Hyperbaric oxygen as an adjunct in the treatment of osteoradionecrosis of the mandible

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Hyperbaric oxygen therapy was used adjunctively in the management of 12 patients who had refractory osteoradionecrosis of the mandible. Eleven of the 12 responded favorably. The mechanism of action is related to increased tissue oxygen tension levels, which support collagen formation and neovascularization.

Various forms of ionizing radiation have been used in the treatment of malignancy.[1] Orthovoltage radiation uses low-voltage X rays, ranging from 150 to 250 kV; the absorbed dose at this energy level is dependent on the atomic number of the tissue being radiated. Bone has an atomic number approximately twice that of either muscle or adipose tissue. This means that orthovoltage has greater damaging effects on bone than on soft tissue. Consequently, orthovoltage is infrequently used today.

Other methods include supervoltage radiation, which is between 500 kV and 8 million electron volts (meV), and megavoltage, which is greater than 8 meV. Cobalt 60 has an energy level of 1.2 meV, and is, therefore, within the range of supervoltage radiation. At this voltage, different tissues tend to absorb approximately the same amount of energy. This has been termed the "sparing" effect of cobalt 60 and is a major factor in its widespread use today. All patients in this study were irradiated with cobalt 60.

Ionizing radiation has a profound effect on both the hard and the soft tissues. In the soft tissues, the blood vessels undergo progressive endarteritis, hyalinization, and fibrosis, which leads to ischemia. Similar changes occur in bone and are secondary to alterations in the vascular and cellular components. Histologically, there is a reduction in the number of osteoblasts and osteocytes, with areas of fatty marrow degeneration. The periosteum undergoes fibrosis, and there is a decrease in remodeling elements. These changes are progressive and may eventually lead to necrosis of bone.

The introduction of bacteria into irradiated bone, either directly through disruption of the overlying mucosa or indirectly through bacteremias, may produce an extensive osteomyelitis as a result of compromised vascularity. Impaired healing will result. The most frequently cultured microorganisms associated with osteoradionecrosis include *Staphylococcus aureus* and *albus, Streptococcus hemolyticus* and *viridans, Pneumococcus, Pseudomonas,* and *Escherichia coli.*

Both conservative and radical treatment methods have been advocated to control osteoradionecrosis.[2-5] Several authors have reported favorable results using hyperbaric oxygen therapy as an adjunct in the treatment of radiation damaged tissues.[6-12]

■ *Methods and Materials*

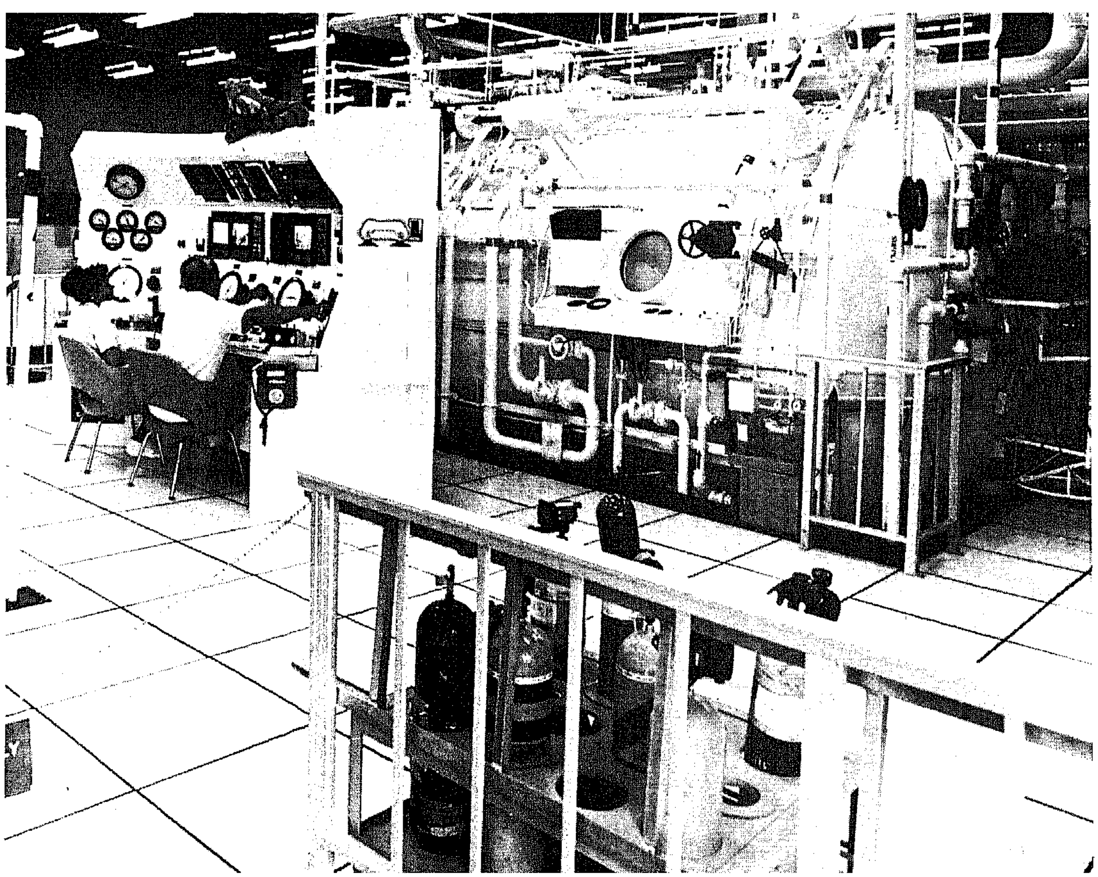
From February 1974 to November 1979, the department of oral and maxillofacial surgery at Wilford Hall USAF Medical Center, in conjunction with the hyperbaric medicine division of the School of Aerospace Medicine, treated 12 patients with refractory osteoradionecrosis of the mandible with adjunctive hyperbaric oxygen therapy. The medical problems of these patients were considered refractory because they had shown no significant improvement with conservative management over a period of two or more months. Before treatment, a complete history was taken of each patient and all patients received a physical examination, chest radiographs, EKG, and appropriate laboratory studies, to delineate possible contraindicating criteria for hyperbaric oxygen therapy, such as viremia or a past history of optic neuritis. Other conditions that required special precautions during hyperbaric oxygen treatment, such as emphysema, asthma, seizure, or psychiatric disorders, were also identified.

All patients had previously been treated with radiotherapy to the oral region, either alone or in combination with surgery, for treatment of malignant tumors. Radiation doses ranged from 4,500 to 7,200

Table • Results of hyperbaric oxygen treatment.

Patient	Type and location of Original lesion	Amount of Radiation (Rads cobalt 60)	Hyperbaric oxygen treatments	Relief of pain	Intraoral wound	Comments
1	Squamous cell; floor of mouth	4,500	133	Marked improvement	Healed	
2	Squamous cell; floor of mouth	4,500; bilateral	79	Marked improvement	Marked improvement	
3	Squamous cell; left tonsil	6,000	62	Asymptomatic	Healed	Orocutaneous fistua healed
4	Squamous cell; right tonsil	6,400	40	Marked improvement	Healed	
5	Adenoid aptic carcinoma; minor salivary gland	6,000	54	Asymptomatic	Healed	
6	Squamous cell; floor of mouth	6,400, floor of mouth; 5,000, neck	68	Slight improvement	Slight improvement	
7	Squamous cell; alveolar process	6,600; 5,000 neck	64	Moderate improvement	Marked improvement	Orocutaneous fistula healed
8	Squamous cell; floor of mouth and soft palate	7,000	71	Marked improvement	Healed	Particulate marrow cancellous bone graft to right mandibular discontinuity defect. Fascia lata graft for closure of orocutaneous fistula
9	Squamous cell right; lateral tongue	6,000	82	Marked improvement	Healed	
10	Squamous cell; left side of tongue and tonsil	6,000	60	Asymptomatic	Healed	
11	Squamous cell; left side of tongue and tonsil	7,200	81	Marked improvement	Marked improvement	
12	Squamous cell; tongue	6,000	102	Marked improvement	Marked improvement	

Fig 1—Control panel and hyperbaric chamber.



rads of cobalt 60. Patients no. 6 and 7 (Table) had additional radiation to the ipsilateral area of the neck.

Factors that contributed to the development of osteoradionecrosis included seven cases of trauma, five of which were directly related to tooth removal. One patient had a pathologic fracture of the mandible, and another developed osteoradionecrosis after irritation from dentures. Initiating causes could not be clearly determined in the remaining five patients.

All patients received vigorous wound care, including multiple daily irrigations of intraoral ulcerations with hydrogen peroxide and normal saline solutions. Orocutaneous fistulas were cleaned with povidone-iodine (Betadine) and dressed with povidone-iodine ointment. Patients were given penicillin parenterally or orally. If cultures showed a penicillin-resistant organism or the patient was allergic to penicillin, appropriate alternative antibiotics were selected.

Hyperbaric oxygenation was achieved by placing the patients in a large, steel hyperbaric chamber (Fig 1), which was compressed with air to 2.4 times normal atmospheric pressure (1,824 mm Hg). Oxygen was administered by an aviator type oronasal mask (Fig 2), or by a headtent (Duke hood) (Fig 3) that provided a high flow of humidified 100% oxygen. Measured Pa_{O_2}s of 1,100 to 1,300 mm Hg were achieved. Exhaled oxygen was evacuated to the exterior of the chamber. The chamber environment was continuously monitored, and constant fresh air ventilation was used to ensure that the oxygen percentage of free chamber air did not exceed 23% and to prevent carbon dioxide build-up.

The patients breathed 100% oxygen for a total of 90 minutes per treatment with an intermittent oxygen-air schedule of 20-minute oxygen periods separated by 5-minute air periods and a final 10-minute oxygen period. This schedule was used to protect the patient from oxygen toxicity.[13] The patients were treated once a day, five days per week. The average number of treatments per patient was 75, with a range of 40 to 133.

Patients remained under the primary care of their referring oral surgeon while undergoing hyperbaric oxygen therapy. Some patients were unable to equalize middle ear pressure by the modified Valsalva maneuver during pressurization; they required the placement of polyethylene tubes through the tympanic membranes.

Fig 2—Standard aviation oronasal mask.

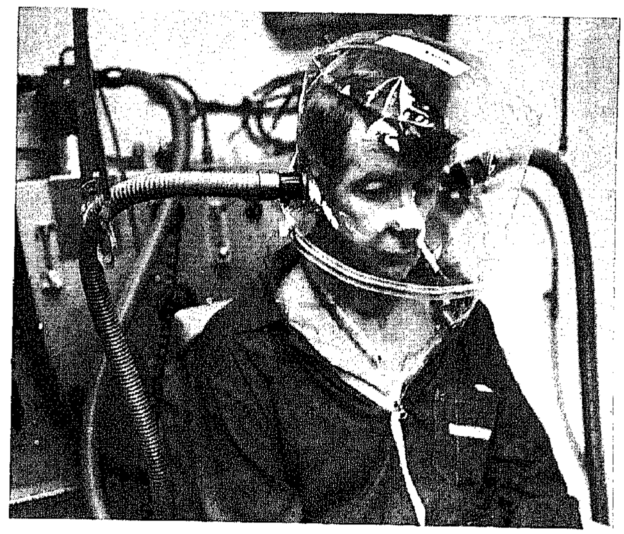


Fig 3—Headtent (Duke hood).

Results

Eleven of 12 patients with osteoradionecrosis of the mandible had excellent responses to treatment with hyperbaric oxygen therapy as an adjunct to conservative management, which included antibiotics, wound care, and superficial sequestrectomy. Seven patients healed completely, and four patients had marked improvement of their intraoral wounds. Only one patient (no. 6) responded poorly. He had received a total course of 6,480 rads to the floor of his mouth and an additional 5,000 rads to the ipsilateral area of the neck for squamous cell carcinoma of the floor of the mouth.

Eight of nine patients who had pretreatment pain had significant relief of symptoms. Three patients noticed pain relief within the first five hyperbaric

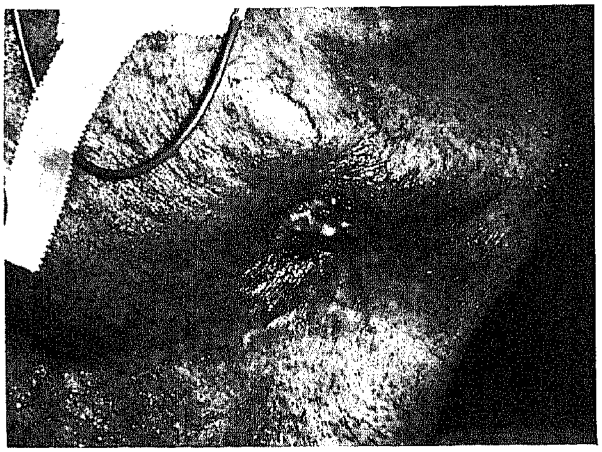


Fig 4—Patient no. 8. Initial appearance of draining orocutaneous fistula.

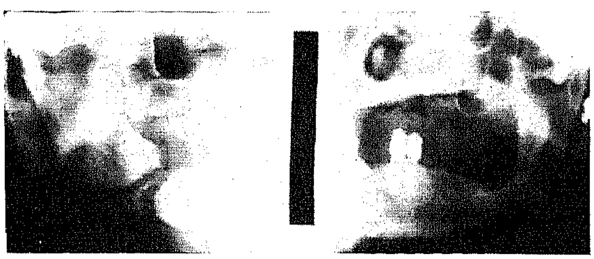


Fig 5—Patient no. 8. Pathologic fracture of mandible.

Fig 6—Patient no. 8. Twelve-month postoperative closure of orocutaneous fistula with fascia lata graft.

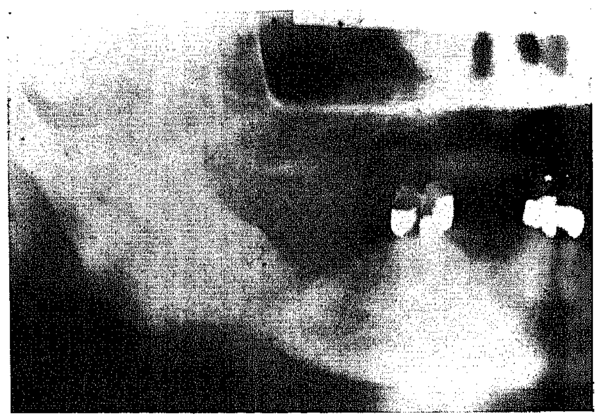


Fig 7—Patient no. 8. Sixteen-month postoperative radiograph after autogenous bone graft and adjunctive hyperbaric oxygen.

oxygen treatments, and five additional patients reported good to excellent relief of pain within the first 12 hyperbaric oxygen treatments. One patient (no. 6) reported little change.

Eight patients underwent sequestrectomies under local anesthesia. One patient (no. 8) required extensive sequestrectomy, which eventually progressed to a pathologic fracture and a discontinuity defect of the right side of the mandible (Fig 4, 5). This was subsequently corrected by using a particulate marrow and cancellous bone graft from the ilium. Stabilization was achieved by external pin fixation. This patient also underwent simultaneous closure of an associated orocutaneous fistula with a fascia lata graft (Fig 6). Sixteen months have elapsed since the bone graft was placed (Fig 7). The patient has excellent mandibular function and total healing of the surgical areas.

Radiographic improvement was noticed in three patients. Deposition of new bone was seen in areas of previous osseous breakdown. However, these changes were not apparent until at least 40 treatments had been completed.

Three patients had orocutaneous fistulas. In two, the fistulas underwent spontaneous closure, and in one patient (no. 8), the fistula required surgical closure.

Discussion

The role of oxygen in the healing of injured tissue has been elucidated by the work of a number of investigators.[14-22] If an adequate blood supply is present in tissue immediately surrounding the site of injury, tissue oxygen tension is high enough (30 to 70 mm Hg) to support new collagen formation. The new collagen establishes a framework that physically supports neovascularization of the injured area. Thus, healing proceeds as a continuous, dynamic process.

If an adequate blood supply is not present, as is the case after high-dose therapeutic irradiation, this dynamic process is not initiated, and persisting tissue hypoxia is the rule. Hunt and others[18] have shown such tissue hypoxia in chronic, nonhealing wounds of both soft tissues and bone, whereas Shaw and Bassett[23] have shown that osteogenesis is enhanced by optimum oxygen tensions of at least 30 mm Hg. Hohn's[24] work suggests that microbial killing by leukocytes in hypoxic tissue is also enhanced when tissue oxygen tension is raised to 30 mm Hg.

Because the oxygen tension at any point in tissue depends on the distance of that point from the nearest functioning capillary, the oxygen demand of the tissue, and the oxygen tension in the capillary, it is clear why repair, which increases the oxygen demand of tissue, does not take place readily in irradiated tissue, where the intercapillary distances are increased because of capillary loss. Exposure to hyperbaric oxygen increases the oxygen tension in the existing capillaries. Oxygen diffusion distances from these capillaries are thus increased, overcoming hypoperfusion, meeting the oxygen demand of tissue, and allowing the healing process to become re-established. As healing progresses, neovascularization eventually re-establishes a more normal physiological state, so that the healed site maintains its integrity.

The opinions contained in this article are those of the authors and are not to be construed as official or as reflecting the view of the Department of Defense or the United States Air Force.

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