Effects of venous gas microemboli on pulmonary
gas transfer function

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Thorsen E, Risberg J, Segadal K, Hope A. Effects of venous gas microemboli on pulmonary gas transfer function. Undersea Hyperbaric Med 1995; 22(4):347-353.—Dynamic lung volumes and flows, slope of phase III of the single breath oxygen test (Δ-N₂), closing volume (CV), and transfer factor for carbon monoxide (Tlco) were measured before and 1 h after an air dive in a hyperbaric chamber to a pressure of 0.49 MPa for 40 min. Six divers had a bottom time of 20 min and a rate of decompression of 50 kPa · min⁻¹, and six divers had a bottom time of 24 min and a rate of decompression of 100 kPa · min⁻¹. Decompression stops were 5 min at 0.16 MPa and 10 min at 0.13 MPa for both groups. As control exposure they were breathing O₂ at atmospheric pressure for 40 min. The dive and control exposure were done on different days within 1 wk, in random order. Doppler ultrasound monitoring for venous gas microemboli (VGM) was done during the first hour after the dive. VGM were detectable in all six divers with the fast decompression rate and in one subject with the slow rate (P < 0.01). In the subjects having VGM there was a significant reduction in Tlco of −5.9 ± 4.4% compared with −0.5 ± 3.4% after the control exposure (P = 0.034). In the five subjects without detectable VGM, the changes in Tlco were −2.8 ± 3.7% and 0.2 ± 3.8% respectively. There were no significant changes in dynamic lung volumes and flows, CV, or Δ-N₂. A reduction in Tlco may reflect effects of VGM after dives in which the effect of O₂ exposure is negligible.

diving, decompression, lung function.

Diving exposure is multifactorial and basically a function of pressure, time, and gas mixture. The exposure takes place with all forms of diving but is quantitatively dependant on the method of diving. Exposure to hyperoxia contributes to reduced pulmonary gas transfer function and reduced small airways conductance after saturation dives (1,2). Exposure to increased gas density and thereby increased work of breathing may cause a training effect of respiratory muscles and increases in vital capacity (3,4). Finally, venous gas microemboli (VGM) encountered during the decompression phase of a dive may be filtered in the pulmonary circulation causing gas exchange abnormalities (5) and inflammatory reactions (6).
Venous gas microemboli contribute to a reduced transfer factor for carbon monoxide ($T_{lCO}$) after deep saturation dives, in which VGM have been shown to form over several days of decompression (7). VGM have also been shown to form with relatively short and shallow air dives (8,9) and with rapid ascent to altitude (10). Dujic et al. (11) found a relationship between reduced $T_{lCO}$ and the presence of VGM after a dive to a pressure of 0.55 MPa.

In this study monitoring for VGM and lung function measurements were done after two different dives to a pressure of 0.49 MPa for 40 min but with different rates of decompression, controlling for the effect of hyperoxia by breathing $O_2$ at atmospheric pressure (0.10 MPa). Reduced $T_{lCO}$ was seen in the divers having VGM.

METHODS

The subjects: Twelve professional divers from The Royal Norwegian Navy and The Norwegian Diving School, age 21–48 yr (median 27), height 176–192 cm (median 181), and weight 69–93 kg (median 82), served as subjects. Eight were never smokers, two were previous smokers, and two were current smokers. They had all passed the annual medical examination required for professional diving by the Norwegian Directorate of Public Health, and they were all licenced as divers by either the Navy or the Norwegian Labour Inspectorate. The protocol for the study was approved by the Regional Ethics Review Committee, and written informed consent was obtained from each subject.

The dives: Each subject performed one dive to a pressure 0.49 MPa corresponding to a depth of 39 meters of sea water, in the hyperbaric chamber complex at The Norwegian Underwater Technology Centre. The gas mixture was compressed air, giving a partial pressure of $O_2$ of 102 kPa during the bottom phase of the dive. In the first six subjects the bottom time was 20 min. Rate of decompression was 50 kPa·min$^{-1}$ with a 5-min decompression stop at a pressure of 0.16 MPa and a 10-min decompression stop at 0.13 MPa. The time for ascent was not included in the time for the decompression stops. In the other six subjects the bottom time was 24 min and decompression was strictly according to The Norwegian Air Diving Tables (12). In between the decompression stops the rate of decompression was 100 kPa·min$^{-1}$, and the time for ascent between the decompression stops was included in the time for the stops. The profiles of the dives for the two groups are shown in Fig. 1.

During the bottom phase of the dives, two bouts of exercise on a mechanically braked cycle ergometer was done at a load of 100 W for 4 min with a 4-min resting period in between and before the start of decompression.
As a control exposure, the subjects were breathing O₂ at normal ambient pressure (97–102 kPa) for 40 min at rest, breathing from a reservoir of pure humidified O₂. The dives and the control exposures were done in random order on different days within 1 wk, with 2 days between exposures.

Protocol: Lung function measurements were done 30–60 min before the exposures and 60–90 min after the exposures. Doppler ultrasound monitoring for VGM was done immediately after and at 20-min intervals in the first hour after the dive. Doppler ultrasound monitoring was not done after the control exposure of O₂ breathing at normal pressure. The experiments were done in the morning at least 2 h after a breakfast without tea or coffee, and smoking was not allowed until all measurements were completed.

Pulmonary function: Forced expired vital capacity (FVC), forced expired volume in 1 s (FEV₁), forced midexpired flow rate (FEF25–75%), forced expiratory flow rates at 50 and 75% of FVC expired (FEF50%, FEF75%), and peak expiratory flow rate (PEF) were taken from at least three satisfactory forced expiratory maneuvers from total lung capacity. FVC, FEV₁, and PEF were taken as the highest readings obtained. FEF25–75%, FEF50%, and FEF75% were taken as the highest values from flow-volume loops not differing by more than 5% from the highest FVC. TlCO was measured by the single breath-holding technique. Effective alveolar volume (VA) was measured simultaneously by helium dilution, and transfer coefficient for carbon monoxide calculated (KCO). The measurements were done on a Morgan Benchmark lung function testing system (P.K. Morgan, London, UK), and all values were corrected to BTPS. The tests were done according to the standardized procedures of the European Respiratory Society (13,14).

The slope of phase III of the single-breath O₂ test (Δ-N₂) and closing volume (CV) were measured by tracing the nitrogen concentration in expired gas during a slow exhalation at a rate of 0.3–0.5 l·s⁻¹ from total lung capacity to residual volume, after the inhalation of pure O₂ from residual volume. These measurements were done on a Gould model 1000IV lung function testing system (Gould Inc., Dayton, OH), according to the standardized procedures of National Heart, Blood and Lung Institute (15).

Doppler ultrasound monitoring for VGM was done 3 times during the first hour after surfacing, using a multifrequency pulsed Doppler ultrasound velocity meter (Alfred, Vingmed, Norway). Monitoring was from the precordial position and the subclavian veins with the subjects standing as described by Nishi (16). For the precordial monitoring, recording was made for 1 min after the heart rate had stabilized to a resting rate. Thereafter one deep knee bend was carried out and the signal recorded for 30 s. This maneuver was performed 3 times. Bubble scores were classified according to the Spencer scale (17). Recordings from the subclavian veins were performed at rest and after hand cranking.

Statistics: The changes in lung function variables were calculated as the percent difference from the mean of the pre- and post-exposure measurements. One-way analysis of variance was used comparing the effects on the subjects with and without VGM with the control exposure. Pearson chi-squared test was used comparing the incidence of VGM with the two decompression profiles. A P value less than 0.05 was considered to be significant.

RESULTS

Venous gas microemboli were detected with precordial monitoring in one of the six subjects having the slow decompression profile and in all six subjects having the faster decompression profile (P < 0.01) on at least one of the three monitoring sessions in the first hour after the dive. The distribution of precordial bubble scores recorded after knee bends is shown in Fig. 2. The incidence of bubbles and the bubble scores were largest in
the period 20–40 min after the dive. In this study the incidence of VGM was not higher when the results from monitoring over the subclavian veins were included.

The $T_{1CO}$ was significantly reduced by $-4.4 \pm 4.1\%$ after the dives compared with $-0.3 \pm 3.4\%$ after the control exposure ($n = 12, P = 0.016$). The reduction in $T_{1CO}$ was $-5.9 \pm 4.4\%$ in the divers who had detectable VGM ($n = 7, P = 0.034$), and $-2.8 \pm 3.7\%$ ($n = 5, P = 0.37$) in the divers who had no detectable VGM. We found no difference in the response to the control exposure in divers who had VGM compared with divers who had not, the changes being $-0.5 \pm 3.4\%$ and $0.2 \pm 3.8\%$, respectively. The results are shown in Fig. 3. No changes were found in effective alveolar volume with either exposure.

No significant changes were seen in dynamic lung volumes and flows or in the indices of distribution of ventilation after the dives or after the control exposures. Nor were there significant differences between the pre-exposure measurements for any of the lung function variables (Table 1).

**DISCUSSION**

The results indicate an acute effect on the lung of dives to a pressure of 0.49 MPa, which is within accepted decompression tables, but no effect of the $O_2$ exposure associated with the dive. The divers having the slow decompression profile and no detectable VGM had no change in any of the lung function variables, indicating that there was no signifi-
Table 1: Changes in Dynamic Lung Volumes and Flows, Tlco, CV, and Slope of Phase III of the Single Breath Nitrogen Washout After the Dives and Control Exposure (n = 12)

<table>
<thead>
<tr>
<th></th>
<th>Control exposure</th>
<th>Dive</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Change, %</td>
</tr>
<tr>
<td>FVC, liter</td>
<td>5.79 ± 0.81</td>
<td>0.9 ± 1.8</td>
</tr>
<tr>
<td>FEV1, liter</td>
<td>4.62 ± 0.71</td>
<td>1.5 ± 2.7</td>
</tr>
<tr>
<td>FEF_{25-75}, liter·s^{-1}</td>
<td>4.35 ± 1.31</td>
<td>1.9 ± 8.3</td>
</tr>
<tr>
<td>PEF, liter·s^{-1}</td>
<td>12.2 ± 1.4</td>
<td>2.4 ± 7.6</td>
</tr>
<tr>
<td>CV, %</td>
<td>10.2 ± 2.0</td>
<td>-3.1 ± 12.6</td>
</tr>
<tr>
<td>Δ-N2, %</td>
<td>0.84 ± 0.23</td>
<td>-2.4 ± 13.3</td>
</tr>
<tr>
<td>Tlco, mmol·min^{-1}·kPa^{-1}</td>
<td>13.1 ± 1.8</td>
<td>-0.3 ± 3.4</td>
</tr>
<tr>
<td>VCO2, liter</td>
<td>7.53 ± 0.78</td>
<td>0.4 ± 2.3</td>
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*Significantly different from control exposure, *P* < 0.05.

cant effect of gas density or pressure per se 1 h after exposure. Reduced Tlco was seen in the subjects having VGM. The difference in the incidence of VGM between the dives could be caused by differences in bottom time, rate of decompression, or differences in ambient temperature during decompression.

Ideally, all subjects should have been exposed to the two different dive profiles and control exposure, including another control of the diurnal variation during the time of day when the exposures took place. However, the control exposure includes the variance caused by diurnal variation, measurement error, and possible effects of hyperoxia. Studies of diurnal variation indicate a small increase in dynamic lung volumes and flows from early morning to noon (18), and a small decrease in Tlco (19). The trend for changes in lung function variables after the control exposure was in that direction. Oxygen exposure of this order has not been shown to result in changes in lung function. No differences were observed in subjects' characteristics between the two groups doing different dives, including age distribution, smoking habits, and baseline pulmonary function.

Our data did not allow for any analysis of dose response relationships between load of VGM on the pulmonary circulation and change in Tlco. The measure of VGM is semiquantitative, and a major problem with all studies of VGM is that monitoring cannot be performed continuously. Most of our subjects had relatively few bubbles within a narrow range of bubble scores. Because of a limited number of subjects any further subdivision of the subjects having detectable VGM could not be done. The study of Dujic et al. (11) indicates, however, that there is a larger reduction in Tlco with higher bubble scores. In that study, 10 divers showed a mean reduction in Tlco of 11% 80 min after a dive to a pressure of 0.55 MPa with a bottom time of 25 min. Three of the 10 divers had VGM grade 3, 5 had VGM grade 2, and 2 VGM grade 1 after knee bends in the first hour after the dive. There was a significant correlation between bubble score and reduction in Tlco. In our study, one, four, and two subjects had VGM grades 3, 2, and 1, respectively. The greater depth and the higher bubble scores may explain the larger reduction in Tlco in the study of Dujic et al. (11). The reason why the dive with the slow decompression rate had a reduction in Tlco not significantly different from the other dive or control exposure may be due to low sensitivity of detection of VGM.

Venous gas microemboli are the cause of respiratory decompression sickness (DCS) or the "chokes," a relatively uncommon manifestation of DCS accounting for approximately 1% of all cases and more common with decompression to altitude than with decompress-
sion from increased pressure (20,21). In these cases, large amounts of VGM filter into the pulmonary circulation, resulting in edema and increased pulmonary arterial pressure. The load of VGM usually seen with otherwise uncomplicated dives, as in this dive series, does not cause symptoms or discomfort. However, they are of concern as long as changes in pulmonary hemodynamics may reduce the effectiveness of the lung as a filter for VGM (22).

The effects of VGM on the lung have been extensively studied in animals. Infusion of VGM gives an immediate response, with an increase in pulmonary arterial pressure that is directly related to the rate of infusion of VGM (23). This could be a vasomotor response or a direct mechanical effect on the pulmonary vascular bed. Some hours after the start of infusion of VGM, and persisting for several hours thereafter, there is increased microvascular permeability and transvascular fluid transport with interstitial edema, indicating capillary endothelial damage. This could be caused by the VGM per se or be associated with an inflammatory response, because a concomitant accumulation of leukocytes occurs (6). It is also known that VGM causes aggregation and activation of platelets (24) which may initiate an inflammatory response.

Hyperoxia may also induce pulmonary vascular changes resembling those seen with infusion of VGM. It has been speculated to be a common mechanism of pulmonary microvascular injury. This effect is, however, seen with hyperoxic exposure far in excess of what is associated with a short, shallow dive as in this study, and no effects of the control exposure were in fact seen. We therefore concluded that VGM, as encountered with operational air diving within accepted decompression tables, have a small but significant effect on pulmonary gas transfer function, and that changes in Tlco reflect the decompression stress of dives in which O2 exposure is negligible.

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