



*Currents: Fall 2002, Volume 3, Number 4*

## Hyperbaric oxygen therapy enhances tissue healing

*Zlatko Anguelov (in collaboration with Eric Greensmith, M.D.)*

**History:** Compressed air has been used as a therapeutic tool since medieval times with variable success and without any knowledge of what may cause its beneficial effect on disease. In the mid-1950s hyperbaric oxygen (HBO) came into use in the U.S. and the Netherlands, especially for conducting surgical operations under pressure. Clinicians noted that patients were less cyanotic after anesthesia in a hyperbaric chamber and since, nitrous oxide became a powerful anesthetic when administered under increased pressure. HBO use declined in the early 1970s because of lack of serious research on the mechanisms of action and appropriate indications. In this country a revival of the field occurred in the late 1970s when the Undersea Medical Society became involved in clinical hyperbarics, and a textbook on HBO therapy was published.

Hyperbaric medicine was naturally restricted at that time to the military for management of decompression sickness and air embolism. Renewed involvement of civilian physicians began as former military physicians from both the Navy and Air Force continued teaching and practicing hyperbaric medicine. Official certification was facilitated through diving medicine courses. An important reason for the swift recognition of the field by mainstream medicine is the hyperbaric community's responsible self-restriction to treating only a limited number of disorders that have been backed by scientific evidence.

**New facts:** In 1976, the then renamed **Undersea and Hyperbaric Medical Society** established a Committee on Hyperbaric Oxygen Therapy to address the evolving applications of HBO. Beyond decompression sickness, CO intoxication, and gas embolism, the currently approved disorders that can be treated with HBO as an adjunctive therapy are: cyanide poisoning; gas gangrene; crush injury, compartment syndrome, and other acute traumatic ischemias; tissue healing in selected problem wounds, such as diabetic wounds, venous-stasis ulcers, decubitus ulcers, and arterial-insufficiency ulcers; exceptional blood loss anemia; necrotizing fasciitis and other necrotizing soft-tissue infections; chronic refractory osteomyelitis; radiation injury to tissues (soft tissue and bone radionecrosis); compromised skin grafts and flaps; and thermal burns. Third-party payors recognize the following disorders for reimbursement: necrotizing infections, all types of radionecrosis, chronic refractory osteomyelitis, and compromised skin grafts.

HBO has only two physiologic effects on the human body: a mechanical effect and the effect of the increased partial pressure of oxygen in all the tissues. Bubbles and gas-containing cavities are subject to **the mechanical effect** of oxygen pressure. Bubble volume is changed in a geometric progression related to the pressure change, thus allowing for very large reductions of volume with only small increases of oxygen pressure. In decompression sickness and gas embolism, the bubbles are intravascular and either spherical or cylindrical in shape. These bubbles mechanically obstruct the microvascular blood flow. Thus, when a gas bubble is compressed by HBO therapy, its volume decreases and the microvascular flow is restored. Beyond mechanical obstruction of blood flow, endothelial cells are injured by direct contact with the gas bubbles, setting off a chain reaction of biochemical events that further limit tissue oxygen intake.

When a patient is breathing 2.8 atmospheres of oxygen in the hyperbaric chamber, oxygen tensions are raised 10 to 13 times above their normal level. Because oxygen dissolves in plasma at a constant rate, the plasma carries a high level of oxygen. Consequently, tissue oxygen needs can be met by plasma-dissolved oxygen alone, thus allowing for hemoglobin to be still fully saturated on the venous side. The high levels of plasma-dissolved oxygen explain the efficacy of HBO in the rare cases of blood-loss anemia. Patients with hematocrits below 6% have been sustained by HBO until life-saving blood transfusion could be started. High oxygen pressure has a variety of effects on various functions, such as the enhancement of killer-cells' activity, vasoconstriction in normal vessels, restoration of fibroblast growth and collagen production, enhancement of osteoclast activity, increased capillary proliferation, etc.

Under **elevated partial pressure** oxygen behaves like any other drug--too little is ineffective and too much will cause harm. Thus, the clinical use of HBO therapy is limited to a maximal partial pressure of three atmospheres. Exceeding this level provides no benefits and increases the toxic effects.

It has been documented that, although HBO causes general vasoconstriction, it doesn't reduce oxygen delivery to hypoxic tissues. To the contrary, HBO results in an increase of peripheral tissue oxygen delivery. Thanks to these and other effects, HBO enhances the healing of hypoxic wounds. Moreover, HBO inhibits the production of clostridial alpha-toxin in gas gangrene, reduces CO toxicity, enhances osteoclast activity, suppresses autoimmune responses, and has a favorable effect on edema in burns and post-ischemic tissues.

Hypoxia is the underlying characteristic of **wounds** that fail to respond to established medical management; they are called problem, or hypoxic, wounds. In a hypoxic environment, wound healing is halted by decreased fibroblast proliferation, collagen production, and capillary angiogenesis. Hypoxia also impairs the ability of oxygen-dependent macrophages to kill aerobic bacteria and creates an ideal environment for anaerobic organisms to thrive. HBO restores the conditions under which the cellular processes of wound healing may occur at a normal pace and efficiency.

**Necrotizing fasciitis** is often a life-threatening infection requiring intensive care. It is characterized by necrosis of the superficial and deep fascia, which manifests with pain, swelling, and foudroyant course. In addition to antibiotics and surgical removal of the necrotic tissue, HBO has proven to be a critical adjunctive therapy aiding in reversing the fatal course of the disease and healing the affected tissues.

We are still short of a clear understanding of the effects of HBO on wound healing. When, for example, a non-healing hypoxic wound is exposed to intermittent hyperoxia, enhanced cell growth leads to the increased formation of connective tissue and microvasculature. Fibroblast proliferation with collagen formation provides the structural support required for angiogenesis. The intermittent increase in oxygen levels allows for closure of small defects and provides an enhanced vascular bed for healing any kind of nonhealing wound as well as cases of radionecrosis, surgical wounds, graft or flap replacement, and thermal burns.

**Practice:** HBO is delivered in hyperbaric chambers, which are monoplace and multiplace. At UI Hospitals and Clinics, the multiplace hyperbaric chamber is functionally associated with the SICU. Pure oxygen is used in the monoplace chambers, whereas pressurized air is used in the multiplace ones, to enhance fire safety. Patients in the latter receive oxygen by a tight-fitting oronasal mask, head tent, or endotracheal tube.

The most important advantage of the multiplace chamber is that direct hands-on care may be given to patients during treatment, including suctioning and neurologic examination. Patients with multiple IV lines may be taken directly into the chamber with all their lines attached. In the event of mass casualty, more than one patient can be treated at a time. This advantage was proven when over a dozen undergraduates at a local college were exposed to Co intoxication due to malfunction in the dormitory heater; all students recovered uneventfully after HBO therapy. If cardiac arrest occurs, defibrillation can be carried out in the air-filled multiplace chamber.

Disadvantages of the multiplace chambers include initial higher cost, the use of oxygen mask or head tent, and the risk of decompression sickness for the inside health care personnel.

Nonhealing wounds of any nature, necrotizing fasciitis, thermal burns, radionecrosis, postoperative abscesses, skin grafts and flaps, and chronic refractory osteomyelitis are the most common conditions treated with HBO **as an adjunctive therapy** at UI Hospitals and Clinics