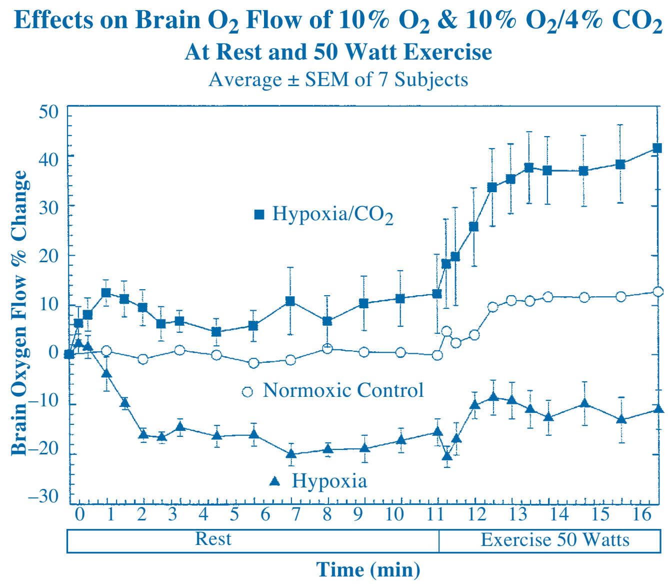

Figure 7 – Brain Oxygen Flow

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The percent change in brain oxygen flow is calculated from the data in Figures 5 and 6, and is shown in Figure 7. This graph shows the significant beneficial effect of the added CO_2 in an INERGEN atmosphere. The amount of oxygen reaching the brain actually *increases* by over 10% during the first minute, as compared to continuing to breath a normal 21% oxygen atmosphere. In other words, an individual exposed to a 10% oxygen INERGEN atmosphere, rather than suffering detrimental effects from oxygen deprivation, in fact feels no effects because the brain is receiving even more oxygen supply than normal air breathing at sea level [17]. In contrast, within two minutes an individual exposed to a 10% oxygen atmosphere caused by an inert gas fire extinguishing agent without added CO_2 will have approximately a 15% *decrease* in oxygen supply to the brain – a drop that can affect a person's ability to function properly (see section D). Also of significance is the rapid response to the presence of CO_2 giving a favorable effect on oxygen flow and brain oxygenation within the first breaths [17].

REFERENCES

[1] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Section 2-3.5.6, National Fire Protection Association, Quincy, MA, USA

[2] *ISO 14520: Standard for Gaseous Fire Extinguishing Systems, Final Draft 2000 Edition, Section 5.2, Safety Precautions,* International Organization for Standards, Geneva, Switzerland

[3] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Section 1-6, National Fire Protection Association, Quincy, MA, USA

[4] *Toxicology of DuPont Halon 1301 Fire Extinguishant*. Report S-35, E.I. Du Pont, de Nemours & Co., 1971.

[5] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Section A 1-6.1.2, National Fire Protection Association, Quincy, MA, USA

[6] Final Rulemaking, 59 FR 13044, March 18, 1994 (USEPA SNAP Program), implementing Section 612 of the Clean Air Act of 1990

[7] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Section 1-6, National Fire Protection Association, Quincy, MA, USA

[8] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Section A 1-6.1.2, National Fire Protection Association, Quincy, MA, USA

[9] *NFPA 2001: Standard for Clean Agent Fire Extinguishing Systems,* 2000 Edition, Sections 1-6.1.2.1, 3-4.2.3, and A-3-4.2, National Fire Protection Association, Quincy, MA, USA

[10] H.H. Emmen, et al. *Human Safety and Pharmacokinetics of CFC Alternative Propellants HFC 134a (1,1,1,2-Tetrafluoroethane) and HFC 227 (1,1,1,2,3,3,3- Heptafluoropropane) Following Whole-Body Exposure*. Regulatory Toxicology and Pharmacology **32**, 22-35 (2000).

[11] Gibbs, F.A., Gibbs, E.L., Lennox, W.G., and Nims, L.F. *The Value of Carbon Dioxide in Counteracting the Effects of Low Oxygen*. J. Aviation. Medicine. 14:250-261, 1943.

[12] *Research Bases for Improvement of Human Tolerance to Hypoxic Atmospheres in Fire Prevention and Extinguishment,* EBRDC Report 10.30.92, Environmental Biomedical Research Data Center, Institute for Environmental Medicine, University of Pennsylvania, 1992

[13] Lambertsen, C.J. and Gelfand, R., *Physiological Effects of Abrupt Exposure to Hypoxic Atmospheres (10% O_2 With 4% CO_2),* EBRDC Report 2.29.95, Environmental Biomedical Research Data Center, Institute for Environmental Medicine, University of Pennsylvania, 1995

[14] Gelfand, R. and Lambertsen, C.J., *Mental Performance, CO_2, and Extension of CNS Tolerance to Acute Inspiratory Hypoxia (0.1 ATA O_2),* Environmental Biomedical Data Center, Institute for Environmental Medicine, University of Pennsylvania, 1998

[15] Lambertsen, C.J., Gelfand, R. and Hopkin, E. *Carbon Dioxide-Oxygen Interactions in Extension of Tolerance to Acute Hypoxia*. National Aeronautics Administration Bioastronautics Investigation Workshop, p. 186-191, Galveston, Texas, January 17-19, 2001

[16] Shapiro, W., Wasserman, A.J. and Patterson, J.L., Jr. *Human Cerebrovascular Response to Combined Hypoxia and Hypercapnia*. Circulation Research, XIX: 903-910, 1966

[17] Gellhorn, E. *Circulatory Studies on Anoxemia in Man with Respect to Posture and Carbon Dioxide*. Annals of Internal Medicine 10 (9): 1267-1278, 1937

[18] Lambertsen, C.J. *Hypoxia, Altitude, and Acclimatization*. Medical Physiology (14th ed.) V.B. Mountcastle, Ed., St. Louis, MO: Mosby, 1980

[19] Gelfand, R., Lambertsen, C.J., and Youdelman, B. *Mental Performance at Rest and in Exercise with Inspired O_2 of 12% and 10% (at 1.0 ATA) Determined by Computerized Human Performance Measurement System* (Abstract). Undersea and Hyperbaric Medicine 24(S): 18, 1997

[20] Consolazio, W.V., Fisher, M.B., Pace, N., Pecora, L.J., Pitts, G.C., and Behnke, A.R. *Effects on Man of High Concentrations of Carbon Dioxide in Relation to Various Oxygen Pressures During Exposures as Long as 72 Hours*. American Journal of Physiology 151: 479-503, 1947

[21] Lambertsen, C.J., Gelfand, R. *Comparison of CO_2-Induced Improvements in Arterial SaO_2 During Abrupt Exposures of Human Subjects to .12 and .10 ATA Inspired O_2 in N_2, in Rest and Exercise* (Abstract). Undersea Hyperbaric Medicine 23(S): 75-76, 1996

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