



UNDERSEA AND HYPERBARIC MEDICAL SOCIETY

# Hyperbaric Oxygen Therapy

# INDICATIONS

14<sup>TH</sup> EDITION

Richard E. Moon MD  
Chair and Editor





UNDERSEA AND HYPERBARIC MEDICAL SOCIETY

# Hyperbaric Oxygen Therapy

# INDICATIONS

14<sup>TH</sup> EDITION

Richard E. Moon MD  
Chair and Editor

Undersea and Hyperbaric Medical Society  
631 US Highway 1, Suite 307  
North Palm Beach, FL 33408  
USA



No responsibility is assumed by the publisher or editor for any injury and or damage to persons or property as a matter of product liability, negligence or otherwise, or from any use or operation of any methods, product, instructions, or ideas contained in the material herein. No suggested test or procedure should be carried out unless, in the reader's judgment, its risk is justified. Because of rapid advances in the medical sciences, we recommend that the independent verification of diagnoses and drug dosages be made.

All rights reserved. No part of this book may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher.

Copyright © 2019 Undersea and Hyperbaric Medical Society

ISBN: 978-1-947239-16-6

Library of Congress Catalog Number: 2019940027

Published by: Best Publishing Company  
631 U.S. Highway 1, Suite 307  
North Palm Beach, Florida 33408

Printed and bound in the United States of America

# Table of Contents

---

|  |      |
|--|------|
| Preface . . . . .  | v    |
| Members of the Hyperbaric Oxygen Therapy Committee . . . . .                         | vii  |
| I. Background . . . . .  | ix   |
| II. Hyperbaric Oxygen: Definition . . . . .  | x    |
| III. Utilization Review For Hyperbaric Oxygen Therapy . . . . .                      | xii  |
| IV. Acceptance (Addition) of New Indications for Hyperbaric Oxygen Therapy . . . . . | xii  |
| V. List of Abbreviations . . . . .   | xiii |
| VI. Author Biographies . . . . .   | xvi  |

## PART I. Indications

|  |     |
|--|-----|
| 1. Hyperbaric Treatment of Air or Gas Embolism: Current Recommendations . . . . .                            | 1   |
| 2. Arterial Insufficiencies  |     |
| A. Central Retinal Artery Occlusion . . . . .  | 15  |
| B. Hyperbaric Oxygen Therapy for Selected Problem Wounds . . . . .   | 31  |
| 3. Carbon Monoxide Poisoning . . . . .   | 81  |
| 4. Clostridial Myonecrosis (Gas Gangrene) . . . . .  | 105 |
| 5. The Effect of Hyperbaric Oxygen on Compromised Grafts and Flaps . . . . .                                 | 117 |
| 6. The Role of Hyperbaric Oxygen for Acute Traumatic Ischemias . . . . .                                     | 135 |
| 7. Decompression Sickness . . . . .  | 153 |
| 8. Delayed Radiation Injuries (Soft Tissue and Bony Necrosis)<br>and Potential for Future Research . . . . . | 163 |
| 9. Sudden Sensorineural Hearing Loss . . . . .   | 203 |
| 10. Intracranial Abscess . . . . .   | 231 |
| 11. Necrotizing Soft Tissue Infections . . . . .   | 239 |
| 12. Refractory Osteomyelitis . . . . .   | 263 |
| 13. Severe Anemia . . . . .  | 293 |
| 14. Adjunctive Hyperbaric Oxygen Therapy in the Treatment of Thermal Burns . . . . .                         | 301 |

## PART II. Additional Considerations

|  |     |
|--|-----|
| 15. Mechanisms of Action of Hyperbaric Oxygen Therapy . . . . .                    | 325 |
| 16. Side Effects of Hyperbaric Oxygen Therapy . . . . .                            | 335 |
| 17. Oxygen Pretreatment and Preconditioning . . . . .                              | 343 |
| 18. Randomized Controlled Trials in Diving and Hyperbaric Medicine . . . . .       | 351 |
| 19. Hyperbaric Oxygen for Symptoms Following Mild Traumatic Brain Injury . . . . . | 379 |

|   |     |
|---|-----|
| Appendix A. Approved Indications for HBO <sub>2</sub> Therapy . . . . . | 393 |
| Index . . . . .   | 399 |



## Preface

---

The application of air under pressure (hyperbaric air) dates back to 1667, when Nathaniel Henshaw proposed a hypo-hyperbaric room pressurized and depressurized with an organ bellows.<sup>1</sup> In the nineteenth century, Simpson wrote a treatise on the use of compressed air for certain respiratory diseases.<sup>2</sup> The medicinal uses of oxygen were first reported by Beddoes in 1794,<sup>3</sup> while the first article describing adjunctive uses of hyperbaric oxygen therapy (HBO<sub>2</sub>) was written by Fontaine in 1879,<sup>4</sup> who constructed a mobile operating room which could be pressurized. He observed that pressurized patients were not as cyanotic after the use of nitrous oxide during induction of anesthesia as compared to patients anesthetized at atmospheric pressure. In addition, he noted that hernias were much easier to reduce. Also around that time, the work of Paul Bert<sup>5</sup> and J. Lorrain-Smith<sup>6</sup> showed that oxygen under pressure had potentially deleterious consequences on the human body with side effects that included central nervous system and pulmonary toxicity. The efforts of Churchill-Davidson and Boerema in the 1950s and 1960s spurred the modern scientific use of clinical hyperbaric medicine.

In 1967, the Undersea Medical Society was founded by six United States Naval diving and submarine medical officers with the explicit goal of promoting diving and undersea medicine. In short order, this society expanded to include those interested in clinical hyperbaric medicine. In recognition of the dual interest by members in both diving and clinical applications of compression therapy, the society was renamed The Undersea and Hyperbaric Medical Society in 1986. It remains the leading not for profit organization dedicated to reporting scientifically and medically efficacious and relevant information pertaining to hyperbaric and undersea medicine.

In 1972, an ad hoc Medicare committee was formed to evaluate the efficacy of hyperbaric oxygen therapy for specified medical conditions. The focus was to determine if this treatment modality showed therapeutic benefit and merited insurance coverage. The growth of the body of scientific evidence that had developed over the preceding years supported this endeavor and recognition for the field. In 1976, the Hyperbaric Oxygen Therapy Committee became a standing committee of what was then the UMS. The first Hyperbaric Oxygen Committee Report was published in 1977 and served as guidance for practitioners and scientists interested in HBO<sub>2</sub>. The report is usually published every three to five years and was last published in 2014. Additionally, this document continues to be used by the Centers for Medicare and Medicaid Services and other third party insurance carriers in determining payment.

The report, currently in its 14<sup>th</sup> edition, has grown in size and depth to reflect the evolution of the literature. To date, the committee recognizes 14 indications for which scientific and clinical evidence supports the use of HBO<sub>2</sub>.

The Undersea and Hyperbaric Medical Society continues to maintain its reputation for its expertise on hyperbaric therapy. With leading experts authoring chapters in their respective fields, this publication continues to provide the most current and up to date guidance and support for scientists and practitioners of hyperbaric oxygen therapy.

Richard E. Moon MD  
Editor, UHMS Committee Chair

## References

1. Henshaw N. Aero-Chalinos or a register for the air for the better preservation of health and cure of diseases, after a new method. London. 1677.
2. Simpson A. Compressed Air as a Therapeutic Agent in the Treatment of Consumption, Asthma, Chronic Bronchitis and Other Diseases. Edinburgh: Sutherland and Knox; 1857.
3. Beddoes T, Watt J. Considerations of the Medicinal Use of Factitious Airs, and on the Manner of Obtaining Them in Large Quantities, First Edition, part II. Bristol: Bulgin and Rossier; 1794.
4. Fontaine JA. Emploi chirurgical de l'air comprime. Union Med. 1879;28:445.
5. Bert P. Barometric Pressure [Hitchcock MS, Hitchcock FA, translation]. Bethesda, MD: Undersea Medical Society; 1978. P. 579.
6. Lorrain-Smith J. The pathological effects due to increase of oxygen tension in the air breathed. J Physiol. 1899; 24:19-35.

## **Members of the Hyperbaric Oxygen Therapy Committee**

---

Richard Moon MD (Chair)

Dirk Bakker MD

Robert Barnes MD

Michael Bennett MD

Enrico Camporesi MD

Paul Cianci MD

James Clark MD

William Dodson, MD

John Feldmeier DO

Laurie Gesell MD

Neil B. Hampson MD

Brett Hart MD

Enoch Huang MD

Irving Jacoby MD

Robert Marx DDS

Heather Murphy-Lavoie MD

Richard Roller MD

Ben Slade MD

Michael Strauss MD

Stephen Thom MD, PhD

Keith Van Meter MD

Lindell Weaver MD

Wilbur T. Workman MS



## I. Background

---

The Undersea and Hyperbaric Medical Society (UHMS) is an international scientific organization which was founded in 1967 to foster exchange of data on the physiology and medicine of commercial and military diving. Over the intervening years, the interests of the Society have enlarged to include clinical hyperbaric oxygen therapy. The society has grown to over 2,000 members and has established the largest repository of diving and hyperbaric research collected in one place. Clinical information, an extensive bibliographic database of thousands of scientific papers, as well as books, and technical reports which represent the results of over 100 years of research by military and university laboratories around the world are contained in the UHMS Schilling Library, holdings are now part of the Duke University Library, Durham, NC. The results of ongoing research and clinical aspects of undersea and hyperbaric medicine are reported annually at scientific meetings and in *Undersea and Hyperbaric Medicine* published bi-monthly. Previously the society supported two journals, *Undersea Biomedical Research* and the *Journal of Hyperbaric Medicine*. These two journals were merged in 1993 into *Undersea and Hyperbaric Medicine*.

UHMS headquarters is located at:

631 US Highway 1, Suite 307  
North Palm Beach, FL 33408  
Phone: 561-776-6110 / 1-877-533-UHMS (8467)  
FAX: 919-490-5149  
Email: [uhms@uhms.org](mailto:uhms@uhms.org)  
Internet: [www.uhms.org](http://www.uhms.org)

## II. Hyperbaric Oxygen: Definition

The UHMS defines hyperbaric oxygen (HBO<sub>2</sub>) as an intervention in which an individual breathes near 100% oxygen intermittently while inside a hyperbaric chamber that is pressurized to greater than sea level pressure (1 atmosphere absolute [ATA]). For clinical purposes, the pressure must equal or exceed 1.4 ATA while breathing near 100% oxygen. The United States Pharmacopoeia (USP) and Compressed Gas Association (CGA) Grade A specify medical grade oxygen to be not less than 99.0% by volume, and the National Fire Protection Association (NFPA) specifies USP medical grade oxygen.

In certain circumstances hyperbaric oxygen therapy represents the primary treatment modality while in others it is an adjunct to surgical or pharmacologic interventions.

The NFPA classifies chambers according to occupancy for the purposes of establishing minimum construction and operation requirements.<sup>1</sup>

1. Class A – Human, multiple occupancy
2. Class B – Human, single occupancy
3. Class C – Animal, no human occupancy

Clinical treatments can be carried out in either a Class A (multi) or B (mono) chamber system. In a Class B system, the entire chamber is pressurized with near 100% oxygen, and the patient breathes the ambient chamber oxygen directly. A Class A system holds two or more people (patients, observers, and/or support personnel); the chamber is pressurized with compressed air while the patients breathe near 100% oxygen via masks, head hoods, or endotracheal tubes. It is important to note that Class B systems can and are pressurized with compressed air while the patients breathe near 100% oxygen via masks, head hoods, or endotracheal tubes.

According to the UHMS definition and the determination of The Centers for Medicare and Medicaid Services (CMS) and other third-party carriers, breathing medical grade near-100% oxygen at 1 atmosphere of pressure or exposing isolated parts of the body to 100% oxygen does not constitute HBO<sub>2</sub> therapy. The patient must receive the oxygen by inhalation within a pressurized chamber. Current information indicates that pressurization should be to 1.4 ATA or higher.

The literature of HBO<sub>2</sub> treatment began to appear during the 1930s as navies and universities around the world began studies in oxygen breathing at elevated pressures as a way to more safely decompress divers and to treat decompression sickness and arterial gas embolism. During the 1960s, HBO<sub>2</sub> was incorporated in standard treatment tables of the U.S. Navy. Extensive research on oxygen toxicity was undertaken to establish safe limits, overall safety, and medical and physiologic aspects of the compressed gas environment. These efforts led to a vast body of literature which underpins modern HBO<sub>2</sub> therapy.



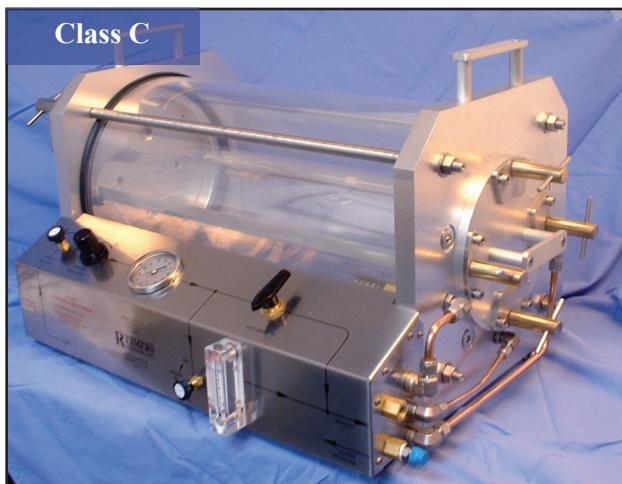
**Figure 1.** Multiplace Chamber

Photograph courtesy of Lindell Weaver MD, of Intermountain Medical Center, Murray, Utah. Fink DL8 multiplace chamber, Fink Engineering, Melbourne, Australia.



**Figure 2.** Monoplace Chamber

Photograph courtesy of Sechrist Industries.



**Figure 3.** Animal Chamber

Photograph courtesy of Reimers Systems.

In 1976, recognizing the need for meticulous scrutiny of emerging clinical applications of HBO<sub>2</sub>, the Executive Committee of the UHMS established the Hyperbaric Oxygen Therapy Committee. The Committee was charged with the responsibility of continuously reviewing research and clinical data and rendering recommendations regarding clinical efficacy and safety of HBO<sub>2</sub>. To achieve this goal, the multispecialty committee is comprised of practitioners and scientific investigators in the fields of internal medicine, infectious diseases, pharmacology, emergency medicine, general surgery, orthopedic surgery, trauma surgery, thoracic surgery, otolaryngology, oral and maxillofacial surgery, anesthesiology, pulmonology, critical care, radiation oncology and aerospace medicine.

Since 1976, the Committee has met annually to review research and clinical data. From the 28 indications for which third-party reimbursement was recommended in the 1976 and 1979 reports, the number of recognized indications has been refined to 14 in the current report. These indications are those for which in vitro and in vivo pre-clinical research data as well as extensive positive clinical experience and study have become convincing.

Evidence considered by the Committee includes sound physiologic rationale; in vivo or in vitro studies that demonstrate effectiveness; controlled animal studies, prospective controlled clinical studies; and extensive clinical experience from multiple, recognized hyperbaric medicine centers.

The Committee requires that experimental and clinical evidence submitted for the efficacy of HBO<sub>2</sub> treatment for a disorder be at least as convincing as that for any other currently accepted treatment modality for that disorder. Studies in progress will continue to clarify mechanisms of action, optimal oxygen dosage, duration of exposure times, frequency of treatments, and patient selection criteria. The Committee recommends third party reimbursement of HBO<sub>2</sub> therapy for the disorders included in the accepted conditions category. Currently, most insurance carriers have established HBO<sub>2</sub> reimbursement policies.

The Committee also reviews cost effectiveness and has established guidelines for each entity. Results show that, in addition to its clinical efficacy, HBO<sub>2</sub> therapy yields direct cost savings by successfully resolving a high percentage of difficult and expensive disorders, thereby minimizing prolonged hospitalization. However, the Committee recommends that each individual hyperbaric facility, whether monoplace or multiplace, establish its own charges consistent with the actual local costs of providing such service.

### **III. Utilization Review for Hyperbaric Oxygen Therapy**

---

A utilization review section is presented for each recognized HBO<sub>2</sub> indication. It is recommended that utilization review be obtained if the number of HBO<sub>2</sub> treatments is to exceed the recommended number of treatments for that indication. Such review should involve discussion of the clinical case with another qualified hyperbaric medicine physician from an outside institution. If that individual agrees that additional HBO<sub>2</sub> therapy is warranted, treatment may exceed the usually prescribed number of treatments.

### **IV. Acceptance (Addition) of New Indications for Hyperbaric Oxygen Therapy**

---

New indications for HBO<sub>2</sub> therapy are considered for acceptance at the meeting of the Hyperbaric Oxygen Therapy Committee during the annual meeting of the Undersea and Hyperbaric Medical Society. This consideration can be initiated from within the Committee itself or may result in response to a written request by a non-Committee member. When a new indication is considered for acceptance, a position paper is written. The information must summarize the *in vitro*, *in vivo*, and clinical aspects of the new indication for HBO<sub>2</sub> therapy. Two members of the Hyperbaric Oxygen Committee review the position paper and each writes a critique. The position paper and critiques are presented to the Hyperbaric Oxygen Committee. A consensus of the Hyperbaric Oxygen Committee is required for recommending the indication be moved into the recognized category. If the Committee determines that a new condition merits acceptance, it makes this recommendation to the Executive Committee of the Society, which ultimately votes whether or not to recognize the new indication.

# **Chapter 1: Hyperbaric Treatment of Air or Gas Embolism: Current Recommendations**

*Richard E. Moon MD*

## **REFERENCES**

1. Benton PJ, Woodfine JD, Westwook PR. Arterial gas embolism following a 1-meter ascent during helicopter escape training: a case report. *Aviat Space Environ Med.* 1996;67:63-4.
2. Mellem H, Emhjellen S, Horgen O. Pulmonary barotrauma and arterial gas embolism caused by an emphysematous bulla in a SCUBA diver. *Aviat Space Environ Med.* 1990;61:559-62.
3. Weiss LD, Van Meter KW. Cerebral air embolism in asthmatic scuba divers in a swimming pool. *Chest.* 1995;107:1653-4.
4. Mason WH, Damon TG, Dickinson AR, Nevison TO, Jr. Arterial gas emboli after blast injury. *Proc Soc Exp Biol Med.* 1971;136(4):1253-5.
5. Freund U, Kopolovic J, Durst AL. Compressed air emboli of the aorta and renal artery in blast injury. *Injury.* 1980;12(1):37-8.
6. Guy RJ, Glover MA, Cripps NP. Primary blast injury: pathophysiology and implications for treatment. Part III: Injury to the central nervous system and the limbs. *J R Nav Med Serv.* 2000;86(1):27-31.
7. Ence TJ, Gong H, Jr. Adult respiratory distress syndrome after venous air embolism. *Am Rev Respir Dis.* 1979;119:1033-7.
8. Frim DM, Wollman L, Evans AB, Ojemann RG. Acute pulmonary edema after low-level air embolism during craniotomy. Case report. *J Neurosurg.* 1996;85(5):937-40.
9. Butler BD, Hills BA. Transpulmonary passage of venous air emboli. *J Appl Physiol (1985).* 1985;59:543-7.
10. Vik A, Brubakk AO, Hennessy TR, Jenssen BM, Ekker M, Slordahl SA. Venous air embolism in swine: transport of gas bubbles through the pulmonary circulation. *J Appl Physiol (1985).* 1990;69(1):237-44.
11. Messina AG, Leslie J, Gold J, Topkins MJ, Devereux RB. Passage of microbubbles associated with intravenous infusion into the systemic circulation in cyanotic congenital heart disease: documentation by transesophageal echocardiography. *Am J Cardiol.* 1987;59(9):1013-4.
12. Vik A, Jenssen BM, Brubakk AO. Paradoxical air embolism in pigs with a patent foramen ovale. *Undersea Biomed Res.* 1992;19(5):361-74.
13. Vik A, Jenssen BM, Brubakk AO. Arterial gas bubbles after decompression in pigs with patent foramen ovale. *Undersea Hyperb Med.* 1993;20(2):121-31.
14. Ries S, Knauth M, Kern R, Klingmann C, Daffertshofer M, Sartor K, Hennerici M. Arterial gas embolism after decompression: correlation with right-to-left shunting. *Neurology.* 1999;52(2):401-4.
15. Spencer MP. Decompression limits for compressed air determined by ultrasonically detected bubbles. *J Appl Physiol (1985).* 1976;40:229-35.
16. Gardette B. Correlation between decompression sickness and circulating bubbles in 232 divers. *Undersea Biomed Res.* 1979;6(1):99-107.
17. Balldin UI, Pilmanis AA, Webb JT. Central nervous system decompression sickness and venous gas emboli in hypobaric conditions. *Aviat Space Environ Med.* 2004;75(11):969-72.
18. Majendie F. Sur l'entree accidentelle de l'air dans les veines. *J Physiol Exp (Paris).* 1821;1:190.
19. Moore RM, Braselton CW. Injections of air and carbon dioxide into a pulmonary vein. *Ann Surg.* 1940;112:212-8.
20. Tunnicliffe FW, Stebbing GF. Intravenous injection of oxygen gas as therapeutic measure. *Lancet.* 1916;2:321-3.
21. Yeakel A. Lethal air embolism from plastic blood storage container. *JAMA.* 1968;204:267-8.
22. Helps SC, Parsons DW, Reilly PL, Gorman DF. The effect of gas emboli on rabbit cerebral blood flow. *Stroke.* 1990;21:94-9.
23. Helps SC, Meyer-Witting M, Rilley PL, Gorman DF. Increasing doses of intracarotid air and cerebral blood flow in rabbits. *Stroke.* 1990;21:1340-5.
24. Helps SC, Gorman DF. Air embolism of the brain in rabbits pre-treated with mechlorethamine. *Stroke.* 1991;22:351-4.
25. Levin LL, Stewart GJ, Lynch PR, Bove AA. Blood and blood vessel wall changes induced by decompression sickness in dogs. *J Appl Physiol (1985).* 1981;50:944-9.
26. Nossom V, Koteng S, Brubakk AO. Endothelial damage by bubbles in the pulmonary artery of the pig. *Undersea Hyperb Med.* 1999;26(1):1-8.
27. Nossom V, Hjelde A, Brubakk AO. Small amounts of venous gas embolism cause delayed impairment of endothelial function and increase polymorphonuclear neutrophil infiltration. *Eur J Appl Physiol.* 2002;86:209-14.
28. Klinger AL, Pichette B, Sobolewski P, Eckmann DM. Mechanotransductional basis of endothelial cell response to intravascular bubbles. *Integrative biology : quantitative biosciences from nano to macro.* 2011;3(10):1033-42.
29. Sobolewski P, Kandel J, Klinger AL, Eckmann DM. Air bubble contact with endothelial cells in vitro induces calcium influx and IP<sub>3</sub>-dependent release of calcium stores. *Am J Physiol Cell Physiol.* 2011;301(3):C679-86.

30. Sobolewski P, Kandel J, Eckmann DM. Air bubble contact with endothelial cells causes a calcium-independent loss in mitochondrial membrane potential. *PLoS ONE*. 2012;7(10):e47254.
31. Pearson RR, Goad RF. Delayed cerebral edema complicating cerebral arterial gas embolism: Case histories. *Undersea Biomed Res*. 1982;9:283-96.
32. Elliott DH, Harrison JAB, Barnard EEP. Clinical and radiological features of 88 cases of decompression barotrauma. In: Shilling CW, Beckett MW, editors. *Underwater Physiology VI Proceedings of the Sixth Symposium on Underwater Physiology*. Bethesda, MD: FASEB; 1978. p. 527-35.
33. Elliott DH, Moon RE. Manifestations of the decompression disorders. In: Bennett PB, Elliott DH, editors. *The Physiology and Medicine of Diving*. Philadelphia, PA: WB Saunders; 1993. p. 481-505.
34. Lam KK, Hutchinson RC, Gin T. Severe pulmonary oedema after venous air embolism. *Can J Anaesth*. 1993;40(10):964-7.
35. Fitchet A, Fitzpatrick AP. Central venous air embolism causing pulmonary oedema mimicking left ventricular failure. *BMJ*. 1998;316(7131):604-6.
36. Blanc P, Boussuges A, Henriette K, Sainty JM, Deleflie M. Iatrogenic cerebral air embolism: importance of an early hyperbaric oxygenation. *Intensive Care Med*. 2002;28(5):559-63.
37. Francis TJR, Mitchell SJ. Manifestations of decompression disorders. In: Brubakk AO, Neuman TS, editors. *Bennett & Elliott's Physiology and Medicine of Diving*. New York, NY: Elsevier Science; 2003. p. 578-99.
38. Neuman TS, Bove AA. Combined arterial gas embolism and decompression sickness following no-stop dives. *Undersea Biomed Res*. 1990;17:429-36.
39. Warren LP, Djang WT, Moon RE, Camporesi EM, Sallee DS, Anthony DC. Neuroimaging of scuba diving injuries to the CNS. *AJNR Am J Neuroradiol*. 1988;9:933-8.
40. Catron PW, Dutka AJ, Biondi DM, Flynn ET, Hallenbeck JM. Cerebral air embolism treated by pressure and hyperbaric oxygen. *Neurology*. 1991;41(2 ( Pt 1)):314-5.
41. Reuter M, Tetzlaff K, Hutzelmann A, Fritsch G, Steffens JC, Bettinghausen E, Heller M. MR imaging of the central nervous system in diving-related decompression illness. *Acta Radiol*. 1997;38(6):940-4.
42. Sayama T, Mitani M, Inamura T, Yagi H, Fukui M. Normal diffusion-weighted imaging in cerebral air embolism complicating angiography. *Neuroradiology*. 2000;42(3):192-4.
43. Benson J, Adkinson C, Collier R. Hyperbaric oxygen therapy of iatrogenic cerebral arterial gas embolism. *Undersea Hyperb Med*. 2003;30(2):117-26.
44. van Hulst RA, Klein J, Lachmann B. Gas embolism: pathophysiology and treatment. *Clin Physiol Funct Imaging*. 2003;23(5):237-46.
45. Krivonyak GS, Warren SG. Cerebral arterial air embolism treated by a vertical head-down maneuver. *Catheter Cardiovasc Interv*. 2000;49(2):185-7.
46. Butler BD, Laine GA, Leiman BC, Warters D, Kurusz M, Sutton T, Katz J. Effects of Trendelenburg position on the distribution of arterial air emboli in dogs. *Ann Thorac Surg*. 1988;45:198-202.
47. Mehlhorn U, Burke EJ, Butler BD, Davis KL, Katz J, Melamed E, Morris WP, Allen SJ. Body position does not affect the hemodynamic response to venous air embolism in dogs. *Anesth Analg*. 1994;79:734-9.
48. Dutka AJ. Therapy for dysbaric central nervous system ischemia: adjuncts to recompression. In: Bennett PB, Moon RE, editors. *Diving Accident Management*. Bethesda, MD: Undersea and Hyperbaric Medical Society; 1990. p. 222-34.
49. Mitchell SJ, Bennett MH, Bryson P, Butler FK, Doolette DJ, Holm JR, Kot J, Lafere P. Pre-hospital management of decompression illness: expert review of key principles and controversies. *Diving Hyperb Med*. 2018;48(1):45-55.
50. Mitchell SJ, Bennett MH, Bryson P, Butler FK, Doolette DJ, Holm JR, Kot J, Lafere P. Consensus guideline: Pre-hospital management of decompression illness: expert review of key principles and controversies. *Undersea Hyperb Med*. 2018;45(3):273-86.
51. Navy Department. US Navy Diving Manual. Revision 6. Vol 5 : Diving Medicine and Recompression Chamber Operations. NAVSEA 0910-LP-106-0957. Washington, DC: Naval Sea Systems Command; 2008.
52. Clarke D, Gerard W, Norris T. Pulmonary barotrauma-induced cerebral arterial gas embolism with spontaneous recovery: commentary on the rationale for therapeutic compression. *Aviat Space Environ Med*. 2002;73(2):139-46.
53. Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H, Kucan JO. Morphological analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg*. 1993;91:1110-23.
54. Martin JD, Thom SR. Vascular leukocyte sequestration in decompression sickness and prophylactic hyperbaric oxygen therapy in rats. *Aviat Space Environ Med*. 2002;73(6):565-9.
55. Ericsson JA, Gottlieb JD, Sweet RB. Closed-chest cardiac massage in the treatment of venous air embolism. *N Engl J Med*. 1964;270:1353-4.

56. Moses HL. Casualties in Individual Submarine Escape 1928-1957. Groton, CT: US Naval Submarine Medical Center; 1964. Report No.: Report No. 438.
57. Van Genderen L. Study of Air Embolism and Extra-aveolar Accidents Associated with Submarine Escape Training. Groton, CT: US Naval Submarine Medical Center; 1967. Report No.: 500.
58. Ingvar DH, Adolfson J, Lindemark C. Cerebral air embolism during training of submarine personnel in free escape: an electroencephalographic study. *Aerospace Med.* 1973;44(6):628-35.
59. Hart GB. Treatment of decompression illness and air embolism with hyperbaric oxygen. *Aerospace Med.* 1974;45:1190-3.
60. Ah-See AK. Review of arterial air embolism in submarine escape. In: Smith G, editor. Proceedings of the Sixth International Congress on Hyperbaric Medicine. Aberdeen, Scotland: Aberdeen University Press; 1977. p. 349-51.
61. Bray P, Myers RA, Cowley RA. Orogenital sex as a cause of nonfatal air embolism in pregnancy. *Obstet Gynecol.* 1983;61(5):653-7.
62. Murphy BP, Harford FJ, Cramer FS. Cerebral air embolism resulting from invasive medical procedures. Treatment with hyperbaric oxygen. *Ann Surg.* 1985;201(2):242-5.
63. Leitch DR, Green RD. Pulmonary barotrauma in divers and the treatment of cerebral arterial gas embolism. *Aviat Space Environ Med.* 1986;57:931-8.
64. Dutka AJ. Air or gas embolism. In: Camporesi EM, Barker AC, editors. *Hyperbaric Oxygen Therapy: A Critical Review.* Bethesda, MD: Undersea and Hyperbaric Medical Society; 1991. p. 1-10.
65. Ziser A, Adir Y, Lavon H, Shupak A. Hyperbaric oxygen therapy for massive arterial air embolism during cardiac operations. *J Thorac Cardiovasc Surg.* 1999;117(4):818-21.
66. Massey EW, Moon RE, Shelton D, Camporesi EM. Hyperbaric oxygen therapy of iatrogenic air embolism. *J Hyperb Med.* 1990;5:15-21.
67. Zwirewich CV, Müller NL, Abboud RT, Lepawsky M. Noncardiogenic pulmonary edema caused by decompression sickness: rapid resolution following hyperbaric therapy. *Radiology.* 1987;163:81-2.
68. Dexter F, Hindman BJ. Recommendations for hyperbaric oxygen therapy of cerebral air embolism based on a mathematical model of bubble absorption. *Anesth Analg.* 1997;84:1203-7.
69. Navy Department. US Navy Diving Manual. Revision 7. Vol 5 : Diving Medicine and Recompression Chamber Operations. NAVSEA 0910-LP-115-1921. Washington, DC: Naval Sea Systems Command; 2016.
70. Moon RE, Sheffield PJ. Guidelines for treatment of decompression illness. *Aviat Space Environ Med.* 1997;68:234-43.
71. Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. *Lancet.* 2011;377(9760):153-64.
72. Cianci P, Slade JB, Jr. Delayed treatment of decompression sickness with short, no-air-break tables: review of 140 cases. *Aviat Space Environ Med.* 2006;77(10):1003-8.
73. Undersea & Hyperbaric Medical Society. UHMS Best Practice Guidelines: Prevention and Treatment of Decompression Sickness and Arterial Gas Embolism. Durham, NC2011.
74. Mitchell SJ. Lidocaine in the treatment of decompression illness: a review of the literature. *Undersea Hyperb Med.* 2001;28(3):165-74.
75. Bennett M, Mitchell S, Dominguez A. Adjunctive treatment of decompression illness with a non-steroidal anti-inflammatory drug (tenoxicam) reduces compression requirement. *Undersea Hyperb Med.* 2003;30(3):195-205.
76. Moon RE, editor. *Adjunctive Therapy for Decompression Illness.* Kensington, MD: Undersea and Hyperbaric Medical Society; 2003.
77. Chang M, Marshall J. Therapeutic hypothermia for acute air embolic stroke. *West J Emerg Med.* 2012;13(1):111-3.
78. Oh SH, Kang HD, Jung SK, Choi S. Implementation of targeted temperature management in a patient with cerebral arterial gas embolism. *Ther Hypothermia Temp Manag.* 2018.
79. Dutka AJ, Hallenbeck JM, Kochanek P. A brief episode of severe arterial hypertension induces delayed deterioration of brain function and worsens blood flow after transient multifocal cerebral ischemia. *Stroke.* 1987;18(2):386-95.
80. van Hulst RA, Haitsma JJ, Lamers TW, Klein J, Lachmann B. Hyperventilation impairs brain function in acute cerebral air embolism in pigs. *Intensive Care Med.* 2004;30(5):944-50.
81. Beevor H, Frawley G. Iatrogenic cerebral gas embolism: analysis of the presentation, management and outcomes of patients referred to The Alfred Hospital Hyperbaric Unit. *Diving Hyperb Med.* 2016;46(1):15-21.
82. Takita H, Olszewski W, Schimert G, Lanphier EH. Hyperbaric treatment of cerebral air embolism as a result of open-heart surgery. Report of a case. *J Thorac Cardiovasc Surg.* 1968;55(5):682-5.
83. Mader JT, Hulet WH. Delayed hyperbaric treatment of cerebral air embolism: report of a case. *Arch Neurol.* 1979;36(8):504-5.
84. Perez MF, Ongkeko Perez JV, Serrano AR, Andal MP, Aldover MC. Delayed hyperbaric intervention in life-threatening decompression illness. *Diving Hyperb Med.* 2017;47(4):257-9.

85. Trytko BE, Bennett MH. Arterial gas embolism: a review of cases at Prince of Wales Hospital, Sydney, 1996 to 2006. *Anaesth Intensive Care*. 2008;36(1):60-4.
86. Morris WP, Butler BD, Tonnesen AS, Allen SJ. Continuous venous air embolism in patients receiving positive end-expiratory pressure. *Am Rev Respir Dis*. 1993;147:1034-7.
87. Halpern P, Greenstein A, Melamed Y, Taitelman U, Sznajder I, Zveibil F. Arterial air embolism after penetrating lung injury. *Crit Care Med*. 1983;11(5):392-3.
88. Brownlow HA, Edibam C. Systemic air embolism after intercostal chest drain insertion and positive pressure ventilation in chest trauma. *Anaesth Intensive Care*. 2002;30(5):660-4.
89. Berlot G, Rinaldi A, Moscheni M, Ferluga M, Rossini P. Uncommon occurrences of air embolism: description of cases and review of the literature. *Case Rep Crit Care*. 2018;2018:5808390.
90. Lattin G, Jr., O'Brien W, Sr., McCrary B, Kearney P, Gover D. Massive systemic air embolism treated with hyperbaric oxygen therapy following CT-guided transthoracic needle biopsy of a pulmonary nodule. *J Vasc Interv Radiol*. 2006;17(8):1355-8.
91. Rehwald R, Loizides A, Wiedermann FJ, Grams AE, Djurdjevic T, Glodny B. Systemic air embolism causing acute stroke and myocardial infarction after percutaneous transthoracic lung biopsy - a case report. *J Cardiothorac Surg*. 2016;11(1):80.
92. Wherrett CG, Mehran RJ, Beaulieu MA. Cerebral arterial gas embolism following diagnostic bronchoscopy: delayed treatment with hyperbaric oxygen. *Can J Anaesth*. 2002;49(1):96-9.
93. Peirce EC, 2d. Specific therapy for arterial air embolism. *Ann Thorac Surg*. 1980;29(4):300-3.
94. Niyibizi E, Kembi GE, Lae C, Pignel R, Sologashvili T. Delayed hyperbaric oxygen therapy for air emboli after open heart surgery: case report and review of a success story. *J Cardiothorac Surg*. 2016;11(1):167.
95. Malik N, Claus PL, Illman JE, Kligerman SJ, Moynagh MR, Levin DL, Woodrum DA, Arani A, Arunachalam SP, Araoz PA. Air embolism: diagnosis and management. *Future Cardiol*. 2017;13(4):365-78.
96. Closon M, Vivier E, Breynaert C, Duperret S, Branche P, Coulon A, De La Roche E, Delafosse B. Air embolism during an aircraft flight in a passenger with a pulmonary cyst: a favorable outcome with hyperbaric therapy. *Anesthesiology*. 2004;101(2):539-42.
97. Jung AS, Harrison R, Lee KH, Genut J, Nyhan D, Brooks-Asplund EM, Shoukas AA, Hare JM, Berkowitz DE. Simulated microgravity produces attenuated baroreflex-mediated pressor, chronotropic, and inotropic responses in mice. *Am J Physiol Heart Circ Physiol*. 2005;289(2):H600-7.
98. Farshchi Zarabi S, Parotto M, Katzenelson R, Downar J. Massive ischemic stroke due to pulmonary barotrauma and cerebral artery air embolism during commercial air travel. *Am J Case Rep*. 2017;18:660-4.
99. Chang C, Dughi J, Shitabata P, Johnson G, Coel M, McNamara JJ. Air embolism and the radial arterial line. *Crit Care Med*. 1988;16(2):141-3.
100. Dube L, Soltner C, Daenen S, Lemariee J, Asfar P, Alquier P. Gas embolism: an exceptional complication of radial arterial catheterization. *Acta Anaesthesiol Scand*. 2004;48(9):1208-10.
101. Yang CW, Yang BP. Massive cerebral arterial air embolism following arterial catheterization. *Neuroradiology*. 2005;47(12):892-4.
102. Murphy GS, Szokol JW, Marymont JH, Avram MJ, Vender JS, Kubasiak J. Retrograde blood flow in the brachial and axillary arteries during routine radial arterial catheter flushing. *Anesthesiology*. 2006;105(3):492-7.
103. Ceponis PJ, Fox W, Tailor TD, Hurwitz LM, Amrhein TJ, Moon RJ. Non-dysbaric arterial gas embolism associated with chronic necrotizing pneumonia, bullae and coughing: a case report. *Undersea Hyperb Med*. 2017;44(1):73-7.
104. Abernathy CM, Dickinson TC. Massive air emboli from intravenous infusion pump: etiology and prevention. *Am J Surg*. 1979;137(2):274-5.
105. Khan M, Schmidt DH, Bajwa T, Shalev Y. Coronary air embolism: incidence, severity, and suggested approaches to treatment. *Catheterization & Cardiovascular Diagnosis*. 1995;36(4):313-8.
106. Baskin SE, Wozniak RF. Hyperbaric oxygenation in the treatment of hemodialysis-associated air embolism. *N Engl J Med*. 1975;293(4):184-5.
107. Ordway CB. Air embolus via CVP catheter without positive pressure: presentation of case and review. *Ann Surg*. 1974;179(4):479-81.
108. Vesely TM. Air embolism during insertion of central venous catheters. *J Vasc Interv Radiol*. 2001;12(11):1291-5.
109. Raju GS, Bendixen BH, Khan J, Summers RW. Cerebrovascular accident during endoscopy - consider cerebral air embolism, a rapidly reversible event with hyperbaric oxygen therapy. *Gastrointest Endosc*. 1998;47(1):70-3.
110. Eoh EJ, Derrick B, Moon R. Cerebral arterial gas embolism during upper endoscopy. A Case Rep. 2015;5(6):93-4.
111. Park S, Ahn JY, Ahn YE, Jeon SB, Lee SS, Jung HY, Kim JH. Two cases of cerebral air embolism that occurred during esophageal ballooning and endoscopic retrograde cholangiopancreatography. *Clin Endosc*. 2016;49(2):191-6.

112. Bassan MM, Dudai M, Shalev O. Near-fatal systemic oxygen embolism due to wound irrigation with hydrogen peroxide. *Postgrad Med J.* 1982;58(681):448-50.
113. Tsai SK, Lee TY, Mok MS. Gas embolism produced by hydrogen peroxide irrigation of an anal fistula during anesthesia. *Anesthesiology.* 1985;63(3):316-7.
114. Rackoff WR, Merton DF. Gas embolism after ingestion of hydrogen peroxide. *Pediatrics.* 1990;85(4):593-4.
115. Christensen DW, Faught WE, Black RE, Woodward GA, Timmons OD. Fatal oxygen embolization after hydrogen peroxide ingestion. *Crit Care Med.* 1992;20(4):543-4.
116. Mullins ME, Beltran JT. Acute cerebral gas embolism from hydrogen peroxide ingestion successfully treated with hyperbaric oxygen. *J Toxicol Clin Toxicol.* 1998;36(3):253-6.
117. Jones PM, Segal SH, Gelb AW. Venous oxygen embolism produced by injection of hydrogen peroxide into an enterocutaneous fistula. *Anesth Analg.* 2004;99(6):1861-3.
118. Smedley BL, Gault A, Gawthrop IC. Cerebral arterial gas embolism after pre-flight ingestion of hydrogen peroxide. *Diving Hyperb Med.* 2016;46(2):117-9.
119. Habegger R, Siebenmann R, Kieser C. Lethal air embolism during arthroscopy. A case report. *J Bone Joint Surg Br.* 1989;71(2):314-6.
120. Faure EAM, Cook RI, Miles D. Air embolism during anesthesia for shoulder arthroscopy. *Anesthesiology.* 1998;89(3):805-6.
121. Hwang SL, Lieu AS, Lin CL, Liu GC, Howng SL, Kuo TH. Massive cerebral air embolism after cardiopulmonary resuscitation. *J Clin Neurosci.* 2005;12(4):468-9.
122. Helmberger TK, Roth U, Empen K. Massive air embolism during interventional laser therapy of the liver: successful resuscitation without chest compression. *Cardiovasc Intervent Radiol.* 2002;25(4):335-6.
123. Kaufman BS, Kaminsky SJ, Rackow EC, Weil MH. Adult respiratory distress syndrome following orogenital sex during pregnancy. *Crit Care Med.* 1987;15:703-4.
124. Bernhardt TL, Goldmann RW, Thombs PA, Kindwall EP. Hyperbaric oxygen treatment of cerebral air embolism from orogenital sex during pregnancy. *Crit Care Med.* 1988;16(7):729-30.
125. Batman PA, Thomlinson J, Moore VC, Sykes R. Death due to air embolism during sexual intercourse in the puerperium. *Postgrad Med J.* 1998;74:612-3.
126. Sadler DW, Pounder DJ. Fatal air embolism occurring during consensual intercourse in a non-pregnant female. *J Clin Forensic Med.* 1998;5(2):77-9.
127. Gariel C, Delwarde B, Beroud S, Soldner R, Floccard B, Rimmele T. Is decompression illness possible during hyperbaric therapy? a case report. *Undersea Hyperb Med.* 2017;44(3):283-5.
128. Raja S, Rice TW, Mason DP, Rodriguez C, Tan C, Rodriguez ER, Manno E, Videtic GM, Murthy SC. Fatal cerebral air embolus complicating multimodality treatment of esophageal cancer. *Ann Thorac Surg.* 2011;92(5):1901-3.
129. Miyamoto S, Mashimo Y, Horimatsu T, Ezoe Y, Morita S, Muto M, Chiba T. Cerebral air embolism caused by chemoradiotherapy for esophageal cancer. *J Clin Oncol.* 2012;30(25):e237-8.
130. Shim CY, Lee SY, Pak HN. Coronary air embolism associated with atrioesophageal fistula after ablation of atrial fibrillation. *Can J Cardiol.* 2013;29(10):Pages 1329 e17- e19.
131. Kapur S, Barbhaiya C, Deneke T, Michaud GF. Esophageal injury and atrioesophageal fistula caused by ablation for atrial fibrillation. *Circulation.* 2017;136(13):1247-55.
132. Thomson M, El Sakr F. Gas in the left atrium and ventricle. *N Engl J Med.* 2017;376(7):683.
133. Peterson C, Elswick C, Diaz V, Tubbs RS, Moisi M. Delayed presentation of cerebral air embolism from a left atrial-esophageal fistula: a case report and review of the literature. *Cureus.* 2017;9(11):e1850.
134. Clark CC, Weeks DB, Gusdon JP. Venous carbon dioxide embolism during laparoscopy. *Anesth Analg.* 1977;56:650-2.
135. Lantz PE, Smith JD. Fatal carbon dioxide embolism complicating attempted laparoscopic cholecystectomy--case report and literature review. *J Forensic Sci.* 1994;39(6):1468-80.
136. Moskop RJ, Jr, Lubarsky DA. Carbon dioxide embolism during laparoscopic cholecystectomy. *South Med J.* 1994;87:414-5.
137. Gillart T, Bazin JE, Bonnard M, Schoeffler P. Pulmonary interstitial edema after probable carbon dioxide embolism during laparoscopy. *Surg Laparosc Endosc.* 1995;5(4):327-9.
138. Cottin V, Delafosse B, Viale JP. Gas embolism during laparoscopy: a report of seven cases in patients with previous abdominal surgical history. *Surg Endosc.* 1996;10(2):166-9.
139. Vacanti CA, Lodhia KL. Fatal massive air embolism during transurethral resection of the prostate. *Anesthesiology.* 1991;74(1):186-7.
140. Tsou MY, Teng YH, Chow LH, Ho CM, Tsai SK. Fatal gas embolism during transurethral incision of the bladder neck under spinal anesthesia. *Anesth Analg.* 2003;97(6):1833-4.

141. Ledowski T, Kiese F, Jeglin S, Scholz J. Possible air embolism during eye surgery. *Anesth Analg.* 2005;100(6):1651-2.
142. Lin SM, Chang WK, Tsao CM, Ou CH, Chan KH, Tsai SK. Carbon dioxide embolism diagnosed by transesophageal echocardiography during endoscopic vein harvesting for coronary artery bypass grafting. *Anesth Analg.* 2003;96(3):683-5, table of contents.
143. Sherlock S, Shearer WA, Buist M, Rasiah R, Edwards A. Carbon dioxide embolism following diagnostic hysteroscopy. *Anaesth Intensive Care.* 1998;26(6):674-6.
144. Imasogie N, Crago R, Leyland NA, Chung F. Probable gas embolism during operative hysteroscopy caused by products of combustion. *Can J Anaesth.* 2002;49(10):1044-7.
145. Michenfelder JD, Martin JT, Altenburg BM, Rehder K. Air embolism during neurosurgery. An evaluation of right-atrial catheters for diagnosis and treatment. *JAMA.* 1969;208:1353-8.
146. Fong J, Gadalla F, Gimbel AA. Precordial Doppler diagnosis of haemodynamically compromising air embolism during caesarean section. *Can J Anaesth.* 1990;37(2):262-4.
147. Jolliffe MP, Lyew MA, Berger IH, Grimaldi T. Venous air embolism during radical perineal prostatectomy. *J Clin Anesth.* 1996;8(8):659-61.
148. Albin MS, Ritter RR, Reinhart R, Erickson D, Rockwood A. Venous air embolism during radical retropubic prostatectomy. *Anesth Analg.* 1992;74(1):151-3.
149. Razvi HA, Chin JL, Bhandari R. Fatal air embolism during radical retropubic prostatectomy. *J Urol.* 1994;151(2):433-4.
150. Lang SA, Duncan PG, Dupuis PR. Fatal air embolism in an adolescent with Duchenne muscular dystrophy during Harrington instrumentation. *Anesth Analg.* 1989;69(1):132-4.
151. Wills J, Schwend RM, Paterson A, Albin MS. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine.* 2005;30(20):E629-35.
152. Andersen KH. Air aspirated from the venous system during total hip replacement. *Anaesthesia.* 1983;38(12):1175-8.
153. Lee SY, Choi BI, Kim JS, Park KS. Paradoxical air embolism during hepatic resection. *Br J Anaesth.* 2002;88(1):136-8.
154. Olmedilla L, Garutti I, Perez-Pena J, Sanz J, Teigell E, Avellaneda M. Fatal paradoxical air embolism during liver transplantation. *Br J Anaesth.* 2000;84(1):112-4.
155. Davies JM, Campbell LA. Fatal air embolism during dental implant surgery: a report of three cases. *Can J Anaesth.* 1990;37(1):112-21.
156. Burrowes P, Wallace C, Davies JM, Campbell L. Pulmonary edema as a radiologic manifestation of venous air embolism secondary to dental implant surgery. *Chest.* 1992;101(2):561-2.
157. Phillips YY. Primary blast injuries. *Ann Emerg Med.* 1986;15(12):1446-50.
158. Pao BS, Hayden SR. Cerebral gas embolism resulting from inhalation of pressurized helium [published erratum appears in Ann Emerg Med 1996 Nov;28(5):588]. *Ann Emerg Med.* 1996;28(3):363-6.

## **Chapter 2A: Arterial Insufficiencies: Central Retinal Artery Occlusion**

*Heather Murphy-Lavoie MD, Frank Butler MD, Catherine Hagan MD*

### **REFERENCES**

1. Cibis GW, Beaver HA, Johns K, et al. Fundamentals and principles of ophthalmology (basic and clinical science course). San Francisco, CA: American Academy of Ophthalmology; 2006. Pp. 38-40.
2. Patz A. Oxygen inhalation in retinal arterial occlusion. Am J Ophthalmol. 1955;40:789-795.
3. Li HK, Dejean BJ, Tang RA. Reversal of visual loss with hyperbaric oxygen treatment in a patient with Susac Syndrome. Ophthalmology. 1996;103(12):2091-2098.
4. Stone R, Zink H, Klingele T, Burde R. Visual recovery after central retinal artery occlusion: two cases. Ann Ophthalmol. 1977;9:445-450.
5. Hayreh SS, Zimmerman MB. Central retinal artery occlusion: visual outcome. Am J Ophthalmol. 2005;140:376-391.
6. David NJ, Norton EWD, Gass JD, Beauchamp J. Fluorescein angiography in central retinal artery occlusion. Arch Ophthal. 1967;77:619-629.
7. Duker JS, Brown GC. Recovery following acute obstruction of the retinal and choroidal circulations. Retina. 1988;8(4):257-260.
8. Hertzog LM, Meyer GW, Carson S, Strauss MB, Hart GB. Central retinal artery occlusion treated with hyperbaric oxygen. J Hyperbaric Medicine. 1992;7:33-42.
9. Jain KK, editor. Textbook of hyperbaric medicine. 4th ed. Cambridge, MA: Hogrefe & Huber Publishers; 2004. Pp. 383- 392.
10. Murphy-Lavoie H, Harch P, VanMeter K. Effect of hyperbaric oxygen on central retinal artery occlusion (abstract). UHMS Scientific Assembly, Australia; 2004.
11. Anderson B, Saltzman H, Heyman A. The effects of hyperbaric oxygenation on retinal arterial occlusion. Arch Ophthal. 1965;73:315-319.
12. Augsburger JJ, Magargal LE. Visual prognosis following treatment of acute central retinal artery obstruction. Br J Ophthalmol. 1980;64:913-917.
13. Miyake Y, Horiguchi M, Matsuura M, et al. Hyperbaric oxygen therapy in 72 eyes with retinal arterial occlusion. In: The 9th international symposium on underwater and hyperbaric physiology. Bethesda, MD: Undersea and Hyperbaric Medical Society; 1987. Pp. 949-953.
14. Yotsukura J, Adachi-Usami E. Correlation of electro-retinographic changes with visual prognosis in central retinal artery occlusion. Ophthalmologica. 1993;207:13-18.
15. Roy M, Bartow W, Ambrus J, Fauci A, Collier B, Titus J. Retinal leakage in retinal vein occlusion: reduction after hyperbaric oxygen. Ophthalmologica. 1989;198:78-83.
16. Miyake Y, Awaya S, Takahashi H, et al. Hyperbaric oxygen and acetazolamide improve visual acuity in patients with cystoid macular edema by different mechanisms. Arch Ophthalmol. 1993;111:1605-1606.
17. Schmidt D. Ocular massage in a case of central retinal artery occlusion the successful treatment of a hitherto undescribed type of embolism. Eur J Med Res. 2000 Apr 19;5(4):157-164.
18. Beard T, Warriner RA, Pasceri P, et al. Adverse events during hyperbaric oxygen therapy (HBOT), a retrospective analysis from 25 centers (abstract). Undersea Hyperbaric Medical Society Annual Scientific Meeting, Las Vegas, NV; 2005.
19. Telander G, Hielweil G, Schwartz S, Butler F. Diagnostic and therapeutic challenges. Retina. 2011;31(8):1726-1731.
20. Gaydar V, Ezraichi D, Dratviman-Storobinsky O, et al. Invest Ophthalmol Vis Sci. 2011;52:7514-7522.
21. Neubauer AS, Mueller AJ, Schriever S, Gruterich M, Ulbig M, Kampik A. Minimally invasive therapy for clinically complete central retinal artery occlusion-results and meta-analysis of literature. Klin Monatsbl Augenheilkd. 2000 Jul;217(1):30-36.
22. Hayreh SS, Podhajsky P. Ocular neovascularization with retinal vascular occlusion: II. Occurrence in central retinal and branch retinal artery occlusion. Arch Ophthalmol. 1982;100:1581-1596.
23. Weber J, Remonda L, Mattle HP, et al. Selective intra-arterial fibrinolysis of acute central retinal artery occlusion. Stroke. 1998;29:2076-2079.
24. Rumelt S, Dorenboim Y, Rehany U. Aggressive systematic treatment for central retinal artery occlusion. Am J Ophthalmol. 1999;128:733-738.
25. Petterson JA, Hill MD, Demchuk AM, et al. Intra-arterial thrombolysis for retinal artery occlusion: The Calgary experience. Can J Neurol Sci. 2005;32:507-511.
26. Garcia-Arumi J, Martinez-Castillo V, Boixadera A, Fonollosa A, Corcostgui B. Surgical embolus removal in retinal artery occlusion. Br J Ophthalmol. 2006;90:1252-1255.
27. Tang WM, Han DP. A study of surgical approaches to retinal vascular occlusions. Arch Ophthalmol. 2000;118:138-143.
28. Mangat HS. Retinal artery occlusion. Surv Ophthalmol. 1995;40:145-156.
29. Butler FK. The eye in the wilderness. In: Auerbach PS, editor. Wilderness medicine. 5th ed. St Louis:MO, Mosby; 2007.

30. Saltzman HA, Hart L, Sieker HO, Duffy EJ. Retinal vascular response to hyperbaric oxygenation. *JAMA*. 1965;191(4):114-116.
31. Haddad HM, Leopold IH. Effect of hyperbaric oxygenation on microcirculation: Use in therapy of retinal vascular disorders. *Invest Ophthalmol*. 1965;4:1141-1151.
32. Yu DY, Cringle SJ. Retinal degeneration and local oxygen metabolism. *Exp Eye Res*. 2005;80:745-751.
33. Phillips D, Diaz C, Atwell G, Chimiak J, Ullman S, et al. Care of sudden blindness: a case report of acute central retinal artery occlusion reversed with hyperbaric oxygen therapy (abstract). *Undersea Hyperb Med*. 1999;26(suppl):23-24.
34. Hayreh SS, Kolder HE, Weingeist TA. Central retinal artery occlusion and retinal tolerance time. *Ophthalmology*. 1980;87(1):75-78.
35. Zhang XZ, Cao JQ. Observations on therapeutic results in 80 cases of central serous retinopathy treated with hyperbaric oxygenation. Presented at the 5th Chinese conference on hyperbaric medicine, Fuzhou, China; 1986 Sept 26-29.
36. Matsuo T. Multiple occlusive retinal arteritis in both eyes of a patient with rheumatoid arthritis. *Jpn J Ophthalmol*. 2001;45:662-664.
37. Beiran I, Reissman P, Scharf J, Nahum Z, Miller B. Hyperbaric oxygenation combined with nifedipine treatment for recent-onset retinal artery occlusion. *Eur J Ophthalmol*. 1993;3(2):89-94.
38. Perkins SA, Magargal LE, Augsburger JJ, Sanborn GE. The idling retina: reversible visual loss in central retinal artery obstruction. *Ann Ophthalmol*. 1987;19:3-6.
39. Beiran I, Goldenberg I, Adir Y, Tamir A, Shupak A, Miller B. Early hyperbaric oxygen therapy for retinal artery occlusion. *Eur J Ophthalmol*. 2001 Oct-Dec;11(4):345-350.
40. Gool VJ, De Jong H. Hyperbaric oxygen treatment in vascular insufficiency of the retina and optic nerve. In: Ledingham IM, editor. *Proceedings of the second international congress on clinical and applied hyperbaric medicine*. Edinburgh: Churchill Livingstone; 1964. Pp. 447-460.
41. Takahashi K, Shima T, Yamamoto M. Hyperbaric oxygenation following stellate ganglion block in patients with retinal artery occlusion. In: Smith G, editor. *Proceedings of the sixth international congress on hyperbaric medicine*. Aberdeen: University of Aberdeen Press; 1977. Pp. 211-215.
42. Pallotta R, Anceschi S, Costagliola N, et al. Recovery from blindness through hyperbaric oxygen in a case of thrombosis on the central retinal artery. *Ann Med Nav*. 1978;83:591-592.
43. Sasaki K, Fukuda M, Otani S, et al. High pressure oxygen therapy in ocular diseases: With special reference to the effect of concomitantly used stellate ganglion block. *Jpn J Anesth*. 1978;27:170-176.
44. Suzuki H, Irie J, Horiuchi T, Fukada J, Matsuzaki H. Hyperbaric oxygenation therapy in ophthalmology. Part 1: Incipient insufficiency of the retinal circulation. *Jpn Clin Ophthalmol*. 1980;34:335-343.
45. Krasnov MM, Kharlap SI, Pereverzina OK, et al. Hyperbaric oxygen in the treatment of vascular disease of the retina. In: Yefunny SN, editor. *Abstracts of the seventh international congress on hyperbaric medicine*. Moscow: USSR Academy of Sciences; 1981. Pp. 301-302.
46. Desola J. Hyperbaric oxygen therapy in acute occlusive retinopathies. In: Schmutz J, editor. *Proceedings of the first Swiss symposium on hyperbaric medicine*. Foundation for Hyperbaric Medicine. Basel; 1987. P. 333.
47. Kindwall EP, Goldmann RW. Hyperbaric medicine procedures. Milwaukee, WI: St. Luke's Medical Center; 1988.
48. Hirayama Y, Matsunaga N, Tashiro J, et al. Bifemelane in the treatment of central retinal artery or vein obstruction. *Clin Ther*. 1990;12:230-235.
49. Aisenbrey S, Krott R, Heller R, et al. Hyperbaric oxygen therapy in retinal artery occlusion. *Ophthalmologe*. 2000;97:461-467.
50. Weinberger AWA, Siekmann UPF, Wolf S, et al. Treatment of acute central retinal artery occlusion (CRAO) by hyperbaric oxygenation therapy (HBO) - a pilot study with 21 patients. *Klin Monatsbl Augenheilkd*. 2002;219:728-734.
51. Imai E, Kunikata H, Udono T, et al. Branch artery occlusion: A complication of iron-deficiency anemia in a young adult with a rectal carcinoid. *Tohoku J Exp Med*. 2004; 203:141-144.
52. Swaby K, Valderrama O, Schiffman J (2005) Treatment of Disc Edema and Retinal Artery Occlusion With Hbo During the Third Trimester of Pregnancy. UHMS Annual Scientific Assembly, Las Vegas, 2005. (Abstract)
53. Weiss JN. Hyperbaric oxygen treatment of nonacute central retinal artery occlusion. *Undersea Hyperb Med*. 2009;36(6):401-405.
54. Inoue, O; Kajiya, S; Yachimori, (2009) Treatment Of Central Retinal Artery Occlusion(Crao) And Branch Retinal Artery Occlusion (Brao) By Hyperbaric Oxygen Therapy(Hbo) - 107 Eyes Over 20 Years. UHMS Annual Scientific Assembly, Las Vegas, 2009. (Abstract)
55. Weiss JN. Hyperbaric oxygen treatment of retinal artery occlusion. *Undersea Hyperb Med*. 2010;37(3):167-172.

56. Aten, LA; Stone, JA; Poli, (2011) T. Treatment of a patient with acute central retinal artery occlusion with hyperbaric oxygen therapy. UHMS Annual Scientific Assembly, Ft Worth, 2011. (Abstract)
57. Cope A, Eggert J, O'Brien E. Retinal artery occlusion: visual outcome after treatment with hyperbaric oxygen. *Diving Hyperb Med.* 2011;40(3):135-138.
58. Menzel-Severing J, Siekmann U, Weinberger A, et al. Early hyperbaric oxygen treatment for nonarteritic central retinal artery obstruction. *Am J Ophthalmol.* 2012;153:454-459.
59. Oguz H, Sobaci G. The use of hyperbaric oxygen in ophthalmology. *Surv Ophthalmol.* 2008;53:112-120.
60. Weiss JN. Treatment of central retinal artery occlusions. *Undersea Hyperb Med.* 2010;37(1):51-53; author reply 54-55.
61. Murphy-Lavoie H, Butler FK. Response to: treatment of central retinal artery occlusions. *Undersea Hyperb Med.* 2010;37(1):54-55.
62. Gibbons RJ, Smith S, Antman E. American College of Cardiology; American Heart Association: American College of Cardiology/American Heart Association clinical practice guidelines: Part I. Where do they come from? *Circulation.* 2003;107:2979-2986.
63. Butler FK, Hagan C, Murphy-Lavoie H. Hyperbaric oxygen therapy and the eye. *Undersea Hyperb Med.* 2008;35:333-387 .
64. Canan H, Ulas B, Altan-Yaycioglu R.(2014) Hyperbaric oxygen therapy in combination with systemic treatment of sickle cell disease presenting as central retinal artery occlusion: a case report. *Journal of Medical Case Reports* 2014;8:370.
65. Hsaio S, Huang Y. (2014) Partial vision recovery after iatrogenic retinal artery occlusion. *Ophthalmology* 2014;14:120.
66. Masters T, Westgard B, Hendrikson S (2015) Central Retinal Artery Occlusion Treated with Hyperbaric Oxygen: A Retrospective Review. UHMS Annual Scientific Assembly, perMontreal, 2015. (Abstract)
67. Desola J, Papoutsidakis E, Martos P (2015) Hyperbaric oxygenation in the treatment of Central Retinal Artery Occlusions: An analysis of 214 cases following a prospective protocol. UHMS Annual Scientific Assembly, Montreal, 2015. (Abstract)
68. Lu C, Wang J, Zhou D (2015) Central retinal artery occlusion associated with persistent truncus arteriosus and single atrium: a case report. *BMC Ophthalmology* 2015; 15:137.
69. Lemos JA, Teixeira C, Carvalho R, et al. (2015) Combined Central Retinal Artery and Vein Occlusion Associated with Factor V Leiden Mutation and Treated with Hyperbaric Oxygen. *Case Rep Ophthalmol.* 2015 Dec 19;6(3):462-8.
70. Hwang K. (2016) Hyperbaric Oxygen Therapy to Avoid Blindness From Filler Injection. *J Craniofac Surg.* 2016 Nov; 27(8):2154-2155.
71. Olson EA, Lentz K. (2016) Central Retinal Artery Occlusion: A Literature Review and the Rationale for Hyperbaric Oxygen Therapy. *Mo Med.* 2016 Jan-Feb;113(1):53-7.
72. Tang P, Engel K, and Parke D (2016) Early Onset of Ocular Neovascularization After Hyperbaric Oxygen Therapy in a Patient with Central Retinal Artery Occlusion. *Ophthalmol Ther.* 2016; 5:263-269.
73. Elder M, Rawstron J, Davis M. Hyperbaric oxygen in the treatment of acute retinal artery occlusion. *Diving Hyperb Med.* 2017; 47:4, 233-238.
74. Hadanny A, Maliar A, Fishlev G, et al. (2017) Reversibility of retinal ischemia due to central retinal artery occlusion by hyperbaric oxygen. *Clin Ophthalmol.* 2017; 11: 115-125.
75. Butler F, Hagan C, Van Hoesen K, et al. Management of Central Retinal Artery Occlusion following successful Hyperbaric Oxygen Therapy: A Case Report. *Undersea Hyperb Med.* 2018; 45:1. 101-107.
76. Gunay C, Altin G, Kersin B, et al. A Rare Complication after Septoplasty: Visual Loss due to Right Retinal Artery Spasm. *J Craniofac Surg* 2018; 29: 466-468.
77. Karaman S, Ozkan B, Yazir Y. Comparison of Hyperbaric Oxygen versus Iloprost Treatment in an Experimental Rat Central Retinal Artery Occlusion Model. *Graefes Arch Clin Exp Ophthalmol.* 2016. 254: 2209-2215.
78. Murphy-Lavoie H, LeGros T, Butler FK, and Jain K. "Hyperbaric Oxygen Therapy and Ophthalmology." In Jain (Ed.), K.K. Jain Textbook of Hyperbaric Medicine, 6th Ed; Springer Publishing. 2016.
79. Youn T, Lavin P, Patrylo M, et al. Current treatment of central retinal artery occlusion: a national survey. *J Neuro.* 2018; 265: 330-335.
80. Callizo J, Feltgen N, Pantenburg S. Cardiovascular Risk Factors in Central Retinal Artery Occlusion: Results of a Prospective Standardized Medical Exam. *Ophthalmology* 2015; 122:1881-1888.
81. Wagner B, Lindenbaum E, Logue C. Rethinking the Standard of Care for Patients with Central Retinal Artery Occlusion. *Ann Emer Med.* 2017; 70:4, Suppl. Pp.S105.

## **Chapter 2B: Arterial Insufficiencies: Hyperbaric Oxygen Therapy for Selected Problem Wounds**

*Enoch T. Huang MD, MPH&TM, FUHM, FACEP, FACCWS,*

*Marvin Heyboer III MD, FUHM, FACEP, FACCWS, Davut J. Savaser MD, MPH, FAAEM, FACEP*

## **REFERENCES**

1. Hunt TK, Ellison EC, Sen CK. Oxygen: at the foundation of wound healing--introduction. *World J Surg.* 2004;28(3):291-293.
2. Janis JE, Harrison B. Wound healing: part I. Basic science. *Plast Reconstr Surg.* 2014;133(2):199e-207e.
3. Sen CK. Wound healing essentials: let there be oxygen. *Wound Repair Regen.* 2009;17(1):1-18.
4. Allen DB, Maguire JJ, Mahdavian M, et al. Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. *Arch Surg.* 1997;132(9):991-996.
5. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet.* 1972;135(4):561-567.
6. Hopf HW, Gibson JJ, Angeles AP, et al. Hyperoxia and angiogenesis. *Wound Repair Regen.* 2005;13(6):558-564.
7. Knighton DR, Silver IA, Hunt TK. Regulation of wound-healing angiogenesis-effect of oxygen gradients and inspired oxygen concentration. *Surgery.* 1981;90(2):262-270.
8. LaVan FB, Hunt TK. Oxygen and wound healing. *Clin Plast Surg.* 1990;17(3):463-472.
9. Knighton DR, Hunt TK, Scheuenstuhl H, Halliday BJ, Werb Z, Banda MJ. Oxygen tension regulates the expression of angiogenesis factor by macrophages. *Science.* 1983;221(4617):1283-1285.
10. Knighton DR, Fiegel VD, Halverson T, Schneider S, Brown T, Wells CL. Oxygen as an antibiotic. The effect of inspired oxygen on bacterial clearance. *Arch Surg.* 1990;125(1):97-100.
11. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. The effect of inspired oxygen on infection. *Arch Surg.* 1984;119(2):199-204.
12. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. A comparison of the effects of inspired oxygen concentration and antibiotic administration on in vivo bacterial clearance. *Arch Surg.* 1986;121(2):191-195.
13. Ruthenborg RJ, Ban JJ, Wazir A, Takeda N, Kim JW. Regulation of wound healing and fibrosis by hypoxia and hypoxia-inducible factor-1. *Mol Cells.* 2014;37(9):637-643.
14. UHMS Position Statement: Topical Oxygen for Chronic Wounds. *Undersea Hyperb Med.* 2018;45(3):379-380.
15. Heughan C, Grislis G, Hunt TK. The effect of anemia on wound healing. *Ann Surg.* 1974;179(2):163-167.
16. Knighton DR, Fiegel VD. Macrophage-derived growth factors in wound healing: regulation of growth factor production by the oxygen microenvironment. *Am Rev Respir Dis.* 1989;140(4):1108-1111.
17. Hunt TK, Aslam RS. Oxygen 2002: wounds. *Undersea Hyperb Med.* 2004;31(1):147-153.
18. Hohn DC. Leukocyte phagocytic function and dysfunction. *Surg Gynecol Obstet.* 1977;144(1):99-104.
19. Babior BM. Oxygen-dependent microbial killing by phagocytes (first of two parts). *N Engl J Med.* 1978;298(12):659-668.
20. Babior BM. The respiratory burst of phagocytes. *J Clin Invest.* 1984;73(3):599-601.
21. Tizard J. Destruction of foreign material - the myeloid system, neutrophils. In: Immunology: an introduction. 3rd ed. Fort Worth, TX: Saunders College Publishing; 1992.
22. Silver IA. Tissue PO<sub>2</sub> changes in acute inflammation. *Adv Exp Med Biol.* 1978;94:769-774.
23. Hohn DC, MacKay RD, Halliday B, Hunt TK. Effect of O<sub>2</sub> tension on microbicidal function of leukocytes in wounds and in vitro. *Surg Forum.* 1976;27(62):18-20.
24. Niinikoski J. Effect of oxygen supply on wound healing and formation of experimental granulation tissue. *Acta Physiol Scand Suppl.* 1969;334:1-72.
25. Pai MP, Hunt TK. Effect of varying oxygen tensions on healing of open wounds. *Surg Gynecol Obstet.* 1972;135(5):756-758.
26. Kivilahti J, Vihersaari T, Renvall S, Niinikoski J. Energy metabolism of experimental wounds at various oxygen environments. *Ann Surg.* 1975;181(6):823-828.
27. Chang N, Goodson WH, 3rd, Gottrup F, Hunt TK. Direct measurement of wound and tissue oxygen tension in postoperative patients. *Ann Surg.* 1983;197(4):470-478.
28. Bullough WS, Johnson M. Epidermal mitotic activity and oxygen tension. *Nature.* 1957;167:488.
29. Udenfriend S. Formation of hydroxyproline in collagen. *Science.* 1966;152:1335.
30. Velazquez OC. Angiogenesis and vasculogenesis: inducing the growth of new blood vessels and wound healing by stimulation of bone marrow-derived progenitor cell mobilization and homing. *J Vasc Surg.* 2007;45 Suppl A:A39-47.
31. Thom SR, Milovanova TN, Yang M, et al. Vasculogenic stem cell mobilization and wound recruitment in diabetic patients: increased cell number and intracellular regulatory protein content associated with hyperbaric oxygen therapy. *Wound Repair Regen.* 2011;19(2):149-161.
32. Winter G, Perrins D. Effects of hyperbaric oxygen treatment on epidermal regeneration. Paper presented at: Fourth International Congress on Hyperbaric Medicine 1970; Tokyo.

33. Utkina O. Regeneration of the skin epithelium in healing wounds under noral conditions and at reduced baroetric pressure. *Biol Abs.* 1964;45:78585.
34. Broughton G, 2nd, Janis JE, Attinger CE. Wound healing: an overview. *Plast Reconstr Surg.* 2006;117(7 Suppl):1e-S-32e-S.
35. Witte MB, Barbul A. General principles of wound healing. *Surg Clin North Am.* 1997;77(3):509-528.
36. Chvapil M, Hurich J, Mirejovska E. Effect of long-term hypoxia on protein synthesis in granuloma and in some organs in rats. *Proc Soc Exp Biol Med.* 1970;135(3):613-617.
37. Fife CE, Buyukcakir C, Otto G, Sheffield P, Love T, Warriner R, 3rd. Factors influencing the outcome of lower-extremity diabetic ulcers treated with hyperbaric oxygen therapy. *Wound Repair Regen.* 2007;15(3):322-331.
38. Fife CE, Buyukcakir C, Otto GH, et al. The predictive value of transcutaneous oxygen tension measurement in diabetic lower extremity ulcers treated with hyperbaric oxygen therapy: a retrospective analysis of 1,144 patients. *Wound Repair Regen.* 2002;10(4):198-207.
39. Fife CE, Smart DR, Sheffield PJ, Hopf HW, Hawkins G, Clarke D. Transcutaneous oximetry in clinical practice: consensus statements from an expert panel based on evidence. *Undersea Hyperb Med.* 2009;36(1):43-53.
40. Londahl M, Katzman P, Hammarlund C, Nilsson A, Landin-Olsson M. Relationship between ulcer healing after hyperbaric oxygen therapy and transcutaneous oximetry, toe blood pressure and ankle-brachial index in patients with diabetes and chronic foot ulcers. *Diabetologia.* 2011;54(1):65-68.
41. Londahl M. Hyperbaric oxygen therapy as adjunctive treatment of diabetic foot ulcers. *Med Clin North Am.* 2013;97(5):957-980.
42. Huang ET, Mansouri J, Murad MH, et al. A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers. *Undersea Hyperb Med.* 2015;42(3):205-247.
43. Margolis DJ, Gupta J, Hoffstad O, et al. Lack of effectiveness of hyperbaric oxygen therapy for the treatment of diabetic foot ulcer and the prevention of amputation: a cohort study. *Diabetes Care.* 2013;36(7):1961-1966.
44. Moon H, Strauss MB, La SS, Miller SS. The validity of transcutaneous oxygen measurements in predicting healing of diabetic foot ulcers. *Undersea Hyperb Med.* 2016;43(6):641-648.
45. Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol.* 2006;290(4):H1378-1386.
46. Heyboer M, 3rd, Milovanova TN, Wojcik S, et al. CD34+/CD45-dim stem cell mobilization by hyperbaric oxygen - changes with oxygen dosage. *Stem Cell Res.* 2014;12(3):638-645.
47. Heyboer M, Byrne J, Pons P, Wolner E, Seargent S, Wojcik SM. Use of in-chamber transcutaneous oxygen measurement to determine optimal treatment pressure in patients undergoing hyperbaric oxygen therapy. *Undersea Hyperb Med.* 2018;45(4):389-394.
48. Wormer BA, Huntington CR, Ross SW, et al. A prospective randomized double-blinded controlled trial evaluating indocyanine green fluorescence angiography on reducing wound complications in complex abdominal wall reconstruction. *J Surg Res.* 2016;202(2):461-472.
49. Colavita PD, Wormer BA, Belyansky I, et al. Intraoperative indocyanine green fluorescence angiography to predict wound complications in complex ventral hernia repair. *Hernia.* 2016;20(1):139-149.
50. Furukawa H, Hayashi T, Oyama A, et al. Effectiveness of intraoperative indocyanine-green fluorescence angiography during inguinal lymph node dissection for skin cancer to prevent postoperative wound dehiscence. *Surg Today.* 2015;45(8):973-978.
51. Wang HD, Singh DP. The use of indocyanine green angiography to prevent wound complications in ventral hernia repair with open components separation technique. *Hernia.* 2013;17(3):397-402.
52. Kitai T, Kawashima M, Fujii H, Mashima S, Shimahara Y. Indocyanine green fluorescence monitoring of perineal wound contamination in abdominoperineal resection: a preliminary report. *Surg Today.* 2011;41(8):1037-1040.
53. Johnson-Arbor K, Falola R, Kelty J, Barbour J, Attinger C. Use of indocyanine green fluorescent angiography in a hyperbaric patient with soft tissue radiation necrosis: a case report. *Undersea Hyperb Med.* 2017;44(3):273-278.
54. Arnold J, Marmolejo V. Visualization of angiogenesis and vasculogenesis in a late tissue radiation injury of the chest wall treated with adjuvant hyperbaric oxygen therapy using fluorescence angiography. *Undersea Hyperb Med.* 2019;46(1):5.
55. Kim D, Rao A, Kaplan S, et al. The use of indocyanine green fluorescence angiography to assess perfusion of chronic wounds undergoing hyperbaric oxygen therapy. *Undersea Hyperb Med.* 2018;45(6):9.
56. Huang E, Nichols T. Indocyanin green angiography results pre- and post-hyperbaric oxygen exposure. *Undersea Hyperb Med.* 2016;43(6):1.
57. Boerema I, Meyne NG, Brummelkamp WH, et al. [Life without blood]. *Ned Tijdschr Geneesk.* 1960;104:949-954.
58. Hopf HW, Rollins MD. Wounds: an overview of the role of oxygen. *Antioxid Redox Signal.* 2007;9(8):1183-1192.
59. Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg.* 2011;127 Suppl 1:131S-141S.

60. Thom SR. Oxidative stress is fundamental to hyperbaric oxygen therapy. *J Appl Physiol* (1985). 2009;106(3):988-995.
61. Schafer M, Werner S. Oxidative stress in normal and impaired wound repair. *Pharmacol Res*. 2008;58(2):165-171.
62. Dennog C, Gedik C, Wood S, Speit G. Analysis of oxidative DNA damage and HPRT mutations in humans after hyperbaric oxygen treatment. *Mutat Res*. 1999;431(2):351-359.
63. Dennog C, Hartmann A, Frey G, Speit G. Detection of DNA damage after hyperbaric oxygen (HBO) therapy. *Mutagenesis*. 1996;11(6):605-609.
64. Dennog C, Radermacher P, Barnett YA, Speit G. Antioxidant status in humans after exposure to hyperbaric oxygen. *Mutat Res*. 1999;428(1-2):83-89.
65. Rothfuss A, Dennog C, Speit G. Adaptive protection against the induction of oxidative DNA damage after hyperbaric oxygen treatment. *Carcinogenesis*. 1998;19(11):1913-1917.
66. Speit G, Dennog C, Eichhorn U, Rothfuss A, Kaina B. Induction of heme oxygenase-1 and adaptive protection against the induction of DNA damage after hyperbaric oxygen treatment. *Carcinogenesis*. 2000;21(10):1795-1799.
67. Speit G, Dennog C, Lampl L. Biological significance of DNA damage induced by hyperbaric oxygen. *Mutagenesis*. 1998;13(1):85-87.
68. Speit G, Dennog C, Radermacher P, Rothfuss A. Genotoxicity of hyperbaric oxygen. *Mutat Res*. 2002;512(2-3):111-119.
69. Juttner B, Scheinichen D, Bartsch S, et al. Lack of toxic side effects in neutrophils following hyperbaric oxygen. *Undersea Hyperb Med*. 2003;30(4):305-311.
70. Thom SR, Mendiguren I, Hardy K, et al. Inhibition of human neutrophil beta2-integrin-dependent adherence by hyperbaric O<sub>2</sub>. *Am J Physiol*. 1997;272(3 Pt 1):C770-777.
71. Thom SR. Functional inhibition of leukocyte B2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol*. 1993;123(2):248-256.
72. Marx RE, Ehler WJ, Tayapongsak P, Pierce LW. Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg*. 1990;160(5):519-524.
73. Svalestad J, Hellem S, Thorsen E, Johannessen AC. Effect of hyperbaric oxygen treatment on irradiated oral mucosa: microvessel density. *Int J Oral Maxillofac Surg*. 2015;44(3):301-307.
74. Svalestad J, Thorsen E, Vaagbo G, Hellem S. Effect of hyperbaric oxygen treatment on oxygen tension and vascular capacity in irradiated skin and mucosa. *Int J Oral Maxillofac Surg*. 2014;43(1):107-112.
75. Thom SR, Milavonova T. Hyperbaric oxygen therapy increases stem cell number and HIF-1 content in diabetics (Abstract). *Undersea Hyperb Med*. 2008;35(4):1.
76. Berra E, Roux D, Richard DE, Pouyssegur J. Hypoxia-inducible factor-1 alpha (HIF-1 alpha) escapes O<sub>2</sub>-driven proteasomal degradation irrespective of its subcellular localization: nucleus or cytoplasm. *EMBO Rep*. 2001;2(7):615-620.
77. Zhang Q, Chang Q, Cox RA, Gong X, Gould LJ. Hyperbaric oxygen attenuates apoptosis and decreases inflammation in an ischemic wound model. *J Invest Dermatol*. 2008;128(8):2102-2112.
78. Sheikh AY, Gibson JJ, Rollins MD, Hopf HW, Hussain Z, Hunt TK. Effect of hyperoxia on vascular endothelial growth factor levels in a wound model. *Arch Surg*. 2000;135(11):1293-1297.
79. Kang TS, Gorti GK, Quan SY, Ho M, Koch RJ. Effect of hyperbaric oxygen on the growth factor profile of fibroblasts. *Arch Facial Plast Surg*. 2004;6(1):31-35.
80. Lin S, Shyu KG, Lee CC, et al. Hyperbaric oxygen selectively induces angiopoietin-2 in human umbilical vein endothelial cells. *Biochem Biophys Res Commun*. 2002;296(3):710-715.
81. Sander AL, Henrich D, Muth CM, Marzi I, Barker JH, Frank JM. In vivo effect of hyperbaric oxygen on wound angiogenesis and epithelialization. *Wound Repair Regen*. 2009;17(2):179-184.
82. Bonomo SR, Davidson JD, Yu Y, Xia Y, Lin X, Mustoe TA. Hyperbaric oxygen as a signal transducer: upregulation of platelet derived growth factor-beta receptor in the presence of HBO<sub>2</sub> and PDGF. *Undersea Hyperb Med*. 1998;25(4):211-216.
83. Boykin JV, Jr., Baylis C. Hyperbaric oxygen therapy mediates increased nitric oxide production associated with wound healing: a preliminary study. *Adv Skin Wound Care*. 2007;20(7):382-388.
84. Godman CA, Chheda KP, Hightower LE, Perdrizet G, Shin DG, Giardina C. Hyperbaric oxygen induces a cytoprotective and angiogenic response in human microvascular endothelial cells. *Cell Stress Chaperones*. 2010;15(4):431-442.
85. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes*. 2005;54(6):1615-1625.
86. Dinh TL, Veves A. A review of the mechanisms implicated in the pathogenesis of the diabetic foot. *Int J Low Extrem Wounds*. 2005;4(3):154-159.
87. Catrina SB, Okamoto K, Pereira T, Brismar K, Poellinger L. Hyperglycemia regulates hypoxia-inducible factor-1alpha protein stability and function. *Diabetes*. 2004;53(12):3226-3232.

88. Gao W, Ferguson G, Connell P, et al. High glucose concentrations alter hypoxia-induced control of vascular smooth muscle cell growth via a HIF-1alpha-dependent pathway. *J Mol Cell Cardiol.* 2007;42(3):609-619.
89. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. *Diabetes Care.* 2003;26(5):1553-1579.
90. Rollins MD, Gibson JJ, Hunt TK, Hopf HW. Wound oxygen levels during hyperbaric oxygen treatment in healing wounds. *Undersea Hyperb Med.* 2006;33(1):17-25.
91. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med.* 1996;334(25):1642-1648.
92. Asano T, Kaneko E, Shinozaki S, et al. Hyperbaric oxygen induces basic fibroblast growth factor and hepatocyte growth factor expression, and enhances blood perfusion and muscle regeneration in mouse ischemic hind limbs. *Circ J.* 2007;71(3):405-411.
93. Gallagher KA, Liu ZJ, Xiao M, et al. Diabetic impairments in NO-mediated endothelial progenitor cell mobilization and homing are reversed by hyperoxia and SDF-1 alpha. *J Clin Invest.* 2007;117(5):1249-1259.
94. Goldstein LJ, Gallagher KA, Bauer SM, et al. Endothelial progenitor cell release into circulation is triggered by hyperoxia-induced increases in bone marrow nitric oxide. *Stem Cells.* 2006;24(10):2309-2318.
95. Liu ZJ, Velazquez OC. Hyperoxia, endothelial progenitor cell mobilization, and diabetic wound healing. *Antioxid Redox Signal.* 2008;10(11):1869-1882.
96. Camporesi, EM, Bosco, G. Mechanisms of action. In: Weaver, LK, ed. Hyperbaric Oxygen Therapy Committee Indications. 13<sup>th</sup> ed. North Palm Beach, Florida: Best Publishing Company. 2014;241-246.
97. Huang E, Heyboer M. Adjunctive hyperbaric oxygen therapy for diabetic foot ulcers. In: Whelan H, Kindwall E, eds. Hyperbaric Medicine Practice. 4<sup>th</sup> ed. North Palm Beach, Florida: Best Publishing Company; 2018.
98. Hart G, Strauss MB. Responses of ischaemic ulcerative conditions to OHP. Paper presented at: Sixth International Congress on Hyperbaric Medicine 1979; Aberdeen, Scotland.
99. Huang ET. Hyperbaric medicine today: an historically noble discipline challenged by loss of critical access and overutilization—an introduction to invited commentary. *Undersea Hyperb Med.* 2017;44(1):1-3.
100. Hart G, Strauss M. Responses of ischaemic ulcerative conditions to OHP. Proceedings of the Sixth International Congress on Hyperbaric Medicine. 1979:312-314.
101. Davis JC. The use of adjuvant hyperbaric oxygen in treatment of the diabetic foot. *Clin Podiatr Med Surg.* 1987;4(2):429-437.
102. Baroni G, Porro T, Faglia E, et al. Hyperbaric oxygen in diabetic gangrene treatment. *Diabetes Care.* 1987;10(1):81-86.
103. Oriani G, Meazza D, Favales F, Pizzi G, Aldeghi A, Faglia E. Hyperbaric Oxygen Therapy in Diabetic Gangrene. *Journal of Hyperbaric Medicine.* 1990;5(3):171-175.
104. Oriani G, Michael M, Meazza D, et al. Diabetic Foot and Hyperbaric Oxygen Therapy: A Ten-Year Experience. *Journal of Hyperbaric Medicine.* 1992;7(4):213-221.
105. Doctor N, Pandya S, Supe A. Hyperbaric oxygen therapy in diabetic foot. *Journal of postgraduate medicine.* 1992;38(3):112-114, 111.
106. Faglia E, Favales F, Aldeghi A, et al. Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer. A randomized study. *Diabetes Care.* 1996;19(12):1338-1343.
107. Fife C. Personal Communication about CMS approval of hyperbaric oxygen therapy for diabetic foot ulcers. 2014.
108. National Coverage Determination (NCD) for Hyperbaric Oxygen Therapy (20.29). In. Version 3 ed: Centers for Medicare and Medicaid Services; 1996.
109. Game F. Classification of diabetic foot ulcers. *Diabetes Metab Res Rev.* 2016;32 Suppl 1:186-194.
110. Wattel F, Mathieu D, Fossati P, Neviere R, Coget JM. Hyperbaric Oxygen in the Treatment of Diabetic Foot Lesions: Search for Predictive Healing Factors. *Journal of Hyperbaric Medicine.* 1991;6(4):263-268.
111. Faglia E, Favales F, Aldeghi A, et al. Change in major amputation rate in a center dedicated to diabetic foot care during the 1980s: prognostic determinants for major amputation. *Journal of diabetes and its complications.* 1998;12(2):96-102.
112. Strauss MB, Bryant BJ, Hart GB. Transcutaneous oxygen measurements under hyperbaric oxygen conditions as a predictor for healing of problem wounds. *Foot Ankle Int.* 2002;23(10):933-937.
113. Moon H, Strauss M, La S, Miller S. The validity of transcutaneous oxygen measurements in predicting healing of diabetic foot ulcers. *Undersea Hyperb Med.* 2016;43(6).
114. Kalani M, Jorneskog G, Naderi N, Lind F, Brismar K. Hyperbaric oxygen (HBO) therapy in treatment of diabetic foot ulcers. Long-term follow-up. *Journal of diabetes and its complications.* 2002;16(2):153-158.
115. Abidia A, Laden G, Kuhan G, et al. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. *Eur J Vasc Endovasc Surg.* 2003;25(6):513-518.
116. Kessler L, Bilbault P, Ortega F, et al. Hyperbaric oxygenation accelerates the healing rate of nonischemic chronic diabetic foot ulcers: a prospective randomized study. *Diabetes Care.* 2003;26(8):2378-2382.

117. Duzgun AP, Satir HZ, Ozozan O, Saylam B, Kulah B, Coskun F. Effect of hyperbaric oxygen therapy on healing of diabetic foot ulcers. *J Foot Ankle Surg.* 2008;47(6):515-519.
118. Londahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. *Diabetes Care.* 2010;33(5):998-1003.
119. Londahl M, Landin-Olsson M, Katzman P. Hyperbaric oxygen therapy improves health-related quality of life in patients with diabetes and chronic foot ulcer. *Diabet Med.* 2011;28(2):186-190.
120. Ma L, Li P, Shi Z, Hou T, Chen X, Du J. A prospective, randomized, controlled study of hyperbaric oxygen therapy: effects on healing and oxidative stress of ulcer tissue in patients with a diabetic foot ulcer. *Ostomy Wound Manage.* 2013;59(3):18-24.
121. Carter MJ, Fife CE, Bennett M. Comment on: Margolis et al. lack of effectiveness of hyperbaric oxygen therapy for the treatment of diabetic foot ulcer and the prevention of amputation: a cohort study. *Diabetes Care.* 2013;36:1961-1966. *Diabetes Care.* 2013;36(8):e131.
122. Margolis D. Personal communication about propensity scoring. 2013.
123. Margolis DJ, Gupta J, Hoffstad O, Papdopoulos M, Thom SR, Mitra N. Response to comments on: Margolis et al. Lack of effectiveness of hyperbaric oxygen therapy for the treatment of diabetic foot ulcer and the prevention of amputation: a cohort study. *Diabetes Care.* 2013;36:1961-1966. *Diabetes Care.* 2013;36(8):e132-133.
124. Fedorko L, Bowen JM, Jones W, et al. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. *Diabetes Care.* 2016.
125. Londahl M, Fagher K, Katzman P. Comment on Fedorko et al. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. *Diabetes Care.* 2016;39:392-399. *Diabetes Care.* 2016;39(8):e131-132.
126. Murad MH. Comment on Fedorko et al. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. *Diabetes Care.* 2016;39:392-399. *Diabetes Care.* 2016;39(8):e135.
127. Huang ET. Comment on Fedorko et al. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. *Diabetes Care.* 2016;39:392-399. *Diabetes Care.* 2016;39(8):e133-134.
128. LeDez K. Serious concerns about the Toronto hyperbaric oxygen for diabetic foot ulcer study. *Undersea Hyperb Med.* 2016;43(6):737-741.
129. Fedorko Study Subject #1121 Testimonial. <https://www.youtube.com/watch?v=1TPNBRHZe1Q> 2016.
130. Santema KTB, Stoekenbroek RM, Koolemay MJW, et al. Hyperbaric oxygen therapy in the treatment of ischemic lower-extremity ulcers in patients with diabetes: Results of the DAMO2CLES multicenter randomized clinical trial. *Diabetes Care.* 2018;41(1):112-119.
131. Huang E. Comment on Santema et al. Hyperbaric oxygen therapy in the treatment of ischemic lower-extremity ulcers in patients with diabetes: results of the DAMO2CLES multicenter randomized clinical trial. *Diabetes Care.* 2018;41:112-119. *Diabetes Care.* 2018;41(4):e61.
132. Santema KTB, Stoekenbroek RM, Koolemay MJW, Ubbink DT, Group DCS. Response to comments on Santema et al. Hyperbaric oxygen therapy in the treatment of ischemic lower-extremity ulcers in patients with diabetes: results of the DAMO2CLES multicenter randomized clinical trial. *Diabetes Care.* 2018;41:112-119. *Diabetes Care.* 2018;41(4):e62-e63.
133. Wunderlich RP, Peters EJ, Lavery LA. Systemic hyperbaric oxygen therapy: lower-extremity wound healing and the diabetic foot. *Diabetes Care.* 2000;23(10):1551-1555.
134. Bishop AJ, Mudge E. Diabetic foot ulcers treated with hyperbaric oxygen therapy: a review of the literature. *Int Wound J.* 2014;11(1):28-34.
135. Goldman RJ. Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. *PM & R : the journal of injury, function, and rehabilitation.* 2009;1(5):471-489.
136. Kranke P, Bennett MH, Martyn-St James M, Schnabel A, Debus SE. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database Syst Rev.* 2012;4:CD004123.
137. Liu R, Li L, Yang M, Boden G, Yang G. Systematic review of the effectiveness of hyperbaric oxygenation therapy in the management of chronic diabetic foot ulcers. *Mayo Clinic Proceedings.* 2013;88(2):166-175.
138. Murad MH, Altayar O, Bennett M, et al. Using GRADE for evaluating the quality of evidence in hyperbaric oxygen therapy clarifies evidence limitations. *J Clin Epidemiol.* 2014;67(1):65-72.
139. O'Reilly D, Pasricha A, Campbell K, et al. Hyperbaric Oxygen Therapy for Diabetic Ulcers: Systematic Review and Meta-Analysis. *International Journal of Technology Assessment in Health Care.* 2013;29(3):269-281.

140. Roeckl-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. *The British Journal of Surgery*. 2005;92(1):24-32.
141. Stoekenbroek RM, Santema TB, Legemate DA, Ubbink DT, van den Brink A, Koelemay MJ. Hyperbaric oxygen for the treatment of diabetic foot ulcers: a systematic review. *Eur J Vasc Endovasc Surg*. 2014;47(6):647-655.
142. Wang Z, Hasan R, Firwana B, et al. A systematic review and meta-analysis of tests to predict wound healing in diabetic foot. *J Vasc Surg*. 2016;63(2 Suppl):29S-36S e21-22.
143. Game FL, Hinchliffe RJ, Apelqvist J, et al. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes Metab Res Rev*. 2012;28 Suppl 1:119-141.
144. Wang C, Schwitzberg S, Berliner E, Zarin DA, Lau J. Hyperbaric oxygen for treating wounds: a systematic review of the literature. *Arch Surg*. 2003;138(3):272-279; discussion 280.
145. Clinical Practice Guidelines We Can Trust. In: Institute of Medicine of the National Academies; 2011.
146. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012;54(12):e132-173.
147. Diabetic foot problems: prevention and management. In: London: National Institute for Health and Care Excellence; 2015.
148. Game FL, Attinger C, Hartemann A, et al. IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes Metab Res Rev*. 2016;32 Suppl 1:75-83.
149. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. *J Vasc Surg*. 2016;63(2 Suppl):3S-21S.
150. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924-926.
151. Moffat AD, Worth ER, Weaver LK. Glycosylated hemoglobin and hyperbaric oxygen coverage denials. *Undersea Hyperb Med*. 2015;42(3):197-204.
152. Ennis W, Huang E, Gordon H. Impact of hyperbaric oxygen on more advanced Wagner Grades 3 and 4 diabetic foot ulcers: matching therapy to specific wound conditions. *Advances in Wound Care*. 2018;7(12):11.
153. Cianci P, Petrone G, Drager S, Lueders H, Lee H, Shapiro R. Salvage of the problem wound and potential amputation with wound care and adjunctive hyperbaric oxygen therapy: An economic analysis. *Journal of Hyperbaric Medicine*. 1988;3(3):127-141.
154. Cianci P, Petrone G, Green B. Adjunctive hyperbaric oxygen in the salvage of the diabetic foot. *Undersea Biomed Res*. 1991;18(Suppl):109.
155. Eggert JV, Worth ER, Van Gils CC. Cost and mortality data of a regional limb salvage and hyperbaric medicine program for Wagner Grade 3 or 4 diabetic foot ulcers. *Undersea Hyperb Med*. 2016;43(1):1-8.
156. Guo S, Counte MA, Gillespie KN, Schmitz H. Cost-effectiveness of adjunctive hyperbaric oxygen in the treatment of diabetic ulcers. *Int J Technol Assess Health Care*. 2003;19(4):731-737.
157. Hailey D, Jacobs P, Perry D, Chuck A, Morrison A, Boudreau R. Adjunctive hyperbaric oxygen therapy for diabetic foot ulcer: an economic analysis. Canadian Agency for Drugs and Technologies in Health; March 2007.
158. Lipsky BA, Berendt AR. Hyperbaric oxygen therapy for diabetic foot wounds: has hope hurdled hype? *Diabetes Care*. 2010;33(5):1143-1145.
159. Chuck AW, Hailey D, Jacobs P, Perry DC. Cost-effectiveness and budget impact of adjunctive hyperbaric oxygen therapy for diabetic foot ulcers. *Int J Technol Assess Health Care*. 2008;24(2):178-183.
160. Santema TB, Stoekenbroek RM, van Steekelenburg KC, van Hulst RA, Koelemay MJ, Ubbink DT. Economic outcomes in clinical studies assessing hyperbaric oxygen in the treatment of acute and chronic wounds. *Diving Hyperb Med*. 2015;45(4):228-234.
161. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-146.
162. Thomas DR. Managing peripheral arterial disease and vascular ulcers. *Clin Geriatr Med*. 2013;29(2):425-431.
163. Hopf HW, Ueno C, Aslam R, et al. Guidelines for the treatment of arterial insufficiency ulcers. *Wound Repair Regen*. 2006;14(6):693-710.
164. Tautenhahn J, Lobmann R, Koenig B, Halloul Z, Lippert H, Buerger T. The influence of polymorbidity, revascularization, and wound therapy on the healing of arterial ulceration. *Vasc Health Risk Manag*. 2008;4(3):683-689.
165. Marston WA, Davies SW, Armstrong B, et al. Natural history of limbs with arterial insufficiency and chronic ulceration treated without revascularization. *J Vasc Surg*. 2006;44(1):108-114.
166. Mlekusch W, Schillinger M, Sabeti S, Maca T, Ahmadi R, Minar E. Clinical outcome and prognostic factors for ischaemic ulcers treated with PTA in lower limbs. *Eur J Vasc Endovasc Surg*. 2002;24(2):176-181.

167. Milovanova TN, Bhopale VM, Sorokina EM, et al. Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo. *J Appl Physiol* (1985). 2009;106(2):711-728.
168. Capla JM, Ceradini DJ, Tepper OM, et al. Skin graft vascularization involves precisely regulated regression and replacement of endothelial cells through both angiogenesis and vasculogenesis. *Plast Reconstr Surg*. 2006;117(3):836-844.
169. Boger RH, Bode-Boger SM, Thiele W, Junker W, Alexander K, Frolich JC. Biochemical evidence for impaired nitric oxide synthesis in patients with peripheral arterial occlusive disease. *Circulation*. 1997;95(8):2068-2074.
170. Heyboer M, 3rd, Grant WD, Byrne J, et al. Hyperbaric oxygen for the treatment of nonhealing arterial insufficiency ulcers. *Wound Repair Regen*. 2014;22(3):351-355.
171. Angelis M, Wong LL, Myers SA, Wong LM. Calciphylaxis in patients on hemodialysis: a prevalence study. *Surgery*. 1997;122(6):1083-1089; discussion 1089-1090.
172. Podymow T, Wherrett C, Burns KD. Hyperbaric oxygen in the treatment of calciphylaxis: a case series. *Nephrol Dial Transplant*. 2001;16(11):2176-2180.
173. Coates T, Kirkland GS, Dymock RB, et al. Cutaneous necrosis from calcific uremic arteriolopathy. *Am J Kidney Dis*. 1998;32(3):384-391.
174. Budisavljevic MN, Cheek D, Ploth DW. Calciphylaxis in chronic renal failure. *J Am Soc Nephrol*. 1996;7(7):978-982.
175. Bhambri A, Del Rosso JQ. Calciphylaxis: a review. *J Clin Aesthet Dermatol*. 2008;1(2):38-41.
176. An J, Devaney B, Ooi KY, Ford S, Frawley G, Menahem S. Hyperbaric oxygen in the treatment of calciphylaxis: A case series and literature review. *Nephrology (Carlton)*. 2015;20(7):444-450.
177. Basile C, Montanaro A, Masi M, Pati G, De Maio P, Gismondi A. Hyperbaric oxygen therapy for calcific uremic arteriolopathy: a case series. *J Nephrol*. 2002;15(6):676-680.
178. Arenas MD, Gil MT, Gutierrez MD, et al. Management of calcific uremic arteriolopathy (calciphylaxis) with a combination of treatments, including hyperbaric oxygen therapy. *Clin Nephrol*. 2008;70(3):261-264.
179. Don BR, Chin AI. A strategy for the treatment of calcific uremic arteriolopathy (calciphylaxis) employing a combination of therapies. *Clin Nephrol*. 2003;59(6):463-470.
180. Dean SM, Werman H. Calciphylaxis: a favorable outcome with hyperbaric oxygen. *Vasc Med*. 1998;3(2):115-120.
181. Vassa N, Twardowski ZJ, Campbell J. Hyperbaric oxygen therapy in calciphylaxis-induced skin necrosis in a peritoneal dialysis patient. *Am J Kidney Dis*. 1994;23(6):878-881.
182. McCulloch N, Wojcik SM, Heyboer M, 3rd. Patient outcomes and factors associated with healing in calciphylaxis patients undergoing adjunctive hyperbaric oxygen therapy. *J Am Coll Clin Wound Spec*. 2015;7(1-3):8-12.
183. Baldwin C, Farah M, Leung M, et al. Multi-intervention management of calciphylaxis: a report of 7 cases. *Am J Kidney Dis*. 2011;58(6):988-991.
184. Hymes SR, Alousi AM, Cowen EW. Graft-versus-host disease: part I. Pathogenesis and clinical manifestations of graft-versus-host disease. *J Am Acad Dermatol*. 2012;66(4):515 e511-518; quiz 533-514.
185. Stussi G, Tsakiris DA. Late effects on haemostasis after hematopoietic stem cell transplantation. *Hamostaseologie*. 2012;32(1):63-66.
186. Biedermann BC, Sahner S, Gregor M, et al. Endothelial injury mediated by cytotoxic T lymphocytes and loss of microvessels in chronic graft versus host disease. *Lancet*. 2002;359(9323):2078-2083.
187. Gassas A, Wayne Evans A, Armstrong C, Doyle JJ. Open wound chronic skin graft-vs-host disease. Are these wounds ischemic? *Pediatr Transplant*. 2007;11(1):101-104.
188. Al-Waili NS, Butler GJ. Effects of hyperbaric oxygen on inflammatory response to wound and trauma: possible mechanism of action. *ScientificWorldJournal*. 2006;6:425-441.
189. Song XY, Sun LN, Zheng NN, Zhang HP. Effect of hyperbaric oxygen on acute graft-versus-host disease after allogeneic bone marrow transplantation. *Zhongguo Shi Yan Xue Ye Xue Za Zhi*. 2008;16(3):623-626.
190. Heyboer M, 3rd, Taylor J, Morgan M, Mariani P, Jennings S. The use of hyperbaric oxygen therapy in the treatment of non-healing ulcers secondary to graft-versus-host disease. *J Am Coll Clin Wound Spec*. 2013;5(1):14-18.
191. Tutrone WD, Green K, Weinberg JM, Caglar S, Clarke D. Pyoderma gangrenosum: dermatologic application of hyperbaric oxygen therapy. *J Drugs Dermatol*. 2007;6(12):1214-1219.
192. Hickman JG, Lazarus GS. Pyoderma gangrenosum: a reappraisal of associated systemic diseases. *Br J Dermatol*. 1980;102(2):235-237.
193. Powell FC, Su WP, Perry HO. Pyoderma gangrenosum: classification and management. *J Am Acad Dermatol*. 1996;34(3):395-409; quiz 410-392.
194. Brooklyn T, Dunnill G, Probert C. Diagnosis and treatment of pyoderma gangrenosum. *BMJ*. 2006;333(7560):181-184.
195. Prystowsky JH, Kahn SN, Lazarus GS. Present status of pyoderma gangrenosum. Review of 21 cases. *Arch Dermatol*. 1989;125(1):57-64.

196. Wolff K, Stingl G. Pyoderma gangrenosum. In: Freedberg E, ed. Fitzpatrick's dermatology in general medicine. New York, NY: McGraw-Hill, Health Professions Division; 2003:969-975.
197. Hurwitz RM, Haseman JH. The evolution of pyoderma gangrenosum. A clinicopathologic correlation. *Am J Dermatopathol.* 1993;15(1):28-33.
198. Fakhar F, Memon S, Deitz D, Abramowitz R, Alpert DR. Refractory postsurgical pyoderma gangrenosum in a patient with Beckwith Wiedemann syndrome: response to multimodal therapy. *BMJ Case Rep.* 2013;2013.
199. Niezgoda JA, Cabigas EB, Allen HK, Simanonok JP, Kindwall EP, Krumenauer J. Managing pyoderma gangrenosum: a synergistic approach combining surgical debridement, vacuum-assisted closure, and hyperbaric oxygen therapy. *Plast Reconstr Surg.* 2006;117(2):24e-28e.
200. Thomas CY, Jr., Crouch JA, Guastello J. Hyperbaric oxygen therapy for pyoderma gangrenosum. *Arch Dermatol.* 1974;110(3):445-446.
201. Fuhrman DL. Letter: Hyperbaric oxygen therapy. *Arch Dermatol.* 1975;111(5):657.
202. Wyrick WJ, Mader JT, Butler ME, Hulet WH. Hyperbaric oxygen treatment of pyoderma gangrenosum. *Arch Dermatol.* 1978;114(8):1232-1233.
203. Davis JC, Landeen JM, Levine RA. Pyoderma gangrenosum: skin grafting after preparation with hyperbaric oxygen. *Plast Reconstr Surg.* 1987;79(2):200-207.
204. Wasserteil V, Bruce S, Sessoms SL, Guntupalli KK. Pyoderma gangrenosum treated with hyperbaric oxygen therapy. *Int J Dermatol.* 1992;31(8):594-596.
205. Fitzpatrick D. Primary treatment of pyoderma gangrenosum with hyperbaric oxygen therapy: a case report. *Wounds.* 1997;9:4.
206. Jacobs P, Wood L, Van Niekerk GD. Therapy: hyperbaric oxygen as the only effective treatment in mutilating and resistant systemic vasculitis. *Hematology.* 2000;5(2):167-172.
207. Vieira WA, Barbosa LR, Martin LM. Hyperbaric oxygen therapy as an adjuvant treatment for pyoderma gangrenosum. *An Bras Dermatol.* 2011;86(6):1193-1196.
208. Hill DS, O'Neill JK, Toms A, Watts AM. Pyoderma gangrenosum: a report of a rare complication after knee arthroplasty requiring muscle flap cover supplemented by negative pressure therapy and hyperbaric oxygen. *J Plast Reconstr Aesthet Surg.* 2011;64(11):1528-1532.
209. Mazokopakis EE, Kofteridis DP, Pateromihelaki AT, Vytiniotis SD, Karastergiou PG. Improvement of ulcerative pyoderma gangrenosum with hyperbaric oxygen therapy. *Dermatol Ther.* 2011;24(1):134-136.
210. Altunay I, Kucukunal A, Sarikaya S, Tukenmez Demirci G. A favourable response to surgical intervention and hyperbaric oxygen therapy in pyoderma gangrenosum. *Int Wound J.* 2014;11(4):350-353.
211. Araujo FM, Kondo RN, Minelli L. Pyoderma gangrenosum: skin grafting and hyperbaric oxygen as adjuvants in the treatment of a deep and extensive ulcer. *An Bras Dermatol.* 2013;88(6 Suppl 1):176-178.
212. Ratnagobal S, Sinha S. Pyoderma gangrenosum: guideline for wound practitioners. *J Wound Care.* 2013;22(2):68-73.
213. Seo HI, Lee HJ, Han KH. Hyperbaric oxygen therapy for pyoderma gangrenosum associated with ulcerative colitis. *Intest Res.* 2018;16(1):155-157.
214. Chiang IH, Liao YS, Dai NT, et al. Hyperbaric oxygen therapy for the adjunctive treatment of pyoderma gangrenosum: a case report. *Ostomy Wound Manage.* 2016;62(5):32-36.
215. Feitosa MR, Feres Filho O, Tamaki CM, et al. Adjunctive hyperbaric oxygen therapy promotes successful healing in patients with refractory Crohn's disease. *Acta Cir Bras.* 2016;31 Suppl 1:19-23.
216. Moran ME. Scleroderma and evidence based non-pharmaceutical treatment modalities for digital ulcers: a systematic review. *J Wound Care.* 2014;23(10):510-516.
217. Dowling GB, Copeman PW, Ashfield R. Raynaud's phenomenon in scleroderma treated with hyperbaric oxygen. *Proc R Soc Med.* 1967;60(12):1268-1269.
218. Chun W, Kim S, Seong H, Chong T. Hyperbaric oxygen therapy in systemic scleroderma. *Korean J Dermatol.* 1974;12(1):4.
219. Slade B. The Effect of hyperbaric oxygen therapy (HBO) on wound healing in patients with collagen-vascular disease: a retrospective analysis. *Undersea Biomed Res.* 1991;18(Suppl):1.
220. Wallace DJ, Silverman S, Goldstein J, Hughes D. Use of hyperbaric oxygen in rheumatic diseases: case report and critical analysis. *Lupus.* 1995;4(3):172-175.
221. Hafner J, Kohler A, Enzler M, Brunner U. Successful treatment of an extended leg ulcer in systemic sclerosis. *Vasa.* 1997;26(4):302-304.
222. Markus YM, Bell MJ, Evans AW. Ischemic scleroderma wounds successfully treated with hyperbaric oxygen therapy. *J Rheumatol.* 2006;33(8):1694-1696.
223. Gerodimos C, Stefanidou S, Kotsiou M, Melekos T, Mesimeris T. Hyperbaric oxygen treatment of intractable ulcers in a systemic sclerosis patient. *Aristotle University Medical Journal.* 2013;40(3):4.

224. Li Y, Pang J, Miao L, Yu M. The long-term effect of hyperbaric oxygen therapy on systemic sclerosis. Guide of China Medicine. 2013.
225. Poirier E, Wind H, Cordel N. [Efficacy of hyperbaric oxygen therapy in the treatment of ischemic toe ulcer in a patient presenting systemic sclerosis]. Ann Dermatol Venereol. 2017;144(1):55-59.
226. Mirasoglu B, Bagli BS, Aktas S. Hyperbaric oxygen therapy for chronic ulcers in systemic sclerosis - case series. Int J Dermatol. 2017;56(6):636-640.
227. Campton-Johnston S, Wilson J, Ramundo JM. Treatment of painful lower extremity ulcers in a patient with sickle cell disease. J Wound Ostomy Continence Nurs. 1999;26(2):98-104.
228. Wethers DL, Ramirez GM, Koshy M, et al. Accelerated healing of chronic sickle-cell leg ulcers treated with RGD peptide matrix. RGD Study Group. Blood. 1994;84(6):1775-1779.
229. Freilich DB, Seelenfreund MH. Hyperbaric oxygen, retinal detachment, and sickle cell anemia. Arch Ophthalmol. 1973;90(2):90-93.
230. Laszlo J, Obenour W, Jr., Saltzman HA. Effects of hyperbaric oxygenation on sickle syndromes. South Med J. 1969;62(4):453-456.
231. Wallyn CR, Jampol LM, Goldberg MF, Zanetti CL. The use of hyperbaric oxygen therapy in the treatment of sickle cell hyphema. Invest Ophthalmol Vis Sci. 1985;26(8):1155-1158.
232. Mychaskiw G, 2nd, Woodyard SA, Brunson CD, May WS, Eichhorn JH. In vitro effects of hyperbaric oxygen on sickle cell morphology. J Clin Anesth. 2001;13(4):255-258.
233. Rudge FW. Hyperbaric oxygen therapy in the treatment of sickle cell ulcers. Journal of Hyperbaric Medicine. 1991;6(1):1-4.
234. Desforges JF, Wang MY. Sickle cell anemia. Med Clin North Am. 1966;50(6):1519-1532.
235. Reynolds JD. Painful sickle cell crisis. Successful treatment with hyperbaric oxygen therapy. JAMA. 1971;216(12):1977-1978.
236. Stirnemann J, Letellier E, Aras N, Borne M, Brinquin L, Fain O. Hyperbaric oxygen therapy for vaso-occlusive crises in nine patients with sickle-cell disease. Diving Hyperb Med. 2012;42(2):82-84.
237. Azik FM, Atay A, Kurekci AE, Ay H, Kibar Y, Ozcan O. Treatment of Priapism with Automated Red Cell Exchange and Hyperbaric Oxygen in an 11-year-old Patient with Sickle Cell Disease. Turk J Haematol. 2012;29(3):270-273.
238. Canan H, Ulas B, Altan-Yaycioglu R. Hyperbaric oxygen therapy in combination with systemic treatment of sickle cell disease presenting as central retinal artery occlusion: a case report. J Med Case Rep. 2014;8:370.
239. Takahashi PY, Kiemele LJ, Jones JP, Jr. Wound care for elderly patients: advances and clinical applications for practicing physicians. Mayo Clinic Proceedings. 2004;79(2):260-267.
240. Valencia IC, Falabella A, Kirsner RS, Eaglstein WH. Chronic venous insufficiency and venous leg ulceration. J Am Acad Dermatol. 2001;44(3):401-421; quiz 422-404.
241. Amsler F, Willenberg T, Blattler W. In search of optimal compression therapy for venous leg ulcers: a meta-analysis of studies comparing diverse [corrected] bandages with specifically designed stockings. J Vasc Surg. 2009;50(3):668-674.
242. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. Br Med J (Clin Res Ed). 1985;290(6485):1855-1856.
243. London NJ, Donnelly R. ABC of arterial and venous disease. Ulcerated lower limb. BMJ. 2000;320(7249):1589-1591.
244. Burton CS, 3rd. Management of chronic and problem lower extremity wounds. Dermatol Clin. 1993;11(4):767-773.
245. Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. Plast Reconstr Surg. 1994;93(4):829-833; discussion 834.
246. Kranke P, Bennett M, Roeckl-Wiedmann I, Debus S. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev. 2004(2):CD004123.
247. Andrade SM, Santos IC. Hyperbaric oxygen therapy for wound care. Rev Gaucha Enferm. 2016;37(2):e59257.
248. Thistlethwaite KR, Finlayson KJ, Cooper PD, et al. The effectiveness of hyperbaric oxygen therapy for healing chronic venous leg ulcers: A randomized, double-blind, placebo-controlled trial. Wound Repair Regen. 2018;26(4):324-331.

## **Chapter 3: Carbon Monoxide Poisoning**

*Lindell K. Weaver MD*

### **REFERENCES**

1. Benzon HT, Claybon L, Brunner EA. Elevated carbon monoxide levels from exposure to methylene chloride. *JAMA*. 1978 Jun 2;239(22):2341.
2. Rioux JP, Myers RA. Hyperbaric oxygen for methylene chloride poisoning: report on two cases. *Ann Emerg Med*. 1989 Jun;18(6):691-695.
3. Huff JS, Kardon E. Carbon monoxide toxicity in a man working outdoors with a gasoline-powered hydraulic machine. *N Engl J Med*. 1989 Jun 8;320(23):1564.
4. DiMaio VJ, Dana SE. Deaths caused by carbon monoxide poisoning in an open environment (outdoors). *J Forensic Sci*. 1987 Nov;32(6):1794-1795.
5. Jumbelic MI. Open air carbon monoxide poisoning. *J Forensic Sci*. 1998 Jan;43(1):228-230.
6. Easley RB. Open air carbon monoxide poisoning in a child swimming behind a boat. *South Med J*. 2000 Apr;93(4):430-432.
7. Hampson NB, Holm JR, Courtney TG. Garage carbon monoxide levels from sources commonly used in intentional poisoning. *Undersea Hyperb Med*. 2017 Jan-Feb;44(1):11-15.
8. Winder C. Carbon monoxide-induced death and toxicity from charcoal briquettes. *Med J Aust*. 2012 Sep 17;197(6):349-350.
9. Hampson NB, Dunn SL, UHMS CDC CO Poisoning Surveillance Group. Symptoms of carbon monoxide poisoning do not correlate with the initial carboxyhemoglobin level. *Undersea Hyperb Med*. 2012 Mar-Apr;39(2):657-665.
10. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2002 Oct 3;347(14):1057-1067.
11. Weaver LK. Clinical practice. Carbon monoxide poisoning. *N Engl J Med*. 2009 Mar 19;360(12):1217-1225.
12. Hampson NB, Piantadosi CA, Thom SR, Weaver LK. Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. *Am J Respir Crit Care Med*. 2012 Dec 1;186(11):1095-1101.
13. Rose JJ, Wang L, Xu Q, et al. Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy. *Am J Respir Crit Care Med*. 2017 Mar 1;195(5):596-606.
14. Penney D, Benignus V, Kephalopoulos S, Kotzias D, Kleinman M, Verrier A. Carbon monoxide. WHO guidelines for indoor air quality: selected pollutants. Bonn, Germany: WHO Regional Office for Europe; 2010. Pp. 55-102.
15. EPA. Air quality criteria for carbon monoxide. Research Triangle Park, NC: U.S. Environmental Protection Agency; 2000.
16. McGrath JJ. The interacting effects of altitude and carbon monoxide. In: Penney DG, editor. Carbon monoxide toxicity. Boca Raton, FL: CRC Press LLC; 2000. Pp. 135-156.
17. Reh CM, Deitchman SD. Health Hazard Evaluation HETA 88-320-2176. U.S. National Institute for Occupational Safety and Health; 1992.
18. NIOSH. Criteria for a recommended standard occupational exposure to carbon monoxide. Cincinnati, OH: National Institute for Occupational Safety and Health; 1972.
19. 29 CFR 1910.1000.
20. NIOSH. 1988 OSHA PEL project documentation. Carbon monoxide. 1988 [updated September 28, 2011]. Available from: <http://www.cdc.gov/niosh/pel88/630-08.html>.
21. ACGIH. Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists; 2005.
22. National Research Council. Carbon monoxide. Emergency and continuous exposure guidance levels for selected submarine contaminants. Washington, D.C.: The National Academies Press; 2007. Pp. 67-702.
23. Yoon SS, Macdonald SC, Parrish RG. Deaths from unintentional carbon monoxide poisoning and potential for prevention with carbon monoxide detectors. *JAMA*. 1998 Mar 4;279(9):685-687.
24. Hampson NB, Courtney TG, Holm JR. Should the placement of carbon monoxide (CO) detectors be influenced by CO's weight relative to air? *J Emerg Med*. 2012 Apr;42(4):478-482.
25. Hampson NB, Courtney TG, Holm JR. Diffusion of carbon monoxide through gypsum wallboard. *JAMA*. 2013 Aug 21;310(7):745-746.
26. Underwriters Laboratories. UL 2034. Standard for safety. Single and multiple station carbon monoxide alarms. 4 ed. Northbrook, IL: Underwriters Laboratories, Inc.; 2017 March 31.
27. Penney DG. Essential reference tables, graphs, and other data. In: Penney DG, editor. Carbon Monoxide Poisoning. Boca Raton, FL: CRC Press; 2008. Pp. 753-764.
28. Kirkpatrick JN. Occult carbon monoxide poisoning. *West J Med*. 1987 Jan;146(1):52-56.

29. Penney DG. Chronic carbon monoxide poisoning: a case series. In: Penney DG, editor. Carbon monoxide poisoning. Boca Raton, FL: CRC Press; 2008. Pp. 551-567.
30. Penney DG. Chronic carbon monoxide poisoning. In: Penney DG, editor. Carbon monoxide toxicity. Boca Raton, FL: CRC Press; 2000. Pp. 393-418.
31. Weaver LK, Valentine KJ, Hopkins RO. Carbon monoxide poisoning: risk factors for cognitive sequelae and the role of hyperbaric oxygen. *Am J Respir Crit Care Med*. 2007 Sep 1;176(5):491-497.
32. Peterson JE, Stewart RD. Absorption and elimination of carbon monoxide by inactive young men. *Arch Environ Health*. 1970 Aug;21(2):165-171.
33. Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxyhemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. *Chest*. 2000 Mar;117(3):801-808.
34. Pace N, Strajman E, Walker EL. Acceleration of carbon monoxide elimination in man by high pressure oxygen. *Science*. 1950 Jun 16;111(2894):652-654.
35. Radford EP, Drizd TA. Blood carbon monoxide levels in persons 3-74 years of age: United States, 1976-80. *Adv Data*. 1982 Mar 17(76):1-24.
36. Touger M, Gallagher EJ, Tyrell J. Relationship between venous and arterial carboxyhemoglobin levels in patients with suspected carbon monoxide poisoning. *Ann Emerg Med*. 1995 Apr;25(4):481-483.
37. Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. *Chest*. 1998 Oct;114(4):1036-1041.
38. Suner S, Partridge R, Sucov A, et al. Non-invasive pulse CO-oximetry screening in the emergency department identifies occult carbon monoxide toxicity. *J Emerg Med*. 2008 May;34(4):441-450.
39. Chee KJ, Nilson D, Partridge R, et al. Finding needles in a haystack: a case series of carbon monoxide poisoning detected using new technology in the emergency department. *Clin Toxicol (Phila)*. 2008 Jun;46(5):461-469.
40. Weaver LK, Churchill SK, Deru K, Cooney D. False positive rate of carbon monoxide saturation by pulse oximetry of emergency department patients. *Respir Care*. 2013 Feb;58(2):232-240.
41. Roughton F, Darling R. The effect of carbon monoxide on oxyhemoglobin dissociation curve. *Am J Physiol*. 1944;141:17-31.
42. Thom SR, Ohnishi ST, Fisher D, Xu YA, Ischiropoulos H. Pulmonary vascular stress from carbon monoxide. *Toxicol Appl Pharmacol*. 1999 Jan 1;154(1):12-19.
43. Piantadosi CA, Zhang J, Demchenko IT. Production of hydroxyl radical in the hippocampus after CO hypoxia or hypoxic hypoxia in the rat. *Free Radic Biol Med*. 1997;22(4):725-732.
44. Zhang J, Piantadosi CA. Mitochondrial oxidative stress after carbon monoxide hypoxia in the rat brain. *J Clin Invest*. 1992 Oct;90(4):1193-1199.
45. Ishimaru H, Katoh A, Suzuki H, Fukuta T, Kameyama T, Nabeshima T. Effects of N-methyl-D-aspartate receptor antagonists on carbon monoxide-induced brain damage in mice. *J Pharmacol Exp Ther*. 1992 Apr;261(1):349-352.
46. Thom SR. Carbon monoxide-mediated brain lipid peroxidation in the rat. *J Appl Physiol*. 1990 Mar;68(3):997-1003.
47. Thom SR. Leukocytes in carbon monoxide-mediated brain oxidative injury. *Toxicol Appl Pharmacol*. 1993 Dec;123(2):234-247.
48. Ischiropoulos H, Beers MF, Ohnishi ST, Fisher D, Garner SE, Thom SR. Nitric oxide production and perivascular nitration in brain after carbon monoxide poisoning in the rat. *J Clin Invest*. 1996 May 15;97(10):2260-2267.
49. Piantadosi CA, Zhang J, Levin ED, Folz RJ, Schmehel DE. Apoptosis and delayed neuronal damage after carbon monoxide poisoning in the rat. *Exp Neurol*. 1997 Sep;147(1):103-114.
50. Meilin S, Rogatsky GG, Thom SR, Zarchin N, Guggenheim-Furman E, Mayevsky A. Effects of carbon monoxide on the brain may be mediated by nitric oxide. *J Appl Physiol*. 1996 Sep;81(3):1078-1083.
51. Thom SR, Bhopale VM, Han ST, Clark JM, Hardy KR. Intravascular neutrophil activation due to carbon monoxide poisoning. *Am J Respir Crit Care Med*. 2006 Dec 1;174(11):1239-1248.
52. Thom SR, Bhopale VM, Fisher D, Zhang J, Gimotty P. Delayed neuropathology after carbon monoxide poisoning is immune-mediated. *Proc Natl Acad Sci USA*. 2004 Sep 14;101(37):13660-13665.
53. Gorman DF, Huang YL, Williams C. Prolonged exposure to one percent carbon monoxide causes a leucoencephalopathy in un-anaesthetised sheep. *Toxicology*. 2001 Aug 28;165(2-3):97-107.
54. Beppu T, Fujiwara S, Nishimoto H, et al. Fractional anisotropy in the centrum semiovale as a quantitative indicator of cerebral white matter damage in the subacute phase in patients with carbon monoxide poisoning: correlation with the concentration of myelin basic protein in cerebrospinal fluid. *J Neurol*. 2012 Aug;259(8):1698-1705.
55. Xu J, Yang M, Kosterin P, et al. Carbon monoxide inhalation increases microparticles causing vascular and CNS dysfunction. *Toxicol Appl Pharmacol*. 2013 Dec 1;273(2):410-417.
56. Thom SR, Bhopale VM, Milovanova TM, et al. Plasma biomarkers in carbon monoxide poisoning. *Clin Toxicol (Phila)*. 2010 Jan;48(1):47-56.

57. Winter PM, Miller JN. Carbon monoxide poisoning. *JAMA*. 1976 Sep 27;236(13):1502.
58. Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. *Arch Neurol*. 1983 Jul;40(7):433-435.
59. Min SK. A brain syndrome associated with delayed neuropsychiatric sequelae following acute carbon monoxide intoxication. *Acta Psychiatr Scand*. 1986 Jan;73(1):80-86.
60. Smith G, Sharp GR. Treatment of carbon-monoxide poisoning with oxygen under pressure. *Lancet*. 1960;276(7156):905-906.
61. Goulon M, Barrios A, Rapin M, Nouailhat F, Grosbuis S, Labrousse J. Carbon monoxide poisoning and acute anoxia due to breathing coal gas and hydrocarbons. *J Hyperb Med*. 1986;1(1):23-41.
62. Myers RA, Snyder SK, Emhoff TA. Subacute sequelae of carbon monoxide poisoning. *Ann Emerg Med*. 1985 Dec;14(12):1163-1167.
63. Mathieu D, Wattel F, Mathieu-Nolf M, et al. Randomized prospective study comparing the effect of HBO versus 12 hours NBO in non comatose CO poisoned patients: results of the interim analysis. *Undersea Hyperb Med*. 1996;23(Suppl):7.
64. Chambers CA, Hopkins RO, Weaver LK, Key C. Cognitive and affective outcomes of more severe compared to less severe carbon monoxide poisoning. *Brain Inj*. 2008 May;22(5):387-395.
65. Rose JJ, Nouraie M, Gauthier MC, et al. Clinical Outcomes and Mortality Impact of Hyperbaric Oxygen Therapy in Patients With Carbon Monoxide Poisoning. *Crit Care Med*. 2018 Jul;46(7):e649-e655.
66. Ginsberg MD, Myers RE. Experimental carbon monoxide encephalopathy in the primate I. Physiologic and metabolic aspects. *Arch Neurol*. 1974 Mar;30(3):202-208.
67. Brown SD, Piantadosi CA. Recovery of energy metabolism in rat brain after carbon monoxide hypoxia. *J Clin Invest*. 1992 Feb;89(2):666-672.
68. Okeda R, Funata N, Song SJ, Higashino F, Takano T, Yokoyama K. Comparative study on pathogenesis of selective cerebral lesions in carbon monoxide poisoning and nitrogen hypoxia in cats. *Acta Neuropathol*. 1982;56(4):265-272.
69. Mayevsky A, Meilin S, Rogatsky GG, Zarchin N, Thom SR. Multiparametric monitoring of the awake brain exposed to carbon monoxide. *J Appl Physiol*. 1995 Mar;78(3):1188-1196.
70. Hopkins RO, Weaver LK, Larson LV, Howe S. Loss of consciousness (LOC) is not required for neurological sequelae due to CO poisoning. *Undersea Hyperb Med*. 1995;22(Suppl):14.
71. Thom SR, Fisher D, Xu YA, Garner S, Ischiropoulos H. Role of nitric oxide-derived oxidants in vascular injury from carbon monoxide in the rat. *Am J Physiol*. 1999 Mar;276(3 Pt 2):H984-992.
72. Thom SR, Garner S, Fisher D, Ischiropoulos H. Vascular nitrosative stress from CO exposure. *Undersea Hyperb Med*. 1998;25(Suppl):47.
73. Cramlet SH, Erickson HH, Gorman HA. Ventricular function following acute carbon monoxide exposure. *J Appl Physiol*. 1975 Sep;39(3):482-486.
74. Anderson EW, Andelman RJ, Strauch JM, Fortuin NJ, Knelson JH. Effect of low-level carbon monoxide exposure on onset and duration of angina pectoris. A study in ten patients with ischemic heart disease. *Ann Intern Med*. 1973 Jul;79(1):46-50.
75. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. *JAMA*. 2006 Jan 25;295(4):398-402.
76. Hampson NB, Rudd RA, Hauff NM. Increased long-term mortality among survivors of acute carbon monoxide poisoning. *Crit Care Med*. 2009 Jun;37(6):1941-1947.
77. Gorman DF, Clayton D, Gilligan JE, Webb RK. A longitudinal study of 100 consecutive admissions for carbon monoxide poisoning to the Royal Adelaide Hospital. *Anaesth Intensive Care*. 1992 Aug;20(3):311-316.
78. Hardy KR, Thom SR. Pathophysiology and treatment of carbon monoxide poisoning. *J Toxicol Clin Toxicol*. 1994;32(6):613-629.
79. Thom SR, Taber RL, Mendiguren, II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med*. 1995 Apr;25(4):474-480.
80. Jasper BW, Hopkins RO, Duker HV, Weaver LK. Affective outcome following carbon monoxide poisoning: a prospective longitudinal study. *Cogn Behav Neurol*. 2005 Jun;18(2):127-134.
81. End E, Long CW. Oxygen under pressure in carbon monoxide poisoning. *J Ind Hyg Toxicol*. 1942;20(10):302-306.
82. Britten JS, Myers RA. Effects of hyperbaric treatment on carbon monoxide elimination in humans. *Undersea Biomed Res*. 1985 Dec;12(4):431-438.
83. Myers RAM, Jones DW, Britten JS. Carbon monoxide half life study. Flagstaff, AZ: Best Publishing Company Co.; 1987. Pp.263-266.
84. Cardellach F, Miro O, Casademont J. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2003 Feb 6;348(6):557-560; author reply 557-560.

85. Thom SR. Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen. *Toxicol Appl Pharmacol.* 1990 Sep 1;105(2):340-344.
86. Thom SR. Functional inhibition of leukocyte B2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol.* 1993 Dec;123(2):248-256.
87. Thom SR, Bhopale VM, Fisher D. Hyperbaric oxygen reduces delayed immune-mediated neuropathology in experimental carbon monoxide toxicity. *Toxicol Appl Pharmacol.* 2006 Jun 1;213(2):152-159.
88. Peirce EC, 2nd, Zacharias A, Alday JM, Jr., Hoffman BA, Jacobson JH, 2nd. Carbon monoxide poisoning: experimental hypothermic and hyperbaric studies. *Surgery.* 1972 Aug;72(2):229-237.
89. Tomaszewski CA, Rudy J, Wathen J, Brent J, Rosenberg N, Kulig K. Prevention of neurologic sequelae from carbon monoxide by hyperbaric oxygen in rats. *Ann Emerg Med.* 1992;21(5):631-632.
90. Haldane J. The relation of the action of carbonic oxide to oxygen tension. *J Physiol.* 1895 Jul 18;18(3):201-217.
91. Douglas CG, Haldane JS, Haldane JB. The laws of combination of haemoglobin with carbon monoxide and oxygen. *J Physiol.* 1912 Jun 12;44(4):275-304.
92. Haldane JB. Carbon monoxide as a tissue poison. *Biochem J.* 1927;21(5):1068-1075.
93. Haldane JS. Respiration. New Haven: Yale University Press; 1922.
94. Boerema I, Meyne NG, Brummelkamp WK, et al. Life without blood (a study of the influence of high atmospheric pressure and hypothermia on dilution of the blood). *J Cardiovasc Surg.* 1960;13:133-146.
95. Weaver LK. Technique of Swan-Ganz catheter monitoring in patients treated in the monoplace hyperbaric chamber. *J Hyperb Med.* 1992;7(1):1-18.
96. Weaver LK, Howe S, Snow GL, Deru K. Arterial and pulmonary arterial hemodynamics and oxygen delivery/extraction in normal humans exposed to hyperbaric air and oxygen. *J Appl Physiol.* 2009 Jul;107(1):336-345.
97. Koehler RC, Jones MD, Jr., Traystman RJ. Cerebral circulatory response to carbon monoxide and hypoxic hypoxia in the lamb. *Am J Physiol.* 1982 Jul;243(1):H27-32.
98. Koehler RC, Traystman RJ, Jones MD, Jr. Regional blood flow and O<sub>2</sub> transport during hypoxic and CO hypoxia in neonatal and adult sheep. *Am J Physiol.* 1985 Jan;248(1 Pt 2):H118-124.
99. Koehler RC, Traystman RJ, Rosenberg AA, Hudak ML, Jones MD, Jr. Role of O<sub>2</sub>-hemoglobin affinity on cerebrovascular response to carbon monoxide hypoxia. *Am J Physiol.* 1983 Dec;245(6):H1019-1023.
100. Barker SJ, Tremper KK. The effect of carbon monoxide inhalation on pulse oximetry and transcutaneous PO<sub>2</sub>. *Anesthesiology.* 1987 May;66(5):677-679.
101. Fuson RL, Saltzman HA, Boineau JP, Smith WW, Spach MS, Brown IW, Jr. Oxygenation and carbonic acidosis in cyanotic dogs exposed to hyperbaric oxygenation. *Surg Gynecol Obstet.* 1966 Feb;122(2):340-352.
102. Keilin D, Hartree EF. Cytochrome and cytochrome oxidase. *Proc R Soc Lond B.* 1939;127(3):167-191.
103. Ball EG, Strittmatter CF, Cooper O. The reaction of cytochrome oxidase with carbon monoxide. *J Biol Chem.* 1951 Dec;193(2):635-647.
104. Chance B, Erecinska M, Wagner M. Mitochondrial responses to carbon monoxide toxicity. *Ann N Y Acad Sci.* 1970 Oct 5;174(1):193-204.
105. Caughey WS. Carbon monoxide bonding in heme proteins. *Ann N Y Acad Sci.* 1970 Oct 5;174(1):148-153.
106. Wald G, Allen DW. The equilibrium between cytochrome oxidase and carbon monoxide. *J Gen Physiol.* 1957 Mar 20;40(4):593-608.
107. Penney DG, Zak R, Aschenbrenner V. Carbon monoxide inhalation: effect on heart cytochrome c in the neonatal and adult rat. *J Toxicol Environ Health.* 1983 Aug-Sep;12(2-3):395-406.
108. Piantadosi CA. Carbon monoxide, oxygen transport, and oxygen metabolism. *J Hyperb Med.* 1987;2(1):27-44.
109. Coburn RF, Mayers LB. Myoglobin O<sub>2</sub> tension determined from measurement of carboxymyoglobin in skeletal muscle. *Am J Physiol.* 1971 Jan;220(1):66-74.
110. Brown SD, Piantadosi CA. In vivo binding of carbon monoxide to cytochrome c oxidase in rat brain. *J Appl Physiol.* 1990 Feb;68(2):604-610.
111. Thom SR, Ohnishi ST, Ischiropoulos H. Nitric oxide released by platelets inhibits neutrophil B2 integrin function following acute carbon monoxide poisoning. *Toxicol Appl Pharmacol.* 1994 Sep;128(1):105-110.
112. Thom SR, Ischiropoulos H. Mechanism of oxidative stress from low levels of carbon monoxide. *Res Rep Health Eff Inst.* 1997 Dec(80):1-19; discussion 21-17.
113. Thom SR, Xu YA, Ischiropoulos H. Vascular endothelial cells generate peroxynitrite in response to carbon monoxide exposure. *Chem Res Toxicol.* 1997 Sep;10(9):1023-1031.
114. Brown SD, Piantadosi CA. Reversal of carbon monoxide-cytochrome c oxidase binding by hyperbaric oxygen in vivo. *Adv Exp Med Biol.* 1989;248:747-754.
115. D'Amico G, Lam F, Hagen T, Moncada S. Inhibition of cellular respiration by endogenously produced carbon monoxide. *J Cell Sci.* 2006 Jun 1;119(Pt 11):2291-2298.

116. Chance B, Williams GR. The respiratory chain and oxidative phosphorylation. *Adv Enzymol Relat Subj Biochem.* 1956;17:65-134.
117. Alonso JR, Cardellach F, Lopez S, Casademont J, Miro O. Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. *Pharmacol Toxicol.* 2003 Sep;93(3):142-146.
118. Daugherty WP, Levasseur JE, Sun D, Rockswold GL, Bullock MR. Effects of hyperbaric oxygen therapy on cerebral oxygenation and mitochondrial function following moderate lateral fluid-percussion injury in rats. *J Neurosurg.* 2004 Sep;101(3):499-504.
119. Lou M, Chen Y, Ding M, Eschenfelder CC, Deuschl G. Involvement of the mitochondrial ATP-sensitive potassium channel in the neuroprotective effect of hyperbaric oxygenation after cerebral ischemia. *Brain Res Bull.* 2006 Mar 31;69(2):109-116.
120. Stewart RJ, Yamaguchi KT, Mason SW, Roshdieh BB, Dabassi NI, Ness NT. Tissue ATP levels in burn injured skin treated with hyperbaric oxygen. *Undersea Biomed Res.* 1989;16(Suppl):53.
121. Piantadosi CA, Tatro L, Zhang J. Hydroxyl radical production in the brain after CO hypoxia in rats. *Free Radic Biol Med.* 1995 Mar;18(3):603-609.
122. Cronje FJ, Carraway MS, Freiberger JJ, Suliman HB, Piantadosi CA. Carbon monoxide actuates O<sub>2</sub>-limited heme degradation in the rat brain. *Free Radic Biol Med.* 2004 Dec 1;37(11):1802-1812.
123. Rothfuss A, Radermacher P, Speit G. Involvement of heme oxygenase-1 (HO-1) in the adaptive protection of human lymphocytes after hyperbaric oxygen (HBO) treatment. *Carcinogenesis.* 2001 Dec;22(12):1979-1985.
124. Speit G, Dennog C, Eichhorn U, Rothfuss A, Kaina B. Induction of heme oxygenase-1 and adaptive protection against the induction of DNA damage after hyperbaric oxygen treatment. *Carcinogenesis.* 2000 Oct;21(10):1795-1799.
125. Gregorevic P, Lynch GS, Williams DA. Hyperbaric oxygen modulates antioxidant enzyme activity in rat skeletal muscles. *Eur J Appl Physiol.* 2001 Nov;86(1):24-27.
126. Kim CH, Choi H, Chun YS, Kim GT, Park JW, Kim MS. Hyperbaric oxygenation pretreatment induces catalase and reduces infarct size in ischemic rat myocardium. *Pflugers Arch.* 2001 Jul;442(4):519-525.
127. Ayvaz S, Kanter M, Aksu B, et al. The effects of hyperbaric oxygen application against cholestatic oxidative stress and hepatic damage after bile duct ligation in rats. *J Surg Res.* 2013 Jul;183(1):146-155.
128. Bosco G, Yang ZJ, Nandi J, Wang J, Chen C, Camporesi EM. Effects of hyperbaric oxygen on glucose, lactate, glycerol and anti-oxidant enzymes in the skeletal muscle of rats during ischaemia and reperfusion. *Clin Exp Pharmacol Physiol.* 2007 Jan-Feb;34(1-2):70-76.
129. Godman CA, Joshi R, Giardina C, Perdrizet G, Hightower LE. Hyperbaric oxygen treatment induces antioxidant gene expression. *Ann N Y Acad Sci.* 2010 Jun;1197:178-183.
130. Ozden TA, Uzun H, Bohloli M, et al. The effects of hyperbaric oxygen treatment on oxidant and antioxidants levels during liver regeneration in rats. *Tohoku J Exp Med.* 2004 Aug;203(4):253-265.
131. Yasar M, Yildiz S, Mas R, et al. The effect of hyperbaric oxygen treatment on oxidative stress in experimental acute necrotizing pancreatitis. *Physiol Res.* 2003;52(1):111-116.
132. Dennog C, Radermacher P, Barnett YA, Speit G. Antioxidant status in humans after exposure to hyperbaric oxygen. *Mutat Res.* 1999 Jul 16;428(1-2):83-89.
133. Shyu WC, Lin SZ, Saeki K, et al. Hyperbaric oxygen enhances the expression of prion protein and heat shock protein 70 in a mouse neuroblastoma cell line. *Cell Mol Neurobiol.* 2004 Apr;24(2):257-268.
134. Wang W, Xue L, Li Y, et al. RNA sequencing analysis reveals new findings of hyperbaric oxygen treatment on rats with acute carbon monoxide poisoning. *Undersea Hyperb Med.* 2016 Nov-Dec;43(7):759-770.
135. Park EJ, Min YG, Kim GW, Cho JP, Maeng WJ, Choi SC. Pathophysiology of brain injuries in acute carbon monoxide poisoning: a novel hypothesis. *Med Hypotheses.* 2014 Aug;83(2):186-189.
136. Juric DM, Finderle Z, Suput D, Brvar M. The effectiveness of oxygen therapy in carbon monoxide poisoning is pressure- and time-dependent: a study on cultured astrocytes. *Toxicol Lett.* 2015 Feb 17;233(1):16-23.
137. Juric DM, Suput D, Brvar M. Hyperbaric oxygen preserves neurotrophic activity of carbon monoxide-exposed astrocytes. *Toxicol Lett.* 2016 Jun 24;253:1-6.
138. Zhang Y, Lv Y, Liu YJ, et al. Hyperbaric oxygen therapy in rats attenuates ischemia-reperfusion testicular injury through blockade of oxidative stress, suppression of inflammation, and reduction of nitric oxide formation. *Urology.* 2013 Aug;82(2):489 e489-489 e415.
139. Miljkovic-Lolic M, Silbergbeit R, Fiskum G, Rosenthal RE. Neuroprotective effects of hyperbaric oxygen treatment in experimental focal cerebral ischemia are associated with reduced brain leukocyte myeloperoxidase activity. *Brain Res.* 2003 May 2;971(1):90-94.
140. Thom SR, Fisher D, Manevich Y. Roles for platelet-activating factor and \*NO-derived oxidants causing neutrophil adherence after CO poisoning. *Am J Physiol Heart Circ Physiol.* 2001 Aug;281(2):H923-930.

141. Thom SR. Dehydrogenase conversion to oxidase and lipid peroxidation in brain after carbon monoxide poisoning. *J Appl Physiol.* 1992 Oct;73(4):1584-1589.
142. Thom SR. Effects of hyperoxia on neutrophil adhesion. *Undersea Hyperb Med.* 2004 Spring;31(1):123-131.
143. Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H, Kucan JO. Morphologic analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg.* 1993 May;91(6):1110-1123.
144. Vlodavsky E, Palzur E, Soustiel JF. Hyperbaric oxygen therapy reduces neuroinflammation and expression of matrix metalloproteinase-9 in the rat model of traumatic brain injury. *Neuropathol Appl Neurobiol.* 2006 Feb;32(1):40-50.
145. Hara S, Mukai T, Kurosaki K, Kuriwa F, Endo T. Characterization of hydroxyl radical generation in the striatum of free-moving rats due to carbon monoxide poisoning, as determined by in vivo microdialysis. *Brain Res.* 2004 Aug 6;1016(2):281-284.
146. Hiramatsu M, Yokoyama S, Nabeshima T, Kameyama T. Changes in concentrations of dopamine, serotonin, and their metabolites induced by carbon monoxide (CO) in the rat striatum as determined by in vivo microdialysis. *Pharmacol Biochem Behav.* 1994 May;48(1):9-15.
147. Newby MB, Roberts RJ, Bhatnagar RK. Carbon monoxide- and hypoxia-induced effects on catecholamines in the mature and developing rat brain. *J Pharmacol Exp Ther.* 1978 Jul;206(1):61-68.
148. Thom SR, Fisher D, Zhang J, Bhopale VM, Cameron B, Buerk DG. Neuronal nitric oxide synthase and N-methyl-D-aspartate neurons in experimental carbon monoxide poisoning. *Toxicol Appl Pharmacol.* 2004 Feb 1;194(3):280-295.
149. Chin BY, Jiang G, Wegiel B, et al. Hypoxia-inducible factor 1alpha stabilization by carbon monoxide results in cytoprotective preconditioning. *Proc Natl Acad Sci U S A.* 2007 Mar 20;104(12):5109-5114.
150. Choi YK, Kim CK, Lee H, et al. Carbon monoxide promotes VEGF expression by increasing HIF-1alpha protein level via two distinct mechanisms, translational activation and stabilization of HIF-1alpha protein. *J Biol Chem.* 2010 Oct 15;285(42):32116-32125.
151. Calvert JW, Cahill J, Yamaguchi-Okada M, Zhang JH. Oxygen treatment after experimental hypoxia-ischemia in neonatal rats alters the expression of HIF-1alpha and its downstream target genes. *J Appl Physiol.* 2006 Sep;101(3):853-865.
152. Li Y, Zhou C, Calvert JW, Colohan AR, Zhang JH. Multiple effects of hyperbaric oxygen on the expression of HIF-1 alpha and apoptotic genes in a global ischemia-hypotension rat model. *Exp Neurol.* 2005 Jan;191(1):198-210.
153. Ostrowski RP, Colohan AR, Zhang JH. Mechanisms of hyperbaric oxygen-induced neuroprotection in a rat model of subarachnoid hemorrhage. *J Cereb Blood Flow Metab.* 2005 May;25(5):554-571.
154. Tofighi R, Tillmark N, Dare E, Aberg AM, Larsson JE, Ceccatelli S. Hypoxia-independent apoptosis in neural cells exposed to carbon monoxide in vitro. *Brain Res.* 2006 Jul 7;1098(1):1-8.
155. Brvar M, Luzar B, Finderle Z, Suput D, Bunc M. The time-dependent protective effect of hyperbaric oxygen on neuronal cell apoptosis in carbon monoxide poisoning. *Inhal Toxicol.* 2010 Oct;22(12):1026-1031.
156. Calvert JW, Zhou C, Nanda A, Zhang JH. Effect of hyperbaric oxygen on apoptosis in neonatal hypoxia-ischemia rat model. *J Appl Physiol.* 2003 Nov;95(5):2072-2080.
157. Rosenthal RE, Silbergliit R, Hof PR, Haywood Y, Fiskum G. Hyperbaric oxygen reduces neuronal death and improves neurological outcome after canine cardiac arrest. *Stroke.* 2003 May;34(5):1311-1316.
158. Garland H, Pearce J. Neurological complications of carbon monoxide poisoning. *Q J Med.* 1967 Oct;36(144):445-455.
159. Thom SR. Hyperbaric-oxygen therapy for acute carbon monoxide poisoning. *N Engl J Med.* 2002 Oct 3;347(14):1105-1106.
160. Hampson NB, Dunford RG, Kramer CC, Norkool DM. Selection criteria utilized for hyperbaric oxygen treatment of carbon monoxide poisoning. *J Emerg Med.* 1995 Mar-Apr;13(2):227-231.
161. Raphael JC, Elkharraf D, Jars-Guincestre MC, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet.* 1989 Aug 19;2(8660):414-419.
162. Ducasse JL, Celsis P, Marc-Vergnes JP. Non-comatose patients with acute carbon monoxide poisoning: hyperbaric or normobaric oxygenation? *Undersea Hyperb Med.* 1995 Mar;22(1):9-15.
163. Schiltz KL. Failure to assess motivation, need to consider psychiatric variables, and absence of comprehensive examination: a skeptical review of neuropsychologic assessment in carbon monoxide research. *Undersea Hyperb Med.* 2000 Spring;27(1):48-50.
164. Amitai Y, Zlotogorski Z, Golani-Katzav V, Wexler A, Gross D. Neuropsychological impairment from acute low-level exposure to carbon monoxide. *Arch Neurol.* 1998 Jun;55(6):845-848.
165. Hampson NB, Mathieu D, Piantadosi CA, Thom SR, Weaver LK. Carbon monoxide poisoning: interpretation of randomized clinical trials and unresolved treatment issues. *Undersea Hyperb Med.* 2001 Fall;28(3):157-164.

166. Weaver LK, Hopkins RO, Chan KJ, et al. Carbon Monoxide Research Group, LDS Hospital, Utah in reply to Scheinkestel et al. and Emerson: the role of hyperbaric oxygen in carbon monoxide poisoning. *Emerg Med Australas.* 2004 Oct-Dec;16(5-6):394-399; discussion 481-392.
167. Jordan BD, Relkin NR, Ravdin LD, Jacobs AR, Bennett A, Gandy S. Apolipoprotein E epsilon4 associated with chronic traumatic brain injury in boxing. *JAMA.* 1997 Jul 9;278(2):136-140.
168. Li L, Bao Y, He S, et al. The Association Between Apolipoprotein E and Functional Outcome After Traumatic Brain Injury: A Meta-Analysis. *Medicine (Baltimore).* 2015 Nov;94(46):e2028.
169. Hopkins RO, Weaver LK, Valentine KJ, Mower C, Churchill S, Carlquist J. Apolipoprotein E genotype and response of carbon monoxide poisoning to hyperbaric oxygen treatment. *Am J Respir Crit Care Med.* 2007 Nov 15;176(10):1001-1006.
170. Tsuang D, Kukull W, Sheppard L, et al. Impact of sample selection on APOE epsilon 4 allele frequency: a comparison of two Alzheimer's disease samples. *J Am Geriatr Soc.* 1996 Jun;44(6):704-707.
171. Hampson NB, Little CE. Hyperbaric treatment of patients with carbon monoxide poisoning in the United States. *Undersea Hyperb Med.* 2005 Jan-Feb;32(1):21-26.
172. Weaver LK, Churchill S, Deru K, Handrahan D. A randomized trial of one v. three hyperbaric oxygen sessions for acute carbon monoxide poisoning. *Undersea Hyperb Med.* 2018;45(5):579.
173. Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y, Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *J Am Coll Cardiol.* 2005 May 3;45(9):1513-1516.
174. De Reuck J, Decoo D, Lemahieu I, et al. A positron emission tomography study of patients with acute carbon monoxide poisoning treated by hyperbaric oxygen. *J Neurol.* 1993 Jul;240(7):430-434.
175. Maeda Y, Kawasaki Y, Jibiki I, Yamaguchi N, Matsuda H, Hisada K. Effect of therapy with oxygen under high pressure on regional cerebral blood flow in the interval form of carbon monoxide poisoning: observation from subtraction of technetium-99m HMPAO SPECT brain imaging. *Eur Neurol.* 1991;31(6):380-383.
176. Murata T, Koshino Y, Nishio M, et al. Serial proton magnetic resonance spectroscopy in a patient with acute carbon monoxide poisoning. *Biol Psychiatry.* 1995 Apr 15;37(8):541-545.
177. Haberstock D, Hopkins RO, Weaver LK, Churchill S. Prospective longitudinal assessment of symptoms in acute carbon monoxide (CO) poisoning. *Undersea Hyperb Med.* 1998;25(Suppl):48.
178. Waisman D, Shupak A, Weisz G, Melamed Y. Hyperbaric oxygen therapy in the pediatric patient: the experience of the Israel Naval Medical Institute. *Pediatrics.* 1998 Nov;102(5):E53.
179. Kim JK, Coe CJ. Clinical study on carbon monoxide intoxication in children. *Yonsei Med J.* 1987;28(4):266-273.
180. Klees M, Heremans M, Dougan S. Psychological sequelae to carbon monoxide intoxication in the child. *Sci Total Environ.* 1985 Aug;44(2):165-176.
181. Cunningham SD, Weaver LK, Deru K, Jensen J, Petty L. Prospective neuropsychological assessment of children with carbon monoxide poisoning. *Undersea Hyperb Med.* 2012;39(5):981-982.
182. Weaver LK, Cunningham SD, Farnsworth K, Layton B, Deru K, Petty L. Prospective vestibular outcomes of children with carbon monoxide poisoning. *Undersea Hyperb Med.* 2012;39(5):982.
183. Koren G, Sharav T, Pastuszak A, et al. A multicenter, prospective study of fetal outcome following accidental carbon monoxide poisoning in pregnancy. *Reprod Toxicol.* 1991;5(5):397-403.
184. Penney DG. Effects of carbon monoxide exposure on developing animals and humans. In: Penney DG, editor. *Carbon monoxide.* Boca Raton, FL: CRC Press, Inc.; 1996. Pp. 109-144.
185. Norman CA, Halton DM. Is carbon monoxide a workplace teratogen? A review and evaluation of the literature. *Ann Occup Hyg.* 1990 Aug;34(4):335-347.
186. Longo LD. The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. *Am J Obstet Gynecol.* 1977 Sep 1;129(1):69-103.
187. Van Hoesen KB, Camporesi EM, Moon RE, Hage ML, Piantadosi CA. Should hyperbaric oxygen be used to treat the pregnant patient for acute carbon monoxide poisoning? A case report and literature review. *JAMA.* 1989 Feb 17;261(7):1039-1043.
188. Elkharrat D, Raphael JC, Korach JM, et al. Acute carbon monoxide intoxication and hyperbaric oxygen in pregnancy. *Intensive Care Med.* 1991;17(5):289-292.
189. Azarov I, Wang L, Rose JJ, et al. Five-coordinate H64Q neuroglobin as a ligand-trap antidote for carbon monoxide poisoning. *Sci Transl Med.* 2016 Dec 7;8(368):368ra173.
190. Weaver LK. Engineered proteins: A carbon monoxide antidote. *Nature Biomedical Engineering.* 2017 02/10/online;1:0030.
191. Kitamoto T, Tsuda M, Kato M, Saito F, Kamijo Y, Kinoshita T. Risk factors for the delayed onset of neuropsychologic sequelae following carbon monoxide poisoning. *Acute Med Surg.* 2016 Oct;3(4):315-319.

192. Kuroda H, Fujihara K, Kushimoto S, Aoki M. Novel clinical grading of delayed neurologic sequelae after carbon monoxide poisoning and factors associated with outcome. *Neurotoxicology*. 2015 May;48:35-43.
193. Pepe G, Castelli M, Nazerian P, et al. Delayed neuropsychological sequelae after carbon monoxide poisoning: predictive risk factors in the Emergency Department. A retrospective study. *Scand J Trauma Resusc Emerg Med*. 2011 Mar 17;19:16.
194. Ruff RM, Iverson GL, Barth JT, et al. Recommendations for diagnosing a mild traumatic brain injury: a National Academy of Neuropsychology education paper. *Arch Clin Neuropsychol*. 2009 Feb;24(1):3-10.
195. Alvarez VM, Parikh M, Weaver LK, Deru K. Cardiac MRI findings in patients with CO poisoning. *Undersea Hyperb Med*. 2015;42(5):468-469.
196. Smith JS, Brandon S. Morbidity from acute carbon monoxide poisoning at three-year follow-up. *Br Med J*. 1973 Feb 10;1(5849):318-321.
197. Hopkins RO, Weaver LK. Cognitive outcomes 6 years after acute carbon monoxide poisoning. *Undersea Hyperb Med*. 2008;35(4):258.
198. Weaver LK, Hopkins RO, Churchill S, Deru K. Neurological outcomes 6 years after acute carbon monoxide poisoning. *Undersea Hyperb Med*. 2008;35(4):258-259.
199. Mimura K, Harada M, Sumiyoshi S, et al. [Long-term follow-up study on sequelae of carbon monoxide poisoning; serial investigation 33 years after poisoning]. *Seishin Shinkeigaku Zasshi*. 1999;101(7):592-618.
200. Huang CC, Ho CH, Chen YC, et al. Increased risk for diabetes mellitus in patients with carbon monoxide poisoning. *Oncotarget*. 2017 Sep 8;8(38):63680-63690.
201. Wong CS, Lin YC, Hong LY, et al. Increased Long-Term Risk of Dementia in Patients With Carbon Monoxide Poisoning: A Population-Based Study. *Medicine (Baltimore)*. 2016 Jan;95(3):e2549.
202. Wong CS, Lin YC, Sung LC, et al. Increased long-term risk of major adverse cardiovascular events in patients with carbon monoxide poisoning: A population-based study in Taiwan. *PLoS One*. 2017;12(4):e0176465.
203. Lai CY, Chou MC, Lin CL, Kao CH. Increased risk of Parkinson disease in patients with carbon monoxide intoxication: a population-based cohort study. *Medicine (Baltimore)*. 2015 May;94(19):e869.
204. Huang CC, Ho CH, Chen YC, et al. Hyperbaric Oxygen Therapy Is Associated With Lower Short- and Long-Term Mortality in Patients With Carbon Monoxide Poisoning. *Chest*. 2017 Nov;152(5):943-953.
205. Keim L, Koneru S, Ramos VFM, et al. Hyperbaric oxygen for late sequelae of carbon monoxide poisoning enhances neurological recovery: case report. *Undersea Hyperb Med*. 2018 Jan-Feb;45(1):83-87.
206. Chang DC, Lee JT, Lo CP, et al. Hyperbaric oxygen ameliorates delayed neuropsychiatric syndrome of carbon monoxide poisoning. *Undersea Hyperb Med*. 2010 Jan-Feb;37(1):23-33.
207. Coric V, Oren DA, Wolkenberg FA, Kravitz RE. Carbon monoxide poisoning and treatment with hyperbaric oxygen in the subacute phase. *J Neurol Neurosurg Psychiatry*. 1998 Aug;65(2):245-247.
208. Myers RA, DeFazio A, Kelly MP. Chronic carbon monoxide exposure: a clinical syndrome detected by neuropsychological tests. *J Clin Psychol*. 1998 Aug;54(5):555-567.
209. Spagnolo F, Costa M, Impellizzeri M, et al. Delayed hyperbaric oxygen treatment after acute carbon monoxide poisoning. *J Neurol*. 2011 Aug;258(8):1553-1554.
210. Vila JF, Meli FJ, Serqueira OE, Pisarello J, Lylyk P. Diffusion tensor magnetic resonance imaging: a promising technique to characterize and track delayed encephalopathy after acute carbon monoxide poisoning. *Undersea Hyperb Med*. 2005 May-Jun;32(3):151-156.
211. Watanuki T, Matsubara T, Higuchi N, et al. [Clinical examination of 3 patients with delayed neuropsychiatric encephalopathy induced by carbon monoxide poisoning, who recovered from severe neurocognitive impairment by repetitive hyperbaric oxygen therapy]. *Seishin Shinkeigaku Zasshi*. 2014;116(8):659-669.
212. Koita N, Mitsuhashi M, Maki T, et al. Two case reports : improvement of delayed leukoencephalopathy after carbon monoxide poisoning more than one month after onset with hyperbaric oxygen therapy. *J Neurol Sci*. 2017;381:499.
213. Weaver LK, Wilson SH, Lindblad AS, et al. Hyperbaric oxygen for post-concussive symptoms in United States military service members: a randomized clinical trial. *Undersea Hyperb Med*. 2018;45(2):129-156.
214. Boussi-Gross R, Golan H, Fishlev G, et al. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury - randomized prospective trial. *PLoS One*. 2013;8(11):e79995.
215. Hampson NB, Weaver LK. Carbon monoxide poisoning: a new incidence for an old disease. *Undersea Hyperb Med*. 2007 May-Jun;34(3):163-168.
216. Mathieu D, Nolf M, Durocher A, et al. Acute carbon monoxide poisoning. Risk of late sequelae and treatment by hyperbaric oxygen. *J Toxicol Clin Toxicol*. 1985;23(4-6):315-324.
217. Norkool DM, Kirkpatrick JN. Treatment of acute carbon monoxide poisoning with hyperbaric oxygen: a review of 115 cases. *Ann Emerg Med*. 1985 Dec;14(12):1168-1171.

218. Huang ET, Hardy KR, Stubbs JM, Lowe RA, Thom SR. Ventriculo-peritoneal shunt performance under hyperbaric conditions. *Undersea Hyperb Med*. 2000 Winter;27(4):191-194.
219. Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust*. 1999 Mar 1;170(5):203-210.
220. Annane D, Chadda K, Gajdos P, Jars-Guincestre MC, Chevret S, Raphael JC. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. *Intensive Care Med*. 2011 Mar;37(3):486-492.
221. Brown SD, Piantadosi CA. Hyperbaric for carbon monoxide poisoning. *Lancet*. 1989 Oct 28;2(8670):1032-1033.
222. Birmingham CM, Hoffman RS. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. *Intensive Care Med*. 2011 Jul;37(7):1218; author reply 1219.
223. Thom SR, Mendiguren I, Hardy K, et al. Inhibition of human neutrophil beta2-integrin-dependent adherence by hyperbaric O<sub>2</sub>. *Am J Physiol*. 1997 Mar;272(3 Pt 1):C770-777.
224. Moher D, Schulz KF, Altman D, Group C. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA*. 2001 Apr 18;285(15):1987-1991.
225. Halperin JL, Levine GN, Al-Khatib SM, et al. Further Evolution of the ACC/AHA Clinical Practice Guideline Recommendation Classification System: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016 Apr 5;67(13):1572-1574.
226. Lin CH, Su WH, Chen YC, et al. Treatment with normobaric or hyperbaric oxygen and its effect on neuropsychometric dysfunction after carbon monoxide poisoning: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2018 Sep;97(39):e12456.
227. Moon RE. Hyperbaric oxygen treatment for decompression sickness. *Undersea Hyperb Med*. 2014 Mar-Apr;41(2):151-157.
228. Hampson NB, Dunn SL, Yip FY, Clower JH, Weaver LK. The UHMS/CDC carbon monoxide poisoning surveillance program: three-year data. *Undersea Hyperb Med*. 2012 Mar-Apr;39(2):667-685.
229. Stoller KP. Hyperbaric oxygen and carbon monoxide poisoning: a critical review. *Neurol Res*. 2007 Mar;29(2):146-155.
230. Anseeuw K, Delvau N, Burillo-Putze G, et al. Cyanide poisoning by fire smoke inhalation: a European expert consensus. *Eur J Emerg Med*. 2013 Feb;20(1):2-9.
231. Norris JC, Moore SJ, Hume AS. Synergistic lethality induced by the combination of carbon monoxide and cyanide. *Toxicology*. 1986 Aug;40(2):121-129.
232. Moore SJ, Ho IK, Hume AS. Severe hypoxia produced by concomitant intoxication with sublethal doses of carbon monoxide and cyanide. *Toxicol Appl Pharmacol*. 1991 Jul;109(3):412-420.
233. Pitt BR, Radford EP, Gurtner GH, Traystman RJ. Interaction of carbon monoxide and cyanide on cerebral circulation and metabolism. *Arch Environ Health*. 1979 Sep-Oct;34(5):345-349.
234. Baud FJ. Cyanide: critical issues in diagnosis and treatment. *Hum Exp Toxicol*. 2007 Mar;26(3):191-201.
235. Lawson-Smith P, Jansen EC, Hyldegaard O. Cyanide intoxication as part of smoke inhalation--a review on diagnosis and treatment from the emergency perspective. *Scand J Trauma Resusc Emerg Med*. 2011;19:14.
236. Beasley DM, Glass WI. Cyanide poisoning: pathophysiology and treatment recommendations. *Occup Med (Lond)*. 1998 Oct;48(7):427-431.
237. Borron SW, Baud FJ. Antidotes for acute cyanide poisoning. *Curr Pharm Biotechnol*. 2012 Aug;13(10):1940-1948.
238. Toon MH, Maybauer MO, Greenwood JE, Maybauer DM, Fraser JF. Management of acute smoke inhalation injury. *Crit Care Resusc*. 2010 Mar;12(1):53-61.
239. Reade MC, Davies SR, Morley PT, Dennett J, Jacobs IC, Australian Resuscitation C. Review article: management of cyanide poisoning. *Emerg Med Australas*. 2012 Jun;24(3):225-238.
240. Thompson JP, Marrs TC. Hydroxocobalamin in cyanide poisoning. *Clin Toxicol (Phila)*. 2012 Dec;50(10):875-885.
241. Desai SS, M. Cyanide poisoning. In: Basow DS, editor. UpToDate. Waltham, MA: UpToDate; 2013.
242. Lee J, Mukai D, Kreuter K, Mahon S, Tromberg B, Brenner M. Potential interference by hydroxocobalamin on cooximetry hemoglobin measurements during cyanide and smoke inhalation treatments. *Ann Emerg Med*. 2007 Jun;49(6):802-805.
243. Pamidi PV, DeAbreu M, Kim D, Mansouri S. Hydroxocobalamin and cyanocobalamin interference on co-oximetry based hemoglobin measurements. *Clin Chim Acta*. 2009 Mar;401(1-2):63-67.
244. Livshits Z, Lugassy DM, Shawn LK, Hoffman RS. Falsely low carboxyhemoglobin level after hydroxocobalamin therapy. *N Engl J Med*. 2012 Sep 27;367(13):1270-1271.
245. Trapp WG. Massive cyanide poisoning with recovery: a boxing-day story. *Can Med Assoc J*. 1970 Mar 14;102(5):517.

246. Litovitz TL, Larkin RF, Myers RA. Cyanide poisoning treated with hyperbaric oxygen. *Am J Emerg Med.* 1983 Jul;1(1):94-101.
247. Amizet L, Pruvot G, Remy S, Kfouri M. Occupational cyanide poisoning. *BMJ Case Rep.* 2011 Nov 21;2011.
248. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. *Ann Emerg Med.* 2007 Jun;49(6):794-801, 801 e791-792.
249. Pearce LL, Bominaar EL, Hill BC, Peterson J. Reversal of cyanide inhibition of cytochrome c oxidase by the auxiliary substrate nitric oxide: an endogenous antidote to cyanide poisoning? *J Biol Chem.* 2003 Dec 26;278(52):52139-52145.
250. Ivanov KP. The effect of elevated oxygen pressure on animals poisoned with potassium cyanide. *Farmakol Toksikol* (in English translation). 1959;22(1959):476-479.
251. Skene WG, Norman JN, Smith G. Effect of hyperbaric oxygen in cyanide poisoning. In: Brown IW, Cox B, editors. *Proceedings of the third international congress on hyperbaric medicine.* Washington, DC: National Academy of Sciences - National Research Council; 1966. Pp. 705-710.
252. Takano T, Miyazaki Y, Nashimoto I, Kobayashi K. Effect of hyperbaric oxygen on cyanide intoxication: in situ changes in intracellular oxidation reduction. *Undersea Biomed Res.* 1980 Sep;7(3):191-197.
253. Way JL, End E, Sheehy MH, et al. Effect of oxygen on cyanide intoxication. IV. Hyperbaric oxygen. *Toxicol Appl Pharmacol.* 1972 Jul;22(3):415-421.
254. Lawson-Smith P, Olsen NV, Hyldegaard O. Hyperbaric oxygen therapy or hydroxocobalamin attenuates surges in brain interstitial lactate and glucose; and hyperbaric oxygen improves respiratory status in cyanide-intoxicated rats. *Undersea Hyperb Med.* 2011 Jul-Aug;38(4):223-237.
255. Houeto P, Borron SW, Sandouk P, Imbert M, Levillain P, Baud FJ. Pharmacokinetics of hydroxocobalamin in smoke inhalation victims. *J Toxicol Clin Toxicol.* 1996;34(4):397-404.
256. Lawson-Smith P, Jansen EC, Hilsted L, Johnsen AH, Hyldegaard O. Effect of acute and delayed hyperbaric oxygen therapy on cyanide whole blood levels during acute cyanide intoxication. *Undersea Hyperb Med.* 2011 Jan-Feb;38(1):17-26.
257. Lawson-Smith P, Jansen EC, Hilsted L, Hyldegaard O. Effect of hyperbaric oxygen therapy on whole blood cyanide concentrations in carbon monoxide intoxicated patients from fire accidents. *Scand J Trauma Resusc Emerg Med.* 2010;18:32.
258. Desola J. Hydroxocobalamin, hyperbaric oxygen and cyanide poisoning. *Undersea Hyperb Med.* 2011 Jul-Aug;38(4):217-220.
259. Hart GB, O'Reilly RR, Broussard ND, Cave RH, Goodman DB, Yanda RL. Treatment of burns with hyperbaric oxygen. *Surg Gynecol Obstet.* 1974 Nov;139(5):693-696.
260. Stewart RJ, Yamaguchi KT, Samadani S, et al. Effects of oxygen and pressure on extravascular lung water following smoke inhalation. *J Hyperb Med.* 1988;3(3):173-178.
261. Ray CS, Green B, Cianci P. Hyperbaric oxygen therapy in burn patients with adult respiratory distress syndrome. *Undersea Biomed Res.* 1989;16(Suppl):81.
262. Thom SR, Mendiguren I, Fisher D. Smoke inhalation-induced alveolar lung injury is inhibited by hyperbaric oxygen. *Undersea Hyperb Med.* 2001 Fall;28(4):175-179.
263. Weaver LK. Hyperbaric oxygen in the critically ill. *Crit Care Med.* 2011 Jul;39(7):1784-1791.

## **Chapter 4: Clostridial Myonecrosis (Gas Gangrene)**

*Robert A. van Hulst, MD, PhD, FUHM, Capt Navy (ret), Dirk J. Bakker MD, PhD, FUHM, Benjamin Chernesky MD, C.R. Soh MD*

## **REFERENCES**

1. Stevens DL. The pathogenesis of clostridial myonecrosis. *Int J Med Microbiol.* 2000;290(4-5):497-502.
2. Van Hulst RA, Bakker DJ. Selected aerobic and anaerobic soft-tissue infections. In: Whelan HT, Kindwall EP, editors. *Hyperbaric Medicine Practice.* North Palm Beach, FL: Best Publishing Company; 2017. Pp. 435-63.
3. Lucey BP, Hutchins GM. William H. Welch, MD, and the discovery of *Bacillus welchii*. *Arch Pathol Lab Med.* 2004;128(10):1193-5.
4. Weinstein L, Barza MA. Gas gangrene. *N Engl J Med.* 1973;289(21):1129-31.
5. Bakker D. Clostridial myonecrosis. In: Bakker DJ, Cramer FS, eds. *Hyperbaric surgery: perioperative care:* Flagstaff, AZ: Best Publishing Co.; 2002:283-316.
6. Srivastava I, Aldape MJ, Bryant AE, Stevens DL. Spontaneous *C. septicum* gas gangrene: A literature review. *Anaerobe.* 2017;48:165-71.
7. Abella BS, Kuchinic P, Hiraoka T, Howes DS. Atraumatic Clostridial myonecrosis: case report and literature review. *J Emerg Med.* 2003;24(4):401-5.
8. Sutton SS, Jumper M, Shah A, Edun B. Clostridium tertium Peritonitis and Concurrent Bacteremia in a Patient With a History of Alcoholic Cirrhosis. *J Investig Med High Impact Case Rep.* 2017;5(3):2324709617731457.
9. Kelesidis T, Tsiodras S. Clostridium sphenoides bloodstream infection in man. *Emerg Infect Dis.* 2011;17(1):156-8.
10. Aldape MJ, Bryant AE, Stevens DL. Clostridium sordellii infection: epidemiology, clinical findings, and current perspectives on diagnosis and treatment. *Clin Infect Dis.* 2006;43(11):1436-46.
11. Williamson ED, Titball RW. A genetically engineered vaccine against the alpha-toxin of *Clostridium perfringens* protects mice against experimental gas gangrene. *Vaccine.* 1993;11(12):1253-8.
12. Stevens DL, Titball RW, Jepson M, Bayer CR, Hayes-Schroer SM, Bryant AE. Immunization with the C-Domain of alpha -Toxin prevents lethal infection, localizes tissue injury, and promotes host response to challenge with *Clostridium perfringens*. *J Infect Dis.* 2004;190(4):767-73.
13. Shreya D, Uppalapati SR, Kingston JJ, Sripathy MH, Batra HV. Immunization with recombinant bivalent chimera r-Cpae confers protection against alpha toxin and enterotoxin of *Clostridium perfringens* type A in murine model. *Mol Immunol.* 2015;65(1):51-7.
14. Titball RW. *Clostridium perfringens* vaccines. *Vaccine.* 2009;27 Suppl 4:D44-7.
15. McLeod JW. Variations in the periods of exposure to air and oxygen necessary to kill anaerobic bacteria. *Acta Pathol Microbiol Scand.* 1930;3(suppl):255.
16. Shimizu T, Ohtani K, Hirakawa H, Ohshima K, Yamashita A, Shiba T, et al. Complete genome sequence of *Clostridium perfringens*, an anaerobic flesh-eater. *Proc Natl Acad Sci U S A.* 2002;99(2):996-1001.
17. Benamar S, Cassir N, Caputo A, Cadoret F, La Scola B. Complete Genome Sequence of *Clostridium septicum* Strain CSUR P1044, Isolated from the Human Gut Microbiota. *Genome Announc.* 2016;4(5).
18. MacLennan JD. The histotoxic clostridial infections of man. *Bacteriol Rev.* 1962;26:177-276.
19. Hitchcock CR, Demello FJ, Haglin JJ. Gangrene infection: new approaches to an old disease. *The Surgical clinics of North America.* 1975;55(6):1403-10.
20. Heimbach RD. Gas gangrene. In: Kindwall EP, ed. *Hyperbaric medicine practice:* Flagstaff, AZ: Best Publishing Co.; 1994:373-94.
21. Kiu R, Hall LJ. An update on the human and animal enteric pathogen *Clostridium perfringens*. *Emerg Microbes Infect.* 2018;7(1):141.
22. Navarro MA, McClane BA, Uzal FA. Mechanisms of Action and Cell Death Associated with *Clostridium perfringens* Toxins. *Toxins (Basel).* 2018;10(5).
23. Takehara M, Takagishi T, Seike S, Ohtani K, Kobayashi K, Miyamoto K, et al. *Clostridium perfringens* alpha-Toxin Impairs Innate Immunity via Inhibition of Neutrophil Differentiation. *Sci Rep.* 2016;6:28192.
24. Takagishi T, Takehara M, Seike S, Miyamoto K, Kobayashi K, Nagahama M. *Clostridium perfringens* alpha-toxin impairs erythropoiesis by inhibition of erythroid differentiation. *Sci Rep.* 2017;7(1):5217.
25. Stevens DL, Troyer BE, Merrick DT, Mitten JE, Olson RD. Lethal effects and cardiovascular effects of purified alpha- and theta-toxins from *Clostridium perfringens*. *J Infect Dis.* 1988;157(2):272-9.
26. Stevens DL, Bryant AE, Adams K, Mader JT. Evaluation of therapy with hyperbaric oxygen for experimental infection with *Clostridium perfringens*. *Clin Infect Dis.* 1993;17(2):231-7.
27. Verherstraeten S, Goossens E, Valgaeren B, Pardon B, Timbermont L, Haesebrouck F, et al. Perfringolysin O: The Underrated *Clostridium perfringens* Toxin? *Toxins (Basel).* 2015;7(5):1702-21.
28. Willis AT. *Clostridia* of wound infection. London: Butterworth; 1969:490.
29. Ohtani K. Gene regulation by the VirS/VirR system in *Clostridium perfringens*. *Anaerobe.* 2016;41:5-9.

30. Stevens DL, Bryant AE. The role of clostridial toxins in the pathogenesis of gas gangrene. *Clin Infect Dis.* 2002;35(Suppl 1):S93-S100.
31. Bryant AE, Stevens DL. Clostridial myonecrosis: new insights in pathogenesis and management. *Curr Infect Dis Rep.* 2010;12(5):383-91.
32. Awad MM, Bryant AE, Stevens DL, Rood JI. Virulence studies on chromosomal alpha-toxin and theta-toxin mutants constructed by allelic exchange provide genetic evidence for the essential role of alpha-toxin in *Clostridium perfringens*-mediated gas gangrene. *Mol Microbiol.* 1995;15(2):191-202.
33. Eaton JT, Naylor CE, Howells AM, Moss DS, Titball RW, Basak AK. Crystal structure of the *C. perfringens* alpha-toxin with the active site closed by a flexible loop region. *J Mol Biol.* 2002;319(2):275-81.
34. Stevens DL, Tweten RK, Awad MM, Rood JI, Bryant AE. Clostridial gas gangrene: evidence that alpha and theta toxins differentially modulate the immune response and induce acute tissue necrosis. *J Infect Dis.* 1997;176(1):189-95.
35. Titball RW, Naylor CE, Basak AK. The *Clostridium perfringens* alpha-toxin. *Anaerobe.* 1999;5(2):51-64.
36. Van U. Inhibition of Toxin Production in *Clostridium Perfringens* in Vitro by Hyperbaric Oxygen. *Antonie Van Leeuwenhoek.* 1965;31:181-6.
37. Kaye D. Effect of hyperbaric oxygen on Clostridia in vitro and in vivo. *Proc Soc Exp Biol Med.* 1967;124(2):360-6.
38. Hill GB, Osterhout S. Experimental effects of hyperbaric oxygen on selected clostridial species. II. In-vitro studies in mice. *J Infect Dis.* 1972;125(1):26-35.
39. Muhvich KH, Anderson LH, Mehm WJ. Evaluation of antimicrobials combined with hyperbaric oxygen in a mouse model of clostridial myonecrosis. *J Trauma.* 1994;36(1):7-10.
40. Demello FJ, Hashimoto T, Hitchcock CR, Haglin JJ. The effect of hyperbaric oxygen on the germination and toxin production of *Clostridium perfringens* spores. In: Wada J, Iwa JT, editors. *Proceedings of the fourth international congress on hyperbaric medicine.* Baltimore, MD: Williams and Wilkins, 1970. 270.
41. Schoemaker G. Oxygen tension measurements under hyperbaric conditions In: Boerema I, Brummelkamp WH, Meijne NG, eds. *Clinical application of hyperbaric oxygen:* Amsterdam: Elsevier; 1964:330-5.
42. Kivilahti J, Niinikoski J. Use of silastic tube and capillary sampling technic in the measurement of tissue PO<sub>2</sub> and PCO<sub>2</sub>. *Am J Surg.* 1973;125(5):623-7.
43. Sheffield PJ. Tissue oxygen measurements. In: Davis JC, Hunt TK, eds. *Problem wounds: the role of oxygen.* New York, NY: Elsevier; 1988:17-51.
44. Nora PF, Mousavipour M, Laufman H. Mechanisms of action of high pressure oxygen in *Clostridium perfringens* exotoxin toxicity. In: Brown IW, Cox BG, eds. *Hyperbaric medicine,* publ 1404. Washington, DC: National Academy of Science National Research Council; 1966:544-51.
45. Nora PF, Mousavipour M, Mittelpunkt A, Rosenberg M, Laufman H. Brain as target organ in *Clostridium perfringens* exotoxin toxicity. *Arch Surg.* 1966;92(2):243-6.
46. Roggentin T, Kleineidam RG, Majewski DM, Tirpitz D, Roggentin P, Schauer R. An immunoassay for the rapid and specific detection of three sialidase-producing clostridia causing gas gangrene. *J Immunol Methods.* 1993;157(1-2):125-33.
47. Scheven M. [Detection of *Clostridium perfringens* in mixed infection patient samples using a modified reverse CAMP test]. *Z Gesamte Hyg.* 1991;37(2):90-1.
48. Hirn M. Hyperbaric oxygen in the treatment of gas gangrene and perineal necrotizing fasciitis. A clinical and experimental study. *Eur J Surg Suppl.* 1993(570):1-36.
49. Demello FJ, Haglin JJ, Hitchcock CR. Comparative study of experimental *Clostridium perfringens* infection in dogs treated with antibiotics, surgery, and hyperbaric oxygen. *Surgery.* 1973;73(6):936-41.
50. Kelley HG, Jr., Pace WG, 3rd. Treatment of Anaerobic Infections in Mice with Hyperpressure Oxygen. *Surg Forum.* 1963;14:46-7.
51. Klopper PJ. Hyperbaric oxygen treatment after ligation of the hepatic artery in rabbits. In: Boerema I, Brummelkamp WH, Meijne NG, eds. *Clinical application of hyperbaric oxygen.* Amsterdam: Elsevier; 1964:31-5.
52. Schott H. [Gas gangrene (principles of treatment, results)]. *Hefte Unfallheilkd.* 1979;138:179-86.
53. Nier H, Kremer K. [Gas gangrene--still a diagnostic and therapeutic problem]. *Zentralbl Chir.* 1984;109(6):402-17.
54. Pailler JL, Labeeu F. [Gas gangrene: a military disease?]. *Acta Chir Belg.* 1986;86(2):63-71.
55. Erttmann M, Havemann D. [Treatment of gas gangrene. Results of a retro- and prospective analysis of a traumatologic patient sample over 20 years]. *Unfallchirurg.* 1992;95(10):471-6.
56. Brummelkamp WH, Hogendijk J, Boerema I. Treatment of anaerobic infections (clostridial myositis) by drenching the tissues with oxygen under high atmospheric pressure. *Surgery.* 1961;49:299-302.
57. Brummelkamp WH. Considerations on Hyperbaric Oxygen Therapy at Three Atmospheres Absolute for Clostridial Infections Type Welchii. *Ann N Y Acad Sci.* 1965;117:688-99.

58. Bakker DJ. The use of hyperbaric oxygen in the treatment of certain infectious diseases, especially gas gangrene and acute dermal gangrene. Wageningen, Holland: Drukkerij Veenman BV; 1984.
59. Hart GB, Lamb RC, Strauss MB. Gas gangrene. J Trauma. 1983;23(11):991-1000.
60. Holland JA, Hill GB, Wolfe WG, Osterhout S, Saltzman HA, Brown IW, Jr. Experimental and clinical experience with hyperbaric oxygen in the treatment of clostridial myonecrosis. Surgery. 1975;77(1):75-85.
61. Van Zijl JJW. Discussion of hyperbaric oxygen. In: Brown IW, Cox BG, eds. Hyperbaric medicine, publ 1404. Washington, DC: National Academy of Science National Research Council; 1966:552-4.
62. Heimbach RD. Gas gangrene. Review and update. HBO Rev. 1980;1:41-6.
63. Peirce EC. Gas gangrene: a critique of therapy. Surg Rounds. 1984;7:17-25.
64. Marroni A, Longobardi P, Cali-Corleo R. Cost-Effectiveness Evaluation of HBO Therapy. In: Mathieu D, ed. Handbook on Hyperbaric Medicine. Dordrecht, The Netherlands: Springer; 2006:674-7.
65. Kindwall EP, chairman. Hyperbaric oxygen therapy committee report. UMS Report Number 5-23-77; 1977:4.
66. Evidence-Based Medicine Working G. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992;268(17):2420-5.
67. Haynes RB, Devereaux PJ, Guyatt GH. Clinical expertise in the era of evidence-based medicine and patient choice. Evid Based Med. 2002;7:36-8.
68. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. N Engl J Med. 1996;334(25):1642-8.
69. Mitton C, Hailey D. Health technology assessment and policy decisions on hyperbaric oxygen treatment. Int J Technol Assess Health Care. 1999;15(4):661-70.
70. Yang Z, Hu J, Qu Y, Sun F, Leng X, Li H, et al. Interventions for treating gas gangrene. Cochrane Database Syst Rev. 2015(12):CD010577.
71. Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. Diving Hyperb Med. 2017;47(1):24-32.

## **Chapter 5: The Effect of Hyperbaric Oxygen on Compromised Grafts and Flaps**

*Shawna Kleban MD, Richard C. Baynosa MD (corresponding author)*

### **REFERENCES**

1. Francis A, Baynosa RC. Hyperbaric Oxygen Therapy for the Compromised Graft or Flap. *Adv Wound Care (New Rochelle)*. 2017 Jan 1;6(1):23-32.
2. Francis A, Baynosa RC. Ischaemia-reperfusion injury and hyperbaric oxygen pathways: a review of cellular mechanisms. *Diving Hyperb Med*. 2017 Jun;47(2):110-117.
3. Kivilisaari J, Niinikoski J. Effects of hyperbaric oxygen and prolonged hypoxia on the healing of open wounds. *Acta Chir Scand*. 1975;141:14-19.
4. Shulman AG, Krohn HL. Influence of hyperbaric oxygen and multiple skin allografts on the healing of skin wounds. *Surgery*. 1967;62:1051-1058.
5. Erdmann D, Roth AC, Hussmann J, et al. Skin allograft rejection and hyperbaric oxygen treatment in immunohistocompatible mice. *Undersea Hyperbaric Med*. 1995;22: 395-399.
6. Erdmann D, Roth AC, Hussman J, et al. Hyperbaric oxygen and cyclosporine as a combined treatment regimen to prevent skin allograft rejection in immunohistocompatible mice. *Ann Plast Surg*. 1996;36:304-308.
7. Renner G, McClane SD, Early E, et al. Enhancement of auricular composite graft survival with hyperbaric oxygen therapy. *Arch Facial Plast Surg*. 2002;4:102-104.
8. Rubin JS, Marzella L, Myers RA, et al. Effects of hyperbaric oxygen on the take of composite skin grafts in rabbit ears. *J Hyperbaric Med*. 1988;3:79-88.
9. Zhang F, Cheng C, Gerlach T, et al. Effect of hyperbaric oxygen on survival of the composite ear graft in rats. *Ann Plast Surg*. 1998;41:530-534.
10. Li EN, Menon NG, Rodriguez ED, et al. The effect of hyperbaric oxygen therapy on composite graft survival. *Ann Plast Surg*. 2004; 53:141-145.
11. Fodor L, Ramon Y, Meilik B, et al. Effect of hyperbaric oxygen on survival of composite grafts in rats. *Scand J Plast Reconstr Surg Hand Surg*. 2006;40:257-260.
12. Kernahan KA, Zingg W, Kay CW. The effect of hyperbaric oxygen on the survival of experimental skin flaps. *Plast Reconstr Surg*. 1965;36:19-25.
13. McFarlane RM, DeYoung G, Henry RA. Prevention of necrosis in experimental pedicle flaps with hyperbaric oxygen. *Surg Forum*. 1965;6:481-482.
14. Wald HI, Georgiade NG, Angelillo J, et al. Effect of intensive hyperbaric oxygen therapy on the survival of experimental skin flaps in rats. *Surg Forum*. 1968;19:497-499.
15. Niinikoski J. Viability of ischemic skin in hyperbaric oxygen. *Acta Chir Scand*. 1970; 136: 567-568.
16. Gruber RP, Heitkamp DH, Lawrence JB. Skin permeability to oxygen and hyperbaric oxygen. *Arch Surg*. 1970;101:69-70.
17. Pellitteri PK, Kennedy TL, Youn BA. The influence of intensive hyperbaric oxygen therapy on skin flap survival in a swine model. *Arch Otolaryngol Head Neck Surg*. 1992;118:1050-1054.
18. Arturson GG, Khanna NN. The effects of hyperbaric oxygen, dimethyl sulfoxide and complamin on survival of experimental skin flaps. *Scand J Plast Reconstr Surg*. 1970;4:8-10.
19. Esclamado RM, Larrabee WF Jr, Zel GE. Efficacy of steroids and hyperbaric oxygen on survival of dorsal skin flaps in rats. *Otolaryngol Head Neck Surg*. 1990;102:41-44.
20. Stewart RJ, Moore T, Bennett B, et al. Effect of free-radical scavengers and hyperbaric oxygen on random-pattern skin flaps. *Arch Surg*. 1994;129:982-987.
21. Da Rocha FP, Fagundes DJ, Rivoire HC, et al. Immunohistochemical expression of apoptosis and VEGF expression on random skin flaps in rats treated with hyperbaric oxygen and N-acetylcysteine. *Undersea Hyperbaric Med*. 2011;38:167-174.
22. Da Rocha FP, Fagundes DJ, Pires JA, et al. Effects of hyperbaric oxygen and N-acetylcysteine in survival of random pattern skin flaps in rats. *Indian J Plast Surg*. 2012;45:453-458.
23. Greenwood TW, Gilchrist AG. The effect of HBO on wound healing following ionizing radiation. In: Trapp WC, et al., Eds. *Proceedings of the fifth international congress on hyperbaric medicine*, Vol I. Barnaby, Canada: Simon Fraser University. 1973;253-263.
24. Nemiroff PM, Merwin GE, Brant T, et al. HBO and irradiation on experimental skin flaps in rats. *Surg Forum*. 1984;35:549-550.
25. Nemiroff PM, Merwin GE, Brant, et al. Effects of hyperbaric oxygen and irradiation on experimental flaps in rats. *Otolaryngol Head Neck Surg*. 1985;93: 485-491.
26. Zhang T, Gong W, Li Z, et al. Efficacy of hyperbaric oxygen on survival of random pattern skin flap in diabetic rats. *Undersea Hyperbaric Med*. 2007;335-339.

27. Selcuk CT, Kuvat SV, Bozkurt M, et al. The effect of hyperbaric oxygen therapy on the survival of random pattern skin flaps in nicotine-treated rats. *J Plast Reconstr Aesthet Surg.* 2012;65:489-493.
28. Demirtas A, Azbo I, Bulut M, et al. Effect of hyperbaric oxygen therapy on healing in an experimental model of degloving injury in tails of nicotine-treated rats. *J Hand Surg Eur Vol.* Epub ahead of print. 2012 Dec 7.
29. Nemiroff PM, Lungu AL. The influence of hyperbaric oxygen and irradiation on vascularity in skin flaps: a controlled study. *Surg Forum.* 1987;38:565-567.
30. Manson PN, Im MJ, Myers RA, et al. Improved capillaries by hyperbaric oxygen in skin flaps. *Surg Forum.* 1980;31:564-566.
31. Hartwig J, Kohnlein HE. The influence of hyperbaric oxygen therapy and Dextran 40 on wound healing. *Eur Surg Res.* 5(Suppl). 1973:109.
32. Meltzer T, Myers B. The effect of hyperbaric oxygen on the bursting strength and rate of vascularization of skin wounds in rats. *Am Surg.* 1986;52: 659-662.
33. Marx RE and Ames JR. The use of hyperbaric oxygen therapy in bony reconstruction of the irradiated and tissue deficient patient. *J Oral Maxillofac Surg.* 1982;40: 412-420.
34. Champion WM, McSherry CK, Goulian D. Effect of hyperbaric oxygen on survival of pedicled skin flaps. *J Surg Res.* 1967;7:583-586.
35. McFarlane RM, Wermuth RE. The use of hyperbaric oxygen to prevent necrosis in experimental pedicle flaps and composite skin grafts. *Plast Reconstr Surg.* 1966;37:422-430.
36. Jurell G, Kaijser L. The influence of varying pressure and duration of treatment with hyperbaric oxygen on the survival of skin flaps: an experimental study. *Scand J Plast Reconstr Surg.* 1973;7:25-28.
37. Tan CM, Im MJ, Myers RA, et al. Effect of hyperbaric oxygen and hyperbaric air on survival of island skin flaps. *Plast Reconstr Surg.* 1974;73:27-30.
38. Ramon Y, Abramovich A, Shupak A, et al. Effect of hyperbaric oxygen on a rat transverse rectus abdominis myocutaneous flap model. *Plast Reconstr Surg.* 1998;102:416-422.
39. Prada FS, Arrunategui G, Alves MC, et al. Effect of allopurinol, superoxide-dismutase, and hyperbaric oxygen on flap survival. *Microsurg.* 2002;22:352-360.
40. Nemiroff PM. Synergistic effects of pentoxifylline and hyperbaric oxygen on skin flaps. *Arch Otolaryngol Head Neck Surg.* 1988;114:977-981.
41. Collins TM, Caimi R, Lynch PR, et al. The effects of nicotinamide and hyperbaric oxygen on skin flap survival. *Scand J Plast Reconstr Surg Hand Surg.* 1991;25:5-7.
42. Lozano DD, Stephenson LL, Zamboni WA. Effect of hyperbaric oxygen and medicinal leeching on survival of axial skin flaps subjected to total venous occlusion. *Plast Reconstr Surg.* 1999;104:1029-1032.
43. Yucel A, Bayramicli. Effects of hyperbaric oxygen treatment and heparin on the survival of unipedicled venous flaps: and experimental study in rats. *Ann Plast Surg.* 2000;295-303.
44. Ulkur E, Yuksel F, Acikel C, et al. Effect of hyperbaric oxygen on pedicle flaps with compromised circulation. *Microsurg.* 2002;22:; 16-20.
45. Zamboni WA, Roth AC, Russell RC, et al. The effect of acute hyperbaric oxygen therapy on axial pattern skin flap survival when administered during and after total ischemia. *J Reconstr Microsurg.* 1989;5:343-347.
46. Zamboni WA, Roth AC, Russell RC, et al. The effect of hyperbaric oxygen on reperfusion of ischemic axial skin flaps: a laser Doppler analysis. *Ann Plast Surg.* 1992;28:339-341.
47. Kaelin CM, Im MJ, Myers RA, et al. The effects of hyperbaric oxygen on free flaps in rats. *Arch Surg.* 1990;125:607-609.
48. Zamboni WA, Roth AC, Russell RC, et al. Morphological analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg.* 91. 1993;1110-1123.
49. Jones SR, Carpin KM, Woodward SM, et al. Hyperbaric oxygen inhibits ischemia-reperfusion-induced CD18 neutrophil polarization by a nitric oxide mechanism. *Plast Reconstr Surg.* 2010;126:403-411.
50. Baynosa RC, Naig AL, Murphy PS, et al. The effect of hyperbaric oxygen on nitric oxide synthase activity and expression in ischemia-reperfusion injury. *J Surg Res.* Epub ahead of print. 2013 Feb 1.
51. Francis A, Kleban SR, Stephenson LL, et al. Hyperbaric Oxygen Inhibits Reperfusion-Induced Neutrophil Polarization and Adhesion Via Plasmin-Mediated VEGF Release. *Plast Reconstr Surg Glob Open.* 2017 Sep 25;5(9):e1497.
52. Hong JP, Kwon H, Chung YK, et al. The effect of hyperbaric oxygen on ischemia-reperfusion injury: an experimental study in a rat musculocutaneous flap. *Ann Plast Surg.* 2003;51:478-487.
53. Tomur A, Etlik O, Gundogan NU. Hyperbaric oxygenation and antioxidant vitamin combination reduces ischemia-reperfusion injury in a rat epigastric island skin-flap model. *J Basic Clin Physiol Pharmacol.* 2005;16: 275-285.

54. Stevens DM, Weiss DD, Koller WA, et al. Survival of normothermic microvascular flaps after prolonged secondary ischemia: Effects of hyperbaric oxygen. *Otolaryngol Head Neck Surg.* 115: 360-364, 1996.
55. Wong HP, Zamboni WA, Stephenson LL. Effect of hyperbaric oxygen on skeletal muscle necrosis following primary and secondary ischemia in a rat model. *Surg Forum.* 1996;47:705-707.
56. Gampper TJ, Zhang F, Mofakhami NF, et al. Beneficial effect of hyperbaric oxygen on island flaps subjected to secondary venous ischemia. *Microsurg.* 2002;22:49-52.
57. Perrins DJD. Hyperbaric oxygenation of skin flaps. *Br J Plast Surg.* 1966;19:110-112.
58. Perrins DJD, Cantab MB. Influence of hyperbaric oxygen on the survival of split skin grafts. *Lancet.* 1967;1: 868-871.
59. Roje Z, Roje Z, Eterovic D et al. Influence of adjuvant hyperbaric oxygen therapy on short-term complications during surgical reconstruction of upper and lower extremity war injuries: retrospective cohort study. *Croat Med J.* 2008;49:224-232.
60. Gonnering RS, Kindwall EP, Goldmann RW. Adjunct hyperbaric oxygen therapy in periorbital reconstruction. *Arch Ophthalmol.* 1986;104: 439-443.
61. Bowersox JC, Strauss MB, Hart GB. Clinical experience with hyperbaric oxygen therapy in salvage of ischemic skin flaps and grafts. *J Hyperbaric Med.* 1986; 141-149.
62. Friedman HI, Stonerock C, Brill A. Composite earlobe grafts to reconstruct the lateral nasal ala and sill. *Ann Plast Surg.* 2003;3:275-281.
63. Qing Y, Cen Y, Chen J, Ke S. Reconstruction of a large through-and-through defect of the nasal tip using a modified auricular composite graft. *J Craniofac Surg.* 2015;26:382-383.
64. Saber AA, Yahya KZ, Rao A, et al. A new approach in the management of chronic nonhealing leg ulcers. *J Invest Surg.* 2005;18: 321-323.
65. Assaad NN, Chong R, Tat LT, et al. Adjuvant hyperbaric oxygen therapy to support limbal conjunctival graft in the management of recurrent pterygium. *Cornea.* 2011;30:7-10.
66. Ueda M, Kaneda T, Takahashi H, et al. Hyperbaric oxygen therapy of ischemic skin flaps: clinical and experimental study. Proceedings of 9<sup>th</sup> International Symposium on Underwater Hyperbaric Physiology. Undersea & Hyperbaric Medical Society. 1987;823.
67. Mathieu D, Neviere R, Pellerin P, et al. Pedicle musculocutaneous flap transplantation: Prediction of final outcome by transcutaneous oxygen measurements in hyperbaric oxygen. *Plast Reconstr Surg.* 1993;91: 329-334.
68. Waterhouse MA, Zamboni WA, Brown RE, et al. The use of HBO in compromised free tissue transfer and replantation, a clinical review. *Undersea Hyperbaric Med.* 1993; 20(Suppl):64.
69. Larson JV, Steensma EA, Flikkema RM, Norman EM. The application of hyperbaric oxygen therapy in the management of compromised flaps. *Undersea Hyperb Med.* 2013;40:499-504.
70. Skeik N, Porten BR, Isaacson E, et al. Hyperbaric oxygen treatment outcome for different indications from a single center. *Ann Vasc Surg* 2015; 29:206-214.
71. Nicther LS, Morwood DT, Williams GS, et al. Expanding the limits of composite grafting: a case report of successful nose replantation assisted by hyperbaric oxygen therapy. *Plast Reconstr Surg.* 1991;87: 337-340.
72. Rapley JH, Lawrence WT, Witt PD. Composite grafting and hyperbaric oxygen therapy in pediatric nasal tip reconstruction after avulsive dog-bite injury. *Ann Plast Surg.* 2001;46: 434-438.
73. Cantarella G, Mazzola RF and Pagani D. The fate of an amputated nose after replantation. *Am J Otolaryngol.* 2005;26: 344-347.
74. Pou JD, Graham HD. Pediatric Nasal Tip Amputation Successfully Treated with Nonmicrovascular Replantation and Hyperbaric Oxygen Therapy. *Ochsner J.* 2017 Summer;17(2):204-207.
75. McCrary BF. Hyperbaric oxygen treatment for a failing facial flap. *Postgrad Med J.* 2007;83: e1-e3.
76. Khandelwal S, Wall J, Kaide C, et al. Case report: successful use of hyperbaric oxygen therapy for a complete scalp degloving injury. *Undersea Hyperbaric Med.* 2008;35: 441-445.
77. Mermans JF, Tuinder S, von Meyenfeldt MF, et al. Hyperbaric oxygen treatment for skin flap necrosis after a mastectomy: a case study. *Undersea Hyperbaric Med.* 2012;39:719-723.
78. Fredman R, Wise I, Friedman T, Heller L, Kami T. Skin-sparing mastectomy flap ischemia salvage using urgent hyperbaric chamber oxygen therapy: a case report. *Undersea Hyperb Med* 2014;41:145-147.
79. Copeland-Halperin LR, Bruce SR, Mesbahi AN. Hyperbaric oxygen following bilateral skin-sparing mastectomies: a case report. *Plast Reconstr Surg Glob Open.* 2016;4:e680.
80. Zhou YY, Liu W, Yang YJ, Lu GD. Use of hyperbaric oxygen on flaps and grafts in China: analysis of studies in the past 20 years. *Undersea Hyperb Med.* 2014;41:209-216.
81. Baynosa RC and Zamboni WA. Compromised grafts and flaps. In: TS Neuman & SR Thom, Eds. *Physiology and Medicine of Hyperbaric Oxygen Therapy.* Philadelphia, PA: Saunders/Elsevier. 2008; 373-395.

82. Friedman HI, Fitzmaurice M, Lefavre JF, et al. An evidence-based appraisal of the use of hyperbaric oxygen on flaps and grafts. *Plast Reconstr Surg.* 2006;117 (Suppl):175S-190S.
83. Nemiroff PM, Rybak LP. Applications of hyperbaric oxygen for the otolaryngologist-head and neck surgeon. *Am J Otolaryngol.* 1988;9:52-57.
84. Reinisch JF. Pathophysiology of skin flap circulation: The delay phenomenon. *Plast Reconstr Surg.* 1974;54:585-598.
85. Reinisch JF. The role of arteriovenous anastomosis in skin flaps. In: Grabb WC, Myers MBG, Eds. *Skin Flaps.* Boston, MA: Little Brown & Co. 1975;81-92.
86. Weber R, Silver A, Williams SJ, et al. Random flap survival with hyperbaric oxygen: daily versus twice-daily treatments. *Undersea Hyperb Med.* 2018 Mar-Apr;45(2):157-164.

## Chapter 6: The Role of Hyperbaric Oxygen for Acute Traumatic Ischemias

Michael B. Strauss MD

### REFERENCES

1. Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma*. 1984;24(8):742-6.
2. Gustilo RB, Williams DN. The use of antibiotics in the management of open fractures. *Orthopedics*. 1984;7(10):1617-9.
3. Caudle RJ, Stern PJ. Severe open fractures of the tibia. *J Bone Joint Surg Am*. 1987;69(6):801-7.
4. Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. *Diving Hyperb Med*. 2017;47(1):24-32.
5. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet*. 1972;135(4):561-7.
6. Hohn DC, Hunt TK. Oxidative metabolism and microbicidal activity of rabbit phagocytes: cells from wounds and from peripheral blood. *Surg Forum*. 1975;26:85-7.
7. Hunt TK, Linsey M, Grislis H, Sonne M, Jawetz E. The effect of differing ambient oxygen tensions on wound infection. *Ann Surg*. 1975;181(1):35-9.
8. Hunt TK, Zederfeldt B, Goldstick TK. Oxygen and healing. *Am J Surg*. 1969;118(4):521-5.
9. Kerrigan CL, Stotland MA. Ischemia reperfusion injury: a review. *Microsurgery*. 1993;14(3):165-75.
10. Strauss MB, Lu LQ. The role of oxygen and hyperbaric oxygen mechanisms. In: Whelan HT, Kindwall EP, editors. *Hyperbaric Medicine Practice*. North Palm Beach, FL: Best Publishing Company; 2017. Pp. 261-322.
11. Weaver LK. Transcutaneous oxygen and carbon dioxide tensions compared to arterial blood gases in normals. *Respir Care*. 2007;52(11):1490-6.
12. Weaver LK, Howe S, Snow GL, Deru K. Arterial and pulmonary arterial hemodynamics and oxygen delivery/extraction in normal humans exposed to hyperbaric air and oxygen. *J Appl Physiol* (1985). 2009;107(1):336-45.
13. Boerema I, Meyne NG, Brummelkamp WH, Bouma S, Mensch MH, Kamermans F, Stern Hanf M, van Aalderen W. Life without blood. *J Cardiovasc Surg (Torino)*. 1960;1:133-46.
14. Krogh A. The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue. *J Physiol*. 1919;52(6):409-15.
15. Bird AD, Telfer AB. Effect of hyperbaric oxygen on limb circulation. *Lancet*. 1965;1(7381):355-6.
16. Nylander G, Lewis D, Nordstrom H, Larsson J. Reduction of postischemic edema with hyperbaric oxygen. *Plast Reconstr Surg*. 1985;76(4):596-603.
17. Sukoff MH, Ragatz RE. Hyperbaric oxygenation for the treatment of acute cerebral edema. *Neurosurgery*. 1982;10:29-38.
18. Strauss MB, Hargens AR, Gershuni DH, Greenberg DA, Crenshaw AG, Hart GB, Akeson WH. Reduction of skeletal muscle necrosis using intermittent hyperbaric oxygen in a model compartment syndrome. *J Bone Joint Surg Am*. 1983;65(5):656-62.
19. Skyhar MJ, Hargens AR, Strauss MB, Gershuni DH, Hart GB, Akeson WH. Hyperbaric oxygen reduces edema and necrosis of skeletal muscle in compartment syndromes associated with hemorrhagic hypotension. *J Bone Joint Surg Am*. 1986;68(8):1218-24.
20. Strauss MB, Hargens AR, Gershuni DH, Hart GB, Akeson WH. Delayed use of hyperbaric oxygen for treatment of a model anterior compartment syndrome. *J Orthop Res*. 1986;4(1):108-11.
21. Wells CH, Goodpasture JE, Horrigan DJ, Hart GB. Tissue gas measurements during hyperbaric oxygen exposure. In: Smith G, editor. *Sixth International Congress on Hyperbaric Medicine*; Aberdeen, Scotland. Aberdeen, Scotland: Aberdeen University Press; 1979. Pp. 118-24.
22. Sheffield PJ. Sheffield PJ. Tissue oxygen measurements with respect to soft-tissue wound healing with normobaric and hyperbaric oxygen. *HBO Review* (1985). 6:18-46. *Hyperbaric Oxygen Review*. 1985;6:18-46.
23. Burt JT, Kapp JP, Smith RR. Hyperbaric oxygen and cerebral infarction in the gerbil. *Surg Neurol*. 1987;28(4):265-8.
24. Thomas MP, Brown LA, Sponseller DR, Williamson SE, Diaz JA, Guyton DP. Myocardial infarct size reduction by the synergistic effect of hyperbaric oxygen and recombinant tissue plasminogen activator. *Am Heart J*. 1990;120(4):791-800.
25. Thom SR. Functional inhibition of leukocyte b2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol*. 1993;123(2):248-56.
26. Thom S. Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen. *Toxicol Appl Pharmacol*. 1990;105:340-4.

27. Zamboni WA, Roth AC, Russell RC, Nemiroff PM, Casas L, Smoot EC. The effect of acute hyperbaric oxygen therapy on axial pattern skin flap survival when administered during and after total ischemia. *J Reconstr Microsurg.* 1989;5(4):343-7; discussion 9-50.
28. Buras J. Basic mechanisms of hyperbaric oxygen in the treatment of ischemia-reperfusion injury. *Int Anesthesiol Clin.* 2000;38(1):91-109.
29. Thom SR, Xu YA, Ischiropoulos H. Vascular endothelial cells generate peroxynitrite in response to carbon monoxide exposure. *Chem Res Toxicol.* 1997;10(9):1023-31.
30. Ferrari R, Ceconi C, Curello S, Guarnieri C, Calderara CM, Albertini A, Visioli O. Oxygen-mediated myocardial damage during ischaemia and reperfusion: role of the cellular defences against oxygen toxicity. *J Mol Cell Cardiol.* 1985;17(10):937-45.
31. Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y. Hyperbaric oxygen and thrombolysis in myocardial infarction: the "HOT MI" pilot study. *Am Heart J.* 1997;134(3):544-50.
32. Strauss MB, Lu LQ. The roles of hyperbaric oxygen In crush Injury and other acute traumatic Ischemias. In: Whelan HT, Kindwall EP, editors. *Hyperbaric Medicine Practice.* North Palm Beach, FL: Best Publishing Company; 2017. Pp. 659-90.
33. Strauss MB. Crush injuries and skeletal muscle-compartment syndromes. In: Weaver LK, editor. *Hyperbaric Oxygen Therapy Indications.* Durham, NC: Undersea & Hyperbaric Medical Society; 2014. Pp. 91-103.
34. Strauss MB. Strauss MB. Role of hyperbaric oxygen therapy in acute ischemias and crush injuries—an orthopedic perspective. *Hyperbaric Oxygen Review.* 1981;2:87-108.
35. Strauss MB, Garcia-Covarrubias L. Crush injuries: Justification of and indications for hyperbaric oxygen therapy. In: Neuman TS, Thom SR, editors. *The Physiology and Medicine of Hyperbaric Oxygen Therapy.* Philadelphia, PA: Saunders Elsevier; 2008. Pp. 427-49.
36. Chiang IH, Tzeng YS, Chang SC. Is hyperbaric oxygen therapy indispensable for saving mutilated hand injuries? *Int Wound J.* 2017;14(6):929-36.
37. Slack WD, Thomas DA, De Jode LR. Hyperbaric oxygen in the treatment of trauma, ischemic disease of limbs and varicose ulceration. In: Brown IW, Cox BG, editors. *Proceeding of the Third International Conference on Hyperbaric Medicine.* Washington, DC: National Academy of Science, National Research Council Publication 1404; 1966. Pp. 621-4.
38. Schramek A, Hashmonai M. Vascular injuries in the extremities in battle casualties. *Br J Surg.* 1977;64(9):644-8.
39. Loder RE. Hyperbaric oxygen therapy in acute trauma. *Ann R Coll Surg Engl.* 1979;61(6):472-3.
40. Nylander G, Nordstrom H, Franzen L, Henriksson KG, Larsson J. Effects of hyperbaric oxygen treatment in post-ischemic muscle. A quantitative morphological study. *Scand J Plast Reconstr Surg Hand Surg.* 1988;22(1):31-9.
41. Bouachour G, Cronier P, Gouello JP, Toulemonde JL, Talha A, Alquier P. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blind placebo-controlled clinical trial. *J Trauma.* 1996;41(2):333-9.
42. Nylander G, Otamiri T, Lewis DH, Larsson J. Lipid peroxidation products in postischemic skeletal muscle and after treatment with hyperbaric oxygen. *Scand J Plast Reconstr Surg Hand Surg.* 1989;23(2):97-103.
43. Bartlett RL, Stroman RT, Nickels M, Kalns JE, Fuhrman CT, Piepmeier EH. Rabbit model of the use of fasciotomy and hyperbaric oxygen in the treatment of compartment syndrome. *Undersea Hyperb Med.* 1998;25(Suppl):29.
44. Malerba F, Oriani G, Farnetti A. HBO in orthopedic disorders In: Oriani G, Marroni A, Wattel F, editors. *Handbook on Hyperbaric Medicine* Milan, Italy: Springer; 1996. Pp. 409-27.
45. Fitzpatrick DT, Murphy PT, Bryce M. Adjunctive treatment of compartment syndrome with hyperbaric oxygen. *Mil Med.* 1998;163(8):577-9.
46. Strauss MB, Hart GB. Hyperbaric oxygen and the skeletal muscle-compartment syndrome. *Contemp Orthop.* 1989;18:167-74.
47. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, Guerci AD, Lima JA, Rader DJ, Rubin GD, Shaw LJ, Wiegers SE, American Heart Association Committee on Cardiovascular I, Intervention, American Heart Association Council on Cardiovascular R, Intervention, American Heart Association Committee on Cardiac Imaging CoCC. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation.* 2006;114(16):1761-91.
48. Berwick DM. Health services research and quality of care. Assignments for the 1990s. *Med Care.* 1989;27(8):763-71.

49. Strauss MB. The role of hyperbaric oxygen in the surgical management of chronic refractory osteomyelitis. In: Bakker DJ, Cramer FS, editors. *Hyperbaric Surgery Perioperative Care*. Flagstaff, AZ: Best Publishing; 2002. Pp. 37-62.
50. Brighton CT. Hospital Tribune. May 9, 1977.
51. Strauss MB, Tan AM, Lu LQ. Fracture healing and the roles of hyperbaric oxygen. In: Whelan HT, Kindwall EP, editors. *Hyperbaric Medicine Practice*. North Palm Beach, FL: Best Publishing Company; 2017. Pp. 623-40.
52. MacKenzie EJ, Bosse MJ, Pollak AN, Webb LX, Swiontkowski MF, Kellam JF, Smith DG, Sanders RW, Jones AL, Starr AJ, McAndrew MP, Patterson BM, Burgess AR, Castillo RC. Long-term persistence of disability following severe lower-limb trauma. Results of a seven-year follow-up. *J Bone Joint Surg Am*. 2005;87(8):1801-9.
53. Strauss MB. Cost-effective issues in hyperbaric oxygen therapy: complicated fractures [Editorial]. *J Hyperbaric Med*. 1988;3(4):199-205.
54. Strauss MB. Why hyperbaric oxygen therapy may be useful in treating crush injuries and skeletal muscle-compartment syndrome [Editorial]. *Undersea Hyperb Med*. 2012;39(4):799-800.

## Chapter 7: Decompression Sickness

Richard E. Moon MD, Simon J. Mitchell MD, MBChB, PhD

### REFERENCES

1. Mitchell SJ. Decompression sickness: pathophysiology. In: Edmonds C, Bennett MH, editors. Diving and Subaquatic Medicine. 5 ed. Boca Raton, FL: Taylor and Francis; 2015. p. 125-40.
2. Hundemer GL, Jersey SL, Stuart RP, Butler WP, Pilmanis AA. Altitude decompression sickness incidence among U-2 pilots: 1994-2010. *Aviat Space Environ Med*. 2012;83(10):968-74.
3. Kohshi K, Wong RM, Abe H, Katoh T, Okudera T, Mano Y. Neurological manifestations in Japanese Ama divers. *Undersea Hyperb Med*. 2005;32(1):11-20.
4. Schipke JD, Gams E, Kallweit O. Decompression sickness following breath-hold diving. *Res Sports Med*. 2006;14(3):163-78.
5. Van Liew HD, Flynn ET. Direct ascent from air and N<sub>2</sub>-O<sub>2</sub> saturation dives in humans: DCS risk and evidence of a threshold. *Undersea Hyperb Med*. 2005;32(6):409-19.
6. Freiberger JJ, Denoble PJ, Pieper CF, Uguccioni DM, Pollock NW, Vann RD. The relative risk of decompression sickness during and after air travel following diving. *Aviat Space Environ Med*. 2002;73:980-4.
7. Vann RD, Pollock NW, Freiberger JJ, Natoli MJ, Denoble PJ, Pieper CF. Influence of bottom time on preflight surface intervals before flying after diving. *Undersea Hyperb Med*. 2007;34(3):211-20.
8. Webb JT, Pilmanis AA, O'Connor RB. An abrupt zero-preoxygenation altitude threshold for decompression sickness symptoms. *Aviat Space Environ Med*. 1998;69(4):335-40.
9. Webb JT, Kannan N, Pilmanis AA. Gender not a factor for altitude decompression sickness risk. *Aviat Space Environ Med*. 2003;74(1):2-10.
10. Francis TJ, Griffin JL, Homer LD, Pezeshkpour GH, Dutka AJ, Flynn ET. Bubble-induced dysfunction in acute spinal cord decompression sickness. *J Appl Physiol* (1985). 1990;68:1368-75.
11. Philp RB, Schacham P, Gowdey CW. Involvement of platelets and microthrombi in experimental decompression sickness: similarities with disseminated intravascular coagulation. *Aerospace Med*. 1971;42(5):494-502.
12. Nossum V, Koteng S, Brubakk AO. Endothelial damage by bubbles in the pulmonary artery of the pig. *Undersea Hyperb Med*. 1999;26(1):1-8.
13. Nossum V, Hjelde A, Brubakk AO. Small amounts of venous gas embolism cause delayed impairment of endothelial function and increase polymorphonuclear neutrophil infiltration. *Eur J Appl Physiol*. 2002;86:209-14.
14. Berry CA, King AH. Severe dysbarism in actual and simulated flight; a follow-up study of five cases. *U S Armed Forces Med J*. 1959;10(1):1-15.
15. Malette WG, Fitzgerald JB, Cockett AT. Dysbarism. A review of thirty-five cases with suggestion for therapy. *Aerospace Med*. 1962;33:1132-9.
16. Brunner F, Frick P, Bühlmann A. Post-decompression shock due to extravasation of plasma. *Lancet*. 1964;1:1071-3.
17. Boussuges A, Blanc P, Molenat F, Bergmann E, Sainty JM. Haemoconcentration in neurological decompression illness. *Int J Sports Med*. 1996;17:351-5.
18. Levin LL, Stewart GJ, Lynch PR, Bove AA. Blood and blood vessel wall changes induced by decompression sickness in dogs. *J Appl Physiol* (1985). 1981;50:944-9.
19. Ward CA, Koheil A, McCullough D, Johnson WR, Fraser WD. Activation of complement at plasma-air or serum-air interface of rabbits. *J Appl Physiol* (1985). 1986;60:1651-8.
20. Ward CA, McCullough D, Yee D, Stanga D, Fraser WD. Complement activation involvement in decompression sickness of rabbits. *Undersea Biomed Res*. 1990;17:51-66.
21. Little T, Butler BD. Pharmacological intervention to the inflammatory response from decompression sickness in rats. *Aviat Space Environ Med*. 2008;79(2):87-93.
22. Helps SC, Gorman DF. Air embolism of the brain in rabbits pre-treated with mechlorethamine. *Stroke*. 1991;22:351-4.
23. Thom SR, Yang M, Bhopale VM, Huang S, Milovanova TN. Microparticles initiate decompression-induced neutrophil activation and subsequent vascular injuries. *J Appl Physiol* (1985). 2011;110(2):340-51.
24. Yang M, Kosterin P, Salzberg BM, Milovanova TN, Bhopale VM, Thom SR. Microparticles generated by decompression stress cause central nervous system injury manifested as neurohypophyseal terminal action potential broadening. *J Appl Physiol* (1985). 2013.
25. Elliott DH, Moon RE. Manifestations of the decompression disorders. In: Bennett PB, Elliott DH, editors. *The Physiology and Medicine of Diving*. Philadelphia, PA: WB Saunders; 1993. p. 481-505.
26. Francis TJR, Mitchell SJ. Manifestations of decompression disorders. In: Brubakk AO, Neuman TS, editors. *Bennett & Elliott's Physiology and Medicine of Diving*. New York, NY: Elsevier Science; 2003. Pp. 578-99.
27. Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. *Lancet*. 2011;377(9760):153-64.

28. Mitchell SJ. Decompression sickness: manifestations. In: Edmonds C, Bennett MH, editors. Diving and Subaquatic Medicine. 5 ed. Boca Raton, FL: Taylor and Francis; 2015. Pp. 141-51.
29. Zwirewich CV, Müller NL, Abboud RT, Lepawsky M. Noncardiogenic pulmonary edema caused by decompression sickness: rapid resolution following hyperbaric therapy. Radiology. 1987;163:81-2.
30. Trytko B, Mitchell SJ. Extreme survival: a deep technical diving accident. SPUMS J. 2005;35:23-7.
31. Warren LP, Djang WT, Moon RE, Camporesi EM, Sallee DS, Anthony DC. Neuroimaging of scuba diving injuries to the CNS. AJNR Am J Neuroradiol. 1988;9:933-8.
32. Reuter M, Tetzlaff K, Hutzemann A, Fritsch G, Steffens JC, Bettinghausen E, Heller M. MR imaging of the central nervous system in diving-related decompression illness. Acta Radiol. 1997;38(6):940-4.
33. Gempp E, Blatteau JE, Stephan E, Pontier JM, Constantin P, Peny C. MRI findings and clinical outcome in 45 divers with spinal cord decompression sickness. Aviat Space Environ Med. 2008;79(12):1112-6.
34. Chung JM, Ahn JY. Relationship between clinical and radiologic findings of spinal cord injury in decompression sickness. Undersea Hyperb Med. 2017;44(1):57-62.
35. Pol B, Wattelle TJJ. Mémoire sur les effets de la compression de l'air appliquée au creusement des puits à houille. Ann Hyg Pub Med Leg. 1854;2:241-79.
36. Moir EW. Tunnelling by compressed air. J Soc Arts. 1896;44(May 15):567-85.
37. Bert P. Barometric Pressure (La Pression Barométrique). Bethesda, MD: Undersea Medical Society; 1978.
38. Zuntz N. Zur Pathogenese und Therapie der durch rasche Luftdruckänderungen erzeugten Krankheiten. Fortschr Med. 1897;15:632-9.
39. Yarbrough OD, Behnke AR. The treatment of compressed air illness using oxygen. J Ind Hyg Toxicol. 1939;21:213-8.
40. Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H, Kucan JO. Morphological analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. Plast Reconstr Surg. 1993;91:1110-23.
41. Martin JD, Thom SR. Vascular leukocyte sequestration in decompression sickness and prophylactic hyperbaric oxygen therapy in rats. Aviat Space Environ Med. 2002;73(6):565-9.
42. Kindwall EP. Use of short *versus* long tables in the treatment of decompression sickness and arterial gas embolism. In: Moon RE, Sheffield PJ, editors. Treatment of Decompression Illness. Kensington, MD: Undersea and Hyperbaric Medical Society; 1996. Pp. 122-6.
43. Thalmann ED. Principles of US Navy recompression treatments for decompression sickness. In: Moon RE, Sheffield PJ, editors. Treatment of Decompression Illness. Kensington, MD: Undersea and Hyperbaric Medical Society; 1996. Pp. 75-95.
44. Moon RE, Sheffield PJ. Guidelines for treatment of decompression illness. Aviat Space Environ Med. 1997;68:234-43.
45. Moon RE, Gorman DF. Treatment of the decompression disorders. In: Neuman TS, Brubakk AO, editors. Bennett & Elliott's Physiology and Medicine of Diving. New York, NY: Elsevier Science; 2003. Pp. 600-50.
46. Hadanny A, Fishlev G, Bechor Y, Bergan J, Friedman M, Maliar A, Efrati S. Delayed recompression for decompression sickness: retrospective analysis. PLoS ONE. 2015;10(4):e0124919.
47. Chin W, Joo E, Ninokawa S, Popa DA, Covington DB. Efficacy of the U.S. Navy Treatment Tables in treating DCS in 103 recreational scuba divers. Undersea Hyperb Med. 2017;44(5):399-405.
48. Moon RE, Gorman DF. Decompression sickness. In: Neuman TS, Thom SR, editors. The Physiology and Medicine of Hyperbaric Oxygen Therapy. Philadelphia, PA: Saunders Elsevier; 2008. Pp. 283-319.
49. Navy Department. US Navy Diving Manual. Revision 7. Vol 5 : Diving Medicine and Recompression Chamber Operations. NAVSEA 0910-LP-115-1921. Washington, DC: Naval Sea Systems Command; 2016.
50. Mitchell SJ, Doolette DJ, Wachholz CJ, Vann RD, editors. Management of Mild or Marginal Decompression Illness in Remote Locations. Durham, NC: Divers Alert Network; 2005.
51. Mitchell SJ, Bennett MH, Bryson P, Butler FK, Doolette DJ, Holm JR, Kot J, Lafere P. Pre-hospital management of decompression illness: expert review of key principles and controversies. Diving Hyperb Med. 2018;48(1):45-55.
52. Ball R. Effect of severity, time to recompression with oxygen, and retreatment on outcome in forty-nine cases of spinal cord decompression sickness. Undersea Hyperb Med. 1993;20:133-45.
53. Ross JAS. Clinical Audit and Outcome Measures in the Treatment of Decompression Illness in Scotland. A report to the National Health Service in Scotland Common Services Agency, National Services Division on the conduct and outcome of treatment for decompression illness in Scotland from 1991-1999. Aberdeen, UK: Department of Environmental and Occupational Medicine, University of Aberdeen Medical School; 2000 27 April 2000.
54. Goodman MW, Workman RD. Minimal recompression oxygen-breathing approach to treatment of decompression sickness in divers and aviators. Washington, DC: US Navy Experimental Diving Unit Report #5-65; 1965.
55. Bennett MH, Mitchell SJ, Young D, King D. The use of deep tables in the treatment of decompression illness: the Hyperbaric Technicians and Nurses Association 2011 Workshop. Diving Hyperb Med. 2012;42(3):171-80.

56. Vann RD, Bute BP, Ugugioni DM, Smith LR. Prognostic factors in DCI in recreational divers. In: Moon RE, Sheffield PJ, editors. *Treatment of Decompression Illness*. Kensington, MD: Undersea and Hyperbaric Medical Society; 1996. Pp. 352-63.
57. Gempp E, Blatteau JE. Risk factors and treatment outcome in scuba divers with spinal cord decompression sickness. *J Crit Care*. 2010;25:236-42.
58. Rivera JC. Decompression sickness among divers: an analysis of 935 cases. *Mil Med*. 1964;129:314-34.
59. Workman RD. Treatment of bends with oxygen at high pressure. *Aerospace Med*. 1968;39:1076-83.
60. How J, Chan G. Management of delayed cases of decompression sickness--3 case reports. *Singapore Med J*. 1973;14(4):582-5.
61. Erde A, Edmonds C. Decompression sickness: a clinical series. *J Occup Med*. 1975;17(5):324-8.
62. Kizer KW. Delayed treatment of dysbarism: a retrospective review of 50 cases. *JAMA*. 1982;247(18):2555-8.
63. Meyers RAM, Bray P. Delayed treatment of serious decompression sickness. *Ann Emerg Med*. 1985;14:254-7.
64. Curley MD, Schwartz HJC, Zwingelberg KM. Neuropsychologic assessment of cerebral decompression sickness and gas embolism. *Undersea Biomed Res*. 1988;15:223-36.
65. Rudge FW, Shafer MR. The effect of delay on treatment outcome in altitude-induced decompression sickness. *Aviat Space Environ Med*. 1991;62:687-90.
66. Kindwall EP. Decompression sickness. In: Davis JC, Hunt TK, editors. *Hyperbaric Oxygen Therapy*. Bethesda, MD: Undersea Medical Society; 1977. Pp. 125-40.
67. Hart GB, Strauss MB, Lennon PA. The treatment of decompression sickness and air embolism in a monoplace chamber. *J Hyperb Med*. 1986;1:1-7.
68. Elliott DH, Kindwall EP. Decompression sickness. In: Kindwall EP, Whelan HT, editors. *Hyperbaric Medicine Practice*. Flagstaff, AZ: Best Publishing Co; 1999. Pp. 433-87.
69. Bond JG, Moon RE, Morris DL. Initial table treatment of decompression sickness and arterial gas embolism. *Aviat Space Environ Med*. 1990;61:738-43.
70. Cianci P, Slade JB, Jr. Delayed treatment of decompression sickness with short, no-air-break tables: review of 140 cases. *Aviat Space Environ Med*. 2006;77(10):1003-8.
71. Weaver LK. Monoplace hyperbaric chamber use of U.S. Navy Table 6: a 20-year experience. *Undersea Hyperb Med*. 2006;33(2):85-8.
72. Farm FP, Jr, Hayashi EM, Beckman EL. Diving and decompression sickness treatment practices among Hawaii's diving fisherman. *Sea Grant Technical Paper UNIHI-SEAGRANT-TP-86-01*. Sea Grant Technical Paper. Honolulu: University of Hawaii; 1986. Report No.: UNIHI-SEAGRANT-TP-86-01.
73. Doolette DJ, Mitchell SJ. In-water recompression. *Diving Hyperb Med*. 2018;48(2):84-95.
74. Pyle RL, Youngblood DA. In-water recompression as an emergency field treatment of decompression illness. *SPUMS J*. 1997;27:154-69.
75. Dituri J, Sadler R, Siddiqi F, Sadler C, Javeed N, Annis H, Whelan H. Echocardiographic evaluation of intracardiac venous gas emboli following in-water recompression. *Undersea Hyperb Med*. 2016;43(2):103-12.
76. Dart TS, Butler W. Towards new paradigms for the treatment of hypobaric decompression sickness. *Aviat Space Environ Med*. 1998;69(4):403-9.
77. Butler WP, Topper SM, Dart TS. USAF treatment table 8: Treatment for altitude decompression sickness. *Aviat Space Environ Med*. 2002;73(1):46-9.
78. Moon RE, editor. *Adjunctive Therapy for Decompression Illness*. Kensington, MD: Undersea and Hyperbaric Medical Society; 2003.

## **Chapter 8: Delayed Radiation Injuries (Soft Tissue and Bony Necrosis) and Potential for Future Research**

*John J. Feldmeier DO, FACRO, FUHM, Laurie B. Gesell MD, FACEP, FUHM*

### **REFERENCES**

1. Studer G, Studer SP, Zwahlen RA et al. Osteoradionecrosis of the mandible: minimized risk profile following intensity-modulated radiation therapy (IMRT). *Strahlen Onko* 2006;182(5):283-8.
2. Rubin P, Casarrett GW. Clinical radiation pathology, vol.1. Philadelphia, PA: WB Saunders; 1968:57-61.
3. Hall EJ, Giaccia A. Radiobiology for the Radiologist. Philadelphia, PA: Lippincot, Williams & Wilkins, and Wolters Kluwer; 2012:9-34.
4. Stone HB, Coleman CN, Anscher MS, McBride WH. Effects of radiation on normal tissues: consequences and mechanisms. *Lancet Oncol* 2003;4:529-36.
5. Metler FA, Upton AC. Medical effects of ionizing radiation. WB Saunders Company; 1995:230.
6. Hall EJ, Giaccia A. Radiobiology for the radiologist. Lippincot, Williams & Wilkins, and Wolters Kluwer; 2012:327-55.
7. Dorr W, Hendry H. Consequential late effects in normal tissues. *Radiotherapy and oncology* 2001;61:223-31.
8. Teguh DN, Levendag PC, Noever I, et al. Early hyperbaric oxygen therapy for reducing radiotherapy side effects: early results of a randomized trial in oropharyngeal and nasopharyngeal cancer. *Int J Radiation Oncology Biol Phys*. 2009;75(3):711-6.
9. Rosenstein BS. Radiogenomics: identification of genomic predictors for radiation toxicity. *Semin Radiat Oncol*. 2017;27:300-9.
10. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg*. 1983;41:283-288.
11. Hojan K, Milecki P. Opportunities for rehabilitation of patients with radiation fibrosis syndrome. *Reports of Practical Oncology and Radiotherapy*. 2014;19:1-6.
12. Delainian S, Lefax JL. The radiation-induced fibrotrophic process: therapeutic perspective via the antioxidant pathway. *Radiother Oncol*. 2004;73(2):119-31.
13. Fleckenstein K, Gauter-Fleckenstein B, Jackson IL, Rabbani Z, Anscher M, Vujaskovic Z. Using biological markers to predict risk of radiation injury. *Semin Radiat Oncol*. 2007;17:89-98.
14. O'Sullivan B, Levin W. Late radiation-related fibrosis: pathogenesis, manifestations, and current management. *Seminars in Radiat Oncol*. 2003;13(3):274-89.
15. Darby IA, Hewitson TD. Hypoxia in tissue repair and fibrosis. *Cell tissue RE*. 2016;365:553-62.
16. Hakenjos L, Bamberg M, Rodemann HP. TGF beta-1-mediated alterations of rat lung fibroblast differentiation resulting in the radiation-induced fibrotic phenotype. *Int J Radiat Biol*. 2000;76:503-9.
17. Andreassen CN, Alsner J, Overgaard J. Does variability in normal tissue reactions after radiotherapy have a genetic basis? Where and how to look for it. *Radiotherapy and oncology*. 2002;64:131-40.
18. Stewart FA, Akleyev AV, Hauer-Jensen M, et al. ICRP publication 118: ICRP statement on tissue reactions and early and late effects of radiation in normal tissues and organ-threshold doses for tissue reactions in radiation protection context. *Ann IRCP*. 2012;41(1-20):1-322.
19. Marx RE, Johnson RP, Kline SN. Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen versus penicillin. *J Am Dent Assoc*. 1985;11:49-54.
20. Deshpande SS, Donneys A, Farberg AS et al. Quantification and characterization of radiation-induced changes to mandibular vascularity using micro-computed tomography. *Ann Plast Surg*. 2014;72(1):100-3.
21. Marx RE. Radiation injury to tissue. In: Kindwall EP, ed. Hyperbaric medicine practice, fourth edition. North Palm Beach, FL: Best Publishing Company; 2017:727- 73.
22. Svalestad J, Thorsen G, VaagboS et al. Effect of hyperbaric oxygen treatment on oxygen tension and vascular capacity in irradiated skin and mucosa. *Int J Oral and Maxillofac Surg*. 2013;43:107-12.
23. Johnson-Arbor K, Falola R, Kelty J et al. Use of indocyanine green fluorescent angiography in a hyperbaric patient with soft tissue radiation necrosis: a case report. *Undersea Hyperb Med*. 2017;44(3):273-8.
24. Feldmeier JJ, Davolt DA, Court WS, Onoda JM, Alecu R. Histologic morphometry confirms a prophylactic effect for hyperbaric oxygen in the prevention of delayed radiation enteropathy. *Undersea Hyperb Med*. 1998; 25(2):93-97.
25. Feldmeier JJ, Jelen I, Davolt DA, Valente PT, Meltz ML, Alecu R. Hyperbaric oxygen as a prophylaxis for radiation induced delayed enteropathy. *Radiotherapy and Oncology*. 1995; 35:138-144.
26. Hamilton SN, Arshad O, Kwok J et al. Documentation and incidence of late effects and screening recommendations for adolescent and young adult patients with head and neck cancer survivors treated with radiotherapy. *Support Care Cancer* 2018;published online 22 Nov 2018.
27. Milanova TN, Bhopale VM, Sorokino EM et al. Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo. *J Appl Physiol*. 1985;106(2):711-28.
28. Thom SR, Bhopale VM, Velazquez OC et al. Stem cell mobilization by hyperbaric oxygen. *AJP-Heart*. 2005;290:1378-86.

29. Hart GB, Manous EG. The treatment of radiation necrosis with hyperbaric oxygen (OHP). *Cancer*. 1976;37:2580-5.
30. Tobey RE, Kelly JF. Osteoradionecrosis of the jaws. *Otolaryngol Clin North Am*. 1979;12(1):183-186.
31. Bedwinek JM, Shukovsky LJ, Fletcher GH, Daly TE. Osteonecrosis in patients treated with definitive radiotherapy for squamous cell cancers of the oral cavity and naso- and oropharynx. *Radiology*. 1976;119:665-667.
32. Emami B, Lyman J, Brown A, Coia L, Gottein M, Munzenrider JE, Shank B, Solin LJ, Wesson M. Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys*. 1991;21:109-122.
33. Reuther T, Schuster T, Mende U, et al. Osteoradionecrosis of the jaws a side effect of radiotherapy of head and neck tumor patients-a report of a thirty-year retrospective review. *Int J Oral and Maxillofac Surg*. 2003;32:289-295.
34. Gomez DR, Estilo L, Wolden SL, Zelefsky MJ, Kraus DH, Wong RJ, Shahar AR, Jatin JP, Mechakos JG, Lee NY. Correlation of osteoradionecrosis and dental events with dosimetric parameters in intensity-modulated radiation therapy for head and neck cancer. *Int J Radiat Oncol Biol Phys*. 2011 Nov 15;81(4):e207-13.
35. Caparotti F, Huang SH, Bratman SV, et al. Osteoradionecrosis of the mandible in carcinoma treated with intensity-modulated radiotherapy. *Cancer*. 2017;123(19):369-373.
36. Maesschaick T, Dulguerov N, Caparotti F, et al. Comparison of the incidence of osteoradionecrosis with conventional radiotherapy and intensity-modulated radiotherapy. *Head Neck*. 2016;38(11):1695-1702.
37. Suntharalingam M. The role of chemotherapy and radiation in the management of patients with squamous cell carcinomas of the head and neck. *Semin Oncol*. 2003;30(4Suppl9):37-45.
38. Parsons JT. The effect of radiation on normal tissues of the head and neck. In: Million RR, Cassisi NJ, eds. *Management of head and neck cancer: A multi-disciplinary approach*. Philadelphia: JB Lippincott; 1994:245-289.
39. Marx RE. Osteoradionecrosis: a new concept of its pathology. *J Oral Maxillofac Surg*. 1983;41:351-8.
40. Marx RE. Osteoradionecrosis of the jaws: review and update. *HBO Rev*. 1984;5:412-9.
41. He Y, Liu Z, Tian Z, et al. Retrospective analysis of osteoradionecrosis of the mandible: proposing a novel clinical classification and staging system. *Int J Oral Maxillofac Surg*. 2015;44:1547-1557.
42. Personal communication with Dr. Robert Marx, January 2019.
43. Lofstrand J, Nyberg M, Karlsson T. Quality of life after fibular free flap reconstruction of segmental mandibular defects. *J Reconstr Microsurg*. 2018;34:108-20.
44. Feldmeier JJ, Hampson NB. A systematic review of the literature reporting the application of hyperbaric oxygen prevention and treatment of delayed radiation injuries: an evidence based approach. *UHM*. 2002;29:4-30.
45. Maier A, Gaggl A, Klemens H, Santler G, Anegg U, Fell B, Karcher H, Smolle-Juttner FM, Friehs GB. Review of severe osteoradionecrosis treated by surgery alone or surgery with postoperative hyperbaric oxygenation. *Br J Oral Maxillofac Surg*. 2000;38:173-6.
46. Freiberger JJ, Yoo DS, de Lisle Dear G, et al. Multimodality surgical and hyperbaric management of mandibular osteoradionecrosis. *Int J Radiat Oncol Bio Phys*. 2008;75(3):717-24.
47. Annane D, Depondt J, Aubert P, et al. Hyperbaric oxygen therapy for radionecrosis of the jaw: a randomized controlled, double-blind trial from ORN96 Study Group. *J Clin Oncol*. 2004;22:4893-4900.
48. Feldmeier JJ, Heimbach RD, Davolt DA, Court WS, Stegmann BJ, Sheffield PJ. Hyperbaric oxygen as an adjunctive treatment for radiation necrosis of the chest wall. *Undersea and Hyperbaric Medicine*. 1995;22(4).
49. Moon RE, McGraw TA, Blakey G. Hyperbaric oxygen therapy for radiation necrosis of the jaw: comments on a randomized study. *UHM*. 2005;32:145-6.
50. Laden G. Hyperbaric oxygen therapy for radionecrosis: clear evidence from confusing data (letter to the editor). *J Clin Oncol*. 2005;23:4465. Mendenhall WM. Mandibular Osteoradionecrosis (editorial) *J Clin Oncol*. 2004;22:4867-8.
51. Mendenhall WM. Mandibular osteoradionecrosis (editorial). *J Clin Oncol*. 2004;22:4867-8.
52. Gal TJ, Yueh B, Futran ND. Influence of prior hyperbaric oxygen therapy in complications following microvascular reconstruction for advanced osteoradionecrosis. *Arch Otolaryngol Head Neck Surg*. 2003;129:72-76.
53. Dielman FJ, Phan TTT, van den Hoogen FJA, et al. The efficacy of hyperbaric oxygen related to clinical stage of osteoradionecrosis of the mandible. *Int J Oral and Maxillofac Surg*. 2017;46:428-33.
54. Hirsch DL, Bell RB, Dierks EJ, et al. Analysis of microvascular free flaps for reconstruction of advanced mandibular osteoradionecrosis: a retrospective cohort study. *J Oral Maxillofac Surg*. 2008;66(12):2545-56.
55. Nolen D, Cannady SB, Wax MK, et al. Comparison of complications in free flap reconstruction for osteoradionecrosis in patients with or without hyperbaric oxygen therapy. *Head Neck*. 2014;36(12):1701-4.
56. Van Gemert JT, Abbink JH, van Es RJ, et al. Early and late complications in the reconstructed mandible with free fibular flaps. *J Surg Oncol*. 2018;117:773-80.
57. Teng MS, Futran ND. Osteoradionecrosis of the mandible. *Cur Opin Otolaryngol Head Neck Surg*. 2005;13:217-21.

58. Delainian S, Chatel CC, Porcher R et al. Complete restoration of refractory mandibular osteoradionecrosis by prolonged treatment with a pentoxifylline-tocopherol-clodronate combination (PENTOCLO): a phase II trial. *Int J Radiation Oncology Biol Phys.* 2011;80(30):832-9.
59. Delainian S, Lefax JL. The radiation-induced fibroatrophic process: therapeutic perspective via the antioxidant pathway. *Radiotherapy and Oncology.* 2003;73:119-31.
60. Hampson NB, Holm JR, Wreford-Brown CE, Feldmeier JJ. Prospective assessment of outcomes in 411 patients treated with hyperbaric oxygen for chronic radiation tissue injury. *Cancer.* 2012;118:3860-8.
61. Lambert PM, Intri N, Eichstaedt R. Management of dental extractions in irradiated jaws: a protocol with hyperbaric oxygen treatment. *J Oral Maxillofac Surg.* 1997;55:268-74.
62. Vudiniabola S, Pirone C, Williamson J, Goss ANN. Hyperbaric oxygen in the prevention of osteoradionecrosis of the jaws. *Australian Dental Journal.* 1999; 44:243-247.
63. David LA, Sandor GK, Evans AW, Brown DH. Hyperbaric oxygen therapy and mandibular osteoradionecrosis: a retrospective study and analysis of treatment outcomes. *J Can Dent Assoc.* 2001; 67:384.
64. Chavez JA, Adkinson CD. Adjunctive hyperbaric oxygen in irradiated patients requiring dental extractions: outcomes and complications. *J Oral Maxillofac Surg.* 2001; 59:518-22.
65. Sulaiman F, Huryn JM, Ziotolow IM. Dental extractions in the irradiated head and neck patient: a retrospective analysis of Memorial Sloan-Kettering Cancer Center protocols, criteria, and end results. *J Oral Maxillofac Surg.* 2003;61:1123-31.
66. Makkonen TA, Kiminski A, Makkonen TK et al. Dental extractions in relation to radiation therapy of 224 patients. *Int J Oral Maxillofac Surg.* 1987; 7;16:56-64.
67. Maxymiw WG, Wood RE, Liu FF. Postradiation dental extractions without hyperbaric oxygen. *Oral Surg Oral Med Oral Pathol.* 1991;72(3):270-4.
68. Lye KW, Wee J, Gao F et al. The effect of prior radiation therapy for treatment of nasopharyngeal cancer on wound healing following extractions: incidence of complications and risk factors. *Int J Oral Maxillofac Surg.* 2007;36:315-20.
69. Clayman L. Management of dental extractions in irradiated jaws: a protocol without hyperbaric oxygen. *J Oral Maxillofac Surg.* 1997;55:275-81.
70. Wahl MJ. Osteoradionecrosis prevention myths. *Int J Radiation Oncology Biol Phys.* 2006;64:661-9.
71. Kim JC, Elkin D, Hendrickson FR. Carcinoma of the vocal cords: results of treatment and time-dose relationships. *Cancer.* 1978;42:1114-9.
72. Stell PM, Morrison ND. Radiation necrosis of the larynx: etiology and management. *Arch Oto Rhin Laryngol.* 1973; 98:111-3.
73. Flood LM, Brightwell AP. Clinical assessment of the irradiated larynx. *J Laryngol Otol.* 1984;98:493-8.
74. Chandler JR. Radiation fibrosis and necrosis of the larynx. *Ann Otol Rhinol & Laryngol.* 1979;88:509-14.
75. Ferguson BJ, Hudson WR, Farmer JC. Hyperbaric oxygen for laryngeal radionecrosis. *Ann Otol Laryngol.* 1987; 96:1-6.
76. Feldmeier JJ, Heimbach RD, Davolt DA, Brakora MJ. Hyperbaric oxygen as an adjunctive treatment for severe laryngeal necrosis: A report of nine consecutive cases. *Undersea Hyper Med.* 1993;20:329-335.
77. Filintis GA, Moon RE, Kraft KL, Farmer JC, Scher RL, Piantadosi CA. Laryngeal radionecrosis and hyperbaric oxygen therapy: report of 18 cases and review of the literature. *Ann Otol Rhinol Laryngol.* 2000;109:554-62.
78. Narzony W, Sicko Z, Kot J et al. Hyperbaric oxygen therapy in the treatment of complications of irradiation in the head and neck area. *Undersea Hyperb Med.* 2005;32:103-10.
79. HSU YC, Lee KW, Tsai KB et al. Treatment of laryngeal necrosis with hyperbaric oxygen therapy: a case report. *Kaohsiung Med.* 2005;21:88-92.
80. Davis JC, Dunn JM, Gates GA, Heimbach RD. Hyperbaric oxygen: a new adjunct in the management of radiation necrosis. *Arch Otolaryngol.* 1979;105:58-61.
81. Neovius EB, Lind MG, Lind FG. Hyperbaric oxygen for wound complications after surgery in the irradiated head and neck: a review of the literature and a report of 15 consecutive cases. *Head and Neck.* 1997;19:315-322.
82. Feldmeier JJ, Newman R, Davolt DA, Heimbach RD, Newman NK, Hernandez LC. Prophylactic hyperbaric oxygen for patients undergoing salvage for recurrent head and neck cancers following full course irradiation (abstract). *Undersea Hyper Med.* 1998;25(Suppl):10.
83. Sessler AM, Esclamado RM, Wolf GT. Surgery after organ preservation therapy. Analysis of wound complications. *Arch Otolaryngol Head Neck Surg.* 1995 Feb;121(2):162-5
84. Agra IM, Carvalho AL, Pontes E, Campos OD, Ulbrich FS, Magrin J, Kowalski LP. Postoperative complications after en bloc salvage surgery for head and neck cancer. *Arch Otolaryngol Head Neck Surg.* 2003 Dec;129(12):1317-21.
85. Gerlach NL, Barkhuysen R, Kaanders JH et al. The effect of hyperbaric oxygen therapy on quality of life in oral and oropharyngeal cancer patients treated with radiotherapy. *Int J of Maxillofac Surg.* 2008;37:255-9.

86. No authors listed. Breast Cancer Treatment (PDQ®)—Patient Version - National Cancer Institute.
87. Feldmeier JJ, Heimbach RD, Davolt DA, Court WS, Stegmann BJ, Sheffield PJ. Hyperbaric oxygen as an adjunctive treatment for delayed radiation injury of the chest wall: a retrospective review of 23 cases. *Undersea Hyperb Med*. 1995;22:383-393.
88. Carl UM, Hartmann KA. Hyperbaric oxygen treatment for symptomatic breast edema after radiation therapy. *Undersea Hyperb Med*. 1998;25:233-234.
89. Carl UM, Feldmeier JJ, Schmitt G et al. Hyperbaric oxygen therapy for late sequelae in women receiving radiation after breast conservation treatment. *Int J Radiat Oncol Biol Phys*. 2001;49(4):1029-31.
90. No Authors Listed. LENT SOMA scales for all anatomic sites. *Int J Radiat Oncol Biol Phys*. 1995;31(5):1049-91.
91. Teguh DN, Bol Raap R, Strikmans H et al. Hyperbaric oxygen therapy for late radiation-induced tissue toxicity: prospectively patient-reported outcome measures in breast cancer patients. *Radiat Oncol*. 2016;11(1):130.
92. Enomoto M, Yagishita K, Okuma K et al. Hyperbaric oxygen for a refractory skin ulcer after radical mastectomy and radiation therapy: a case report. *J Med Case Rep*. 2017;11(1):electronically published.
93. Bevers RF, Bakker DJ, Kurth KH. Hyperbaric oxygen treatment for haemorrhagic radiation cystitis. *Lancet*:1995;346:803-805.
94. Neheman A, Nativ O, Moskovitz B, Melamed Y, Stein A. hyperbaric oxygen therapy for radiation-induced haemorrhagic cystitis. *BJU Int*. 2005;96:107-9.
95. Corman JM, McClure D, Pritchett R, Kozlowski P, Hampson NB. Treatment of radiation induced hemorrhagic cystitis with hyperbaric oxygen. *J Urol*. 2003;160:2200-2.
96. Chong KT, Hampson NB, Corman JM. Early hyperbaric oxygen improves outcome for radiation-induced hemorrhagic cystitis. *Urology*. 2005;65:649-53.
97. Cardinal J, Slade A, McFarland M et al. Scoping review and meta-analysis of hyperbaric oxygen therapy for radiation-induced hemorrhagic cystitis. *Current Urology Reports*. 2018;19:38 published on line.
98. Cheng C, Foo KT. Management of severe chronic radiation cystitis. *Ann Acad Med Singapore*:1992;21:368-71.
99. Li A, Sun J, Chao H. Late bladder complications following radiotherapy of carcinoma of the uterine cervix. *Zhonghua Fu Chan Ke*. 1995;30:741-3.
100. Neurath MF, Branbrink A, Meyer zum Buschenfelde KH, Lohse AW. A new treatment for severe malabsorption due to radiation enteritis. *Lancet*. 1996;347:1302.
101. Jones K, Evans AW, Bristow RG et al. Treatment of radiation proctitis with hyperbaric oxygen. *Radiotherapy and Oncology*. 2006;78:91-4.
102. Girinius S, Ceronsky N, Gesell L et al. Treatment of refractory radiation-induced hemorrhagic proctitis with hyperbaric oxygen therapy. *Am J Clin Oncol*. 2006;29:588-92.
103. Dall'Era MA, Hampson NB, His RA et al. Hyperbaric oxygen therapy for radiation induced proctopathy in men treated for prostate cancer. *J Urol*. 2006;176:87-90.
104. Marshall GT, Thirlby RC, Bredfeldt JE, Hampson NB. Treatment of gastrointestinal radiation injury with hyperbaric oxygen *Undersea Hyperb Med*. 2007;34:35-42.
105. Clarke RE, Tenorio LMC, Hussey JR et al. Hyperbaric oxygen treatment of chronic refractory radiation proctitis: a randomized and controlled double-blind crossover trial with long term follow-up. *Int J Radiat Oncol Biol Phys*. 2008;72(1):134.
106. Glover M, Smerdon GR, Andeyev HJ et al. Hyperbaric oxygen for patients with chronic bowel dysfunction after pelvic radiotherapy (HBO<sub>2</sub>T): a randomized double-blind, sham-controlled phase 3 trial. *Lancet Oncol*. 2016;17(2):224-33.
107. Paquette IM, Vogel JD, Abbas MA, et al. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the treatment of chronic radiation proctitis. *Dis Colon Rectum*. 2018;61:1135-40.
108. Farmer JC, Shelton DL, Bennett PD, Angelillo JD, Hudson MD. Treatment of radiation-induced injury by hyperbaric oxygen. *Ann Otol*. 1978; 87;707-15.
109. Williams JAA, Clarke D, Dennis WAA, Dennis EJJ, Smith STT. Treatment of pelvic soft tissue radiation necrosis with hyperbaric oxygen. *Am J Obstet Gynecol*. 1992; 167:415-416.
110. Feldmeier JJ, Heimbach RD, Davolt DA, Court WS, Stegmann BJ, Sheffield PJ. Hyperbaric oxygen as an adjunctive treatment for delayed radiation injuries of the abdomen and pelvis. *Undersea Hyperb Med*. 1997;23(4):205-213.
111. Fink D, Chetty N, Lehm JP, Marsden DE, Hacker NF. Hyperbaric oxygen therapy for delayed radiation injuries in gynecological cancers. *Int J Gynecol Cancer*. 2006;16:638-42.
112. Craighead P, Shea-Budgell MA, Nation J, Esmail R, Evans AW, Parliament M, Oliver TK, Hagen NA. Hyperbaric oxygen for late radiation tissue injury in gynecologic malignancies. *Curr Oncol*. 2011;18(5):220-7.
113. Feldmeier JJ, Heimbach RD, Davolt DA, McDonough MJ, Stegmann BJ, Sheffield PJ. Hyperbaric oxygen in the treatment of delayed radiation injuries of the extremities *Undersea Hyperb Med*. 2000;27(1):15-19.

114. Marcus RB Jr, Million RR. The incidence of transverse myelitis after radiation of the cervical spinal cord. *Int J Radiat Oncol Biol Phys.* 1990;19:3-8.
115. Marcus RB Jr, Million RR. The incidence of transverse myelitis after radiation of the cervical spinal cord. *Int J Radiat Oncol Biol Phys* 1990;19:3-8.
116. Glassburn JR, Brady LW. Treatment with hyperbaric oxygen for radiation myelitis. *Proc. 6th Int Cong on Hyperbaric Medicine.* 1977:266-77.
117. Calabro F, Jinkins JR. MRI of radiation myelitis: a report of a case treated with hyperbaric oxygen. *Eur Radiol.* 2000;10:1079-84.
118. Feldmeier JJ, Lange JD, Cox SD, Chou L, Ciaravino V. Hyperbaric oxygen as a prophylaxis or treatment for radiation myelitis. *Undersea Hyper Med.* 1993;20(3):249-255.
119. Sminia P, Van der Kleij AJ, Carl UM, Feldmeier JJ, Hartmann KA. Prophylactic hyperbaric oxygen treatment and rat spinal cord re-irradiation. *Cancer Lett.* 2003 Feb 28;191(1):59-65.
120. Feldmeier J, Borrillo D Siebenhaler G. The benefits of hyperbaric oxygen in the treatment of delayed spinal cord radiation induced injury. *Undersea Hyper Med.* 2009;36(4).
121. Schulteiss TE, Stephen LC, Peters LJ. Survival in radiation myelopathy. *Int J Radiat Oncol Biol Phys.* 1986;12:1765-9.
122. Chuba PJ, Aronin P, Bhamhani K, Eichenhorn M, Zamarano L, Cianci P, Muhlbauer M, Porter AT, Fontanesi J. Hyperbaric oxygen therapy for radiation-induced brain injury in children. *Cancer.* 1997;80:2005-2012.
123. Leber KA, Eder HG, Kovac H, Anegg U, Pendl G. Treatment of cerebral radionecrosis by hyperbaric oxygen therapy. *Sterotact Funct Neurosurg.* 1998;70(Suppl 1):229-36.
124. Cirafisi C, Verderame F. Radiation-induced rhomboencephalopathy. *Ital J Neurol Sci.* 1999;20:55-8.
125. Dear GdeL, Rose RE, Dunn R, Piantadosi CA, Stolp BW, Carraway MS, Thalmann ED, Kraft K, Rice JR, Friedman AH, Friedman HS, Moon RE. Treatment of neurological symptoms of radionecrosis of the brain with hyperbaric oxygen: a case series. Presented at the 35th Annual Undersea and Hyperbaric Medical Society Scientific Meeting. San Diego, CA: 28-30 June 2002.
126. Gesell LB, Warnick R, Breneman J, Albright R, Racadio J, Mink, S. Effectiveness of hyperbaric oxygen for the treatment of soft tissue radionecrosis of the brain. Presented at the 35th Annual Undersea and Hyperbaric Medical Society Scientific Meeting. San Diego, CA: 28-30 June, 2002.
127. Fetko K, Lukas RV, Watson L et al. Survival and complications of stereotactic radiosurgery:a systematic review of stereotactic radiosurgery for newly diagnosed and recurrent high-grade gliomas. *Medicine (Baltimore).* 2017; 96(43):e8293.
128. Furuse M, Nonoguchi N, Kuroiwa T et al. A prospective multi-centre, single-arm clinical trial of bevacizumab for patients with surgically untreatable symptomatic brain radiation necrosis. *Neurooncol Pract.* 2016;3(4):272-80.
129. Borruat FXX, Schatz NJJ, Glaser JSS, Feun LGG, Matos L. Visual recovery from radiation-induced optic neuropathy. The role of hyperbaric oxygen therapy. *J Clin Neuroophthalmol.* 1993;13:98-101.
130. Fontanesi J, Golden EB, Cianci PC, Heideman RL. Treatment of radiation-induced optic neuropathy in the pediatric population. *Journal of Hyperbaric Medicine.* 1991;6(4):245-248.
131. Boschetti M; De Lucchi M; Giusti M; Spena C; Corallo G; Goglia U; Ceresola E; Resmini E; Vera L; Minuto F; Ferone D. Partial visual recovery from radiation-induced optic neuropathy after hyperbaric oxygen therapy in a patient with Cushing disease. *Eur J Endocrinol.* 01 June 2006;154(6):813-8.
132. Guy J, Schatz NJJ. Hyperbaric oxygen in the treatment of radiation-induced optic neuropathy. *Ophthalmology.* 1986;93:1083-8.
133. Roden D, Bosley TM, FowbleB, Clark J, Savino PJ, Sergott RC, Schatz NJ. Delayed radiation injury to the retrobulbar optic nerves and chiasm. Clinical syndrome and treatment with hyperbaric oxygen and corticosteroids. *Ophthalmolgoy.* 1990;97:346-51.
134. Guy J. Letter to the Editor. *Ophthalmology.* 1990;97:1246-7.
135. Malik A, Golnik K. Hyperbaric oxygen in the treatment of radiation optic neuropathy. *J Neuroophthalmol.* 2012;32(2):128-31.
136. Li CQ, Gerson S, Snyder B. Case report; hyperbaric oxygen and MRI findings in radiation-induced optic neuropathy. *Undersea Hyperb Med.* 2014;41(1):59-63.
137. Videtic GM, Venkatesan VM. Hyperbaric oxygen corrects sacral plexopathy due to osteoradionecrosis appearing 15 years after pelvic irradiation. *Clin Oncol (R Coll Radiol).* 1999;11(3):198-9.
138. Pritchard J, Anand P, Broome J,et al. Double-blind randomized phase II study of hyperbaric oxygen in patients with radiation-induced brachial plexopathy. *Radiother Oncol.* 2001;58:279-86.
139. Granstrom G. Placement of dental implants in irradiated bone: the case for hyperbaric oxygen. *Int J Oral Maxillofac.* 2006;64:812-8.

140. Ueda M, Kaneda T, Takahashi H. Effect of hyperbaric oxygen therapy on osseointegration of titanium implants in irradiated bone: A preliminary report. *Int J Oral Maxillofac Implants*. 1993;8:41-44.
141. Pomeroy BD, Keim LW, Taylor RJ. Preoperative hyperbaric oxygen therapy for radiation induced injuries. *J Urol*. 1998;159:1630-1632.
142. Sessler AM, Esclamado RM, Wolf GT. Surgery after organ preservation therapy: analysis of wound complications. *Arch Otolaryngol Head and Neck Surg*. 1995; 121(2):162-5.
143. Gray LH, Conger AD, Ebert M et al. The concentration of oxygen dissolved in tissues at the time of radiation as a factor in radiotherapy. *Br J Radiol*. 1953;26:638-48.
144. Churchill-Davidson I. The oxygen effect in radiotherapy: historical review. *Front Radiat Ther Oncol*. 1968;1:1-15.
145. Koshi K, Kinoshita Y, Imada H et al. Effects of radiotherapy after hyperbaric oxygenation on malignant gliomas. *Br J Cancer*. 1990;80:236-41n.
146. Beppu T, Kamada K, Arai H et al. Change of oxygen pressure in glioblastoma tissue under various conditions. *J Neurooncol*. 2002;58:47-52.
147. Becker A, Kuhnt T, Liedtke H et al. Oxygenation measurements in head and neck cancers during hypervbaric oxygenation . *Strahlenther Onkol*. 2002;178:105-8.
148. Hartford AC, Davis TH, Buckey JC et al. Hyperbaric oxygen as radiation sensitizer for locally advanced squamous cell carcinoma of the oropharynx: a Phase 1 Dose-escalation study.
149. Personal communication with Mr. Richard E. Clarke, CHT. June 2018.
150. Allen BG, Bhatia SK, Anderson CM et al. Ketogenic diets as an adjuvant to cancer therapy: history and potential mechanism. *Redox Biol*. 2014;2:963-70.
151. Warburg O Wind F, Negelein E. The metabolism of tumors in the body. *Journal of Physiol*. 1926;519-30.
152. Poff AM, Ari C, Seyfried TN and D'Agostino DP. The ketogenic diet and hyperbaric oxygen therapy prolong survival in mice with systemic metastatic cancer. *PLOS One*. 2013.;8(6):1-9. |
153. Iyikesici MS, Slocum AK, Slocum A, et al. Efficacy of metabolically supported chemotherapy combined with ketogenic diet, hyperthermia and hyperbaric oxygen therapy for stageIV triple-negative breast cancer. *Cureus*. 2017;9(7):e1445.
154. Feldmeier J, Carl U, Hartmann K, Sminia P. Hyperbaric oxygen: Does it promote growth or recurrence of malignancy. *UHM*. 2003; 30(1):1-18.
155. Daruwalla J, Christophi C. Hyperbaroc oxygen therapy for malignancy. *World J Surg*. 2006;30:2112-31.
156. Moen I, Stuhr LE. Hyperbaric oxygen therapy and cancer-review. *Targ Oncol*. 2012;7:233-42.
157. Chong KT, Hampson NB, Bostwick DG, Vessella RL, Corman JM. Hyperbaric oxygen does not accelerate latent in vivo prostate cancer: implications for the treatment of radiation-induced haemorrhagic cystitis. *BJU Int*. 2004;94(9):1275-8.
158. Stuhr LE, Iverson VV, Straume O, Maehle BO, Reed RK. Hyperbaric oxygen alone or combined with 5-FU attenuates growth of DMBA induced rat mammary tumors. *Cancer Lett*. 2004;210(1):3540.
159. Sun TB, Chen RL, Hsu YH. The effect of hyperbaric oxygen on human oral cancer cells. *Undersea Hyperb Med*. 2004;31(2):251-60.
160. Shi Y, Lee CS, Wu J, Koch CJ, Thom SR, Maity A, Bernhard EJ. Effects of hyperbaric oxygen exposure on experimental head and neck tumor growth, oxygenation, and vasculature. *Head Neck*. 2005 May;27(5):362-9.
161. Granowitz EV, Tonomura N, Benson RM, Katz DM, Band V, Makari-Judson GP, Osborne BA. Hyperbaric oxygen inhibits benign and malignant human mammary epithelial cell proliferation. *Anticancer Res*. 2005;25:3833-42.
162. Daruwalla J, Christophi C. The effect of hyperbaric oxygen therapy on tumour growth in a mouse model of colorectal cancer liver metastases. *Eur J Cancer*. 2006 Dec;42(18):3304-11.
163. Haroon AT, Patel M, Al-Mehdi AB. Lung metastatic load limitation with hyperbaric oxygen. *Undersea Hyperb Med*. *Int J Radiat Oncol Biol Phys*. 2009;74(4):1077-82. 2007 Mar-Apr;34(2):83-90.
164. Eltorai I, Hart GB, Strauss MB. Et al. Does hyperbaric oxygen provoke an occult carcinoma in man? In Kindwall EP, ed. *Proceedings of the eighth international congress on hyperbaric medicine*. San Pedro, CA. 1987:18-29.
165. Bradfield JJ, Kinsella JB, Mader JT et al. Rapid progression of head and neck squamous carcinoma after hyperbaric oxygen. *Otolaryngol Head and Neck Surg*. 1996;114:793-7.
166. Lin HY, Ku CH, Liu DW et al. Hyperbaric oxygen therapy for late radiation-associated tissue necroses: Is it safe in patients with locoregionally recurrent and the successfully salvaged head-and-neck cancers? *Int J Radiat Oncol Biol Phys*. 2009;74:1077-82.
167. Elbers JBW, Veldhuis LI, Bhairosing PA et al. Salvage surgery for advanced stage head and neck squamous cell carcinoma following radiotherapy or chemoradiation. *Eur Arch Otorhinolaryngol*. 2019; Epub ahead of print.

## **Chapter 9: Sudden Sensorineural Hearing Loss**

*Tracy Leigh LeGros MD, PhD, and Heather Murphy-Lavoie MD*

### **REFERENCES**

1. Fetterman BL, Saunders JE, Luxford WM. Prognosis and treatment of sudden sensorineural hearing loss. *Am J Otol.* 1996 Jul; 17(4):529–536.
2. O'Malley MR, Haynes DS. Sudden hearing loss. *Otolaryngol Clin N Am.* 2008;41: 633–649.
3. Haberkamp TJ, Tanyeri HM. Management of idiopathic sudden sensorineural hearing loss. *Am J Otol.* 1999 Sept;20:587–592.
4. Stachler R, Chandrasekhar S, Archer S, Rosenfeld R, Schwartz S, Barrs D, Brown S, Fife T, Ford P, Ganiats T, Hollingsworth D, Lewandowski C, Montano J, Saunders J, Tucci D, Valente M, Warren B, Yaremchuk K, Robertson P. Clinical practice guidelines: sudden hearing loss. *Otolaryngology – Head and Neck Surgery.* 2012;146:S1-35.
5. Rauch SD. Idiopathic sudden sensorineural hearing loss. *N Engl J Med.* 2008 Aug 21;359(8):833–840.
6. Byl FM Jr. Sudden hearing loss: eight years' experience and suggested prognostic table. *Laryngoscope.* 1984 May; 94 (5 Pt 1): 647–661.
7. Alexander TH, Harris JP. Incidence of sudden sensorineural hearing loss." *Otol Neurotol.* 2013;34:1586–1589.
8. Teranishi M, Katayama N, Uchida Y, Tominaga M, Nakashima T. Thirty-year trends in sudden deafness from four nationwide epidemiological surveys in Japan. *Acta Otolaryngol.* 2007;127:1259–1265.
9. Klemm E, Deutscher A, Mosges R. A Present investigation of the epidemiology in idiopathic sudden sensorineural hearing loss." *Larygorhinootologie.* 2009;88:524 –527.
10. Hallberg OE. Sudden deafness of obscure origin. *Laryngoscope.* 1956 Oct; 66(10):1237–1267.
11. Byl FM. Seventy-six cases of presumed sudden hearing loss occurring in 1973; prognosis and incidence. *Laryngoscope.* 1977 May;87(5 Pt 1):817–825.
12. Mattox DE, Simmons FB. Natural history of sudden sensorineural hearing loss. *Ann Otol Rhinol Laryngol.* 1977 Jul-Aug; 86(4 Pt 1):463–480.
13. Shaia FT, Sheehy JL. Sudden sensori-neural hearing impairment: a report of 1,220 cases. *Laryngoscope.* 1976 Mar; 86(3):389–398.
14. Jourdy DN, Donatelli LA, Victor JD, Selesnick SH. Assessment of variation throughout the year in the incidence of idiopathic sudden sensorineural hearing loss. *Otol Neurotol.* 2010 Jan;31(1):53–57.
15. Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study." *Arch Otolaryngol.* 1980 Dec; 106(12):772–776.
16. Chandrasekhar SS. Intratympanic dexamethasone for sudden sensorineural hearing loss: clinical and laboratory evaluation. *Otol Neurotol.* 2001 Jan; 22(1):18 –23.
17. Battaglia A, Burchette R, Cueva R. Combination therapy (intratympanic dexamethasone + high-dose prednisone taper) for the treatment of idiopathic sudden sensorineural hearing loss." *Otol Neurotol.* 2008 Jun;29(4):453–460.
18. De Kleyn A. Sudden complete or partial loss of function of the octavus system in apparently normal persons. *Acta Otolaryngologica.* 1944(32):407–429.
19. Cole RR, Jahrdoerfer RA. Sudden hearing loss: an update. *Am J Otol.* 1988 May; 9 (3):211–215.
20. Hughes GB, Freedman MA, Haberkamp TJ, Guay ME. Sudden sensorineural hearing loss. *Otolaryngol Clin North Am.* 1996 Jun; 29(3):393–405.
21. Alimoglu Y, Inci E, Edizer DT, Ozdilek A, Aslan M. Efficacy comparison of oral steroid, intratympanic steroid, hyperbaric oxygen and oral steroid and hyperbaric oxygen treatments in idiopathic sudden sensorineural hearing loss cases. *Eur Arch Otorhinolaryngol.* 2011 Dec; 268(12):1735–1741.
22. Lamm C, Walliser U, Schumann K, Lamm K. Oxygen partial pressure measurements in the perilymph and the scala tympani in normo- and hyperbaric conditions. An animal experiment study. *HNO.* 1988 Sept;35(9):363–366.
23. Lamm K, Lamm C, Lamm H, Schumann K. Simultaneous determinations of oxygen partial pressure in the scala tympani, electrocochleography and blood pressure measurements in noise stress in guinea pigs. *HNO.* 1988 Sep; 36(9):367–372.
24. Belal A Jr. Pathology of vascular sensorineural hearing impairment. *Laryngoscope.* 1980 Nov;90(11 Pt 1):1831–1839.
25. Yoon TH, Paparella MM, Schachern PA, Alleva M. Histopathology of sudden hearing loss. *Laryngoscope.* 1990 Jul;100(7):707–715.
26. Piroddi A, Ferri GG, Modugno GC, Borghi C. Systemic hypotension and the development of acute sensorineural hearing loss in young healthy subjects." *Arch Otolaryngol Head Neck Surg.* 2001 Sep;127:1049–1052.
27. Lehnhardt E, Hesch RD. Causes of inner ear deafness: a critique of therapy. *HNO.* 1980;28:73–79.
28. Maass B. Autonomic nervous system and hearing. *Adv Otorhinolaryngol.* 1981;27:14–25.

29. Pirodd A, Saggese D, Giausa G, Ferri GG, Nascetti S, Gaddi A. Can hypotension episodes cause cochlear damage in young subjects? *Med Hypotheses*. 1997;48:195–186.
30. Pirodd A, Ferri Gg, Modugno GC, Gaddi A. Hypotension and sensorineural hearing loss: a possible correlation. *Acta Otolaryngol*. 1999;119(7):758–762.
31. Kawakami M, Makimoto K, Fukuse S, Takahashi H. Autoregulation of cochlear blood flow. A comparison of cerebral blood flow with muscular blood flow. *Eur Arch Otorhinolaryngol*. 1991;248:471–474.
32. Ciccone MM, Cortese F, Pinto m, Di Teo C, Fornarelli F, Gesualdo M, Mezzina A, Sabatelli E, Scicchitano P, Quaranta N. Endothelial function and cardiovascular risk in patients with idiopathic sudden sensorineural hearing loss. *Atherosclerosis*. 2012;225:511–516.
33. Brant LJ, Gordon-Salant S, Pearson JD, Klein LL, Morrell CH, Metter EJ, Fozard JL. Risk factors related to age-associated hearing loss in the speech frequencies. *J Am Acad Audiol*. 1996;7:152–160.
34. Rudack C, Langer C, Stoll W, Rust S., Walter M. Vascular risk factors in sudden hearing loss. *Thromb Haemost*. 2006;95:454–561.
35. Aimoni C, Bianchini C, Borin M, Ciorba A, Fellin R, Martini A, Scanelli G, Volpati S. Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: a case-control study. *Audio Neurotol*. 2010;15(2):111–115.
36. Lin HC, Chao PZ, Lee HC. Sudden sensorineural hearing loss increases the risk of stroke: a 5-year follow-up study. *Stroke*. 2008 Oct;39 (10):2744–2748.
37. Ozler GS. Increased neutrophil-lymphocyte ratio in patients with idiopathic sudden sensorineural hearing loss. *J Craniofac Surg*. 2014 May;25(3): e260–e263.
38. Gloddek B, Lamm K, Arnold W. Pharmacological influence on inner ear endothelial cells in relation to the pathogenesis of sensorineural hearing loss. *Adv Otorhinolaryngol*. 2002;59:75–83.
39. Merchant SN, Durand ML, Adams JC. Sudden deafness: is it viral? *ORL J Otorhinolaryngol Relat Spec*. 2008;70:52–62.
40. Merchant SN, Adams JC, Nadol JB Jr. Pathology and pathophysiology of idiopathic sudden sensorineural hearing loss. *Otol Neurotol*. 2005 Mar;26(2):151–160.
41. Stokroos RJ, Albers FW, Schirm J. The etiology of idiopathic sudden sensorineural hearing loss: experimental herpes simplex virus infection of the inner ear. *Am J Otol*. 1998 Jul;19(4):447–452.
42. Shirwany NA, Seidman MD, Tang W. Effect of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity, and histology in the guinea pig. *Am J Otol* 1998; 19:230 –235.
43. Nagura M, Iwasaki S, Wu R, Mizuta K, Umemura K, Hoshino T. Effects of corticosteroid, contrast medium and ATP on focal microcirculatory disorders of the cochlea. *Eur J Pharmacol*. 1999 Jan 29;366(1):47–53.
44. Tabuchi K, Oikawa K, Uemaetomari I, Tsuji S, Wada T, Hara A. Glucocorticoids and dehydroepiandrosterone sulfate ameliorate ischemia-induced injury of the cochlea. *Hear Res*. 2003 Jun; 180(1-2):51–56.
45. Lin DW, Trune DR. Breakdown of stria vascularis blood-labyrinth barrier in C3H/lpr autoimmune disease mice. *Otolaryngol Head Neck Surg*. 1997 Nov;117(5):530– 534.
46. Trune DR, Wobig RJ, Kempton JB, Hefeneider SH. Steroid treatment improves cochlear function in the MRL-MpJ-Fas(lpr) autoimmune mouse. *Hear Res*. 1999 Nov;137(1-2):160–166.
47. Alexiou C, Arnold W, Fauser C, Schratzenstaller B, Gloddek B, Fuhrmann S, Lamm K. Sudden sensorineural hearing loss: does application of glucocorticoids make sense? *Arch Otolaryngol Head Neck Surg*. 2001, Mar; 127(3):253–258.
48. Slattery WH, Fisher LM, Iqbal Z, Friedman RA, Liu N. Intratympanic steroid injection for treatment of idiopathic sudden hearing loss. *Otolaryngol Head Neck Surg*. 2005 Aug; 133(2):251–259.
49. Dispenza F, Amadio E, De Stefano A, Gallina S, Marchese D, Mathur N, Riggio F. Treatment of sudden sensorineural hearing loss with transtympanic injection of steroids as single therapy: a randomized clinical study. *Eur Arch Otorhinolaryngol*. 2011 Sep;268(9):1273-1278.
50. Seggas I, Koltsidopoulos P, Bibas A, Tzonou A, Sismanis A. Intratympanic steroid therapy for sudden hearing loss: a review of the literature. *Otol Neurotol*. 2011 Jan; 32(1):29–35.
51. Spear SA, Schwartz SR. Intratympanic steroids for sudden sensorineural hearing loss. A systematic review. *Otolaryngol Head Neck Surg*. 2011 Oct;145(4):534–543.
52. Ferri E, Frisina A, Fasson AC, Armato E, Spinato G, and Amadori M. Intratympanic steroid treatment for idiopathic sudden sensorineural hearing loss after failure of intravenous therapy. *ISRN Otolaryngology*. 2012;1–6.
53. Haynes DS, O’Malley M, Cohen S, Watford K, Labadie RF. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. *Laryngoscope*. 2007 Jan;117(1):3–15.
54. Cinamon U, Bendet E, Kronenberg J. Steroids, carbogen or placebo for sudden hearing loss: a prospective double-blind study. *Eur Arch Otorhinolaryngol*. 2001 Nov;258(9):477–480.

55. Zadeh MH, Storper IS, Spitzer JB. Diagnosis and treatment of sudden-onset sensorineural hearing loss: a study of 51 patients. *Otolaryngol Head Neck Surg.* 2003 Jan;128(1):92–98.
56. Parnes LS, Sun AH, Freeman DJ. Corticosteroid pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. *Laryngoscope.* 1999 Jul; 109(7 Pt 2):1–17.
57. Bird PA, Begg EJ, Zhang M, Keast AT, Murray DP, Balkany TJ. Intratympanic versus intravenous delivery of methylprednisolone to cochlear perilymph. *Otol Neurotol.* 2007 Dec; 28(8):1124–1130.
58. Plontke SK, Biegner T, Kammerer B, Delabar U, Salt AN. Dexamethasone concentration gradients along scala tympani after application to the round window membrane. *Otol Neurotol.* 2008 Apr; 29(3):401–406.
59. Wei BPC, Stathopoulos D, O’Leary S. Steroids for idiopathic sudden sensorineural hearing loss. *Cochrane Database of Systematic Reviews.* 2013;Issue 7. Art. No.: CD003998.
60. Gao Y, Liu D. Combined intratympanic and systemic use of steroids for idiopathic sudden sensorineural hearing loss: a meta-analysis. *Eur Arch Otorhinolaryngol.* 2016; 273:3699–3711.
61. Qiang Q, Wu X, Yang T, Yang C, Sun H. A comparison between systemic and intratympanic steroid therapies as initial therapy for idiopathic sudden sensorineural hearing loss: a meta-analysis. *Acta Oto-Laryngologica.* 2016 Dec 6: 1–8 ISSN:0001-6489.
62. Ho HG, Lin HC, Shu MT, Yang CC, Tsai HT. Effectiveness of intratympanic dexamethasone injection in sudden-deafness patients as salvage treatment. *Laryngoscope.* 2004 Jul;114(7):1184–1189.
63. Xenellis J, Papadimitriou N, Nikolopoulos T, Maragoudakis P, Segas J, Tzagaroulakis A, Ferekidis E. Intratympanic steroid treatment in idiopathic sudden sensorineural hearing loss: a control study. *Otolaryngol Head Neck Surg.* 2006 Jun;134(6):940–945.
64. Ahn JH, Han MW, Kim JH, Chung JW, Yoon TH. Therapeutic effectiveness over time of intratympanic dexamethasone as salvage treatment of sudden deafness. *Acta Otolaryngol.* 2008 Feb;128(2):128–131.
65. Kilic R, Safak MA, Oguz H, Kargin S, Demirci M, Samim E, Ozluoglu LN. Intratympanic methylprednisolone for sudden sensorineural hearing loss. *Otol Neurotol.* 2007 Apr;28(3):312–316.
66. Plaza G, Herraiz C. Intratympanic steroids for treatment of sudden hearing loss after failure of intravenous therapy. *Otolaryngol Head Neck Surg.* 2007 Jul;137(1): 74–78.
67. Hong SM, Park CH, Lee JH. Hearing outcomes of daily intratympanic dexamethasone alone as a primary treatment modality for ISSHL. *Otolaryngol Head Neck Surg.* 2009 Nov;141(5):579–583.
68. Tsai YJ, Liang JG, Wu WB, Ding YF, Chiang RP, Wu SM. Intratympanic injection with dexamethasone for sudden sensorineural hearing loss. *J Laryngol Otol.* 2011 Feb; 125(2):133–137.
69. Cavallazzi GM. Relations between O<sub>2</sub> and hearing function. Eds: Marroni A, Oriani G, Wattel F. *Proceedings of International Joint Meeting on Hyperbaric and Underwater Medicine.* Milano, Italy. 1996a Sept 4–8; 633–645.
70. Nagahara K, Fisch U, Yagi N. Perilymph oxygenation in sudden and progressive sensorineural hearing loss. *Acta Otolaryngol.* 1983 Jul – Aug;96(1–2):57–68.
71. Lamm H. Der einfluss der hperbaren sauerstofftherapie auf den tinnitus und horverlust bei akuten und chronischen innenohrschaden. *Otorhinolaryngol Nova.* 1995; 5:161–169.
72. Tsunoo M, Perlman MB. Temporary arterial obstruction. Effects on perilymph oxygen and microphonics. *Acta Otolaryngol.* 1969;67:460–466.
73. Schwab B, Flunkert C, Heermann R, Lenarz T. HBO in the therapy of cochlear dysfunctions – first results of a randomized study. *EUBS diving and hyperbaric medicine, collected manuscripts of XXIV Annual Scientific Meeting of the European Underwater and Baromedical Society.* Stockholm: EUBS. 1998:40–42.
74. Fattori B, Berrettini S, Casani A, Nacci A, De Vito A, De Iaco G. Sudden hypoacusis treated with hyperbaric oxygen therapy: a controlled study. *Ear Nose Throat J.* 2001 Sept;80(9):655–660.
75. Racic G, Maslovara S, Roje Z, Dogas Z, Tafra R. Hyperbaric oxygen in the treatment of sudden hearing loss. *ORL J Otorhinolaryngol Relat Spec.* 2003 Nov–Dec;65(6): 317–320.
76. Dundar K, Gumus T, Ay H, Yetiser S, Ertugrul E. Effectiveness of hyperbaric oxygen on sudden sensorineural hearing loss: prospective clinical research. *J Otolaryngol.* 2007 Feb;36(1):32–37.
77. Hoffmann G, Bohmer D, Desloovere C. Hyperbaric oxygenation as a treatment for sudden deafness and acute tinnitus. *Proceedings of the Eleventh International Congress on Hyperbaric Medicine.* Flagstaff, AZ: Best Publishing Company; 1995. Pp:146–151.
78. Lamm K, Lamm H, Arnold W. Effect of hyperbaric oxygen therapy in comparison to conventional or placebo therapy or no treatment in idiopathic sudden hearing loss, acoustic trauma, noise-induced hearing loss and tinnitus. A Literature Survey. *Adv Otorhinolaryngol.* 1998;54:86–89.
79. Marchesi G, Valetti TM, Amer M, Ross M, Tiberti R, Ferani R, Mauro G Di. The HBO effective in sudden hearing loss treatment. *UHMS Meeting Abstracts,* 2000. <http://archive.rubicon-foundation.org/6781>.

80. Murakawa T, Kosaka M, Mori Y, Fukazawa M, Misaki K. Treatment of 533 patients with sudden deafness performed oxygenation at high pressure. *Nihon Jibiinkoka Gakkai Kaiho*. 2000 May;103(5):506–515.
81. Muzzi E, Zennaro B, Visentin R, Soldano F, Sacilotto C. Hyperbaric oxygen therapy as salvage treatment for sudden sensorineural hearing loss: review of rationale and preliminary report. *J Laryngol Otol*. 2010;124(2):e2.
82. Ohno K, Noguchi Y, Kawashima Y, Yagishita K, Kitamura K. Secondary hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss in the subacute and chronic phases. *J Med Dent Sci*. 2010;57(2):127–132.
83. Cvorovic L, Jovanovic MG, Milutinovic Z, Arsovic N, Djeric D. Randomized prospective trial of hyperbaric oxygen therapy and intratympanic steroid injection as salvage treatment of sudden sensorineural hearing loss. *Otol and Neurotology*. 2013;34(6):1021–1026.
84. Yang CH, Wu RW, Hwang CF. Comparison of intratympanic steroid injection, hyperbaric oxygen and combination therapy in refractory sudden sensorineural hearing loss. *Otol and Neurotology*. 2013;34:1411–1416.
85. Pezzoli M, Magnano M, Maffi L, Pezzoli L, Marcato P, Orione M, Cupi D, Bongioannini G. Hyperbaric oxygen therapy as salvage treatment for sudden sensorineural hearing loss: a prospective controlled study. *Eur Arch Otorhinolaryngol*. 2015 Jul; 272(7):1659–1666.
86. Schumann K, Lamm K, Hettich M. Effect and effectiveness of hyperbaric oxygen therapy in chronic hearing disorders. Report of 557 cases 1989. *HNO*. 1990 Nov; 38(11):408–411.
87. Hoffman G, Bohmer D, Desloovere C. Hyperbaric oxygenation as a treatment of chronic forms of inner ear hearing loss and tinnitus. Proceedings of the Eleventh International Congress on Hyperbaric Medicine. Flagstaff, AZ: Best Publishing Company; 1995. Pp:141–145.
88. Kramer MR, Springer C, Berkman N, Glazer M, Bubil M, Bar-Yishay E, Godfrey S. Rehabilitation of hypoxemic patients with COPD at low altitude at the dead sea, the lowest place on earth. *Chest*. 1998 Mar;113(3):571–575.
89. Dean JB, Mulkey DK. Continuous Intracellular recordings from mammalian neurons exposed to hyperbaric helium, oxygen, or air. *J Appl Physiol*. 2000 Aug 89 (2):807–822.
90. Kau RJ, Sendtner-Gress K, Ganzer U, Arnold W. Effectiveness of hyperbaric oxygen therapy in patients with acute and chronic cochlear disorders. *ORL J Otorhinolarygnol Relat Spec*. 1997 Mar–Apr; 59(2):78–83.
91. Giger HL. Therapy of sudden deafness with O<sub>2</sub> / CO<sub>2</sub> inhalation. *HNO*. 1979 Mar; 27(3):107–109.
92. Goto F, Fujiita T, Kitani Y, Kanno M, Kamei T, Ishii H. Hyperbaric oxygen and stellate ganglion blocks for idiopathic sudden hearing loss. *Acta Otolaryngol*. 1979;88(5– 6):335–342.
93. Pilgramm M, Lamm H, Schumann K. Hyperbaric oxygen therapy in sudden deafness. *Laryngol, Rhinol, Otol*. 1985 Jul;64(7):351–354.
94. Dauman R, Poisot D, Cros AM, Zennaro O, Bertrand B, Duclos JY, Esteban D, Milacic M, Boudey C, Bebear JP. Sudden deafness: a randomized comparative study of 2 administration modalities of hyperbaric oxygenotherapy combined with naftidrofuryl. *Rev Laryngol Otol Rhinol (Bord)*. 1993;114(1):53–58.
95. Zennaro O, Dauman R, Poisot A, Esteben D, Duclose JY, Bertrand B, Cros AM, Milacic M, Bebear JP. Value of the association of normovolemic dilution and hyperbaric oxygenation in the treatment of sudden deafness. A retrospective study. *Ann Otolaryngol Cir Cervicofac*. 1993;110(3):162–169.
96. Cavallazzi G, Pignataro L, Capaccio P. Italian experience in hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. Proceedings of the International Joint Meeting on Hyperbaric and Underwater Medicine. Bologna: Grafica Victoria; 1996. Pp: 647–649.
97. Aslan I, Oysu C, Veyseller B, Baserer N. Does the addition of hyperbaric oxygen therapy to the conventional treatment modalities influence the outcome of sudden deafness? *Otolaryngol Head Neck Surg*. 2002 Feb;126(2):121–126.
98. Topuz E, Yigit O, Cinar U, Seven H. Should hyperbaric oxygen be added to treatment in idiopathic sudden sensorineural hearing loss? *Eur Arch Otorhinolaryngol*. 2004 Aug;261(7):393–396.
99. Narozny W, Kuczkowski J, Kot J, Stankiewicz C, Sicko Z, Mikaszewski B. Prognostic factors in sudden sensorineural hearing loss: our experience and a review of the literature. *Ann Otol Rhinol Laryngol*. 2006 Jul;115(7):553–558.
100. Suzuki H, Fujimura T, Shiromori T, Ohbuchi T, Kitamura T, Hashida K, Ueda T. Prostaglandin E1 versus steroid in combination with hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. *Auris Nasus Larynx*. 2008 Jun;35 (2):192–197.
101. Suzuki H, Fujimura T, Ikeda K, Shiromori T, Ueda T, Ohbuchi T, Nagatani G. Prostaglandin E1 in combination with hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. *Acta Otolaryngol*. 2008 Jan;128(1):61–65.
102. Cekin E, Cincik H, Ulubil SA, Gungor A. Effectiveness of hyperbaric oxygen therapy in management of sudden hearing loss. *J Laryngol Otol*. 2009;123:609–612.

103. Liu Y, Sun D, Shao S, Jiang W, Sun Z, Li Z. The effect of hyperbaric oxygen therapy to different degree of hearing loss and types of threshold curve in sudden deafness patients. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2010 Oct; 24(19):890– 894.
104. Korpinar S, Alkan Z, Yigit O, Gor AP, Toklu AS, Cakir B, Soyuyuce OG, Ozkul H. Factors influencing the outcome of idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol*. 2011 Jan; 268 (1):41–47.
105. Holy R, Navara M, Dosel P, Fundova P, Prazenica P, Hahn A. Hyperbaric oxygen therapy in idiopathic sudden sensorineural hearing loss (ISSHL) in association with combined treatment. *Undersea Hyperb Med*. 2011 Mar – Apr;38(2):137–142.
106. Liu SC, Kang BH, Lee JC, Lin YS, Huang KL, Liu DW, Su WF, Kao CH, Chu YH, Chen HC, Wang CH. Comparison of therapeutic results in sudden sensorineural hearing loss with/without additional hyperbaric oxygen therapy: a retrospective review of 465 audiologically controlled cases. *Clin Otolaryngol*. 2011 Apr;36(2):121–128.
107. Fujimura T, Suzuki H, Shiromori T, Ueda T, Mori T. Hyperbaric oxygen and steroid therapy for idiopathic sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol*. 2007 Aug;264(8):861–866.
108. Suzuki H, Mori T, Hashida K, Shibata M, Nguyen KH, Wakasugi T, Hohchi N. Prediction model for hearing outcome in patients with idiopathic sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol*. 2011;268(4):497–500.
109. Filipo R, Attanasio G, Viccaro M, Russo FY, Mancini P, Rocco M, Pietropaoli P, Covelli E. Hyperbaric oxygen therapy with short duration intratympanic steroid therapy for sudden hearing loss. *Acta Otolaryngol*. 2012 May;132(5):475–481.
110. Capuano L, Cavaliere M, Parente G, Damiano A, Pezzuti G, Lopardo D, Lemma M. Hyperbaric oxygen for idiopathic sudden hearing loss: is the routine application helpful? *Acta Oto-Laryngologica*. 2015 Jul;135(7):692–697.
111. Carneiro SN, Guerreiro DV, Cunha AM, Camacho OF, Aguiar IC. Hyperbaric oxygen therapy in sudden sensorineural hearing loss following spinal anesthesia: case reports. *Undersea Hyperb Med*. 2016;43(2):153 –159.
112. Hosokawa S, Sugiyama K, Takashashi G, Takebayashi S, Mineta H. Prognostic factors for idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy and intravenous steroids. *J Laryngol and Otol*. 2017;131:77–82.
113. Bennett MH, Kertesz T, Perleth M, Yeung P, Lehm JP. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2012; Issue 10. Art. No.:CD004739.
114. Yildirim E, Murat Ozcan K, Palah M, Ali Cetin M, Ensari S, Dere H. Prognostic effect of hyperbaric oxygen therapy starting time for sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol*. 2015;272:23–28.
115. Bennett MH, Kertesz T, Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2005 Jan 25 (1):CD004739.
116. Bennett MH, Kertesz T, Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2007 Jan 24 (1):CD004739.
117. Bennett MH, Kertesz T, Matthias P, Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2010 Jan 20(1):CD004739.
118. Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss. A systematic review. *Arch Otolaryngol Head Neck Surg*. 2008 Jun;133:573–581.
119. Agarwal L, Pothier Dd. Vasodilators and vasoactive substances for idiopathic sudden sensorineural hearing loss. *Cochrane Database Syst Rev*. 2009 Oct 7;(4): CD003422.
120. Tucci DL, Farmer JC, Kitch RD, Witsell DL. Treatment of sudden sensorineural hearing loss with systemic steroids and valacyclovir. *Otol Neurotol*. 2002;23:301– 308.
121. Stokroos RJ, Albers FWJ, Ten Vergert EM. Antiviral treatment of idiopathic sudden sensorineural hearing loss: a prospective, randomized, double-blinded clinical trial. *Acta Otolaryngol*. 1998b;118: 488–485.
122. Westerlaken BO, Stokroos RJ, Dhooge IJ, Wit HP, Albers FW. Treatment of idiopathic sudden sensorineural hearing loss with antiviral therapy: a prospective, randomized, double-blind clinical trial. *Ann Otol Rhinol Laryngol*. 2003;112:993– 100.
123. Uri N, Doweck I, Cohen-Kerem R, Greenberg E. Acyclovir in the treatment of idiopathic sudden sensorineural hearing loss. *Otolaryngol Head Neck Surg*. 2003; 128:544–549.
124. Awad Z, Huins C, Pothier DD. Antivirals for idiopathic sudden sensorineural hearing loss. *Cochrane Database Syst Rev*. 2012 Aug 15;(8):1–22.
125. Wei BP, Mubiru S, O’Leary S. Steroids for idiopathic sudden sensorineural hearing loss. *Cochrane Database Syst Rev*. 2006 Jan 25;(1):CD003998.
126. Nosrati-Zarenoe R, Hultcrantz E. Corticosteroid Treatment of Idiopathic Sudden sensorineural hearing loss: randomized triple-blind placebo-controlled trial. *Otol Neurotol*. 2012 Jun; 22(4):523–531.

127. Plontke SK, Meisner C, Caye-Thomasen P, Parnes L, Agrawal S, Mikulee T. Intratympanic glucocorticoids for sudden sensorineural hearing loss. *Cochrane Database Syst Rev*. 2009 Oct 7(1):CD0088080.
128. Kranke P, Bennett MH, Debus SE, Roeckl-Wiedmann I, Schnabel A. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database Syst Rev*. 2009 Jul 8(1): CD004123.
129. Piper SM, Murphy-Lavoie H, LeGros TL. Idiopathic sudden sensorineural hearing loss. In: *Hyperbaric Oxygen Therapy Indications: The Hyperbaric Oxygen Therapy Committee Report*. North Palm Beach, Florida; 2014. Best Publishing Company.
130. Uzun G, Mutluoglu M, Metin S. The use of hyperbaric oxygen treatment for sudden sensorineural hearing loss in europe. *Diving Hyperb Med*. 2016 Mar;46 (1):43– 46.
131. Grades of Hearing Impairment. World Health Organization. 2011. [http://www.who.int/pbd/deafness/hearing\\_impairment\\_grades/en/index.html](http://www.who.int/pbd/deafness/hearing_impairment_grades/en/index.html).
132. Deafness and Hearing Impairment. World Health Organization Fact Sheet. April 2010. <http://www.who.int/mediacentre/factsheets/fs300/en/index.html>.
133. World Health Organization. The Global Burden of Disease: 2004 Update. 2008. WHO, Geneva, Switzerland. WHO Press. ISBN 978 92 4 156371 0.
134. Narozny W, Sicko Z, Przewony T, Stankiewicz C, Kot J, Kuczkowski J. Sudden sensorineural hearing loss: a treatment protocol including glucocorticoids and hyperbaric oxygen therapy. *Otolaryngol Pol*. 2004;58(4): 821-830.

## **Chapter 10: Intracranial Abscess**

*Edward O. Tomoye DO, Richard E. Moon MD*

### **REFERENCES**

1. Brouwer MC, Tunkel AR, McKhann GM, 2nd, van de Beek D. Brain abscess. *N Engl J Med.* 2014;371(5):447-56.
2. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. *Neurology.* 2014;82(9):806-13.
3. Tunkel AR. Brain abscess. In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition. 8 ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1164-76.
4. Tekkok IH, Erbengi A. Management of brain abscess in children: review of 130 cases over a period of 21 years. *Childs Nerv Syst.* 1992;8(7):411-6.
5. Udayakumaran S, Onyia CU, Kumar RK. Forgotten? Not Yet. Cardiogenic Brain Abscess in Children: A Case Series-Based Review. *World Neurosurg.* 2017;107:124-9.
6. Gelfand MS, Stephens DS, Howell EI, Alford RH, Kaiser AB. Brain abscess: association with pulmonary arteriovenous fistula and hereditary hemorrhagic telangiectasia: report of three cases. *Am J Med.* 1988;85(5):718-20.
7. Press OW, Ramsey PG. Central nervous system infections associated with hereditary hemorrhagic telangiectasia. *Am J Med.* 1984;77(1):86-92.
8. Chang YT, Lu CH, Chuang MJ, Huang CR, Chuang YC, Tsai NW, et al. Supratentorial deep-seated bacterial brain abscess in adults: clinical characteristics and therapeutic outcomes. *Acta Neurol Taiwan.* 2010;19(3):178-83.
9. Sukoff MH, Ragatz RE. Hyperbaric oxygenation for the treatment of acute cerebral edema. *Neurosurgery.* 1982;10:29-38.
10. Mader JT, Brown GL, Guckian JC, Wells CH, Reinarz JA. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. *J Infect Dis.* 1980;142:915-22.
11. Siddiqui A, Davidson JD, Mustoe TA. Ischemic tissue oxygen capacitance after hyperbaric oxygen therapy: a new physiologic concept. *Plast Reconstr Surg.* 1997;99(1):148-55.
12. Price JC, Stevens DL. Hyperbaric oxygen in the treatment of rhinocerebral mucormycosis. *Laryngoscope.* 1980;90:737-47.
13. Ferguson BJ, Mitchell TG, Moon R, Camporesi EM, Farmer J. Adjunctive hyperbaric oxygen for treatment of rhinocerebral mucormycosis. *Rev Infect Dis.* 1988;10(3):551-9.
14. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis.* 2005;41(5):634-53.
15. Verklin RM, Jr., Mandell GL. Alteration of effectiveness of antibiotics by anaerobiosis. *J Lab Clin Med.* 1977;89(1):65-71.
16. Madsen ST. Sepsis, endocarditis, and brain abscess. *Scand J Gastroenterol Suppl.* 1983;85:48-54.
17. Kaide CG, Khandelwal S. Hyperbaric oxygen: applications in infectious disease. *Emerg Med Clin North Am.* 2008;26(2):571-95, xi.
18. Larsson A, Engstrom M, Uusijarvi J, Kihlstrom L, Lind F, Mathiesen T. Hyperbaric oxygen treatment of postoperative neurosurgical infections. *Neurosurgery.* 2008;62 Suppl 2:652-71.
19. Bartek J, Jr., Jakola AS, Skyrmans S, Forander P, Alpkvist P, Schechtman G, et al. Hyperbaric oxygen therapy in spontaneous brain abscess patients: a population-based comparative cohort study. *Acta Neurochir (Wien).* 2016;158(7):1259-67.
20. Kutlay M, Colak A, Yildiz S, Demircan N, Akin ON. Stereotactic aspiration and antibiotic treatment combined with hyperbaric oxygen therapy in the management of bacterial brain abscesses. *Neurosurgery.* 2008;62 Suppl 2:540-6.
21. Lampl LA. Hyperbaric oxygen in intracranial abscess. In: Whelan HT, Kindwall EP, editors. *Hyperbaric Medicine Practice.* 4th ed. North Palm Beach, FL: Best Publishing Company; 2017. p. 467-83.
22. Baechli H, Schmutz J, Mayr JM. Hyperbaric oxygen therapy (HBO) for the treatment of an epidural abscess in the posterior fossa in an 8-month-old infant. *Pediatr Neurosurg.* 2008;44(3):239-42.
23. Kohshi K, Abe H, Mizoguchi Y, Shimokobe M. Successful treatment of cervical spinal epidural abscess by combined hyperbaric oxygenation. *Mt Sinai J Med.* 2005;72(6):381-4.
24. Kurschel S, Mohia A, Weigl V, Eder HG. Hyperbaric oxygen therapy for the treatment of brain abscess in children. *Childs Nerv Syst.* 2006;22(1):38-42.
25. Nakahara K, Yamashita S, Ideo K, Shindo S, Suga T, Ueda A, et al. Drastic therapy for listerial brain abscess involving combined hyperbaric oxygen therapy and antimicrobial agents. *J Clin Neurol.* 2014;10(4):358-62.

## **Chapter 11: Necrotizing Soft Tissue Infections**

*Caesar A. Anderson MD, MPH, Irving Jacoby MD, FACP, FACEP, FAAEM, FUHM*

### **REFERENCES**

1. Kao LS, Lew DF, et al. Local variations in the epidemiology, microbiology, and outcome of necrotizing soft tissue infections: a multicenter study. *Am J Surg* 2011;202:139.
2. Wilkinson D, Dolette D. Hyperbaric Oxygen treatment and survival from necrotizing soft tissue infection. *Arch Surg.* 2004;139:1339 -1345.
3. Escobar SJ, Slade JB. Adjuvant hyperbaric oxygen therapy for treatments of necrotizing fasciitis reduces mortality and amputation rates. *Undersea and Hyperb Med.* 2006;32(6):437-443.
4. Anaya DA, Predictors of mortality and limb loss in necrotizing soft tissue infections. *Arch Surg.* 2005.
5. Shupak A, Shoshani O, Goldberg I, et al. Necrotizing fasciitis: An indication for hyperbaric oxygen therapy? *Surgery.* 1995;118:873-878.
6. Shaw JJ, Psoinos C, Emhoff TA, et al. Not just full of hot air: Hyperbaric oxygen therapy increases survival in cases of necrotizing soft tissue infections. *Surg Infect (Larchmt).* 2014;15:328-335.
7. Hakkaranen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: Review and current concepts in treatment, systems of care, and outcomes. *Curr Probl Surg.* 2014 August;51(8):344-362.
8. Sudarsky LA, Laschinger JC, et al. Improved results from a standardized approach in treating patients with necrotizing fasciitis. *Ann Surg.* 1987;206:661-665.
9. Faraklas I, Yang D, et al. A Multicenter Review of Care Patterns and Outcomes in Necrotizing Soft Tissue Infections. *Surgical Infections.* 2016;Volume 17(6).
10. Mandell G. Bactericidal activity of aerobic and anaerobic polymorphonuclear neutrophils. *Infect Immun.* 1974;9:337-341.
11. Mader JT, Adams KR, Sulton TE. Infectious diseases: pathophysiology and mechanisms of hyperbaric oxygen. *J Hyperbaric Med.* 1987;2:133-140.
12. Hunt TK, Linsey M, Grislis G, et al. The effect of differing ambient oxygen tension on wound infection. *Ann Surg.* 1975 Jan;181(1):35-39.
13. Thom SR, Mendiguren I, Hardy K, Bolotin T, Fisher D, Nebolon M, et al. Inhibition of human neutrophil beta2--integrin-dependent adherence by hyperbaric O<sub>2</sub>. *Am J Physiol.* 1997 Mar;272(3 Pt 1):C770-777.
14. Park MK, Muhvich KH, Myers RA, Marsella L. Hyperoxia prolongs the aminoglycoside-induced postantibiotic effect in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother.* 1991;35(4):691-695.
15. Jones J. *Surgical Memoirs of the War of the Rebellion. Investigation Upon the Nature, Causes, and Treatment of Hospital Gangrene as Prevailed in the Confederate Armies 1861-1865.* United States Sanitary Commission;New York, NY. p.1871.
16. Meleney FL. Hemolytic streptococcus gangrene. *Arch Surg.* 1924;9:317-364.
17. Wilson B. Necrotizing fasciitis. *Am Surg.* 1952;18:416-431.
18. Simonsen E, Orman E, et al. Cellulitis incidence in a defined population. *Epidemiol Infect.* 2006;134(2):293-299.
19. Gozal D, Ziser A, et al. Necrotizing fasciitis. *Arch Surg.* 1986;121:233.
20. Anaya DA, Patchen Dellinger E. Necrotizing soft-tissue infection: diagnosis and management. *Clin Infect Dis.* 2007;44:705-710.
21. Miller LG, Perdreau-Remington F, Rieg G, Mehdi S, Perlroth J, Bayer AS, Tang AW, Phung TO, Spellberg B. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N Engl J Med.* 2005;352:1445-1453.
22. Giuliano A, Lewis F, et al. Bacteriology of necrotizing fasciitis. *Am J Surg.* 1977;1134(1):52-57.
23. Miller L, Carrick M, et al. Necrotizing fasciitis caused by community associated methicillin-resistant *Staphylococcal aureus* in Los Angeles. *N Engl J Med.* 2005;352(14):1445-1453.
24. Bryant AE, Stevens DL, et al. clostridial myonecrosis: new insights in pathogenesis and management. *Curr Infect Dis Rep.* 2010;12(5):383-391.
25. Stevens DL, Aldape MJ, et al. Life threatening clostridial infections. *Anaerobe.* 2011;18(2):254-259.
26. Eke N. Fournier's gangrene: a review of 1726 cases. *Br J Surg.* 2000;87:718.
27. Toro C, Castillo A, et al. Cervical necrotizing fasciitis: Report of 6 cases and review of literature. *European Annals Otorhinolaryngology, Head and Neck Diseases.* 2014;131:357-359.
28. Flanagan C, Daramola O, et al. Surgical debridement and adjunctive hyperbaric oxygen in cervical necrotizing fasciitis. *Otorhinolaryngology, Head and Neck Diseases.* 2009;140 (5):730-4.h
29. Stevens DL, Bryant AE. Necrotizing soft tissue infections. *N Engl J Med.* 2017;377:2253.
30. Shiroff A, Herlitz G, Gracias V. Necrotizing soft tissue infections. *J Intensive Care Med.* 2014;29(3):138-144.
31. Darenberg J, Luca-Harari B, et al. Molecular and clinical characteristics of invasive GAS infection in Sweden. *Clin Infect Dis.* 2007;45:450.

32. Goodell J, Jordan M, et al. Rapidly advancing necrotizing fasciitis caused by *Phytobacterium* (*Vibrio*) damsels: a hyperaggressive variant. *Crit Care Med.* 2004;32(1):278-281.
33. Hau V, Ho CO. Necrotizing fasciitis caused by *Vibrio vulnificans* in the lower limb following exposure to seafood on the hand. *Hong Kong Med J.* 2011;17:335.
34. Brogan TV, Nizet V, Waldhausen JHT, Rubens CE, Clarke W. Group A streptococcal necrotizing fasciitis complicating primary varicella: a series of fourteen patients. *Pediatr Infect Dis J.* 1995;14:588-594.
35. <https://www.fda.gov/downloads/drugs/drugsafety/ucm618466.pdf>
36. Stevens DL, Bryant AE, et al. Necrotizing soft tissue infections. *N Engl J Med.* 2017;377:2253.
37. Hamilton SM, Bayer CR, Stevens DL, and Bryant AE. Effects of selective and nonselective nonsteroidal anti-inflammatory drugs on antibiotic efficacy of experimental Group A Streptococcal myonecrosis. *Jour Infect Dis.* 2014; 209:1429-1435.
38. Bell AL, Adamson H, Kirk F, McCaigue MD, Rotman H. Diclofenac inhibits monocyte superoxide production ex vivo in rheumatoid arthritis. *Rheumatol Int.* 1991;11:27-30.
39. Stevens DL. Could nonsteroidal anti-inflammatory drugs (NSAIDS) enhance the progression of bacterial infections to toxic shock syndrome? *Shock.* 2013;21(4):977-980.
40. LaRock CN, Todd J, LaRock DL et al. IL-1 $\beta$  is an innate immune sensor of microbial proteolysis. *Sci. Immunol.* 2016;1,eaah3539.
41. Sawin RS, Schaller RT, Tapper D, Morgan A, Cahill J. Early recognition of neonatal abdominal wall necrotizing fasciitis. *Am J Surg.* 1994;167:481-484.
42. Wang TL, Hung CR. Role of tissue oxygen saturation monitoring in diagnosing necrotizing fasciitis of the lower limbs. *Ann Emerg Med.* 2004;44:222-228.
43. Lally KP, Atkinson JB, Wooley MM, Mahour GH. Necrotizing fasciitis: a serious sequela of omphalitis in the newborn. *Ann Surg.* 1984;199:101-103.
44. Sawin RS, Schaller RT, Tapper D, Morgan A, Cahill J. Early recognition of neonatal abdominal wall necrotizing fasciitis. *Am J Surg.* 1994;167:481-484.
45. Keung E, Liu X, et al. Immunocompromised status in patients with necrotizing soft tissue infections. *JAMA Surg.* 2013;148(5):419-426.
46. Stamenkovic I, Lew PD. Early recognition of potentially fatal necrotizing fasciitis: the use of frozen-section biopsy. *N Engl J Med.* 1984;310:1689-1693.
47. Carbonetti F, Cremona A, et al. The role of contrast enhanced computed tomography in the diagnosing of necrotizing fasciitis and comparison with the Laboratory risk indicator for Necrotizing fasciitis (LRINEC). *Radiol Med.* 2016 Feb;121(2):106-121.
48. Wysoki MG, Santora TA, Shah RM, Friedman AC. Necrotizing fasciitis: CT characteristics. *Radiology.* 1997;203:859-863.
49. Schmid MR, Kossman T, Duewell S. Differentiation of necrotizing fasciitis and cellulitis using MR imaging. *Am J Roentgenol.* 1998;170:615-620.
50. Wong C, Khin L, et al. The LRINEC (laboratory risk indicator for necrotizing fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med.* 2004;32(7):1535-1541.
51. Bechar J, Sephripour S, et al. Laboratory risk indicator for necrotizing fasciitis (LRINEC) score for the assessment of early necrotizing fasciitis: a systematic review of the literature. *Ann R Coll Surg Engl.* 2017;99:341-346.
52. Borschitz T, Schlicht S, et al. Improvement of a clinical score for necrotizing fasciitis: 'pain out of proportion' and high CRP levels aid the diagnosis. *PLoS One* 2015;10(7):e0132775.
53. Hansen M, Rasmussen L, et al. Pentraxin-3 as a marker of disease severity and risk of death in patients with necrotizing soft tissue infections: a nationwide, prospective, observational study. *Critical Care.* 2016;(20)40.
54. Su YC, Chen HW, et al. Laboratory risk indicator for necrotizing fasciitis score and outcomes. *ANZ J Surg.* 2008;78:968-972.
55. Hansen MB, Rasmussen LS, et al. Association between cytokine response, the LRINEC score and outcome in patients with necrotizing soft tissue infection: a multicenter, prospective study. *Sci Rep.* 2017; 7:42179.
56. Stevens DL, Bisno AL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections:2014 update by the infectious diseases society of America. *Clin Infect Dis.* 2014;59:147.
57. Faraklas I, Yang D, et al. A Multicenter Review of Care Patterns and Outcomes in Necrotizing Soft Tissue Infections. *Surgical Infections.* 2016; Volume 17(6).
58. Sablier F, Slaouti T, et al. Nosocomial transmission of necrotizing fasciitis. *Lancet.* 2010;375:1052.
59. Bilbault P, Castelain V, et al. Life threatening cervical necrotizing fasciitis after a common dental extraction. *Am J Emerg Med.* 2008;26:5-7

60. Soh CR, Pietroban R, Freiberger JJ, et al. Hyperbaric Oxygen therapy in necrotizing soft tissue infections:a study of patients in the US Nationwide Inpatient sample. *Intensive Care Med.* 2012;38:1143.
61. Wilkinson D, Dolette D. Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. *Arch Surg.* 2004;139:1339-1345.
62. Escobar SJ, Slade JB, Hunt TK, Cianci P. Adjuvant hyperbaric oxygen therapy (HBO<sub>2</sub>) for treatment of necrotizing fasciitis reduces mortality and amputation rate. *Undersea Hyperb Med.* 2006;32(6):437-443.
63. Brown DR, Davis NL, Lepawsky M, Cunningham J, Kortbeek J. A multicenter review of the treatment of major truncal necrotizing infections with and without hyperbaric oxygen therapy. *Am J Surg.* 1994;167:485-489.
64. Monestersky JH, Myers RAM. Letter to the editor: hyperbaric oxygen treatment of necrotizing fasciitis. *Am J Surg.* 1995;169:187-188.
65. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. *Arch Surg.* 2005;140:151-157.
66. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. *Ann Surg.* 1995;221:558-563.
67. Hsieh WH, Yang PH, Chao HC, Lai JY. Neonatal necrotizing fasciitis: report of 3 cases and review of the literature. *Pediatrics.* 1999;103(4):e53. Available at: <http://pediatrics.aappublications.org/cgi/content/full/103/4/e53>
68. Lally KP, Atkinson JB, Wooley MM, Mahour GH. Necrotizing fasciitis: a serious sequela of omphalitis in the newborn. *Ann Surg.* 1984;199:101-103.
69. Sawin RS, Schaller RT, Tapper D, Morgan A, Cahill J. Early recognition of neonatal abdominal wall necrotizing fasciitis. *Am J Surg.* 1994;167:481-484.
70. Gozal D, Ziser A, Shupak A, Ariel A, Melamed Y. Necrotizing fasciitis. *Arch Surg.* 1986;121:233-235.
71. Riseman JA, Zamboni WA, Curtis A, Graham DR, Konrad HR, and Ross DS. Hyperbaric oxygen therapy for necrotizing fasciitis reduces mortality and the need for debridements. *Surgery.* 1990;108:847-850.
72. Laor E, Palmer LS, Tolia BM. Outcome prediction in patients with Fournier's gangrene. *J Urol.* 1995;154:89-92.
73. Dahm P, Roland FH, Vaslef SN, Moon RE, Price DT, Georgiade GS, Viewig J. Outcome analysis in patients with primary necrotizing fasciitis of the male genitalia. *Urol.* 2000;56:31-36.
74. Mallikarjuna M, Vijayakumar A, et al. Fournier's gangrene: current practices. *ISRN Surgery* 2012(ID 942437):1-8.
75. Hollabaugh RS, Dmochowski RR, Hickerson WL. Fournier's gangrene: therapeutic impact of hyperbaric oxygen. *Plast Reconstr Surg.* 1998;101:94-100.
76. Pizzorno R, Bonini F, Donelli A, Stubinski R, Medica M, Carmignani G. Hyperbaric oxygen therapy in the treatment of Fournier's disease in 11 male patients. *J Urol.* 1997;158:837-840.
77. Korhonen K, Him M, Niinikoski J. Hyperbaric oxygen in the treatment of Fournier's gangrene. *Eur J Surg.* 1998;164:251-255.
78. Willy C, Rieger H, et al. Hyperbaric oxygen therapy for NSTI. *Chirug* 2012;83:960.
79. Eggerstedt M, Gamelli RL, et al. The care of necrotizing soft tissue infections. Patterns of definitive intervention at a large referral center. *J Burn Care Res.* 2015;36:105-110.
80. Holena DN, Mills AM, et al. Transfer status: A risk factor for mortality in patients with necrotizing fasciitis. *Surgery.* 2011;150:363-370.
81. Davaney B, Frawley G, et al. Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. *Anaesth Intensive Care.* 2015;43:6.
82. Gore M. Odontogenic necrotizing fasciitis: a systematic review of the literature. *BMC Ear, Nose and Throat Disorders.* 2018;18:14.
83. Shaw JJ, Psoinos C, Emhoff TA, et al. Not just full of hot air: Hyperbaric oxygen therapy increases survival in cases of necrotizing soft tissue infections. *Surg Infect (Larchmt).* 2014;15:328-335.
84. Torp KD, Caraway MS. Safe administration of hyperbaric oxygen after bleomycin:a case series of 15 patients. *Undersea Hyperb Med.* 2012;39:873.
85. Karagoz B, Suleymanoglu S, et al. Hyperbaric Oxygen therapy does not potentiate doxorubicin-induced cardiotoxicity in rats. *Basic Clin Pharmacol Toxicol.* 2008;102:287.
86. Stone HH, Martin JD. Synergistic necrotizing cellulitis. *Ann Surg.* 1972;175:702-711.
87. Bessman AN, Wagner W. Nonclostridial gas gangrene. *JAMA.* 1975;233:958.
88. Cullen TS. A progressively enlarging ulcer of abdominal wall involving the skin and fat, following drainage of an abdominal abscess, apparently of appendiceal origin. *Surg Gynecol Obstetr.* 1924;38:579-582.
89. Ledingham IM, Tehrani MA. Diagnosis, clinical course and treatment of acute dermal gangrene. *Br J Surg.* 1975;62:364-372.
90. Chayakulkeeree M, Ghannoum MA, Perfect JR. Zygomycosis: the re-emerging fungal infection. *Eur J Clin Microbiol Infect Dis.* 2006;25:215-229.

91. McNulty JS. Rhinocerebral mucormycosis: predisposing factors. *Laryngoscope*. 1982;92:1140-1143.
92. Windus DW, Stokes TJ, Julian BA, Fenves AZ. Fatal Rhizopus infections in hemodialysis patients receiving deferoxamine. *Ann Int Med*. 1987;107:678-680.
93. Boelaert JR, Van Roost GF, Vergauwe PL, Verbanck C, De Vroey C, Segaert MF. The role of deferoxamine in dialysis-associate mucormycosis: report of three cases and review of the literature. *Clin Nephrol*. 1988; 29:261-266.
94. Cocanour CS, Miller-Crouchett P, Reed RL, Johnson PC, Fischer RP. Mucormycosis in trauma patients. *J Trauma*. 1992;32:12-15.
95. Tedder MJ, Spratt JA, Anstadt MP, Hegde SS, Tedder SD, Lowe JE. Pulmonary mucormycosis: results of medical and surgical therapy. *Ann Thorac Surg*. 1994;57:1044-1050.
96. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *Clin Microbiol Revs*. 2000;13:236-301.
97. Murray HW. Pulmonary mucormycosis with massive fatal hemoptysis. *Chest*. 1975;68:65-68.
98. Michalak DM, Cooney DR, Rhodes KH, Telander RL, Kleinberg F. Gastrointestinal mucormycosis in infants and children: a cause of gangrenous intestinal cellulitis and perforation. *J Pediatr Surg*. 1980;15:320-324.
99. Chamilos G, Marom EM, Lewis RE, Lionakis MS, Kontoyiannis DP. Predictors of pulmonary zygomycosis versus invasive pulmonary aspergillosis in patients with cancer. *Clin Infect Dis*. 2005;41:60-66.
100. Diamond RD, Haudenschild CC, Erickson III NF. Monocyte-mediated damage to Rhizopus oryzae hyphae in vitro. *Infect Immun*. 1982;38:292-297.
101. Waldorf AR. Pulmonary defense mechanisms against opportunistic fungal pathogens. *Immunol Ser*. 1989;47: 243-271.
102. Waldorf AR, Ruderman N, Diamond RD. Specific susceptibility to mucormycosis in murine diabetes and bronchoalveolar macrophage defense against Rhizopus. *J Clin Invest*. 1984;74:150-160.
103. Ibrahim AS, Spellberg B, Avanessian V, Fu Y, Edwards, Jr. E. Rhizopus oryzae adheres to, is phagocytosed by, and damages endothelial cells in vitro. *Infect Immun*. 2005;73:778-783.
104. Imperatore F, Cuzzocrea S, De Lucia D, Sessa M, Rinaldi B, Capuano A, Liguori G, Filippelli A, Rossi F. Hyperbaric oxygen therapy prevents coagulation disorders in an experimental model of multiple organ failure syndrome. *Intensive Care Med*. 2006;32:1881-1888.
105. Buras JA, Holt D, Orlow D, Belikoff B, Pavlides S, Reenstra WR. Hyperbaric oxygen protects from sepsis mortality via an interleukin-10-dependent mechanism. *Crit Care Med*. 2006;34(10):2624-2629.
106. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, Sein M, Sein T, Chiou CC, Chu JH, Kontoyiannis DP. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Inf Dis*. 2005;41:634-653.
107. Almyroudis NG, Konoyiannis DP, Sepkowitz KA, De Pauw BE, Walsh TJ, Segal BH. Issues related to the design and interpretation of clinical trials of salvage therapy for invasive mold infection. *Clin Inf Dis*. 2006;43:1449-1455.
108. Bentur Y, Shupak A, Ramon Y, Abramovich A, Wolfson G, Stein H, Krivoi N. Hyperbaric oxygen therapy for cutaneous/soft-tissue zygomycosis complicating diabetes mellitus. *Plastic and Reconstr Surg*. 1998;102:822-824.
109. Temple ME, Brady MT, Koranyi KI, Nahata MC. Periorbital cellulitis secondary to Conidiobolus incongruous. *Pharmacotherapy*. 2001;21(3):351-354.
110. Powers JH. Salvage therapy trials in fungal disease: challenges and opportunities. *Clin Inf Dis*. 2006;43:1456-1459.
111. Trifilio SM, Bennett CL, Yarnold PR, McKoy JM, Parada J, Mehta J, Chamilos G, Palella F, Kennedy L, Mullane K, Tallman MS, Evens A, Scheetz MH, Blum W, Kontoyiannis DP. Breakthrough zygomycosis after voriconazole administration among patients with hematologic malignancies who receive hematopoietic stem-cell transplants or intensive chemotherapy. *Bone Marrow Transplant*. 2007;39:425-429.
112. Greenberg RN, Mullane K, van Burick JAH, Raad I, Abzug MJ, Herbrecht R, Langston A, Marr KA, Schiller G, Schuster M, Wingard JR, Gonzalez CE, Revankar SG, Corcoran G, Kryscio RJ, Hare R. Posaconazole as salvage therapy for zygomycosis. *Antimicrob Agents and Chemother*. 2006;50(1):126-133.
113. Langford JD, McCartney DL, Wang RC. Frozen section-guided surgical debridement for management of rhino-orbital mucormycosis. *Am J Ophthalmol*. 1997;124:265-267.
114. Jallali N, Withey S, Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. *Am J Surg*. 2005;189(4):462-466.

## **Chapter 12: Refractory Osteomyelitis**

*Brett B. Hart MD*

### **REFERENCES**

1. Strauss MB. Refractory osteomyelitis. *J Hyperbaric Med.* 1987;2:147-159.
2. Perrins DJD, et al. OHP in the management of chronic osteomyelitis. In third international conference on hyperbaric medicine. Washington D.C.: National Academy of Sciences-National Research Council;1966.
3. Slack WK, Thomas DA, Perrins D. Hyperbaric oxygenation chronic osteomyelitis. *Lancet.* 1965;14:1093-4.
4. Hamblen DL. Hyperbaric oxygenation. Its effect on experimental staphylococcal osteomyelitis in rats. *J Bone Joint Surg Am.* 1968;50(6):1129-41.
5. Sippel HW, Nyberg CD, Alvis HJ. Hyperbaric oxygen as an adjunct to the treatment of chronic osteomyelitis of the mandible: report of case. *J Oral Surg.* 1969;27(9):739-41.
6. Niinikoski J, Hunt TK. Oxygen tensions in healing bone. *Surg Gynecol Obstet.* 1972;134(5):746-50.
7. Mader JT, et al. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. *J Infect Dis.* 1980;142(6):915-22.
8. Park MK, Myers RA, Marzella L. Oxygen tensions and infections: modulation of microbial growth, activity of antimicrobial agents, and immunologic responses. *Clin Infect Dis.* 1992;14(3):720-40.
9. Hohn DC. Oxygen and leukocyte microbial killing, in hyperbaric oxygen therapy. Davis JC, Hunt TK eds. Bethesda, Maryland: Undersea Medical Society; 1977. Pp.101-10.
10. Kindwall EP. Uses of hyperbaric oxygen therapy in the 1990s. *Cleve Clin J Med.* 1992;59(5):517-28.
11. Esterhai Jr, JL, et al. Effect of hyperbaric oxygen exposure on oxygen tension within the medullary canal in the rabbit tibial osteomyelitis model. *J Orthop Res.* 1986;4(3):330-6.
12. Verklin Jr, RM, Mandell GL. Alteration of effectiveness of antibiotics by anaerobiosis. *J Lab Clin Med.* 1977;89(1):65-71.
13. Mader JT, Adams KR, Couch LA. Potentiation of tobramycin by hyperbaric oxygen in experimental *Pseudomonas aeruginosa* osteomyelitis. In 27th interscience conference on antimicrobial agents and chemotherapy. New York;1997.
14. Mader JT, et al. Hyperbaric oxygen as adjunctive therapy for osteomyelitis. *Infect Dis Clin North Am.* 1990;4(3):433-40.
15. Mendel V, et al. Therapy with hyperbaric oxygen and cefazolin for experimental osteomyelitis due to *Staphylococcus aureus* in rats. *Undersea Hyperb Med.* 1999;26(3):169-74.
16. Mader J, Shirtliff M, Calhoun JH. The use of hyperbaric oxygen in the treatment of osteomyelitis. In hyperbaric medicine practice. Kindwall EP, Whelan HT, eds. Flagstaff, AZ: Best Publishing Company, 1999. Pp.603-616.
17. Sugihara A, et al. The effect of hyperbaric oxygen therapy on the bout of treatment for soft tissue infections. *J Infect.* 2004;48(4):330-3.
18. Mader JT, Ortiz M, Calhoun JH. Update on the diagnosis and management of osteomyelitis. *Clin Podiatr Med Surg.* 1996;13(4):701-24.
19. Coulson DB, Ferguson Jr, AB, Diehl Jr, RC. Effect of hyperbaric oxygen on the healing femur of the rat. *Surg Forum.* 1966;17:449-50.
20. Niinikoski J, Penttinen R, Kulonen K. Effect of hyperbaric oxygenation on fracture healing in the rat: a biochemical study. *Calcif Tissue Res.* 1970;p.Suppl:115-6.
21. Penttinen R. Biochemical studies on fracture healing in the rat, with special reference to the oxygen supply. *Acta Chir Scand Suppl.* 1972;432:1-32.
22. Yablon IG, Cruess RL. The effect of hyperbaric oxygen on fracture healing in rats. *J Trauma.* 1968;8(2):186-202.
23. Steed DL. Enhancement of osteogenesis with hyperbaric oxygen therapy. A clinical study. *J Dent Res.* 1982;61A: 288.
24. Ueng SW, et al. Bone healing of tibial lengthening is enhanced by hyperbaric oxygen therapy: a study of bone mineral density and torsional strength on rabbits. *J Trauma.* 1998;44(4):676-81.
25. Sawai T, et al. Histologic study of the effect of hyperbaric oxygen therapy on autogenous free bone grafts. *J Oral Maxillofac Surg.* 1996;54(8):975-81.
26. Jones Jr, JP. The effect of hyperbaric oxygen on osteonecrosis. Anaheim, CA: Orthopaedic Research Society;1991.
27. Strauss MB. Effect of hyperbaric oxygen on bone resorption in rabbits. In seventh annual conference on the clinical applications of hyperbaric oxygen. Anaheim, CA; 1982.
28. Strauss MB, Bryant B. Hyperbaric oxygen. *Orthopedics.* 2002;25(3):303-10.
29. Skyhar MJ, et al. Hyperbaric oxygen reduces edema and necrosis of skeletal muscle in compartment syndromes associated with hemorrhagic hypotension. *J Bone Joint Surg Am.* 1986;68(8):1218-24.
30. Strauss MB, et al. Reduction of skeletal muscle necrosis using intermittent hyperbaric oxygen in a model compartment syndrome. *J Bone Joint Surg Am.* 1983;65(5):656-62.

31. Zamboni WA, et al. Morphologic analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg.* 1993;91(6):1110-23.
32. Nylander G, et al. Reduction of postischemic edema with hyperbaric oxygen. *Plast Reconstr Surg.* 1985;76(4):596-603.
33. Hunt TK, Halliday B, Knighton DR.. Impairment of microbial function in wounds: correction with oxygenation, in soft and hard tissue repair. Hunt TK, Heppenstall RB, Pines E, eds. Praeger: New York; 1984;455-68.
34. Hohn DC, et al. Effect of O<sub>2</sub> tension on microbial function of leukocytes in wounds and in vitro. *Surg Forum.* 1976;27(62):18-20.
35. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet.* 1972;135(4):561-7.
36. Connolly WB, et al. Influence of distant trauma on local wound infection. *Surg Gynecol Obstet.* 1969;128:713-8.
37. Wald ER. Risk factors for osteomyelitis. *Am J Med.* 1985;78(6B):206-12.
38. Le Saux N, et al. Shorter courses of parenteral antibiotic therapy do not appear to influence response rates for children with acute hematogenous osteomyelitis: a systematic review. *BMC Infect Dis.* 2002;2:16.
39. Lew DP, Waldvogel FA. Osteomyelitis. *Lancet.* 2004;364(9431):369-79.
40. Davis JC, Heckman JD. Refractory osteomyelitis, in problem wounds: the role of oxygen. Davis JC, Hunt TK, eds. New York: Elsevier Science Publishing Co., Inc.; 1988. Pp.125-142.
41. Attinger C, Cooper P. Soft tissue reconstruction for calcaneal fractures or osteomyelitis. *Orthop Clin North Am.* 2001;32(1):135-70.
42. Lazzarini L, Lipsky BA, Mader JT. Antibiotic treatment of osteomyelitis: what have we learned from 30 years of clinical trials? *Int J Infect Dis.* 2005;9(3):127-38.
43. Zalavras CG, Singh A, Patzakis MJ. Novel technique for medullary canal debridement in tibia and femur osteomyelitis. *Clin Orthop Relat Res.* 2007;461:31-4.
44. Thonse R, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. *J Orthop Trauma.* 2007;21(4):258-68.
45. Kocaoglu M, et al. Reconstruction of segmental bone defects due to chronic osteomyelitis with use of an external fixator and an intramedullary nail. *J Bone Joint Surg Am.* 2006;88(10):2137-45.
46. Chen F, et al. [The treatment of deep wound infection after posterior thoracic and lumbar instrumentation]. *Zhonghua Wai Ke Za Zhi.* 2005;43(20):1325-7.
47. Varzos PN, et al. Chronic osteomyelitis associated with monofilament wire fixation. *J Foot Surg.* 1983;22(3):212-7.
48. Chang WC, et al. Successful treatment of extended epidural abscess and long segment osteomyelitis: a case report and review of the literature. *Surg Neurol.* 2008 Feb;69(2):117-20. Note original 2007 citation was for an Epub.
49. Barbarossa V, et al. Treatment of osteomyelitis and infected non-union of the femur by a modified Ilizarov technique: follow-up study. *Croat Med J.* 2001;42(6):634-41.
50. Pappou IP, et al. Postoperative infections in interbody fusion for degenerative spinal disease. *Clin Orthop Relat Res.* 2006;444:120-8.
51. Talmi YP, et al. Postsurgical prevertebral abscess of the cervical spine. *Laryngoscope.* 2000;110(7):1137-41.
52. Przybylski GJ, Sharan AD. Single-stage autogenous bone grafting and internal fixation in the surgical management of pyogenic discitis and vertebral osteomyelitis. *J Neurosurg.* 2001;94(1 Suppl):1-7.
53. May Jr. JW, Gallico III, GG, Lukash FN. Microvascular transfer of free tissue for closure of bone wounds of the distal lower extremity. *N Engl J Med.* 1982;306(5):253-7.
54. Steinlechner CW, Mkandawire NC. Nonvascularised fibular transfer in the management of defects of long bones after sequestrectomy in children. *J Bone Joint Surg Br.* 2005;87(9):1259-63.
55. Simard S, Marchant M, Mencio G. The Ilizarov procedure: limb lengthening and its implications. *Phys Ther.* 1992;72(1):25-34.
56. Daver NG, et al. Oral step-down therapy is comparable to intravenous therapy for *Staphylococcus aureus* osteomyelitis. *J Infect.* 2007;54(6):539-44.
57. Aneziokoro CO, et al. The effectiveness and safety of oral linezolid for the primary and secondary treatment of osteomyelitis. *J Chemother.* 2005;17(6):643-50.
58. Cole WG, Dalziel RE, Leitl S. Treatment of acute osteomyelitis in childhood. *J Bone Joint Surg Br.* 1982;64(2):218-23.
59. Gentry LO. Overview of osteomyelitis. *Orthop Rev.* 1987;16(4):255-8.
60. Ketterl R, et al. Use of ofloxacin in open fractures and in the treatment of post-traumatic osteomyelitis. *J Antimicrob Chemother.* 1988;22 (Supp.C):159-66.
61. Lamp KC, et al. Clinical experience with daptomycin for the treatment of patients with osteomyelitis. *Am J Med.* 2007;120(10 Sup p.1):S13-20.
62. Miller,DJ, Mejicano GC, Vertebral osteomyelitis due to *Candida* species: case report and literature review. *Clin Infect Dis.* 2001;33(4):523-30.

63. Petersen S, et al. Acute haematogenous osteomyelitis and septic arthritis in childhood. A 10-year review and follow-up. *Acta Orthop Scand*. 1980;51(3):451-7.
64. Powers T, Bingham DH. Clinical and economic effect of ciprofloxacin as an alternative to injectable antimicrobial therapy. *Am J Hosp Pharm*. 1990;47(8):1781-4.
65. Rayner CR et al. Linezolid in the treatment of osteomyelitis: results of compassionate use experience. *Infection*. 2004;32(1):8-14.
66. Schurman DJ, Dillingham M. Clinical evaluation of cefoxitin in treatment of infections in 47 orthopedic patients. *Rev Infect Dis*. 1979;1(1):206-9.
67. Stefanovski N, Van Voris LP. Pyogenic vertebral osteomyelitis: report of a series of 23 patients. *Contemp Ortho*. 1995;31(3):159-64.
68. Stratov I, Korman TM, Johnson PD. Management of Aspergillus osteomyelitis: report of failure of liposomal amphotericin B and response to voriconazole in an immunocompetent host and literature review. *Eur J Clin Microbiol Infect Dis*. 2003;22(5):277-83.
69. Bingham EL, Hart GB. Hyperbaric oxygen treatment of refractory osteomyelitis. *Postgrad Med*. 1977;61(6):70-6.
70. Depenbusch FL, Thompson RE, Hart GB. Use of hyperbaric oxygen in the treatment of refractory osteomyelitis: a preliminary report. *J Trauma*. 1972;12(9):807-12.
71. Davis JC, et al. Chronic non-hematogenous osteomyelitis treated with adjuvant hyperbaric oxygen. *J Bone Joint Surg Am*. 1986;68(8):1210-7.
72. Morrey BF, et al. Hyperbaric oxygen and chronic osteomyelitis. *Clin Orthop Relat Res*. 1979(144):121-7.
73. Sheps SB. Hyperbaric oxygen for osteomyelitis and osteoradionecrosis. Vancouver: University of British Columbia;1992. Pp.1-21.
74. Senneville E, et al. Effectiveness and tolerability of prolonged linezolid treatment for chronic osteomyelitis: a retrospective study. *Clin Ther*. 2006;28(8):1155-63.
75. Priest DH, Peacock, Jr JE. Hematogenous vertebral osteomyelitis due to *Staphylococcus aureus* in the adult: clinical features and therapeutic outcomes. *South Med J*. 2005;98(9):854-62.
76. Gomez J, et al. [Orthopedic implant infection: prognostic factors and influence of long-term antibiotic treatment on evolution. Prospective study, 1992-1999]. *Enferm Infect Microbiol Clin*. 2003;21(5):232-6.
77. Eckardt JJ, Wirganowicz PZ, Mar T. An aggressive surgical approach to the management of chronic osteomyelitis. *Clin Orthop Relat Res*. 1994(298):229-39.
78. Hall BB, Fitzgerald, Jr., RH, Rosenblatt JE. Anaerobic osteomyelitis. *J Bone Joint Surg Am*. 1983;65(1):30-5.
79. Marx RE. Chronic osteomyelitis of the jaws. *Oral Maxillofac Surg Clin North Am*. 1991;3:367-81.
80. Mercuri LG. Acute osteomyelitis of the jaws. *Oral Maxillofac Surg Clin North Am*. 1991;3:355-65.
81. Mader JT, et al. Antimicrobial treatment of chronic osteomyelitis. *Clin Orthop Relat Res*. 1999(360):47-65.
82. Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects (second of three parts). *N Engl J Med*. 1970;282(5):260-6.
83. Gomis M, et al. Oral ofloxacin versus parenteral imipenem-cilastatin in the treatment of osteomyelitis. *Rev Esp Quimioter*. 1999;12(3):244-9.
84. Mader JT, Cantrell JS, Calhoun J. Oral ciprofloxacin compared with standard parenteral antibiotic therapy for chronic osteomyelitis in adults. *J Bone Joint Surg Am*. 1990;72(1):104-10.
85. Gentry LO, Rodriguez-Gomez G. Ofloxacin versus parenteral therapy for chronic osteomyelitis. *Antimicrob Agents Chemother*. 1991;35(3):538-41.
86. Jauregui LE, Hageage G, Martin M. Oral enoxacin versus conventional intravenous antimicrobial therapy for chronic osteomyelitis. *J Chemother*. 1989;1(4 Suppl):735-6.
87. Swionkowski MF, et al. A comparison of short- and long-term intravenous antibiotic therapy in the postoperative management of adult osteomyelitis. *J Bone Joint Surg Br*. 1999;81(6):1046-50.
88. Spencer CH. Bone and joint infections in children. *Curr Opin Rheumatol*. 1998;10(5):494-7.
89. Tetzlaff TR, McCracken Jr. GH, Nelson JD. Oral antibiotic therapy for skeletal infections of children. II. Therapy of osteomyelitis and suppurative arthritis. *J Pediatr*. 1978;92(3):485-90.
90. Wall EJ. Childhood osteomyelitis and septic arthritis. *Curr Opin Pediatr*. 1998;10(1):73-6.
91. Higuchi T, et al. Preliminary report of the safety and efficacy of hyperbaric oxygen therapy for specific complications of lung transplantation. *J Heart Lung Transplant*. 2006;25(11):1302-9.
92. Larsson A, et al. Hyperbaric oxygen treatment of postoperative neurosurgical infections. *Neurosurgery*. 2002;50(2):287-95; discussion 295-6.
93. Luente FE, Parisier SC, Som PM. Complications of the treatment of malignant external otitis. *Laryngoscope*. 1983;93(3):279-81.

94. Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects. *N Engl J Med.* 1970;282(4):198-206.
95. Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects. Osteomyelitis associated with vascular insufficiency. *N Engl J Med.* 1970;282(6):316-22.
96. Ger R. Muscle transposition for treatment and prevention of chronic post-traumatic osteomyelitis of the tibia. *J Bone Joint Surg Am.* 1977;59(6):784-91.
97. Gordon L, Chiu EJ. Treatment of infected nonunions and segmental defects of the tibia with staged microvascular muscle transplantation and bone-grafting. *J Bone Joint Surg Am.* 1988;70(3):377-86.
98. Kelly PJ. Infected nonunion of the femur and tibia. *Orthop Clin North Am.* 1984;15(3):481-90.
99. May Jr. JW, et al. Clinical classification of posttraumatic tibial osteomyelitis. *J Bone Joint Surg Am.* 1989;71(9):1422-8.
100. Weiland AJ, Moore JR, Daniel RK. The efficacy of free tissue transfer in the treatment of osteomyelitis. *J Bone Joint Surg Am.* 1984;66(2):181-93.
101. Mader JT, Shirtliff M, Calhoun JH. Staging and staging application in osteomyelitis. *Clin Infect Dis.* 1997;25(6):1303-9.
102. Cierny III G, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. *Clin Orthop Relat Res.* 2003(414):7-24.
103. Fanning WJ, Vasko JS, Kilman JW. Delayed sternal closure after cardiac surgery. *Ann Thorac Surg.* 1987;44(2):169-72.
104. Clarkson JH, et al. Our experience using the vertical rectus abdominis muscle flap for reconstruction in 12 patients with dehiscence of a median sternotomy wound and mediastinitis. *Scand J Plast Reconstr Surg Hand Surg.* 2003;37(5):266-71.
105. Farinas MC, et al. Suppurative mediastinitis after openheart surgery: a case-control study covering a seven-year period in Santander, Spain. *Clin Infect Dis.* 1995;20(2):272-9.
106. Athanassiadi K, et al. Omental transposition: the final solution for major sternal wound infection. *Asian Cardiovasc Thorac Ann.* 2007;15(3):200-3.
107. Rezai AR, et al. Contemporary management of spinal osteomyelitis. *Neurosurgery.* 1999;44(5):1018-25; discussion 1025-6.
108. Osei-Yeboah C, et al. Osteomyelitis of the frontal bone. *Ghana Med J.* 2007;41(2):88-90.
109. Blomstedt GC. Craniotomy infections. *Neurosurg Clin N Am.* 1992;3(2):375-85.
110. Malone DG, et al. Osteomyelitis of the skull base. *Neurosurgery.* 1992;30(3):426-31.
111. Stieg PE, Mulliken JB. Neurosurgical complications in craniofacial surgery. *Neurosurg Clin N Am.* 1991;2(3):703-8.
112. Gallagher RM, Gross CW, Phillips CD. Suppurative intracranial complications of sinusitis. *Laryngoscope.* 1998;108(11 Pt 1):1635-42.
113. Lucente FE, et al. Malignant external otitis: a dangerous misnomer? *Otolaryngol Head Neck Surg.* 1982;90(2):266-9.
114. Tisch M, Maier H. [Malignant external otitis]. *Laryngorhinootologie.* 2006;85(10):763-9; quiz 770-3.
115. Bhandary, S, Karki P, Sinha BK. Malignant otitis externa: a review. *Pac Health Dialog.* 2002;9(1):64-7.
116. Slattery III, WH. Brackmann DE. Skull base osteomyelitis. Malignant external otitis. *Otolaryngol Clin North Am.* 1996;29(5):795-806.
117. Triplett RG, et al. Experimental mandibular osteomyelitis: therapeutic trials with hyperbaric oxygen. *J Oral Maxillofac Surg.* 1982;40(10):640-6.
118. Mendel V, Simanowski HJ, Scholz H. Synergy of HBO<sub>2</sub> and a local antibiotic carrier for experimental osteomyelitis due to *Staphylococcus aureus* in rats. *Undersea Hyperb Med.* 2004;31(4):407-16.
119. Mader JT, et al. Therapy with hyperbaric oxygen for experimental osteomyelitis due to *Staphylococcus aureus* in rabbits. *J Infect Dis.* 1978;138(3):312-8.
120. Triplett RG, Branham GB. Treatment of experimental mandibular osteomyelitis with hyperbaric oxygen and antibiotics. *Int J Oral Surg.* 1981;10(Sup p.1):178-82.
121. Esterhai Jr. JL, et al. Adjunctive hyperbaric oxygen therapy in the treatment of chronic refractory osteomyelitis. *J Trauma.* 1987;27(7):763-8.
122. Esterhai Jr. JL, et al. Treatment of chronic osteomyelitis complicating nonunion and segmental defects of the tibia with open cancellous bone graft, posterolateral bone graft, and soft-tissue transfer. *J Trauma.* 1990;30(1):49-54.
123. MacGregor RR, Graziani AL, Esterhai JL. Oral ciprofloxacin for osteomyelitis. *Orthopedics.* 1990;13(1):55-60.
124. Barili F, et al. Role of hyperbaric oxygen therapy in the treatment of postoperative organ/space sternal surgical site infections. *World J Surg.* 2007;31(8):1702-6.

125. Welsh FML, Matos LU, deTreville TP. Medical hyperbaric oxygen therapy: 22 cases. *Aviat Space Environ Med.* 1980;51(6):611-4.
126. Eltorai I, Hart GB, Strauss MB. Osteomyelitis in the spinal cord injured: a review and a preliminary report on the use of hyperbaric oxygen therapy. *Paraplegia.* 1984;22(1):17-24.
127. Maynor ML, et al. Chronic osteomyelitis of the tibia: treatment with hyperbaric oxygen and autogenous microsurgical muscle transplantation. *J South Orthop Assoc.* 1998;7(1):43-57.
128. Chen CY, et al. Chronic refractory tibia osteomyelitis treated with adjuvant hyperbaric oxygen: a preliminary report. *Changgeng Yi Xue Za Zhi.* 1998;21(2):165-71.
129. Chen CE, et al. Hyperbaric oxygen therapy in the treatment of chronic refractory osteomyelitis: a preliminary report. *Chang Gung Med J.* 2003;26(2):114-21.
130. Chen CE, et al. Results of chronic osteomyelitis of the femur treated with hyperbaric oxygen: a preliminary report. *Chang Gung Med J.* 2004;27(2):91-7.
131. Calhoun KH, et al. Osteomyelitis of the mandible. *Arch Otolaryngol Head Neck Surg.* 1988;114(10):1157-62.
132. Jamil MU, Eckardt A, Franko W. [Hyperbaric oxygen therapy. Clinical use in treatment of osteomyelitis, osteoradionecrosis and reconstructive surgery of the irradiated mandible]. *Mund Kiefer Gesichtschir.* 2000;4(5):320-3.
133. Handschel J, et al. Evaluation of hyperbaric oxygen therapy in treatment of patients with osteomyelitis of the mandible. *Mund Kiefer Gesichtschir;* 2007.
134. Lentrodt S, et al. Hyperbaric oxygen for adjuvant therapy for chronically recurrent mandibular osteomyelitis in childhood and adolescence. *J Oral Maxillofac Surg.* 2007;65(2):186-91.
135. Mainous EG. Hyperbaric oxygen in maxillofacial osteomyelitis, osteoradionecrosis, and osteogenesis enhancement. In hyperbaric oxygen therapy. Davis JC, Hunt TK, eds. Bethesda, Maryland: Undersea Medical Society; 1977. Pp.191-203.
136. Van Merkesteyn JP, et al. Hyperbaric oxygen treatment of chronic osteomyelitis of the jaws. *Int J Oral Surg.* 1984; 13(5):386-95.
137. Aitasalo K, et al. A modified protocol for early treatment of osteomyelitis and osteoradionecrosis of the mandible. *Head Neck.* 1998;20(5):411-7.
138. Carragee EJ, et al. The clinical use of erythrocyte sedimentation rate in pyogenic vertebral osteomyelitis. *Spine.* 1997;22(18):2089-93.
139. Kovalenko DG, Savchenko AV, Milovanova EM. [Osteoplasty in surgical treatment of hematogenous osteomyelitis of the spine]. *Vestn Khir Im I I Grek.* 1978;120(3):89-93.
140. Ibarra S, et al. [Osteomyelitis of the frontal bone (Pott's puffy tumor). A report of 5 patients]. *Enferm Infect Microbiol Clin.* 1999;17(10):489-92.
141. Balm AJ, Tiwari RM, de Rijcke TB. Osteomyelitis in the head and neck. *J Laryngol Otol.* 1985;99(10):1059- 65.
142. Boeckx WD, et al. The role of free flaps in the treatment of persistent scalp osteomyelitis. *Neurosurgery.* 2006;59 (1 Sup p.1).ONS64-7; discussion ONS64-7.
143. Marshall AH, Jones NS. Osteomyelitis of the frontal bone secondary to frontal sinusitis. *J Laryngol Otol.* 2000;114(12):944-6.
144. Levy R, et al. Oral ofloxacin as treatment of malignant external otitis: a study of 17 cases. *Laryngoscope.* 1990; 100(5):548-51.
145. Lang R, et al. Successful treatment of malignant external otitis with oral ciprofloxacin: report of experience with 23 patients. *J Infect Dis.* 1990;161(3):537-40.
146. Gehanno P. Ciprofloxacin in the treatment of malignant external otitis. *Chemotherapy.* 1994;(40 Sup p.1):35-40.
147. Martel, J. et al. [Malignant or necrotizing otitis externa: experience in 22 cases]. *Ann Otolaryngol Chir Cervicofac.* 2000. 117(5): p.291.
148. Narozny W, et al. Value of hyperbaric oxygen in bacterial and fungal malignant external otitis treatment. *Eur Arch Otorhinolaryngol.* 2006; 263(7):680-4.
149. Davis JC, et al. Adjuvant hyperbaric oxygen in malignant external otitis. *Arch Otolaryngol Head Neck Surg.* 1992;118(1):89-93.
150. Strecker T, et al. Sternal wound infections following cardiac surgery: risk factor analysis and interdisciplinary treatment. *Heart Surg Forum.* 2007;10(5):E366-71.
151. Newman LG, et al. Unsuspected osteomyelitis in diabetic foot ulcers. Diagnosis and monitoring by leukocyte scanning with indium in 111 oxyquinoline. *Jama.* 1991;266(9):1246-51.
152. Grayson ML, et al. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. *Jama.* 1995;273(9):721-3.
153. Roeckl-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg.* 2005;92(1):24-32.

154. Zamboni WA, et al. Evaluation of hyperbaric oxygen for diabetic wounds: a prospective study. Undersea Hyperb Med. 1997;24(3):175-9.
155. Abidia A, et al. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. Eur J Vasc Endovasc Surg. 2003;25(6):513-8.
156. Kessler L, et al. Hyperbaric oxygenation accelerates the healing rate of nonischemic chronic diabetic foot ulcers: a prospective randomized study. Diabetes Care. 2003;26(8):2378-82.
157. Warriner III RA, Hopf HW. Enhancement of healing in selected problem wounds, in hyperbaric oxygen 2003: indications and results: the hyperbaric oxygen therapy committee report. Feldmeier JJ, Editor. Kensington: Undersea and Hyperbaric Medical Society; 2003. Pp.41-55.
158. Strauss MB. Economic considerations in chronic refractory osteomyelitis. In fifth annual conference on clinical applications of hyperbaric oxygen. Long Beach, CA; 1980.
159. Riddick M. Sternal wound infections, dehiscence, and sternal osteomyelitis: the role of hyperbaric oxygen therapy, in hyperbaric medicine practice. Kindwall EP, Whelan HT, eds. 1999, Flagstaff, AZ: Best Publishing Company; 1999. Pp.617-39.
160. Shandley S, et al. Hyperbaric oxygen therapy in a mouse model of implant-associated osteomyelitis. J Orthop Res. 2012;30(2):203-8.
161. Chen CY, et al. Adjuvant hyperbaric oxygen therapy in the treatment of hemodialysis patients with chronic osteomyelitis. Ren Fail. 2008;30(2):233-7.
162. Roje Z, et al. Influence of adjuvant hyperbaric oxygen therapy on short-term complications during surgical reconstruction of upper and lower extremity war injuries: retrospective cohort study. Croat Med J. 2008;49(2):224-32.
163. Ahmed R, Severson MA, Traynelis VC. Role of hyperbaric oxygen therapy in the treatment of bacterial spinal osteomyelitis. J Neurosurg Spine. 2009;10(1):16-20.
164. Sandner A, et al. [Value of hyperbaric oxygen in the treatment of advanced skull base osteomyelitis]. Laryngorhinootologie. 2009;88(10):641-6.
165. Yu WK, et al. Hyperbaric oxygen therapy as an adjunctive treatment for sternal infection and osteomyelitis after sternotomy and cardiothoracic surgery. J Cardiothorac Surg. 2011;6:141.
166. Hart BB. Refractory osteomyelitis, in Hyperbaric oxygen therapy indications. Thirteenth edition. Weaver, LK, ed. North Palm Beach, FL: Best Publishing Company; 2014. Pp.179-207.
167. Onen MR, et al. Efficacy of hyperbaric oxygen therapy in iatrogenic spinal infections. Spine. 2015;40(22):1743-8.
168. Coulson A, Peek A, Haugen D. Femoral vein cannulation in the treatment of osteomyelitis. Wounds. 2016;28(6):194-9.
169. Skeik N, et al. Hyperbaric oxygen treatment outcome for different indications from a single center. Ann Vasc Surg. 2015;29(2):206-214.
170. Yeheskeli E, et al. Temporomandibular joint involvement as a positive clinical prognostic factor in necrotizing external otitis. J Laryngol Otol. 2016;130(5):435-9.
171. Kawashima M, et al. Hyperbaric oxygen therapy in orthopedic conditions. Undersea Hyperb Med. 2004 Spring;31(1):155-62.

## Chapter 13: Severe Anemia

Keith W. Van Meter MD

### REFERENCES

1. Van Slyke DD, Neill JM. The determination of gases in blood and other solutions by vacuum extraction and manometric measurement. *J Biol Chem.* 1924;61:523-573.
2. Chance EM, Chance B. Oxygen delivery to tissue: calculation of oxygen gradient in the cardiac cell. *Adv Exp Med Biol.* 1988;222:69-75.
3. Fick A. Über die messung des blut quantums in der herzventrikeln. *SB Phys-Med Ges Wurzburg.* 1870;16.
4. Shoemaker WC, Appel PL, Kram HB. Tissue oxygen debt as a determinant of lethal and nonlethal post-operative organ failure. *Crit Care Med.* 1988;16:1117-1120.
5. Goodnough LT, Schander A, Brecher ME. Transfusion medicine: looking into the future. *Lancet.* 2003;361:161-169.
6. Johnson JL, Moore EE, Gonzalez RJ, et al. Alteration of the post-injury hyperinflammatory response by means of resuscitation with a red cell substitute. *J Trauma.* 2003;54:133-140.
7. Vamvakas EC. Transfusion associated cancer recurrence and post-operative infection: meta-analysis of randomized controlled clinical trials. *Transfusion.* 1996;36:175-186.
8. Winslow RM. Blood substitutes. *Curr Opin Hematol.* 2002;9:146-151.
9. Cohn C, Cushing M. Oxygen therapeutics: perfluorocarbons and blood substitute safety. *Crit Care Med.* 2009;25:399-414.
10. Kindwall EP, editor. Hyperbaric oxygen therapy: a committee report. Bethesda, MD: Undersea and Hyperbaric Medical Society; 1977.
11. Hampson NB, editor. Hyperbaric oxygen therapy: a committee report. Bethesda, MD: Undersea and Hyperbaric Medical Society; 1999. Pp. 35-36.
12. Hart GB. Hyperbaric oxygen and exceptional blood loss anemia. In: Kindwall EP, Whelan HT, editors. *Hyperbaric medicine practice.* 2nd ed. revised. Flagstaff, AZ: Best Publishing Co.; 2002. Pp. 741-751.
13. DeBets D, Theunissen S, Devriendt J, et al. The normobaric oxygen paradox: does it increase hemoglobin. *Diving and Hyperbar Med.* 2012;42(2):67-71.
14. Brozak J, Grande F. Body composition and basal metabolism in man correlation analysis versus physiologic approach. *Human Biol.* 1955;27:22-31.
15. Boerema I, Meyne NG, Brummelkamp WH, et al. Life without blood. *Arch Chir Neerl.* 1959;11:70-84.
16. McLoughlin PL, Cope TM, Harrison JC. Hyperbaric oxygen therapy in management of severe acute anemia in a Jehovah's witness. *Anesthesia.* 1999;54:879-898.
17. Cummins RO, Hazinski MF, Kerber RE, et al. Low-energy biphasic waveform defibrillation: evidence-based review applied to emergency cardiovascular care guidelines. *Circulation.* 1998;97:1654-1667.
18. Burnet W, Clark RG, Duthie HL, et al. The treatment of shock by oxygen under pressure. *Scot Med J.* 1959;4:535-538.
19. Cowley RA, Attar S, Esmond WG, et al. Electrocardiographic and biochemical study in hemorrhagic shock in dogs treated with hyperbaric oxygen. *Circulation.* 1963;27:670-675.
20. Blair E, Henning G, Esmond WG, et al. The effect of hyperbaric oxygenation (OHP) on three forms of shock – traumatic, hemorrhagic, and septic. *J Trauma.* 1964;4:652-663.
21. Clark RG, Young DG. Effects of hyperoxygenation and sodium bicarbonate in hemorrhagic hypotension. *Brit J Surg.* 1965;52:705-708.
22. Cowley RA, Attar S, Blair E, et al. Prevention and treatment of shock by hyperbaric oxygenation. *Ann NY Acad Sci.* 1965;117:673-683.
23. Elliot DP, Paton BC. Effect of 100% oxygen at 1 and 3 atmospheres on dogs subjected to hemorrhagic hypotension. *Surg.* 1965;57:401-408.
24. Attar S, Scanlan E, Cowley RA. Further evaluation of hyperbaric oxygen in hemorrhagic shock. In: Brown IW, Cox B, editors. *Proceedings of the third international congress on hyperbaric medicine.* Washington DC: NAS/NRC; 1965. Pp. 417-424.
25. Jacobson YG, Keller ML, Mundth ED, et al. Hyperbaric oxygen therapy in experimental hemorrhagic shock. In: Brown IW, Cox B, editors. *Proceedings of the third international congress on hyperbaric medicine.* Washington DC: NAS/NRC; 1966. Pp. 425-431.
26. Jacobson YG, Keller ML, Mundth ED, et al. Hemorrhagic shock: influence of hyperbaric oxygen on metabolic parameters. *Calif Med.* 1966;105:93-96.
27. Navarro RU, Ferguson CC. Treatment of experimental hemorrhagic shock by the combined use of hyperbaric oxygen and low-molecular weight dextran. *Surg.* 1968;63:775-781.

28. Doi Y, Onji Y. Oxygen deficit in hemorrhagic shock under hyperbaric oxygen. In: Wada J, Iwa JT, editors. Proceedings of the fourth international congress on hyperbaric medicine. Baltimore, MD: Williams and Wilkins; 1970. P. 181-184.
29. Necas E, Neuwirt J. Lack of erythropoietin in plasma of anemic rats exposed to hyperbaric oxygen. *Life Sci.* 1969;8:1221-1228.
30. Oda T, Takeori M. Effect of viscosity of the blood on increase in cardiac output following acute hemodilution. In: Wada J, Iwa JT, editors. Proceedings of the fourth international congress on hyperbaric medicine. Baltimore, MD: Williams and Wilkins; 1970. Pp. 191-196.
31. Norman JN. Hemodynamic studies in total blood replacement. *Biblio Haema.* 1975;41:203-208.
32. Luenov AN, Yakovlev VN. Role played by cerebral nitrogen metabolism in the mechanism of the therapeutic oxygen effects under high pressure in the hemorrhagic shock. *Biull Eksp Biol Med.* 1977;83:418-420.
33. Gross DR, Moreau PM, Jabor M, Welch DW, Fife WP. Hemodynamic effects of dextran-40 on hemorrhagic shock during hyperbaria and hyperbaric hyperoxia. *Aviat Space Environ Med.* 1983;54:413-419.
34. Gross DR, Moreau PM, Chaikin BN, et al. Hemodynamic effects of lactated Ringers' solution on hemorrhagic shock during exposure to hyperbaric air and hyperbaric hyperoxia. *Aviat Space Environ Med.* 1983;54:701-708.
35. Gross DR, Dodd KT, Welch DW, Fife WP. Hemodynamic effects of 10% dextrose and of dextran-70 on hemorrhagic shock during exposure to hyperbaric air and hyperbaric hyperoxia. *Aviat Space Environ Med.* 1984;55:1118-1128.
36. Bitterman H, Reissman P, Bitterman N, et al. Oxygen therapy in hemorrhagic shock. *Circ Shock.* 1991;33:183-191.
37. Wen-Ren L. Resection of aortic aneurysms under 3 ATA of hyperbaric oxygenation. In: Bakker DJ, Cramer JS, editors. Proceedings of the tenth international congress of hyperbaric medicine. Flagstaff, AZ: Best Publishing Co.; 1992. Pp. 94-95.
38. Adir Y, Bitterman N, Katz E, et al. Salutary consequences of oxygen therapy or long-term outcome of hemorrhagic shock in awake, unrestrained rats. *Undersea Hyperb Med.* 1995;22:23-30.
39. Yamashita M, Yamashita M. Hyperbaric oxygen treatment attenuates cytokine induction after massive hemorrhage. *Am J Physiol Endocrinol Metab.* 2000;28:E811-E816.
40. Boerema I, Meyne NG, Brummelkamp WH, et al. Life without blood: a study of the influence of high atmosphere pressure and hypothermia on dilution of the blood. *J Cardiovasc Surg.* 1960;1:133-146.
41. Attar S, Esmond WG, Cowley RA. Hyperbaric oxygenation in vascular collapse. *J Thoracic Cardiovasc Surg.* 1962;42:759-770.
42. Trytyshnikov IM. Effect of acute massive blood loss during hyperbaric oxygen therapy on nucleic and metabolism in the albino rat liver. *Biull Eksp Biol Med.* 1974;77:23-25.
43. Frank HA, Fine J. Traumatic shock V: a study of the effect of oxygen on hemorrhagic shock. *J Clin Invest.* 1943;22: 305-314.
44. Whalen RE, Moor GF, Mauney FM, et al. Hemodynamic responses to "Life Without Blood." In: Brown IW, Cox B, editors. Proceedings of the third international congress on hyperbaric medicine. Washington DC: NAS/NRC; 1965. Pp. 402-408.
45. Barkova EN, Petrov AV. The effect of oxygen barotherapy on erythropoiesis in the recuperative period following hemorrhagic collapse. *Biull Eksp Biol Med.* 1976;81:156-158.
46. Marzella L, Yin A, Darlington D, et al. Hemodynamic responses to hyperbaric oxygen administration in a rat model of hemorrhagic shock. *Circ Shock.* 1992;37:12.
47. Cancer.Net. Levels of evidence: explanation in therapeutic studies (PDQ). Internet Service of the National Cancer Institute, 1999.
48. Barton S, editor. Clinical evidence. London: BMJ Publishing Group; 2001.
49. Wiggers CJ, Werle JM. Exploration of method for standardizing hemorrhagic shock. *Proc Soc Exper Biol Med.* 1942;49:604.
50. Bellamy RF, Maningas PA, Wenger BA, et al. Current shock models and clinical correlations. *Ann Emerg Med.* 1986;15:1392-1395.
51. Ledingham IM. Hyperbaric oxygen in shock. *Anes Clin.* 1969;7:819-839.
52. Amonic RS, Cockett ATK, Lonhan PH, et al. Hyperbaric oxygen therapy in chronic hemorrhagic shock. *JAMA.* 1969;208:2051-2054.
53. Hart GB. Exceptional blood loss anemia. *JAMA.* 1974;228:1028-1029.
54. Myking O, Schreinen A. Hyperbaric oxygen in hemolytic crisis. *JAMA.* 1974;227:1161-1162.
55. Hart GB, Lennon PA, Strauss MB. Hyperbaric oxygen in exceptional acute blood loss anemia. *J Hyperbar Med.* 1987;2:205-210.

56. Meyerstein N, Mazor D, Tsach T, et al. Resistance of human red blood cells to hyperbaric oxygen under therapeutic conditions. *J Hyperbar Med.* 1989;4:1-5.
57. Young BA, Burns JR. Management of the severely anemic Jehovah's Witness. *Ann Int Med.* 1992;119:170.
58. Van Meter KW. A systematic review of the literature reporting the application of hyperbaric oxygen in the treatment of exceptional blood loss anemia: an evidence-based approach. *Undersea Hyperb Med.* 2005;32(1):61-83.
59. Hillard JR. Severe claustrophobia in a patient requiring hyperbaric oxygen treatment. *Psychosomatics.* 1990;31:107-108.
60. Ross ME, Yolton DP, Yolton RL, et al. Myopia associated with hyperbaric oxygen therapy. *Optometry and Vision Sci.* 1996;73:487-494.
61. Ueno S, Sakoda M, Kurahara H, et al. Safety and efficacy of early post-operative hyperbaric oxygen therapy with restriction of transfusions in patient with HCC who have undergone partial hepatectomy. *Arch Surg.* 2011;396:99-106.
62. Blanchard J, Toma A, Bryson P, et al. Middle ear barotrauma in patients undergoing hyperbaric oxygen therapy. *Clin Otolaryn.* 1996;21:400-403.
63. Youngberg JT, Myers AM. Complications from hyperbaric oxygen therapy. *Ann Emerg Med.* 1990;19:1356-1357.
64. Van Meter KW, Harch PG. HBO in emergency medicine. In: Jain KK, editor. *Textbook of hyperbaric medicine.* Cambridge, MA: Hogrefe & Huber Publishers; 1996. Pp. 453-481.
65. Van Meter KW. Hyperbaric oxygen therapy as an adjunct to pre-hospital advanced life support. *Surg Technol Int.* 2011 Dec 1;XXI:61-73.
66. Donat A, Damani E, Zuccan S, et al. Effects of short-term hyperoxia on erythropoietin levels and microcirculation in critically ill patients: a prospective, observational pilot study. *MMC Anesthesiology* 2017;17:49-59.
67. Van Meter K, Van Meter KW. The effect of hyperbaric oxygen on severe anemia. *Undersea Hyperb Med.* 2012;39(5):937-42.
68. Saa P, Proctor M, Foster-Getal. Investigational testing for Zika virus among US blood donors. *NEJM* 2018;378:1778-1788.
69. Harrington T, Kuehnent MJ, Kamel H, et al. West Nile virus infection transmitted by blood transfusion. *Transfusion* 2004;3:1018-1022.
70. Graffeo C, Dishong W. Severe blood loss anemia in a Jehovah's Witness treated with adjunctive hyperbaric oxygen therapy. *American Journal of Emergency Medicine.* 2013;31:756.e3-756.e4.
71. Gutierrez G, Brotherton J. Management of severe anemia secondary to menorrhagia in a Jehovah's Witness: a case report and treatment algorithm. *American Journal of Obstetrics & Gynecology.* 2011;205(2):e5-8.
72. Wright JK, Ehler W, McGlasson DL, Thompson W. Facilitation of recovery from acute blood loss with hyperbaric oxygen. *Archives of Surgery.* 2002;137:850-853.

## **Chapter 14: Adjunctive Hyperbaric Oxygen Therapy in the Treatment of Thermal Burns**

*Paul Cianci MD, FAC, FUHM (Corresponding Author), Ronald M. Sato MD, Julia Faulkner*

### **REFERENCES**

1. American Burn Association Report of Data from 2008-2017 National Burn Repository 2017 Update. Available from [http://ameriburn.org/wp-content/uploads/2018/04/2017\\_aba\\_nbr\\_annual\\_report\\_summary.pdf](http://ameriburn.org/wp-content/uploads/2018/04/2017_aba_nbr_annual_report_summary.pdf).
2. American Burn Association, National Burn Repository Version 12.0. 2016.
3. Wolf SE, Tompkins RG, Herndon DN. On the Horizon – Research Priorities in Burns for the Next Decade. *Surg Clin N Am.* 2014;94:917-930.
4. Burd F, Chiu T. Allogenic skin in the treatment of burns. *Clin Dermatol.* 2005;23:376-387.
5. Atiyeh BS, Gunn SW, Hayek SN. State of the art in burn treatment. *World J Surg.* 2005;29(2):131-148.
6. Arturson G. Pathophysiology of the burn wound. *Ann Chir Gynaecol.* 1980;69:178-190.
7. Demling RH. The burn edema process: current concepts. *J Burn Care Rehabil.* May/June 2005;26:207-227.
8. Boykin JV, Eriksson E, Pittman RN. In vivo microcirculation of a scald burn and the progression of postburn dermal ischemia. *Plast Reconstr Surg.* 1980;66:191-198.
9. Monafo WW. Initial management of burns. *NEJM.* 1996;335(21):1581-1586.
10. Arturson G. The pathophysiology of severe thermal injury. *J Burn Care Rehabil.* 1985;6(2):129-146.
11. Heggers JP, Robson MC, Zachary LS. Thromboxane inhibitor for the prevention of progressive dermal ischemia due to the thermal injury. *J Burn Care Rehabil.* 1985;6:466-468.
12. Miller TA, Korn HN. Epithelial burn injury and repair, In: Davis JC, Hunt TK, editors. *Hyperbaric oxygen therapy.* Bethesda, MD: Undersea Medical Society, Inc.; 1977. P. 251.
13. Demling RH. Burns and other thermal injuries. In: Way LW, Doherty GM, editors. *Current surgical diagnosis and treatment.* 11th ed. New York, NY: McGraw-Hill Medical; 2003. P. 267.
14. Alexander JW, Meakins JL. A physiological basis for the development of opportunistic infections in man. *Annals of Surgery.* 1972;176:273.
15. Alexander JW, Wixson D. Neutrophil dysfunction and sepsis in burn injury. *Surg Gynec Obstet.* 1970;130:431.
16. Barber RC, Aragaki CC, Rivera-Chavez FA. TLR4 and TNF-alpha polymorphisms are associated with an increased risk for severe sepsis following burn injury. *J Med Genet.* 2004;41:808-813.
17. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. *Clin Microbiol Rev.* 2006;19(2):403-434.
18. Deitch EA, Wheelahan TM, Rose MP, Clothier J, Cotter J. Hypertrophic burn scars: Analysis of variables. *J Trauma.* 1983;23:895-898.
19. Ikeda K, Ajiki H, Nagao H, Karino K, Sugii S, Iwa T, Wada J. Experimental and clinical use of hyperbaric oxygen in burns. In: Wada J, Iwa JT, editors. *Proceedings of the fourth international congress on hyperbaric medicine.* Baltimore, MD: Williams and Wilkins; 1970. P. 370.
20. Hartwig J, Kirste G. Experimentelle untersuchungen über die revaskularisierung von verbrennungswunden unter hyperbarer sauerstofftherapie. *Zbl Chir.* 1974;99:1112-1117.
21. Nylander G, Nordstrom H, Eriksson E. Effects of hyperbaric oxygen on oedema formation after a scald burn. *Burns Incl Therm Inj.* 1984 Feb;10(3):193-196.
22. Kaiser W, Schnaidt U, von der Leith H. Auswirkungen hyperbaren sauerstoffes auf die frische brandwunde. *Handchir Mikrochir Plast Chir.* 1989;21:158-163.
23. Kaiser W, Voss K. Influence of hyperbaric oxygen on the edema formation in experimental burn injuries. *Iugoslav Physiol Pharmacol Acta.* 1992;28(9):87-98.
24. Ketchum SA, Zubrin JR, Thomas AN, Hall AD. Effect of hyperbaric oxygen on small first, second and third degree burns. *Surg Forum.* 1967;18:65-67.
25. Ketchum SA, Thomas AN, Hall AD. Angiographic studies of the effect of hyperbaric oxygen on burn wound revascularization. In: Wada J, Iwa JT, editors. *Proceedings of the fourth international congress on hyperbaric medicine.* Tokyo: Igaku Shoin Ltd.; 1970. P. 388.
26. Niccole MW, Thornton JW, Danet RT, Bartlett RH, Tavis MJ. Hyperbaric oxygen in burn management: a controlled study. *Surgery.* 1977;82:727-733.
27. Gruber RP, Brinkley B, Amato JJ, Mendelson JA. Hyperbaric oxygen and pedicle flaps, skin grafts, and burns. *Plast and Recon Surg.* 1970;45:24-30.
28. Wells CH, Hilton JG. Effects of hyperbaric oxygen on post-burn plasma extravasation. In: Hunt TK, Davis JC, editors. *Hyperbaric oxygen therapy.* Bethesda, MD: Undersea and Hyperbaric Medical Society; 1977. P. 259.
29. Stewart RJ, Yamaguchi KT, Cianci PE, Knost PM, Samadani S, Mason SW, Roshdiah B. Effects of hyperbaric oxygen on adenosine triphosphate in thermally injured skin. *Surg Forum.* 1988;39:87.

30. Stewart RJ, Yamaguchi KT, Cianci PE, Mason WW, Roshdiah BB, Dabbasi N. Burn wound levels of ATP after exposure to elevated levels of oxygen. In: Proceedings of the American Burn Association, New Orleans, LA; 1989. P. 67.
31. Germonpré P, Reper P, Vanderkelen A. Hyperbaric oxygen therapy and piracetam decrease the early extension of deep partial thickness burns. *Burns*. 1996;22(6):468-473.
32. Korn HN, Wheeler ES, Miller TA. Effect of hyperbaric oxygen on second-degree burn wound healing. *Arch Surg*. 1977;112:732-737.
33. Saunders J, Fritz E, Ko F, Bi C, Gottlieb L, Krizek T. The effects of hyperbaric oxygen on dermal ischemia following thermal injury. In: Proceedings of the American Burn Association. New Orleans, LA; 1989. P. 58.
34. Perrins DJD. Failed attempt to limit tissue destruction in scalds of pig's skin with hyperbaric oxygen. In: Wada J, Iwa T, editors. Proceedings of the fourth international congress on hyperbaric medicine. Tokyo, Japan: Igaku Shoin Ltd.; 1970. P. 381.
35. Traystman RJ, Kirsch JR, Koehler RC. Oxygen radical mechanisms of brain injury following ischemia and reperfusion. *J Appl Physiol*. 1991;71:1185-1195.
36. Ward PA, Mulligan MS. New insights into mechanisms of oxyradical and neutrophil mediated lung injury. *Klin Wochenschr*. 1991;69:1009-1011.
37. Ward PA, Till GO. The autodestructive consequences of thermal injury. *J Burn Care Rehabil*. 1985;6:251-255.
38. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. *N Engl J Med*. 1985;312:159-163.
39. Yogaratnam JZ, Laden G, Madden LA, Griffin S, et al. Hyperbaric oxygen: a new drug in myocardial revascularization and protection? *Cardiovasc Revasc Med*. 2006 Jul-Sep;7(3):146-154.
40. Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H, Kucan JO. Morphological analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg*. 1993;91: 1110-1123.
41. Zamboni WA, Stephenson LL, Roth AC, Suchy H, Russell RC. Ischemia-reperfusion injury in skeletal muscle: CD18 dependent neutrophil-endothelial adhesion. *Undersea Hyperb Med*. 1994;21(Suppl):53.
42. Wasiak J, Bennett M, Cleland H. Hyperbaric oxygen as adjuvant therapy in the management of burns: can evidence guide clinical practice? *Burns*. 2006;32:650-652.
43. Buras JA, Stahl GL, Svoboda KK, Weenstra WR. Hyperbaric oxygen down regulates ICAM-1 expression induced by hypoxia and hypoglycemia: the role of NOS. *Am J Physiol Cell Physiol*. 2000;278:C292-302.
44. Ueno S, Tanabe G, Kihara K et al. Early post-operative hyperbaric oxygen therapy modifies neutrophile activation. *Hepatogastroenterology*. 1999;46:1798-1799.
45. Miljkovic-Lolic M, Silbergliit R, Fiskum G, Rosenthal RE. Neuroprotective effects of hyperbaric oxygen treatment in experimental focal cerebral ischemia are associated with reduced brain leukocyte myeloperoxidase activity. *Brain Res*. 2003 May 2;971(1):90-94.
46. Shoshani O, Shupak A, Barak Y, Ullman Y, Ramon Y, Lindenbaum E, Peled Y. Hyperbaric oxygen therapy for deep second degree burns: an experimental study in the guinea pig. *Brit J Plast Surg*. 1998;51:67-73.
47. Bleser F, Benichoux R. Experimental surgery: The treatment of severe burns with hyperbaric oxygen. *J Chir (Paris)*. 1973;106:281-290.
48. Tenenhaus M, Hansbrough JF, Zapata-Sirvent R, Neumann T. Treatment of burned mice with hyperbaric oxygen reduces mesenteric bacteria but not pulmonary neutrophil deposition. *Arch Surg*. 1994;129:1338-1342.
49. Magnotti LJ, Deitch EA. Burns, bacterial translocation, gut barrier function, and failure. *J of Burn Care Rehab*. 2005;26(5):383-391.
50. Yamada T, Taguchi T, Hirata Y, Suita S, Yugi H. The protective effect of hyperbaric oxygenation on the small intestine in ischemia-reperfusion injury. *J Pediatr Surg*. 1995;30:786-790.
51. Nylander G, Nordstrom H, Lewis D, Larsson J. Metabolic effects of hyperbaric oxygen in postischemic muscle. *Plast Reconstr Surg*. 1987;79:91-97.
52. Takahashi M, Iwatsuki N, Ono K, Koga Y. Hyperbaric oxygen therapy accelerates neurologic recovery after 15-minute complete global cerebral ischemia in dogs. *Crit Care Med*. 1992;20(11):1588-1594.
53. Thom SR. Functional inhibition of leukocyte B2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol*. 1993;123:248-256.
54. Veltkamp R, Siebing DA, Schwab S, Schwaninger M. Hyperbaric oxygen reduces blood-brain barrier damage and edema after transient focal cerebral ischemia. *Stroke*. 2005;36:1679-1683.
55. Kolski JM, Mazolewski PJ, Stephenson LL, Zamboni WA. Effect of hyperbaric oxygen therapy on testicular ischemia-reperfusion injury. *J of Urology*. Aug 1998;160:601-604.
56. Shandling AH, Ellestad MH, Hart GB, et al. Hyperbaric oxygen and thrombolysis in myocardial infarction: The hot MI pilot study. *Am Heart J*. 1997;134:544-550.

57. Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D; Hyperbaric Oxygen Therapy in Percutaneous Coronary Interventions Investigators. Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol.* 2004 Jun 15;93(12):1533-1535.
58. Thomas MP, Brown LA, Sponseller DR, et al. Myocardial infarct size reduction by synergistic effect of hyperbaric oxygen and recombinant tissue plasminogen activator. *Am Heart J.* 1990 Oct;120(4):791-800.
59. Xu N, Li Z, Luo X. Effects of hyperbaric oxygen therapy on the changes in serum sIL-2R and Fn in severe burn patients. *Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi.* 1999;15(3):220-223.
60. Deitch EA, Xu DZ, Franko L, et al. Evidence favoring the role of the gut as a cytokine generating organ in rats subjected to hemorrhagic shock. *Shock.* 1994;1:141-146.
61. Deitch EA. Role of the gut lymphatic system in multiple organ failure. *Current Opin Crit Care.* 2001;7:92-98.
62. Hohn DC, McKay RD, Halliday B, Hunt TK. Effect of oxygen tension on the microbicidal function of leukocytes in wounds and in vitro. *Surg Forum.* 1976;27:18-20.
63. Allen DB, Maguire JJ, Mahdavian M, et al. Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. *Arch Surg.* 1997;132:991-996.
64. Mader JT, Brown GL, Guckian JC, et al. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. *J Infect Dis.* 1980;142:915-922.
65. Hussman J, Hebebrand D, Erdmann D, Moticka J. Lymphocyte subpopulations in spleen and blood after early wound debridement and acute/chronic treatment with hyperbaric oxygen. *Hanchir Mikrochir Plast Chir.* 1996;28(2):103-107.
66. Bilic I, Petri NM, Bota B. Effects of hyperbaric oxygen therapy on experimental burn wound healing in rats: A randomized controlled study. *Undersea Hyperb Med.* 2005;32(1):1-9.
67. Turkaslan T, Yogum N, Cimsit M, Solakoglu S, Ozdemir C, Ozsoy Z. Is HBOT treatment effective in recovering zone of stasis? An experimental immunohistochemical study. *Burns.* 2010;36(4):539-544.
68. Gallagher KA, Goldstein LJ, Thom SR, Velazquez OC. Hyperbaric oxygen and bone marrow-derived endothelial progenitor cells in diabetic wound healing. *Vascular.* 2006;14(6):328-337.
69. Gallagher KA, Liu ZJ, Xiao M, Chen H, Goldstein LJ, Buerk DG, Nedeau A, Thom SR, Velazquez OC. Diabetic impairments in NO-mediated endothelial progenitor cell mobilization and homing are reversed by hyperoxia and SDF-1 alpha. *J Clin Invest.* 2007;117:1249-1259.
70. Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol.* 2006;290:H1378-1386.
71. Goldstein LJ, Gallagher KA, Bauer SM et al. Endothelial progenitor cell release into circulation is triggered by hyperoxia-induced increases in bone marrow nitric oxide. *Stem Cells.* 2006;24:2309-2318.
72. Thom SR, Milovanova TN, Yang M, Bhopale VM, Sorokina EM, Uzun G, Malay DS, Troiano MA, Hardy KR, Lambert DS, Logue CJ, Margolis DJ. Vasculogenic stem cell mobilization and wound recruitment in diabetic patients: increased cell number and intracellular regulatory protein content associated with hyperbaric oxygen therapy. *Wound Repair Regen.* 2011;19(2):149-161.
73. Milovanova TN, Bhopale VM, Sorokina EM, Moore JS, Hunt TK, Hauer-Jensen M, Velazquez OC, Thom SR. Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo. *J Appl Physiol.* 2009;106:711-728.
74. Milovanova TN, Bhopale VM, Sorokina EM, Moore JS, Hunt TK, Hauer-Jensen M, Velazquez OC, Thom SR. Lactate stimulates vasculogenic stem cells via the thioredoxin system and engages an autocrine activation loop involving hypoxia-inducible factor 1. *Mol Cell Biol.* 2008;28:6248-6261.
75. Wada J, Ikeda T, Kamata K, Ebuoka M. Oxygen hyperbaric treatment for carbon monoxide poisoning and severe burn in coal mine (hokutanyubari) gas explosion. *Igakunoaymi* (Japan). 1965;5:53.
76. Ikeda K, Ajiki H, Kamiyama T, Wada J. Clinical application of oxygen hyperbaric treatment. *Geka* (Japan). 1967;29:1279.
77. Wada J, Ikeda K, Kagaya H, Ajiki H. Oxygen hyperbaric treatment and severe burn. *Jap Med J.* 1966;13:2203.
78. Lamy ML, Hanquet MM. Application opportunity for OHP in a general hospital - a two year experience with a monoplace hyperbaric oxygen chamber. In: Wada J, Iwa JT, editors. *Proceedings of the fourth international congress on hyperbaric medicine.* Tokyo: Igaku Shoin Ltd.; 1970. P. 517.
79. Tabor CG. Hyperbaric oxygenation in the treatment of burns of less than forty percent. *Korean J Intern Med.* 1967;10(4):267-275.
80. Grossman AR, Grossman AJ. Update on hyperbaric oxygen and treatment of burns. *Hyperbaric Oxygen Review.* 1982;3:51.
81. Niu AKC, Yang C, Lee HC, Chen SH, Chang LP. Burns treated with adjunctive hyperbaric oxygen therapy: A comparative study in humans. *J Hyperbar Med.* 1987;2:75.

82. Cianci P, Lueders H, Lee H, Shapiro R, Sexton J, Williams C, Green B. Adjunctive hyperbaric oxygen reduces the need for surgery in 40-80% burns. *J Hyperbar Med.* 1988;3:97.
83. Cianci P, Lueders HW, Lee H, Shapiro RL, Sexton J, Williams C, Sato R. Adjunctive hyperbaric oxygen therapy reduces length of hospitalization in thermal burns. *J Burn Care Rehabil.* 1989;10:432-435.
84. Cianci P, Lueders H, Lee H, Shapiro R, Green B, Williams C. Hyperbaric oxygen and burn fluid requirements: Observations in 16 patients with 40-80% TBSA burns. *Undersea Biomed Res.* 1988;15(Suppl):14.
85. Hart GB, O'Reilly RR, Broussard ND, Cave RH, Goodman DB, Yanda RL. Treatment of burns with hyperbaric oxygen. *Surg Gynecol Obstet.* 1974 Nov;139(5):693-696.
86. Waisbren BA, Schutz D, Collentine G, Banaszak E. Hyperbaric oxygen in severe burns. *Burns.* 1982;8:176-179.
87. Merola L, Piscitelli F. Considerations on the use of HBO in the treatment of burns. *Ann Med Nav.* 1978;83:515.
88. Cianci P, Williams C, Lueders H, Lee H, Shapiro R, Sexton J, Sato R. Adjunctive hyperbaric oxygen in the treatment of thermal burns - an economic analysis. *J Burn Care Rehabil.* 1990;11:140-143.
89. Cianci P, Sato R. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns: A review. *Burns.* 1994 Feb;20(1):5-14.
90. Maxwell G, Meites H, Silverstein P. Cost effectiveness of hyperbaric oxygen therapy in burn care. Presented at: Winter Symposium on Baromedicine; 1991; Aspen, CO.
91. Cianci P, Sato R, Green B. Adjunctive hyperbaric oxygen reduces length of hospital stay, surgery, and the cost of care in severe burns. *Undersea Biomed Research Suppl.* 1991;18:108.
92. Hammarlund C, Svedman C, Svedman P. Hyperbaric oxygen treatment of healthy volunteers with UV-irradiated blister wounds. *Bums.* 1991;17:296-301.
93. Niegzoda JA, Cianci P, Folden BW, Ortega RL, Slade JB, Storrow AB. The effect of hyperbaric oxygen therapy on a burn wound model in human volunteers. *Plast Reconstr Surg.* 1997;99(6):1620-1625.
94. Brannen AL, Still J, Haynes M, Orlet H, Rosemblum F, Law E, Thompson WO. A randomized prospective trial of hyperbaric oxygen in a referral burn center population. *Am Surg.* 1997;63:205-208.
95. Sutherland AM, Clarke HA, Katz J, Katzenelson R. Hyperbaric Oxygen Therapy: A New Treatment for Chronic Pain? *Pain Practice.* 2015;2(1):1-9.
96. Ramussen VM, Borgen AE, Jansen EC, Rotboll Nielsen PH, Werner MU. Hyperbaric Oxygen Therapy Attenuates Central Sensitization Induced by a Thermal Injury in Humans. *Acta Anaesthesiologica Scandinavica.* 2015;59:749-762.
97. Chong SJ, Kan EM, Song C, Soh CR, Lu J. Work in Progress – Characterization of Early Thermal Burns and the Effects of Hyperbaric Oxygen Treatment: A Pilot Study. *Diving and Hyperbaric Medicine.* 2013;43(3):157-161.
98. Jones LM, Rubadue C, Brown NV, Khandelwal S, Coffey RA. Evaluation of TCOM/HBOT Practice Guideline for the Treatment of Foot Burns Occurring in Diabetic Patients. *Burns.* 2015;41:536-541.
99. Zhang Q, Chang Q, Cox RA, Gong X, Gould LJ. Hyperbaric Oxygen Attenuates Apoptosis and Decreases Inflammation in an Ischemic Wound Model. *J Invest Dermatol.* 2008;128(8):2102-2112.
100. Fosen KM, Thom SR. Hyperbaric Oxygen, Vasculogenic Stem Cells, and Wound Healing. *Antioxidants & Redox Signaling.* 2014;21(11):1634-1646.
101. Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem Cell Mobilization by Hyperbaric Oxygen. *Am J Physiol Heart Circ. Physiol.* 2006;290:H1378-H1386.
102. Thom SR, Milovanova TN, Yang M, Bhopale VM, Sorokina EM, Uzun G, Malay DS, Troiano MA, Hardy KR, Lambert DW, Logue CJ, Margolis DJ. Vasculogenic Stem Cell Mobilization and Wound Recruitment in Diabetic Patients: Increased Cell Number and Intracellular Protein Content Associated with Hyperbaric Oxygen Therapy. *Wound Rep Reg.* 2011;19:149-161.
103. Stewart RJ, Yamaguchi KT, Cianci PE, Knost PM, Samadani S, Mason SW, Roshdiah B. Effects of Hyperbaric Oxygen on Adenosine Triphosphate in Thermally Injured Skin. *Surg Forum.* 1988;39:87.
104. Stewart RJ, Yamaguchi KT, Cianci PE, Mason WW, Roshdiah BB, Dabbasi N. Burn wound Levels of ATP after Exposure to Elevated Levels of Oxygen. *Proceedings of the American Burn Association, New Orleans.* 1989:67.
105. Sureda A, Batle JM, Martorell M, Capo X, Tejada S, Tur JA, Pons A. "Antioxidant Response of Chronic Wounds to Hyperbaric Oxygen Therapy." *PLoS One* 2016;11(9):e0163371.
106. Shirani K, Pruitt B, Mason A. The influence of inhalation injury and pneumonia on burn mortality. *Ann Surg.* 1986;205:82-87.
107. Balkissoon R, Shusterman DJ. Occupational upper airway disorders. *Semin Respir Crit Care Med.* 1999;20:569-580.
108. Rabinowitz, PM, Siegel MD. Acute inhalation injury. *Clin Chest Med.* 2002;23(4):707.
109. Grim PS, Nahum A, Gottlieb L, Wilbert C, Hawe E, Sznajder J. Lack of measurable oxidative stress during HBO therapy in burn patients. *Undersea Biomed Res.* 1989;16(Suppl):22.

110. Ray CS, Green G, Cianci P. Hyperbaric oxygen therapy in burn patients: Cost effective adjuvant therapy (abstract). Undersea Biomed Res. 1991;18(Suppl):77.
111. Villanueva E, Bennett MH, Wasik J, Lehm JP. Hyperbaric oxygen therapy for thermal burns (Review). Cochrane Database Syst Rev. 2004;(3):CD004727.
112. Hunt JL, Sato RM, Baxter CR. Early Tangential Excision and Immediate Mesh Auto-grafting of Deep Dermal Hand Burns. Annals Surg. 1979;189(2):147-151. (Orig paper)
113. Sato RM, Beesinger DE, Hunt JL, Baxter CR. Early Excision and Closure of the Burn Wound. Current Topics in Burn Care. TL Wachtel et al.(eds) Rockville, Aspen Publication;1983. Pp.65-76.(Orig paper)
114. Sato RM, Baxter CT. Tangential Excision of the Burn Wound. Recent Advances in Emergency and Definitive Burn Wound Care. Proceedings of a Symposium Sponsored by Valley Medical Center (Fresno, CA). March 1977:16-24. CV2.
115. Sato R, Beesinger D, Hunt J, Baxter C. Early Excision and Closure of the Burn Wound. Critical Care Quarterly. 1978;1(3):51-62. CV4.
116. Hunt JL, Sato RM. Acute Electrical Burns. Uncommon Problems in Emergency Medicine. Miahcel I. Greenberg (ed). Philadelphia, F. A. Davis Company; 1982. Pp:183-195. CV11.
117. Hunt JL, Sato RM. Early Excision of Full Thickness Hand and Digit Burns: Factors Affecting Morbidity. J Trauma. 1982;22(5):414-419. CV12.
118. Kowalczyk L. Catastrophic costs: hospitals, insurers, some R.I. fire victims face huge medical bills. The Boston Globe. 2003 Feb 28.
119. Hunt JL, Sato RM, Baxter CR. Early tangential excision and immediate mesh auto-grafting of deep dermal hand burns. Annals Surg. 1979;189(2):147-151.
120. Sato RM, Beesinger DE, Hunt JL, Baxter CR. Early excision and closure of the burn wound. In: Wachtel TL et al., editors. Current topics in burn care. Rockville, MD: Aspen Publications; 1983. Pp. 65-76.
121. Nicther LS, Morwood DT, Williams GS, Spence RJ. Expanding the limits of composite grafting: A case report of successful nose replantation assisted by hyperbaric oxygen therapy. Plast Reconstr Surg. 1991;87:337-340.
122. Kindwall EP. The use of drugs under pressure. In: Kindwall EP, Whelan HT, editors. Hyperbaric medicine practice. 2nd ed. Flagstaff, AZ: Best Publishing Co.; 1999. P. 326.
123. Personal experience of the authors in a regional burn center.
124. Grube BJ, Marvin JA, Heimbach DM. Therapeutic hyperbaric oxygen: Help or hindrance in burn patients with carbon monoxide poisoning? J Burn Care Rehabil. 1988;9.
125. Cost statistics (1997-98) from hospital patient accounts, home facility of the authors.
126. Ong YS, Samual M, Song C. Meta-analysis of early excision of burns. Burns. 2006;32(2):145-150.
127. Engrav LH, Heimbach DM, Rivara FP et al. Harborview burns 1974-2009. PlosOne. 2012;7(7):1-23.
128. Blaisdell LL, Chace R, Hallagan LD, Clark DE. A half century of burn epidemiology and burn care in a rural state. J Burn Care Res. 2012 May-Jun;33(3):347-353.
129. Rowan MP, Cancio LC, Elster EA, Burmeister DM, Rose LF, Natesan S, Chan RK, Christy RJ, Chung KK. Burn Wound Healing and Treatment: Review and Advancements. Critical Care. 2015;DOI 10.1186/s13054-01509861-2.
130. Boykin JV Jr. Letter to the Editor, Undersea Hyperb Med. 2013Mar-Apr;40(2):212.

## Chapter 15: Mechanisms of Action of Hyperbaric Oxygen Therapy

Gerardo Bosco MD, PhD (corresponding author), Alex Rizzato MSc., Enrico M. Camporesi MD

### REFERENCES

1. Yarbrough O, Behnke A. The treatment of compressed air illness. *J Ind Hyg Toxicol.* 1939;21:213–8.
2. Churchill-Davidson I, Sanger C, Thomlinson R. High-pressure oxygen and radiotherapy. *Lancet (London, England).* 1955 May 28;268(6874):1091–5.
3. Boerema I, Huiskes J, Kroll J, Kroon B, Lokin E, Meyne N. High atmospheric pressure as an aid to cardiac surgery. *Arch Chir Neerl.* 1956;8(3):193–211.
4. Brummelkamp WH, Hogendijk J, Boerema I. Treatment of anaerobic infections (clostridial myositis) by drenching the tissues with oxygen under high atmospheric pressure. *Surgery.* 1961 Mar 1;49(3):299–302.
5. Smith G, Ledingham IM, Sharp GR, Norman JN, Bates EH. Treatment of coal-gas poisoning with oxygen at 2 atmospheres pressure. *Lancet.* 1962 Apr 21 [cited 2019 Feb 22];279(7234):816–9.
6. Muth CM, Shank ES. Gas Embolism. *N Engl J Med [Internet].* 2000 Feb 17;342(7):476–82.
7. Thom SR. Oxidative stress is fundamental to hyperbaric oxygen therapy. *J Appl Physiol.* 2009 Mar;106(3):988–95.
8. Vorosmarti J. Hyperbaric oxygen therapy. *Am Fam Physician.* 1981 Jan;23(1):169–73.
9. Clark J, Whelan HT. Hyperbaric medicine practice. In: Kindwall & H.T. Whelan, editor. Best Publishing Company; 1994.
10. Davis JC. Hyperbaric oxygen therapy. *J Intensive Care Med.* 1989 Mar 30;4(2):55–7.
11. Camporesi EM, Bosco G. Mechanisms of action of hyperbaric oxygen therapy. *Undersea Hyperb Med.* 2014;41(3):247–52.
12. Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg.* 2011 Jan;127:131S–141S.
13. Falanga V. Wound healing and its impairment in the diabetic foot. *Lancet.* 2005 Nov 12;366(9498):1736–43.
14. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg.* 1983 May;41(5):283–8.
15. Hunt TK, Aslam RS, Beckert S, Wagner S, Ghani QP, Hussain MZ, et al. Aerobically derived lactate stimulates revascularization and tissue repair via redox mechanisms. *Antioxid Redox Signal.* 2007 Aug;9(8):1115–24.
16. Milovanova TN, Bhopale VM, Sorokina EM, Moore JS, Hunt TK, Hauer-Jensen M, et al. Lactate stimulates vasculogenic stem cells via the thioredoxin system and engages an autocrine activation loop involving hypoxia-inducible factor 1. *Mol Cell Biol.* 2008 Oct 15;28(20):6248–61.
17. Bosco G, Yang Z, Nandi J, Wang J, Chen C, Camporesi EM. Effects of hyperbaric oxygen on glucose, lactate, glycerol and anti-oxidant enzymes in the skeletal muscle of rats during ischaemia and reperfusion. *Clin Exp Pharmacol Physiol.* 2007 Jan;34(1–2):70–6.
18. Sharifi M, Fares W, Abdel-Karim I, Petrea D, Koch JM, Adler D, et al. Inhibition of restenosis by hyperbaric oxygen: a novel indication for an old modality. *Cardiovasc Radiat Med.* 2002;3(3–4):124–6.
19. Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D, et al. Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol.* 2004 Jun 15;93(12):1533–5.
20. Yang ZJ, Bosco G, Montante A, Ou XI, Camporesi EM. Hyperbaric O<sub>2</sub> reduces intestinal ischemia-reperfusion-induced TNF-alpha production and lung neutrophil sequestration. *Eur J Appl Physiol.* 2001 Jul 5;85(1–2):96–103.
21. Yang Z, Nandi J, Wang J, Bosco G, Gregory M, Chung C, et al. Hyperbaric oxygenation ameliorates indomethacin-induced enteropathy in rats by modulating TNF- $\alpha$  and IL-1 $\beta$  production. *Dig Dis Sci.* 2006 Aug 13;51(8):1426–33.
22. Baynosa RC, Naig AL, Murphy PS, Fang XH, Stephenson LL, Khiabani KT, et al. The effect of hyperbaric oxygen on nitric oxide synthase activity and expression in ischemia-reperfusion injury. *J Surg Res.* 2013 Jul;183(1):355–61.
23. Hampson NB, Piantadosi CA, Thom SR, Weaver LK. Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. *Am J Respir Crit Care Med.* 2012 Dec 1;186(11):1095–101.
24. Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. In: *The Lancet.* Elsevier; 2011. Pp: 153–64.
25. Moon RE. Hyperbaric oxygen treatment for air or gas embolism. *Undersea Hyperb Med.* 2014;41(2):159–66.
26. Thom SR, Bhopale VM, Mancini DJ, Milovanova TN. Actin S-nitrosylation inhibits neutrophil beta2 integrin function. *J Biol Chem.* 2008 Apr 18;283(16):10822–34.
27. Mori H, Shinohara H, Arakawa Y, Kanemura H, Ikemoto T, Imura S, et al. Beneficial effects of hyperbaric oxygen pretreatment on massive hepatectomy model in rats. *Transplantation [Internet].* 2007 Dec 27 [cited 2019 Feb 22];84(12):1656–61.
28. Yang ZJ, Xie Y, Bosco GM, Chen C, Camporesi EM. Hyperbaric oxygenation alleviates MCAO-induced brain injury and reduces hydroxyl radical formation and glutamate release. *Eur J Appl Physiol.* 2010 Feb 23;108(3):513–22.
29. Bosco G, Vezzani G, Mrakic Spusta S, Rizzato A, Enten G, Abou-Samra A, et al. Hyperbaric oxygen therapy ameliorates osteonecrosis in patients by modulating inflammation and oxidative stress. *J Enzyme Inhib Med Chem.* 2018 Dec;33(1):1501–5.
30. Gorbach SL, Bartlett JG. Anaerobic Infections. *N Engl J Med.* 1974 May 23;290(21):1177–84.

31. Zanon V, Rossi L, Castellani E, Camporesi EM, Palù G, Bosco G. Oxybiotest project: microorganisms under pressure. Hyperbaric oxygen (HBO) and simple pressure interaction on selected bacteria. *Med Gas Res.* 2012 Sep 11;2(1):24.
32. Mader JT, Brown GL, Guckian JC, Wells CH, Reinarz JA. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. *J Infect Dis.* 1980 Dec;142(6):915–22.
33. Almzaiei AJ, Billington R, Smerdon G, Moody AJ. Effects of hyperbaric oxygen treatment on antimicrobial function and apoptosis of differentiated HL-60 (neutrophil-like) cells. *Life Sci.* 2013 Jul 30;93(2–3):125–31.
34. Wu Y, Klapper I, Stewart PS. Hypoxia arising from concerted oxygen consumption by neutrophils and microorganisms in biofilms. *Pathog Dis.* 2018 Jun 1;76(4).
35. Kolpen M, Lerche CJ, Kragh KN, Sams T, Koren K, Jensen AS, et al. Hyperbaric oxygen sensitizes anoxic *pseudomonas aeruginosa* biofilm to ciprofloxacin. *Antimicrob Agents Chemother.* 2017 Nov;61(11).
36. Lerche CJ, Christophersen LJ, Kolpen M, Nielsen PR, Trøstrup H, Thomsen K, et al. Hyperbaric oxygen therapy augments tobramycin efficacy in experimental *Staphylococcus aureus* endocarditis. *Int J Antimicrob Agents.* 2017 Sep;50(3):406–12.
37. Sanford NE, Wilkinson JE, Nguyen H, Diaz G, Wolcott R. Efficacy of hyperbaric oxygen therapy in bacterial biofilm eradication. *J Wound Care.* 2018 Jan 1;27(Sup1):S20–8.
38. Ishii Y, Miyanaga Y, Shimojo H, Ushida T, Tateishi T. Effects of hyperbaric oxygen on procollagen messenger RNA levels and collagen synthesis in the healing of rat tendon laceration. *Tissue Eng.* 1999 Jun;5(3):279–86.
39. Weisz G, Lavy A, Adir Y, Melamed Y, Rubin D, Eidelman S, et al. Modification of in vivo and in vitro TNF-alpha, IL-1, and IL-6 secretion by circulating monocytes during hyperbaric oxygen treatment in patients with perianal Crohn's disease. *J Clin Immunol.* 1997 Mar;17(2):154–9.
40. Tsai H-M, Gao C-J, Li W-X, Lin M-T, Niu K-C. Resuscitation from experimental heatstroke by hyperbaric oxygen therapy. *Crit Care Med.* 2005 Apr;33(4):813–8.
41. Zhao LL, Davidson JD, Wee SC, Roth SI, Mustoe TA. Effect of hyperbaric oxygen and growth factors on rabbit ear ischemic ulcers. *Arch Surg.* 1994 Oct 1;129(10):1043.
42. Gleadle JM, Ratcliffe PJ. Hypoxia and the regulation of gene expression. *Mol Med Today.* 1998 Mar 1;4(3):122–9.
43. Haroon ZA, Raleigh JA, Greenberg CS, Dewhirst MW. Early wound healing exhibits cytokine surge without evidence of hypoxia. *Ann Surg.* 2000 Jan;231(1):137–47.
44. Thom SR, Bhopale V, Fisher D, Manevich Y, Huang PL, Buerk DG. Stimulation of nitric oxide synthase in cerebral cortex due to elevated partial pressures of oxygen: an oxidative stress response. *J Neurobiol.* 2002 May;51(2):85–100.
45. Thom SR, Fisher D, Zhang J, Bhopale VM, Ohnishi ST, Kotake Y, et al. Stimulation of perivascular nitric oxide synthesis by oxygen. *Am J Physiol Circ Physiol.* 2003 Apr;284(4):H1230–9.
46. Boykin J V, Baylis C. Hyperbaric oxygen therapy mediates increased nitric oxide production associated with wound healing: a preliminary study. *Adv Skin Wound Care.* 2007 Jul;20(7):382–8.
47. Kendall AC, Whatmore JL, Harries LW, Winyard PG, Smerdon GR, Eggleton P. Changes in inflammatory gene expression induced by hyperbaric oxygen treatment in human endothelial cells under chronic wound conditions. *Exp Cell Res.* 2012 Feb 1;318(3):207–16.
48. Oter S, Korkmaz A, Topal T, Ozcan O, Sadır S, Ozler M, et al. Correlation between hyperbaric oxygen exposure pressures and oxidative parameters in rat lung, brain, and erythrocytes. *Clin Biochem.* 2005 Aug;38(8):706–11.
49. Palzur E, Zaaroor M, Vlodavsky E, Milman F, Soustiel JF. Neuroprotective effect of hyperbaric oxygen therapy in brain injury is mediated by preservation of mitochondrial membrane properties. *Brain Res.* 2008 Jul 24;1221:126–33.
50. Brentnall M, Rodriguez-Menocal L, De Guevara R, Cepero E, Boise LH. Caspase-9, caspase-3 and caspase-7 have distinct roles during intrinsic apoptosis. *BMC Cell Biol.* 2013 Jul 9;14(1):32.
51. Hink J, Jansen E. Are superoxide and/or hydrogen peroxide responsible for some of the beneficial effects of hyperbaric oxygen therapy? *Med Hypotheses.* 2001 Dec;57(6):764–9.
52. Vlodavsky E, Palzur E, Soustiel JF. Hyperbaric oxygen therapy reduces neuroinflammation and expression of matrix metalloproteinase-9 in the rat model of traumatic brain injury. *Neuropathol Appl Neurobiol.* 2006 Feb;32(1):40–50.
53. Tracey DJ, Walker JS. Pain due to nerve damage: are inflammatory mediators involved? *Inflamm Res.* 1995 Oct;44(10):407–11.
54. Zhang J-M, An J. Cytokines, inflammation, and pain. *Int Anesthesiol Clin.* 2007;45(2):27–37.
55. Ren K, Torres R. Role of interleukin-1beta during pain and inflammation. *Brain Res Rev.* 2009 Apr;60(1):57–64.
56. Thompson CD, Uhelski ML, Wilson JR, Fuchs PN. Hyperbaric oxygen treatment decreases pain in two nerve injury models. *Neurosci Res.* 2010 Mar;66(3):279–83.
57. Gu N, Niu J-Y, Liu W-T, Sun Y-Y, Liu S, Lv Y, et al. Hyperbaric oxygen therapy attenuates neuropathic hyperalgesia in rats and idiopathic trigeminal neuralgia in patients. *Eur J Pain.* 2012 Sep;16(8):1094–105.

58. Inamoto Y, Okuno F, Saito K, Tanaka Y, Watanabe K, Morimoto I, et al. Effect of hyperbaric oxygenation on macrophage function in mice. *Biochem Biophys Res Commun.* 1991 Sep 16;179(2):886–91.
59. Li F, Fang L, Huang S, Yang Z, Nandi J, Thomas S, et al. Hyperbaric oxygenation therapy alleviates chronic constrictive injury-induced neuropathic pain and reduces tumor necrosis factor-alpha production. *Anesth Analg.* 2011 Sep;113(3):626–33.
60. Ohgami Y, Zylstra CC, Quock LP, Chung E, Shirachi DY, Quock RM. Nitric oxide in hyperbaric oxygen-induced acute antinociception in mice. *Neuroreport.* 2009 Oct 7;20(15):1325–9.
61. Zelinski LM, Ohgami Y, Chung E, Shirachi DY, Quock RM. A prolonged nitric oxide-dependent, opioid-mediated antinociceptive effect of hyperbaric oxygen in mice. *J Pain.* 2009 Feb;10(2):167–72.
62. Camporesi EM, Vezzani G, Bosco G, Mangar D, Bernasek TL. Hyperbaric oxygen therapy in femoral head necrosis. *J Arthroplasty.* 2010 Sep 1;25(6):118–23.
63. Bosco G, Vezzani G, Enten G, Manelli D, Rao N, Camporesi EM. Femoral condylar necrosis: treatment with hyperbaric oxygen therapy. *Arthroplast today.* 2018 Dec;4(4):510–5.
64. Camporesi EM, Vezzani G, Zanon V, Manelli D, Enten G, Quartesan S, et al. Review on hyperbaric oxygen treatment in femoral head necrosis. *Undersea Hyperb Med.* 2017;44(6):497–508.
65. Hadi H Al, Smerdon GR, Fox SW. Hyperbaric oxygen therapy suppresses osteoclast formation and bone resorption. *J Orthop Res.* 2013 Jul;31(11).
66. Vezzani G, Quartesan S, Cancellara P, Camporesi EM, Mangar D, Bernasek T, et al. Hyperbaric oxygen therapy modulates serum OPG/RANKL in femoral head necrosis patients. *J Enzyme Inhib Med Chem.* 2017;32(1):707–11.

## **Chapter 16: Side Effects of Hyperbaric Oxygen Therapy**

*Matteo Paganini MD, Enrico M. Camporesi MD*

### **REFERENCES**

1. Cousins JL, Wark PA, McDonald VM. Acute oxygen therapy: a review of prescribing and delivery practices. *Int J Chron Obstruct Pulmon Dis.* 2016;11:1067-75.
2. Heyboer M, Sharma D, Santiago W, McCulloch N. Hyperbaric oxygen therapy: side effects defined and quantified. *Adv Wound Care (New Rochelle).* 2017;6(6):210-224.
3. Davis JC, Dunn JM, Heimbach RD. Hyperbaric medicine: patient selection, treatment procedures, and side effects. In: Davis JC, Hunt TK, eds. *Problem wounds: the role of oxygen.* New York: Elsevier; 1988. Pp:225-235.
4. Davis JC. Hyperbaric oxygen therapy. *J Intensive Care Med* 1989;4:55-57.
5. Brown M, Jones J, Krohmer J. Pseudoephedrine for the prevention of barotitis media: a controlled clinical trial in underwater divers. *Ann Emerg Med.* 1992;21:849-852.
6. Carlson S, Jones J, Brown M, Hess C. Prevention of hyperbaric-associated middle ear barotrauma. *Ann Emerg Med.* 1992;21:1468-1471.
7. Fernau JL, Hirsch BE, Derkay C, Ramasastry S, Schaefer SE. Hyperbaric oxygen therapy: effect on middle ear and eustachian tube function. *Laryngoscope.* 1992;102:48-52.
8. Shupak A, Atias J, Aviv J, Melamed Y. Oxygen diving-induced middle ear under-aeration. *Acta Otolaryngol Stockh.* 1995;115:422-426.
9. McMonnies CW. Hyperbaric oxygen therapy and the possibility of ocular complications or contraindications. *Clin Exp Optom.* 2015;98(2):122-5.
10. Anderson B Jr, Farmer JC Jr. Hyperoxic myopia. *Trans Am Ophthalmol Soc* 1978;76:116-124.
11. Anderson B Jr, Shelton DL. Axial length in hyperoxic myopia. In: Bove AA, Bachrach AJ, Greenbaum LJ Jr, eds. *Underwater and hyperbaric physiology IX. Proceedings of the ninth international symposium on underwater and hyperbaric physiology.* Bethesda, MD: Undersea and Hyperbaric Medical Society; 1987. Pp:607-611.
12. Lyne AJ. Ocular effects of hyperbaric oxygen. *Trans Ophthalmol Soc.* 1978; 98:66-68.
13. Palmquist BM, Philipson B, Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. *Br J Ophthalmol.* 1984;68:113-117.
14. Churchill S, Hopkins RO, Weaver LK. Incidence and duration of myopia while receiving hyperbaric oxygen (HBO<sub>2</sub>) therapy. *Undersea Hyperbaric Med* 1997;24 (Suppl):36.
15. Dedi D, Prager T, Jacob R, Chan A, Fife C. Visual acuity changes in patients undergoing hyperbaric oxygen therapy. *Undersea Hyperbaric Med* 1998;25(Suppl):34.
16. Evanger K, Haugen OH, Irgens A, Aanderud L, Thorsen E. Ocular refractive changes in patients receiving hyperbaric oxygen administered by oronasal mask or hood. *Acta Ophthalmol.* 2004;82:449-453.
17. Gesell LB, Adams BS, Kob DG. De novo cataract development following a standard course of hyperbaric oxygen therapy. *Undersea Hyperbaric Med* 2000;27 (Suppl): 56-57.
18. Behnke AR, Forbes HS, Motley EP. Circulatory and visual effects of oxygen at 3 atmospheres pressure. *Am J Physiol.* 1936;114:436-442.
19. Lambertsen CJ, Clark JM, Gelfand R, Pisarello J, Cobbs WH, Bevilacqua JE, Schwartz DM, Montabana DJ, Leach CS, Johnson PC, Fletcher DE. Definition of tolerance to continuous hyperoxia in man. An abstract report of predictive studies V. In: Bove AA, Bachrach AJ, Greenbaum LJ Jr, eds. *Underwater and hyperbaric physiology IX. Proceedings of the ninth international symposium on underwater and hyperbaric physiology.* Bethesda, MD: Undersea and Hyperbaric Medical Society; 1987. Pp:717-735.
20. Clark JM, Lambertsen CJ, Montabana DJ, Gelfand R, Cobbs WH. Comparison of visual function effects in man during continuous oxygen exposures at 3.0 and 2.0 ATA for 3.4 and 9.0 hours. *Undersea Biomed Res.* 1988;15(suppl):32.
21. Nichols CW, Lambertsen CJ, Clark JM. Transient unilateral loss of vision associated with oxygen at high pressure. *Arch Ophthalmol.* 1969;81:548-552.
22. Clark JM, Thom SR. Oxygen under pressure. In: Brubakk AO, Neuman TS, eds. *Bennett and Elliott's physiology and medicine of diving,* 5th ed. Philadelphia: W.B. Saunders; 2003. Pp:358-418.
23. Lambertsen CJ. Effects of hyperoxia on organs and their tissues. In: Robin E, ed. *Extrapulmonary manifestation of respiratory disease.* New York: Marcel Dekker; 1978. Pp:239-303.
24. Kindwall EP. Working under increased barometric pressure. In: Francis TJR, ed. *Encyclopedia of Occupational Health and Safety.* Geneva: International Labor Organization; 2011.
25. Tsan MF. Superoxide dismutase and pulmonary oxygen toxicity: lessons from transgenic and knockout mice (Review). *Int J Mol Med.* 2001 Jan;7(1):13-9.
26. Clark JM, Lambertsen CJ. Rate of development of pulmonary O<sub>2</sub> toxicity in man during O<sub>2</sub> breathing at 2.0 ATA. *J Appl Physiol.* 1971;30:739-752.

27. Thorsen E, Aanderud L, Aasen TB. Effects of a standard hyperbaric oxygen treatment protocol on pulmonary function. *Eur Respir J.* 1998;12:1442-1445.
28. Weaver LK, Howe S. Normobaric measurement of O<sub>2</sub> tension of blood in subjects exposed to hyperbaric oxygen. *Chest.* 1992;102:1175-1181.
29. Weaver LK, Howe S. Arterial oxygen tension of patients with abnormal lungs treated with hyperbaric oxygen is greater than predicted. *Chest.* 1994;106:1134-1139.
30. Bond GF. Arterial gas embolism. In: Davis JC, Hunt TK, eds. *Hyperbaric oxygen therapy.* Bethesda, MD: Undersea Medical Society;1977. Pp:141-152.
31. Wolf HK, Moon RE, Mitchell PR, Burger PC. Barotrauma and air embolism in hyperbaric oxygen therapy. *Am J Forensic Med Pathol.* 1990;11:149-153.
32. Sloan EP, Murphy DG, Hart R, Cooper MA, Turnbull T, Barreca RS, Ellerson B. Complication and protocol considerations in carbon monoxide-poisoned patients who require hyperbaric oxygen therapy: report from a ten-year experience. *Ann Emerg Med.* 1989;18:629-634.
33. K.W. Donald: Oxygen poisoning in man. I. *Br Med J.* 1:667-672. 1947.
34. K.W. Donald: Oxygen poisoning in man. II. *Br Med J.* 1:712-717. 1947.
35. Hart GB, Strauss MB. Central nervous system oxygen toxicity in a clinical setting. In: Bove AA, Bachrach AJ, Greenbaum LJ, eds. *Undersea and hyperbaric physiology IX. Proceedings of the ninth international symposium on underwater and hyperbaric physiology.* Bethesda, MD: Undersea and Hyperbaric Medical Society; 1987. Pp:695-699.
36. Sherlock S, Way M, Tabah A. Audit of practice in Australasian hyperbaric units on the incidence of central nervous system oxygen toxicity. *Diving Hyperb Med.* 2018;48(2):73-78.
37. Keenan HT, Bratton SL, Norkool DM, Brogan TV, Hampson NB. Delivery of hyperbaric oxygen therapy to critically ill, mechanically ventilated children. *J Crit Care.* 1998;13:7-12.
38. Patz A. Effect of oxygen on immature retinal vessels. *Invest Ophthalmol.* 1965;4:988-999.
39. Sola A, Chow L, Rogido M. [Retinopathy of prematurity and oxygen therapy: a changing relationship]. *An Pediatr (Barc).* 2005;62(1):48-63.
40. Lind F. A pro/con review comparing the use of mono- and multiplace hyperbaric chambers for critical care. *Diving Hyperb Med.* 2015;45(1):56-60.
41. Beard T, Watson B, Barry R, Stewart D, Warriner R: Analysis of adverse events occurring in patients undergoing adjunctive hyperbaric oxygen treatment: 2009-2010 (Abstract) UHM Vol. 38-5 - section G, p. 455. 2011.
42. Zadik Y, Drucker S. Diving dentistry: a review of the dental implications of scuba diving. *Australian Dent J.* 2011;56:265-271.

## **Chapter 17: Oxygen Pretreatment and Preconditioning**

*Enrico M. Camporesi MD, Matteo Paganini MD, Gerardo Bosco MD, PhD*

### **REFERENCES**

1. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation*. 1986;74(5):1124-36.
2. Bourroche G, Bourgain JL. Preoxygenation and general anesthesia: a review. *Minerva Anestesiol*. 2015;81(8):910-20.
3. Otis AB, Rahn H, Fenn WO. Alveolar gas changes during breath holding. *Am J Physiol*. 1948;152(3):674-86.
4. Waring WS, Thomson AJ, Adwani SH, Rosseel AJ, Potter JF, Webb DJ, Maxwell SR. Cardiovascular effects of acute oxygen administration in healthy adults. *J Cardiovasc Pharmacol*. 2003;42:245-250.
5. Thomson AJ, Drummond GB, Waring WS, Webb DJ, Maxwell SR. Effects of short-term isocapnic hyperoxia and hypoxia on cardiovascular function. *J Appl Physiol*. 2006;101:809-816.
6. Castagna O, Gempp E, Blatteau JE. Pre-dive normobaric oxygen reduces bubble formation in scuba divers. *Eur J Appl Physiol*. 2009;106:167-172.
7. Piepho T, Ehrmann U, Werner C, Muth CM. Oxygen therapy in diving accidents. *Anaesthesist*. 2007;56:44-52.
8. Vann RD, Denoble PJ, Howle LE, Weber PW, Freiberger JJ, Pieper CF. Resolution and severity in decompression illness. *Aviat Space Environ Med*. 2009;80:466-471.
9. Bosco G, Yang ZJ, Di Tano G, Camporesi EM, Faralli F, Savini F, Landolfi A, Doria C, Fano G. Effect of in-water oxygen prebreathing at different depths on decompression-induced bubble formation and platelet activation. *J Appl Physiol*. 2010;108:1077-1083.
10. Evans A, Walder DN. Significance of gas micronuclei in the aetiology of decompression sickness. *Nature*. 1969;222(5190):251-2.
11. Arieli R, Boaron E, Arieli Y, Abramovich A, Katsenelson K. Oxygen pretreatment as protection against decompression sickness in rats: pressure and time necessary for hypothesized denucleation and renucleation. *Eur J Appl Physiol*. 2011;111:997-1005.
12. Landolfi A, Yang Z, Savini F, Camporesi E, Faralli F, Bosco G. Pre-treatment with hyperbaric oxygenation reduces bubble formation and platelet activation. *Sport Sciences for Health*. 2006;1:122-128.
13. Arieli Y, Arieli R, Marx A. Hyperbaric oxygen may reduce gas bubbles in decompressed prawns by eliminating gas nuclei. *J Appl Physiol*. 2002;92:2596-2599.
14. Butler BD, Little T, Cogan V, Powell M. Hyperbaric oxygen pre-breathe modifies the outcome of decompression sickness. *Undersea Hyperb Med*. 2006;33:407-417.
15. Katsenelson K, Arieli Y, Abramovich A, Feinsod M, Arieli R. Hyperbaric oxygen pretreatment reduces the incidence of decompression sickness in rats. *Eur J Appl Physiol*. 2007;101:571-576.
16. Behnke AR. The isobaric (oxygen window) principle of decompression. In: The new thrust seaward. Transactions of the third annual conference of marine technology society. San Diego, CA: Marine Technology Society; 1967.
17. Balestra C, Germonpre P, Snoeck T, Ezquer M, Leduc O, Leduc A, Willeput F, Marroni A, Cali Corleo R, Vann R. Normobaric oxygen can enhance protein captation by the lymphatic system in healthy humans. *Undersea Hyperb Med*. 2004;31:59-62.
18. Webb JT, Pilmanis AA. Preoxygenation time versus decompression sickness incidence. *SAFE J*. 1999;29:75-78.
19. Youngh DE. On the evolution, generation, and regeneration of gas cavitation nuclei. *J Acoust Soc Am*. 1982;71:1473-1481.
20. Dunford RG, Vann RD, Gerth WA, Pieper CF, Huggins K, Wacholtz C, Bennett PB. The incidence of venous gas emboli in recreational diving. *Undersea Hyperb Med*. 2002;29:247-259.
21. Hamilton RW, Thalmann ED. Decompression practice. In: Brubakk AO, Neuman TS, editors. *Bennett & Elliott's Physiology and Medicine of Diving*. 5th ed. New York, NY: Elsevier Science; 2003. Pp. 455-500.
22. Pontier JM, Gempp E, Ignatescu M. Blood platelet-derived microparticles release and bubble formation after an open-sea air dive. *Appl Physiol Nutr Metab*. 2012;37(5):888-92.
23. Morabito C, Bosco G, Pilla R, Corona C, Mancinelli R, Yang Z, Camporesi EM, Fano G, Mariggio MA. Effect of pre-breathing oxygen at different depth on oxidative status and calcium concentration in lymphocytes of scuba divers. *Acta Physiol (Oxf)*. 2011;202:69-78.
24. Gorsuch WB, Chrysanthou E, Schwaebel WJ, Stahl GL. The complement system in ischemia-reperfusion injuries. *Immunobiology*. 2012;217(11):1026-33.
25. Yu SY, Chiu JH, Yang SD, Yu HY, Hsieh CC, Chen PJ, Lui WY, Wu CW. Preconditioned hyperbaric oxygenation protects the liver against ischemia-reperfusion injury in rats. *J Surg Res*. 2005;128:28-36.
26. Grisotto PC, dos Santos AC, Coutinho-Netto J, Cherri J, Piccinato CE. Indicators of oxidative injury and alterations of the cell membrane in the skeletal muscle of rats submitted to ischemia and reperfusion. *J Surg Res*. 2000;92:1-6.

27. Yang ZJ, Bosco G, Montante A, Ou XI, Camporesi EM. Hyperbaric O<sub>2</sub> reduces intestinal ischemia-reperfusion-induced TNF-alpha production and lung neutrophil sequestration. *Eur J Appl Physiol.* 2001;85(1-2):96-103.
28. Bosco G, Yang ZJ, Nandi J, Wang J, Chen C, Camporesi EM. Effects of hyperbaric oxygen on glucose, lactate, glycerol and anti-oxidant enzymes in the skeletal muscle of rats during ischaemia and reperfusion. *Clin Exp Pharmacol Physiol.* 2007;34(1-2):70-6.
29. Yang ZJ, Xie Y, Bosco GM, Chen C, Camporesi EM. Hyperbaric oxygenation alleviates MCAO-induced brain injury and reduces hydroxyl radical formation and glutamate release. *Eur J Appl Physiol.* 2010;108(3):513-22.
30. Jadhav V, Ostrowski RP, Tong W, Matus B, Chang C, Zhang JH. Hyperbaric oxygen preconditioning reduces postoperative brain edema and improves neurological outcomes after surgical brain injury. *Acta Neurochir Suppl.* 2010;106:217-20.
31. Wang L, Li W, Kang Z, et al. Hyperbaric oxygen preconditioning attenuates early apoptosis after spinal cord ischemia in rats. *J Neurotrauma.* 2009;26(1):55-66.
32. Gu GJ, Li YP, Peng ZY, et al. Mechanism of ischemic tolerance induced by hyperbaric oxygen preconditioning involves upregulation of hypoxia-inducible factor-1alpha and erythropoietin in rats. *J Appl Physiol.* 2008;104(4):1185-91.
33. Ozyurt H, Ozyurt B, Koca K, Ozgocmen S. Caffeic acid phenethyl ester (CAPE) protects rat skeletal muscle against ischemia-reperfusion-induced oxidative stress. *Vascul Pharmacol.* 2007;47:108-112.
34. Mebazaa A, Pitsis AA, Rudiger A, Toller W, Longrois D, Ricksten SE, Bobek I, De Hert S, Wieselthaler G, Schirmer U, von Segesser LK, Sander M, Poldermans D, Ranucci M, Karpati PC, Wouters P, Seeberger M, Schmid ER, Weder W, Follath F. Clinical review: practical recommendations on the management of perioperative heart failure in cardiac surgery. *Crit Care.* 2010;14(2):201.
35. Bolli R, Becker L, Gross G, Mentzer R Jr, Balshaw D, Lathrop DA. Myocardial protection at a crossroads: the need for translation into clinical therapy. *Circ Res.* 2004;95:125- 134.
36. Hentia C, Rizzato A, Camporesi E, et al. An overview of protective strategies against ischemia/reperfusion injury: The role of hyperbaric oxygen preconditioning. *Brain Behav.* 2018;8:e00959.
37. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation.* 1986;74:1124-1136.
38. Hausenloy DJ, Mwamure PK, Venugopal V, Harris J, Barnard M, Grundy E, Ashley E, Vichare S, Di Salvo C, Kolvekar S, Hayward M, Keogh B, MacAllister RJ, Yellon DM. Effect of remote ischaemic preconditioning on myocardial injury in patients undergoing coronary artery bypass graft surgery: a randomised controlled trial. *Lancet.* 2007;370:575-579.
39. Wu ZK, Iivainen T, Pehkonen E, Laurikka J, Tarkka MR. Arrhythmias in off-pump coronary artery bypass grafting and the antiarrhythmic effect of regional ischemic preconditioning. *J Cardiothorac Vasc Anesth.* 2003;17:459-464.
40. Yellon DM, Alkhulaifi AM, Pugsley WB. Preconditioning the human myocardium. *Lancet.* 1993;342:276-277.
41. Berger MM, Macholz F, Mairbaurl H, Bärtsch P. Remote ischemic preconditioning for prevention of high-altitude diseases: fact or fiction?. *J Appl Physiol.* 2015;119(10):1143-51.
42. Yogaratnam JZ, Laden G, Guvendik L, Cowen M, Cale A, Griffin S. Hyperbaric oxygen preconditioning improves myocardial function, reduces length of intensive care stay, and limits complications post coronary artery bypass graft surgery. *Cardiovasc Revasc Med.* 2010;11:8-19.
43. Li Y, Dong H, Chen M, Liu J, Yang L, Chen S, Xiong L. Preconditioning with repeated hyperbaric oxygen induces myocardial and cerebral protection in patients undergoing coronary artery bypass graft surgery: a prospective, randomized, controlled clinical trial. *J Cardiothorac Vasc Anesth.* 2011 Dec;25(6):908-916.
44. Alex J, Laden G, Cale A, Bennett S, Flowers K, Madden L, Gardiner E, McCollum T, Griffin S. Pretreatment with hyperbaric oxygen and its effect on neuropsychometric dysfunction and systemic inflammatory response after cardiopulmonary bypass: A prospective randomised double-blind trial. *J Thorac Cardiovasc Surg.* 2005;130(6):1623-1630.
45. Jeysen ZY, Gerard L, Levant G, Cowen M, Cale A, Griffin S. Research report: the effects of hyperbaric oxygen preconditioning on myocardial biomarkers of cardioprotection in patients having coronary artery bypass graft surgery. *Undersea Hyperb Med.* 2011;38(3):175-85.
46. Li Q, Li J, Zhang L, Wang B, Xiong L. Preconditioning with hyperbaric oxygen induces tolerance against oxidative injury via increased expression of heme oxygenase-1 in primary cultured spinal cord neurons. *Life Sci.* 2007;80:1087-1093.
47. Sterling DL, Thornton JD, Swafford A, Gottlieb SF, Bishop SP, Stanley AW, Downey JM. Hyperbaric oxygen limits infarct size in ischemic rabbit myocardium *in vivo*. *Circulation.* 1993 Oct;88(4 Pt 1):1931-1936.
48. Wada K, Ito M, Miyazawa T, Katoh H, Nawashiro H, Shima K, Chigasaki H. Repeated hyperbaric oxygen induces ischemic tolerance in gerbil hippocampus. *Brain Res.* 1996;740:15-20.

49. Liska GM, Lippert T, Russo E, Nieves N, Borlongan CV. A dual role for hyperbaric oxygen in stroke neuroprotection: preconditioning of the brain and stem cells. *Cond Med.* 2018;1(4):151-166.
50. Gao L, Taha R, Gauvin D, Othmen LB, Wang Y, Blaise G. Postoperative cognitive dysfunction after cardiac surgery. *Chest.* 2005;128:3664-3670.
51. Sato Y, Laskowitz DT, Bennett ER, Newman MF, Warner DS, Grocott HP. Differential cerebral gene expression during cardiopulmonary bypass in the rat: evidence for apoptosis? *Anesth Analg.* 2002;94:1389-1394, table of contents.
52. Gao ZX, Rao J, Li YH (2017) Hyperbaric oxygen preconditioning improves postoperative cognitive dysfunction by reducing oxidant stress and inflammation. *Neural Regen Res* 12(2):329-336.
53. Liu Y, Sun XJ, Liu J, Kang ZM, Deng XM. Heme-oxygenase-1 could mediate the protective effects of hyperbaric oxygen preconditioning against hepatic ischemia-reperfusion injury in rats. *Clin Exp Pharmacol Physiol.* 2011;38:675-682.
54. Bosco G, Casarotto A, Nasole E, et al. Preconditioning with hyperbaric oxygen in pancreaticoduodenectomy: a randomized double-blind pilot study. *Anticancer Res.* 2014;34(6):2899-906.
55. Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D; Hyperbaric Oxygen Therapy in Percutaneous Coronary Interventions Investigators. Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol.* 2004 Jun 15;93(12):1533-1535.
56. Kang N, Hai Y, Liang F, Gao CJ, Liu XH. Preconditioned hyperbaric oxygenation protects skin flap grafts in rats against ischemia/reperfusion injury. *Mol Med Rep.* 2014;9(6):2124-30.
57. Yang Z, Nandi J, Wang J, et al. Hyperbaric oxygenation ameliorates indomethacin-induced enteropathy in rats by modulating TNF-alpha and IL-1beta production. *Dig Dis Sci.* 2006;51(8):1426-33.

## **Chapter 18: Randomized Controlled Trials in Diving and Hyperbaric Medicine**

*Michael H. Bennett*

### **REFERENCES**

1. Medicare Services Advisory Committee. Review of interim funded service: Hyperbaric oxygen therapy for the treatment of chronic non-diabetic wounds and non-neurological soft tissue radiation injuries. MSAC Application 1054.1 Assessment Report, Commonwealth Government of Australia. ISBN 978-1-74241-605-2, 18 July 2016. <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1054.1-public>.
2. Health Quality Ontario. Hyperbaric oxygen therapy for the treatment of diabetic foot ulcers: a health technology assessment. Ontario health technology assessment series. 2017;17(5):1.
3. Health Technology Assessment Program, Washington State Health Care Authority. Hyperbaric oxygen therapy (HBOT) for tissue damage, including wound care and treatment of central nervous system (CNS) conditions. Final Evidence Report. 15 February 2013. [https://www.hca.wa.gov/assets/program/021513\\_hbot\\_final\\_report\[1\].pdf](https://www.hca.wa.gov/assets/program/021513_hbot_final_report[1].pdf)
4. Wittes J, ed. (Special Design Issue). Controlled clinical trials. 1998;19(4):313-418.
5. Frieden TR. Evidence for health decision making—beyond randomized, controlled trials. New England Journal of Medicine. 2017 Aug 3;377(5):465-75.
6. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 Explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.
7. Machin D, Campbell MJ, Fayers PM, Pinol APY. Sample size tables for clinical studies, 2nd ed. Blackwell Science Ltd. Malden, MA. 1997.
8. Phillips B, Ball C, Sackett D, et al. Oxford Centre for Evidence-based Medicine <http://www.cebm.net/> (last accessed January 2013).
9. Ho PM, Peterson PN, Masoudi FA. Key issues in outcomes research Evaluating the evidence. Is there a rigid hierarchy? Circulation. 2008;118:1675-1684.
10. Hopewell S, Dutton S, Yu LM, Chan AW, Altman DG. The quality of reports of randomised trials in 2000 and 2006: comparative study of articles indexed in PubMed. BMJ 340: c723.
11. Treweek S, Zwarenstein M. What kind of randomised trials do patients and clinicians need? Evidence Based Medicine 2009;14:101-103.
12. Zwarenstein M, Treweek S, Gagnier JJ, et al. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008;337:a2390.
13. Foëx BA. The ethics of clinical trials. Anaesthesia & Intensive Care Medicine. 2009 Feb 1;10(2):98-101.
14. Freedman B. Equipoise and the ethics of clinical research. N Engl J Med. 1987;317:141-145.
15. Veatch R. The irrelevance of equipoise. Journal of Medical Philosophy 2007;32:167-183.
16. Ubel PA, Silbergliet R. Behavioral equipoise: A way to resolve ethical stalemates in clinical research. The American Journal of Bioethics. 2008;11:1-8.
17. Kahneman D, Tversky A. The psychology of preferences. Scientific American. 1982;246:160–173.
18. Truzzi M. On the extraordinary: an attempt at clarification. Zetetic Scholar. 1978;1:11.
19. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB (2000). Evidence-based medicine: How to practice and teach EBM (2nd ed.). Edinburgh: Churchill Livingstone, 2000:1.
20. Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA 1992; 268:2420-2425.
21. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Teaching methods relevant to the clinical application of the results of critical appraisals to individual patients. In: Evidence-based medicine. How to practice and teach EBM (2nd Ed). Churchill Livingstone; London. 2000.
22. Bennett MH, Connor D, Lehm JP. The database of randomized controlled trials in hyperbaric medicine (DORCTHIM). <http://hboevidence.unsw.wikispaces.net/>.
23. Morris AH. Randomized clinical trials (Editorial). Trans Am Soc Artif Intern Organs 1991;27:41-42.
22. The Oxford Centre for Evidence-based Medicine. <http://www.cebm.net/> (Accessed January 2013).
24. Turner JA, Deyo RA, Loeser JD, Korff MV, Fordyce WE. The importance of placebo effects in pain treatment and research. JAMA 1994;271:1609-1614.
25. UK Parliamentary Committee Science and Technology Committee. Evidence Check 2: Homeopathy 2010. February 2010:10-12. Evidence Check 2: Homoeopathy 2010 (accessed January 2013).
26. McCarney R, Warner J, Iliffe S, van Haselen R, Griffin P, Fisher P. The Hawthorne effect: a randomised, controlled trial. BMC Medical Research Methodology. 2007;7:30.
27. Clarke RE, Catalina Tenorio LM, Hussey JR, Toklu AS, Cone DL, Hinojosa JG, et al. Hyperbaric oxygen treatment of chronic refractory radiation proctitis: a randomised and controlled double-blind crossover trial with long-term follow-up. International Journal of Radiation Oncology, Biology, Physics. 2008;72:134-143.

28. Weaver LK, Hopkins RO, Churchill S, Haberstock D. Double-blinding is possible in hyperbaric oxygen (HBO<sub>2</sub>) randomized clinical trials (RCT) using a minimal chamber pressurization as control (abstract). Undersea and Hyperbaric Med. 1997;24(Suppl):36.
29. Weaver LK, Churchill SK, Bell J, Deru K, Snow GL. A blinded trial to investigate whether 'pressure familiar' individuals can determine chamber pressure. Undersea and Hyperbaric Medicine. 2012;39:801-5.
30. Jansen T, Mortensen CR, Tvede MF. It is possible to perform a double-blind hyperbaric session: a double-blinded randomized trial performed on healthy volunteers. Undersea Hyperb Med. 2009 Sep-Oct;36(5):347-51.
31. Wolf G, Cifu D, Baugh L, Carne W, Profenna L. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. Journal of Neurotrauma. 2012. Pp:2606-2612.
32. Efrati S, Fishlev G, Bechor Y, Volkov O, Bergan J, et al. Hyperbaric oxygen induces late neuroplasticity in post stroke patients – randomized prospective trial. PLoS ONE 2013;8(1):e53716.
33. Mitchell SJ, Bennett MH. Unestablished indications for hyperbaric oxygen therapy. Diving Hyperb Med. 2014 Dec 1;44(4):228-34.
34. Bennett MH. Hyperbaric medicine and the placebo effect. Diving Hyperb Med. 2014 Dec 1;44:235-40.
35. Fedorko L, Bowen JM, Jones W, Oreopoulos G, Goeree R, Hopkins RB, O'Reilly DJ. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. Diabetes Care. 2016 Mar 1;39(3):392-9.
36. Santema KT, Stoekenbroek RM, Koelemay MJ, Reekers JA, van Dortmont LM, Oomen A, Smeets L, Wever JJ, Legemate DA, Ubbink DT. Hyperbaric Oxygen Therapy in the Treatment of Ischemic Lower-Extremity Ulcers in Patients With Diabetes: Results of the DAMO2CLES Multicenter Randomized Clinical Trial. Diabetes care. 2018 Jan 1;41(1):112-9.
37. Bennett MH. The evidence basis of diving and hyperbaric medicine - a synthesis of the high level clinical evidence with meta-analysis. <http://trove.nla.gov.au/>.
38. Jørgensen AW, Hilden J, Gøtzsche PC. Cochrane reviews compared with industry supported meta-analyses and other meta-analyses of the same drugs: systematic review. BMJ 2006;333:782.

## **Appendix 1: Randomized Clinical Trials in Hyperbaric Medicine**

This list includes abstracts when there has been no more complete report.

### **Acute Thermal Burns**

1. Hart GB, O'Reilly RR, Broussard N, Cave RH, Goodman DB, Yanda RL. Treatment of burns with hyperbaric oxygen. *Surg Gynecol Obstet.* 1974;139:693-696.
2. Hammarlund C, Svedman C, Svedman P. Hyperbaric oxygen treatment of healthy volunteers with U.V.-irradiated blister wounds. *Burns.* 1991;17(4):296-301.
3. Brannen AL, Still J, Haynes M, Orlet H, Rosenblum F, Law E, Thompson WO. A randomized prospective trial of hyperbaric oxygen in a referral burn center population. *Am Surgeon.* 1997;63(3):205-208.
4. Niezgoda JA, Cianci P, Folden BW, Ortega RL, Slade JB, Storrow AB. The effect of hyperbaric oxygen therapy on a burn wound model in human volunteers. *Plastic and Reconstructive Surgery.* 1997;99:1620-1625.
5. Xu N, Li Z, Luo X. [Effects of hyperbaric oxygen therapy on the changes in serum sIL-2R and Fn in severe burn patients]. *Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi.* 1999; 15(3):220-223.
6. Villanueva E, Bennett MH, Wasiak J, Lehman JP. Hyperbaric oxygen therapy for thermal burns (Cochrane Review). In: The Cochrane Library (Issue 3, 2004). Chichester, UK: John Wiley & Sons, Ltd.
7. Ma L, Li P, Shi Z, Hou T, Chen X, Du J. A prospective, randomized, controlled study of hyperbaric oxygen therapy: effects on healing and oxidative stress of ulcer tissue in patients with a diabetic foot ulcer. *Ostomy Wound Manage.* 2013 Mar 1;59(3):18-24.
8. Rasmussen VM, Borgen AE, Jansen EC, Rotbøll Nielsen PH, Werner MU. Hyperbaric oxygen therapy attenuates central sensitization induced by a thermal injury in humans. *Acta Anaesthesiologica Scandinavica.* 2015 Jul 1;59(6):749-62.

### **Acute Myocardial Ischemia and Cardiac Surgery**

9. Cameron AJV, Gibb BH, Ledingham IMcA. A controlled clinical trial of hyperbaric oxygen in the treatment of acute myocardial infarction. *Proceedings of the Second International Congress.* London: ES Livingston; 1965. P:277.
10. Thurston JGB, Greenwood TW, Bending MR, Connor H, Curwen MP. A controlled investigation into the effects of hyperbaric oxygen on mortality following acute myocardial infarction. *Q J Med, New Series,* XLII. 1973;168:751-770.
11. Swift PC, Turner JH, Oxer HF, O'Shea JP, Lane GK. Myocardial hibernation identified by hyperbaric oxygen treatment and echocardiography in postinfarction. *Am Heart J.* 1992;124:1151-1158.
12. Dekleva MN, Ostojic M, Vujnovic D. Hyperbaric oxygen and thrombolysis in acute myocardial infarction: a preliminary report. In: Sitinen SA, Leinio M, eds. *Proceedings of the Twenty-first Annual Meeting of the European Underwater and Baromedical Society (EUBS), Helsinki, Finland;* 1995. Pp:9-13.
13. Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y. Hyperbaric oxygen and thrombolysis in myocardial infarction: The "Hot MI" Study. *Am Heart J.* 1997;143(3):544-550.
14. Stavitsky Y, Shandling AH, Ellestad MH, Hart GB, Van Natta B, Messenger JC, Strauss M, Dekleva MN, Alexander JM, Mattice M, Clarke D. Hyperbaric oxygen and thrombolysis in myocardial infarction: the 'HOT MI' randomised multicenter study. *Cardiology.* 1998; 90:131-136.
15. Vlahovic A, Neskovic AN, Dekleva M, Putnikovic B, Popovic ZB, Otasevic P, Ostojic M. Hyperbaric oxygen treatment does not affect left ventricular chamber stiffness after myocardial infarction treated with thrombolysis. *American Heart Journal.* 2004;148:J1-J7.
16. Sharifi M, Fares W, Abdel-Karim I, Koch MJ, Sopko J, Adler D. Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol.* 2004;93:1533-1535.
17. Dekleva M, Neskovic A, Vlahovic A, Putnikovic B, Beleslin B, Ostojic M. Adjunctive effect of hyperbaric oxygen treatment after thrombolysis on left ventricular function in patients with acute myocardial infarction. *Am Heart J.* 2004 Oct;148(4).

18. Alex J, Laden G, Cale A, Bennett S, Flowers K, Madden L, Gardiner E, McCollum T, Griffin S. Pretreatment with hyperbaric oxygen and its effect on neuropsychometric dysfunction and systemic inflammatory response after cardiopulmonary bypass: A prospective randomised double-blind trial. *Journal of Thoracic and Cardiovascular Surgery*. 2005;130(6):1623-30.
19. Yoganathan JZ, Laden G, Madden LA, Guvendik L, Cowen M, Greenman M, Seymour AM, Cale A, Griffin S. Hyperbaric oxygen preconditioning promotes cardioprotection following ischemic reperfusion injury by improving myocardial function, limiting necrosis and enhancing the induction of Hsp72. *Undersea and Hyperbaric Medicine*. 2007;34(4):301-302.
20. Li Y, Dong H, Chen M, Liu J, Yang L, Chen S, Xiong L. Preconditioning with repeated hyperbaric oxygen induces myocardial and cerebral protection in patients undergoing coronary artery bypass graft surgery: a prospective, randomized, controlled clinical trial. *J Cardiothorac Vasc Anesth*. 2011 Dec;25(6):908-16. doi:10.1053/j.jvca.2011.06.017. Epub 2011 Aug 25.
21. Jeysen ZY, Gerard L, Levant G, Cowen M, Cale A, Griffin S. Research report: the effects of hyperbaric oxygen preconditioning on myocardial biomarkers of cardioprotection in patients having coronary artery bypass graft surgery. *Undersea Hyperb Med*. 2011 May-Jun;38(3):175-85.
22. Bennett MH, Lehm JP, Jepson N. Hyperbaric oxygen therapy for acute coronary syndrome. *Cochrane Database of Systematic Reviews* 2015, Issue 7. Art. No.: CD004818. DOI: 10.1002/14651858.CD004818.pub4.

### **Altitude Sickness**

23. Kasic J, Yaron M, Nicholas R, Lickteig J, Roach R. Treatment of acute mountain sickness: hyperbaric versus oxygen therapy. *Annals of Emergency Medicine*. 1991;20:1109-1112.
24. Bartsch P, Merki B, Hofstetter D, Maggiorini M, Kayser B, Oelz O. Treatment of acute mountain sickness by simulated descent: a randomised controlled trial. *British Medical Journal*. 1993;306:1098-1101.
25. Kayser B, Jean D, Herry JP. Pressurization and acute mountain sickness. *Aviation Space and Environmental Medicine*. 1993;64(10):928-37.

### **Audiovestibular**

26. Goto F, Fujita T, Kitoni Y, Kanno M, Kamei T, Ishii H. Hyperbaric oxygen and stellate ganglion blocks for idiopathic sudden hearing loss. *Acta Otolaryngol*. 1979;88:335-342.
27. Pilgramm M, Schumann K. Hyperbaric oxygen therapy for acute acoustic trauma. *Archives of Otolaryngology*. 1985;241:247-254.
28. Pilgramm M. Clinical and animal experiment studies to optimise the therapy for acute acoustic trauma. *Scandinavian Audiology (Suppl)*. 1991;34:103-122.
29. Carlson S, Jones J, Brown M, Hess C. Prevention of hyperbaric-associated middle ear barotrauma. *Annals of Emergency Medicine*. 1992;21:1468-1471.
30. Hoffman G, Bohmer D, Desloovere C. Hyperbaric oxygenation as a treatment of chronic forms of inner ear hearing loss and tinnitus. In: Wen-ren Li, pres. *Proceedings of the Eleventh 30. International Congress on Hyperbaric Medicine* (Fuzhou, China). Flagstaff, Arizona: Best Publishing Co.; 1993. Pp.146-152.
31. Hoffman G, Bohmer D, Desloovere C. Hyperbaric oxygenation as a treatment of chronic forms of inner ear hearing loss and tinnitus (abstract). In: Wen-ren Li, pres. *Proceedings of the Eleventh International Congress on Hyperbaric Medicine* (Fuzhou, China). Flagstaff, Arizona: Best Publishing Co.; 1993. Pp:26-27.
32. Hoffman G, Bohmer D, Desloovere C. Hyperbaric oxygenation as a treatment for sudden deafness and acute tinnitus. In: Wen-ren Li, pres. *Proceedings of the Eleventh International Congress on Hyperbaric Medicine* (Fuzhou, China). Flagstaff, Arizona: Best Publishing Co.; 1993. Pp:141-145.
33. Dauman, R, Poisot D, Cros AM, Zennaro O, Bertrand B, Duclos JY, Esteben D, Milacic M, Boudey, Bebear JP. (Sudden deafness: A randomized comparative study of 2 administration modalities of hyperbaric oxygen therapy combined with naftidrofuryl). *Rev Laryngol Otoal Rhino*. 1993;114(1):53-58.
34. Cavallazzi G, Pignataro L, Capaccio P. Italian experience in hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. In *Proceedings of the International Joint Meeting on Hyperbaric and Underwater Medicine*. Marroni A, Oriani G, Wattel F, eds. Grafica Victoria, Bologna; 1996. Pp:647-649.
35. Schwab B, Flunkert C, Heermann R, Lenarz T. HBO in the therapy of cochlear dysfunctions - first results of a randomized study. Collected manuscripts of XXIV Annual Scientific Meeting of the European Underwater and Baromedical Society, M Gennser, ed. Stockholm; 1998. Pp:40-42.
36. Mutzbauer T, Mueller P, Tetzlaff K, et al. Is eustachian tube ventilatory function (ETVF) impairment after oxygen diving mediated by free radicals? *Undersea and Hyperbaric Medicine* 2000; 27(suppl):16.

37. Fattori B. Sudden hypoacusis treated with hyperbaric oxygen therapy: a controlled study. *Ear, Nose and Throat Journal* 2001;80(9):655-660.
38. Topuz E., Yigit O, Cinar U, Seven H. Should hyperbaric oxygen be added to treatment in idiopathic sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol.* 2004;261:393-396.
39. Phillips JS, Jones SEM. Hyperbaric oxygen as an adjuvant treatment for malignant otitis externa. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD004617.
40. Stiegler P, Matzi V, Lipp C, Kontaxis A, Klemen H, Walch C, Smolle-Jüttner F. Hyperbaric oxygen (HBO2) in tinnitus: influence of psychological factors on treatment results? *Undersea Hyperb Med.* 2006 Nov-Dec;33(6):429-37.
41. Cekin E, Cincik H, Ulubil SA, Gungor A. Effectiveness of hyperbaric oxygen therapy in management of sudden hearing loss. *J Laryngol Otol.* 2009 Jun;123(6):609-12.
42. Cvorovic L, Jovanovic MB, Milutinovic Z, Arsovic N, Djeric D. Randomized prospective trial of hyperbaric oxygen therapy and intratympanic steroid injection as salvage treatment of sudden sensorineural hearing loss. *Otology & Neurotology.* 2013 Aug 1;34(6):1021-6.
43. Ng AW, Muller R, Orton J. Incidence of middle ear barotrauma in staged versus linear chamber compression during hyperbaric oxygen therapy: a double blinded, randomized controlled trial. *Undersea & Hyperbaric Medicine: Journal of the Undersea and Hyperbaric Medical Society, Inc.* 2017;44(2):101-7.
44. Bennett MH, Weibel S, Wasiak J, Schnabel A, French C, Kranke P. Hyperbaric oxygen therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD004954. DOI: 10.1002/14651858.CD004954.pub3.

### **Avascular Necrosis**

45. Vezzani G, Caberti L, Cantadori L, Mordacci M, Nicolopolou A, Pizzola A, Valesi M. Hyperbaric oxygen therapy (HBO<sub>2</sub>) for idiopathic avascular femoral head necrosis (IAFHN): a prospective double-blind randomized trial. *Undersea and Hyperbaric Medicine* 2005; 32(4):272-273.
46. Hsu SL, Wang CJ, Lee MS, Chan YS, Huang CC, Yang KD. Cocktail therapy for femoral head necrosis of the hip. *Arch Orthop Trauma Surg.* 2010 Jan;130(1):23-9. doi: 10.1007/s00402-009-0918-5.
47. Camporesi EM, Vezzani G, Bosco G, Mangar D, Bernasek TL. Hyperbaric oxygen therapy in femoral head necrosis. *J Arthroplasty.* 2010 Sep;25(6 Suppl):118-23.

### **Carbon Monoxide Poisoning**

48. Raphael JC, Elkharrat D, Jars-Guincestre MC, Chastang C, Chasles V, Verken JB, Gajdos P. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet.* 1989;2(8660):414-419.
49. Ducasse JL, Izard PH, Celsis P, Leclercq Ch, Marc-Vergnes JP, Cathala B. Moderate carbon monoxide poisoning: Hyperbaric or normobaric oxygenation? In: Bakker DJ, Schmutz J, eds. *Hyperbaric Medicine Proceedings*, 2nd Swiss Symposium on Hyperbaric Medicine. Basel, Switzerland: Foundation for Hyperbaric Medicine; 1990. Pp:289-297.
50. Ducasse JL, Celsis P, Marc-Vergnes JP. Non-comatose patients with acute carbon monoxide poisoning: Hyperbaric or normobaric oxygenation? *Undersea Hyperbaric Med.* 1995;22(1):9-15.
51. Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: Prevention by treatment with hyperbaric oxygen. *Ann Emerg Med.* 1995;25(4):474-480.
52. Jay GD, Tetz DJ, Hartigan CF, Lane LL, Aghababian RV. Portable hyperbaric oxygen therapy in the emergency department with the modified Gamow bag. *Annals of Emergency Medicine.* 1995;26:707-711.
53. Mathieu D, Wattel F, Mathieu-Nolf M, Durak C, Tempe JP, Bouachour G, Sainty JM. Randomized prospective study comparing the effect of HBO versus 12 hours NBO in non-comatose CO poisoned patients: results of the interim analysis. In: *Proceedings of the International Joint Meeting on Hyperbaric and Underwater Medicine*, Marroni A, Oriani G, Wattel F eds. Grafica Victoria, Bologna; 1996. P:331.
54. Scheinkestel CD, Bailey M, Myles PS, Jones K, Cooper DJ, Millar IL, Tuxen DV. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Medical Journal of Australia.* 1999;170:203-210.
55. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *New England Journal of Medicine.* 2002;347(14):1057-1066.
56. Hampson NB, Dunford RG, Ross DE, Wreford-Brown CE. A prospective, randomized clinical trial comparing two hyperbaric treatment protocols for carbon monoxide poisoning. *Undersea and Hyperbaric Medicine.* 2006;33(1):27-32.

57. Hopkins RO, Weaver LK, Valentine KJ, Mower C, Churchill S, Carlquist J. Apolipoprotein E genotype and response of carbon monoxide poisoning to hyperbaric oxygen treatment. *Am J Respir Crit Care Med.* 2007 Nov 15;176(10):1001-6.
58. Annane D, Chadda K, Gajdos P, Jars-Guincestre M-C, Chevret S, Raphael J-C. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomised controlled trials. *Intensive Care Medicine.* 2011;8658:414-419.
59. Buckley NA, Stanbrook MB, McGuigan MA, Bennett M, Lavonas E. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev.* 2011;(1):CD002041.

### **Cerebral Palsy and Autism**

60. Collet J-P, Vannasse M, Marois P, et al. Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. *Lancet.* 2001;357:582-586.
61. Hardy P, Collet JP, Goldberg J, Ducruet T, Vannasse M, Lambert J, Marois P, et al. Neuropsychological effects of hyperbaric oxygen therapy in cerebral palsy. *Developmental Medicine and Child Neurology.* 2002;44:436-446.
62. Mathai SS, Bansali P, Singh Gill B, Nagpal S, John MJ, Aggarwal H, Bhatt V. Effects of hyperbaric oxygen therapy in children with cerebral palsy. Proceedings of the International Conference on Diving and Hyperbaric Medicine, Barcelona 7-10 September 2005:193-197.
63. Packard M. The Cornell Study. <http://www.netnet.net/mums/>.
64. Rossignol, DA, et al. Hyperbaric treatment for children with autism: a multicenter, randomised, double blind, controlled trial. *BMC Paediatrics.* 2009;9:21.
65. Granpeesheh D, Tarbox J, Dixon D, Wilke A, Allen M, Bradstreet J. Randomized trial of hyperbaric oxygen therapy for children. *Research in Autism Spectrum Disorders.* 2010;4:268-275.
66. Sampanthavivat M, Singkhwa W, Chaiyakul T, Karoonyawanich S, Ajpru H. Hyperbaric oxygen in the treatment of childhood autism: a randomised controlled trial. *Diving Hyperb Med.* 2012 Sep;42(3):128-33.
67. Xiong T, Chen H, Luo R, Mu D. Hyperbaric oxygen therapy for people with autism spectrum disorder (ASD). *Cochrane Database of Systematic Reviews* 2016, Issue 10. Art. No.: CD010922. DOI: 10.1002/14651858. CD010922.pub2

### **Cognitive Performance and Psychology**

68. Boyle E, Aparico A, Canosa F, Owen D, Dash HH. Hyperbaric oxygen and acetazolamide in the treatment of senile cognitive functions. In: Trapp WG, Bannister EW, Davison AJ, Trapp PA, eds. *Proceedings of the Fifth International Hyperbaric Conference.* Burnaby, Canada: Simon Fraser University; 1974. Pp:432-438.
69. Raskin A, Gershon S, Crook T, Sathananthan G, Ferris S. The effects of hyperbaric and normobaric oxygen on cognitive impairment in the elderly. *Archives of General Psychiatry* 1978;35:50-56.
70. Allen KD, Danforth JS, Drabman RS. Videotaped modeling and film distraction for fear reduction in adults undergoing hyperbaric oxygen therapy. *Journal of Consulting and Clinical Psychology.* 1989;57:554-558.
71. Xiao Y, Wang J, Jiang S, Luo H. Hyperbaric oxygen therapy for vascular dementia. *Cochrane Database of Systematic Reviews* 2012, Issue 7. Art. No.: CD009425.
72. Vadas D, Kalichman L, Hadanny A, Efrati S. Hyperbaric Oxygen Environment Can Enhance Brain Activity and Multitasking Performance. *Frontiers in integrative neuroscience.* 2017 Sep 27;11:25.
73. Feng JJ, Li YH. Effects of hyperbaric oxygen therapy on depression and anxiety in the patients with incomplete spinal cord injury (a STROBE-compliant article). *Medicine.* 2017 Jul;96(29).

### **Crush Injury**

74. Bouachour G, Cronier P, Gouello JP, Toulemonde JL, Talha A, Alquier PH. Hyperbaric oxygen therapy in the management of crush injuries: A randomized double-blind placebo-controlled clinical trial. *J Trauma.* 1996;41(2):333-339.
75. Cronier P, Bouachour G, Talha A, Gouello JP, Toulemonde JL, Merienne JF, Alquier P. The effectiveness of hyperbaric oxygen in post-traumatic skin lesions. *Journal of Bone and Joint Surgery – British Volume.* 1997;79(Suppl 1):56.
76. Lindstrom T, Gullichsen K, Lertola K, Niinikoski J. Effects of hyperbaric oxygen therapy on perfusion parameters and transcutaneous oxygen measurements in patients with intramedullary nailed tibial shaft fractures. *Undersea and Hyperbaric Medicine.* 1998;25:87-91.
77. Millar IL, Williamson OD, Cameron PA. Hyperbaric oxygen in lower limb trauma (HOLLT): Designing a randomised controlled multi-centre study. *Undersea and Hyperbaric Medicine.* 2007;34(4):299.

78. Bennett MH, Stanford RE, Turner R. Hyperbaric oxygen therapy for promoting fracture healing and treating fracture non-union. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD004712.

### **Enhancement of Radiotherapy**

79. Cade IS, McEwen JB. Megavoltage radiotherapy in hyperbaric oxygen: A controlled trial. *Cancer*. 1967;20:817-821.
80. Brenk Van den HAS. Hyperbaric oxygen in radiation therapy: Investigations of dose-effect relationships in tumour response and tissue damage. *Am J Roentgenology*. 1968;102:8-26.
81. Van Den Brenk HA. Hyperbaric oxygen in radiation therapy. An investigation of dose-effect relationships in tumour response and tissue damage. *American Journal of Roentgenology*. 1968;102:8-26.
82. Faust DS, Brady LW, Kazem B, Germon PA. Hybaroxia and radiation therapy in carcinoma of the cervix (Stage III and IV): A clinical trial. In: Wada J, Takashi I, eds. *Proceedings of the Fourth International Congress on Hyperbaric Medicine* (Sapporo, Japan). Baltimore: Williams & Wilkins; 1970. Pp:410-414.
83. Henk JM. Hyperbaric oxygen in radiotherapy of head and neck carcinoma. *Clin Radiol*. 1970;21:223-231.
84. Tobin DA, Vermund H. A randomised study of hyperbaric oxygen as an adjunct to regularly fractionated radiation therapy for clinical treatment of advanced neoplastic disease. *Am J Roentgenol Radium Ther Nucl Med*. 1971;3:613-621.
85. Plenk HP. Hyperbaric radiation therapy. Preliminary results of a randomized study of cancer of the urinary bladder and review of the "oxygen experience." *Am J Roentgenol Radium Ther Nucl Med*. 1972;114(1):152-157.
86. Shigematsu Y, Fuchihata, Makino T, Inoue T. Radiotherapy with reduced fraction in head and neck cancer, with special reference to hyperbaric oxygen radiotherapy in maxillary sinus carcinoma (a controlled study). In: Sugahara T, Scott OCA, eds. *Fraction Size in Radiobiology and Radiotherapy*. Tokyo: Igaku Shoin; 1973. Pp:180-187.
87. Dische S. The hyperbaric oxygen chamber in the radiotherapy of carcinoma of the uterine cervix. *Br J Radiol*. 1974. Pp:99-107.
88. Glassburn JR, Damsker JI, Brady LW, Faust DS, Antoniades J, Prasavinichai S, Lewis GC, Torpie RJ, Asbell SO. Hyperbaric oxygen and radiation treatment of advanced cervical cancer. *Proceedings of the Fifth International Hyperbaric Congress*. Simon Fraser University; 1974. Pp:813-819.
89. Chang CH, Conley JJ, Herbert C. Radiotherapy of advanced carcinoma of the oropharyngeal region under hyperbaric oxygenation. *Am J Roentgenol Radium Ther Nucl Med*. 1975;117(3):509-516.
90. Fletcher GH, Lindberg RD, Carderao JB, Wharton JT. Hyperbaric oxygen as a radiotherapeutic adjuvant in advanced cancer of the uterine cervix: Preliminary results of a randomized trial. *Cancer*. 1977;39(2):617-23.
91. Henk JM, Smith CW. Radiotherapy and hyperbaric oxygen in head and neck cancer. Interim report of second clinical trial. *Lancet*. 1977;8029(2):104-105.
92. Henk JM, Kunkler PB, Smith CW. Radiotherapy and hyperbaric oxygen in head and neck cancer: Final report of first controlled clinical trial. *Lancet*. 1977;8029(2):101-103.
93. Perrins D, Wiernik G. The medical research council's working party on radiotherapy and hyperbaric oxygen. Controlled trials in carcinoma of the bladder. *Br J Radiol*. 1978;51(611):876-878.
94. Watson ER, Halnan KE. Hyperbaric oxygen and radiotherapy: A medical research council trial in carcinoma of the cervix. *Br J Radiol*. 1978;51:879-887.
95. Cade IS, Dische S, Watson ER, Wiernik G, Sutherland I. Hyperbaric oxygen and radiotherapy: a medical research council trial in carcinoma of the bladder. *Br J Radiol*. 1978; 51:876-878.
96. Cade IS, McEwen JB, Dische S, Saunders MI, Watson ER, Halnan KE, Wiernik G, Perrins DJD, Sutherland I. Hyperbaric oxygen and radiotherapy: A medical research council trial in carcinoma of the bladder. *Br J Radiol*. 1978;51(611):876-878.
97. Cade IS, McEwen JB. Clinical trials of radiotherapy in hyperbaric oxygen at Portsmouth (1964-1976). *1978;29:333-338*.
98. Ward AJ, Dixon B. Carcinoma of the cervix: Results of a hyperbaric oxygen trial associated with the use of the cathetron. *Clin Radiology*. 1979;30(4):383-387.
99. Berry GH, Dixon B, Ward AJ. The leeds results of radiotherapy in HBO for carcinoma of the head and neck. *Clin Radiol*. 1979;30:591-592.
100. Sause WT, Plenk HP. Radiation therapy of head and neck tumours: a randomised study of treatment in air vs. treatment in hyperbaric oxygen. *International Journal of Radiation Oncology, Biology and Physics*. 1979;5:1833-1836.
101. Brady Lw, Plenk HP; Hanley JA, Glassburn JR, Kramer S, Parker RG. Hyperbaric oxygen for carcinoma of the cervix - stages IIB, IIIB and IVA: Results of a randomized study by the radiation therapy oncology group. *Int J Radiation Oncology Biol Phys* 1981;7(8):991-998.

102. Henk JM. Late results of a trial of hyperbaric oxygen and radiotherapy in head and neck cancer: A rationale for hypoxic cell sensitizers? *Int J Radiat Oncol Biol Phys.* 1986;12(8):1339-1341.
103. Sealy R, Cridland S, Barry L. Irradiation with misonidazole and hyperbaric oxygen: Final report on a randomized trial in advanced head and neck cancer. *Int J Radiat Oncol Biol Phys.* 1986;12(8):1343-1346.
104. Dische S, Saunders M, Sealy R, Werner I, Verma N, Foy C, Bentzen S. Carcinoma of the cervix and the use of hyperbaric oxygen with radiotherapy: a report of a randomised controlled trial. *Radiotherapy and Oncology.* 1999;53:93-98.
105. Haffty BG, Peters LJ. Radiation therapy with hyperbaric oxygen at 4 atmospheres pressure in the management of squamous cell carcinoma of the head and neck: results of a randomized clinical trial. *The Cancer Journal from Scientific American,* 1999;5:341-347.
106. Bennett MH, Feldmeier J, Smee R, Milross C. Hyperbaric oxygenation for tumour sensitisation to radiotherapy. *Cochrane Database of Systematic Reviews* 2018, Issue 4. Art. No.: CD005007. DOI: 10.1002/14651858.CD005007.pub4.

## **Headache**

107. Fife CE, Meyer JS, Berry JM. Hyperbaric oxygen and acute migraine pain: Preliminary results of a randomized blinded trial. *Undersea Biomed Res.* 1992;19(5):106-107.
108. Hill RK. A blinded, cross-over controlled study on the use of hyperbaric oxygen in the treatment of migraine headache. *Undersea Biomed Res.* 1992;19(5):106.
109. Myers DE, Myers RAM. A preliminary report on hyperbaric oxygen in the relief of migraine headache. *Headache.* 1995;35:197-199.
110. Wilson JR, Foresman BH, Gamber RG, Wright T. Hyperbaric oxygen in the treatment of migraine with aura. *Headache.* 1998;38:112-115.
111. Nilsson Remahl AIM, Ansjon R, Lind F, Waldenlind E. Hyperbaric oxygen treatment of active cluster headache: a double-blind placebo-controlled cross-over study. *Cephalgia.* 2002; 22:730-739.
112. Eftedal OS, Lydersen S, Helde G, White L, Brubakk AO, Stovner LJ. A randomised, double-blind study of the prophylactic effect of hyperbaric oxygen therapy on migraine. *Cephalgia.* 2004; 24:639-644.
113. Bennett MH, French C, Schnabel A, Wasiak J, Kranke P, Weibel S. Normobaric and hyperbaric oxygen therapy for the treatment and prevention of migraine and cluster headache. *Cochrane Database of Systematic Reviews* 2015, Issue 12. Art. No.: CD005219. DOI: 10.1002/14651858.CD005219.pub3.

## **Inflammatory and Autoimmune Clinical Conditions**

114. Racic G, Denoble PJ, Sprem N, Bojic L, Bota B. Hyperbaric oxygen as a therapy of Bell's palsy. *Undersea and Hyperbaric Medicine.* 1997;24:35-38.
115. Van Hoof E, Coomans D, De Becker P, Meeusen R, Cluydts R, De Meirlier K. Hyperbaric therapy in chronic fatigue syndrome. *Journal of the Chronic Fatigue Syndrome.* 2003;11(3):37-49.
116. Yildiz S, Kiralp MZ, Akin A, Keskin, I, Ay H, Dursun H, Cimsit M. A new treatment modality for fibromyalgia syndrome: hyperbaric oxygen therapy. *Journal of International Medical Research.* 2004;32: 263-267.
117. van Ophoven A, Rossbach G, Pajonk F, Hertle L. Safety and efficacy of hyperbaric oxygen therapy for the treatment of interstitial cystitis a randomised, sham controlled, double blind trial. *Journal of Urology.* 2006;176:1442-1446.
118. Holland NJ, Bernstein JM, Hamilton JW. Hyperbaric oxygen therapy for Bell's palsy. *Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No.: CD007288.
119. Pagoldh M, Hultgren E, Arnell P, Eriksson A. Hyperbaric oxygen therapy does not improve the effects of standardized treatment in a severe attack of ulcerative colitis: a prospective randomized study. *Scandinavian journal of gastroenterology.* 2013 Sep 1;48(9):1033-40.
120. Gallego-Vilar D, García-Fadrique G, Povo-Martin I, Salvador-Marin M, Gallego-Gomez J. Maintenance of the response to dimethyl sulfoxide treatment using hyperbaric oxygen in interstitial cystitis/painful bladder syndrome: a prospective, randomized, comparative study. *Urologia internationalis.* 2013;90(4):411-6.
121. Efrati S, Golan H, Bechor Y, Faran Y, Daphna-Tekoah S, Sekler G, Fishlev G, Ablin JN, Bergan J, Volkov O, Friedman M. Hyperbaric oxygen therapy can diminish fibromyalgia syndrome—prospective clinical trial. *PloS one.* 2015 May 26;10(5):e0127012.

## **Miscellaneous**

122. Hutchinson JH, Kerr MM, Inall JA, Shanks RA. Controlled trials of hyperbaric oxygen and tracheal intubation in asphyxia neonatorum. *Lancet.* 1966;7444:935-939.

123. Allen KD, Danforth JS, Drabman RS. Videotaped modeling and film distraction for fear reduction in adults undergoing hyperbaric oxygen therapy. *Journal of Consulting and Clinical Psychology*. 1989;57:554-558.
124. Verrizo G, Coppola L, Luongo C, Sammartino A, Giunta R, Grassia A, Ragone R, Tirelli A. Hyperbaric oxygen, oxygen-ozone therapy, and rheological parameters of blood in patients with peripheral occlusive arterial disease. *Undersea and Hyperbaric Medicine*. 1995; 22:17-22.
125. Kiralp MZ, Yildiz S, Vural D, Keskin I, Ay H, Dursun H. Effectiveness of hyperbaric oxygen therapy in the treatment of complex regional pain syndrome. *The Journal of International Medical Research*. 2004; 32:258-262.
126. Risberg J, Englund M, Aanderud L, Eftedal O, Flook V, Thorsen E. Venous gas embolism in chamber attendants after hyperbaric exposure. *Undersea Hyperb Med*. 2004 Winter;31(4):417-29.
127. Levett D, Bennett MH, Millar I. Adjunctive hyperbaric oxygen for necrotizing fasciitis (Protocol). *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD007937.
128. Nogueira-Filho GR, Rosa BT, David-Neto JR. Effects of hyperbaric oxygen therapy on the treatment of severe cases of periodontitis. *Undersea Hyperb Med*. 2010 Mar-Apr;37(2):107-14.
129. Xiong T, Li H, Zhao J, Dong W, Qu Y, Wu T, Mu D. Hyperbaric oxygen for term newborns with hypoxic ischemic encephalopathy (Protocol). *Cochrane Database of Systematic Reviews* 2011, Issue 8. Art. No.: CD009248.
130. Wu Z, Cai J, Chen J, Huang L, Wu W, Luo F, Wu C, Liao L, Tan J. Autologous bone marrow mononuclear cell infusion and hyperbaric oxygen therapy in type 2 diabetes mellitus: an open-label, randomized controlled clinical trial. *Cytotherapy*. 2014 Feb 1;16(2):258-65.

### **Multiple Sclerosis**

131. Fischer BH, Marks M, Reigh T. Hyperbaric oxygen treatment of multiple sclerosis: A randomized, placebo controlled, double-blind study. *New Engl J Med*. 1983;308:181-186.
132. Wood J, Stell R, Unsworth I, Lance J, Skuse N. A double-blind trial of hyperbaric oxygen in the treatment of multiple sclerosis. *Medical Journal of Australia*. 1985;143:238-241.
133. Erwin CW, Massey EW, Brendle AC. Hyperbaric oxygen influences on the visual evoked potentials in multiple sclerosis patients. *Neurology*. 1985;35(suppl 1):104.
134. Barnes MP, Cartlidge NEF, Bates D, French JM, Shaw DA. Hyperbaric oxygen and multiple sclerosis: Short-term results of a placebo-controlled, double-blind trial. *Lancet*. 1985;1:297-300.
135. Murthy KN, Maurice PB, Wilmeth JB. Double-blind randomized study of hyperbaric oxygen (HBO) versus placebo in multiple sclerosis (MS). *Neurology*. 1985;35(Suppl):104.
136. Nieman J, Nilsson B, Barr P, Perrins D. Hyperbaric oxygen in chronic progressive multiple sclerosis: visual evoked potentials and clinical effects. *Journal of Neurology, Neurosurgery and Psychiatry*. 1985;48:497-500.
137. Slater GE, Anderson DA, Sherman R, Ettinger MG, Haglin J, Hitchcock C. Hyperbaric oxygen and multiple sclerosis: a double-blind, controlled study. *Neurology*. 1985;35(Suppl 1):315.
138. Wiles CM, Clarke CRA, Irwin HP, Edgar EF, Swan AV. Hyperbaric oxygen in multiple sclerosis: A double blind trial. *Br Med J*. 1986;292(6517):367-371.
139. Confavreux C, Mathieu C, Chacornac R, Aimard G, Devic M. Hyperbaric oxygen in multiple sclerosis. A double-blind randomised placebo-controlled study. *La Presse Medicale*. 1986;15:1319-1322.
140. L'Hermitte F, Roullet E, Lyon-Caen O, et al. Hyperbaric oxygen treatment of chronic multiple sclerosis. Results of a placebo-controlled, double-blind study in 49 patients. *Revue de Neurologie*. 1986;142:201-206.
141. Harpur GD, Suke R, Bass BH. Hyperbaric oxygen therapy in chronic stable multiple sclerosis: double-blind study. *Neurology*. 1986;36:988-991.
142. Barnes MP, Bates D, Cartlidge NEF, French JM, Shaw DA. Hyperbaric oxygen and multiple sclerosis: Final results of a placebo-controlled, double-blind trial. *J Neurol Neurosurg Psychiatry*. 1987;50:1402-1406.
143. Worthington JA, DeSouza LH, Forti A. A double-blind controlled cross-over trial investigating the efficacy of hyperbaric oxygen in patients with multiple sclerosis. In: Rose FS, Jones R, eds. *Multiple Sclerosis: Immunological, Diagnostic and Therapeutic Aspects*. London: John Libbey Publications;1987.
144. Hart G, Rowe MJ, Myers LW. A controlled study of hyperbaric oxygen treatment in multiple sclerosis. *J Hyperbaric Med*. 1987;2(1):1-5.
145. Massey EW, Shelton DL, Greenberg J, Wewin W, Saltzman H, Bennett PB. Hyperbaric oxygen in multiple sclerosis: Double blind crossover study of 18 patients. *Neurology*. 1985;35(Suppl. 1):104. (Also in: Bove AA, Bachrach AJ, Greenbaum LJ, Jr., eds. *9th International Symposium on Underwater and Hyperbaric Physiology*. Bethesda, Maryland: Undersea and Hyperbaric Medical Society;1987. Pp:859-857.)
146. Oriani G, Barbieri S, Cislaghi G. Long-term hyperbaric oxygen in multiple sclerosis: A placebo-controlled, double-blind trial with evoked potentials studies. *J Hyperbaric Med*. 1990;5(4):237-245.

147. Oriani G, Magni R, Musini A, Meazza D, Brancato R. A new electrophysiological test to assess ophthalmological benefits of hyperbaric therapy. Proceedings of the 10th International Congress on Hyperbaric Medicine, Amsterdam. Best Publishing, Flagstaff, Arizona; 1992.Pp:104-109.
148. Bennett MH, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD003057.

## Ophthalmology

149. Bojic L, Kovacevic H, Gosavic S, Denoble P. The effect of hyperbaric oxygen on glaucoma: A prospective study. In: Bakker DJ, Schmutz J, eds. Hyperbaric Medicine Proceedings, 2nd Swiss Symposium on Hyperbaric Medicine. Basel, Switzerland: Foundation for Hyperbaric Medicine;1990. Pp:273-275.
150. Oriani G, Magni R, Musini A, Meazza D, Brancato R. A new electrophysiological test to assess ophthalmological benefits of hyperbaric therapy. In: Bakker DJ, Cramer FS, Kley AJvd, van Merkesteyn JPR, eds. Proceedings of the Tenth International Congress on Hyperbaric Medicine (Amsterdam, Netherlands), Flagstaff, Arizona: Best Publishing Co.;1990. Pp:104-109.
151. Recupero SM, Cruciani F, Picardo V, Sposito PA, Tamanti N, Abdolrahimzadeh S. Hyperbaric oxygen therapy in the treatment of secondary keratoendotheliosis. Ann Ophthalmol. 1992;24(12):448-452.
152. Bojic L, Kovacevic H, Andric d, Romanovic D, Petri NM. Hyperbaric oxygen dose of choice in the treatment of glaucoma. Arh Hig Rada Toksikol .1993;44(3):239-247.
153. Bojic L, Racic G, Gosovic S. The effect of hyperbaric oxygen breathing on the visual field in glaucoma. Acta Ophthalmol. 1993;71:315-319.
154. Vingolo E, Pelaia, Forte R, Rocco M, Giusti C, Rispoli E. Does hyperbaric oxygen (HBO) delivery rescue retinal photoreceptors in retinitis pigmentosa? Documenta Ophthalmologica; 1999;97:33-39.
155. Jalabi MW, Abidia A, Kuhan G. The safety and effect of hyperbaric oxygen therapy in patients with diabetic retinopathy - a double-blind randomised-controlled trial. Undersea and Hyperbaric Medicine. 2001;28(suppl):57.
156. Rozenek R, Brennan FF, Banks JC, Russo AC, Lacour MG, Strauss MB. Does hyperbaric oxygen exposure affect high-intensity, short-duration exercise performance? Journal of Strength and Conditioning Research. 2007;21(4):1037-1041.

## Physiology and Pharmacology

157. Merritt GJ, Slade JB. Influence of hyperbaric oxygen on the pharmacokinetics of single-dose gentamicin in healthy volunteers. Pharmacotherapy. 1993;13(4):382-385.
158. Peliai P, Rocco M, De Blasi R, Spadetta G, Alampi D, Araimo F, Nicolucci S. Assessment of lipid peroxidation in hyperbaric oxygen therapy: protective role of N-acetylcysteine. Minerva Anestesiologia. 1995;61:133-139.
159. Shupak A, Abramovich A, Adir Y, Goldenberg I, Ramon Y, Halpern P, Ariel A. Effects on pulmonary function of daily exposure to dry or humidified hyperbaric oxygen. Respiratory Physiology.1997;108:241-246.
160. Stephens M, Frey M, Mohler H. Effect of caffeine consumption on tissue oxygen levels during hyperbaric oxygen treatment. Undersea and Hyperbaric Medicine. 1999;26:93-97.
161. Thomas PS, Hakim TS, Trang LQ, Hosain SI, Camporesi EM. The synergistic effect of sympathectomy and hyperbaric oxygen exposure on transcutaneous PO<sub>2</sub> in healthy volunteers. Anesthesia and Analgesia. 1999;88:67-71.
162. Ueno S, Tanabe G, Kihara K, Aoki D, Arikawa K, Dogomori H, Aikou T. Early postoperative hyperbaric oxygen therapy modifies neutrophile activation. Hepato-Gastroenterology. 1999;46:1798-1799.
163. Granowitz EV, Skulsky EJ, Benson RM, Wright J, Garb JL, Cohen ER, Smithline EC, Brown RB. Exposure to increased pressure or hyperbaric oxygen suppresses interferon-gamma secretion in whole blood cultures of healthy humans. Undersea and Hyperbaric Medicine. 2002;29(3):216-225.
164. Muth CM, Glenz Y, Klaus M, Radermacher P, Speit G, Leverve X. Influence of an orally effective SOD on hyperbaric oxygen-related cell damage. Free Radic Res. 2004 Sep;38(9):927-32.
165. Bader N, Bosy-Westphal A, Koch A, Mueller MJ. Influence of vitamin C and E supplementation on oxidative stress induced by hyperbaric oxygen in healthy men. Ann Nutr Metab. 2006;50(3):173-6.
166. Fagher K, Katzman P, Löndahl M. Hyperbaric oxygen therapy reduces the risk of QTc interval prolongation in patients with diabetes and hard-to-heal foot ulcers. Journal of Diabetes and its Complications. 2015 Nov 1;29(8):1198-202.
167. Mutzbauer TS, Schneider M, Neubauer B, Weiss M, Tetzlaff K. Antioxidants may Attenuate Plasma Erythropoietin Decline after Hyperbaric Oxygen Diving. International journal of sports medicine. 2015 Nov;36(13):1035-40.

## **Preconditioning, Postoperative Care and Transplantation**

168. Williamson OD, Millar I, Venturoni C. Hyperbaric oxygen and the management of open tibial fractures. *Journal of Bone and Joint Surgery – British Volume, Orthopaedic proceedings* 2005;88-B(Suppl II):323.
169. Tang X, Yin X, Zhang T, Peng H. The effect of hyperbaric oxygen therapy on clinical outcomes of patients after resection of meningiomas with conspicuous peritumoral brain edema. *Undersea and Hyperbaric Medicine*. 2011;38(2):109-115.
170. Yuan JB, Yang LY, Wang YH, Ding T, Chen TD, Lu Q. Hyperbaric oxygen therapy for recovery of erectile function after posteriorurethral reconstruction. *Int Urol Nephrol*. 2011 Sep;43(3):755-61.
171. Ueno S, Sakoda M, Kurahara H, Iino S, Minami K, Ando K, Mataki Y, Maemura K, Ishigami S, Shinchi H, Natsugoe S. Safety and efficacy of early postoperative hyperbaric oxygen therapy with restriction of transfusions in patients with HCC who have undergone partial hepatectomy. *Langenbecks Arch Surg*. 2011 Jan;396(1):99-106.
172. Eskes A, Vermeulen H, Lucas C, Ubbink DT. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD008059. DOI: 10.1002/14651858.CD008059.pub3.
173. Bosco G, Casarotto A, Nasole E, Camporesi E, Salvia R, Giovinazzo F, Zanini S, Malleo G, Di Tano A, Rubini A, Zanon V. Preconditioning with hyperbaric oxygen in pancreaticoduodenectomy: a randomized double-blind pilot study. *Anticancer research*. 2014 Jun 1;34(6):2899-906.
174. Ravaioli M, Baldassare M, Vasuri F, Pasquinelli G, Laggetta M, Valente S, De VP, Neri F, Siniscalchi A, Zanfi C, Bertuzzo VR. Strategies to Restore Adenosine Triphosphate (ATP) Level After More than 20 Hours of Cold Ischemia Time in Human Marginal Kidney Grafts. *Annals of transplantation*. 2018 Jan;23:34-44.

## **Sham and Blinding**

175. Weaver LK, Hopkins RO, Churchill S, Haberstock D. Double-blinding is possible in hyperbaric oxygen (HBO<sub>2</sub>) randomized clinical trials (RCT) using a minimal chamber pressurization as control (abstract). *Undersea and Hyperbaric Med*. 1997;24(Suppl):36.
176. Abidia A, Kuhan G, Laden G. The placebo effect of hyperbaric oxygen therapy- fact or fiction? *Undersea and Hyperbaric Medicine*. 2001;28(suppl):57-58.
177. Jansen T, Mortensen CR, Tvede MF. It is possible to perform a double-blind hyperbaric session: a double-blinded randomized trial performed on healthy volunteers. *Undersea Hyperb Med*. 2009 Sep-Oct;36(5):347-51.
178. Weaver LK, Churchill SK, Bell J, Deru K, Snow GL. A blinded trial to investigate whether 'pressure-familiar' individuals can determine chamber pressure. *Undersea Hyperb Med*. 2012 Jul-Aug;39(4):801-5.

## **Sports and Athletic Performance**

179. Cabric M, Medved R, Denoble P, Zivkovic M, Kovacevic H. Effect of hyperbaric oxygenation on maximal aerobic performance in a normobaric environment. *Journal of Sports Medicine and Physical Fitness*. 1991;31:362-366.
180. Soolsma SJ, Clement DB, Connell DC, McKenzie DC, Taunton JB, Staples JR, Logan MA, Davidson RD. The effect of intermittent hyperbaric oxygen on short term recovery from grade II medial collateral injuries. Allan McGavin Sports Medicine Centre, Vancouver BC, Canada. 1995.
181. Borromeo CN, Ryan JL, Marchetto PA, Peterson R, Bove AA. Hyperbaric oxygen therapy for acute ankle sprains. *American Journal of Sports Medicine*. 1997;25:619-625.
182. Borer RC, Rozenek R, Russo AC, Strauss MB. Delayed onset of muscle soreness, neutrophil inflammatory response and hyperbaric oxygen therapy. *Undersea and Hyperbaric Medicine*. 1999 (Suppl); 26:12.
183. Staples JR, Clement DB, Taunton JE, McKenzie DC. Effects of hyperbaric oxygen on a human model of injury. *Am Journal of Sports Medicine*. 1999;27:600-605.
184. McGavock J, Lecomte J, Delaney J. Effect of hyperbaric oxygen on aerobic performance in a normobaric environment. *Undersea and Hyperbaric Medicine*. 1999; 26(4):219-224.
185. Mekjavić IB, Exner J, Tesch PA, Eiken O. Hyperbaric oxygen therapy does not affect recovery from delayed onset muscle soreness. *Medicine and Science in Sports and Exercise*. 2000;32:558-563.
186. Harrison BC, Robinson D, Davison BJ, Foley B, Seda E, Byrnes WC. Treatment of exercise-induced muscle injury via hyperbaric oxygen therapy. *Medicine and Science in Sports and Exercise*. 2001;33(1):36-42.
187. Webster AL, Syrotuik DG, Bell GJ, Jones RL, Hanstock CC. Effects of hyperbaric oxygen on recovery from exercise-induced muscle damage in humans. *Clinical Journal of Sport Medicine*. 2002;12:139-150.
188. Babul S, Rhodes EC, Taunton J, Lepawsky M. Effects of intermittent exposure to hyperbaric oxygen for the treatment of acute soft tissue injury. *Clinical Journal of Sports Medicine*. 2003;13:138-147.

189. Germain G, Delaney J, Moore G, Lee P, Lacroix V, Montgomery D. Effect of hyperbaric oxygen therapy on exercise-induced muscle soreness. *Undersea and Hyperbaric Medicine*. 2003;30(2):135-145.
190. Bennett MH, Best TM, Babul-Wellar S, Taunton JE. Hyperbaric oxygen therapy for delayed onset muscle soreness and closed soft tissue injury. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD004713.
191. Shimoda M, Enomoto M, Horie M, Miyakawa S, Yagishita K. Effects of hyperbaric oxygen on muscle fatigue after maximal intermittent plantar flexion exercise. *The Journal of Strength & Conditioning Research*. 2015 Jun 1;29(6):1648-56.
192. Branco BH, Fukuda DH, Andreato LV, da Silva Santos JF, Esteves JV, Franchini E. The effects of hyperbaric oxygen therapy on post-training recovery in jiu-jitsu athletes. *PloS one*. 2016 Mar 9;11(3):e0150517.

## **Stroke**

193. Sarno MT, Sarno JE, Diller L. The effect of hyperbaric oxygen on communication function in adults with aphasia secondary to stroke. *Journal of Speech and Hearing Research*. 1972;15:42-48.
194. Anderson DC, Bottini AG, Jagiella WM, Westphal B, Ford S, Rockswold GL, Leowenson RB. A pilot study of hyperbaric oxygen in the treatment of human stroke. *Stroke* 1991;22(9):1137-1142.
195. Nighoghossian N, Trouillas P, Adeleine P, Salord F. Hyperbaric oxygen in the treatment of acute ischemic stroke. A double-blind pilot study. *Stroke*. 1995;26(8):1369-1372.
196. Sansone A, Gulotta G, Sparacia B, Alongi A, Savoia G, Sparacia GV. Effect of hyperbaric oxygen therapy on neurologic recovery after focal cerebral ischaemia. *British Journal of Anaesthesia*. 1997;78(Suppl 1):73-4.
197. Rusyniak DE, Kirk MA, May JD, et al. Hyperbaric oxygen therapy in acute ischemic stroke. Results of the hyperbaric oxygen in acute ischaemic stroke trial pilot study. *Stroke*. 2003;34:571-574.
198. Imai K, Mori T, Izumoto H, Takabatake N, Kuneida T, Watanabe M. Hyperbaric oxygen combined with intravenous edaravone for treatment of acute embolic stroke: a pilot clinical trial. *Neurological Medicine and Surgery (Tokyo)*. 2006;46:373-378.
199. Tang X-P, et al. Effects of early hyperbaric oxygen therapy on clinical outcome in postoperative patients with intracranial aneurysm. *UHM*. 2011;38(6):493-501.
200. Efrati S, Fishlev G, Bechor Y, Volkov O, Bergan J, et al. Hyperbaric oxygen induces late neuroplasticity in post stroke patients – randomized prospective trial. *PLoS ONE*. 2013;8(1):e53716.
201. Bennett MH, Weibel S, Wasik J, Schnabel A, French C, Kranke P. Hyperbaric oxygen therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD004954. DOI: 10.1002/14651858.CD004954.pub3.
202. Xu Q, Fan SB, Wan YL, Liu XL, Wang L. The potential long-term neurological improvement of early hyperbaric oxygen therapy on hemorrhagic stroke in the diabetics. *Diabetes research and clinical practice*. 2018 Apr 1;138:75-80.

## **Tissue Injury and Chemotherapy**

203. Xin PJ, Miao GC, Zong WC, Rong WS, Min LJ, Yingying C, An ZS, Song LT. The influence of hyperbaric oxygenation on chemotherapy effect in patients with malignant lymphoma. In: Wen-ren Li, pres. *Proceedings of the Eleventh International Congress on Hyperbaric Medicine (Fuzhou, China)*. Flagstaff, Arizona: Best Publishing Co.;1993. Pp:44-47.
204. Heys SD, Smith IC, Ross JA, Gilbert FJ, Brooks J, Semple S, Miller ID, Hutcheon A, Sarker T, Eremin O. A pilot study with long term follow up of hyperbaric oxygen pretreatment in patients with locally advanced breast cancer undergoing neo-adjuvant chemotherapy. *Undersea and Hyperbaric Medicine*. 2006;33(1):33-43.

## **Tissue Injury Due to Radiation and Bisphosphonates**

205. Tobey RE, Kelly JF. Osteoradionecrosis of the jaws. *Otolaryngol Clin North Am*. 1979;12(1):183-186.
206. Marx RE. Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen versus penicillin. *J Am Dent Assoc*. 1985;(III):49-54.
207. Marx RE. Radiation injury to tissue. In: Kindwall EP, ed. *Hyperbaric Medicine Practice*. Flagstaff, Arizona: Best Publishing Co.;1994. Pp:447-503.
208. Hulshof M, Stark N, Van der Kleij A, Sminia P, Smeding M, Gonzalez D. Hyperbaric oxygen therapy for cognitive disorders after irradiation of the brain. *Strahlentherapie und Onkol*. 2001;177:192-8.
209. Pritchard J, Anand P, Broome J, Davis C, Gothard L, Hall E, Maher J, McKinna F, Millington J, Misra VP, Pitkin A, Yarnold JR. Double-blind randomized phase II study of hyperbaric oxygen in patients with radiation-induced brachial plexopathy. *Radiother Oncol* 2001. Mar;58(3):279-86.

210. Denton AS, Andreyev JJ, Forbes A, Maher J. Non surgical interventions for late radiation proctitis in patients who have received radical radiotherapy to the pelvis. Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD003455.
211. Denton AS, Maher J. Interventions for the physical aspects of sexual dysfunction in women following pelvic radiotherapy. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD003750.
212. Annane D, Depondt J, Aubert P, Villart M, Gehanno P, Gajdos P, Chevret S. Hyperbaric oxygen therapy for radionecrosis of the jaw: a randomised, placebo-controlled, double-blind trial from the ORN96 study group. *Journal of Clinical Oncology*. 2004;22(24):1-8.
213. Lewis AL, Hardy KR, Huang ET, Bolotin T, Clark JM, Thom SR. Hyperbaric oxygen therapy decreases gross haematuria and improves quality of life in patients with radiation cystitis. *Undersea and Hyperbaric Medicine*. 2005;32(4):236.
214. Gesell LB, Warnick RE, Brenerman JC, Vogt CJ, Lindsell CJ. A randomized, controlled trial of hyperbaric oxygen therapy for brain radionecrosis. *Undersea and Hyperbaric Medicine*; 2005;32(4): 235-236.
215. Sidik S, Hardjodisastro D, Setiabudy R, Gondowiardjo S. Does hyperbaric oxygen administration decrease side effect and improve quality of life after pelvic radiation? *Acta Med Indones*. 2007;39(4):169-173.
216. Schoen PJ, Raghoobar GM, Bouma J, Reintsema H, Vissink A, Sterk W, Roodenburg JL. Rehabilitation of oral function in head and neck cancer patients after radiotherapy with implant-retained dentures: effects of hyperbaric oxygen therapy. *Oral Oncol*. 2007 Apr;43(4):379-88.
217. Clarke RE, Catalina Tenorio LM, Hussey JR, Toklu AS, Cone DL, Hinojosa JG, et al. Hyperbaric oxygen treatment of chronic refractory radiation proctitis: a randomised and controlled doubleblind crossover trial with long-term follow-up. *International Journal of Radiation Oncology, Biology, Physics*. 2008;72:134-143.
218. Esposito M, Grusovin MG, Patel S, Worthington HV, Coulthard P. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD003603.
219. Teguh DN, Levendag PC, Noever I, Voet P, van der Est H, van Rooij P, Dumans AG, de Boer MF, van der Huls MP, Sterk W, Schmitz PI. Early hyperbaric oxygen therapy for reducing radiotherapy side effects: early results of a randomized trial in oropharyngeal and nasopharyngeal cancer. *Int J Radiat Oncol Biol Phys*. 2009 Nov 1;75(3):711-6.
220. Gothard J, Haviland J, Bryson P. Randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema after radiotherapy for cancer. *Radiotherapy and Oncology*. 2010;97:101-107.
221. Shao Y, Lu GL, Shen ZJ. Comparison of intravesical hyaluronic acid instillation and hyperbaric oxygen in the treatment of radiation-induced hemorrhagic cystitis. *BJU Int*. 2012 Mar;109(5):691-4.
222. Freiberger JJ, Padilla-Burgos R, McGraw T, Suliman HB, Kraft KH, Stolp BW, Moon RE, Piantadosi C. What is the role of hyperbaric oxygen in the management of bisphosphonate-related osteonecrosis of the jaw: a randomized controlled trial of hyperbaric oxygen as an adjunct to surgery and antibiotics. *J Oral Maxillofac Surg*. 2012 Jul;70(7):1573-83.
223. Esposito M, Worthington HV. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD003603. DOI: 10.1002/14651858.CD003603.pub3.
224. Svalestad J, Hellem S, Thorsen E, Johannessen AC. Effect of hyperbaric oxygen treatment on irradiated oral mucosa: microvessel density. *International journal of oral and maxillofacial surgery*. 2015 Mar 1;44(3):301-7.
225. Glover M, Smerdon GR, Andreyev HJ, Benton BE, Bothma P, Firth O, Gothard L, Harrison J, Ignatescu M, Laden G, Martin S. Hyperbaric oxygen for patients with chronic bowel dysfunction after pelvic radiotherapy (HOT<sub>2</sub>): a randomised, double-blind, sham-controlled phase 3 trial. *The Lancet Oncology*. 2016 Feb 1;17(2):224-33.
226. Rollason V, Laverrière A, MacDonald LCI, Walsh T, Tramèr MR, Vogt-Ferrier NB. Interventions for treating bisphosphonate-related osteonecrosis of the jaw (BRONJ). Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD008455. DOI: 10.1002/14651858.CD008455.pub2.
227. Bennett MH, Feldmeier J, Hampson NB, Smee R, Milross C. Hyperbaric oxygen therapy for late radiation tissue injury. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD005005. DOI: 10.1002/14651858.CD005005.pub4.

## Traumatic Brain Injury

228. Holbach KH, Wassman H, Kolberg T. Improved reversibility of the traumatic mid-brain syndrome following the use of hyperbaric oxygen. *Acta Neurochirurgica*. 1974;30:247-256.
229. Artru F, Chacornac R, Deleuze R. Hyperbaric oxygenation for severe head injuries. Preliminary results of a controlled study. *European Neurology*. 1976;14:310-318.

230. Rockswold GL, Ford SE. Preliminary results of a prospective randomized trial of treatment of severely brain-injured patients with hyperbaric oxygen. *Minn Med.* 1985;68:533-535.
231. Rockswold GL, Ford SE, Anderson DC, Bergman TA, Sherman RE. Results of a prospective randomized trial for treatment of severely brain-injured patients with hyperbaric oxygen. *J Neurosurg.* 1992;76(6):929-934.
232. Ren H, Wang W, Ge Z. Glasgow coma scale, brain electrical activity mapping and Glasgow outcome scale after hyperbaric oxygen treatment of severe brain injury. *Chinese Journal of Traumatology.* 2001;4(4):239-241.
233. Shi X, Tang Z, Xiong B, Bao J, Sun D, Zhang Y, Yao Y. Cerebral perfusion SPECT imaging for assessment of the effect of hyperbaric oxygen therapy on patients with postbrain injury neural status. *Chinese Journal of Traumatology.* 2003;6(6):346-349.
234. Xie Z, Zhuang M, Lin L, Xu H, Chen L, Hu, L. Changes of plasma C-reactive protein in patients with craniocerebral injury before and after hyperbaric oxygenation: a randomly controlled study. *Neural Regeneration Research.* 2007;2(5):314-317.
235. Lin JW, Tsai JT, Lee LM, Lin CM, Hung CC, Hung KS, Chen WY, Wei L, Ko CP, Su YK, Chiu WT. Effect of hyperbaric oxygen on patients with traumatic brain injury. *Acta Neurochirurgica.* 2008;101(Supplement):145-149.
236. Rockswold SB, Rockswold GL, Zaun DA, Zhang X, Cerra CE, Bergman TA, Liu J. A prospective, randomized clinical trial to compare the effect of hyperbaric to normobaric hyperoxia on cerebral metabolism, intracranial pressure, and oxygen toxicity in severe traumatic brain injury. *Journal of Neurosurgery.* 2010;112:1080-1094.
237. Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. *Cochrane Database of Systematic Reviews* 2012, Issue 12. Art. No.: CD004609.
238. Wolf G, Cifu D, Baugh L, Carne W, Profenna L. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. *Journal of Neurotrauma.* 2012. Pp:2606-2612.
239. Weaver LK, Cifu D, Hart B, Wolf G, Miller S. Hyperbaric oxygen for post-concussion syndrome: design of Department of Defense clinical trials. *Undersea Hyperb Med.* 2012 Jul-Aug;39(4):807-14.
240. Rockswold SB, Rockswold GL, Zaun DA, Liu J. A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury. *Journal of neurosurgery.* 2013 Jun;118(6):1317-28.
241. Boussi-Gross R, Golan H, Fishlev G, Bechor Y, Volkov O, Bergan J, Friedman M, Hoofien D, Shlamkovich N, Ben-Jacob E, Efrati S. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury-randomized prospective trial. *PloS one.* 2013 Nov 15;8(11):e79995.
242. Cifu DX, Walker WC, West SL, Hart BB, Franke LM, Sima A, Graham CW, Carne W. Hyperbaric oxygen for blast-related postconcussion syndrome: Three-month outcomes. *Annals of neurology.* 2014 Feb 1;75(2):277-86.
243. Wares JR, Cifu DX, Hoke KW, Wetzel PA, Gitchel G, Carne W. Effects of hyperbaric oxygen on eye tracking abnormalities in males after mild traumatic brain injury. *Journal of rehabilitation research and development.* 2014;51(7):1047.
244. Walker WC, Franke LM, Cifu DX, Hart BB. Randomized, Sham-controlled, feasibility trial of hyperbaric oxygen for service members with postconcussion syndrome: cognitive and psychomotor outcomes 1 week postintervention. *Neurorehabilitation and neural repair.* 2014 Jun;28(5):420-32.
245. Miller RS, Weaver LK, Bahraini N, Churchill S, Price RC, Skiba V, Caviness J, Mooney S, Hetzell B, Liu J, Deru K. Effects of hyperbaric oxygen on symptoms and quality of life among service members with persistent postconcussion symptoms: a randomized clinical trial. *JAMA internal medicine.* 2015 Jan 1;175(1):43-52.
246. Wolf EG, Baugh LM, Kabban CM, Richards MF, Prye J. Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial. School of Aerospace Medicine Wright Patterson AFB OH Aerospace Medicine Dept; 2015 Aug 7.
247. Weaver LK, Chhoeu A, Lindblad AS, Churchill S, Wilson SH. Hyperbaric oxygen for mild traumatic brain injury: Design and baseline summary. *Undersea & hyperbaric medicine: journal of the Undersea and Hyperbaric Medical Society, Inc.* 2016;43(5):491-509.
248. Weaver LK, Chhoeu A, Lindblad AS, Churchill S, Deru K, Wilson SH. Executive summary: The Brain Injury and Mechanism of Action of Hyperbaric Oxygen for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (mTBI)(BIMA) Study. *Undersea & hyperbaric medicine: journal of the Undersea and Hyperbaric Medical Society, Inc.* 2016;43(5):485-9.
249. Churchill S, Miller RS, Deru K, Wilson SH, Weaver LK. Simple and procedural reaction time for mild traumatic brain injury in a hyperbaric oxygen clinical trial. *Military medicine.* 2016 May 1;181(suppl\_5):40-4.

## **Wound Healing**

250. Perrins DJD. Influence of hyperbaric oxygen on the survival of split skin grafts. *Lancet.* 1967;1:868-871.
251. Doctor N, Pandya S, Supe A. Hyperbaric oxygen therapy in diabetic foot. *J Postgrad Med.* 1992;38(3):112-114.
252. Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: A randomized double-blind study. *Plast Reconstr Surg.* 1994;93(4):829-834.
253. Faglia E, Favales F, Aldeghi A, Calia P, Quarantiello A, Oriani G, Michael M, Campagnoli P, Morabito A. Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer: A randomized study. *Diabetes Care.* 1996;19(12):1338-1343.
254. Abidia A, Laden G, McCollum P. Hyperbaric oxygen therapy improves reflex vasoconstriction induced by leg dependency in patients with diabetic neuropathy. *Undersea and Hyperbaric Medicine.* 2000;27(suppl):44.
255. Chin K, Xie Y, Abidia A, Laden G, Greenman J, Monson J, Grout P, McCollum P. The relationship of hyperbaric oxygen therapy and vascular endothelial growth factor in diabetic patients with leg ulcers: a double-blind randomised controlled trial. *Undersea and Hyperbaric Medicine.* 2001;28(Suppl):63.
256. Lin TF, Chen SB, Niu KC. The vascular effects of hyperbaric oxygen therapy in treatment of early diabetic foot. *Undersea and Hyperbaric Medicine.* 2001;28 (Suppl):67.
257. Kalani M, Jorneskog G, Naderi N, Lind F, Brisimar K. Hyperbaric oxygen (HBO) therapy in treatment of diabetic foot ulcers. Long term follow-up. *Journal of Diabetes and its Complications.* 2002;16:153-158.
258. Kessler L, Bilbault P, Ortega F, Grasso C, Passemard R, Stephan D, Pinget M, Schneider F. Hyperbaric oxygenation accelerates the healing rate of nonischemic chronic diabetic foot ulcers. *Diabetes Care.* 2003;26:2378-82.
259. Sun TB, Yang CC, Kuo TB. Effect of hyperbaric oxygen on cardiac neural regulation in diabetic individuals with foot complications. *Diabet Med.* 2006 Apr;23(4):360-6.
260. Duzgun AP, Satir HZ, Ozozan O, Saylam B, Kulah B, Coskun F. Effect of hyperbaric oxygen therapy on healing of diabetic foot ulcers. *J Foot Ankle Surg.* 2008 Nov-Dec;47(6):515-9.
261. Alleva R, Tomasetti M, Sartini D, Emanuelli M, Nasole E, Di Donato F, Borghi B, Santarelli L, Neuzil J. Alpha-lipoic acid modulates extracellular matrix and angiogenesis gene expression in non-healing wounds treated with hyperbaric oxygen therapy. *Mol Med.* 2008 Mar-Apr;14(3-4):175-83.
262. Efrati S, Gall N, Bergan J, Fishlev G, Bass A, Berman S, Hamad-Abu R, FeigenzonM, Weissgarten J. Hyperbaric oxygen, oxidative stress, NO bioavailability and ulcer oxygenation in diabetic patients. *Undersea Hyperb Med.* 2009 Jan-Feb;36(1):1-12.
263. Londahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. *Diabetes Care.* 2010;33(5):998-1003.
264. Chong SJ, Kwan TM, Weihao L, Joang KS, Rick SC. Maintenance of negative-pressure wound therapy while undergoing hyperbaric oxygen therapy. *Diving Hyperb Med.* 2011 Sep;41(3):147-50.
265. O'Reilly D, Linden R, Fedorko L, Tarride JE, Jones WG, Bowen JM, Goeree R. A prospective, double-blind, randomized, controlled clinical trial comparing standard wound care with adjunctive hyperbaric oxygen therapy (HBOT) to standard wound care only for the treatment of chronic, non-healing ulcers of the lower limb in patients with diabetes mellitus: a study protocol. *Trials.* 2011 Mar 7;12:69.
266. Wang CJ, Wu RW, Yang YJ. Treatment of diabetic foot ulcers: a comparative study of extracorporeal shock wave therapy and hyperbaric oxygen therapy. *Diabetes Res Clin Pract.* 2011 May;92(2):187-93.
267. Löndahl M, Katzman P, Hammarlund C, Nilsson A, Landin-Olsson M. Relationship between ulcer healing after hyperbaric oxygen therapy and transcutaneous oximetry, toe blood pressure and ankle-brachial index in patients with diabetes and chronic foot ulcers. *Diabetologia.* 2011 Jan;54(1):65-8.
268. Kaur S, Pawar M, Banerjee N, Garg R. Evaluation of the efficacy of hyperbaric oxygen therapy in the management of chronic nonhealing ulcer and role of periwound transcutaneous oximetry as a predictor of wound healing response: A randomised prospective controlled trial. *Journal of Anaesthesia and Clinical Pharmacology.* 2012;28(1):70-75.
269. Igor S, Mirko T, Dalibor P, Milutin R, Dusica D, Vladimir Z, Vladimir J. Hyperbaric oxygenation accelerates prosthetic rehabilitation of lower limb amputees. *Undersea Hyperb Med.* 2013 May 1;40:289-97.
270. Kranke P, Bennett MH, Martyn-St James M, Schnabel A, Debus SE, Weibel S. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database of Systematic Reviews* 2015, Issue 6. Art. No.: CD004123. DOI: 10.1002/14651858.CD004123.pub4.
271. Ersoz F, Arikan S, Sari S, Korpinar S, Ozcan O, Poyraz B, Purisa S, Toklu AS. Effect of hyperbaric oxygen treatment on pilonidal disease surgery. *Undersea & hyperbaric medicine: journal of the Undersea and Hyperbaric Medical Society, Inc.* 2016 Nov 1;43(7):821-5.

272. Fedorko L, Bowen JM, Jones W, Oreopoulos G, Goeree R, Hopkins RB, O'Reilly DJ. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. *Diabetes Care*. 2016 Mar 1;39(3):392-9.
273. Yildiz H, Senol L, Ercan E, Bilgili ME, Karabudak Abuaf O. A prospective randomized controlled trial assessing the efficacy of adjunctive hyperbaric oxygen therapy in the treatment of hidradenitis suppurativa. *International journal of dermatology*. 2016 Feb 1;55(2):232-7.
274. Chen CY, Wu RW, Hsu MC, Hsieh CJ, Chou MC. Adjunctive Hyperbaric Oxygen Therapy for Healing of Chronic Diabetic Foot Ulcers: A Randomized Controlled Trial. *Journal of Wound Ostomy & Continence Nursing*. 2017 Nov 1;44(6):536-45.
275. Zhao D, Luo S, Xu W, Hu J, Lin S, Wang N. Efficacy and Safety of Hyperbaric Oxygen Therapy Used in Patients With Diabetic Foot: A Meta-analysis of Randomized Clinical Trials. *Clinical therapeutics*. 2017 Oct 1;39(10):2088-94.
276. Li G, Hopkins RB, Levine MA, Jin X, Bowen JM, Thabane L, Goeree R, Fedorko L, O'Reilly DJ. Relationship between hyperbaric oxygen therapy and quality of life in participants with chronic diabetic foot ulcers: data from a randomized controlled trial. *Acta diabetologica*. 2017 Sep 1;54(9):823-31.
277. Santema KT, Stoekenbroek RM, Koelemay MJ, Reekers JA, van Dortmont LM, Oomen A, Smeets L, Wever JJ, Legemate DA, Ubbink DT. Hyperbaric Oxygen Therapy in the Treatment of Ischemic Lower-Extremity Ulcers in Patients With Diabetes: Results of the DAMO2CLES Multicenter Randomized Clinical Trial. *Diabetes care*. 2018 Jan 1;41(1):112-9.

# **Chapter 19: Hyperbaric Oxygen for Symptoms Following Mild Traumatic Brain Injury**

*Lindell K. Weaver MD*

## **REFERENCES**

1. Zaloshnja E, Miller T, Langlois JA, Selassie AW. Prevalence of long-term disability from traumatic brain injury in the civilian population of the United States, 2005. *J Head Trauma Rehabil.* 2008 Nov-Dec;23(6):394-400.
2. Crawford C, Teo L, Yang E, Isbister C, Berry K. Is hyperbaric oxygen therapy effective for traumatic brain injury? A rapid evidence assessment of the literature and recommendations for the field. *J Head Trauma Rehabil.* 2017 May/Jun;32(3):E27-E37.
3. Peterson K, Bourne D, Anderson J, Boundy E, Helfand M. Evidence brief: hyperbaric oxygen therapy (HBOT) for traumatic brain injury and/or post-traumatic stress disorder. Portland, OR: Evidence-Based Synthesis Program (ESP), Portland VA Health Care System; 2018.
4. Weaver LK, Wilson SH, Lindblad AS, et al. Hyperbaric oxygen for post-concussive symptoms in United States military service members: a randomized clinical trial. *Undersea Hyperb Med.* 2018;45(2):129-156.
5. Terrio H, Brenner LA, Ivins BJ, et al. Traumatic brain injury screening: preliminary findings in a US Army Brigade Combat Team. *J Head Trauma Rehabil.* 2009 Jan-Feb;24(1):14-23.
6. Harch PG. The dosage of hyperbaric oxygen in chronic brain injury. In: Joiner JT, editor. The proceedings of the 2nd international symposium on hyperbaric oxygenation for cerebral palsy and the brain-injured child. Flagstaff, AZ: Best Publishing; 2002. Pp. 31-56.
7. Neubauer RA, Gottlieb SF, Pevsner NH. Hyperbaric oxygen for treatment of closed head injury. *South Med J.* 1994 Sep;87(9):933-936.
8. Weaver LK, Cifu D, Hart B, Wolf G, Miller S. Hyperbaric oxygen for post-concussion syndrome: design of Department of Defense clinical trials. *Undersea Hyperb Med.* 2012 Jul-Aug;39(4):807-814.
9. Boussi-Gross R, Golan H, Fishlev G, et al. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury - randomized prospective trial. *PLoS One.* 2013;8(11):e79995.
10. Wolf G, Cifu D, Baugh L, Carne W, Profenna L. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. *J Neurotrauma.* 2012 Nov 20;29(17):2606-2612.
11. Cifu DX, Hart BB, West SL, Walker W, Carne W. The effect of hyperbaric oxygen on persistent postconcussion symptoms. *J Head Trauma Rehabil.* 2014 Jan-Feb;29(1):11-20.
12. Miller RS, Weaver LK, Bahraini N, et al. Effects of hyperbaric oxygen on symptoms and quality of life among service members with persistent postconcussion symptoms: a randomized clinical trial. *JAMA Intern Med.* 2015 Jan;175(1):43-52.
13. Lindblad AS, Weaver LK, Wetzel PA, et al. Eyetracker outcomes in a randomized trial of hyperbaric oxygen or sham in participants with persistent post-concussive symptoms. *Undersea Hyperb Med.* 2017;44(5):441-442.
14. Skipper LD, Churchill S, Wilson SH, Deru K, Labutta RJ, Hart BB. Hyperbaric oxygen for persistent post-concussive symptoms: long-term follow-up. *Undersea Hyperb Med.* 2016;43(5):601-613.
15. Hoge CW, Jonas WB. The ritual of hyperbaric oxygen and lessons for the treatment of persistent postconcussion symptoms in military personnel. *JAMA Intern Med.* 2015 Jan;175(1):53-54.
16. Harch PG. Hyperbaric oxygen therapy for post-concussion syndrome: contradictory conclusions from a study mischaracterized as sham-controlled. *J Neurotrauma.* 2013 Dec 01;30(23):1995-1999.
17. Weaver LK, Churchill SK, Bell J, Deru K, Snow GL. A blinded trial to investigate whether 'pressure-familiar' individuals can determine chamber pressure. *Undersea Hyperb Med.* 2012 Jul-Aug;39(4):801-805.
18. Neubauer R. The effect of hyperbaric oxygen in prolonged coma. Possible identification of marginally functioning brain zones. *Medicina Subacquea ed Iperbarica.* 1985;5(3):75-79.
19. Eltorai I, Monroy R. Hyperbaric oxygen therapy leading to recovery of a 6-week comatose patient afflicted by anoxic encephalopathy posttraumatic edema. *Journal of Hyperbaric Medicine.* 1991;6(3):189-198.
20. Neubauer R, Gottlieb SF. Amelioration of long term head injuries with hyperbaric oxygen-documentation via SPECT brain imaging (abs). *Undersea Biomed Res.* 1992;19(Suppl):66-67.
21. Harch P, Gottlieb SF, Van Meter K, Staab P. HMPAO SPECT brain imaging and low pressure HBOT in the diagnosis and treatment of chronic traumatic, ischemic, hypoxic and anoxic encephalopathies (abs). *Undersea Hyperb Med.* 1994;21 (Suppl):30.
22. Harch P, Van Meter K, Neubauer R, Gottlieb SF. Use of HMPAO SPECT for assessment of response to HBO in ischemic/hypoxic encephalopathies. In: Jain K, editor. *Textbook of hyperbaric medicine.* 1996. Pp. 480-491.
23. Keim L, Aita J, Hankins J, Spethman T, Shalberg P. Quantitative SPECT scanning in the assessment of patients with ischemic/traumatic brain injury treated with HBO (abs). *Chest.* 1997 112(3 (suppl)):918.
24. Golden ZL, Neubauer R, Golden CJ, Greene L, Marsh J, Mleko A, editors. *Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy.* 2nd International Symposium on Hyperbaric Oxygenation for Cerebral Palsy and the Brain-injured Child. Flagstaff, AZ: Best Publishing Company; 2002.

25. Neubauer R, Gerstenbrand F, editors. Hyperbaric oxygen facilitates neurorehabilitation. 3rd World Congress in Neurological Rehabilitation; 2002 April 3-6, 2002; Venice, Italy: Medimond Inc.
26. Harch P, editor. The dosage of hyperbaric oxygen in chronic brain injury. 2nd International Symposium on Hyperbaric Oxygenation for Cerebral Palsey and the Brain-injured Child. Flagstaff, AZ: Best Publishing Company; 2002.
27. Barrett K, Harch P, Masel B, Patterson J, Corson K, Mader J. Cognitive and cerebral blood flow improvements in chronic stable traumatic brain injury induced by 1.5 ATA hyperbaric oxygen (abs). Undersea Hyperb Med. 1998;25(Suppl):9.
28. Barrett K, Masel B, Patterson J, Scheibel R, Corson K, Mader J. Regional CBF in chronic stable TBI treated with hyperbaric oxygen. Undersea Hyperb Med. 2004 Winter;31(4):395-406. Epub 2005/02/03. eng.
29. Harch PG, Neubauer R. HBO therapy in global cerebral ischemia/anoxia and coma. In: Jain K, editor. Textbook of hyperbaric medicine. 4th ed. Cambridge, MA: Hogrefe & Huber Publishers; 2004. Pp. 223-261.
30. Golden Z, Golden CJ, Neubauer RA. Improving neuropsychological function after chronic brain injury with hyperbaric oxygen. Disabil Rehabil. 2006 Nov 30;28(22):1379-1386.
31. Shi XY, Tang ZQ, Sun D, He XJ. Evaluation of hyperbaric oxygen treatment of neuropsychiatric disorders following traumatic brain injury. Chin Med J (Engl). 2006 Dec 5;119(23):1978-1982. Epub 2007/01/04. eng.
32. Hardy P, Johnston KM, De Beaumont L, et al. Pilot case study of the therapeutic potential of hyperbaric oxygen therapy on chronic brain injury. J Neurol Sci. 2007 Feb 15;253(1-2):94-105. Epub 2007/01/20. eng.
33. Lin JW, Tsai JT, Lee LM, et al. Effect of hyperbaric oxygen on patients with traumatic brain injury. Acta Neurochir Suppl. 2008;101:145-149. Epub 2008/07/23. eng.
34. Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report. Cases J. 2009;2:6538.
35. Wright JK, Zant E, Groom K, Schlegel RE, Gilliland K. Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen. Undersea Hyperb Med. 2009 Nov-Dec;36(6):391-399.
36. Harch P, Andrews S, Fogarty E, et al. Hyperbaric oxygen therapy treatment of chronic mild-moderate blast-induced traumatic brain injury/post concussion syndrome with post traumatic stress disorder: pilot trial (abs). Eight World Congress on Brain Injury; March 10-14, 2010; Washington DC2010.
37. Wolf EG, Prye J, Michaelson R, Brower G, Profenna L, Boneta O. Hyperbaric side effects in a traumatic brain injury randomized clinical trial. Undersea Hyperb Med. 2012 Nov-Dec;39(6):1075-1082.
38. Scorza KA, McCarthy W, Miller RS, Carne W, Wolf EG. Hyperbaric oxygen effects on PTSD and mTBI symptoms: a subset analysis. Undersea Hyperb Med. 2013;40(6):548.
39. Wolf EG, Baugh LM, Kabban CM, Richards MF, Prye J. Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial. Undersea Hyperb Med. 2015 Jul-Aug;42(4):313-332.
40. Shandley S, Wolf EG, Schubert-Kabban C, et al. Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy. Undersea Hyperb Med. 2017;44(3):257-269.
41. Churchill S, Weaver LK, Deru K, et al. A prospective trial of hyperbaric oxygen for chronic sequelae after brain injury (HYBOBI). Undersea Hyperb Med. 2013 Mar-Apr;40(2):165-193.
42. Cifu DX, Walker WC, West SL, et al. Hyperbaric oxygen for blast-related postconcussion syndrome: three-month outcomes. Ann Neurol. 2014 Feb;75(2):277-286.
43. Walker WC, Franke LM, Cifu DX, Hart BB. Randomized, sham-controlled, feasibility trial of hyperbaric oxygen for service members with postconcussion syndrome: cognitive and psychomotor outcomes 1 week postintervention. Neurorehab Neural Repair. 2014;28(5):420-432.
44. Cifu DX, Hoke KW, Wetzel PA, Wares JR, Gitchel G, Carne W. Effects of hyperbaric oxygen on eye tracking abnormalities in males after mild traumatic brain injury. J Rehabil Res Dev. 2014;51(7):1047-1056.
45. Churchill S, Miller RS, Deru K, Wilson SH, Weaver LK. Simple and procedural reaction time for mild traumatic brain injury in a hyperbaric oxygen clinical trial. Mil Med. 2016 May;181(5 Suppl):40-44.
46. Tal S, Hadanny A, Berkovitz N, Sasson E, Ben-Jacob E, Efrati S. Hyperbaric oxygen may induce angiogenesis in patients suffering from prolonged post-concussion syndrome due to traumatic brain injury. Restor Neurol Neurosci. 2015;33(6):943-951.
47. Harch PG, Andrews SR, Fogarty EF, Lucarini J, Van Meter KW. Case control study: hyperbaric oxygen treatment of mild traumatic brain injury persistent post-concussion syndrome and post-traumatic stress disorder. Med Gas Res. 2017 Jul-Sep;7(3):156-174.
48. Tal S, Hadanny A, Sasson E, Suzin G, Efrati S. Hyperbaric oxygen therapy can induce angiogenesis and regeneration of nerve fibers in traumatic brain injury patients. Front Hum Neurosci. 2017;11:508.
49. Hadanny A, Abbott S, Suzin G, Bechor Y, Efrati S. Effect of hyperbaric oxygen therapy on chronic neurocognitive deficits of post-traumatic brain injury patients: retrospective analysis. BMJ Open. 2018 Sep 28;8(9):e023387.