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REVIEW ARTICLE

# Hyperbaric Oxygen Therapy

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**KEYWORDS:**
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**Abstract** Hyperbaric oxygen is a treatment in which a patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than at sea level pressure (ie, >1 atm). In certain circumstances, it represents the primary treatment modality, whereas in others it is an adjunct to surgical or pharmacologic interventions. After reviewing all the scientific evidence available to date, the Undersea and Hyperbaric Medical Society, in its latest publication, *Hyperbaric Oxygen Therapy Indications* (12th ed.), recommends 13 indications for hyperbaric oxygen therapy. Several of these indications are related to our practice of wound care. The article discusses these indications in detail.


## Introduction

Hyperbaric oxygen is a treatment in which a patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than at sea level pressure (ie, >1 atm abs). In certain circumstances, hyperbaric oxygen therapy (HBOT) is the primary treatment modality, whereas in others, it is an adjunct to surgical or pharmacologic interventions.[1]

Treatment can be carried out in either a monoplace or a multiplace chamber. In a monoplace chamber, a single patient is accommodated, the entire chamber is pressurized with 100% oxygen, and the patient breathes the ambient chamber oxygen directly. A multiplace chamber holds 2 or more people and is pressurized with compressed air while patients breathe 100% oxygen via masks, head hoods, or endotracheal tubes.

Topical oxygen therapy is not HBOT. The patient must receive the oxygen by inhalation within a pressurized chamber, and the Undersea and Hyperbaric Medical Society position paper indicates that pressurization should be at least 1.4 abs or higher for the therapy to be considered HBOT.[2]

After reviewing all the scientific evidence available to date, the Undersea and Hyperbaric Medical Society, in its latest publication, *Hyperbaric Oxygen Therapy Indications* (12th ed.), recommends the following 13 indications for HBOT.[1]

1. Air or gas embolism
2. Carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning
3. Clostridial myositis and myonecrosis (gas gangrene)
4. Crush injury, compartment syndrome and other acute traumatic ischemias
5. Decompression sickness
6. Arterial insufficiencies
   a. Central retinal artery occlusion
   b. Enhancement of healing in selected problem wounds

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7. Severe anemia
8. Intracranial abscess
9. Necrotizing soft tissue infections
10. Osteomyelitis (refractory)
11. Delayed radiation injury (soft tissue and bony necrosis)
12. Compromised grafts and flaps
13. Acute thermal burn injury

Most of these indications are approved by Medicare and other insurance, but it is advisable to check with local Medicare intermediaries and insurance companies for coverage determination.

The indications that we commonly see in our wound care practice are discussed in detail in the following sections of this article.

## Clostridial Myositis and Myonecrosis (Gas Gangrene)

Clostridial myositis and myonecrosis, or gas gangrene, is an acute, rapidly progressive nonpyogenic, invasive clostridial infection of the muscles, characterized by profound toxemia, extensive edema, massive death of tissue, and a variable degree of gas production. This infection is most commonly caused by anaerobic, spore forming, gram-positive, encapsulated bacilli of the genus *Clostridium*. The most commonly isolated organism is *Clostridium perfringens* type A.[3]

The onset of gas gangrene may occur between 1 and 6 hours after injury or an operation. It begins with severe and sudden pain in the infected area, and the pain is out of proportion to the lesion. Usually, pain starts after the trauma or an operation. The skin initially appears shiny and tense but quickly becomes dusky and progresses to a bronze discoloration. Any delay in recognition of this condition can be fatal. Other clinical findings are hemorrhagic bulla, vesicles, swelling and edema of the infected area, and noncontractile dark red to black or greenish muscles that do not bleed when cut. Crepitus is usually present.[3]

X-ray shows featherlike figures between muscle fibers, an early and highly characteristic sign of clostridial myonecrosis.[3]

A serious concern in gas gangrene is the rapidly advancing phlegmon caused by continuous production of alpha toxin in the infected but still viable tissue. It is essential to stop alpha toxin production as soon as possible and to continue HBOT until the advancement of the disease process has clearly been arrested.[2,3] Van Unnik found that it is necessary to achieve tissue $Po_2$ of 250 mm Hg to stop toxin production, and this $Po_2$ can be achieved only by starting HBOT as soon as possible.[1,3]

The recommended treatment profile consists of hyperbaric oxygen at 3.0 atm abs for 90 minutes, 3 times a day for the first 24 hours, followed by twice per day for the next 2 to 5 days. If patient remains toxic, the treatment profile needs to be extended.[1,3]

## Crush Injuries and Skeletal Muscle Compartment Syndromes

Crush Injuries represent a spectrum of injury to body parts as a result of trauma. Typically the injury may involve skin, subcutaneous tissue, muscle, tendons, bone and joint. Complications arising from crush injuries can be osteomyelitis, nonunion of fractures, failed flap and amputations that occur in approximately 50% of the cases. HBOT can be used as an adjunct to get better outcomes.[1,4]

Compartment syndrome is another consequence of trauma. Edema, bleeding, or a combination within the confined fascial envelope increases the pressure within the skeletal muscle compartment. When tissue fluid pressure increases above the capillary pressure, signs of ischemia set in. In early stages, HBOT assists with slowing the progression and complication before fasciotomy is required.[1,5,6,7]

In crush injuries and compartment syndrome, HBOT helps in one of the following 3 ways: (1) supplements oxygen to poorly perfused areas in early postinjury period, (2) reduces edema, and (3) mitigates the reperfusion injury.[1,5,6,7]

Patients with crush injuries benefit from HBOT based on the seriousness of injury and the ability of the host to respond to the injury. However, the best time to start HBOT is with the initial management of the crush injuries, when complications are predictable, such as the Gustilo IIIB and C fractures and in lesser Gustilo grades in impaired and decompensated hosts.[6,7]

Compartment syndrome is divided into 3 stages: *suspected*, *impending*, and *established*. HBOT is not recommended in the suspected stage, when compartment syndrome is not actually present but there is a suspicion that a compartment syndrome may develop.[7] In the established stage, the patient should be monitored with frequent neurocirculatory checks of the injured extremity.[7]

In the impending stage, the patient develops signs such as increasing pain, hyperesthesias, muscle weakness, discomfort with passive stretch, and tenseness in the compartment. The compartment pressure should be measured. If the compartment cannot be measured or if pressure is such that immediate fasciotomy is not needed, then HBOT should be started as soon as possible. However, the patient should demonstrate 3 or more clinical findings suggestive of compartment syndrome.[1,5,6,7]

In the established stage, symptoms, signs, and pressure measurement suggest compartment syndrome and immediate fasciotomy must be done. However, after fasciotomy, HBOT is used if the patient has significant residual problems, such as ischemic muscle, threatened flaps, residual neuropathy, massive swelling, or significant host impairment.[1,7]

Treatment criteria for HBOT in crush injuries varies depending on suspected pathophysiology. HBOT is given at 2 ATA in monoplace chambers and 2.4 ATA in multiplace chambers, with 3 treatments in 24 hours for critical

ischemia; twice a day for threatened flaps, and once a day when one is dealing with infections or healing delay because of impaired host.[1,7]

HBOT for compartment syndrome is given at 2.0 to 2.4 ATA for 90 to 120 minutes, twice a day, for 7 to 10 days.[1,7]

## Problem Wounds

Problem wounds represent a significant and growing challenge to our health care. The hypoxic nature of all wounds has been demonstrated, and the hypoxia, when pathologically increased, correlates with impaired wound healing and increased rates of wound infection.[1,8] The rate at which all normal wounds heal has been shown to be oxygen dependent.[8,9] Fibroblast replication, collagen deposition, angiogenesis, resistance to infection, and intracellular leukocyte bacterial killing are oxygen-sensitive responses essential to normal wound healing. Evidence suggests that intermittent oxygenation of hypoperfused wound beds, a process achievable only in selected patients by exposing them to HBOT, sets in motion a cascade of events that leads to wound healing.[8,9]

Although HBOT is used in a variety of problem wounds, the best evidence exists for treatment of Wagner grade 3 or worse diabetic foot ulcers.[1]

For a cost-effective application of HBOT, identifying wounds that would most likely benefit from HBOT is paramount. Although aggressive distal lower-extremity bypass grafting and lower-extremity angioplasty do increase limb salvage rates, the microcirculation component causes difficulty with salvage in spite of aggressive lower extremity revascularization.[10,11]

Transcutaneous oxygen tension measurements provide a direct, quantitative assessment of oxygen availability to the periwound skin and an indirect measurement of periwound microcirculatory blood flow. Hypoxia (ie, wound $Po_2 < 40$ mm Hg) generally best defines wounds appropriate for HBOT. It is important to note that transcutaneous oxygen study is a better predictor of failure than success.[10,11]

### Diabetic Foot Ulcer

While the evidence suggests that all hypoxic diabetic lower extremity wounds could benefit from HBOT, the majority of clinical trials on HBOT have included wounds on the basis of severity and level of tissue involvement. The Centers for Medicare and Medicaid Services has approved coverage for HBOT in patients with diabetic wounds of the lower extremities who met the following criteria:

1. Patient has type 1 or 2 diabetes mellitus and has lower-extremity wound due to diabetes.
2. Patient has wound classified as Wagner grade 3 or higher.
3. Patient has failed an adequate course of standard wound therapy. (Standard wound therapy is defined as 30 days of standard treatment, including assessment and correction of vascular abnormalities, optimization of nutritional status and glucose control, debridement, moist wound dressings, off-loading, and treatment of infection.)

For HBOT to continue, reevaluation at 30-day intervals must show continued progress in healing.[1] The usual treatment protocol for HBOT in diabetic wounds is HBOT given at 2.0 to 2.4 ATA for 90 minutes daily for 30 to 40 days.[1,12,13]

HBOT may be recommended in other wound indications in a specific situation, but it may not be reimbursed by some third-party payers.

### Arterial Insufficiency Ulcer

The Wound Healing Society clinical practice guidelines for arterial insufficiency ulcer were published in 2006. Guideline 6B1a states, "In patients with non-reconstructable anatomy or whose ulcer is not healing despite revascularization, HBOT should be considered as adjuvant therapy." Selection criteria include ulcers that are hypoxic (because of ischemia) and whose hypoxia is reversible by hyperbaric oxygenation. Guideline 6B1b states, "HBOT should be investigated in the treatment of ischemia-reperfusion injury after revascularization in patients with arterial ulcers."[1,14]

### Venous Stasis Ulcer

HBOT is not indicated in the primary management of venous stasis ulcers of the lower extremities. HBOT may be required to support skin grafting in patients with concomitant peripheral arterial occlusive disease and in diabetic patients whose hypoxia is not corrected by control of edema.[1]

### Pressure Ulcer

HBOT is not indicated in routine decubitus ulcer management. It may be necessary for the support of skin grafts or flaps showing evidence of ischemic failure, for ulcer developing in previously radiated fields, in presence of refractory osteomyelitis, or in presence of progressive necrotizing infections.[1]

## Necrotizing Soft Tissue Infections

Necrotizing fasciitis is an acute, potentially fatal infection of the superficial and deep fascia of the skin and soft tissues and progresses to ischemic dermal necrosis after involvement of the dermal blood vessels, which traverse through the fascial layers.[1,15]

## Clinical Presentation

A patient with necrotizing fasciitis usually presents with pain out of proportion to the skin findings, swelling, fever, and chills. Mistakenly, the area of infection is assumed to be cellulitis and not a serious form of infection. However, with time, the infection will progress rapidly, causing areas of blisters and bullae formation. Eventually, skin starts appearing dusky, grayish, or frankly black. A surgeon confirms the diagnosis during debridement when the necrotic fascia are found.[1,15]

## Microbiology

Common organisms are groups A, C, or G β-hemolytic streptococci; other commonly isolated organisms are *Enterobacteriaceae*, *Enterococcus* species, *Bacteroides* species, *Peptococcus* species, *Candida* species, and methicillin-resistant *Staphylococcus aureus*—community acquired. The occurrence of *S aureus* plus anaerobic streptococci is also known as Meleney's synergistic gangrene.[1,15]

## Clinical Management

Numerous studies have continued to demonstrate the beneficial effect of HBOT in the management of necrotizing fasciitis. The protocol for treating necrotizing fasciitis with HBOT includes initiating therapy at 2.0 to 2.5 atm abs for 90 minutes of oxygen given twice a day for the first few days until there appears to be no further extension of necrosis in previously debrided areas and the infection is controlled. Patients will need standard wound care; debridement of necrotic tissue; drainage of fluid collections and abscesses; antibiotics directed at the expected range of organisms; intravenous gamma globulin, particularly if the necrotizing soft tissue infection is associated with group A hemolytic streptococcal infection and toxic shock syndrome; and goal-directed management of sepsis.[1,15,16]

# Refractory Osteomyelitis

Osteomyelitis is an infection of bone or bone marrow, usually caused by pyogenic bacteria or mycobacteria. Refractory osteomyelitis is defined as a chronic osteomyelitis that persists or recurs either after definitive surgical debridement or after a period of 4 to 6 weeks of appropriate antibiotic therapy.[1,17]

The Cierny-Mader classification of osteomyelitis can be used as a guide to determine which patients will most likely benefit from adjunctive HBOT. Stage 1 disease in the Cierny-Mader classification is primarily managed with antibiotics alone. Stage 2 disease generally responds well to appropriate antibiotics and superficial debridement of the affected bone and soft tissues. Patients with stage 3 or 4 osteomyelitis, complicated by adverse local or systemic risk factors, are most likely to benefit from HBOT as an adjunct to continued antibiotics and repeat surgical debridement.[1]

HBOT is usually given on a daily basis, 5 to 7 times per week, and timed to begin just after the most recent surgical debridement. Initial treatment at 2.4 to 2.5 ATA may provide the best theoretical balance between clinical efficacy and oxygen toxicity risk. A total of 30 to 40 treatments are required to attain the desired clinical results. If osteomyelitis fails to resolve or recurs after a total of 6 to 8 weeks of continuous, culture-directed antibiotics and hyperbaric oxygen treatment (30-40 sessions), then nidus for reinfection, such as occult sequestra or fixation hardware refractory to sterilization, should be suspected.[1,17]

# Delayed Radiation Injuries (Soft Tissue and Bony Necrosis)

Delayed radiation injuries are typically seen after a latent period of 6 months or more and may develop many years after the radiation exposure. Sometimes, delayed injuries are precipitated by an additional tissue insult such as surgery within the radiation field.[1,18]

Delayed radiation injury causes vascular changes characterized by obliterative endarteritis and stromal fibrosis. HBOT induces neovascularization in hypoxic tissues by stimulating angiogenesis and improving tissue oxygenation, reduces fibrosis, and mobilizes and stimulates an increase of stem cells within the irradiated tissues.[1,18]

The most widely applied and most extensively documented indication of HBOT in chronic radiation injury is in the treatment and prevention of radiation necrosis of the mandible.[1,18] The likelihood of mandibular necrosis because of therapeutic radiation varies widely among several reports. Reports indicate 0% incidence below doses of 6,000 cGy, increasing to 1.8% at doses from 6,000 to 7,000 cGy and 9% at doses greater than 7,000 cGy.[1,18] Usual HBOT protocol for treatment of osteoradionecrosis is given at 2.4 ATA for 30 daily treatments, followed if necessary by 10 additional daily treatments.[1,18] For prevention of osteoradionecrosis in patients who require dental surgery and dental extraction in a previously radiated field, 20 hyperbaric oxygen treatments before and 10 treatments after tooth removal are recommended.[1,18]

HBOT is also useful for radiation-induced soft tissue radionecrosis, mainly laryngeal necrosis, soft tissue necrosis of the head and neck, chest wall necrosis, radiation cystitis, proctitis, enteritis, myelitis, and brain necrosis. HBOT protocol is 2.0 to 2.5 ATA for 90 to 120 minutes for 30 to 60 treatments.[1,18]

# Compromised Grafts and Flaps

All flaps, by definition, have an inherent blood supply, whereas grafts are avascular tissues that rely on quality of the recipient bed for survival and revascularization.

Therefore, diagnosis of a compromised graft begins with proper assessment of the recipient wound bed. Compromised grafts can be salvaged by prompt institution of HBOT.[1,19]

There are many etiologies for flap compromise, mainly random ischemia, venous congestion, and occlusion to arterial circulation.

Free flaps can be exposed in both ischemia-reperfusion injury and secondary ischemic insults, which can compromise the viability of the flap. In many cases, there is no correctable mechanical cause for decreased flap perfusion. HBOT can reduce the need for repeat flap procedures, decreasing overall patient morbidity.[1,19]

Usual HBOT protocol is 2.0 to 2.5 ATA for 90 to 120 minutes. Initial treatment should be twice a day. Once the graft and flap are more viable, the patient can get once-a-day treatment. HBOT should be started as soon as signs of flap compromise appear. Usually, 20 treatments are required for wound bed preparation, and another 20 treatments are required after a flap or graft has been placed into its recipient bed.[1,19]

## Acute Thermal Burn Injury

Severe thermal injury is one of the most devastating physical and psychological injuries a person can suffer. The goal of burn treatment include survival of the patient, with rapid wound healing, minimal scarring and abnormal pigmentation, and cost-effectiveness.[1,20]

The burn wound is a complex and dynamic injury characterized by a central zone of coagulation surrounded by an area of stasis, bordered by an area of erythema. The zone of coagulation or complete capillary occlusion may progress during the first 48 hours after injury. Local microcirculation is compromised to the worst extent 12 to 24 hours postburn. Usually, ischemic necrosis and edema follow.[1,20]

HBOT is recommended in treatment of serious burns, burns that are greater than 20% of total body surface area or with involvement of the hands, face, feet, or perineum, that are deep partial- or full-thickness injuries.[1,20]

Adjunctive HBOT is helpful in decreasing healing time in major burn injuries, especially if the wounds are deep second-degree burns. It is also used to support a skin graft and flap.[1,20] Ideally, HBO is initiated as soon as possible after injury, often during initial resuscitation. Treatments are attempted 3 times within the first 24 hours and twice daily thereafter on a regimen of 90 minutes at 2.0 to 2.4 ATA. A total of 30 to 40 treatments may be needed. In large burns of 40% or greater, treatment is rendered for 10 to 14 days, in close consultation with the burn surgeon.[1,20]

Current data show that HBOT, when used as an adjunct in a comprehensive program of burn care, can significantly reduce morbidity and mortality, reduce length of hospital stay, and lessen the need for surgery.[1,20]

## Conclusion

HBOT has proved to be an useful adjunct in the treatment of multiple conditions in the wound care clinic. Judicious use of HBOT will greatly increase wound healing rates in patients with compromised split thickness skin grafts or flaps, refractory osteomyelitis, radiation injury, and progressive necrotizing fasciitis.

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