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Comparison of Simulated High Altitude Pilot Effective Performance Time Between Habitual Smokers' and Non-Smokers'

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The combined effects of low oxygen content at high altitudes and reduced oxygen diffusion because of the smokers' impaired ventilation efficiency, can significantly compromise pilot performance.

Smoking attenuates the amount of oxygen that diffuses from the lung tissue and oxygenates the blood (Guyton, 1996). High altitudes attenuate the oxygen available for transport to the blood. However, little has been reported on the combined effects of these two forms of hypoxia (inadequate oxygenation of the blood). It may be that, together, these two hypoxic conditions react exponentially to critically affect human performance.

Fifty-two participants were screened for cotinine serum values >200 ng/dl^{-1}, to flesh out nicotine usage, through urine sampling. Nineteen participants were entered into the smoker's group and 33 into the non-smoker's group. All of the participants were active student pilots. All of them held current instrument ratings and all of them had approximately the same amount of time and experience in instrument meteorological conditions (IMC).

Data were analyzed using Microsoft Excel and SPSS computer software statistic programs. The criterion for significance (alpha) was set at 0.05. The test was a non-directional *t*-test (two-tailed), which means that an effect in either direction was interpreted. Statistical significance existed when comparing the mean effective performance times between smoking pilots and nonsmoking pilots $t = 3.541$ (39), $p = .05$ in the experimental (simulated altitude) groups. Within the limitations of this study it can be concluded that the combined hypoxic effects of smoking and high altitude result in a statistically significant detriment in pilot effective performance time.

Smoking attenuates the amount of oxygen that diffuses from the lung tissue and oxygenates the blood (Guyton, 1996). High altitudes attenuate the oxygen available for transport to the blood (Poliler, 1971). However, little has been reported on the combined effects of these two forms of hypoxia (inadequate oxygenation of the blood) (Nesthus, Garner, Mills, 1997; Yoneda, Watanabe, 1997). It may be that together, these two hypoxic conditions react exponentially to critically affect human performance. Such may be the case for pilots who are chronic smokers' and are required to fly at high altitudes to avoid severe weather or oncoming aircraft. The combined effects of low oxygen content at high altitudes and reduced oxygen diffusion because of the smokers' impaired ventilation efficiency, can significantly compromise pilot performance. This possibility leads to the prediction that pilots who are chronic smokers' will evidence a reduction in effective performance time when they fly at a simulated altitude of 10,000 feet mean sea-level (MSL) which has demonstrated a reduction in cognitive and motor performance (Tune, 1964).

Pilot Effective Performance Time (PEPT)

Pilot effective performance time represents the time in seconds that a pilot takes to maneuver an aircraft to maintain an assigned steady course of flight. During actual flight, specific external environmental forces act upon the flight surfaces causing changes in aircraft attitude. These conditions include changes in temperature lapse rate, density altitude, wind velocity and atmospheric pressures. These changes may cause the aircraft to unfavorably pitch (nose up or down), yaw (tail movement right or

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left), or roll (wing tips rise or fall). As these meteorological phenomena occur, the pilot is required to respond skillfully, maneuvering the aircraft back to its assigned course, heading, and altitude. Hence, the time required to return the aircraft to the proper attitude is PEPT.

For this study, aircraft control, orientation, navigation, and communication changes were simulated using a personal computer aviation-training device (PCATD). The PCATD (Appendix A) used in this study was programmed to simulate many of the atmospheric changes that may occur during an actual flight.

In this study, PEPT was measured over a time window of forty-five seconds, starting with the 40th minute of simulated flight time. Individual pilot PEPT recorded during the 45-second window represents the total time it took the participant to return to an assigned indicated altitude of 7,000 feet MSL (for visual reference) straight and level flight without any adverse pitch, yaw, or roll. The hypobaric chamber was used to simulate atmospheric conditions at 3,049 meters (10,000 feet) MSL.

Physiological Principles of Oxygen Transport

To appreciate the significance of the combined effects of high altitude and chronic smokers" hypoxias, it is necessary to make clear the physiological principles of oxygen transport. Oxygen occupies about 21% of the air we breathe. When we inhale, oxygen makes its way to the alveoli of the lungs; it diffuses across the thin alveolar membrane into the blood stream and crosses the membranes of the arterial erythrocytes. The erythrocytes carry the oxygen to the left side of the heart where it is pumped into the body's systemic circulation and carried to awaiting tissue. The tissue exchanges the oxygen for carbon dioxide and is subsequently sent to the right side of the heart as venous return via the inferior and superior vena cava.

Hemoglobin (Hb) is the principal transport system for oxygen. The oxygen-hemoglobin dissociation curve demonstrates, graphically, the progressive increase/decrease in the percentage of hemoglobin bound with oxygen. As the partial pressure of oxygen ($P[O_2]$) increases, so too does the percent saturation of hemoglobin.

Oxygen is fundamental for metabolic activity of the cells in the body. This metabolism can be compromised in an assortment of ways, including rapid or continuous change in atmospheric pressures or the introduction or ingestion of harmful gasses or materials. (Ernsting, 1988)

This compromise of the metabolic pathways makes it difficult for cells to utilize oxygen that has diffused across the membranes. This in turn forces the body to compensate accordingly by increasing respiratory rate and depth, as well as cardiac output. This condition of increased cardiopulmonary activity increases the rate at which carbon dioxide is removed from the body. Paradoxically, carbon dioxide is important to stimulate respiration, as it is necessary for converting carbonate, a base into carbonic acid. Chemoreceptors in the dorsal medulla of the brainstem continuously monitor pH levels. Decreased pH enhances the neuronal firing rate of these cells, which in turn increases respiratory rate and depth. Consequently, decreased carbon dioxide content due to hyperventilation results in decreased carbonic acid concentrations, increased pH and a progressively weakened breathing signal. (Pitts, and Pace, 1947, DeHart, 2002).

Background

Only two studies could be found that investigated the effects of chronic smoking and high altitude performance (Nesthus, Garner, Mills, 1997; Yoneda and Watanabe, 1997). Both studies concluded that the smokers' performed better in the early portion of the studies while both cognitive and motor response rates deteriorated with prolonged exposure to high altitudes. The two studies differed in altitude exposures. Nesthus et al performed their study at a simulated altitude of 8,000 feet MSL for a period of two hours while the Yoneda & Wantanbe study investigated responses at a simulated altitude of 25,000 feet MSL.

Denison, Ledewith, and Poulton (1966) and Ledewith and Denison (1964) suggested their studies showed task impairment at 8,000 feet. However, later studies have been unable to demonstrate similar effects (Fowler, Paul, Porlier, Elcombe, and Taylor, 1985; Crow and Kelman, 1971, 1973; Kelman and Crow, 1969; Kelman, Crow, and Bursil, 1969). Eight thousand feet is the accepted maximum allowable cabin pressure on commercial jet aircraft.

The sparse literature that has reported the combined effects of high altitude hypoxia (hypoxic) and chronic smokers' hypoxia (hypemic) makes clear the need to study the effects of simulated high altitude PEPT in smokers' compared to non-smokers'.

The effects of altitude on the human body are described in terms of atmospheric thermodynamics (Appendix D). As a person ascends in altitude they pass through "layers" or levels of the atmosphere. From sea level to an altitude of about 91.5 km (300,000 ft.) the relative concentrations of atmospheric gases remains fairly constant.

Nitrogen and oxygen are the most abundant gases; 78% and 21% respectively. Compensatory physiological changes occur continuously with changes in altitude. Gas laws (Appendix C) that attempt to describe each and every atmospheric condition in part, govern these physiological changes. The greatest concentrations of work

involving these gas laws were born in aviation with the invention of the hot air or hot gas balloons.

The level where high altitude affects human performance has been long in debate. Experiments performed by the Federal Aviation Administration's (FAA) Civil Aeromedical Institute demonstrated that exposure to a simulated altitude of 12,500 feet caused decrements in complex task performance (Mertens and Collins, 1986, 1985; Mertens McKenzie, Funkhouser, White and Milburn, 1982). Tune (1964) determined in his study that perceptual-motor performance degraded significantly at 10,000 feet. Some studies showed task impairment at 8,000 feet. (Denison, Ledewith, and Poulton, 1966; and Ledewith and Denison, 1964) However, later studies have been unable to demonstrate similar effects (Fowler, Paul, Porlier, Elcombe, and Taylor, 1985; Crow and Kelman, 1971, 1973; Kelman and Crow, 1969; Kelman, Crow, and Bursil, 1969). Eight thousand feet is the accepted maximum allowable cabin pressure on commercial jet aircraft.

Rick Curtis (1999) labeled the atmospheric levels of altitude as follows: high altitude (8,000 - 12,000 feet [2,438-3,658 meters]), very high altitude (12,000 - 18,000 feet [3,658 - 5,487 meters]), and extremely high altitude (18,000 + feet [5,500+ meters]). The aviation community has accepted 3,049 meters (10,000 feet) as the lowest point on the altitude scale that hypoxia has noticeable influence on cognitive and functional performance.

With ascent to altitude the atmospheric pressure decreases, the partial pressure of oxygen becomes increasingly reduced and the reduction in pressure results in an extremely harsh environment, making survival increasingly unlikely.

The atmosphere has been divided into three physiological zones (physiological efficient zone, physiological deficient zone, and space equivalent zone) in which human survival eventually becomes dependent on specialized equipment (pressurized aircraft, pressure suits, sealed cabins/capsules, etc.).

Purpose of this Study

The purpose of this study is to investigate the combined effects of high altitude hypoxia and chronic smokers' hypoxia on PEPT. Questions that guided this study are:

1. Is there a difference in smoker's PEPT at sea level compared to non-smokers' PEPT at sea level?
2. Is there a difference between the smokers' PEPT at sea level compared to their PEPT at a simulated altitude of 3,049 meters (10,000 feet MSL)?
3. Is there a difference in non-smokers' PEPT at sea level compared to their PEPT at a simulated altitude of 3,049 meters (10,000 feet MSL)?

ANOVA tests were applied to the captured data to determine whether there was a difference in effective performance times between smoking and nonsmoking pilots at a simulated altitude of 3,049 meters (10,000 feet) and sea level. Additional tests were applied to the data to compare effective performance times for smoking pilots at altitude and sea level and again with non-smoking pilots at altitude and sea level.

Null Hypothesis

There is no statistical significant difference in pilot effective performance time at an altitude of 3,049 meters (10,000 feet MSL) in smokers' when compared to non-smokers'.

Hypoxia and Smoking

Fowler and Kelso (1991) stated, "It is well known that hypoxia increases visual reaction time." Evidence gathered by Kobrick and Dusek (1970) and again by Fowler, et al (1988) conducted studies in high altitude chambers. These studies also found there was potential for barotraumas due to the reduction of atmospheric pressures.

A reduced oxygen-breathing device (ROBD) involving mixed gases and regulatory devices to induce hypoxic effects were developed by Sausen, Wallick, Slobodnic, Bower, and Clark (1999). Successful experiments performed on U.S. Navy personnel using analytical tools to determine cognitive assessment ranged from simple juvenile games to complex neuropsychological assessment instruments, i.e., selected memory instruments, math problem solving, computerized tracking, and so on.

Original research conducted by Yoneda and Watanabe, (1997) measured the response rates of pilots who were habitual smokers' at an altitude of 7,620 meters (25,000 ft). Their conclusions showed that smokers' were slightly resistant to altitude hypoxia because of their affinity toward anemic (hypemic) hypoxia brought about by increased carboxyhemoglobin levels due to habitual smoking. Most of the data gathered were considered subjective. Observations included: warm sensation or heat flush, thinking impairment, visual impairment, lethargy, fatigue, dyspnea, sweating, tremor, anxiety headache, euphoria, and nausea. However, the statistics were not conclusive enough to determine long-term effects. In addition, comparisons of habitual smokers' and non-smokers'' were not made at sea level. The study involved only short duration exposure to high altitude. The most frequently used profile for pilot and aircrew member training was a decompression of 25,000 ft. Mean Sea Level (7,620m) for approximately 4-8 minutes with a hypoxia experience and subsequent descent (U.S. Navy Hypobaric Type II and Type IIa flight profiles). These

profiles were used for investigating altitude tolerance and hypoxia symptoms. Time of useful consciousness (TUC) was determined with written instruments, handwriting samples, and simple numeric testing. Baseline TUC was determined for both groups whether they were smokers' or not. The research only made conclusions regarding TUC and did not make statements regarding PEPT.

Atmospheric Physics

The composition of the atmosphere is remarkably constant between sea level and an altitude of 91.5 km (300,000 ft.). Nitrogen and oxygen are the most abundant gases in the atmosphere. From a practical standpoint, in studies concerning the effects of altitude on the human body, the percent concentrations of the other gases are considered negligible and are ignored. Air has an approximate composition of 78% nitrogen and 21% oxygen by *volume*, which is directly affected by temperature and pressure. The measure of dry air at sea level is usually seen defined by its mass (mmHg). The region of the atmosphere to which humans are adapted physiologically extends from sea level to 3,049 m (10,000 feet). The oxygen level within this zone is sufficient to keep a normal, healthy person physiologically fit without the aid of special protective equipment. The changes in pressure encountered with rapid ascents or descents within this zone can produce ear or sinus difficulties.

A physiologically deficient region extends from 3,049 m to about 15.3 km. Because of reduced atmospheric pressure, this is the zone in which oxygen deficiency becomes an ever-increasing problem. Supplemental oxygen is required when flying above 3,811 m (12,500 feet) (FAR 91.211). Trapped gas in the intestinal tract and evolved gas problems occur within this zone. In addition, protection must be provided against decreasing temperature.

The space-equivalent region begins when 50,000 feet is reached since supplemental oxygen (100%), even when supplied under pressure, no longer protects one from the problem of hypoxia. The means of protecting a person above 50,000 feet are such that they will also offer protection in true space (i.e., pressure suits, sealed cabins). The only additional physiological problems occurring within this zone, which extends from 50,000 feet to 120 miles, are possible radiation effects and the boiling of body fluids in an unprotected individual. Boiling of body fluids will occur when the total barometric pressure is less than the vapor pressure of water at 37oC (47 mmHg), which is reached at 19.6 km (63,500 feet, Armstrong Line) (Boothby, Lovelace, Benson, & Strehler, 1954).

Physiological Requirements of Oxygen

The periodic and rhythmic characteristics of respiration are maintained by means of comparatively clear nervous pathways between the lungs and respiratory muscles and the brain. The medulla oblongata is the location for neural control of respiration. Within the compact, definitively located segment of the medulla is the respiratory center. There are two distinct aggregations of nerve cells. These are the inspiratory and expiratory centers. It is believed that the inspiratory center is located caudal to the expiratory center. Specialized nerve cells are located in the pons, which also influence respiratory activity. This higher center is sometimes referred to as the pneumotaxic center (Fisher, 1991).

Ventilation is a cyclic process by which fresh air or a gas mixture enters the lungs and pulmonary air is expelled. The inspired volume is greater than the expired volume because the volume of oxygen absorbed by the blood is greater than the volume of carbon dioxide, which is released from the blood. Since gas exchange occurs solely in the alveoli and not in the conducting airways, the estimation of alveolar ventilation rate (i.e. the amount of gas which enters the alveoli per minute) is the single most important variable of ventilation (Guyton & Hall, 2000).

Oxygenation of the tissue yields the metabolic conversion of oxygen to carbon dioxide. Carbon dioxide (CO_2) is exchanged for oxygen at the cellular level and is converted to carbonic acid (H_2CO_3). The direct effects of CO_2 on the respiratory centers produce a lower signal frequency than oxygen, which triggers an autonomic response reminding the body to breathe. These responses at the pneumotaxic center have a lesser effect than the peripheral chemoreceptors. This would indicate that the peripheral chemoreceptors receive and transmit signals to the respiratory center before blood containing carbonic acid reaches the pneumotaxic center. The respiratory center is also sensitive to low pH levels (acidity) caused by rising carbonic acid levels. Both low oxygen levels and acidic pH levels cause the brain to increase both the rate and depth of breathing which, in turn, increases the amount of oxygen available to the body. Unfortunately, increased depth and rate of breathing also causes the body to expel CO_2 at an increased rate. As a result, there is rapid loss of carbonic acid, which again is an important breathing stimulus for the brain (Ernsting, 1988).

Metabolism of Smoking

Nicotine is rapidly metabolized and has a short half-life; cotinine, the major metabolite of nicotine, is metabolized and eliminated at a much lower rate. Because of the resulting increase with time in the cotinine to nicotine ratio in the body, including in the brain, it is of interest to

examine the effect of cotinine on nicotine-induced changes (Sziraki, Sershen, Benuck, Lipovac, Hashim, Cooper, Allen, Lajtha, Nathan, Kline, 1999).

Because cotinine is a major metabolite of nicotine it is currently regarded as the best biomarker for exposure to tobacco. Cotinine measurement is preferred over measuring nicotine because its retention in the body is much longer than nicotine. Cotinine can be measured in blood (i.e., in serum), urine, saliva, and hair. Nonsmokers' exposed to typical levels of environmental tobacco smoke (ETS) have cotinine levels less than 1 nanogram per milliliter (ng/mL), with heavy exposure to ETS producing levels in the 1 to 15-ng/mL ranges. Active smokers' almost always have levels higher than 15 ng/mL, sometimes over 500 ng/mL (Pirkle, Flegal, Bernert, Brody, Etzel, Maurer, 1996).

Cotinine Immunoassays

The assay chosen to determine which participants were cigarette users in this study was the Sure Step ™ smoke check test. This test was a lateral flow, one-step immunoassay for the qualitative detection of cotinine, the major metabolite of nicotine in human urine, at a cutoff concentration of 200 ng/dl^{-1}. This product was used to obtain visual, qualitative results and was intended to provide objective means to determine the chronic smokers' from the non-smokers'.

Findings and Discussion

Smokers' vs. Non-smokers' Pilot Effective Performance Time at High Altitude

An independent samples *t*-test that compared the mean smokers' (n = 19), PEPT at 3,049 meters (10,000 feet MSL) to the non-smokers' (n=33) PEPT at 3,049 meters (10,000 feet MSL) revealed that the smokers' PEPT was 17.0356 seconds, Table 4, and the mean non-smokers' PEPT was 15.0870 seconds, Table 6. The computed *t* (df) between these two means was 3.541 (df=51), which was significant at the .001 level. These results show that the smokers' pilot effective performance time was longer than the non-smokers'' PEPT. These results reject the null hypothesis that there was no difference in pilot effective performance time at high altitude between smokers' and non-smokers'. These findings suggest that the combined altitude and smoking hypoxias were significantly more detrimental to pilot performance skills required to maintain the assigned altitude of 7,000 feet MSL than high altitude hypoxia alone.

Table 1 Independent samples *t* test to compare the means of pilot effective performance times.

Smokers' and nonsmokers'	N	Mean time (sec)	*t* (df)	p
Pilot performance at altitude-smoker nonsmoker	19 33	17.3056 15.0870	3.541 (51)	.001
Pilot performance at sea level-smoker nonsmoker	19 33	10.6389 12.9348	-1.538(51)	.132

Table 2 Paired samples *t* test comparing smoker pilot effective performance time at altitude and sea level.

Independent Variable	Mean	Std. Dev	Std.Er.	*t* (df)	p
Smoker performance time at altitude	17.3056	3.80069	.89583	-6.624(18)	.000
Smoker performance time at sea level	10.6398	5.59886	1.31966		

Table 3 Paired samples *t* test comparing non-smoking pilot effective performance time at altitude and sea level.

Independent Variable	Mean	Std. Dev	Std.Er.	*t* (df)	p
Nonsmoker performance time at altitude	15.0870	5.6421	1.1765	2.827 (32)	.010
Nonsmoker performance time at sea level	12.9348	3.9580	.825		

This objective evidence agrees with original research conducted by Yoneda and Watanabe (1997). They measured response rates of pilots who were habitual smokers', at an altitude of 25,000 feet MSL. They concluded that smokers' were slightly resistant to altitude hypoxia because of their affinity toward hypemic hypoxia brought about by the increase of carboxyhemoglobin levels due to habitual smoking. Their data was based on subjective observations, e.g. warm sensations, visual and thinking impairment, fatigue, and headaches. Never the less, their subjective data support the findings of the present study.

Smokers' vs. Non-smokers' PEPT at Sea Level

An independent samples *t*-test compared the mean smokers' (n = 19) at sea level to the mean of the non-smokers" (n = 33) at sea level. The respective pilot effective performance times were 10.6398 seconds for the smokers' and 12.9348 seconds for the non-smokers', Table 4. The computed *t*(df) between the two means was 1.538 (n = 51). It was not significant (p = .132). These results show there was not a difference in the pilot effective performance time at sea level between the smokers' and non-smokers'. These data suggest that smoking hypoxia alone is not sufficiently detrimental to pilot effective performance skills required to maintain the assigned navigational course at sea level. These findings answer question number one of the related questions proposed to guide this study: Is there a difference between smokers' PEPT at sea level compared to the non-smokers' pilot effective performance time at sea level? The answer is no.

Smokers' Pilot Effective Performance Time at 3,049 meters (10,000 feet MSL) vs. Sea Level

A paired samples *t*-test compared smoker effective performance time at high altitude and sea level (Table 5). The mean pilot effective performance time at altitude (17.3056 seconds) was significantly greater than their pilot effective performance time at sea level (10.6398 seconds). This difference was significant at the 0.000 level. These data suggest that high altitude hypoxia, by itself; can cause significant attenuation of PEPT. And that only when smokers' fly at high altitudes and experience the effects of high altitude hypoxia is PEPT significantly affected. These findings answer question number two of the related questions guiding this study: Is there a difference in the smokers" pilot effective performance time at sea level compared to high altitude? The answer is yes.

Non-Smokers' Pilot Effective Performance Time at High Altitude vs. Sea Level

A paired samples *t*-test compared the non-smokers" PEPT at 3,049 meters (10,000 feet MSL) and sea level (Table 6). The mean pilot effective performance time at 3,049 meters (10,000 feet MSL) (15.08 seconds) was significantly greater than their PEPT at sea level (12.9348 seconds). This difference was significant at the 0.01 level. These data suggest that high altitude hypoxia, by itself; can cause a significant attenuation of PEPT. These data answer the question number three of the related questions guiding the study: Is there a difference in the non-smokers" PEPT at sea level compared to high altitude? The answer is yes.

References

Benowitz N., (1996). Cotinine as biomarker of environmental tobacco smoke exposure. Epidemiological Reviews; 18 {2}: 188-204

Boren, C. F., Albrecht, B. A. (1998) Atmospheric Thermodynamics, Oxford University Press,

Boothby, W.M., Lovelace, W.R. II, Benson, O.O. Jr., & Strehler, A.F. (1954). Volume and partial pressures of respiratory gases at altitude. In W.M. Boothby (Ed). Handbook of respiratory physiology. Randolph AFB, Texas: Air University, USAF School of Aviation Medicine, September.

Carlson, L.D. Gas exchange and transportation. (1965a). In T.C. Ruch & J.F. Fulton (Eds). Medical physiology and geophysics (18th ed). Philadelphia: W. B. Saunders,

Carlson, L.D. (1965b) Gas exchange and transportation. In T.C. Ruch & J.F. Fulton (Eds.), Physiology and biophysics (19th ed.). Philadelphia: W.B. Saunders.

Clark, J.M., & Lambertsen, C.J. (1971). Pulmonary oxygen toxicity: A Review. Pharmacological Review; 23: 37-133.

Comroe, J.H., Jr. (1965). Physiology of respiration. Chicago: Yearbook Medical Publishers,

Corvall, M., and Vala I. (1993). Nicotine and metabolites: analysis and levels in body fluids. Nicotine and related alkaloids: absorption, distribution, metabolism, and excretion. Edited by Gorrod, J. W. and Wahren, J. Chapman & Hall. ISBN 0.14255740-1.

DeHart, R. L. Davis, J., R. (2002). (Eds) *Fundamentals of Aerospace Medicine*, (3rd ed). Williams and Wilkins, Baltimore

Ernsting, J. (1965). The physiological requirements of aircraft oxygen systems. In J.A. Gillies (Ed). A textbook of aviation physiology. New York: Pergamon Press.

Ernsting, J. (1965a). The physiology of pressure breathing. In J.A. Gillies (Ed). A textbook of aviation physiology. New York: Pergamon Press,.

Ernsting, J. (1965b). Respiration and anoxia. In J.A. Gillies (Ed). A textbook of Aviation physiology. New York: Pergamon Press.

Ernsting, J. (1966). Some effects of raised intrapulmonary pressure in man (AGARD Monograph 106).Maidenhead, England: Technivision.

Ernsting, J., & King, P. (1988). Aviation medicine. Boston: Butterworths.

Ernsting, J. (1964). The use of the pressure economizer oxygen system in high performance aircraft in which crewmembers are routinely exposed to positive acceleration (FPRC Memo 215). Farnborough, England: RAF Institute of aviation medicine, September.

Fellenius, E., & Samuelson, R. (1973). Effects of severe systemic hypoxia on myocardial energy metabolism. Journal of Scandinavian Physiology; 88, 256-266.

Fowler, B., Kelso, B. (1992).The effects of hypoxia on components of the human event-related potential and relationship to reaction time. Aviat. Space Environ Med.; 63:510-6

Fowler, B., Kelso, B., Landolt, J.P., Porlier, G. (1988). The effects of hypoxia on P300 and reaction time. Electric and magnetic activities of the central nervous system: research and clinical application in aerospace medicine. AGARD Conference Proceedings 432. Neuilly Sur Sein, France: AGARD: 16-1-7

Fukata Y, Amano M, & Kaibuchi K. (2001). Rho-Rho-kinase pathway in smooth muscle contraction and cytoskeletal reorganization of non-muscle cells Trends Pharmacol Sci.; 22(1), 32-39, decompression sickness. Aerospace Medicine; 38, 825-828.

Gillies, J.A. (Ed). (1965). A textbook of aviation physiology. New York: Pergamon Press, (or latest edition).

Guyton, A. C. (1998). Textbook of medical physiology (6th ed.). Philadelphia: W. B. Saunders.

Guyton, A. C. & Hall, , J..E., (2000). Textbook of medical physiology (7th ed.).Philadelphia: W. B. Saunders.

Horvath, S.M. (1972). Physiology of work at altitude In: *Physiological Adaptations: Desert and Mountain*, M.K. Yousef, S.M. Horvath, and R.W. Bullard (Eds). pp 183-190, New York.

Hultgren, N.H., & Grover, R.F. (1968) Circulatory adaptation to high altitude. Annual Review of Medicine; 19: 119-151.

Kobrick, J.L., Dusek, E. R., (1970). Effects on voluntary response time to peripherally allocated visual stimuli. J. Appl. Physio.1970; 29: 444-8.Medicine; 1971; 284: 1298-1308.

Luft, U.C., & Finkelstein, S. (1968) Hypoxia: A clinical-physiological approach. Aerospace Medicine; 39: 105-109.

Luft, U.C. (1961). Altitude sickness. In H.G. Armstrong (Ed.), Aerospace medicine. Baltimore: The Williams & Wilkins.

Luft, U.C. (1965) Aviation Physiology - The effects of altitude. In Fenn W.O., & Rahn, H. (Eds.). Handbook of physiology. Section 3, Vol.II, Respiration. Washington, DC: American Physiological Society.

Mohler, S.R. (1985). Medication and Flying: A Pilot's Guide, Aircraft Owners and Pilots Association.

Samuelsson, R. (1973). Effects of severe systemic hypoxia on myocardial excitation, Journal of Scandinavian Physiology; 88: 267-280.

Sausen, K.P., Wallick, M.T., Slobodnic B., Bower, E.A., Chimiak, J. M., Bower, E. A., and Clark, J., B. (2001). The reduced oxygen-breathing paradigm for hypoxia training: physiological, cognitive, and subjective effects. Aviation, Space and Environmental Medicine; 72: 539-545.

Schupp P, Mucha RF, Pauli P. (1999). Topography of sham and real puffing examined using a paced smoking regimen. Addict Behav. Sep-Oct; 24(5):695-9.

Yoneda, I., Wantanabe, Y. (1997). Comparisons of altitude tolerance and hypoxia symptoms between nonsmokers' and habitual smokers'. Aviat. Space and Environ. Med., 68: 807-811.