Hyperbaric Oxygen Therapy for Trauma: Crush Injury, Compartment Syndrome, and Other Acute Traumatic Peripheral Ischemias

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Hyperbaric oxygen (HBO) can be used as adjunctive therapy for trauma patients with crush injury, compartment syndrome, and acute traumatic peripheral ischemia (ATPI). ATPI conditions as well as burns, frostbite, threatened flaps, and reimplantations can be grouped together for discussion of treatment strategies because of their similarities in regard to injury mechanism, pathophysiology, and receptivity to hyperbaric oxygen. Broadly speaking, the rationale for hyperbaric oxygen therapy is the need to counter the effects of tissue hypoxia arising as a direct consequence of vascular injury and as a secondary consequence of trauma and infection. The unifying factors among these various conditions include a self-perpetuating cycle of ischemia, edema, injury gradient, and comorbid conditions such as age, compromised status, and immunological deficiencies.

■ Crush Injury/Compartment Syndrome

Three aspects of a diffuse crushing injury contribute to the development of compartment syndrome: (1) tissue destruction, (2) type of tissue involved, and (3) gradient of injury. Tissue is destroyed at the site of injury. The extent of this destruction depends on the acceleration/deceleration force applied to the tissue. Chapman demonstrated, using cadavers, that the crushing force applied to a limb caught between two bumpers colliding at 20 mph is 100,000 foot-pounds (personal communication).[1] In motor vehicle deceleration injury, it is obvious that no single tissue is spared from the direct impact forces. Thus, the injury is regional, with full-thickness involvement of skin, subcutaneous tissue, bone, muscles, vessels, and nerves.[2] It also follows that not all tissues are damaged equally. A gradient of tissue destruction, from complete to partial to noninvolvement, is thus present. The goal of therapy is to limit the spread of injury. Because it is difficult to describe the effect of injury on

each system comprehensively, clinical descriptions are usually confused and/or incomplete.

In their description of compartment syndrome, Mubarak and associates[3] place crush injury on a continuum, with severity being determined by the extent of muscle damage and subsequent clinical presentation and duration of injury. Compartment syndrome itself emerges in both acute and chronic forms in relationship to its etiology and reversibility. The acute syndrome is usually severe and most common after trauma. This form manifests as an increase in compartment pressure, which produces necrosis and loss of limb viability if it is not relieved by decompression. Fractures and soft tissue injuries following blunt trauma are the major causes. Other forms of trauma are compression from debris, crushing, and wringer mechanisms of injury. In addition, the acute syndrome may also be associated with contusions, bleeding disorders, burns, vascular repair, exercise, drug or alcohol overdose, tight constrictive dressings, venous obstruction, and other forms of ischemia.

Pathophysiology

Pressure of 30 to 40 mm Hg occludes the capillary flow in patients with normal central arterial blood flow through the collateral arteriovenous shunts and the skin. Because of circulatory disruption, fluid accumulates within the compartment. The extent of tissue injury increases progressively with increasing time (Table 1). In ischemic tissue, high intracellular calcium concentrations cause water to shift into the muscle fibers. Extracellular calcium moves into the aqueous sarcoplasm, localizing particularly in the mitochondria and sarcoplasmic reticulum. Intracompartment pressure of 80 mm Hg over 30 minutes inhibits arterial perfusion, suggesting that compartment tamponade originates from intracellular swelling.

Ischemia

Ischemia may arise after direct injury of blood vessels. As a consequence, forward flow of blood is lost. Ischemia also occurs after indirect

Table 1. *Ischemic Effect vs Time*

Time (h)	Effect
0.5–2	Functional nerve changes (hypoesthesia/paresthesia)
2–4	Functional muscle changes (motor weakness)
3	Decreased capillary integrity (postischemic swelling)
4	Onset of myoglobinuria
4–12	Irreversible muscle damage begins
12+	Postischemic contracture as a sequela

injury subsequent to vascular collapse from external pressure, as a result of decreased flow in the microcirculation. The amount of tissue fluid (blood, plasma, transudates) increases, setting up conditions for development of compartment syndrome. Another result of an increase in external pressure is stasis, leading to vasoconstriction and total vessel occlusion. Oxygenation of the tissues thus diminishes and metabolic requirements are not met. This is a critical issue. Injured patients have dramatically increased metabolic needs to facilitate the healing process. Failure to meet those needs results in nonhealing wounds, tissue necrosis, and heightened risk of infection—all of which further increase ischemic insults.

Edema

Edema is caused by accumulation of either intravascular or extravascular fluid due to multiple causes, including intracellular fluid leakage to extracellular spaces and cytogenic causes. Direct trauma to blood and lymphatic vessels results in vasogenic fluid collection. With this increase, the tissue perfusion pressure rises and the venous outflow is inhibited; the ultimate insult is hypoxia, with further intracellular water content loss into the tissues. As hypoxia progresses, the intracellular energy production and cellular transport mechanisms are disrupted and further cellular destruction occurs. The diffusion distance from capillaries to cells increases with the edema, and the thin-walled vessels collapse, inhibiting forward flow of intravascular contents. A vicious cycle is established. Edema progresses in the tissues, and in a muscle compartment surrounded by tight fascia, compartment syndromes develop. The ultimate effect is total collapse of the vasculature, with inhibition of both venous emptying and arterial flow entering. When interstitial fluid pressure exceeds capillary profusion pressure, the capillary bed closes and all flow ceases.

Gradient of Injury

There is a great variety in degrees of tissue injury, which makes it very difficult to accurately describe the amount of tissue destruction and the extent of the injury. Multiple systems have been devised for this purpose. The most commonly used are the classification scheme developed by Gustilo and colleagues[4] (Table 2) and the mangled extremity severity score (MESS) developed by Johansen and associates[5] (Table 3).

Self-perpetuating mechanisms play into traumatic peripheral ischemias, all leading toward compromised microcirculation. This self-progression and perpetuation of the mechanisms ultimately leads to irreversible damage. Therefore, time becomes an essential player in the

Table 2. *HBO Therapy for Fractured Crush Injury (Gustilo Classification)*

				Use of HBO and Host Status		
Type	Characteristic	Infection Rate	Amputation Rate	Normal Host	Impaired Host	Compromised Host
I	Small (<1 cm) laceration, from inside out	Almost nil	0	No	No	Yes
II	Laceration, with minimal soft tissue injury	3%	0	No	Yes	Yes
III-A	Crush with adequate soft tissue coverage	<10%	0	No	Yes	Yes
III-B	Crush with extensive soft tissue injury, insufficient to cover bone	52%	16%	Yes	Yes	Yes
III-C	Crush with major vascular injury	42%	42%	Yes	Yes	Yes

HBO = hyperbaric oxygen.
Adapted from Gustilo et al.[4]

continuum. In the skeletal muscle compartment syndrome, the full extent of the injury may not be recognized until several hours after injury. This time delay may result in irreversible damage to the tissue, primarily from the trauma itself and secondarily from the effects of increased edema, inhibition of perfusion, the ultimate "no-flow" with microcirculatory destruction followed by infection, impaired wound healing, and ultimate contractures.

Anatomy of Extremity Compartments

Crucial to the understanding of compartment syndrome is an understanding of the vasculature that is affected by increased pressure. The efferent circulating system branches into smaller and smaller muscular wall precapillaries or arterioles. These smaller structures can form arteriovenous shunts. Precapillaries pass into capillaries, join with venules, and then form the venous system.

Elevation of tissue fluid pressure decreases capillary blood flow. Ischemia of sufficient duration produces tissue necrosis. This compromise of the microcirculation occurs at tissue pressures as low as 30 to 40 mm Hg of capillary perfusion.

Muscles have isolated vascular support systems with limited internal and external anastomoses. Abundant communications exist in the soleus and peroneus longus muscles, but others such as the anterior tibialis and flexor hallucis longus have mainstem arteries and branches.

Table 3. *Mangled Extremity Scoring Scale*

A. Skeletal/Soft Tissue Injury
- 1 > Low energy (stab, simple fracture), low velocity (gunshot wound)
- 2 > Medium energy (open or multiple fractures)
- 3 > High energy (close range gunshot wound, crush injury)
- 4 > Very high energy (above + gross contamination, avulsion)

B. Limb Ischemia (double time if ischemia time is >6 h)
- 0 > Perfusion normal
- 1 > Pulse reduced/absent—perfusion still present
- 2 > No pulse, paresis, diminished capillary refill
- 3 > Cool, paralyzed, insensate, numb

C. Shock
- 0 > Systolic blood pressure always >90 mm Hg
- 1 > Hypotension transiently
- 2 > Persistent hypotension

D. Age
- 1 > <30
- 2 > 30–50
- 3 > >50

Source: Johansen et al.[5] With permission.

Those with single radiating patterns (e.g., biceps) or quadrilateral patterns (e.g., extensor hallucis longus) are very susceptible to circulatory compromise. Increased pressure in a muscle compartment affects nerves within that compartment and, with vascular ischemia, functional disturbance to the nerves can occur.

Veins are thin walled and therefore more compressible and more susceptible to changes in muscle pressure and interstitial fluid volumes. There are two networks of veins: superficial and deep. Superficial veins lie outside the fascia, under the skin, and lack support. The deep vein system is enclosed within the muscles and fascial compartments; valves within this system allow the forward passage of blood.

Clinical Diagnosis

The diagnosis of compartment syndrome is based on the mnemonic of "five Ps": pain, pressure, paresthesia, paresis, and pulses.

Pain Patients experience pain that is greater than expected from the primary fracture or contusion. There is a deep, throbbing, unrelenting pressure that is not relieved by immobilization. Absence of pain usually is related to central or peripheral sensory deficits. Stretching the muscle (e.g., with toe or ankle movement) aggravates the pain significantly.

Pressure The limb is swollen and palpably tense and may have shiny, warm skin, giving the appearance of cellulitis. It is essential to remove all dressings for adequate exposure and examination, even though fracture reduction may be lost. All constrictive dressings and casts must be removed. One must remain cognizant of the fact that the deep posterior compartment is the most difficult to assess.

Paresthesia Paresthesia occurs in the distribution of the involved nerve. All prolonged pressures over 30 mm Hg ultimately result in sensory deficits. Compartment syndrome can lead to complete sensory loss.

Paresis Motor weakness secondary to nerve ischemia occurs relatively late and can progress to paralysis. The large, fast-conducting fibers are blocked selectively at lower intracompartmental pressures.

Pulses Intracompartmental pressures of 30 to 60 mm Hg can readily produce nerve and muscle ischemia but are insufficient to occlude arterial flow. In the normotensive patient, a pressure of about 100 mm Hg would be necessary to hydrodynamically occlude distal pulses. Thus, if peripheral pulses are absent, one should usually seek another cause and undertake angiography.

Pressure Measurements

In order to monitor intracompartmental pressures, various techniques have been employed. The major problem is that, in general, the reading represents the pressure at only one time. Measurements must be repeated to monitor trends. A needle technique was introduced by White-

sides and colleagues[6] in 1975. Subsequently, Mubarak and colleagues[3,7] developed the wick catheter technique, in which a catheter is placed within the tissue to be monitored. This allows long-term monitoring but requires invasive surgery for placement of the catheter. Concern also arises about the degree of local injury secondary to edema induced by the procedure. The authors use a needle injection technique in which a needle is placed into the tissue, and a few milliliters of fluid is injected to clear it. This conduit is then attached to a manometer, giving a direct readout on a gauge. Similarly, with the continuous infusion technique, a needle inserted into the tissue is connected to a monitor to obtain direct readings.

Rationale for Hyperbaric Oxygen Therapy

Hyperoxygenation The basis of all clinical hyperbaric oxygen treatment is its property of increasing the amount of oxygen dissolved in plasma as a result of breathing 100% oxygen in an environment of increased atmospheric pressure. Henry's law states that, at constant temperature, the amount of gas dissolved in a liquid or tissue is proportional to the partial pressure of the gas in contact with the liquid or tissue. Under pressure—between 2 and 3 atmospheres of absolute pressure (ATA)—the amount of plasma-transported oxygen is equivalent to the total metabolic needs of the body. Red cells are not necessary for transport of this oxygen load. With an extremely high diffusion gradient, oxygen diffuses into the tissues and thus elevates tissue levels. Alveolar oxygen levels of more than 2,200 mm Hg have been documented at 3 ATA of pressure.[8] This massive tissue load of oxygen counteracts trauma-related tissue hypoxia and edema. The ability of plasma to enter areas where red cell flow is obstructed in the microcirculation allows physically dissolved oxygen to enter the tissues.[9]

Vasoconstriction Vasoconstriction occurs as a protective reaction to hyperoxia. A 20% reduction in blood flow lessens extravasation of fluid and thus edema, with reduced collapse of capillaries.[10] The net effect is an increase in oxygenation to the tissues, with improvement in microcirculation.

Cellular Function With enhanced oxygenation at the injury zone, host factors related to healing and infection control come into play. Tissue oxygen levels less than 30 mm Hg inhibit fibroblast proliferation, which in turn inhibits neovascularization and repair.[11]

Inhibition of Infection Neutrophils need an oxidative burst to kill bacteria. Raising oxygen tensions can assist neutrophil killing function toward both anaerobic and aerobic organisms.[12] Clostridia and *Bacteroides* (anaerobic organisms) are specifically inhibited by increased oxygen tensions. Other organisms such as streptococci, pneumococci, *Candida*, and microbacteria are slowed by oxygen-enriched environments. Anaerobic organisms are affected by the facilitation of leukocyte oxidative killing.

Reperfusion Injury Over the years, our understanding of reperfusion injury has progressed from the original work of Zamboni and colleagues,[13] who demonstrated a reduction in the necrosis of axial-pattern skin flaps with immediate treatment with hyperbaric oxygen. This confirmed studies on tourniquet ischemia with significant postinjury muscle necrosis and edema and also the presence of an aerobic versus anaerobic tissue environment.[14] The adenosine triphosphatase (ATPase) and phosphocreatine kinase levels in the HBO-treated group were more like the levels in the normal controls, and the lactate levels were low. In the ischemic group, the reverse occurred with high lactate levels, indicating anaerobic metabolism. Thom[15] demonstrated that the interaction of toxic oxygen radicals with lipids of cell membranes producing lipid peroxidation is inhibited by hyperbaric oxygenation. The sequestration of neutrophils in the postcapillary venules that occurs with initiation of reperfusion is inhibited by hyperbaric oxygen.[13] Antagonism of the CD-18 (beta-2 integrin) adhesion molecule, which binds the endothelial intercellular adhesion molecule receptor in the postcapillary venule endothelium, is inhibited by hyperbaric oxygen.[16] This initiates the adherence response of neutrophils to the endothelium. A combination of hyperbaric oxygen and platelet-derived growth factor (PDGF) treatment has been shown to mediate upregulation of PDGF receptor messenger RNA expression. Hyperbaric oxygen increases expression of PDGF receptor protein levels in dermal fibroblast, which may be one of the factors responsible for enhanced wound healing.[17]

Two forces oppose leukocyte adhesion to the endothelium: (1) the shear force generated by blood flow and (2) the inherent adhesiveness of the endothelium. Cellular adhesion molecules (CAMS) are located on the endothelium. Changes in intracellular metabolism, pH, redox potential, and production of inflammatory cytokines and lipid mediators are signals inducing the synthesis of CAMS. Cellular surface CAMS interact with endothelial cells and their binding partners (ligands) on the polymorphonuclear leukocytes (PMNL). Initially the opposing shearing and adhesive forces cause tethering and rolling of the PMNL on the surface endothelium. As the rolling overcomes the shear force, adhesive interaction oc-

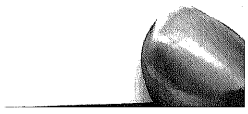
curs between the PMNL and endothelium cells. The CAMS exchange their expression, and chemoattractants affect the adhesiveness of the endothelial cells for PMNL, overcoming the shear force of blood flow and resulting in binding of PMNL to the endothelial cell.[18] Transendothelial migration then occurs into the surrounding tissues.

Recent work on nitric oxide and reperfusion injury shows that there are three subtypes of nitric oxide synthase. These are found on different cells, including endothelial cells, PMNL, and macrophages, and also on neuronal populations. Controversy exists at present regarding the physiological concentrations of nitric oxide present in tissues and how much is needed to produce an antiadhesive effect.

■ Clinical Experience

Clinical experience with acute traumatic peripheral ischemia is limited. Randomized clinical trials are difficult to conduct because of the complexity and diversity of the injuries. The first clinical work was done by Perrins,[19] who demonstrated that threatened flaps had a threefold increase in survival with the use of hyperbaric oxygen therapy. Strauss[20] described 700 cases, reporting subjective benefits of hyperbaric oxygen, in which frequent use of hyperbaric oxygen therapy produced better clinical responses. The Russian and Eastern European literature indicates far more experience than the English language literature. Shupak and colleagues[21] described a 75% reduction of amputation rate after trauma and acute ischemic injury with the use of adjunctive hyperbaric oxygen. Radonic and associates[22] reported improved outcomes after popliteal vessel injury and better wound healing with HBO therapy.

The first double-blind, randomized, placebo-controlled clinical trial of Gustilo grade III-B and III-C injuries was reported by Bouachour and associates.[23] Complete healing occurred in 94% of the hyperbaric group versus 59% of controls ($P < 0.01$). There was also a reduction in the need for additional surgical procedures in both groups (6% in the hyperbaric group and 33% in the control groups [$P < .05$]). Among patients older than 40 years of age, there was a significant improvement in outcome in the hyperbaric group ($P < .05$). Transcutaneous oxygen measurements were significantly improved in the HBO-treated patients compared with the control group. In making the decision to use adjunctive hyperbaric oxygen for acute traumatic peripheral ischemia, the Gustilo or MESS system should be applied (see Tables 2 and 3). It is essential to consider timely introduction of hyperbaric oxygen therapy because, with time delays in making this decision, changes are being induced by edema and ischemia, until, at some point, it becomes irreversible (see Table 1).



Cost Impact

Complications of infection and/or amputations necessitated by nonunion occur in 50% of patients with Gustilo grade III-B and III-C open fractures and crush injuries. Bouachour and associates[23] reported that the use of hyperbaric oxygen was associated with fewer surgeries, improved healing rates, and improved responses in older age patients.

■ Skin Grafts and Flaps

Hyperbaric oxygen therapy is not recommended for uncompromised skin grafts or flaps. However, compromise caused by radiation, fibrosis, decreased perfusion, or hypoxia is a good indication for flap salvage with hyperbaric oxygen. Hyperoxygenation improves fibroblast stimulation, collagen synthesis, and neovascularization; thus, skin flap survival can be improved. Both animal and clinical studies have been undertaken to support these claims. Champion and colleagues,[24] using a rabbit model pedicle flap, demonstrated a 100% flap survival rate in the HBO group, whereas the control group showed a necrosis rate of more than 40%. The increased oxygen levels achieved under repetitive treatments (2 ATA for 120 minutes twice a day for 5 days) sustained the compromised flap until neovascularization had occurred.

Niinikoski[25] suggested that enhanced diffusion of oxygen into a disrupted circulation area produced increased tissue viability and that this mechanism was responsible for the 51% improved viability in tubular skin grafts in rats treated with hyperbaric oxygen compared with air-breathing controls. Arturson and Khanna,[26] using a dorsal random skin flap in rats, revealed a significant improvement in flap survival among HBO-treated animals over untreated controls ($P < .05$). In this model, a predictable and constant degree of necrosis was produced. The importance of timeliness of treatment on response was noted by Jurell and Kaijser,[27] HBO therapy was administered intermittently during 24 hours to rats with cranial pedicle flaps: the oxygen-treated group had a flap-survival rate 50% higher than the rate among controls ($P < .001$). Delaying the hyperbaric oxygen for 24 hours still yielded better flap survival ($P < .01$).

Greenwood and Gilchrist,[28] reported a reduction of the extent of ischemic necrosis of skin flaps in previously irradiated rats. Six months after exposure to 2,600 rads, rectangular pedicle flaps were created. Mean flap necrosis was greater in the control group ($P < .05$). Tan and associates[29] and Nemiroff and coworkers,[30] demonstrated increased survival of island flaps and experimental skin flaps in randomized controlled studies on rats.

Work by Ketchum and colleagues[31] in the burn animal model showed enhanced capillary proliferation following hyperbaric oxygen. This was confirmed in the experimental skin flap model developed by Nemiroff and Lungu,[32] which showed a significantly greater increase in the number of blood vessels in the hyperbaric group compared with air controls ($P < .01$). To be most effective, hyperbaric oxygen must be administered as

soon after surgery as possible. Histochemical staining with ATPase to demonstrate small blood vessels revealed three times greater capillary distal growth in HBO-treated pedicle flaps compared with aged-matched controls.[33] Zamboni and colleagues,[13] using axial pattern flaps in male rats following prolonged total ischemia, showed that hyperbaric oxygen treatment during ischemia or reperfusion significantly reduced the mean flap necrosis from 28% to a range of 9% to 12%. The axial-pattern skin flap survival was significantly increased with hyperbaric oxygen, and the effect was systemic, not local.

All types of flaps—free-skin grafts, pedicle flaps, random flaps, irradiated wounds/flaps, composite grafts, and axial pattern flaps—with different blood supplies have shown increased viability when hyperbaric oxygen is used to reduce the hypoxic insult.

Many clinical studies of the use of hyperbaric oxygen for grafts have been undertaken. Perrins,[19] Greenwood and Gilchrist,[28] and Bowersox and associates[34] have all shown significant flap survival and salvage after hyperbaric oxygen therapy. The 10% failure rate of Bowersox and associates[34] compared favorably with other studies, in which the failure rates were up to 67% in compromised tissues. Zamboni[35] provides a critical review of the use of hyperbaric oxygen in flap and skin graft enhancement and survival.

It must be emphasized that hyperbaric oxygen therapy is not necessary or recommended for normal, uncompromised skin grafts or flaps. However, for patients who received radiation before or after surgery and in those with compromised flaps, hyperbaric oxygen can make the difference between flap survival and death. From a cost-containment perspective, a failed flap may increase costs (surgical fees and hospitalization fees) by $30,000. In contrast, 10 to 20 hyperbaric oxygen treatments for flap salvage may cost $3,000 to $6,000. In their study on mandibular radionecrosis, Marx and coworkers[36] calculated a potential cost savings per patient of $60,000 related to postradiation with extraction of teeth. In the group that did not receive hyperbaric oxygen therapy, 29.9% of patients developed osteoradionecrosis, compared with 5.4% in the HBO-treated group.

■ Summary

In the future, the indications for HBO therapy in acute peripheral ischemic injuries will likely be based on objective criteria rather than, as at present, on clinical diagnoses alone. This chapter offers objective criteria for using HBO in crush injuries and compartment syndromes. The pathophysiology of ATPI are well defined. Hyperbaric oxygen mediates the effects of ATPI through four mechanisms: hyperoxygenation, vasoconstriction, reperfusion, and host factors. The cost benefits of using HBO will be substantial, since complications from ATPI are very expensive. As

objective criteria replace the presently used subjective criteria, hyperbaric oxygen therapy will become an integral part of trauma management of these injuries.

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