

No changes in lung function after a saturation dive to 2.5 MPa with intermittent reduction in P_{O_2} during decompression

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Abstract Decompression stress and exposure to hyperoxia may cause a reduction in transfer factor of the lung for carbon monoxide and in maximal aerobic capacity after deep saturation dives. In this study lung function and exercise capacity were assessed before and after a helium–oxygen saturation dive to a pressure of 2.5 MPa where the decompression rate was reduced compared with previous deep dives, and the hyperoxic exposure was reduced by administering oxygen intermittently at pressures of 50 and 30 kPa during decompression. Eight experienced divers of median age 41 years (range 29–48) participated in the dive. The incidence of venous gas microemboli was low compared with previous deep dives. Except for one subject having treatment for decompression sickness,

no changes in lung function or angiotensin converting enzyme, a marker of pulmonary endothelial cell damage, were demonstrated. The modified diving procedures with respect to decompression rate and hyperoxic exposure may have contributed to the lack of changes in lung function in this dive compared with previous deep saturation dives.

Keywords Angiotensin converting enzyme · Decompression · Hyperoxia · Lung function · Venous gas microembolism

Introduction

A reduction in lung function has been demonstrated after deep saturation dives to depths of 300 m or more, corresponding to pressures of ≥ 3.1 MPa (Cotes et al. 1987; Suzuki et al. 1991; Thorsen et al. 1994; Lehnigk et al. 1997). A mean reduction in transfer factor for carbon monoxide (Tl_{CO}) of 10–15% is the most consistent finding, and in some studies a reduction in peak oxygen uptake ($V_{O_{2peak}}$) has been demonstrated. The lung function changes appear to be at least partially reversible within 6–8 weeks after the dives, but some studies indicate that residual effects may accumulate to long term effects with repeated saturation and compressed air diving (Thorsen et al. 1990a; Tetzlaff et al. 1998).

Diving is associated with several exposure factors known to have effects on the lung. Hyperoxia has toxic effects on the lung at partial pressures of more than 40 kPa commonly used in the different phases of saturation dives (Thorsen et al. 1993). Decompression stress is associated with the risk of formation of free

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gas (microbubbles) either in the venous circulation or interstitially in the tissues causing decompression sickness. The changes in lung function immediately after saturation dives is associated with the cumulative hyperoxic exposure higher than 21 kPa, which is the normal atmospheric pressure of oxygen, and with the cumulative load of venous gas microemboli (VGM) lodged in the pulmonary circulation during the decompression phase (Thorsen et al. 1994).

The capillary endothelial cells are vulnerable to hyperoxia, and endothelial cell injury and vascular structural changes appear before epithelial cell injury in the lung (Fracica et al. 1991). Pulmonary oxygen toxicity is attenuated when exposure is intermittent (Hendricks et al. 1977). VGM may cause direct mechanical injury to the vascular surface layer and endothelial cells with shedding of the endothelial layer in arterioles (Nossum et al. 1999), and mechanical obstruction of pulmonary blood flow. All mechanisms can explain the reduction in Tl_{CO} after saturation dives by a reduction in the capillary blood volume available for gas exchange. Angiotensin converting enzyme (ACE) is an enzyme specific for the pulmonary endothelial cells, and converts angiotensin I to the active form angiotensin II. It could be a marker of pulmonary endothelial cell damage (Brizio-Molteni et al. 1992).

In this study a dive was conducted where the partial pressure of oxygen (P_{O_2}) during the decompression phase was intermittently reduced, and the rate of decompression was slower compared with previous deep experimental saturation diving profiles (Thorsen et al. 1990b). The hypothesis was that by reducing the hyperoxic exposure and the decompression stress, the effects on the lung were expected to be less.

Methods

A simulated dry helium-oxygen dive with saturation at 240 m corresponding to a pressure of 2.5 MPa was carried out in the hyperbaric chamber complex of the Norwegian Underwater Intervention A/S in Bergen in October 2002. Participation in the study was based on written informed consent and the study was approved by the Regional Committee for Medical Research Ethics. Measurements of lung function were done within 3 days before the dive, within 2 days after the dive and 6–8 weeks after the dive. Measurements of ACE were also done in the isopression phase on dive day 7 and in the decompression phase on dive day 17.

The dive

The compression phase was 20 h 35 min, and there was a 1 h stop at 0.9 MPa and a 2 h stop at 1.7 MPa, with a decrease in the rate of compression after each stop. The P_{O_2} during the compression phase was kept at ~40 kPa. The isopression phase at 2.5 MPa was 6.6 days with a P_{O_2} at ~35 kPa, and during this period, excursions of 8 h duration to a maximal pressure of 2.64 MPa with a P_{O_2} of ~70 kPa were conducted. The divers were working in two teams of four divers each, having the excursions at different times during the isopression phase, one team having four excursions and the other team six. The decompression phase was 11.9 days and the mean rate of decompression was 202 kPa 24 h⁻¹, with 8 h night stops. The P_{O_2} was kept at ~50 kPa during the decompression phase except for the first ten nights when it was reduced to ~30 kPa.

Total time for the dive was 19.3 days. The cumulative hyperoxic exposure calculated as the integrated product of P_{O_2} higher than 21 kPa and time (Thorsen et al. 1994) was 432 and 433 kPa 24 h for the two teams of divers respectively (Fig. 1).

Precordial Doppler ultrasound monitoring for VGM in the decompression phase was done in each diver in the morning and in the afternoon (Segadal et al. 2003). VGM were detected in four of the eight divers in 14 out of 200 monitoring sessions. There was one observation of VGM at rest, all other observations were made after limb movement. Doppler bubble scores according to the Spencer Scale (Spencer and Clark 1972) were grade III on two occasions, grade II on three and grade I on nine occasions. In four divers VGM were not observed during the decompression phase at all. No VGM was observed after surfacing in any subject.

Moderate exercise of 60 min duration was done daily during decompression by all divers. A treadmill, a

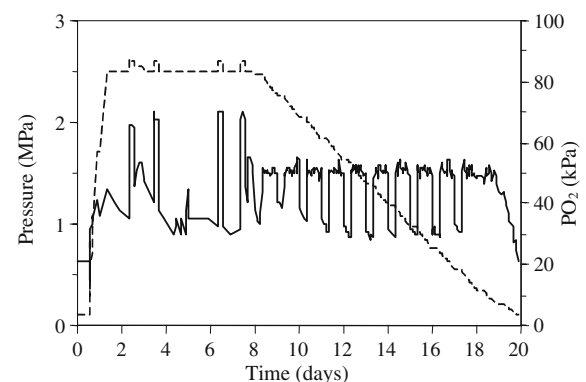


Fig. 1 The profile of the dive with respect to total pressure (broken line) and partial pressure of oxygen, P_{O_2} (solid line)

cycle ergometer and a rowing ergometer were available for the training, and the divers could alternate between the three alternatives. The intensity of the exercise was moderate, at a heart rate (HR) corresponding to ~50% of that measured during the measurement of $V_{O_{2peak}}$ before the dive.

The divers

Eight men participated in the study. Seven were commercial divers certified for saturation diving and one was a medically qualified scientist with experience in scuba and saturation diving. The divers' median age was 41 years (range 29–48). Three were current smokers. Median height was 179 cm (range 168–189), body mass 85 kg (range 69–105) and body mass index (BMI) 28.6 kg m⁻² (range 24.2–30.7).

Lung function testing

The measurements included forced expiratory lung volumes, maximal expiratory flow rates and the transfer factor for carbon monoxide. The measurements were taken on a Morgan Benchmark lung function testing apparatus (PK Morgan Ltd., Kent, England), and were done by the same technician and according to the standardized procedures of the European Respiratory Society (Quanjer et al. 1993; Cotes et al. 1993). Volume calibration of the spirometer and calibration of the gas analyzers were done before each measurement. All measurements were corrected to the “body temperature pressure saturated” condition.

The forced vital capacity (FVC), forced expired volume in one second (FEV₁) and peak expiratory flow rate (PEF) were taken as the highest readings obtained from at least three satisfactory forced expiratory maneuvers. Mean midexpiratory flow rate (FEF_{25–75%}) was taken as the best value from flow-volume loops not differing by more than 5% from the highest FVC. Tl_{CO} was measured by the single breath holding technique. Effective alveolar volume (V_A) was measured simultaneously by helium dilution and the transfer coefficient for carbon monoxide (K_{CO}) was calculated as Tl_{CO} V_A^{-1} . A correction in Tl_{CO} to a haemoglobin concentration of 146 g l⁻¹ was done (Cotes 1979). The mean of the best 2 measurements not differing by more than 10% was used in the analysis.

$V_{O_{2peak}}$ was measured in six divers when exercising on a treadmill. After a 10 min warm up period at an individually set speed of 8–10 km h⁻¹ and 2% inclination, the speed was increased in steps of 1 or 2 km h⁻¹ every second minute. Exercise was continued to the symptom limited maximum. Minute ventilation (V_E),

V_{O_2} , carbon dioxide output (V_{CO_2}) and HR were measured with an integrated exercise testing system (V_{max} 200, SensorMedics, Anaheim, CA, USA). The measurements of V_{O_2} and V_{CO_2} were corrected to the “standard temperature pressure dry” condition. In two divers $V_{O_{2peak}}$ was measured by incremental cycle ergometry. For each subject $V_{O_{2peak}}$ was assessed with the same exercise mode and protocol each time. Exercise testing was done pre-dive and 1–2 days post-dive only. In one subject exercise testing could not be done post-dive.

Angiotensin converting enzyme

ACE was measured in serum by a spectrophotometric method using 3-(2-furylacryloyl)-L-phenylalanyl-glycyl-glycine as the substrate (Johansen et al. 1987). Venous blood was drawn from a cubital vein. Blood samples taken at increased ambient pressure during the dive were gently decompressed in the medical lock, and there was no evidence of haemolysis of the blood samples (Hofsø et al. 2005).

Statistics

The results of the lung function and exercise test variables are given as mean and one standard deviation (SD). One way analysis of variance (ANOVA) was used to test for differences between the pre- and post-dive measurements. For ACE the results of the measurements taken during the dive were also included in the ANOVA. A *P* value < 0.05 was considered to be statistically significant.

Results

There were no significant changes in any of the lung function variables or in exercise capacity after the dive (Table 1). Exercise was continued to the same peak HR, and $V_{O_{2peak}}$, $V_{CO_{2peak}}$ and V_E at $V_{O_{2peak}}$ were unchanged. Exercise testing was not done in one subject post-dive.

There were no significant changes in ACE between the pre- and post-dive measurements (Fig. 2; Table 1). There was, however, an increase in ACE from the end of the bottom phase to the end of the decompression phase, from 56.8 (19.6) to 70.4 (24.7) U l⁻¹ (*P* = 0.038).

One subject had treatment for neurological decompression sickness before post-dive lung function testing was done. This subject's Tl_{CO} was reduced by 11.3% and $V_{O_{2peak}}$ by 17.5%, while HR_{peak} was 6.3% lower. This subject had a 52% increase in ACE from the end

Table 1 Lung function, peak exercise responses and angiotensin converting enzyme before and after a 19-day saturation dive to 2.5 MPa, mean (SD)

	Before	1–2 days after	6–8 weeks after
<i>n</i> = 8			
FVC (l)	5.64 (0.82)	5.65 (0.87)	5.55 (0.89)
FEV ₁ (l)	4.48 (0.70)	4.49 (0.75)	4.45 (0.74)
FEF _{25–75%} (l s ⁻¹)	4.07 (0.91)	4.04 (0.89)	4.14 (0.83)
PEF (l s ⁻¹)	11.55 (2.21)	11.97 (2.15)	11.19 (2.08)
Tl _{CO} (mmol min ⁻¹ kPa ⁻¹)	11.20 (1.25)	11.09 (1.41)	11.39 (1.31)
K _{CO} (mmol min ⁻¹ kPa ⁻¹ l ⁻¹)	1.63 (0.11)	1.63 (0.17)	1.65 (0.15)
<i>n</i> = 7			
V _{O₂peak} (ml min ⁻¹ kg ⁻¹)	42.3 (7.1)	40.3 (7.4)	
V _{CO₂peak} (ml min ⁻¹ kg ⁻¹)	45.8 (6.9)	45.0 (7.8)	
V _{Epeak} (l min ⁻¹)	132.6 (22.3)	136.3 (25.0)	
HR _{peak} (beats min ⁻¹)	178 (9)	174 (11)	
<i>n</i> = 8			
ACE (U l ⁻¹)	53.8 (16.9)	64.5 (25.8)	61.1 (21.5)

FVC Forced vital capacity, FEV₁ Forced expired volume in 1 s, FEF_{25–75%} Mean midexpiratory flow rate, PEF Peak expiratory flow rate, Tl_{CO} Transfer factor of the lung for carbon monoxide, K_{CO} Transfer factor of the lung for carbon monoxide per unit alveolar volume, V_{O₂peak} Peak oxygen uptake, V_{CO₂peak} Peak carbon dioxide output, V_{Epeak} Ventilation at peak oxygen uptake, HR_{peak} Heart rate at peak oxygen uptake, ACE Angiotensin converting enzyme

of the bottom phase to the end of the decompression phase (Fig. 2). The range of changes in Tl_{CO} in the other subjects was from -4.4 to +7.5%, and in V_{O₂peak} it was from -8.7 to +3.4%.

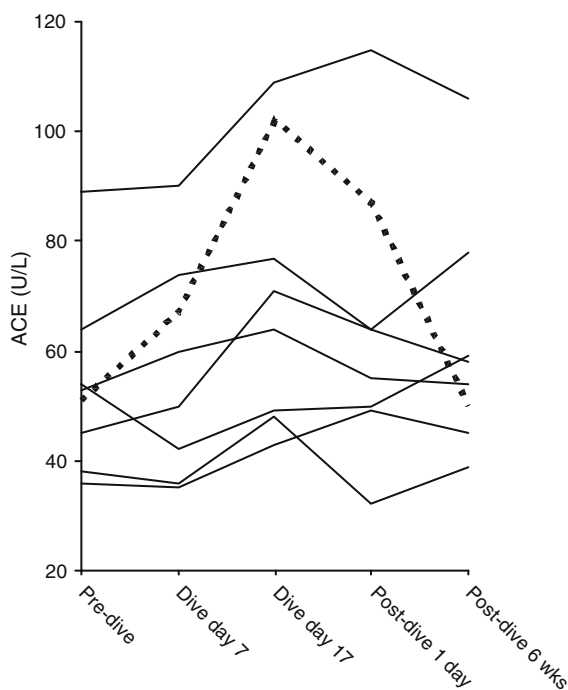


Fig. 2 Angiotensin converting enzyme (ACE) before, during and after the dive. Data for each diver are shown, and the subject with decompression sickness is represented by the broken bold line

Discussion

Compared with other deep experimental saturation dives there was a low incidence of venous gas microembolism and no changes in pulmonary function after this dive. In a series of experimental dives to 360 m (3.7 MPa), the mean rate of decompression was 276 kPa 24 h⁻¹ and the P_{O₂} was kept at 50 kPa throughout the decompression period (Thorsen et al. 1990b). VGM were demonstrated in all 18 divers during decompression, and VGM were present on all monitoring sessions after the session where the first VGM had been demonstrated. In this dive the mean decompression rate was 202 kPa 24 h⁻¹. VGM was demonstrated only sporadically during decompression and in only four of the eight divers. The cumulative load of VGM in the pulmonary circulation appears to be considerably less than in the dives to 360 m where the mean reduction in Tl_{CO} was 11.4% and in V_{O₂peak} 19.5% (Thorsen et al. 1990b).

The hyperoxic exposure was administered intermittently during the decompression phase ranging from 30–50 kPa. Pulmonary oxygen toxicity is attenuated when oxygen is administered intermittently, but that is within a range of oxygen pressures of 42–200 kPa, which is much higher than in this study (Hendricks et al. 1977). In an analysis of experimental deep dives in the depth range of 110–450 m including 118 dives where P_{O₂} was constant at 50–60 kPa during decompression, there was a relationship between the reduction in Tl_{CO} and cumulative hyperoxic exposure (Thorsen et al. 1994). Based on this regression, a reduction in Tl_{CO} of 8.1% would have been expected

after this dive where the cumulative hyperoxic exposure was 432 kPa 24 h. The intermittent reduction in the hyperoxic exposure may contribute to less effects on pulmonary function in this dive.

A reduction in P_{O_2} without a concomitant reduction in decompression rate will increase the risk of decompression sickness. This interdependence between P_{O_2} and decompression rate with respect to risk for decompression sickness is established for saturation dives with air and mixtures of nitrogen and oxygen (Eckenhoff and Vann 1985), and for saturation dives with mixtures of helium and oxygen (Hamilton and Thalmann 2003). A control dive to the same depth with a reduced P_{O_2} , without a reduction in decompression rate, would be associated with an unacceptable risk of decompression sickness. Historical controls have therefore been used for comparison in this study.

Compared with previous deep dive series, the divers in this dive were older, with a higher BMI and lower exercise capacity. However, they were all medically fit for diving and were active as commercial divers in the North Sea when included in this study. A high BMI, low exercise capacity and age are associated with increased VGM formation associated with air bounce dives (Carturan et al. 2002), but definite studies on these relationships with deep saturation dives are lacking. In this group of experienced divers, there may be a self-selection of subjects being less susceptible to the effects of a dive on the lung. However, there was a case of decompression sickness and neurological deficits after this dive that is of concern (Grønning et al. 2003).

In the previous deep dive series to a pressure of 3.7 MPa (Thorsen et al. 1990b) moderate exercise during the decompression phase was optional, and was practiced by ~50% of the divers. In those dives exercise did not seem to have any influence on VGM. In this dive daily moderate exercise during decompression may have contributed to the $V_{O_{2peak}}$ being unchanged. Furthermore, exercise will increase peripheral blood flow and inert gas washout from the tissues, and, thereby, contribute to the low VGM formation during decompression.

There were no significant changes in ACE after the dive. However, the trend for an increase in ACE during the decompression phase and the finding of the largest increase in ACE in the subject with decompression sickness should be followed up with further studies. There can be several reasons for an increase in ACE, including hyperoxia and VGM. Marbotti et al. (1999) found an increase in ACE only after dives where VGM was detected by Doppler ultrasound. The lack of changes in lung function after this deep

saturation dive could be due to the intermittent reduction in P_{O_2} during the decompression phase and the reduced decompression stress.

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References

- Brizio-Molteni L, Piano G, Warpeha RL, Solliday NH, Molteni A, Angelats J, Lewis N, Patejak-Radwanski H (1992) Angiotensin-1-converting enzyme activity as an index of pulmonary damage in thermal injury with or without smoke inhalation. *Ann Clin Lab Sci* 22:1–10
- Carturan D, Boussuges A, Vanuxem P, Bar-Hen A, Burnet H, Gardette B (2002) Ascent rate, age, maximal oxygen uptake, adiposity and circulating venous bubbles after diving. *J Appl Physiol* 93:1349–1356
- Cotes JE (1979) Allowance for the effect on transfer factor of variation in haemoglobin concentration and in capillary oxygen tension. In: Cotes JE (ed) *Lung function*, 4th edn. Blackwell Scientific Publications, London, pp 245–246
- Cotes JE, Davey JS, Reed JW, Rooks M (1987) Respiratory effects of a single saturation dive to 300 m. *Br J Ind Med* 44:76–82
- Cotes JE, Chinn DJ, Quanjer PhH, Roca J, Yernault J-C (1993) Standardization of the measurement of transfer factor (diffusion capacity). *Eur Respir J* 6(suppl 16):41–52
- Eckenhoff RG, Vann RD (1985) Air and nitrox saturation decompression. A report of 4 schedules and 77 subjects. *Undersea Biomed Res* 12:41–52
- Fracica PJ, Knapp MJ, Piantadosi CA, Takeda K, Fulkerson WJ, Coleman RE, Wolfe WG, Crapo DJ (1991) Responses of baboons to prolonged hyperoxia: physiology and qualitative pathology. *J Appl Physiol* 71:2352–2362
- Grønning M, Hjelle J, Segadal K, Skeidsvoll H, Thorsen E, Troland K, Sundal E, Nyland H (2003) Neurological deficits during and after a simulated dive to 250 MSW. In: Jansen EC, Mortensen CR, Hyldegaard O (eds) *Proceedings of 29th Annual meeting of European Underwater and Baromedical Society*, Copenhagen, p 138
- Hamilton RW, Thalmann ED (2003) Decompression practice. In: Brubakk AO, Neuman TS (eds) *Bennett and Elliott's physiology and medicine of diving*. Saunders, Edinburgh, pp 455–500
- Hendricks PL, Hall DA, Hunter WL Jr, Haley PJ (1977) Extension of pulmonary oxygen tolerance in man at 2 ATA by intermittent oxygen exposure. *J Appl Physiol* 42:593–599
- Hofsø D, Ulvik RJ, Segadal K, Hope A, Thorsen E (2005) Changes in erythropoietin and haemoglobin concentrations in response to saturation diving. *Eur J Appl Physiol* 95:191–196
- Johansen KB, Marstein S, Aas P (1987) Automated method for the determination of angiotensin converting enzyme in serum. *Scand J Clin Lab Invest* 47:411–414
- Lehnigk B, Jorres RA, Elliott DH, Holthaus J, Magnussen H (1997) Effects of a single saturation dive on lung function and exercise performance. *Int Arch Occup Environ Health* 69:201–208
- Marabotti C, Chiesa F, Scalzini A, Antonelli F, Lari R, Franchini C, Data PG (1999) Cardiac and humoral changes induced by recreational scuba diving. *Undersea Hyperb Med* 26:151–158

- Nossum V, Koteng S, Brubakk AB (1999) Endothelial damage by bubbles in the pulmonary artery of the pig. *Undersea Hyperb Med* 26:1–8
- Quanjer PhH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault J-C (1993) Lung volumes and forced ventilatory flows. *Eur Respir J* 6(suppl 16):5–40
- Segadal K, Risberg J, Eftedal O, Hope A, Thorsen E, Suzuki S, Stuhr L, Marstein S, Sundland H, Holand B, Hjelle J, Brubakk AO (2003) A simulated 250 MSW saturation dive: venous gas emboli, pulmonary function, maximum oxygen uptake and angiotensin converting enzyme. In: Jansen EC, Mortensen CR, Hyldegaard O (eds) *Proceedings of 29th Annual meeting of European Underwater and Baromedical Society*, Copenhagen, p 98
- Spencer MP, Clark HF (1972) Precordial monitoring of pulmonary gas embolism and decompression sickness. *Aerosp Med* 43:762–767
- Suzuki S, Ikeda T, Hashimoto A (1991) Decrease in the single breath diffusing capacity after saturation dives. *Undersea Biomed Res* 18:103–109
- Tetzlaff K, Friege L, Reuter M (1998) Expiratory flow limitation in compressed air divers and oxygen divers. *Eur Respir J* 12:895–899
- Thorsen E, Segadal K, Kambestad BK, Gulsvik A (1990a) Divers' lung function: small airways disease? *Br J Ind Med* 47:519–523
- Thorsen E, Hjelle J, Segadal K, Gulsvik A (1990b) Exercise tolerance and pulmonary gas exchange after deep saturation dives. *J Appl Physiol* 68:1809–1814
- Thorsen E, Segadal K, Reed JW, Elliott C, Gulsvik A, Hjelle J (1993) Contribution of hyperoxia to reduced pulmonary function after deep saturation dives. *J Appl Physiol* 75:657–662
- Thorsen E, Segadal K, Kambestad BK (1994) Mechanisms of reduced pulmonary function after a saturation dive. *Eur Respir J* 7:4–10