

Hyperbaric Oxygen Therapy in the Treatment of Open Fractures and Crush Injuries

Mark F. Buettner, DO, ABEM*,
Derek Wolkenhauer, RRT, CHT

*Great River Wound and Hyperbaric Clinic, Center for Rehabilitation,
1401 West Axia Road, West Burlington, IA 52655, USA*

Traumatic injuries to the extremities that involve tissue ischemia are known to share a common dynamic pathophysiology. In the practice of hyperbaric medicine such injuries fall within a group known as the acute traumatic peripheral ischemias (ATPIs). These injuries include open fractures and crush injuries, skeletal muscle compartment syndromes, thermal burns, frost bite and threatened flaps, and grafts and replantations. In their various forms, these injuries share a common pathophysiology involving (1) a triad of tissue ischemia, hypoxia, and edema, (2) a gradient of tissue injury, and (3) a capacity for the injury to become self perpetuating. Early administration of hyperbaric oxygen therapy (HBOt) is reported to be beneficial when provided as an adjunct to appropriate surgical interventions for the ATPIs. Emergency department management of these injuries is part of the core curriculum of emergency medicine residency training. Emergency physicians should familiarize themselves with this treatment modality because of their role in the early management of these injuries. The focus of this article is on the use of HBOt in the treatment of open fractures and crush injuries.

Background

Hyperbaric oxygen is a therapy in which a patient breathes 100% oxygen while inside a treatment chamber at a pressure greater than that of sea level. The earliest cited application of treating patients under pressure dates back to 1662 when the British clergyman Henshaw [1] constructed a sealed

* Corresponding author.

E-mail address: mbuettner@pol.net (M.F. Buettner).

chamber he called a “domicilium.” By connecting his vessel to valved organ bellows, he was able to increase or decrease the air pressure within. Without any scientific basis he treated a variety of acute and chronic illnesses. In the nineteenth century discoveries were made allowing safer and more effective delivery of anesthesia within a compressed air environment. Decompression sickness was first identified among bridge caisson workers in the 1850s. Compression therapy for this disorder was first provided in 1889. Modern-day use of hyperbaric oxygen therapy emerged in 1955 with the work of Churchill-Davidson [2]. The high-oxygen environment was used to potentiate the effects of radiation therapy in cancer patients. That same year, the Dutch surgeon Ite Boerema [3] proposed using HBOt to enhance tolerance to circulatory arrest during cardiac surgery. The promising results of his animal studies led to the construction of a large hyperbaric operating chamber at the University of Amsterdam. Boerema [3] performed a variety of surgeries within this chamber for conditions such as transposition of the great vessels, tetralogy of Fallot, and pulmonic stenosis. His first publication appeared in 1956. In the early 1960s the first reports on the positive effects of HBOt for anaerobic infections and carbon monoxide poisonings were published [4,5]. The 1970s witnessed both degradation and decline in the field. On the heels of the discoveries found in the 1960s researchers eagerly sought other applications for HBOt. Experiments were performed using it in a variety of debilitating conditions. Positive reports were largely anecdotal, touting the “good results” without regard for scientific methodology [6]. Indiscriminate use of HBOt led to the need for regulation. There were no formal guidelines for insurers to reference regarding payment for the valid use of HBOt. In 1976, the Undersea Medical Society formed an ad hoc committee to work with Medicare and Blue Cross. As a result, the first edition of the Hyperbaric Oxygen Therapy Committee Report was published. Formal indications for the valid use of HBOt were established based on scientific merit. With periodic revisions, the committee report remains the authority on approved indications for HBOt within the United States (Fig. 1).

Physiology

The primary means for oxygen transport is in the form of oxyhemoglobin bound within the erythrocyte. At sea level the barometric pressure is 1 atmosphere absolute (ata). At 1 ata the partial pressure of alveolar oxygen (PAO_2) is about 100 mm Hg. Also at 1 ata hemoglobin is about 97% oxygen saturated ($SaO_2 = 97$) and yields an oxygen content ($HbO_2 + \text{plasma dissolved } O_2$) of about 19.8 mL oxygen per dL blood. Under pressure, as the PAO_2 reaches 200 mm Hg, hemoglobin becomes fully saturated with oxygen ($SaO_2 = 100\%$). Further increases in pressure beyond a PAO_2 of 200 mm Hg will not result in an increase in oxyhemoglobin. Therefore, the superoxygenated state achieved in a hyperbaric oxygen environment is attributed to the amount of oxygen physically dissolved in the plasma. When air is breathed



Fig. 1. Monoplace hyperbaric oxygen chamber at Great River Wound and Hyperbaric Clinic West Burlington, Iowa. (Courtesy of Perry Baromedical, Riviera Beach, FL; with permission.)

at sea level (1 ata), only 1.5% of the oxygen content is related to oxygen dissolved in plasma. Comparatively, when 100% oxygen is breathed at a pressure of 3 ata, a PAO_2 of 2200 mm Hg is generated, dissolving another 6.8 mL of oxygen into each dL of blood, resulting in an arterial oxygen tension (PaO_2) of about 2000 mm Hg (Fig. 2). A healthy adult at rest uses about 6 mL of oxygen per dL of circulating blood. Therefore, as demonstrated in Boerema's 1960 study "Life Without Blood" [7], life can be sustained without the need for erythrocytes while in a hyperbaric oxygen environment at a pressure of 3 ata.

Crush injury pathophysiology

If the amount of energy transfer during a crush injury is sufficient, a gradient of tissue injury expands from the impact site (Fig. 3). The most immediate injury is the primary zone of tissue destruction. This region of

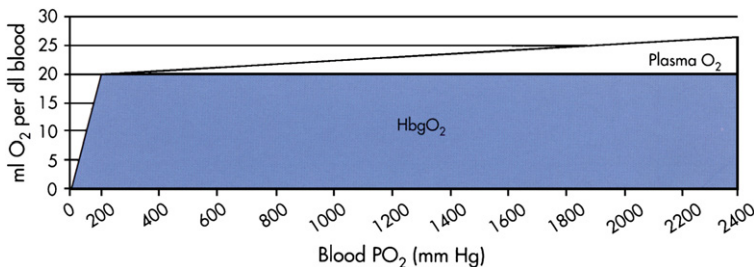


Fig. 2. Combined blood oxygen content bound to hemoglobin and dissolved in plasma at high levels of blood PO_2 . (From Sheffield PJ, Smith PS. Physiologic and pharmacological basis of hyperbaric oxygen therapy. In: Bakker DJ, Cramer FS, editors. Hyperbaric surgery perioperative care. Flagstaff (AZ): Best Publishing Company; 2002. p. 68; with permission.)

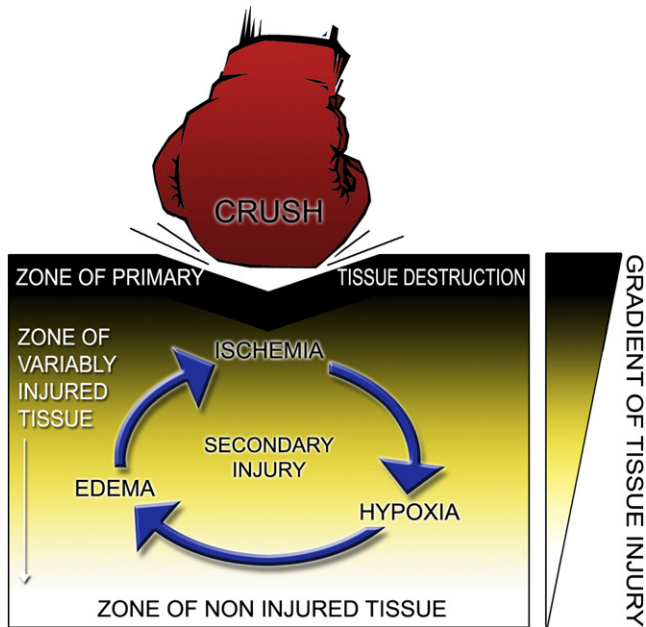


Fig. 3. Zones of injured tissues relative to the crush impact and the secondary perpetuation of injury.

injured tissue may be rendered nonviable regardless of intervention. The next zone along the gradient of injury is composed of variably injured or variably ischemic tissues. Most therapeutic interventions are targeted within this penumbra of tissues. The outermost zone along the gradient of injury is composed of minimally injured to noninjured tissues. A self-perpetuating secondary injury may occur to tissues at any point along the injury gradient.

Secondary injury

Ischemia

A decrease in blood perfusion to the variably injured tissues is the initial event leading to secondary injury. Ischemia may result from direct traumatic injury to blood vessels. Ischemia also may arise indirectly. The indirect mechanism for ischemia often is multifactorial and may include one or more of the following: fluid leakage (edema, hemorrhage) with or without vascular collapse from the external pressure of the tissue fluid (compartment syndrome); vasoconstriction; stasis; occlusion. The indirect mechanisms for ischemia within the microcirculation are the largest contributor to the secondary injury.

Hypoxia

Cellular processes involved in wound repair are heavily oxygen dependant. The zone of variably injured tissues has an increased oxygen demand at a time of diminished perfusion. Oxygen demands may increase by a factor of greater than 20 [8]. Wound-repair mechanisms such as fibroblast activity and collagen formation are compromised under hypoxic conditions [9]. An increased risk of infection develops with the failure of oxygen-dependant host immune functions. Hypoxic cells cannot retain intracellular water, leading to cytogenic edema.

Edema

Edema is a profound contributor to tissue hypoxia. When fluid accumulates within the extracellular space, the distance from the capillary wall to the injured cell is greater. Therefore, less oxygen reaches the injured cell to exert repair. Vasodilatation of the proximal arterial vasculature increases blood flow to the site of injury. This reflex results in vasogenic edema. When combined with increased bleeding from the injured vessels, fluid accumulates in the interstitial space. Collapse of the capillary bed occurs as the pressure within the interstitial space exceeds capillary filling pressures (12–32 mm Hg). Cellular hypoxia is propagated.

Reperfusion injury

Reperfusion contributes to the perpetuation of the secondary injury. Neutrophils adhere to postcapillary venules after a period of ischemia and during reperfusion. This process results in a release of toxic oxygen free radicals. Oxygen free radicals are destructive to tissues in several ways: the induction of a no-reflow phenomenon by the vasoconstriction of precapillary arterioles, lipid peroxidation of cell membranes, and the formation of peroxynitrite when the oxygen free radicals react with endothelial-generated nitric oxide.

The net result is a self-perpetuating secondary injury. If left unchecked, this secondary injury may result in a volume of tissue necrosis much larger than and remote from the primary zone of tissue destruction. When the drug oxygen is delivered within a hyperbaric environment, its pharmacodynamics mitigates the pathophysiology of ischemia.

Pharmacodynamics of hyperbaric oxygen therapy

Diffusion radius

To exert its effects, oxygen must travel out of the arterial end of the capillary wall through the interstitial space to the injured cell. This diffusion

radius of oxygen from the arterial end of the capillary into the interstitial space has been calculated to traverse a distance of 64 μm . With HBOt at 3 ata, this diffusion radius has been calculated to traverse a distance of 247 μm (Fig. 4) [10]. During the immediate postinjury period of a crush injury the maintenance of tissue oxygenation is critical [11].

Vascular response

Oxygen breathing results in smooth muscle contraction of the arterial vasculature resulting in up to a 20% reduction of blood flow to the limb [12]. This response is physiologic, and it is observed in healthy tissues. With an increase in upstream arterial resistance comes a drop in downstream capillary hydrostatic pressure. The drop in local capillary hydrostatic pressure creates an environment that favors absorption. The increase in oxygen dissolved in plasma compensates for the reduction in blood flow. Conversely, Hammerlund and colleagues [13,14] have shown that with oxygen breathing blood flow increases within the local microvasculature of both acute and chronic wounds. The net response to HBOt within the variably injured tissues is a redistribution of perfusion and physiologic resorption of edema.

Cellular function

Cellular function is restored when HBOt corrects the Po_2 to normal or slightly elevated values. This restoration is manifested by enhanced

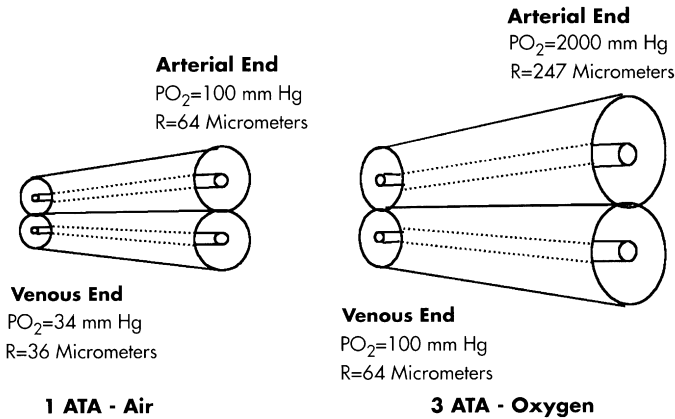


Fig. 4. Krogh-Erlang oxygen diffusion model used to estimate oxygen diffusion from the capillaries to surrounding tissue and the potential increase in oxygen diffusion distances with hyperbaric oxygenation. ATA, atmosphere absolute; R, radius. (From Sheffield PJ, Smith PS. Physiologic and pharmacological basis of hyperbaric oxygen therapy. In: Bakker DJ, Cramer FS, editors. Hyperbaric surgery perioperative care. Flagstaff (AZ): Best Publishing Company; 2002. p. 68; with permission.)

epithelialization, fibroplasia, collagen synthesis, angiogenesis, and leukocyte bactericidal-killing mechanisms [15,16]. The enhanced fibroblast activity can last up to 72 hours following a hyperbaric oxygen exposure. HBOt reduces the secondary injury by blunting the release of oxygen free radicals. More specifically, the Beta2 integrin system is disrupted, preventing neutrophil adherence to the postcapillary venules [17]. Hyperbaric oxygen also antagonizes lipid peroxidation of the cell membrane [18]. Erythrocyte sludging is reduced because of enhanced erythrocyte deformability in response to HBOt (Fig. 5) [19].

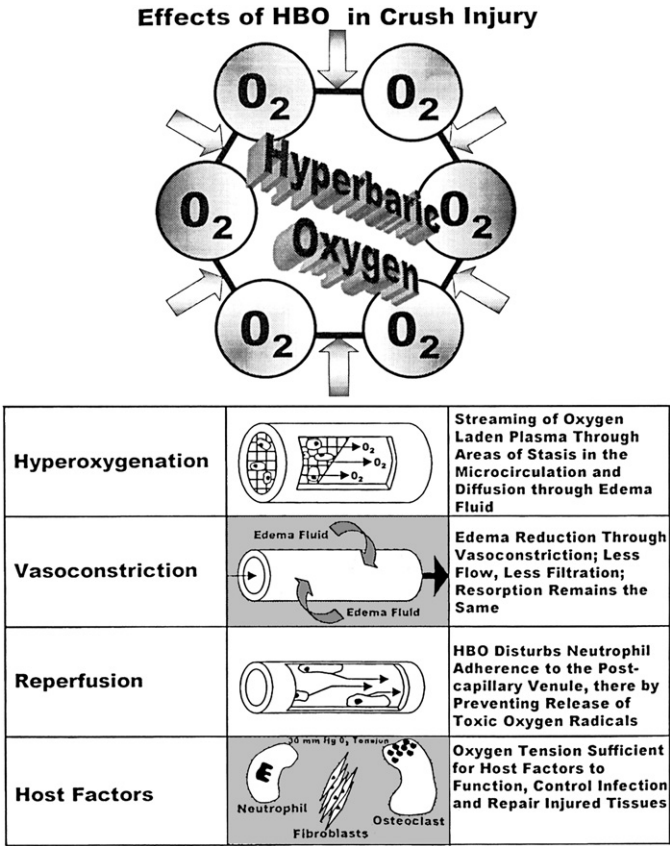


Fig. 5. Hyperbaric oxygen mediates the effects of crush injuries primarily through four mechanisms. These mechanisms also are useful adjuncts in managing the injuries in the other acute traumatic peripheral ischemias. HBO, hyperbaric oxygen. (From Strauss B. Crush injury, compartment syndrome and other acute traumatic peripheral ischemias. In: Kindwall E, Whalen H, editors. Hyperbaric medicine practice. 2nd (revised) edition. Flagstaff (AZ): Best Publishing Company; 2002. p. 760; with permission.

Clinical application

Despite all that is understood about the physiologic and pharmacodynamic properties of hyperbaric oxygen, guidelines for its clinical application in the treatment of the ATPIs as a group are limited. The lack of guidelines is related to a noticeable paucity of randomized clinical trials in the literature. The vast majority of the clinical literature is in the form of case reports. A well-designed clinical trial allows comparison between treatment groups so that it is possible to identify which patients actually need the therapy to heal and which ones do not. Clinical guidelines are derived more accurately from such studies. Unfortunately, the complex and variable nature of these injuries as a group makes it difficult to develop well-designed clinical trials.

The clinical recommendations for the use of HBOt in open fractures and crush injuries are perhaps the best founded. In 1979 Strauss [20] had summarized more than 700 positive case reports in the use of HBOt for crush injuries. Perhaps the highest level of evidence for its use was reported in the results of Bouachour's [21] 1996 randomized, clinical trial of hyperbaric oxygen therapy in the management of crush injuries [21]. The severity of injury was graded objectively using the widely accepted Gustilo classification scheme (Table 1). The more severe injuries (Gustilo grade III-B and III-C) have been associated with a 50% complication rate (infection, non-union, nonhealing, amputation) [22–24]. Thirty-six patients who had Gustilo grade II or III injuries were assigned in a blinded, randomized fashion to the HBOt treatment group or the placebo group. All the patients received the same standard therapies (antibiotics, anticoagulants, and wound dressings). The two groups were similar in terms of subject age, risk factors, number,

Table 1
Gustilo classification of open fractures and crush injuries

Grade	Findings	Complications (infections, nonhealing, amputation)
I	Puncture type wound, usually from inside to out	Almost nil
II	Laceration associated with the open fracture	10%
III	Crush component to the injury	Vary with the subtype
A	Sufficient soft tissue to cover the bone	~ 10%
B	Exposed bone remains after débridement	~ 50%
C	Concomitant major vascular injury to the extremity	> 50%

Data from Gustilo R. Management of open fractures and their complications. Philadelphia: WB Saunders; 1962. p. 202–8; Gustilo R, Williams DN. The use of antibiotics in the management of open fractures. Orthopedics 1984;7:1617–9; and 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;24:742.

type and location of vascular injuries, neurologic injuries, or fractures. They were similar as well in type, location, and timing of surgical procedures. The results revealed complete healing in 94% of the HBOt group versus 59% of the controls ($P < .01$). Subsequent surgeries were required in 6% of the HBOt group versus 33% of the controls ($P < .05$). The healing of fractures in patients over the age of 40 years was significantly improved within the HBOt group ($P < .05$). Finally, transcutaneous oxygen measurements were significantly improved in the HBOt group as compared with the control group. The patients who healed had higher transcutaneous oxygen levels than those who did not heal.

The results of Bouachour's clinical trial revealed which crush-injured patients benefit from HBOt. Such information provides the basis for formulating objective guidelines for patient selection. Factors to consider are severity of injury, age, and host comorbidities. Strauss [11] has published the most comprehensive guidelines. The Strauss guidelines incorporate the Gustilo grade of injury with a five-criteria 10-point host assessment (Table 2). Because of the 50% complication rate, HBOt is recommended for all Gustilo grade III-B and III-C injuries regardless of host status (Table 3). With this high grade of injury, however, a primary amputation should be considered in severely compromised hosts (host score, 0–3). For the moderately compromised host (host score, 4–7) HBOt is indicated for both Gustilo grades II and III-A. HBOt should be considered for a Gustilo grade I fracture if the host is severely compromised. Finally, the decisions regarding surgical management should be made independently of whether HBOt is provided. Although HBOt should not delay any necessary surgical intervention, it should be provided as soon after the injury as possible [11]. Clinical

Table 2
Strauss evaluation system: five criteria, 10-point host assessment

Criteria	Findings			Interpretation
	2 Points ^a	1 Point ^a	0 Points ^a	
Age in years	< 40	40–60	> 60	Healthy 8-10 Points
Ambulation ^b	Community	Household	None	
Cardiovascular/renal function ^c	Normal	Impaired	Decompensate	Impaired 8-10 Points
Smoking/steroid use ^c	None	Past	Current	Marginal 3-10 Points
Neuropathy/deformity ^c	None	Mild-to-Moderate	Severe	

^a Use half-points if observations fall between two findings.

^b Subtract one-half point if walking aids required.

^c Whichever gives the lower score.

From Strauss MB. Hyperbaric oxygen for crush injuries and compartment syndromes. In: Bakker DJ, Cramer FS, editors. Hyperbaric surgery perioperative care. Flagstaff (AZ): Best Publishing Company; 2002. p. 344; with permission.

Table 3
Objective indications for using hyperbaric oxygen in open fracture–crush injuries

Gustilo Grade	Host status		
	Normal	Impaired	Marginal (severely compromised)
I	—	—	Yes
II	—	Yes	Yes
III -A	—	Yes	Yes
III-B	Yes	Yes	Yes/No ^a
III-C	Yes	Yes/No ^a	Yes/No ^a

^a Consider primary amputation.

From Strauss MB. Hyperbaric oxygen for crush injuries and compartment syndromes. In: Bakker DJ, Cramer FS, editors. Hyperbaric surgery perioperative care. Flagstaff (AZ): Best Publishing Company; 2002. p. 344; with permission.

guidelines for patient selection are now well defined, but there is no single standard treatment protocol for HBOt in crush-injured patients. The Boua-chour study called for two hyperbaric oxygen treatments per day for 6 days to be initiated within 24 hours of injury. Each treatment provided a pressure of 2.5 ata for 90 minutes. Strauss [11] has published his recommended treat-ment protocol with consideration for maintenance of tissue oxygenation during the immediate injury period, edema reduction, host responses to in-jury, and metabolic state stabilization. This protocol calls for three treat-ments per day for the first 2 days, two treatments per day for the next 2 days, and once-daily treatments for the last 2 days. Each of the 12 treat-ments is to be delivered at a pressure of 2 to 2.4 ata.

Cost impact

The cost impact of treating crush-injured patients with HBOt is favor-able. In 1977 Brighton [25] reported that in the United States the average cost was \$140,000.00 to resolve each case of crush-type fracture that failed to heal primarily. When projected to today’s costs, that amount would be significantly higher. The Gustilo grade III-B and III-C injuries are associ-ated with a 50% complication rate. The grade II injuries are associated with a 10% complication rate. For these fractures, Bouachour’s [21] study demonstrated an overall 35% improvement in primary healing and a 27% decrease in the need for additional surgeries within the group treated with hyperbaric oxygen. At the authors’ institution the total Medicare reimburse-ment cost for a patient to receive one hyperbaric oxygen treatment is \$466.00.

Summary

In crush injuries, HBOt has objective indications based on the highest level of clinical evidence supporting its use. It meets the American Heart

Association's criteria for a category 1 indication. Both Medicare and Undersea and Hyperbaric Medical Society guidelines list crush injuries as an approved indication for HBOt [26,27]. Based on the clinical evidence and cost analysis, medical institutions that treat these types of injuries are justified in incorporating HBOt as a standard of care. As more hyperbaric programs go online, emergency physicians increasingly will be involved in coordinating the early administration of HBOt with the plans for surgical intervention. In such cases the phrase "time is muscle" also applies to skeletal muscle. The United States has recently witnessed a resurgence in the use of HBOt coinciding, in large part, with the technological advances in the treatment of chronic wounds. The practice of hyperbaric medicine as a whole remains challenged to develop evidence-based guidelines like those derived for the treatment of crush injuries.

Acknowledgments

The authors acknowledge the efforts of Craig Borchard and Shawn Mears, Great River Medical Center Public Relations, Lynette Collier and the talented GRMC wound clinic staff, and Derek and Jen, for the quality delivery of HBOt.

References

- [1] Henshaw IN, Simpson A. Compressed air as a therapeutic agent in the treatment of consumption, asthma, chronic bronchitis and other diseases. Edinburgh (UK): Sutherland and Knox; 1857.
- [2] Churchill-Davidson I, Sanger C, Thomlinson RH. High-pressure oxygen and radiotherapy. *Lancet* 1955;1:1091–5.
- [3] Boerema I, Kroll JA, Meijne NG, et al. High atmospheric pressure as an aid to cardiac surgery. *Arch Chir Neerl* 1956;8:193–211.
- [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;49:299–302.
- [5] Smith G, Sharp GR. Treatment of coal gas poisoning with oxygen at two atmospheres pressure. *Lancet* 1962;1:816–9.
- [6] Kindwall Eric. A history of hyperbaric medicine. In: Kindwall E, Whalen H, editors. *Hyperbaric medicine practice*. 2nd (revised) edition. Flagstaff (AZ): Best Publishing Company; 2002. p. 1–20.
- [7] Boerema I, Meyne NG, Brummelkamp WH, et al. Life without blood: a study of the influence of high atmospheric pressure and hypothermia on dilution of blood. *J Cardiovasc Surg* 1960;1:133–46.
- [8] Strauss MB. Introduction to nonhealing wounds. *Current concepts in wound care*. 1986;Fall:5–6.
- [9] Hunt TK, Niinikoski J, Zederfeldt BH, et al. Oxygen in wound healing enhancement: cellular effects of oxygen. In: Davis JC, Hunt TK, editors. *Hyperbaric oxygen therapy*. Bethesda (MD): The Undersea Medical Society; 1977. p. 111–2.
- [10] Krogh A. The number and distribution of capillaries in muscle with calculations of the oxygen pressure head necessary for supplying the tissue. *J Physiol* 1919;52:409–15.

- [11] Strauss MB. Hyperbaric oxygen for crush injuries and compartment syndromes; surgical considerations. In: Bakker DJ, Cramer FS, editors. *Hyperbaric surgery perioperative care*. Flagstaff (AZ): Best Publishing Company; 2002. p. 341–57.
- [12] Bird AD, Telfer ABM. Effect of hyperbaric oxygen on limb circulation. *Lancet* 1965;(1): 355–6.
- [13] Hammerlund C, Kutlu N. Effects of oxygen breathing on blister wound microcirculation in man. In: *Hyperbaric oxygenation and wound repair. Effects on the dermal microcirculation* [dissertation]. Lund University, Sweden; 1995.
- [14] Hammerlund C, Castenfors J, Svedman P. Dermal vascular response to hyperoxia in healthy volunteers. In: Bakker DJ, Schmutz J, editors. *Proceedings of the second Swiss symposium on hyperbaric medicine*. Basel (Switzerland): Foundation for Hyperbaric Medicine; 1988. p. 55–9.
- [15] Sheffield PJ, Smith PS. Physiologic and pharmacologic basis of hyperbaric oxygen therapy. In: Bakker DJ, Cramer FS, editors. *Hyperbaric surgery perioperative care*. Flagstaff (AZ): Best Publishing Company; 2002. p. 63–109.
- [16] Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet* 1972;135:561–7.
- [17] Thom SR. Functional inhibition of neutrophil B2 integrins by hyperbaric oxygen in carbon monoxide mediated brain injury. *Toxicol Appl Pharmacol* 1993;123:248–56.
- [18] Thom SR. Antagonism of co-mediated brain lipid peroxidation by hyperbaric oxygen. *Toxicol Appl Pharmacol* 1990;105:340–4.
- [19] Mathieu D, Coget J, Vinkier L, et al. Red blood cell deformability and hyperbaric oxygen therapy [abstract]. *HBO Review* 1985;6(4):280.
- [20] Strauss MB. Role of hyperbaric oxygen therapy in acute ischemias and crush injuries—an orthopedic perspective. *HBO Review* 1981;2:87–108.
- [21] Bouachour G, Cronier P, Gouello JP, et al. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blinded placebo-controlled clinical trial. *J Trauma* 1996;41:333–9.
- [22] Gustilo R. *Management of open fractures and their complications*. Philadelphia: WB Saunders; 1982. p. 202–8.
- [23] Gustilo R, Williams DN. The use of antibiotics in the management of open fractures. *Orthopedics* 1984;7:1617–9.
- [24] 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;24:742–6.
- [25] Brighton CT. *Hospital Tribune*. May 9, 1977:4.
- [26] Medicare bulletin 424. Hyperbaric oxygen (HBO) therapy. May 11, 1999.
- [27] Hampson NB, editor. *Hyperbaric oxygen therapy: 1999 committee report*. Kensington (MD): Undersea and Hyperbaric Medical Society, Inc; 1999. p. 17–21.