

## HYPERBARIC MEDICINE PROGRAM CASE OF THE MONTH

*A series of case presentations identifying the improved clinical and cost outcomes that characterize the addition of hyperbaric oxygen therapy to standard medical and surgical measures, in carefully selected patients.*

An 81 yowm was referred to the hyperbaric medicine service for evaluation and treatment recommendations. The patient presented with a compromised full thickness scalp skin graft.

**Pertinent Medical History:** Squamous cell carcinoma of the head and neck.

**Other Significant Medical History:** Atherosclerotic heart disease with MI and stent placements; chronic atrial fibrillation; renal insufficiency; hyperlipidemia and prostate cancer (treated with seed implants).

The patient had undergone several wide scalp excisions, the most recent measuring 8cm x 9cm, and was closed with a full thickness skin graft. Excisional margins proved positive. Further surgery was decided against and external beam radiotherapy planned. Given uncertain flap viability and the potentially damaging effect of radiotherapy on this tissue pre-radiation hyperbaric oxygen therapy was sought.

### Assessment:

- i Compromised full thickness anterior scalp skin graft
- ii Unresolved malignant squamous cell carcinoma; multiple sites
- iii No longer a surgical candidate; radiotherapy planned, with potential negative impact on an already threatened flap
- iv No patient-specific risks related to hyperbaric oxygenation

### Recommendation:

Proceed immediately with hyperbaric oxygen therapy, per compromised skin flap protocol, in order to maximize number of treatments prior to radiotherapy.

This treatment plan was agreed to by the patient and his referring physician team. The informed consent process was completed.

Hyperbaric oxygen therapy commenced, and was tolerated with complaint or apparent side-effect. A total of five uneventful treatments were completed, with a generalized improvement in the appearance of the flap. The patient then underwent 7,000 cGy of external beam radiotherapy, without further hyperbaric oxygenation. In follow-up several months post-radiation the scalp graft appeared globally threatened, with a central area consistent with soft tissue radionecrosis. The threat of chronically exposed bone resulted in re-referral to the hyperbaric medicine service.

It was elected to re-start hyperbaric oxygen treatments for the dual indications of compromised skin flap and soft tissue radionecrosis. Following 10 treatments much of the graft had evolved to a healthier overall appearance, with the exception of the central area, which remained hypoperfused and somewhat necrotic (Figure 1).

Following 22 treatments the margins of the wound have closed. The central area of the lesion remains a concern, although now somewhat smaller (Figure 2). Healing continues in concert with continued daily hyperbaric oxygen (Figure 3). It was elected to hold hyperbaric oxygen at treatment number 45, as the patient appeared close to the point of maximum benefit. The lesion continued to improve and had fully healed within the ensuing three weeks (Figure 4).

### Discussion:

This elderly patient with complex medical problems faced a potentially devastating outcome should his scalp graft fail. The reconstructive procedure was threatened prior to radiotherapy, and was further and significantly compromised as a result of it; an acceptable and necessary risk given unresolved cancer. Hyperbaric oxygen therapy was sought in order to improve vascular density within the graft. The basis for this referral is evidence that exposure to hyperbaric doses of oxygen stimulates healing responses in tissues compromised by hypoxia and hypoperfusion. There is solid cellular and sub-cellular evidence for refractory wounds in general<sup>1,2,3</sup> and compromised skin grafts and flaps in particular.<sup>4,5</sup> Clinical experience is encouraging but, as with every other medical and surgical option, not presently supported by high level evidence.<sup>6</sup> Given the different types of skin grafts and flaps, and their infrequent complications, it would take a multicenter trial involving many institutions and several years to generate Level I<sup>7</sup> evidence of efficacy. Funding for such a trial would be equally problematic. No significant commercial incentive exists given the inability to control access to oxygen.

In the above case, a skin graft compromised by relative ischemia was further injured during the radiotherapy process. Brief (90 minute) daily elevations to supra-physiologic levels of oxygen (1,520 mmHg) stimulated healing responses to the point that a critical mass of angiogenesis was generated. Local compromise was reversed and the entire flap salvaged.

### References:

- 1) Thom SR, Bhople VM, Velazquez OC, et al.: Stem Cell Mobilization by Hyperbaric Oxygen. *AM J Physiol Heart Circ Physiol* 2006;290:H1378-H1386
- 2) Lee CC, Chen SC, Tsai SC, et al.: Hyperbaric Oxygen Induces VEGF Expression Through ERK, JNK and C-JUN/AP-1 Activation in Human Umbilical Vein Endothelial Cells. *Journal of Biomedical Science* 2006;13:143-156
- 3) Lin S, Shyu KG, Lee CC, et al.: Hyperbaric Oxygen Selectively Induces Angiopoietin-2 in Human Umbilical Vein Endothelial Cells. *Biochemical and Biophysical Research Communication* 2002;296:710-715
- 4) Stevens DM, Weiss DW, Koller WA, et al.: Survival of Normothermic Microvascular Flaps After Prolonged Secondary Ischemia: Effects of Hyperbaric Oxygen. *Otolaryngology-Head and Neck Surgery* 1996;115(4):360-364
- 5) Gampper TJ, Zhang F, Mofakhami NF, et al.: Beneficial Effect of Hyperbaric Oxygen on Island Flaps Subjected to Secondary Venous Ischemia. *Microsurgery* 2002;22:49-52
- 6) Friedman HIF, Fitzmaurice M, Lefavre JF, et al.: An Evidence-Based Medicine of the Use of Hyperbaric Oxygen on Flaps and Grafts. *Plastic Reconstr. Surgery* 2006;117(Suppl.):175S-192S
- 7) American Heart Association Guidelines for Clinical Efficacy



Fig. 1



Fig. 2



Fig. 3



Fig. 4

## INDICATIONS AND RATIONALE FOR HBO THERAPY \*

Indications	Rationale
Acute carbon monoxide poisoning	Relieve hypoxia; hasten elimination of CO; antagonize brain lipid peroxidation
Acute exceptional blood loss anemia	Increase physically dissolved oxygen; treat hypoxia; support marginally perfused tissues
Acute thermal burns	Relieve hypoxia; decrease fluid losses; limit burn wound extension and conversion; treat edema; promote wound closure
Cerebral arterial gas embolism	Overcome free gas volume; relieve hypoxia; antagonize leukocyte mediated ischemia-reperfusion injury
Chronic osteomyelitis	Augment host antimicrobial defenses; induce angiogenesis; potentiate leukocytic superoxide dismutase and myeloperoxidase production; relieve hypoxia; augment antibiotic therapy; extend post-antibiotic effect; augment osteoclast activity
Clostridial gas gangrene	Reduce size of gaseous bullae; inactivate clostridial alpha toxin; inhibit alpha toxin production; induce bacteriostasis; potentiate leukocytic superoxide dismutase and myeloperoxidase production
Compromised skin flaps	Support marginally perfused/oxygenated tissues; antagonize ischemic-reperfusion injury; accelerate angiogenesis
Crush injury; acute ischemia	Provide interim tissue oxygenation in relative states of ischemia; reduce edema; reduce compartment pressures; antagonize ischemic-reperfusion injury; augment limb salvage
Decompression sickness	Overcome free gas volume- induced ischemia; relieve hypoxia; hasten elimination of offending inert gas; treat edema
Diabetic foot wounds	Re-establish wound oxygen gradients; relieve hypoxia; induce angiogenesis; augment host antimicrobial defenses; prepare for definitive coverage
Late radiation tissue injury	Re-establish wound oxygen gradients; relieve hypoxia; induce angiogenesis; prepare for definitive coverage
Late radiation tissue injury prophylaxis	Re-establish wound oxygen gradients; induce angiogenesis prior to surgical wounding
Necrotizing soft tissue infections	Induce bacteriostasis of anaerobes; (fasciitis and cellulitis) potentiate leukocytic superoxide dismutase and myeloperoxidase production; relieve hypoxia; more closely demarcate potentially viable tissue
Non-healing marginally perfused wounds	Re-establish wound oxygen gradients; relieve hypoxia; reduce edema; induce angiogenesis; correct diabetic-induced leukocyte changes; prepare for definitive coverage

\*UNDERSEA AND HYPERBARIC MEDICAL SOCIETY, 2003