Effects of cigarette smoking on tissue gas exchange during hyperbaric exposures

GEORGE B. HART¹, MICHAEL B. STRAUSS²

¹Department of Hyperbaric Medicine, Long Beach Memorial Medical Center, Long Beach, California, University of California Irvine, School of Medicine, Irvine, California, USA
²Department of Hyperbaric Medicine, Long Beach Memorial Medical Center, Long Beach, California, Department of Orthopedics, University of California Irvine School of Medicine, Irvine, California, USA

CORRESPONDING AUTHOR: Dr. George Hart – gbabehart@hotmail.com

ABSTRACT

Objectives: In this study we investigate whether differences exist in human skeletal muscle (MM) and subcutaneous (SC) tissue gas tensions between chronic cigarette smokers and non-smokers measured under room air and hyperbaric conditions.

Methods: Gas tensions in resting MM and SC tissues were recorded using a mass spectrometer at four-minute intervals during two and one-half to three-hour period in smokers and non-smokers during normobaric, normoxic (room air) and hyperbaric conditions. Two hyperbaric oxygen (HBO₂) protocols were utilized: Protocol A employed the continuous breathing of oxygen (O₂) at 2 ATA, a typical monoplace hyperbaric chamber treatment, while Protocol B utilized intermittent air breaks between O₂ breathing periods at 2 ATA representative of a multiplace hyperbaric chamber treatment.

Results: All tissue gas tensions changed significantly (repeated measures of variance, \( p=0.00001 \)) with time as pressures and gas mixtures breathed were altered. Significant Individual Step Analysis (ISA) differences occurred with unloading of nitrogen (N₂) from the muscle compartment in both protocols (T-test and Wilcoxon Rank Sum). The interaction of grouping variable and time revealed significant differences between smokers and non-smokers in unloading MM N₂ in both protocols: protocol a \( (p=0.02) \) and in protocol B \( (p=0.022) \). Carbon dioxide (CO₂) levels in both protocols decreased significantly with time when exposed to HBO₂ while increasing when breathing air at 2 ATA.

Conclusions: This study demonstrates: 1) Smokers release MM N₂ more slowly than nonsmokers during hyperbaric oxygen exposures regardless of the treatment protocol used; 2) There were no significant differences in O₂ loading of MM and SC tissues during HBO₂ exposures between smokers and nonsmokers; 3) The CO₂ levels in both protocols decrease with time when exposed to HBO₂ while increasing with breathing air at 2 ATA; 4) The known vasoconstriction effect in subcutaneous tissue from nicotine lasts less than one hour with the topical adiabatic heating increasing the O₂ loading specifically in the SC tissues of smokers; 5) Wounds heal more slowly due to the chronically injured endothelium from carbon monoxide, hydrogen cyanide, and other toxic products in smoke rather than from the transient elevations of nicotine.

INTRODUCTION

Hyperbaric oxygen (HBO₂) increases tissue oxygen (O₂) partial pressures while lowering partial pressures of inert gases. The toxic constituents of cigarette smoke – particularly nicotine, carbon monoxide (CO), and hydrogen cyanide (HCN) – provide potential mechanisms to explain how cigarette smoking interferes with O₂ availability to tissues and perturb wound healing. The hypoxia immediately following inhalation of cigarette smoke was documented as lasting approximately an hour in human volunteers and is attributed to peripheral vasoconstriction, from nicotine (1). HBO₂ exposure appears to magnify the effects of
hyperoxygenation in smokers. Transcutaneous O$_2$ (P$_{tcO_2}$) levels increments doubled in room air while magnified fourfold by HBO$_2$ exposure in a patient who was a 75 pack-per-year cigarette smoker 46 hours after cessation of smoking (2). In order to test the hypothesis that cigarette smoking alters the tissue transport of O$_2$, nitrogen (N$_2$), and/or carbon dioxide (CO$_2$) we used recently reported (3,4), techniques to compare tissue partial pressures between smokers and non-smokers with two different HBO$_2$ treatment protocols. Tissue O$_2$ uptake, N$_2$ loading and N$_2$ and CO$_2$ washout using low-permeability Teflon® probes in muscle (MM) and subcutaneous (SC) tissues were measured with a mass spectrometer.

From over 16,000 human tissue gas measurements, the following (3) baseline data was obtained: First, mean room air O$_2$, CO$_2$ and N$_2$ partial pressures for resting MM and SC tissue were O$_2$ = 28mm ± 7 Hg; N$_2$ = 437 ± 47 Hg; CO$_2$ = 45mm ± 4 Hg in MM; and O$_2$ = 44mm Hg ± 10; N$_2$ = 540 mm ± 55 Hg; CO$_2$ = 38mm ± 4 Hg in the SC tissues. The differences between MM and SC tissues were significantly (p<0.001) different.

Second, there were differences in gas exchange between the two HBO$_2$ treatment protocols. In Protocol A (typical monoplace treatment), MM N$_2$ tensions decreased 9% more than in Protocol B (a treatment schedule representative of multiplace chambers) with 11% less O$_2$ exposure time (p<0.001). SC O$_2$ increased 12% more in Protocol A than Protocol B with 9% less exposure time (p<0.001). In Protocol B muscle, the zenith O$_2$ tension at 2 atmospheres absolute (ATA) was 9% higher than Protocol A (p<0.001).

Third, the skin was an organ of gas exchange for O$_2$, N$_2$ and CO$_2$. Fourth, air used for air breaks in Protocol B was a source of rapid N$_2$ deposition into the tissues and may be a partial explanation of why patients with mixed arterial gas embolism and decompression sickness presentations were reported to deteriorate using diving treatment tables with air breaks (5,6). Finally, the absence of air breaks in protocol A was not a cause of demonstrable central nervous system O$_2$ toxicity.

The present study is a redefined cohort of the initial study (3) and the recent male versus female study (4) focuses on differences in tissue gas tensions between smokers and non-smokers. The purposes of this study are threefold: First to learn whether there are differences with respect to O$_2$ on-gassing and N$_2$ off-gassing from MM and SC tissues; second, to measure the differences in the tissue O$_2$ tensions of these gases with continuous HBO$_2$ and intermittent HBO$_2$ with air breaks; and, finally, to quantify the amount of MM and SC CO$_2$ washout under these conditions between smokers and non-smokers.

From this information we propose: The harmful effects of cigarette smoking are due to the chronic effects of carbon monoxide and other toxic agents in cigarette smoke on the capillary endothelium rather than from the transient vasoconstriction from nicotine.

**METHODS**

Changes in MM and SC tissue gas tensions were studied in smokers and non-smokers using normobaric and hyperbaric conditions using two treatment protocols. Protocol A, a typical monoplace HBO$_2$ treatment schedule, did not employ air breaks during the HBO$_2$ exposure. Protocol B, an exposure representative of a multiplace chamber HBO$_2$ treatment included air breaks *(Table 1, facing page).* Subjects in Protocol A were pressurized in an air environment, breathing air directly from within the chamber at 2 ATA during the initial 30 minutes of the protocol and then breathed O$_2$ directly from the nearly pure O$_2$ atmosphere in the chamber by switching the inflow gas from air to O$_2$. During the last 30 minutes of the 150-minute protocol, the subjects breathed air at 1 ATA.

Subjects in Protocol B were pressurized in 2 ATA air and breathed O$_2$ by a SCUBA (self-contained underwater breathing apparatus) regulator for each HBO$_2$ exposure. Inhalation of gas from within the chamber by the subjects of Protocol B was prevented during the O$_2$ breathing periods by occluding the external nares with a soft rubber nose clamp. The air exposures *(i.e., air breaks)* were archived by removing the nose clamp and the SCUBA regulator and breathing the gas (air) within the chamber.
Protocol A also differed from Protocol B in two other ways: First, the total HBO2 exposure time of Protocol B exceeded that of Protocol A by 10 minutes; and second, Protocol B’s HBO2 exposures were interrupted with a total of four five-minute air breaks breathing hyperbaric air at 2 ATA interspersed between the five 20-minute O2 breathing periods (Table 1). The gas (air or O2) flows through the chamber were maintained at 400 liters per minute in both protocols at both pressures.

**Study population**

Thirty-six healthy volunteers participated in the study; their anthropomorphic data is summarized in Table 2 (next page). All participated in Protocol A, and 33 (92%) participated in Protocol B. The smokers’ cohort smoked a pack or more daily and all said they typically inhaled the smoke. The non-smokers did not use any tobacco products, such as chewing tobacco, snuff, cigars and/or cigarettes recently or remotely. Three males (8%), one smoker and two non-smokers, did not return for Protocol B for personal reasons. No subject participated in Protocol B less than 30 days after completing Protocol A. All were informed of the risks and objectives of the study. The study protocol was performed in accordance with the standards using human subjects: the Helsinki Accords and approved by the institutional review board of our medical center. Catheter insertion technique, mass spectroscopy calibration, sampling site temperature effects with the correction constants (K) for gender tissue temperature, mass spectrometer response delays, chamber pressurizations and administration of breathing gases were done as described in previous reports (3,4)

**Statistical Assessments**

The F-Test analyzed variance, while the paired t-Test and Wilcoxon Rank Sum demonstrated the probability of differences between variables. Further evaluation was performed using the p Values for Repeated Measures Analysis of Variance. Individual Step Analysis (ISA) was done to distinguish the significance of differences between the SC and MM spaces at each four-minute interval (Tables 3-6, Pages 77-78). Non-significant conclusions are noted as NS while significant differences are described in the text as well as tabulated with their levels of significance.

---

**Table 1**

<table>
<thead>
<tr>
<th>Step</th>
<th>Protocol A³</th>
<th>Protocol B⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ATA²</td>
<td>Gas</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>Air</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Air</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>O2</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>Air</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>O2</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Air</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>O2</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Air</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>O2</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>Air</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>O2</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>Air</td>
</tr>
</tbody>
</table>

Notes:

1. Compressed in O2 and breathing O2
2. Compressed in air with O2 breathing by SCUBA regulator
3. ATA = atmospheres absolute
4. Green-shaded areas = O2 breathing intervals
Comparison of Protocol A versus Protocol B (Pooled Data): As the first two steps in both protocols were identical (measurements in room air and at 2 atmospheres absolute air), the differences were computed of the pooled data to discover the effects, if any, the first exposure (Protocol A) may have had on the subsequent exposure (Protocol B) one month later.

Statistical assessment of the combined 2 ATA air exposure in both protocols, where the mean differences between the smokers in Protocol A (excluding the three dropouts) were compared with those in Protocol B using $p^1 = \text{paired } t\text{-Test}$ and $p^2 = \text{Wilcoxon Rank Sum}$ and in the non-smokers using $p^3 = \text{paired } t\text{-Test}$ and $p^4 = \text{Wilcoxon Rank Sum}$.

The following measurements were also used to note differences in tissue partial pressures between the protocols: First, $p^5 = F\text{-test for homogeneity of variances}$; second, $p^6 = T\text{-test comparing the groups (smokers vs. non-smokers)}$; and third, $p^7 = \text{Wilcoxon Rank Sum test}$ (The pooled variance estimate is used when $p^5 > 0.05$, while the separate variance is used when $p^5 \leq 0.05$).

RESULTS

The loading and unloading of $N_2$ and $O_2$ in the SC are graphically displayed in Figures 1 and 2 (Page 79) for the monoplace chamber exposures and in Figures 3 and 4 (Page 80) for the multiplace exposure. Nitrogen unloads at a significantly slower rate during the $O_2$ exposure from the smoker’s MM compartment in both protocols [Table 3 (facing page) with $t\text{-Test}$: Steps O6 through A1 with $p = 0.01$ to 0.04 and Wilcoxon Rank Sum: Steps O6 through A4 with $p = 0.04$ to 0.02]. Tables 4, 5 and 6 (Pages 77-78) reveal the significant variations at each individual step analysis (ISA), while Table 7 (Page 81) confirms these changes.

There were no significant changes between $O_2$ loading in MM and SC tissues of smokers and non-smokers. The SC $CO_2$ and MM $CO_2$ are graphically displayed in Figures 5 – Protocol A and 6 – Protocol B (Page 82). ISA values are recorded in Table 5. The $p$ values for Repeated Measures Analysis of Variance confirm the significant differences seen in MM $N_2$ in both protocols (Table 7).

Table 2: The anthropomorphic characteristics of the smoker volunteers are compared with those of the non-smoker volunteers.
Table 3: Protocol A – wherein smokers’ muscle oxygen (MM O₂), muscle nitrogen (MM N₂) plus the subcutaneous oxygen (SC O₂) and subcutaneous nitrogen (SC N₂) are measured for any significant changes during the prescribed exposures: 1 ATA prior to chamber insertion, 30 minutes at 2 ATA air, 90 minutes of O₂ at 2 ATA, with a closing exposure of 30 minutes 1 ATA air.

Table 4: Protocol B – wherein smokers’ muscle oxygen (MM O₂), muscle nitrogen (MM N₂) plus the subcutaneous oxygen (SC O₂) and subcutaneous nitrogen (SC N₂) are measured for any significant changes during the prescribed exposures: 1 ATA prior to insertion, compressed in 2 ATA air, breathes 2 ATA O₂ by SCUBA regulator X 20 minutes with five-minute 2 ATA air breaks for five cycles and a last 30-minute exposure at ambient air.
**Table 5: SMOKERS (S) vs. NON-SMOKERS (NS)**

<table>
<thead>
<tr>
<th>ISA</th>
<th>A/S vs NS SC CO₂</th>
<th>A/S vs NS MM CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₀</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₁</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₄</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₅</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₇</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₈</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blank Spaces Indicates No significant Differences at Each Individual Step Analysis (ISA)

**Table 6: Protocol A** – wherein smokers’ subcutaneous carbon dioxide (SC CO₂) and muscle carbon dioxide (MM CO₂) are measured for any significant changes during the prescribed exposures: One ATA prior to chamber insertion, 30 minutes at 2 ATA air, 90 minutes of O₂ at 2 ATA, with a closing exposure of 30 minutes 1 ATA air.

**Table 6: NON-SMOKERS (NS)**

<table>
<thead>
<tr>
<th>ISA</th>
<th>R/S vs NS SC CO₂</th>
<th>R/S vs NS MM CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₀</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₁</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₄</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₅</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₇</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A₈</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blank Spaces Indicates No significant Differences at Each Individual Step Analysis (ISA)

**Table 6: Protocol B** – wherein smokers’ subcutaneous carbon dioxide (SC CO₂) and muscle carbon dioxide (MM CO₂) are measured for any significant changes during the prescribed exposures: One ATA prior to insertion, compressed in 2 ATA air, breathes 2 ATA O₂ by SCUBA regulator X 20 minutes with five-minute 2 ATA air breaks for five cycles and a last 30-minute exposure at ambient air.
Figure 1 — Protocol A: The comparison of changes observed in the mid-thigh of subcutaneous oxygen (O₂) and nitrogen (N₂) at ambient air, 30 minutes of 2 ATA air breathing, followed by 90 minutes 2 atmospheres O₂; the observations terminated after 30 minutes at ambient air (1 ATA air).

Figure 2 — Protocol A: The comparison of changes observed in the quadriceps femoris muscle oxygen (O₂) and nitrogen (N₂) at ambient air, 30 minutes of 2 ATA Air breathing, followed by 90 minutes 2 ATA O₂; the observations terminated after 30 minutes at ambient air (1 ATA air).
Figure 3 – Protocol B: The comparison of changes observed in the mid-thigh of subcutaneous oxygen (O₂) and nitrogen (N₂) at ambient air, 30 minutes of 2 ATA air breathing, followed by 2 ATA O₂ breathing for 20 minutes with a five-minute 2 ATA air breathing period; the cycle was repeated five times. The total exposure was terminated after 30 minutes at ambient air (1 ATA air).

Figure 4 – Protocol B: The comparison of changes observed in the mid-thigh of muscle oxygen (O₂) and nitrogen (N₂) at ambient air, 30 minutes of 2 ATA air breathing, followed by 2 ATA O₂ breathing for 20 minutes with a five-minute 2 ATA air breathing period; the cycle was repeated five times. The total exposure terminated after 30 minutes at ambient air (1 ATA air).
The change of pressure and/or inspired gas with time (r) dynamically changes the concentration of the measured gases in the tissues ($p = 0.0001$) in both protocols. During the first 30 minutes of air breathing at 2ATA the mean differences between the smokers in Protocol A (excluding the three dropouts) were compared with those in Protocol B using $p_1 = \text{paired t-test}$ and $p_2 = \text{Wilcoxon rank Sum}$ and in the non-smokers using $p_3 = \text{paired t-test}$ and $p_4 = \text{Wilcoxon rank Sum}$. There were no significant differences found in the pooled data of the combined 2 ATA air data.

**DISCUSSION**

The harmful effects of cigarette smoking are well documented (7,8,9,10,11,12,13,14,15,16,17,18). Orthopedic complications such as osteomyelitis, non-union, failure of spine fusions and flap sloughs are twice as high or more in smokers as compared to non-smokers (10,11). It is noteworthy that hyperbaric oxygen (HBO$_2$) mitigated the harmful effects of cigarette smoking for bone healing of tibial lengthening in a rabbit model (12). Equally high complication rates are noted in smokers from the plastic surgery literature (9,13,14). Decompression illness occurred more frequently and from significantly shallower dives in divers who smoked than for non-smokers and were more likely to cause cerebral rather than spinal cord symptoms (19). The Divers Alert Network (DAN) database from 1989-1997 shows that there was an increase in severity of symptoms from decompression illness in recreational divers who smoked than those who did not smoke (20).

Numerous reports confirm the association between cigarette smoking and the development of malignancies as well as the use of smokeless tobacco (16,17,18,21,22). Although nicotine is usually implicated as the primary cause of the harmful effects of cigarette smoking its effects are short-lived and paradoxical (1,7,8,9,10,11,12,13,14). Nicotine, a potent transient vasoconstrictor, appears to act directly on the musculature of the blood vessel...
Figure 5 – **Protocol A**: The comparison of the subcutaneous and muscle CO₂: Non-smokers vs. smokers using a 90-minute 2 ATA oxygen exposure after a 30-minute 2 ATA air exposure and ending with observations at ambient air (1 ATA air).

Figure 6 – **Protocol B**: Comparison of the subcutaneous and muscle CO₂: Non-smokers vs. smokers using four air breaks of five minutes at 20-minute intervals during the O₂ exposure and ending with observations at ambient air (1 ATA air).
wall (23). This effect lasts less than an hour (1,23,24). Following the transient vasoconstriction, there is a rebound vasodilatation, probably secondary to signaling mechanisms from tissue hypoxia that arises as a consequence of ischemia from vasoconstriction (24,25). Consequently, nicotine may not be the cause of the harmful effects of cigarette smoking. We opine that conclusions from this cohort of our comprehensive tissue gas studies reconciles the nicotine paradox and provides the most tenable explanation to date to explain the harmful effects of cigarette smoking.

The following analysis of our conclusions clarifies the deductions our data supports: First, smokers release muscle N₂ more slowly than non-smokers during hyperbaric oxygen exposures regardless of the protocol used. Since it took more than an hour to prepare the volunteers, insert the mass spectrometer probes, obtain baseline recordings and pressurize the hyperbaric chamber, nicotine cannot be implicated as the agent that alters the peripheral circulation. Tissue O₂ tension is a function of perfusion rather than tissue O₂ saturation, and is consistent with the report that by two days after cessation from smoking, transcutaneous O₂ tensions improved remarkably (2).

The slowing of N₂ release from the muscle, while the subcutaneous tissues shows no significant difference in the release of molecular N₂ reflects a change within the afferent microvasculature of the muscle, the tissue of higher metabolic demand (7,8). We conclude that the more resolute combination of carbon monoxide (CO) with myoglobin and the many harmful products other than nicotine in cigarette smoke such as hydrogen cyanide (HCN) and tars, in addition to CO, cause long-lasting injury to the endothelium of the microvasculature first evidenced in the afferent capillary loop (Figure 7, Page 84), over 40 toxic products have been identified in cigarette smoke (26,27). The capillary injury delays N₂ off-gassing from the tissues to the capillary bed, accounting for approximately 50 % delay of N₂ escaping from the muscle compartment observed in smokers versus non-smokers. An animal project first notes this afferent effect of cigarette smoking.

**CONSEQUENCES/RECOMMENDATIONS**

First: Compressed-gas divers and multiplace hyperbaric chamber attendants who smoke should slow their ascents and increase their decompression times by 50% before surfacing.

Second: The anticipated differences in tissue O₂ between smokers and non-smokers in both MM and SC tissues when exposed to 2 ATA O₂ did not occur. The explanations for these observations are twofold.

1) The mean age of the smoker (as well as the non-smoker) was 33 years. The relatively young age of the smoker group and duration of smoking were probably insufficient for the non-nicotine products to cause enough long-standing damage to affect O₂ on-gassing to MM and SC tissues.

2) The transient vasoconstrictive effects of nicotine, as explained before, was well beyond the duration of the effect. At the time of the HBO₂ exposures, the microvasculature may well have been in a post-nicotine vasodilatation phase. Furthermore, this vasodilatation may have mitigated the early effects that CO, nicotine, tars and other substances in cigarette smoke may have had on the relatively youthful vasculature of these smokers.

The differences just discussed of the on- and off-loading of O₂ and N₂ between smokers and non-smokers under hyperbaric oxygen conditions is attributed to the physiological mechanisms for the transport of these gases in blood. Whereas 100% of N₂ is transported by plasma, only 2.5% of O₂ is normally transported in plasma in room air; the other 97.5% is carried by hemoglobin (24). Hyperbaric oxygen at 2 ATA increases the physical dissolved O₂ in plasma, a tenfold factor and then accounts for 25% of the O₂ transport (29). Consequently, the improved ability of whole blood to transport O₂ due to hemoglobin explains differences observed between O₂ on-gassing and CO₂ and N₂ tissue off-gassing in smokers and non-smokers.

Hyperbaric oxygen mitigates the harmful effects of cigarette smoking on O₂ on-gassing to tissues...
Figure 7: Schematic of the microcirculation: Note the arterial (efferent) capillary flow into voluntary muscle wherein the carbon monoxide in the smoker releases from the myoglobin, thereby unfavorably altering/injuring the venous (afferent) capillary wall and slowing the nitrogen movement out of the muscle.

during HBO2 exposure. This consequence is consistent with the report: HBO2 significantly improves outcomes of fracture healing in an animal model exposed to cigarette smoke by two days after cessation of smoking, transcutaneous O2 tensions improve in room air and even to a greater extent during HBO2 (2,12). Consequently, we do not withhold HBO2 treatments in limb injuries and/or life-threatening conditions in the inveterate smoker, as the patient is routinely hospitalized and smoking is forbidden.

Third: CO2 levels in both protocols decrease with time when exposed to HBO while increasing with breathing air at 2 ATA. The decreases are not due to hyperventilation from pain and/or anxiety associated with cannulae insertion, confinement in a pressure vessel, or imperceptible hyperventilation as a response to HBO2, but rather from changes in the partial pressures of the inspired gas. Although CO2 is 20 times more permeable through tissue fluids and in its ability to be transported in blood than O2, it is an indirect marker of perfusion. Apparently, the microvascular injury from smoking in the relatively young smoker cohort was not sufficient to interfere with CO2 off-gassing and transport at rest. Increases of CO2 tensions while the subjects breathed air at 2 ATA reflects the mass effect of breathing air with 0.5% CO2 versus pure O2 with essentially no CO2 in it. Carbon dioxide retention is not a concern with HBO2 treatments whether the patient smokes in this relatively young group of smokers.

Fourth, the vasoconstrictive effects from nicotine in the subcutaneous tissue last less than one hour, with adiabatic heating increasing O2 loading specifically in the subcutaneous tissues of smokers. The significant rise in tissue O2 in the first air breathing period at 2 ATA in Protocol B of the smokers cohort is noteworthy. We postulate that this occurred once the
nicotine effect expired after smoking the last cigarette, coupled with adiabatic heating from pressurization of the chamber. This preferentially affects the subcutaneous tissues with resultant vasodilatation and increased O2 tensions while not affecting the deeper tissues (24,30). Gas flow rates were maintained at 400 liters per minute to minimize adiabatic temperature effects and prevent exhaled gas accumulation within the hyperbaric chamber (3,25). Because of a hematoma complication at the cannulae insertion site in a subject during the Protocol A studies, the time to pressurization after cannulae insertion was increased an additional 30 minutes to ensure bleeding was not occurring at the site. This provided additional time for the transient vasoconstrictive effects of nicotine to dissipate, while the carbon monoxide effect requiring significantly longer time for clearance persists (1,24, 31).

Spuriously high transcutaneous tissue O2 measurement may occur from a rebound vasodilatation plus adiabatic heating in the subcutaneous tissues of smokers. This observation should be remembered when interpreting transcutaneous oxygen tensions and providing recommendations for management of problem wounds in smokers.

Finally, the reason wounds heal more slowly and post-operative wound healing complications are increased in smokers is due to the chronically injured endothelium from CO, hydrogen cyanide (HCN) and other tissue toxic products (26) in cigarette smoke, rather than the transient elevations of nicotine in smoke. The endothelium injury is accumulative, and we believe the differences observed between the smoker and non-smoker would have been more pronounced if the mean age and duration of smoking had been greater than that of our smoker cohorts (mean age 33 years). Another observation implicating CO and other harmful products of smoke rather than nicotine as the toxic agent is that inhaled cigarette smoke significantly increases the permeability of the arterial wall to fibrinogen; this effect is observed with CO alone, but not with intravenous nicotine (7).

Since 1972 we have advised our patients to discontinue the use of all tobacco products prior to and during their course of hyperbaric oxygen treatments (32,33,34). Again, in light of the findings in this report we opine that HBO2 is of value in intractable smokers with life- and/or limb-threatening wounds and/or complications within the hospital setting. Regardless, we do not recommend smoking or the use of smokeless tobacco or chewing tobacco in any habitual form because of their association with malignancies, myocardial infarction and cerebrovascular accidents (18,21,22,35).

Further, we note that the United Kingdom’s screening tests for covert smokers is an important consideration before performing elective surgery to reduce healthcare costs (14). Alternatively, a venous carbon monoxide level may be used as a rapid low-cost screening test (31,32,33). Likewise, we do not recommend the use of marijuana, regardless of its tetrahydrocannabinol content, because of its substantially increased respiratory burden of carbon monoxide and tars similar to smoking a similar quantity of tobacco (15).

In summary, smokers and non-smokers demonstrate differences in their abilities to off-gas nitrogen and on-gas oxygen with hyperbaric oxygen. The differences are not attributed to the effects of nicotine, which are transient, but rather to the chronic, repetitive injury to the epithelium of the microvasculature from carbon monoxide, hydrogen cyanide and other toxic products in tobacco smoke. Cigarette smoking first causes injury to the afferent low-pressure vascular (venous) endothelium due to the persistent release of CO from the myoglobin, thereby delaying the escape of N2 from the muscle compartment in this relatively young smoker (33 years) cohort. Regardless, hyperbaric oxygen improves tissue oxygenation, even in the presence of the endothelial injury.
References


