For most indolent wounds, hypoxia is a major contributor to failure to heal. Many guidelines to patient selection for HBO_2T include the interpretation of transcutaneous oxygen tensions around the wound while breathing air and oxygen at pressure (Fig. 477e-4). Wound healing is a complex and incompletely understood process. While it appears that in acute wounds healing is stimulated by the initial hypoxia, low pH, and high lactate concentrations found in freshly injured tissue, some elements of tissue repair are extremely oxygen dependent, for example, collagen elaboration and deposition by fibroblasts, and bacterial killing by macrophages. In this complicated interaction between wound hypoxia and peri-wound oxygenation, successful healing relies on adequate tissue oxygenation in the area surrounding the fresh wound. Certainly, wounds that lie in hypoxic tissue beds are those that most often display poor or absent healing. Some causes of tissue hypoxia will be reversible with HBO_2T, whereas some will not (e.g., in the presence of severe large vessel disease). When tissue hypoxia can be overcome by a high driving pressure of oxygen in the arterial blood, this can be demonstrated by measuring the tissue partial pressure of oxygen using an implantable oxygen electrode or, more commonly, a modified transcutaneous Clarke electrode.

The intermittent presentation of oxygen to those hypoxic tissues facilitates a resumption of healing. These short exposures to high oxygen tensions have long-lasting effects (at least 24 h) on a wide range of healing processes (Fig. 477e-3). The result is a gradual improvement in oxygen tension around the wound that reaches a plateau in experimental studies at about 20 treatments over 4 weeks. Improvements in oxygenation are associated with an eight- to ninefold increase in vascular density over both normobaric oxygen and air-breathing controls.

Clinical Evidence The typical course of HBO_2T consists of 20–30 once-daily compressions to 2–2.4 ATA for 1.5–2 h each session, but is highly dependent on the clinical response. There are many case series in the literature supporting the use of HBO_2T for a wide range of problem wounds. Both retrospective and prospective cohort studies suggest that 6 months after a course of therapy, about 70% of indolent ulcers will be substantially improved or healed. Often these ulcers have been present for many months or years, suggesting that the application of HBO_2T has a profound effect, either primarily or as a facilitator of other strategies. A recent Cochrane review included nine randomized controlled trials (RCTs) and concluded that the chance of ulcer healing improved about fivefold with HBO_2T (RR 5.20; 95% CI 1.25–21.66; $p = .02$). Although there was a trend to benefit with HBO_2T, there was no statistically significant difference in the rate of major amputations (RR 0.36; 95% CI 0.11–1.18).

CARBON MONOXIDE POISONING

Carbon monoxide (CO) is a colorless, odorless gas formed during incomplete hydrocarbon combustion. Although CO is an essential endogenous neurotransmitter linked to NO metabolism and activity, it is also a leading cause of poisoning death, and in the United States alone results in more than 50,000 emergency department visits per year and about 2000 deaths. Although there are large variations from country to country, about half of nonlethal exposures are due to self-harm. Accidental poisoning is commonly associated with defective or improperly installed heaters, house fires, and industrial exposures. The motor vehicle is by far the most common source of intentional poisoning.

Pathology and Clinical Course The pathophysiology of carbon monoxide exposure is incompletely understood. CO binds to hemoglobin with an affinity more than 200 times that of oxygen, directly reducing the oxygen-carrying capacity of blood, and further promoting tissue hypoxia by shifting the oxyhemoglobin dissociation curve to the left. CO is also an anesthetic agent that inhibits evoked responses and narcotizes experimental animals in a dose-dependent manner. The associated loss of airway patency together with reduced oxygen carriage in blood may cause death from acute arterial hypoxia in severe poisoning. CO may also cause harm by other mechanisms including direct disruption of cellular oxidative processes, binding to myoglobin and hepatic cytochromes, and peroxidation of brain lipids.

The brain and heart are the most sensitive target organs due to their high blood flow, poor tolerance of hypoxia, and high oxygen requirements. Minor exposure may be asymptomatic or present with vague constitutional symptoms such as headache, lethargy, and nausea, whereas higher doses may present with poor concentration and cognition, short-term memory loss, confusion, seizures, and loss of consciousness. While carboxyhemoglobin (COHb) levels on admission do not necessarily reflect the severity or the prognosis of CO poisoning, cardiorespiratory arrest carries a very poor prognosis. Over the longer term, surviving patients commonly have neuropsychological sequelae. Motor disturbances, peripheral neuropathy, hearing loss, vestibular abnormalities, dementia, and psychosis have all been reported. Risk

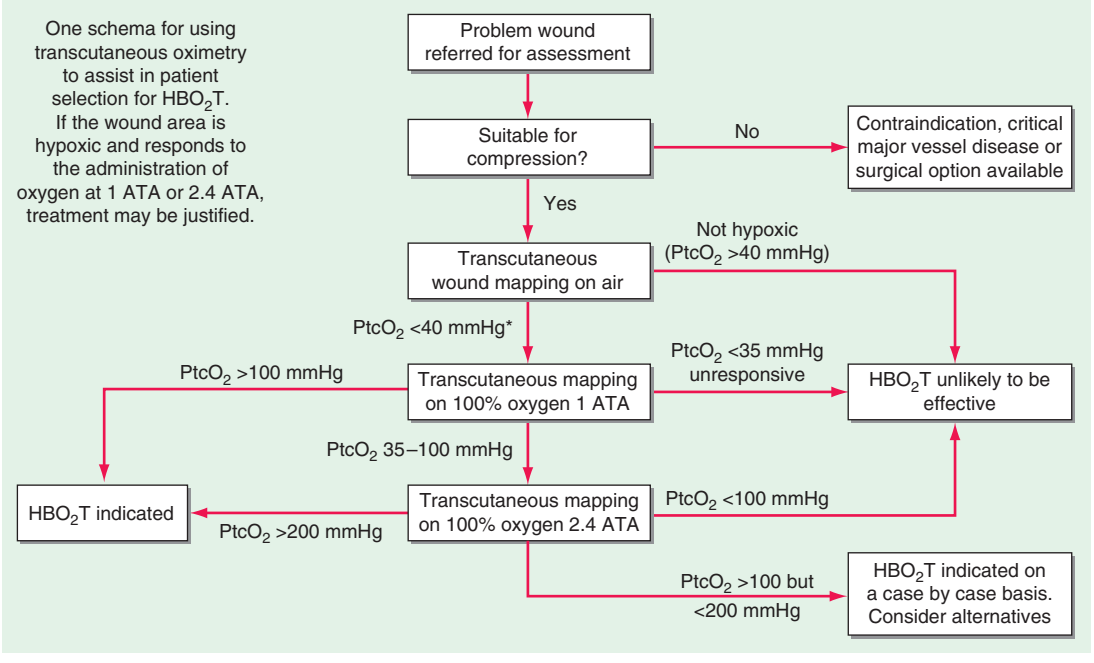

FIGURE 477e-4 Determining suitability for hyperbaric oxygen therapy (HBO_2T) guided by transcutaneous oximetry around the wound bed. *In diabetic patients, <50 mmHg may be more appropriate. $PtcO_2$, transcutaneous oxygen pressure.