

## INDICATIONS FOR HYPERBARIC OXYGEN

The appropriate indications for HBO<sub>2</sub>T are controversial and evolving. Practitioners in this area are in an unusual position. Unlike most branches of medicine, hyperbaric physicians do not deal with a range of disorders within a defined organ system (e.g., cardiology), nor are they masters of a therapy specifically designed for a single category of disorders. Inevitably, the encroachment of hyperbaric physicians into other medical fields generates suspicion from specialist practitioners in those fields. At the same time this relatively benign therapy, the prescription and delivery of which requires no medical license in most jurisdictions (including the United States), attracts both charlatans and well-motivated proselytizers who tout the benefits of oxygen for a plethora of chronic incurable diseases. This battle on two fronts has meant that mainstream hyperbaric physicians have been particularly careful to claim effectiveness only for those conditions where there is a reasonable body of supporting evidence.

In 1977, the UHMS systematically examined claims for the use of HBO<sub>2</sub>T in more than 100 disorders and found sufficient evidence to support routine use in only 12. The Hyperbaric Oxygen Therapy Committee of that organization has continued to update this list periodically with an increasingly formalized system of appraisal for new indications and emerging evidence (Table 477e-1). Around the world, other relevant medical organizations have generally taken a similar approach, although indications vary considerably—particularly those recommended by hyperbaric medical societies in Russia and China where HBO<sub>2</sub>T has gained much wider support than in the United States, Europe, and Australasia. Recently, several Cochrane reviews have examined the randomized trial evidence for many putative indications, including attempts to examine the cost-effectiveness of HBO<sub>2</sub>T. Table 477e-2 is a synthesis of these two approaches and lists the estimated cost of attaining health outcomes with the use of HBO<sub>2</sub>T. Any savings associated with alternative treatment strategies avoided as a result of HBO<sub>2</sub>T are not accounted for in these estimates (e.g., the avoidance of lower leg amputation in diabetic foot ulcers). Following are short reviews of three important indications currently accepted by the UHMS.

### LATE RADIATION TISSUE INJURY

Radiotherapy is a well-established treatment for suitable malignancies. In the United States alone, approximately 300,000 individuals annually will become long-term survivors of cancer treated by irradiation. Serious radiation-related complications developing months or years after treatment (late radiation tissue injury [LRTI]) will significantly affect between 5 and 15% of those long-term survivors, although inci-

dence varies widely with dose, age, and site. LRTI is most common in the head and neck, chest wall, breast, and pelvis.

**Pathology and Clinical Course** With time, tissues undergo a progressive deterioration characterized by a reduction in the density of small blood vessels (reduced vascularity) and the replacement of normal tissue with dense fibrous tissue (fibrosis). An alternative model of pathogenesis suggests that rather than a primary hypoxia, the principle trigger is an overexpression of inflammatory cytokines that promote fibrosis, probably through oxidative stress and mitochondrial dysfunction, and a secondary tissue hypoxia. Ultimately, and often triggered by a further physical insult such as surgery or infection, there may be insufficient oxygen to sustain normal function, and the tissue becomes necrotic (radiation necrosis). LRTI may be life-threatening and significantly reduce quality of life. Historically, the management of these injuries has been unsatisfactory. Conservative treatment is usually restricted to symptom management, whereas definitive treatment traditionally entails surgery to remove the affected part and extensive repair. Surgical intervention in an irradiated field is often disfiguring and associated with an increased incidence of delayed healing, breakdown of a surgical wound, or infection. HBO<sub>2</sub>T may act by several mechanisms to improve this situation, including edema reduction, vasculogenesis, and enhancement of macrophage activity (Fig. 477e-3). The intermittent application of HBO<sub>2</sub> is the only intervention shown to increase the microvascular density in irradiated tissue.

**Clinical Evidence** The typical course of HBO<sub>2</sub>T consists of 30 once-daily compressions to 202.6–243.1 kPa (2–2.4 ATA) for 1.5–2 h each session, often bracketed around surgical intervention if required. Although HBO<sub>2</sub>T has been used for LRTI since at least 1975, most clinical studies have been limited to small case series or individual case reports. In a review, Feldmeier and Hampson located 71 such reports involving a total of 1193 patients across eight different tissues. There were clinically significant improvements in the majority of patients, and only 7 of 71 reports indicated a generally poor response to HBO<sub>2</sub>T. A Cochrane systematic review with meta-analysis included six randomized trials published since 1985 and drew the following conclusions (see Table 477e-2 for numbers needed to treat): HBO<sub>2</sub>T improves healing in radiation proctitis (relative risk [RR] of healing with HBO<sub>2</sub>T 2.7; 95% confidence interval [CI] 1.2–6) and after hemimandibulectomy and reconstruction of the mandible (RR 1.4; 95% CI 1.1–1.8); HBO<sub>2</sub>T improves the probability of achieving mucosal coverage (RR 1.4; 95% CI 1.2–1.6) and the restoration of bony continuity with osteoradionecrosis (ORN) (RR 1.4; 95% CI 1.1–1.8); HBO<sub>2</sub>T prevents the development of ORN following tooth extraction from a radiation field (RR 1.4; 95% CI 1.08–1.7) and reduces the risk of wound dehiscence following grafts and flaps in the head and neck (RR 4.2; 95% CI 1.1–16.8). Conversely, there was no evidence of benefit in established radiation brachial plexus lesions or brain injury.

### SELECTED PROBLEM WOUNDS

A problem wound is any cutaneous ulceration that requires a prolonged time to heal, does not heal, or recurs. In general, wounds referred to hyperbaric facilities are those where sustained attempts to heal by other means have failed. Problem wounds are common and constitute a significant health problem. It has been estimated that 1% of the population of industrialized countries will experience a leg ulcer at some time. The global cost of chronic wound care may be as high as U.S. \$25 billion per year.

**Pathology and Clinical Course** By definition, chronic wounds are indolent or progressive and resistant to the wide array of treatments applied. Although there are many contributing factors, most commonly these wounds arise in association with one or more comorbidities such as diabetes, peripheral venous or arterial disease, or prolonged pressure (decubitus ulcers). First-line treatments are aimed at correction of the underlying pathology (e.g., vascular reconstruction, compression bandaging, or normalization of blood glucose level), and HBO<sub>2</sub>T is an adjunctive therapy to good general wound care practice to maximize the chance of healing.

**TABLE 477e-1 CURRENT LIST OF INDICATIONS FOR HYPERBARIC OXYGEN THERAPY**

1. Air or gas embolism (includes diving-related, iatrogenic, and accidental causes)
2. Carbon monoxide poisoning (including poisoning complicated by cyanide poisoning)
3. Clostridial myositis and myonecrosis (gas gangrene)
4. Crush injury, compartment syndrome, and acute traumatic ischemias
5. Decompression sickness
6. Arterial insufficiency
  - Central retinal artery occlusion
  - Enhancement of healing in selected problem wounds
7. Exceptional blood loss (where transfusion is refused or impossible)
8. Intracranial abscess
9. Necrotizing soft tissue infections (e.g., Fournier's gangrene)
10. Osteomyelitis (refractory to other therapy)
11. Delayed radiation injury (soft-tissue injury and bony necrosis)
12. Skin grafts and flaps (compromised)
13. Thermal burns
14. Sudden sensorineural hearing loss

**Source:** The Undersea and Hyperbaric Medical Society (2013).