Journal of Hyperbaric Medicine, Vol. 2, No. 3, 1987

The Role of Hyperbaric Oxygen in Infectious Disease: Introduction

J. C. Davis

Hyperbaric Medicine, Methodist Hospital and Nix Medical Center, San Antonio, TX

During the 1960s, when results of experimental and clinical work on anaerobic clostridial infections came from the University of Amsterdam, one concern was that with wound oxygenation we would see overgrowth of aerobic microorganisms in these mixed wound infections. That not only failed to happen but there seemed to be favorable effects. In vitro and in vivo studies during the 1960s showed mixed results of the direct effects of hyperbaric oxygen (HBO) on various aerobic bacteria. In 1968, a landmark study by Hamblin (1) demonstrated a significant effect of HBO on 21-d established *Staphylococcus aureus* osteomyelitis in rats. In part of the study, HBO was compared to sea level air in 21-d established *S. aureus* osteomyelitis with no surgery or antibiotics and only oxygen effect studied. A significant difference was found, using very rigid criteria for success. For an animal to be categorized as healed it had to have sterile cultures, histologic evidence of no remaining sequestrum, no draining sinus, and radiologic evidence of no remaining bone infection. Table 1 shows that of 80 treated animals, 56 were healed and 24 remained infected. Among the 79 control animals, 54 remained infected and 25 were healed. A significant difference occurred in all groups, the most significant occurring in the groups treated at 2 ATA, 3 times a day ($P < 0.01$). In the groups treated for 1 h at 3 ATA twice a day, the difference was still significant but only at a $P < 0.05$. In view of previous studies showing disappointing results of direct HBO effect on bacteria, Hamblin (1) suggested some alteration in host response to infection as the mechanism, although in 1968 the nature of that host response was unknown. Subsequent studies by Hohn (2, 3), Hunt et al. (4), Hunt and Pai (5), Mader et al. (6), Niinikoski et al. (7), Knighton et al. (8), and Sheffield (9) confirmed hypoxia in infected wounds, impaired bacterial killing by hypoxic leukocytes, and correction by wound Po_2 elevation.

Among the indications currently accepted by the Undersea and Hyperbaric Medical Society, Hyperbaric Oxygen Committee (10) and by Medicare, almost half involve infection. Among the current Medicare accepted indications, infection is involved in gas gangrene and to some extent in crush injury and so-called Meleney ulcers, as well as in chronic refractory osteomyelitis and actinomycosis. The 1986 Hyperbaric Oxygen Committee Report (10) recognizes the indications shown in Table 2.

TABLE 1: Results of Hyperbaric Oxygen vs. Air Controls After a 21 d Follow-up Period

	Healed	Infected	Total
Treated	56	24	80
Controls	25	54	79

$P < 0.01$ T.I.D. groups. $P < 0.05$ B.I.D. groups. Adapted from Hamblin (1)

TABLE 2: Accepted Conditions, Hyperbaric Oxygen Committee Report, 1986

Air or gas embolism (acute)
Carbon monoxide poisoning, acute smoke inhalation and assumed carbon monoxide/cyanide poisoning
Crush injury, compartment syndrome and other acute traumatic ischemias
Cyanide poisoning (acute)
Decompression sickness
Enhancement of healing of selected problem wounds
Exceptional blood loss (anemia)
Gas gangrene (clostridial)
Necrotizing soft tissue infections
Osteomyelitis (refractory)
Radiation necrosis: osteoradionecrosis and soft tissue radiation necrosis
Selected refractory anaerobic infections: actinomycosis
Skin grafts or flaps (compromised)
Special Consideration
Burns (thermal)

Unquestionably, more basic studies in HBO therapy are needed, but a review of the literature shows the extensive work on which current practice is based. To introduce this symposium, a few exerpts are presented from the preface to the forthcoming *Problem Wounds: The Role of Oxygen,* edited by J.C. Davis and T.K. Hunt, to be published by Elsevier in 1987. An infected wound must be visualized as an area with an elevated metabolic rate. Regardless of the etiology, the common denominator of problem wounds is hypoxia. A wound with adequate perfusion may be hypoxic because infection raises oxygen consumption. Whether the oxygen tension of a relatively ischemic wound can be elevated by any tolerable dose of inspired oxygen depends on the status of regional perfusion. Data from research during the past 2 decades support the following "knowns."

1. Hypoxia in partially ischemic and infected wounds or irradiated tissue can often be corrected by high-dose oxygen inhalation. The dose of

inspired oxygen required varies from wound to wound and ranges from 40% oxygen at sea level to 100% oxygen at 2 to 3 ATA.

2. Elevation of wound oxygen tension significantly increases the capacity of leukocytes to kill many pathogenic bacteria. Elevating the wound Po_2 may be as effective as specific antibiotics and is additive to some.
3. Intermittent correction of problem wound hypoxia increases fibroblast replication and production of collagen to support capillary proliferation.
4. Anaerobic microorganisms that lack superoxide dismutase or catalase are killed by elevated wound oxygen tension and their ability to produce toxins is impaired.
5. Healing in previously irradiated tissue is significantly improved following surgery if it is preceded by 20 to 30 d of intermittent HBO inhalation.

Hyperbaric oxygen is a powerful adjuvant to surgery and antibiotics in certain infections of bone and soft tissue. However, its adjuvant role is stressed. It must be used only as part of a coordinated medical-surgical approach to patients with wound infection.

References

1. Hamblin DL. Hyperbaric oxygenation: Its effect on experimental staphylococcal osteomyelitis in rats. J Bone Joint Surg 1968; 50A:1129–1141.
2. Hohn, DC, MacKay RD, Halliday B, Hunt TK. The effect of oxygen tension on the microbicidal function of leukocytes in wounds and *in-vitro*. Surg Forum 1976; 27:18–20.
3. Hohn DC. Oxygen and leukocyte microbial killing. In: Davis JC, Hunt TK, eds. Hyperbaric oxygen therapy. Bethesda, MD: Undersea Medical and Hyperbaric Society 1977:101–110.
4. Hunt TK, Zederfeldt BH, Goldstick TK. Oxygen and healing. Am J Surg 1969; 118:521–525.
5. Hunt TK, Pai, MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. Surg Gynecol Obstet 1972; 135:561–567.
6. Mader JT, Brown GL, Guckian JC, Wells CH, Reinerz JA. A mechanism for the amelioration by hyperbaric oxygen of experimental staphyloccal osteomyelitis in rabbits. J Infect Dis 1980; 142(6):915–922.
7. Niinikoski J, Grislis G, Hunt TK. Respiratory gas tensions and collagen in infected wounds. Ann Surg 1972; 175:588–593.
8. Knighton DR, Halliday B, Hunt TK, Goldstick TK. Oxygen as an antibiotic; the effect of inspired oxygen on infection. Arch Surg 1984; 119:199–204.
9. Sheffield PJ. Tissue oxygen measurements with respect to soft tissue wound healing with normobaric and hyperbaric oxygen. HBO Rev 1985; 6(1):18–46.
10. Myers, RAM, ed. Hyperbaric oxygen therapy: a committee report. Bethesda, MD, Undersea and Hyperbaric Medical Society, 1986.