477e Hyperbaric and Diving Medicine

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WHAT IS HYPERBARIC AND DIVING MEDICINE?

Hyperbaric medicine is the treatment of health disorders using whole-body exposure to pressures greater than 101.3 kPa (1 atmosphere or 760 mmHg). In practice, this almost always means the administration of *hyperbaric oxygen therapy* (HBO_2T). The Undersea and Hyperbaric Medical Society (UHMS) defines HBO_2T as: "a treatment in which a patient breathes 100% oxygen … while inside a treatment chamber at a pressure higher than sea level pressure (i.e., >1 atmosphere absolute or ATA)." The treatment chamber is an airtight vessel variously called a hyperbaric chamber, recompression chamber, or decompression chamber, depending on the clinical and historical context. Such chambers may be capable of compressing a single patient (a monoplace chamber) or multiple patients and attendants as required (a multiplace chamber) **(Figs. 477e-1 and 477e-2)**. Historically, these compression chambers were first used for the treatment of divers and compressed air workers suffering decompression sickness (DCS; "the bends"). Although the prevention and treatment of disorders arising after decompression in diving, aviation, and space flight has developed into a specialized field of its own, it remains closely linked to the broader practice of hyperbaric medicine.

Despite an increased understanding of mechanisms and an improving evidence basis, hyperbaric medicine has struggled to achieve widespread recognition as a "legitimate" therapeutic measure. There are several contributing factors, but high among them are a poor grounding in general oxygen physiology and oxygen therapy at medical schools and a continuing tradition of charlatans advocating hyperbaric therapy (often using air) as a panacea. Funding for both basic and clinical research has been difficult in an environment where the pharmacologic agent under study is abundant, cheap, and unpatentable. Recently, however, there are signs of an improved appreciation of the potential importance of HBO_2T with significant National Institutes of Health (NIH) funding for mechanisms research and from the U.S. military for clinical investigation.

MECHANISMS OF HYPERBARIC OXYGEN

Increased hydrostatic pressure will reduce the volume of any bubbles present within the body (see "Diving Medicine"), and this is partly responsible for the success of prompt recompression in DCS and arterial gas embolism. Supplemental oxygen breathing has a dose-dependent effect on oxygen transport, ranging from improvement in hemoglobin oxygen saturation when a few liters per minute are delivered by simple mask at 101.3 kPa (1 ATA) to raising the dissolved plasma oxygen sufficiently to sustain life without the need for hemoglobin at all when 100% oxygen is breathed at 303.9 kPa (3 ATA). Most HBO_2T regimens involve oxygen breathing at between 202.6 kPa and 283.6 kPa (2 and 2.8 ATA), and the resultant increase in arterial oxygen tensions to >133.3 kPa (1000 mmHg) has widespread physiologic and pharmacologic consequences **(Fig. 477e-3)**.

FIGURE 477e-1 A monoplace chamber. *(Prince of Wales Hospital, Sydney.)*

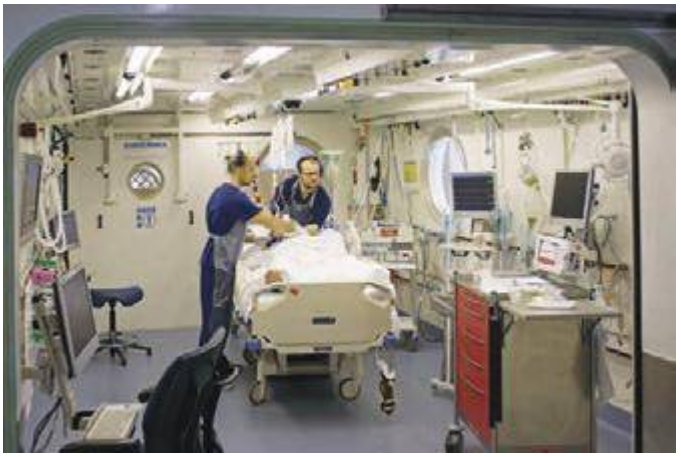

FIGURE 477e-2 A chamber designed to treat multiple patients. *(Karolinska University Hospital.)*

One direct consequence of such high intravascular tension is to increase greatly the effective capillary-tissue diffusion distance for oxygen such that oxygen-dependent cellular processes can resume in hypoxic tissues. Important as this may be, the mechanism of action is not limited to this restoration of oxygenation in hypoxic tissue. Indeed, there are pharmacologic effects that are profound and long-lasting. Although removal from the hyperbaric chamber results in a rapid return of poorly vascularized tissues to their hypoxic state, even a single dose of HBO_2T produces changes in fibroblast, leukocyte, and angiogenic functions and antioxidant defenses that persist many hours after oxygen tensions are returned to pretreatment levels.

It is widely accepted that oxygen in high doses produces adverse effects due to the production of reactive oxygen species (ROS) such as superoxide (O_2^-) and hydrogen peroxide (H_2O_2). It has become increasingly clear over the last decade that both ROS and reactive nitrogen species (RNS) such as nitric oxide (NO) participate in a wide range of intracellular signaling pathways involved in the production of a range of cytokines, growth factors, and other inflammatory and repair modulators. Such mechanisms are complex and at times apparently paradoxical. For example, when used to treat chronic hypoxic wounds, HBO_2T has been shown to enhance the clearance of cellular debris and bacteria by providing the substrate for macrophage phagocytosis; stimulate growth factor synthesis by increased production and stabilization of hypoxia-inducible factor 1 (HIF-1); inhibit leukocyte activation and adherence to damaged endothelium; and mobilize CD34+ pluripotent vasculogenic progenitor cells from the bone marrow. The interactions between these mechanisms remain a very active field of investigation. One exciting development is the concept of *hyperoxic preconditioning* in which a short exposure to HBO_2 can induce tissue protection against future hypoxic/ischemic insult, most likely through an inhibition of mitochondrial permeability transition pore (MPTP) opening and the release of cytochrome c. By targeting these mechanisms of cell death during reperfusion events, HBO_2 has potential applications in a variety of settings including organ transplantation. One randomized clinical trial suggested that HBO_2T prior to coronary artery bypass grafting reduces biochemical markers of ischemic stress and improves neurocognitive outcomes.