Issue: Hyperbaric Oxygen Therapy
Released: June 2012

Evidence *in* Context

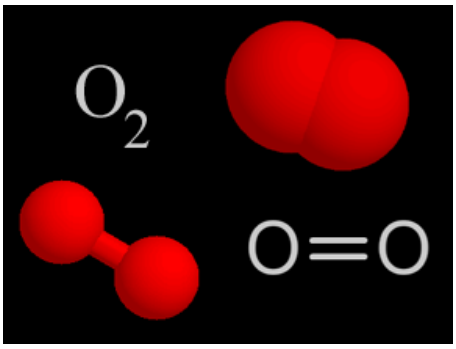
Health research – synthesized and contextualized for use in Newfoundland & Labrador

Synthesis topic

Hyperbaric Oxygen Therapy for Difficult Wound Healing in Newfoundland & Labrador

Hyperbaric Oxygen Therapy (HBOT) delivers pure, pressurized oxygen into a sealed chamber. HBOT is conventionally used to treat decompression sickness, carbon monoxide poisoning, certain kinds of wounds, and delayed radiation injuries.

Eastern Health is in the process of developing policies for clinical hyperbaric oxygen therapies in the province. The health authority has increased HBOT capacity, in terms of infrastructure and human resources. It intends to continue these increases to meet an expected rising demand for HBOT services in Newfoundland and Labrador.



The Oxygen Molecule: described in four ways

In partnering with CHRSP, Eastern Health sought research-based evidence to guide decision making about the clinical and cost effectiveness of HBOT for difficult wounds.

For this project, NLCAHR has partnered with Eastern Health, as well as with the Canadian Agency for Drugs in Technology and Health (CADTH). The CHRSP Project Team included senior administrators from Eastern Health (who proposed the topic), local clinical and research experts in HBOT and difficult wound healing, and CHRSP staff at NLCAHR. The CHRSP Project Team and CADTH refined the original research question for this project. CADTH searched for and identified the relevant research literature, critically appraised and synthesized the evidence, and produced a report, which was then peer-reviewed. The work by CADTH was published as an independent report available at: www.nlcahr.mun.ca/chrsp.

The CHRSP Project Team then took the CADTH results, and, with input from key stakeholders throughout the province, provided additional analysis and contextualization of the research for Newfoundland and Labrador. Research findings and key messages for decision makers are outlined in the following pages. The full CHRSP report is available at www.nlcahr.mun.ca/chrsp together with a companion report by CADTH, "Hyperbaric Oxygen Therapy for Difficult Wound Healing: A Systematic Review of Clinical Effectiveness and Cost Effectiveness."

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The Research Question:

What does the scientific literature tell us about the clinical and economic effectiveness of hyperbaric oxygen treatment for difficult wound healing (i.e., diabetic foot ulcers, pressure ulcers, delayed radiation-induced injuries, thermal burns, skin grafts and flaps, and revascularization after organ transplantation) considering the expected patient populations and given the social, geographic, economic and political contexts of Newfoundland & Labrador?

Background

Hyperbaric oxygen therapy in Newfoundland & Labrador

Hyperbaric oxygen therapy (HBOT) facilities for Newfoundland and Labrador were originally located in, and administered by, the Centre for Offshore and Remote Medicine (MEDICOR), which was established in 1982 as a research centre within the Faculty of Medicine at Memorial University. MEDICOR had an initial mandate to conduct health research in diving and related industries. Initially, the focus of operation for HBOT was therefore research. Over time, HBOT was increasingly employed by MEDICOR in clinical emergency cases, particularly for decompression illness and carbon monoxide poisoning. Recommended clinical applications for HBOT in non-emergency cases also increased, resulting in significant additional demand for this treatment.

The shift in focus from research activity to clinical applications was conducted on an *ad hoc* basis. By 2008, research involving HBOT had decreased effectively to nothing. In February 2009, staffing issues forced the closure of the facility altogether. In September 2009, responsibility for HBOT transferred to Eastern Health. In March 2010, Eastern Health and Memorial University agreed that Eastern Health would take formal responsibility for the HBOT facility for clinical case work, while Memorial University would retain access to the equipment for the purposes of research and education.

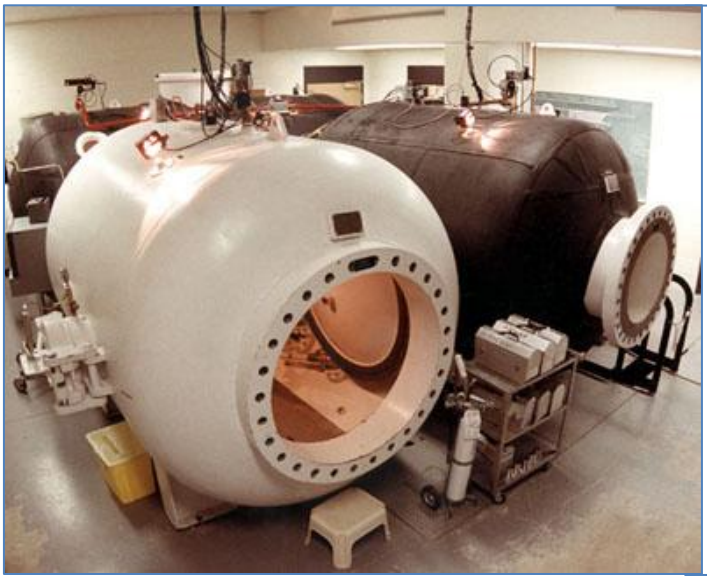
About the therapy

How does HBOT actually work?

In essence, patients receiving hyperbaric oxygen therapy (HBOT) absorb pure oxygen gas (O_2) at higher than normal pressure. HBOT chambers come in two basic types: a multi-place chamber that can accommodate more than one patient at a time and a mono-place chamber designed to accommodate a single patient. In multi-place chambers, patients breathe pure pressurized oxygen through a mask or hood and oxygen is absorbed exclusively through the lungs. Equipment and attendant staff can remain inside the multi-place chamber, making this an effective option for complex case management and multiple co-morbidities requiring monitoring by specialists.

In mono-place chambers, one patient, (or in special cases, a child and parent) can be treated. Mono-place chambers are typically designed as enclosed beds. No hoods or masks are worn; instead, pure O_2 is pumped directly into the chamber at elevated pressure.

In both designs, the combination of elevated pressure and the higher concentration of inhaled O_2 increases the amount of oxygen absorbed by the patient. Oxygen plays a critical role in wound metabolism. Most important to wound healing is oxygen's influence on cytokines, which are intercellular mediators of immune function. Recent evidence indicates that particular combinations of cytokines trigger the production of specific proteins and the expression of specific genes involved in wound metabolism. Oxygen levels therefore influence the subsequent immune reaction to a wound. Oxygen levels may also affect tissues and the immune system prior to sustaining a wound and may reduce the severity of tissue damage and the degree of immune-related inflammation. HBOT influences cytokine signatures in complex and inter-related ways.



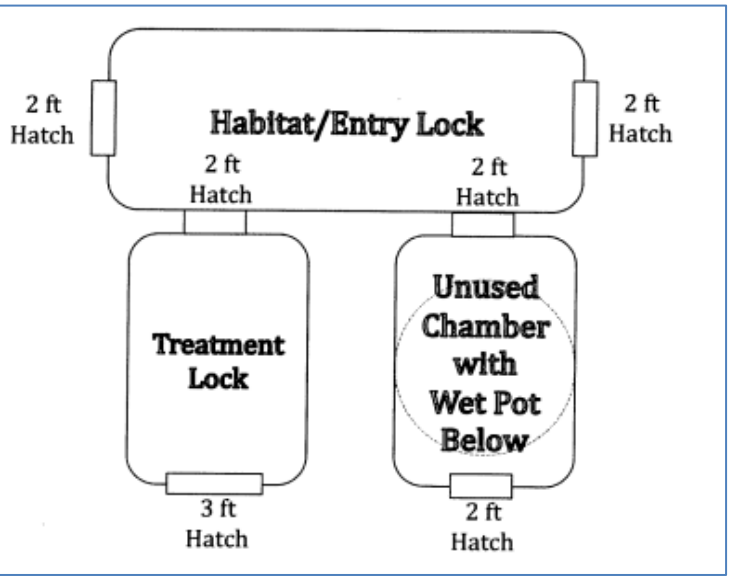


Photo of the HBOT multi-place chamber in the Health Sciences Centre, St. John's, Newfoundland and Labrador and schematic layout of HBOT facilities

HBOT and health

What health conditions are approved for HBOT in Canada?

Conditions Approved for HBOT in Canada	Conditions Under Investigation for HBOT	Conditions Not Approved for HBOT
Emergency conditions: • Clostridal myositis & myonecrosis (gas gangrene) • CO poisoning • Decompression illness & gas embolism • Necrotizing soft tissue infections (flesh-eating disease) • Crush injuries, compartment syndromes, traumatic ischemias • Exceptional blood loss or anemia	**Emergency conditions:** • Acute peripheral arterial insufficiency • Anoxic encephalopathy • Cyanide poisoning	Pre-treatment for organ storage or transplantation, Acute cerebral oedema, Acute or chronic cerebral vascular insufficiency, Aerobic or anaerobic septicemia & infection (non-clostridial), Arthritic Diseases, Cardiogenic shock, Chronic peripheral vascular insufficiency, Exceptional blood loss anaemia, Hepatic necrosis, Myocardial infarction, Nonvascular causes of chronic brain syndrome, Pulmonary emphysema, Senility, Sickle cell anaemia, Smoke inhalation, Systemic aerobic infection, Tetanus, Acute coronary syndrome, Acute traumatic brain damage, Cerebral hypoxia, traumatic or after a stroke, Malign otitis externa, Multiple Sclerosis, Radionecrosis of the central nervous system, Tinnitus.
Adjunctive therapies: • Diabetic foot ulcers • Hemorrhagic cystitis after irradiation • Osteoradionecrosis • Radiation proctitis & enteritis • Chronic refractory osteomyelitis • Larynx radionecrosis • Skin grafts and myocutaneous flaps • Soft tissue radionecrosis • Intracranial abscess • Non-diabetic ulcers • Thermal burns	**Adjunctive therapies:** • Acute deafness • Chronic critical ischemia in case of arteriosclerosis • Ischemic ocular disorders/abnormalities • Neuroblastoma Stage IV • Pneumatosis Cystoides Intestinalis **Pre-Treatment therapy:** • Re-implantation of fingers/extremities	

Focus of the synthesis

What research did we look for?

Health conditions included in this project were selected in consultation with our health system partners and CADTH. They were: diabetic foot ulcers, pressure ulcers, delayed radiation-induced injuries, thermal burns, skin grafts and flaps, and revascularization after organ transplantation. Because HBOT is not the standard of care for chronic or non-emergency cases, research evidence was limited. On our behalf, CADTH's Health Technology Inquiry Service (HTIS) identified the evidence for this project, focusing on high-level research, systematic reviews, meta-analyses, health technology assessments (HTA) and very recent high-quality primary studies. Screening resulted in thirteen relevant sources being selected as the focus of our synthesis.

Summary of Findings

What is the evidence?

Systematic review literature about hyperbaric oxygen therapy for difficult wound healing has limitations. The most significant of these is the lack of large-scale randomized controlled trials. Also, applying findings from existing research to the situation in St. John's has inherent limitations due to the specifics of service delivery. For this study, the most important variables are differences in the extent to which HBOT is integrated into a wound-care program and the availability of support services for patients undergoing weeks or months of treatment.

HBOT for Pressure Ulcers/Diabetic Foot Ulcers:
There is sufficient evidence to indicate that HBOT is clinically beneficial and cost-effective as an adjunctive therapy for diabetic foot ulcers, but not for pressure ulcers. For diabetic foot ulcers, there is broad agreement that HBOT is an effective adjunctive treatment that reduces the risk of major amputation. The available evidence is, however, limited in sample size and power.

HBOT for Delayed Radiation Induced Injuries (DRII):
Evidence indicates that adjunctive HBOT is beneficial for osteoradionecrosis and radiation rectitis/proctitis. While the strength of the evidence is insufficient to call for *routine* use of HBOT for these conditions, experts noted that 'routine use' of HBOT in Newfoundland is rare: most patients with non-healing wounds are referred for HBOT only after having undergone other unsuccessful treatments. HBOT treatment of radiation proctitis/rectitis produces consistent, statistically-significant improvements across a range of clinical outcomes. Similarly, evidence for HBOT treatment in head and neck injuries to soft and bony tissue indicates improvement, but findings are of limited strength. It should also be noted that the research studies on adjuvant HBOT for other types of DRII are consistent in finding no significant negative effects. Instead, where data are available, there are consistent findings of small improvements in healing. As such, while there is insufficient evidence for HBOT as an effective treatment for other forms of DRII, it should not be considered ineffective either. →

Summary of Findings continued…

HBOT for Thermal Burns: The incidence of thermal burns in Canada is low. In locating evidence, only two studies were identified that met eligibility criteria, both of which were of poor quality with small sample sizes. Consequently, there is not adequate evidence to support or contradict the use of HBOT for thermal burns.

HBOT for Skin Grafts and Flaps: As with thermal burns, there is insufficient evidence to support or contradict HBOT treatment for skin grafts or flaps. Most research in this area involves animal models, which has found evidence for improved healing of skin grafts. The single identified clinical study on humans did find an increased percentage of healed surface area and of overall graft success; however, a small sample size limited the strength of these findings.

HBOT for Revascularization After Organ Transplantation: CADTH did not identify any evidence for HBOT for revascularization after organ transplantation. Published articles in this field of research consist mainly of animal models or human case studies, neither of which provides an adequate evidence base for the purposes of this report.

The Local Context

With increased awareness of the effectiveness of HBOT for wound care, HBOT referrals are likely to increase in the province. The incidence of health conditions that may result in non-healing wounds is also expected to rise. The province will therefore require greater capacity and more efficient chamber use to meet a growing demand for HBOT. The province may also need to consider a methodology for ensuring HBOT is an appropriate treatment option.

Eastern Health may benefit from knowledge exchange with HBOT units across Canada to learn more about service development and appropriate clinical applications.

Patients from outside St. John's may benefit from telehealth consultations prior to HBOT; they may also need service options that are designed to reduce their length of stay for treatment.

The current HBOT location in the Health Sciences Centre may pose problems for those with limited mobility. Exposure to public areas when accessing the HBOT facility may also pose an infection risk.

Cost effectiveness might be improved by addressing overtime issues, training, specialized pediatric options, and remuneration models, and by optimizing human resources and capacity.

Organizational considerations include integrating HBOT into a wound-care management program and addressing acute/chronic care service issues.

Contextualized Synthesis: Hyperbaric Oxygen Therapy

Implications for Decision Makers

Research evidence supports HBOT as a clinically-effective and cost-effective treatment for diabetic foot ulcers and as clinically-effective, but not cost-effective, for delayed radiation-induced injuries in the head, neck and pelvis.

There is insufficient evidence about the clinical or cost effectiveness of HBOT for pressure ulcers, delayed radiation-induced injuries in other parts of the body, thermal burns, skin grafts, skin flaps, or revascularization after organ transplantation.

The cost effectiveness of HBOT for appropriate non-healing wounds will increase as the number of treated patients increases.

The appropriate and timely referral of patients for HBOT treatment improves with integration of wound-care management into existing chronic and acute health service programs.

Evidence for the clinical and cost effectiveness of HBOT for non-healing wounds is limited. As a result, future studies will be needed to augment the evidence base concerning HBOT for a number of conditions.

For the complete CHRSP report and a companion report on the project, including details on the evidence reviewed by the project team, and for more information about the CHRSP process, please visit the NLCAHR website: www.nlcahr.mun.ca/chrsp

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