Conseil *d'***É**valuation *des* **T**echnologies *de la* **S**anté *du* Québec

Report - December – 2001
(CETS 2000-3 RE)

HYPERBARIC OXYGEN THERAPY IN QUÉBEC
(Summary)

Report submitted to the

Minister of Research, Science and Technology of Québec

Conseil d'évaluation des technologies de la santé du Québec

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Agence d'évaluation des technologies et des
modes d'intervention en santé
2021, avenue Union, Bureau 1040
Montréal (Québec) H3A 2S9

Telephone: (514) 873-2563
Fax: (514) 873-1369
E-mail: aetmis@aetmis.gouv.qc.ca
Web site address: http://www.aetmis.gouv.qc.ca

Legal deposit	-	Bibliothèque nationale du Québec, 2001
	-	National Library of Canada
ISBN		2-550-38540-3

How to cite this report :

Agence d'évaluation des technologies et des modes d'intervention en santé. Hyberbaric Oxygen Therapy in Québec (AÉTMIS 2000-3 RE). Montréal: AÉTMIS, 2001, x-124 p.

Conseil d'évaluation des technologies de la santé du Québec

MANDATE

To promote and support health technology assessment, disseminate the results of the assessments and encourage their use in decision making by all stakeholders involved in the diffusion of these technologies.

To advise the Minister on matters concerning the introduction, diffusion and use of health technologies and, to this end, give advice based on the assessment of their effectiveness, safety and cost, their impact on the health-care system, and their economic, ethical and social implications.

THE CONSEIL'S MEMBERS

The Conseil normally consists of 12 members. It is therefore waiting for six new members to be appointed by the Québec Cabinet.

DIRECTOR

Jean-Marie R. Lance

Note : This information about the mandate and the Conseil's members reflects the situation when the French official report was published. On June 28, 2000, the name and the mandate were modified and new members were appointed.

HYPERBARIC OXYGEN THERAPY IN QUÉBEC

Hyperbaric oxygen (HBO) therapy has been medically available in Québec since 1982. Until recently, this technology was available only at one hospital. Recognized as the treatment of choice for carbon monoxide poisoning and diving-related decompression sickness, HBO therapy has evolved, given that it is now being used more and more as an adjuvant treatment for a number of chronic, nonemergency medical conditions.

This led the Ministère de la Santé et des Services sociaux to ask the *Conseil d'évaluation des technologies de la santé* (*CETS*) to determine if it would be useful to support broader diffusion of this technology in Québec and, if so, to define the guidelines for this diffusion. After describing the technology, this report examines its efficacy in the treatment of various conditions and its complications, explains what safety measures are needed to control its risks, and estimates the potential demand for new facilities in Québec.

Although HBO therapy has been tried out on nearly 130 medical conditions, it is *CETS's* conclusion that this technology can be recommended for only 13 of them. Its efficacy in the treatment of cerebral palsy, although not demonstrated, is still controversial, given the results of a randomized, comparative trial recently conducted in Québec.

CETS also believes that the potential demand justifies installing hyperbaric chambers in the Greater Québec City Area and gradually installing others in the Greater Montreal Area. These decisions would lead to considerable expenses that would probably be offset by the decrease in the lengths of hospital stay for chronic cases. Studies would be necessary in order to validate the clinical and administrative efficacy. Lastly, steps would need to be taken to ensure the presence of a multidisciplinary team, permanent medical supervision and compliance with safety standards.

In disseminating this report, *CETS* wishes to provide the best information possible to the policymakers concerned with the effective and safe use of HBO therapy, at all levels in Québec's health-care system.

Renaldo N. Battista
President

SUMMARY

INTRODUCTION

Hyperbaric oxygen (HBO) therapy has been medically available in Québec since 1982. However, it is an "old" technology that originated in the 1920s. Recognized as the treatment of choice for carbon monoxide poisoning and diving-related decompression sickness, HBO therapy is being used more and more as an adjuvant treatment for a certain number of chronic, nonemergency medical conditions.

In Québec, until quite recently, hyperbaric medical services were available only at the Hôpital du Sacré-Coeur de Montréal. Given that hyperbaric medicine has evolved worldwide, the Ministère de la Santé et des Services sociaux would like to know if it would be useful to support wider diffusion of this technology in Québec and, if so, what the guidelines should be for this diffusion.

The purpose of this *Conseil d'évaluation des technologies de la santé* (*CETS*) report is to enlighten the Ministry and the other policymakers concerned as to the decision-making issues regarding this technology.

Objectives

CETS's specific objectives in this report are as follows:

- To describe hyperbaric oxygen therapy and its mechanisms of action.
- To systematically review the scientific literature in order to determine which pathologies and in what conditions HBO therapy is effective.
- To review the adverse effects and complications of HBO therapy.
- To examine the risks associated with operating a hyperbaric chamber and the necessary safety measures relating thereto.
- To estimate the potential demand for HBO therapy in Québec and the costs that would be generated in meeting this demand.
- To define the guidelines for meeting this potential demand, if applicable.

Hyperbaric oxygen therapy

In hyperbaric oxygen therapy, the patient is placed in a steel, aluminum or polymer chamber in which he or she breathes pure oxygen (100%) at greater than atmospheric pressure (1.5 to 3 ATA[1]). Chambers can be of the mono- or multiplace type. Through different mechanisms of action, HBO therapy seems to play a role in the revitalization, revascularization and healing of tissues, grafts and organs, in the preservation and regeneration of bone, and in potentiating certain pharmacologic effects.

Therapeutic modalities

At present, there are no standard protocols for specific medical conditions. The therapeutic procedures vary according to the condition (acute or chronic) and the treatment centre (physicians caring for the patient, etc.). The treatment can be administered on a one-time basis and vary in duration, as is the case with carbon monoxide poisoning, or by way of several daily or twice-daily sessions of predetermined duration (30 to 90 minutes). The pressure at which HBO is administered depends on several factors: the medical condition, the patient's characteristics and the centre's practices (1.5 to 3 ATA or even 6 ATA).

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[1] ATA: Atmosphere absolute (1 ATA is the pressure at sea level, 2 ATA is the equivalent pressure at a depth of 33 feet of seawater).

Efficacy of HBO therapy

HBO therapy has reportedly been tried out on nearly 130 medical conditions, but very few of them have been the subject of randomized, controlled, prospective trials. Based on an exhaustive review of the available scientific literature and on the opinions of expert organizations, *CETS* concludes that hyperbaric oxygen therapy is recommended in the following medical conditions:

- Carbon monoxide poisoning
- Decompression sickness
- Gas embolism
- Gas gangrene
- Refractory tissue or bony necrosis due to a single microorganism or a mixed population of microorganisms (aerobic or anaerobic)
- Post-radiation therapy tissue damage: osteoradionecrosis and soft-tissue damage
- Chronic tissue lesions associated with chronic critical ischemia: diabetic foot, chronic leg ulcers
- Severe burns which are refractory to treatment and/or which compromise graft take

The treatment of cerebral palsy with HBO is presently a controversial topic worldwide. Until very recently, there were no clinical studies evaluating the beneficial effect of hyperbaric oxygen on the evolution of this condition, which is classified as a cerebral ischemia. However, one randomized, prospective, double-blind, multicentre clinical study was just conducted by Québec researchers and provides the first rigorous data on this application. The results showed an improvement in an equal proportion of children in the experimental group and in the placebo group. Although the investigators conclude that hyperbaric oxygenation has no effect, other possible interpretations are suggested and raise questions about the factors for improvement, all of which points to the need for further research.

Complications

Middle ear barotrauma heads the list of complications. Pulmonary barotrauma rarely occurs. Impaired visual acuity in the form of myopia or hyperopia secondary to hyperbaric oxygen therapy has been reported, most often in the context of prolonged treatment. These symptoms are generally transient, but studies specifically concerning these complications are few in number. A few experimental studies (involving animals and in specific study conditions) report oxygen toxicity to certain organs, especially the central nervous system. The origin and mechanisms of this toxicity remain poorly elucidated.

Safety measures

HBO is a treatment that requires continual, close monitoring before, during and after administration. Regardless of the medical condition to be treated, a potential candidate for HBO therapy must meet strict physiological and psychological criteria (even if they have not yet been standardized). Furthermore, this procedure requires a professionally and technically competent environment.

The safety measures pertain to the equipment and its maintenance, the conditions for operating a chamber, and training of both the treatment team, the technical team and the patients. *CETS* believes that all hyperbaric medical centres (private and public) operating in Québec should be subject to, as a minimum, the Canadian Standards Association (CSA) standard for the use of hyperbaric facilities (Z275.1-93).

Potential demand in Québec and need for new facilities

On the basis only of the medical conditions for which HBO therapy is recognized as being effective, *CETS* considers that the potential demand in the Greater Québec City Area justifies installing a hyperbaric chamber. If a decision were made to operate a multiplace chamber, it would be advisable to install a monoplace chamber along with it.

As for the Greater Montréal Area, the potential demand could justify the addition of hyperbaric chambers. This assessment assumes that the multiplace chamber at the Hôpital du Sacré-Coeur can operate at full capacity, with a multidisciplinary mode of organization. The number of treatments per year could, in effect, increase from 900 to 5,200.

The number and type of additional facilities will depend on the pace at which the potential demand materializes and on institutions' and professionals' interest in using this therapy. Whatever develops in the future, *CETS* believes that a monoplace chamber should also be added at the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre in order to deal with emergency cases without having to interrupt the treatments in progress in the multiplace chamber.

Adding these resources could have a significant economic impact. The operating budget for a multiplace chamber is approximately $500,000 a year. The cost of purchasing and installing a new multiplace chamber varies from $1.5 to $2 million.

These costs would very likely be offset by a reduction in the lengths of stay, the extent of which has yet to be determined, at least for chronic cases that require hospitalization. As an illustration, we estimated that for the Montréal area, the decreasing break-even point for HBO therapy would require about a 20% reduction in the lengths of stay. In other words, the addition of HBO therapy would have to result in a length-of-stay reduction of 20% in order for the benefits (in terms of hospitalization costs only) to equal the cost of the treatments. For the Québec City area, the decreasing break-even point would require a 26% reduction.

It would be desirable if studies could be undertaken in Québec to determine the extent of these reductions and to assess the impact, on resources, of the therapeutic benefit that hyperbaric oxygen therapy might have for patients treated mainly on an outpatient basis.

Lastly, adding hyperbaric chambers does not merely involve adding new facilities. To exploit their full potential, steps must be taken to ensure:

1) the presence of a multidisciplinary team that includes specialists from all the areas in which HBO therapy can be of benefit;
2) permanent medical supervision
3) and compliance with safety standards, such as the one published by the CSA.

ACKNOWLEDGMENTS

This report was prepared at the request of the *Conseil d'évaluation des technologies de la santé du Québec* by **Raouf M.R. Hassen-Khodja**, **M.D., MSc**, a researcher-consultant for the *Conseil*, and **Guy Régnier, Ph.D.**, a research officer at the *Conseil*. We wish to express our sincere gratitude for their work.

The *Conseil* also cordially thanks the external reviewers who, through their numerous comments, helped improve the quality and contents of this report:

Dr. Maxime Amar	Head of the Hyperbaric Medicine Unit, Centre hospitalier régional de Rimouski and Institut maritime du Québec, Rimouski, Québec
Dr. Mario Côté	Head of the Hyperbaric Medicine Unit, Hôtel-Dieu de Lévis, Lévis, Québec
Dr. Mario Dugas	Pneumologist, physician in charge of the hyperbaric chamber, Hôpital du Sacré-Cœur de Montréal, Montréal, Québec
Dr. François Paquet	Member of the Hyperbaric Medicine Unit, Hôtel-Dieu de Lévis, Lévis, Québec
Prof. Francis Wattel	Physician, Respiratory Emergency, Medical Resuscitation and Hyperbaric Medicine Unit, Centre hospitalier régional universitaire de Lille, Lille, France

Lastly, the *Conseil* wishes to express its gratitude to Marc-André Thibodeau, library technician, and Pierre Vincent, librarian, for their bibliographic support, and to Maria-Edith Jacques, secretary, for the final layout of this report.

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

1. INTRODUCTION

Hyperbaric oxygen (HBO) therapy has been medically available in Québec since 1982. However, it is an "old" technology that originated in the 1920s. Recognized as the treatment of choice for carbon monoxide poisoning and diving-related decompression sickness, HBO therapy is being used more and more as adjuvant treatment for a certain number of chronic, nonemergency medical conditions.

In Québec, until quite recently, hyperbaric medical services were available only at the Hôpital du Sacré-Coeur de Montréal. Given that hyperbaric medicine has evolved worldwide, the Ministère de la Santé et des Services sociaux would like to know if it would be useful to support wider diffusion of this technology in Québec and, if so, what the guidelines should be for this diffusion.

The purpose of this *Conseil d'evaluation des technologies de la santé (CETS)* report is to provide information to enlighten the Ministry and the other policymakers concerned as to the decision-making issues regarding this technology.

CETS's specific objectives in this report are:

- To describe hyperbaric oxygen therapy and its mechanisms of action.
- To systematically review the scientific literature in order to determine which pathologies and in what conditions HBO therapy is effective.
- To review the risks associated with operating a hyperbaric chamber and the necessary safety measures relating thereto.
- To review the adverse effects and complications of HBO therapy.
- To estimate the potential demand for HBO therapy in Québec and the costs that would be generated in meeting this demand.
- To define the guidelines for meeting this potential demand, if applicable.

2. HYPERBARIC OXYGEN THERAPY

2.1 REVIEW OF THE LAWS OF PHYSICS

Hyperbaric conditions, or increased atmospheric pressure (air or oxygen), is at the basis of the treatment of decompression sickness and gas embolism. The use of oxygen at greater than atmospheric pressure (hyperbaric oxygen) has widened the scope of this technology.

Most applications of hyperbaric conditions and HBO therapy derive directly from principles and laws developed over the centuries.

- The theory of the compressibility of gases, better known as *Boyle's law,* underlies the use of compressed air as a therapeutic modality in decompression sickness. This law states that, at a constant temperature, the volume (V) of a gas is inversely proportional to the pressure (P). In other words, the product PV is a constant.

- *Dalton's law*, or the law of partial pressures, states that the pressure of a gaseous mixture can be considered the sum of the pressures, the partial pressures (PP), of its constituent gases.

  $$(PPgas_1 + PPgas_2 + \ldots + PPgas_n = P_{mixture})$$

  This law is fundamental in diving. It alone explains the mechanisms of nitrogen narcosis, oxygen poisoning (Lorrain Smith effect, Paul Bert effect) and the need to proceed in stages, this together with Henry's law and tissue nitrogen saturation and desaturation during diving.

- *Henry's law*: This law is crucial in explaining the physiopathogenesis of diving accidents and in hyperbaric treatment, especially of decompression sickness. It defines the mechanisms of gas dissolution in liquids at a constant temperature.

  At a given temperature, the quantity of gas dissolved to the point of saturation in a liquid is proportional to the pressure of the gas above the liquid. At atmospheric pressure, the fluids in our bodies are saturated to certain levels by the different gases that constitute air (oxygen, nitrogen, etc.). When there is a change in pressure, such as when ascending from a dive, our tissues become supersaturated with gas. The tendency to reestablish equilibrium between these levels and the ambient pressure accounts for the release of gas. If the drop in pressure due to the ascent is too fast, bubbles form, which can be very hazardous to the body. The application of this law is at the basis of the therapeutic protocol for decompression sickness.

These laws and an understanding of the mechanisms of gas saturation-desaturation has enabled HBO technology to evolve and has permitted its use in numerous medical conditions. The development of increasingly safer hyperbaric equipment (monoplace chambers, multiplace chambers and medicalized chambers) is making it possible to meet various therapeutic needs, e.g., carbon monoxide poisoning, gas embolism and osteoradionecrosis. The equipment and mechanisms of action will be discussed in greater detail in the chapter on hyperbaric oxygen therapy.

2.2 BACKGROUND

Even though Priestly (1775), then Scheele and Lavoisier in 1777 acknowledged the existence of oxygen, it was not until 1789 that Lavoisier, in his *Treatise on Elementary Chemistry*, introduced the term *oxygen* as the name of a component and the basic principle of certain substances, such as acids, bases and salts. Previously, and in contrast to harmful expelled air (an allusion to carbon dioxide, which was discovered by Black in 1756), ambient air was considered indispensable to life.

However, it was not until 1878 that the physical and physiological principles, therapeutic applications and potential toxicity of oxygen were demonstrated, by Paul Bert (Paul Bert effect). It is now known that oxygen accounts for 89% of the weight of water and 23% of that of air and that the main minerals consist of 50% oxygen. Ambient air with an oxygen content below 17% can result in serious lesions. If the content drops below 12%, death by suffocation can occur.

Although the theory of the compressibility of gases (Boyle's law) was set forth in 1676, the first hyperbaric chamber for therapeutic use had already been set up in London by Henshow in 1664. However, it was not until 1840 that hyperbaric centres for treating patients with compressed gas were created, by Tabarie and Pravaz (in Lyon). In 1854, Pol and Wattelle were the first to report the beneficial effect of gradual recompression in improving the health of a patient with decompression sickness [249], but it was only in 1909 that Keays demonstrated, statistically, the positive effects of gradual recompression in the treatment of this condition, based on 3,700 cases of decompression sickness that had occurred during the construction of the Hudson River Tunnel in New York City [163].

It took nearly 300 years to realize the importance of the therapeutic effects of hyperbaric conditions, of oxygen and of the effects of combining them. Bert (1878), Zuntz (1897) and Von Schrotter (1906) were the first to recommend including oxygen therapy during recompression sessions [24, 308, 329]. Inadequate knowledge of the adverse effects of this treatment and the absence of adequate technologies delayed its use.

It was in 1920 that, concurrently with the development of diving and improvements to support technologies, experimental work on hyperbaric oxygen really began to take off. Decompression sickness aside, the first medical use of HBO (adjuvant treatment at 3 ATA) was by Boerema in 1959 during open-heart surgery [28, 29]. HBO was first incorporated into a treatment protocol in 1961 by Brummelkamp, for patients with gas gangrene [43].

The offshore oil industry and the development of diving operations led to increased interest in and the evolution of this technology. The numerous incidents (decompression sickness, fires, explosions, etc.) between 1960 and 1970 led many specialists to look into the problem of making hyperbaric compartments safer and into standardizing the operating procedures (dive duration, number of stages, etc.). In 1924, the United States Navy was the first to publish standards (diving table) for the treatment of decompression sickness. Presently, the most widely used diving tables are those of COMEX (France) [63], the Defense and Civil Institute of Environmental Medicine (DCIEM) and the United States Navy.

In the past 30 years or so, with knowledge evolving, the advent of new technologies and the numerous potential applications of hyperbaric oxygen therapy, a very large number of hyperbaric centres have opened worldwide, especially in the United States, Italy, France, Germany and Japan [213].

2.3 DESCRIPTION OF THE TECHNOLOGY AND ITS MECHANISMS OF ACTION

In hyperbaric oxygen therapy, the patient breathes pure oxygen (100%) at greater than atmospheric pressure (1.5 to 3 ATA) while in a steel or polymer chamber.

Through different mechanisms of action, which are explained later, HBO seems to play a role in:

- The revitalization, revascularization and healing of tissues, grafts and organs.

- The preservation and regeneration of bone.
- The potentiation of certain pharmacologic effects.

Hyperbaric oxygen is used for different therapeutic purposes, although Ishihara *et al* report its use for evaluative purposes in predicting recovery after surgery in patients with cervical compression myelopathy [154]. The therapeutic applications concern the central nervous system, cardiovascular system and respiratory system, as well as soft tissues, the locomotive system and hematologic disorders [142, 154, 187, 307].

According to Gabb *et al* [107], HBO therapy has been tried out in over 130 medical conditions, although very few of them have been the subject of randomized, controlled, prospective trials. Depending on the author or school, the number of medical conditions in which the efficacy of HBO therapy is recognized varies from seven to 20. It should be noted that, in most cases, the observed difference is due to the manner in which they are grouped rather than to greater diversity.

HBO is known mainly for its use as the treatment of choice in carbon monoxide poisoning, gas embolism and decompression sickness (underwater diving accidents). In such cases, it constitutes emergency care for life-threatened patients. In general, only one or two "dives" in a chamber suffice for this type of use.

The experience of hyperbaric medicine specialists and, to a certain extent, the scientific literature also support the use of HBO as an adjuvant treatment for a number of other, more “chronic” medical conditions, such as certain complex, refractory wounds [215]. However, such use requires numerous visits, with up to as many as sixty 90-minute sessions, depending on the illness. Such treatments necessarily require a multidisciplinary team consisting of specialists involved in hyperbaric medicine, such as plastic surgeons, orthopedic surgeons and endocrinologists, which implies a more complex mode of organization.

Despite the recommendations of expert organizations, such as the Undersea and Hyperbaric Medical Society, concerning the "recognized indications", HBO therapy is presently a technology whose applications, apart from the emergency situations mentioned above, are still controversial [46, 128].

2.3.1 Equipment

There are two types of hyperbaric chambers: monoplace and multiplace. The purpose of a hyperbaric chamber is to create an ambient air pressure that is in equilibrium with the pressure of the oxygen that the patient is breathing.

Monoplace chamber

A monoplace chamber usually consists of a small-diameter, airtight cylinder in which the patient is placed. The chamber is then pressurized with pure oxygen. In this type of setup, the patient cannot be physically examined; only visual and auditory communication is possible.

Multiplace chamber

Not only can several patients be treated at the same time in a multiplace chamber, but they can also be clinically monitored by nurses and/or physicians throughout the treatment. The chamber is pressurized with compressed air, and only the patient breathes oxygen, through an airtight mask, endotracheal tube or a plastic or Plexiglas head hood. Different monitoring or therapeutic instruments and devices (infusions, medical vacuum cleaner, etc.) can be placed in the chamber.

There have been different developments over the years, with the result that there are now mobile hyperbaric chambers and medical hyperbaric chambers (multiplace chambers which can accommodate a gurney and which permit complete management of patients whose condition is unstable).

The use of a hyperbaric chamber is not without its risks, both to the patient and personnel. The risks include explosive decompression, fire, oxygen poisoning and decompression sickness (an error or a series of errors is always determined to be the cause of an accident, although such events are fortunately rare, considering the high number of daily sessions worldwide). Furthermore, the treatment may be accompanied by complications. These topics are discussed in detail in Section 7.

2.3.2 Therapeutic modalities

The clinical application of HBO requires heavy equipment (physically and financially speaking) and specialized training for the teams in charge of the centre.

At present, there are no standard protocols for specific medical conditions. The therapeutic procedures vary according to the condition (acute or chronic) and the treatment centre (physicians caring for the patient, etc.). The treatment can be administered on a one-time basis and vary in duration, as is the case with carbon monoxide poisoning, or by way of several daily or twice-daily sessions of predetermined duration (30 to 90 minutes). The pressure at which HBO is administered depends on several factors: the medical condition, the patient's characteristics, the type of chamber and the centre's practices (1.5 to 3 ATA or even 6 ATA).

Depending on the type of chamber and the patient's disease state, and after following the usual safety instructions (Chapter 8), the patient is placed in the chamber in a comfortable manner in a sitting or lying position, and the appropriate oxygen breathing system is installed (mask, hood, etc.). The patient is monitored closely throughout the session.

2.3.3 Effects of HBO: mechanisms of action

HBO seems to play a role in the revitalization, revascularization and healing of tissues, grafts and organs, in the preservation and regeneration of bone, and in potentiating certain pharmacologic effects. These effects are the direct or indirect consequence of six main mechanisms of action.

2.3.3.1 Effect of increased pressure

According to Boyle’s law, any volume of gas trapped in the body decreases as the pressure increases. Reducing the volume of gas bubbles allows them to move through the bloodstream or at least into small vessels, thus reducing the surfaces that could be potential sites for an infarction. This hyperbaric effect is exploited in the treatment of gas embolism and decompression sickness.

2.3.3.2 Effect of increasing the oxygen pressure

Administering oxygen at a high pressure results in the rapid elimination of toxic gases, such as carbon monoxide, and therefore reduces their harmful effects. Breathing 100% oxygen at pressures of 2.5 to 3 atmospheres (1 ATA = 760 mm Hg) increases by 15- to 20-fold the partial pressure of oxygen in the blood and tissues. This significant increase explains the efficacy of hyperbaric oxygen therapy in the treatment of carbon monoxide poisoning.

2.3.3.3 Effect of reactive vasoconstriction

Hyperbaric oxygen acts as an alpha-adrenergic agent. The increase in the partial pressure of oxygen (PaO_2) causes reactive vasoconstriction of the small vessels, which reduces vasogenic edema without altering normal tissue oxygenation. Thanks to this property, HBO is used in the treatment of severe injuries, such as crush injuries and thermal burns.

2.3.3.4 Antibacterial effect

Certain conditions are caused by anaerobic bacteria that have no natural defenses against superoxide ions, peroxides or other entities formed in the presence of a high oxygen concentration. Most of an individual's antibacterial defense mechanisms are oxygen-dependent, and any decrease in oxygen delays and prevents the phenomena of phagocytosis and the destruction of foreign microorganisms by white blood cells. Increasing the PO_2 (oxygen pressure) optimizes the antiinfective properties of white blood cells, especially polymorphonuclear neutrophils, through the formation of enzymes and oxygenated free radicals (superoxide ions), which enhance the body's antibacterial capability. Certain bacteria, such as *E. coli*, grow in an environment that contains oxygen but are inhibited by high-pressure oxygen.

2.3.3.5 Antiischemic effect

Two phenomena give HBO therapy an antiischemic effect:

- HBO therapy results in excess oxygen dissolving in the plasma (Henry's law).
- HBO improves the elasticity and therefore deformability of red blood cells, which enables them to reach ischemic tissues.

These two mechanisms make for enhanced tissue oxygenation and increased local metabolism.

2.3.3.6 Healing effect

HBO promotes osteoclast and osteoblast growth, facilitates collagen synthesis as a result of its positive action on fibroblast proliferation, and stimulates neovascularization, or angiogenesis. The medical conditions in which HBO has this effect include treatment-refractory lesions, radionecrosis (bony and tissue), compromised grafts, and severe, extensive burns.

Appendix A explains, in synoptic form, the physiopathogenesis of the different conditions, and, for each one, the mechanisms involved and the anticipated effects of HBO therapy.

3. EFFICACY OF HYPERBARIC OXYGEN THERAPY

3.1 UNDERSEA AND HYPERBARIC MEDICAL SOCIETY RECOMMENDATIONS

The Undersea and Hyperbaric Medical Society is an international, non-profit organization with about 2,500 members in 50 countries. The UHMS, which was founded in 1967, describes itself as the primary source of information on diving and hyperbaric medicine.

In 1976, recognizing the need for closer scrutiny of the emerging applications of hyperbaric oxygen therapy, the UHMS's executive committee created the Hyperbaric Oxygen Therapy Committee. The committee was charged with reviewing, on a regular basis, the available clinical and scientific data and issuing recommendations concerning the clinical efficacy and safety of HBO therapy. To this end, the multidisciplinary committee consists of clinicians and researchers in the following specialties: internal medicine, infectious diseases, pharmacology, emergency medicine, general surgery, orthopedic surgery, thoracic surgery, otorhinolaryngology, facial and maxillary surgery, anesthesia, pneumology, resuscitation and aerospace medicine.

From 1976 to 1999 (year of the last available report), the number of indications recommended by the committee decreased from 28 to 13.

The committee's recommendations are based on various types of evidence: physiological explanations, in vivo and in vitro efficacy studies, animal studies, controlled trials (prospective, controlled clinical studies) and the clinical experience of numerous recognized hyperbaric medical centres.

The committee requires that clinical and scientific evidence demonstrating the efficacy of HBO in the treatment of a given medical condition be at least as convincing as that supporting the accepted treatments for that condition.

In its latest report, dated 1999 [128], the Undersea and Hyperbaric Medical Society recommends the use of HBO therapy in the following 13 conditions:

- Gas embolism
- Carbon monoxide poisoning
- Gas gangrene (clostridial myonecrosis)
- Crush injuries, compartment syndromes and acute traumatic ischemias
- Decompression sickness
- Problem wounds
- Exceptional blood loss anemia
- Necrotizing soft-tissue infections
- Refractory osteomyelitis
- Radionecrosis
- Compromised skin grafts and flaps
- Burns
- Intracranial abscesses

It should be noted that the UHMS's recommendations are based both on an analysis of the scientific literature and on the clinical experience of hyperbaric medical specialists.

3.2 ALBERTA ASSESSMENT REPORT

The Alberta Heritage Foundation for Medical Research and the Center for Advancement of Health [210] systematically reviewed the scientific literature in order to determine the acceptable indications for HBO therapy. Their analysis was complemented by expert opinions.

Their findings were as follows:

- There is a high level of evidence supporting the use of HBO in the treatment of the following conditions:
  - Maxillary osteoradionecrosis
  - Diabetic leg ulcers
- There is an acceptable level of evidence supporting the use of HBO in the treatment of the following conditions:
  - Decompression sickness and gas embolism
  - Gas gangrene (clostridial)
  - Severe carbon monoxide poisoning
- There is an acceptable level of evidence suggesting a potential role for HBO—although the evidence does not demonstrate its efficacy—in the treatment of the following conditions:
  - Soft-tissue radionecrosis
  - Necrotizing soft-tissue infections
- The available hard data do not support the use of HBO in the treatment of the following conditions:
  - Refractory osteomyelitis
  - Burns
  - Compromised skin grafts
  - Anemia
  - Crush injuries

3.3 ANALYSIS OF CLINICAL STUDIES

The Conseil d'évaluation des technologies de la Santé chose to conduct its own assessment of the scientific literature on the efficacy of HBO in the treatment of various conditions. The literature published in French and English up until July 1999 was identified by means of an automated MEDLINE search and by a manual search of the bibliographies in published articles and reports. The sample size, the publication date and the medical condition treated were used when initially selecting the studies and reports to be evaluated. Table 1 shows the studies chosen for each indication according to design type.

In general, there is a paucity or even a complete absence of randomized, controlled trials of the efficacy of hyperbaric oxygen in treating disease. The inadequacies encountered most often in the publications consulted were as follows:

- No clear definition of the study population in whom the treatment was to be instituted.
- No introduction of the specialists in charge of the treatment.
- The comparator treatment is most often poorly defined or not mentioned.
- No subject inclusion or exclusion criteria for the study presented.
- No double-blinding.
- Duration of treatment not stated or not defined.
- Long-term follow-up often not mentioned.

In the following sections, the medical conditions treated in at least one efficacy study are examined. The studies are presented on a quality-of-evidence basis according to the hierarchy presented below, from the most rigorous to the least rigorous design.

Table 1: Synopsis of the types of studies presented, by medical condition

MEDICAL CONDITION(S)	Randomized, double-blind, controlled trials	Randomized, Controlled trials	Nonrandomized, controlled trials	Observational, controlled studies	Case series
Carbon monoxide poisoning	Scheinkestel 1999 [269] Weaver 1995 [316]	Ducassé 1995 [81] Raphael 1989 [257] Thom 1995 [294]			
Decompression sickness/gas embolism		Keller 1995 [165]		Ziser 1999 [328]	
Gas gangrene				Gibson 1986 [110]	Hart 1990 [136]
Infectious diseases characterized by tissue necrosis				Brown 1994 [42] Hollabaugh 1998 [148] Riseman 1990 [262]	Pizzorno 1997 [247]
Osteoradionecrosis (ORN)		Warren 1997 [313]	Neovius 1997 [223] Marx 1985 [195]		Bevers 1995 [27] Feldemeier 1996 [98] McKenzie 1993 [204]
Diabetic lesions			Doctor 1992 [79]	Faglia 1998 [93] Stone 1998 [287]	
Problem wounds **Burns** **Leg ulcers** **Crush injuries**	Niezgodda 1997 [226] Hammarlund 1995 [127] Bouachour 1996 [33]	Brannen 1997 [36]			
Myocardial ischemia		Shandling 1997 [273]			
Cerebral ischemias	Nighoghossian 1995 [228]	Rockswold 1992 [263]			Holbach 1979 [146] Cordoba-Cabeza 1998 [66]
Anemias					Mazin 1992 [202]
Migraines	Wilson 1998 [318]	Myers 1995 [218]	Di Sabato 1997 78]		
Facial palsies		Racic 1997 [253]			
Malignant conditions		Cade 1978 [44] Fletcher 1977 [101] Watson 1978 [314]			
Ear/hearing disorders					Kau 1997 [161] Lamm 1998 [176]
Multiple sclerosis	Confavreux 1986 [64] Harpur 1986 [132] Wood 1985 [324]	Kleijnen 1995 (systematic review of 14 RCTs) [170]			

For each medical condition in question, only those studies with the most robust level of evidence are discussed and analyzed here.

Controlled trial: A planned, prospective experiment for the purpose of comparing the efficacy of the study treatment with at least one other appropriate therapeutic modality under specific conditions and in which the participants are assigned to one or more experimental groups and a control group.

The manner in which the participants are assigned (randomly or otherwise) and the steps taken to blind the study personnel as to which participants are receiving which treatment will have a determining effect on the strength of the evidence gathered.

Randomized, double-blind, controlled trial: The participants are randomly assigned to one or more experimental groups and a control group. Neither the observer nor the participant knows which group the latter has been assigned to. Scientifically, this method is considered the most rigorous. From a methodological standpoint, the quality of the evidence gathered in such a study is indisputable.

Randomized, controlled trial: The participants are randomly assigned to one or more experimental groups and a control group. Only the participants do not know which group they have been assigned to. This method is subject to observer bias.

Nonrandomized, controlled trial: The participants are not randomly assigned to the experimental group or control group. This method is subject to selection bias and the influence of confounding variables, as well as observer bias.

Observational, controlled study: A retrospective, analytical study for the purpose of comparing the results obtained in a group of subjects who underwent the treatment of interest with those obtained in a group that received another type of treatment (control group). At no time are the investigators involved in assigning the subjects to either group. This method suffers considerably from selection bias.

Case series: A descriptive study of the course of a disease in a group of patients who have undergone the treatment of interest. This method suffers from the absence of a comparator control group for assessing the actual value of the reported observations.

3.3.1 Carbon monoxide poisoning

Since the hyperbaric chamber at the Hôpital du Sacré-Coeur de Montréal was put into service in 1982, 80% of the 1,500 patients treated in it have been so for carbon monoxide (CO) poisoning. In the United States, in a retrospective study covering a period of 10 years, 56,000 deaths due to CO exposure were recorded [59, 131, 254].

Different mechanisms are responsible for the toxicity of CO. The main consequence of CO poisoning is reduced tissue oxygen transport as a result of the binding of CO to hemoglobin. The affinity of the Hb-CO bond is 200 times greater than that of the HB-oxygen bond.

Clinically, CO poisoning can have cardiac, pulmonary and even renal sequelae, but most often they are neurological in nature [115]. The symptomatology is highly variable, and the patient may present with a hyperactive state, lethargy, chorea, apraxia, psychotic states or a coma. More rarely, peripheral neuropathy and cortical blindness are reported. Early and even late sequelae can occur (disorientation, epileptic seizures, behavioral problems, etc.) [1, 40, 174, 197, 200, 294].

Table 2: Studies of hyperbaric oxygen in the treatment of carbon monoxide poisoning

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Scheinkestel *et al* 1999 [269]	Randomized, double-blind, controlled trial	To determine the efficacy of HBO vs. NBO.	– All cases of CO poisoning between Sept. 1, 1993 and Dec. 30, 1995. – Excluded: pregnant women, children, burn victims and those refusing to give consent.	– 191 subjects (104 HBO, 87 NBO). – 60 minutes a day for 3 to 6 days. – HBO: 2.8 ATA. – NBO: 1.0 ATA.	– 28% of the subjects in the HBO group required additional treatments vs. 15% in the NBO group (significant difference). – The NBO group did not score as well on the neurological tests at the end of the treatments: significant difference.
Weaver *et al* 1995 [316]	Randomized, double-blind, controlled trial	To determine the efficacy of HBO vs. NBO.	– Poisoning occurred within less than 23 hrs. – Age: ≥ 16. – Consent. – Pregnant women excluded.	– 49 subjects (24 HBO, 25 NBO). – HBO vs. NBO at 2.2 ATA. – Initial treatment with HBO vs. O_2 at 2.2 ATA. – + 2 sessions at 6 hrs and 12 hrs with HBO vs. air at 2.2 ATA.	– Symptoms persisted in 8 subjects (4 and 4). – 4 subjects presented with delayed neurological sequelae (DNS*).
Thom *et al* 1995 [294]	Nonrandomized, controlled trial	To test the hypothesis that HBO would have no effect on the incidence of delayed neurological sequelae (DNS)*.	– Subjects who presented within 6 hours of exposure. – Mild to moderate poisoning. – No loss of consciousness or cardiac instability.	– 60 patients. – 30 patients received 100% O_2 at atmospheric pressure. – 30 patients received HBO (2.8 ATA for 30 min, then at 2 ATA for 90 min). – Measurement of DNS*.	– 7/30 in the control group presented with DNS. – 0/30 in the experimental group ($p < 0.05$). – DNS appeared 6 ± 1 days after poisoning and persisted for 41 ± 1 days. – At 4 weeks of follow-up, the control group patients who had not sustained any DNS had a worse score on one particular test.
Raphael *et al* 1989 [257]	Nonrandomized, controlled trial	To evaluate the effect of HBO in the treatment of CO poisoning.	– Subjects presenting within 12 hrs after exposure.	– 629 subjects with CO poisoning. – Group A: no impairment of consciousness. – A0 (n=170): 6 hrs of NBO. – A1 (n=173): 2 hrs of HBO. – 2 ATA, then 4 hrs of NBO. – Group B had impaired consciousness: all received HBO (both groups received 4 hrs of NBO). – B0 (n=145): 1 session of HBO. – B1 (n=141): 2 sessions of HBO.	Group A At 1 month: – 66% of the A0 subjects and 68% of the A1 subjects recovered. Group B At 1 month: – Recovery 54% of the B0 subjects 52% of the B1 subjects – Neuropsychological sequelae – Deaths 2 in B0, 2 in B1
Ducassé *et al* 1995 [81]	Nonrandomized, controlled trial	Controlled study of the treatment of CO-poisoned patients without impaired consciousness: HBO vs. NBO.	– Noncomatose CO-poisoned subjects.	– 26 patients treated within 2 hours of exposure. – Control group (13): 100% NBO. – Exp. group (13): 100% HBO followed by NBO for 10 hours.	At the end of 1st period The HBO-treated patients showed a significant improvement in their clinical and biological parameters compared to the NBO group. At the end of 2nd period No significant difference in the COHb level. However, a few patients in the control group had ECG abnormalities.

* DNS (delayed neurological sequelae): Defined as the appearance of new symptoms after oxygen therapy and deterioration on one or more neurological evaluation tests (NPSB).

Basically, the severity of CO poisoning depends on three things: the CO concentration and the length of exposure to the toxic gas, the length of time the victim is unconscious, and a combination of other factors, such as age and concurrent diseases (cardiovascular, etc.). In their study of 302 cases, Goulon *et al* observed a mortality rate of 13.5% when the treatment was administered within six hours after the poisoning occurred but of 35.8% when it was administered later than that [117]. Whether hyperbaric oxygen or normobaric oxygen should be used is still being debated [65, 269, 316].

Randomized, controlled trials of HBO therapy in carbon monoxide poisoning are rare. Some of the few studies identified were conducted in a double-blind fashion but were limited to one category of patients (with mild or moderate CO poisoning). The studies selected are presented in Table 2.

Up until now, only those studies by Scheinkestel et al [269] and Weaver *et al* [316] provide a high level of evidence. The latter study showed no significant difference in the persistence of neurological sequelae when HBO therapy was compared with treatment with normobaric oxygen (NBO). In their double-blind study, Scheinkestel *et al* even observed worse neurological sequelae in the subjects who underwent HBO treatments than in those who received normobaric treatments. However, Ducassé *et al* [81] report that HBO was effective in reducing the time to recovery in CO poisoning. This had previously been reported by Jiang [156] in experimental work. These observations are supported by the results obtained by Pace *et al*, who showed that the half-life of Hb-CO is 90 minutes at 1 atmosphere (ATA), 35 minutes at 2 ATA and 22 minutes at 3 ATA [235].

The results obtained by Raphael *et al* [257], then by Thom *et al* [294] are similar to those obtained by Norkool and Kirkpatrick [232], who report that HBO is effective in the recovery, without sequelae, of victims of CO poisoning. Although randomized, these studies were not conducted in a double-blind fashion.

In a critical review of clinical studies (nonrandomized and uncontrolled) carried out by Tibbles *et al*, it is seen that HBO offers a clear advantage over NBO in reducing morbidity and mortality [297]. The use of HBO in pregnant women is still controversial [41, 88, 302].

In short, most studies demonstrating the efficacy of HBO and its advantage over normobaric oxygen provide a low level of evidence or are only retrospective studies (e.g., Tibbles [297], Gorman [113] and Gorman and Runcinam [116]). Nonetheless, given the clinical results obtained over the past several years by HBO specialists, hyperbaric oxygen therapy is the treatment of choice for carbon monoxide poisoning. However, the criteria for using it (level of consciousness, clinical signs and/or COHb level) vary according to the medical facility [67, 114, 129, 279].

In conclusion, it can be said that the level of the available scientific evidence is low but that the clinical results obtained and the experimental data support the use of HBO in the treatment of carbon monoxide poisoning, based on criteria that need to be standardized.

3.3.2 Gas embolism

Gas embolism can occur when there is a sudden change in barometric pressure (compression/ decompression) or at normal atmospheric pressure, as during traumatic and iatrogenic injuries. Gas embolism resulting from decompression sickness will be discussed in a separate section. Gas embolism can be a sequela of:

- Traumatic injuries to the heart and large vessels or sudden trauma to the chest in the presence of a closed glottis [254, 255].

Table 3: Study of hyperbaric oxygen in the treatment of massive gas embolism

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Ziser *et al* 1999 [328]	Case series	Efficacy of HBO in the early treatment of gas embolism following cardiac surgery.	Patients referred for massive gas embolism between 1985 and 1998.	17 patients followed.	- 8 patients experienced complete recovery. - 6 patients had significant neurological sequelae. - 3 patients died. - The 5 patients who received HBO within 3 hours after their operation recovered without sequelae. - 2 of the 4 patients treated 3 to 5 hours after their operation recovered without sequelae. - 1 of the 8 patients who received HBO 9 to 20 hours after their operation recovered without sequelae. The association between the improvement in neurological signs and the time to treatment was significant.

- Iatrogenic injuries: perforation of a vessel wall during surgical, diagnostic, medical (catheterizations, laparoscopies, organ biopsies, etc.) [8, 162, 209, 258, 270] or therapeutic (curettage, hemodialysis, etc.) procedures [31].

Gas embolism can affect all of the body's systems and organs. The sequelae range from transient ischemia to a major tissue infarction [237], the symptoms from ordinary malaise to circulatory collapse. Damage to the nervous system is life-threatening.

Most articles dealing with gas embolism concern experimental or observational studies [77, 83, 141, 328] and state that hyperbaric oxygen therapy is effective.

In an observational study with no control group and only 17 patients, Ziser *et al* [328] observed a relationship between the persistence of sequelae and the time to hyperbaric treatment.

In conclusion, there are no studies with a high level of evidence demonstrating the efficacy of HBO in the treatment of gas embolism. However, the theoretical data and observational studies have led to HBO being accepted as the standard treatment for certain severe cases of gas embolism.

3.3.3 Decompression sickness

Decompression sickness is still a frequent phenomenon [4]. It is due to a decrease in the ambient pressure with, as a result, the formation of gas bubbles and mechanical blockage of the blood and/or lymphatic vessels. These "foreign bodies" give rise to various lesional (vascular endothelium), inflammatory (reactive secretion of histamine) and procoagulant manifestations due to cell disturbances (leukocytes and platelets). The necrosis secondary to ischemia of the affected tissues is usually nonreversible and the sequelae very debilitating. Different hypotheses have been advanced concerning the mechanisms of gas bubble formation [75, 187, 225, 275]. The bubbles can form in intracellular, extracellular or intravascular sites.

Table 4: Study of the treatment of decompression sickness: HBO vs. dexamethasone

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Keller *et al* 1995 [165]	Randomized, controlled trial	To compare HBO and dexamethasone in the treatment of mountain sickness.	Mountain climbers with symptoms of mountain sickness.	- 31 subjects: 15 treated with HBO (1.93 ATA, 1 hour), 16 with dexamethasone, 8 mg followed by 4 mg every 6 hours. - Outcome measures by means of checklists (Lake Louise score, clinical score and AMS-C score) before and after 11 hours of treatment.	- Significant improvement observed in all three scores in the HBO group. - Significant improvement observed in the different scores in the dexamethasone group. - After 1 hour of treatment, the SaO_2 was significantly higher in the HBO group. - This difference was significant after 11 hours in the dexamethasone group.

Gas embolism can accompany or be a complication of decompression sickness. In both conditions, the treatment is the same [113]. The presence of gas bubbles in the vessels is most often due to explosive decompression or passage through an arteriovenous shunt (suggestive symptomatology) [186].

Based on data from basic physics, hyperbaric oxygen therapy is the most effective treatment [240]. The purpose of recompression (HBO) is to reduce the size of the gas bubbles in the tissues and vessels, which results in improved blood and lymph flow and the resolution of the gases. The other effect of recompression is tissue reoxygenation and the elimination of inert gases (e.g., nitrogen) and a decrease in inflammatory process activation. The question as to which therapeutic doses of HBO are optimal is a matter of debate [69].

Controlled trials, such as that by Keller *et al* [165] (Table 4), have been carried out to evaluate the efficacy of HBO used alone and of certain drugs (dexamethasone, lidocaine). The results are unconvincing [2, 97, 165]. Use of a portable hyperbaric chamber for therapeutic purposes usually occurs within a research context [82].

In conclusion, decompression sickness does not lend itself well to randomized, controlled trials, which explains, in part, why so few such trials were identified and which affects the level of the available scientific evidence. However, data from basic physics, observational studies and clinical experience have made HBO the treatment of choice for decompression sickness.

3.3.4 Gas gangrene

Gas gangrene, or clostridial myonecrosis (myositis), is an invasive infection of the muscles by a strict anaerobic, toxinogenic bacterium (nearly 96% of cases of gas gangrene are caused by *Clostridium perfringens* or *welchii*). It is characterized by toxemia, severe edema, tissue necrosis and the production of a relatively large quantity of gas [14, 142]. It is a serious disease that is often fatal if it is not diagnosed early. The contamination may be of endogenous origin due to the presence of an existing bacterial focus or of exogenous origin due to an injury (open wound, severe burn, etc.). The history of the disease and clinical signs of toxic shock may arouse suspicion of such an infection, which is quickly confirmed by a stain: the presence of rod-shaped, grampositive bacilli.

Table 5: Studies of hyperbaric oxygen therapy in the treatment of gas gangrene

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Gibson and Davies 1986 [110]	Observational, controlled study	To demonstrate the benefit of adjuvant HBO therapy in the early management of gas gangrene.	Patients diagnosed with gas gangrene.	- Retrospective review covering a 14-year period. - 46 cases. - 29 received specific treatment and HBO. - 17 received specific treatment only.	- HBO group: 9 deaths (31%). - Non-HBO group: 12 deaths (71%).
Hart and Strauss 1990 [136]	Case series	Benefit of antibiotic therapy + surgery + HBO in gas gangrene.	Patients admitted for clostridial infections.	- Series of 139 cases over a 15-year period.	- 81% survived the infection. - 5% of deaths caused by post-injury clostridial myonecrosis. - The mortality rate increased as the time from diagnosis to treatment increased.

The basic treatment for gas gangrene is antibiotic therapy (penicillin), most often multiple antibiotic therapy. The life prognosis depends on how soon treatment is initiated and on the patient's condition at the time of diagnosis (whether he or she is in a state of shock).

After experimental studies reporting the benefit of including HBO in the treatment of induced gas gangrene in dogs [72] and guinea pigs [144, 145], Hart, in a literature review covering a period of 20 years, concluded that hyperbaric oxygen therapy is effective as an adjuvant treatment to antibiotic therapy and surgery [134, 136].

HBO owes its efficacy to a blocking effect on anaerobic bacteria and/or a facilitating action via the stimulation of cellular defenses. However, this technology should only be used as an adjuvant to the specific treatment [110, 304], and its use must, under no circumstances, result in the specific treatment being delayed [123]. Gas gangrene is what might be called "an application II level indication" for HBO, i.e., necessary for preventing the occurrence of complications or sequelae.

In conclusion, the theoretical data, together with the experimental results, point to the efficacy of HBO as an adjuvant treatment in gas gangrene. However, the positive effects of this adjuvant treatment, as suggested by the observational, controlled studies, need to be confirmed by randomized, controlled trials.

3.3.5 Infectious diseases characterized by tissue necrosis

The use of HBO in certain necrotizing infectious diseases (apart from *Clostridium perfringens* gas gangrene) is on the increase. The use of HBO as adjuvant therapy in these diseases is based on the double efficacy of pressurized oxygen: the antibacterial effect on anaerobes due to the production of superoxide free radicals that are toxic to such microorganisms (which do not have any degradation enzymes, such as peroxidases), with a simultaneous effect on the body's cellular defense system, in particular, leukocytes. Furthermore, some authors mention the fact that HBO increases the efficacy of certain antibiotics (specifically, those whose intracellular transport is oxygen-dependent).

In their experimental study on induced streptococcal myositis in rats, Zamboni *et al* reported that the efficacy of the antibiotic treatment increased when combined with HBO

[326].

HBO is presently used in therapeutic protocols for necrotizing soft-tissue infections [198]. The different diseases of interest here include pro-gresssive necrotizing infections and Meleney's ulcer, an infection due to a combination of two or more microorganisms (nonhemolytic strepto-coccus and Streptococcus aureus and even amebae or a Proteus species). It is characterized by a central ulcer with necrotic edges surrounded by painful erythema. A microscopic examination reveals microthrombi. This condition is sometimes observed in diabetic foot ulcers.

Hollabaugh *et al* [148] and Pizzorno *et al* [247] report that combining HBO with the usual medical and surgical treatments has a beneficial effect in a disease similar to Meleney's ulcer, Fournier's gangrene, whose etiology is still debated (polymicrobial infection). Bell devised a decision tree for evaluating HBO therapy according to the medical condition [18].

In an observational, controlled study involving 54 patients with truncal necrotizing infections, Brown et al found no significant difference between the group that received specific treatment together with HBO and the control group, which received specific treatment only [42]. The authors mention the possibility of selection bias and recommend that studies with a higher degree of validity be conducted.

Riseman *et al* report that the use of HBO in combination with the specific treatment for necrotizing fasciitis (NF) had a beneficial effect [262]. A group of 29 patients with NF was followed for eight years. They were treated with antibiotics and surgery alone or in combination with HBO. The authors observed less mortality and morbidity (fewer surgical debridements) in the patients with nonclostridial infections.

The beneficial effects of hyperbaric oxygen therapy in combination with specific treatments in refractory cases have been reported by different authors [130, 191, 198, 199, 301]. Most often, the patients had polymicrobial diseases of the soft tissues (skin, subcutaneous tissue, fascia), where there is often a mixed bacterial flora (anaerobes/aerobes).

Hyperbaric oxygen therapy has been used, with positive results, in the treatment of botry-omycosis (due to *Streptococcus aureus*) [89] and in actinomycosis. The efficacy in such cases is, however, the subject of debate, since, unlike Drake [80], Eugster *et al* [92] did not report any benefit with the use of HBO therapy in group A beta-hemolytic streptococcal infections (necro-tizing fasciitis).

Most of the studies identified suffer from methodological problems and sampling weak-nesses [91]. The only studies in which the variables are controlled are those involving animal models [145]. Mader *et al* studied induced *Staphylococcus aureus* osteomyelitis in rabbits [188]. They conclude that HBO is not directly responsible for microbial destruction and that the efficacy of this treatment is due to increased intramedullar oxygenation, which maximizes the efficacy of the activity of phagocytes (polynuclears, a macropnages). Niinikoski and Hunt confirmed the occurrence of bone marrow hypoxia (20 mm of Hg less) in osteomyelitis [149, 150, 229].

Osteomyelitis is one of the target medical conditions for hyperbaric oxygen therapy. Slack *et al* and subsequently Depenbusch *et al* reported an improvement in health and lesion healing in 100% and 71%, respectively, of the patients with chronic refractory osteomyelitis [74, 282]. Perrins et al obtained similar results in their study (70%) [242]. Davis *et al* reported that HBO is effective in the treatment of external malignant otitis (involving osteomyelitis with intracranial extension) [70].

Table 6: Studies of hyperbaric oxygen in the treatment of infectious diseases characterized by tissue necrosis (other than gas gangrene)

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Hollabaugh *et al* 1998 [148]	Observational, controlled study	To assess the impact of HBO as adjuvant therapy in Fournier's gangrene (FG).	- Patients diagnosed with FG at the University of Tennessee.	- 26 cases (diabetes, alcohol abuse, immunosuppression or other associated diseases). - 14 patients received HBO. - 12 patients received the usual treatments (controls).	- 1 death (7%) in the HBO group and 5 (42%) in the control group.
Brown *et al* 1994 [42]	Observational, controlled study	To evaluate the efficacy of HBO in truncal tissue-necrotizing infections.	- Patients admitted between 1/1/80 and 31/12/91 for major truncal necrosis with a diagnosis of necrotizing fasciitis, necrotizing cellulitis, gangrene, Fournier's gangrene or clostridial or nonclostridial myonecrosis. - Excluded: patients for whom information was incomplete or whose hospital stay was longer than 100 days, and cases of nonbacterial tissue necrosis.	- 2 centres: Vancouver General Hospital and Calgary General Hospital. - 30 patients received HBO as adjuvant therapy (2.5 to 3 ATA for 90 min); 80% of the patients underwent 4 or fewer sessions of HBO. - 24 patients received standard treatment (control group). *Note*: There were more clostridial infections in the HBO group than in the control group. - Determination of the mean length of hospital stay (LHS), the mean length of intensive care unit (ICU) stay and the duration of antibiotic therapy.	- No significant difference in the mean LHS, the mean ICU stay or the duration of antibiotic therapy. - No significant difference in mortality: 9/30 (30%) in the HBO group and 10/24 (42%) in the control group.
Riseman *et al* 1990 [262]	Observational, controlled study	To assess the impact of HBO on life prognosis and the number of surgical interventions in patients with necrotizing fasciitis receiving the usual treatment.	- Patients treated between 1980 and 1988 for necrotizing fasciitis, gas gangrene or Fournier's gangrene.	- 12 patients in the ATBs + debridements group. - 17 patients in the experimental group: same treatment + HBO (2.5 ATA for 90 min; mean, 7.3 sessions).	Group without HBO: - Deaths: 8/12 (67%). - 13 debridements (3.25 per patient). Group with HBO: - Deaths: 4/17 (24%). - 14 debridements (1.16 per patient).
Pizzorno *et al* 1997 [247]	Case series	To determine the effect of HBO in Fournier's gangrene (FG).	- Patients with FG associated with diabetes.	- 11 patients treated with ATBs and HBO (5 to 24 90-minute sessions at 2.5 ATA).	- No deaths. - All the patients experienced healing.

Osteomyelitis is currently one of the recognized indications for HBO. Hyperbaric oxygen therapy (35 sessions of oxygen therapy) is strictly an adjuvant treatment to medical, surgical and nutritional therapy [87, 201].

In conclusion, the theoretical data and experimental results point to the efficacy of HBO as adjuvant treatment in tissue-necrotizing infections (soft and bony tissues). However, the benefits of this adjuvant treatment, as suggested by observational, controlled studies, need to be confirmed by randomized, controlled trials.

3.3.6 Soft and bony tissue necrosis due to radiation therapy

This category comprises numerous morbid manifestations due to exposure to therapeutic or accidental radiation, one of the sequelae of which is ischemia or even soft-tissue and bony necrosis. These conditions can occur after certain radiation treatments. Most often, they develop after local injury. This type of pathology frequently occurs in the face, especially the jaw, after dental extraction or dental prosthesis placement. If left untreated, it will exhibit a chronic course with complications, infections and fractures. The associated pain is often intense and refractory.

In soft tissues, high doses of radiation cause inflammation and injury to the inner coat of the blood vessels (proliferative endarteritis), with resulting ischemia and tissue necrosis. Because of its density, which is 1.8 times greater than that of tissue, bone absorbs more radiation, which explains the lack of oxygen and nutrient delivery. Also, radiation is responsible for the imbalance in the osteoclast (destruction) and osteoblast (production) system, which leads to osteoporosis and bony necrosis, or osteoradionecrosis (ORN).

These complications occur in numerous regions, especially the pelvic region (lumbar vertebrae, femur and pelvis because of their function as supporting structures, which are therefore susceptible to injury) and the maxillaries (high density, poor vascularization and functionality) [196]. The incidence of ORN is high in the maxillaries because of the number of cancer tumors of the head and neck, which are treated effectively with radiation.

In 1979, Marx *et al* showed that ORN results from a healing defect due to a state of chronic tissue hypoxia [193]. In 1984, he published a study concerning 150 cases of patients with osteoradionecrosis of the jaws [192]. He divided the disease into three stages of clinical evolution (see Appendix B). The results showed that 14% of the stage I, 18% of the stage II and 68% of the stage III patients saw their condition normalize. It should be noted that most of these patients had been refractory (for months or even years) to the standard treatments [192].

In a prospective study published in 1985, Marx *et al* had already demonstrated the prophylactic efficacy of HBO in post-radiation therapy dental extraction [195].

A number of case series [27, 53, 98, 205], an observational, controlled study [223] and a nonrandomized, controlled trial [313] have shown that hyperbaric oxygen therapy has a beneficial effect in preventing the complications of radiation therapy. Similar results (with a few exceptions [153]) are reported in numerous studies of the efficacy of hyperbaric oxygen in healing and in preventing the adverse effects of radiation therapy [5, 11, 20, 39, 48, 50, 52, 99, 137, 139, 196, 204, 211, 212, 216, 231, 250, 312, 323]. These effects concern both visceral and bone injuries.

In a 1990 consensus report on the treatment of ORN, the National Institutes of Health [221] stresses the facts that adequate oxygenation of injured tissue (bone) is the basis of effective treatment of ORN and that HBO is considered the best support.

In a study published in 1993 that concerned 26 cases of osteoradionecrosis, McKenzie *et al* conclude that HBO therapy is effective and safe [205].

Radiation therapy-induced tissue and bony necrosis is one of the indications and target medical conditions for hyperbaric oxygenation and often takes up much of the operating time of hyperbaric chambers [9, 90, 97, 276, 295]. Hyperbaric oxygen therapy for patients with ORN is lengthy, taking about 30 to 40 of 90-minute sessions at more than 2 ATA (2.4). At the Hôpital du Sacré-Coeur de Montréal, ORN accounts for 40% of the hyperbaric treatment time, although the patients in question account for only 10% of those treated in the chamber. In 1997, Dempsey *et al* published a cost-effectiveness analysis of HBO therapy in osteoradionecrosis [73]. The costs for the study group were determined from a retrospective study of 21 patients who had undergone the modified HBO protocol at Hamilton Civic Hospitals in Hamilton, Ontario. A hypothetical control group was created and matched with the study group. The authors concluded that the modified HBO protocol was less expensive and more effective than the usual treatment.

In conclusion, HBO therapy seems to be an accelerating factor in cases of complete healing of radiation therapy-induced tissue and bony necrosis. Hyperbaric oxygen therapy can be used preventively, in early treatment or both [99, 196, 250]. The treatment protocols for soft-tissue necrosis and osteoradionecrosis are, however, not uniform. The level of evidence supporting the efficacy of HBO in the treatment of osteoradionecrosis is fair, whereas that concerning soft-tissue necrosis is lower. Nonetheless, the results for soft-tissue necrosis are promising.

3.3.7 Problem wounds

Problem wounds include severe burns, leg ulcers, diabetic lesions and grafts. Oxygen therapy is often used in these different conditions. Since the therapeutic principle of HBO, the mechanism of action and the results obtained are similar [168], diabetic foot, burns, grafts and leg ulcers are discussed in the same section, together, when useful, with the particular aspects of each of these conditions. For most of them, hyperbaric oxygen therapy is used in combination with or as an adjunct to preexisting therapy [103, 291, 300].

Hyperbaric oxygen provides several different benefits [14, 71]:

- Increased tissue oxygen delivery.
- The activation of epithelialization [226] and collagen synthesis thanks to the role of oxygen in fibroblast replication and thus in promoting angiogenesis [150, 168].
- The double antimicrobial effect: directly on anaerobic organisms and indirectly by facilitating the killing activity of leukocytes (greatly reduced in hypoxia).
- An antiedemic effect, which is more perceptible in certain severe lesions (e.g., crush injuries, severe burns).

There have been numerous studies of the use of hyperbaric oxygen therapy for wounds that are refractory to the usual treatments. For all of these pathologies, the objective is to transform the chronic wound into an acute wound in order to maintain it in a state conducive to reparative therapy [215, 320]. However, there still remains some doubt as to when HBO can still have an effect (early stage) and as to the level of reepithelialization [287]. HBO does not cause normal wounds to heal more quickly but, under certain circumstances, does induce activation of the healing of certain problem wounds [168].

In combination with allogenic grafts or an HSE (human skin equivalent), HBO can have a positive effect on the healing of problem wounds. However, the long-term prognosis depends more on the underlying neuropathies and vascular diseases than on the local microangiopathy. For example, diabetic neuropathies are the pathogenic basis of diabetic ulcers [95, 96].

Table 7: Studies of hyperbaric oxygen in the treatment of post-radiation therapy tissue necrosis

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Marx *et al* 1985 [195]	Nonrandomized, controlled Trial	To determine if HBO can prevent the development of ORN* after tooth removal in high-risk patients.	- Patients requiring the removal of one or more teeth in a segment of the mandible that had previously received an irradiation dose of 6,000 or more rads and agreeing to maintain follow-up visits for at least 6 months. - Excluded: patients who had received radiation therapy within the previous six months or more than 15 years earlier; individuals with a CI to penicillin or HBO (100% O_2 at 2.4 ATA); and individuals who had received chemotherapy in the 6 months pre- ceding the test or who had a systemic disease (e.g., diabetes, systemic lupus erythematosus, lichen planus).	- 74 patients. - Same lidocaine- and epinephrine-based treatment. - Same surgical procedure. - Control group: 37 pa- tients; antibiotic therapy before and after surgery. - Experimental group: 37 patients; no antibiotic therapy but 20 sessions of HBO before surgery and 10 after surgery (100% O_2 at 2.4 ATA once daily 5 or 6 days a week).	Control group - 11/37 (29.9%) failed to heal in 6 months. HBO group - 2/37 (5.4%) failed to heal in 6 months.
Warren *et al* 1997 [313]	Nonrandomized, controlled Trial	To confirm the beneficial effect of HBO in the treatment of radiation proctitis.	- Patients with radiation proctitis.	- 2 centres. - 14 patients. - 20 to 72 sessions. - Group A: 9 patients (120 min, 2.0 ATA, 5 or 6 per week), monoplace chamber. - Group B: 5 patients (90 min, 2.36 ATA 5 days a week), multiplace chamber.	- Symptoms disappeared completely in 8 patients: 6 in group A and 2 in group B. - 1 patient (group A) experienced a 64% improvement. - 5 patients in whom HBO had no effect. - No significant difference between the two groups.
Neovius *et al* 1997 [223]	Observational, controlled study	To evaluate the role of HBO in inducing and accelerating the healing of irradiated tissue.	- Patients with soft-tissue wounds without signs of healing after radiation therapy of 64 Gy to the head and neck regions.	- 15 received standard treatment plus HBO. - Controlled study with patients treated without HBO (reference group, n=15).	- 12 of the 15 patients healed completely, 2 healed partially, and 1 patient did not heal at all. - 7 of the 15 patients in the reference group healed properly, and 2 had complications, which proved fatal in one case.
Bevers *et al* 1995 [27]	Case series	To evaluate the role of HBO in the treatment of hematuria associated with radiation-induced cystitis.	- Radiation therapy-induced hemorrhagic cystitis (histologic diagnosis) not responding to the standard treatments. - Exclusion criteria: tumor recurrence in the bladder, bleeding or coagulation disorders, severe pulmonary disease.	- 40 subjects followed for 13 months. - 20 90-minute sessions of 100% O_2 at 3 ATA. - Multiplace chamber.	- 11 patients died after 23.8 months (mean). - Causes of death: 4 due to metastases, 3 unrelated, 4 with unknown diagnosis. - Of the 40 patients treated, 30 had good results (absence of hematuria). - In 12 of the 18 patients with severe hematuria, the symptom disappeared.
McKenzie *et al* 1993 [205]	Case series	To evaluate the effect of HBO in the treatment of ORN.	- Patients diagnosed with ORN.	- 26 patients (aged 28 to 80). - 9 to 84 sessions of HBO.	- 21 showed improvement, with 13 experiencing complete healing.
Feldmeier *et al* 1996 [98]	Case series	To determine the effect of HBO in the treatment of radionecrosis of the abdomen and pelvis.	- Patients with injuries of the abdomen and/or pelvis following radiation therapy.	- 41 patients followed in 1979.	- 26 of the 41 patients healed. - 6 failures. 9 had an inadequate course of treatment. - 80% of the patients who underwent at least 20 sessions of HBO healed.

*ORN: osteoradionecrosis; CI: contraindication.

Studies of the effects of HBO on this type of pathology have not been rigorously controlled, and the cases involved are often associated diseases or diseases for which the patient is receiving a specific treatment. There is a lack of well-defined protocols for treating problem wounds.

3.3.7.1 Diabetic foot

One of the accepted indications for the use of HBO concerns infectious complications in diabetics, especially those in the feet (diabetic foot).

The two disease substrates reported most often are:

- *Neuropathies*. These are due to damage to the peripheral and autonomic nervous systems and are characterized by a loss of sensitivity to pain, with a tendency toward an increase in lesions that go unnoticed and in secondary complications. The loss of muscle innervation results in abnormalities and deformations, which lead to an increase in the rubbing and pressure surfaces. This, together with an increase in skin dryness, results in cracks and portals of entry for microorganisms.
- *Angiopathies*. Chronic, obstructive arterial micro- or macroangiopathies often occur that contribute to the development of wounds, with resulting inhibition of the phenomenon of leukocyte diapedesis and impaired defense factor involvement. Doppler studies showed that vascular deterioration was more frequent in diabetics with wounds of this type [319].

Lastly, there is a decrease in cellular immunity as a result of cell migration (polynuclears, macrophages, lymphocytes) slowing or even coming to a halt and therefore a predisposition to infections.

The anticipated efficacy of hyperbaric oxygen therapy lies in its ability to enhance tissue oxygenation, promote oxygen-dependent transmembrane transport (leukocytes, antibiotics) and stimulate healing through increased collagen synthesis. This efficacy depends on the type of diabetic lesion and on how far advanced it is (Wagner's classification: 0 to 5). Apart from these mechanisms of action, the bactericidal effect of oxygen on anaerobic bacteria is a possibility. The efficacy of HBO has been reported for other sites of infection (in particular, the eyes) and for other microorganisms (*Rhizopus*) [184].

Researchers are specifically interested in diabetic lesions for several reasons [79, 287]:

- Foot wounds in diabetics are the leading cause of hospitalization in this population. In the United States, foot care entails $1.5 billion in expenses a year.
- 25% of the 11 million diabetics (in the United States) have foot problems, and one diabetic in 15 will require amputation during his or her lifetime (the amputation rate is estimated at nearly 6 per 1,000 diabetics).
- Amputations in diabetics account for 50 to 70% of all amputations (152,000 in 1986), with 10% involving the loss of a foot, 35% of the loss of the lower leg and 30% the lower leg and knee.
- In 24% of cases, an ipsilateral amputation is performed, with a 10% contralateral complication rate.
- The 5-year probability of survival after amputation is 50%.
- The costs associated with treatment are high.

These different statistics explain, in part, the investment in studies of the potential efficacy of HBO therapy in diabetics.

The government of Taiwan approved the reimbursement of oxygen therapy for diabetic foot wounds. This decision was made in light of the results of studies of the efficacy of HBO in treating wounds and reducing the number of amputations in diabetics [181].

One of the rare randomized, controlled trials was that by Doctor *et al*, who reported that HBO was effective in decreasing the number of amputations and in producing negative cultures in patients with chronic diabetic lesions [79]. However, the authors observed no significant difference in the length of hospital stay in these patients in relation to the subjects who did not receive HBO as adjunctive therapy. This trial involved a total of only 30 subjects.

Faglia, in a nonrandomized, controlled trial, reported a major amputation rate 2.9 times lower in diabetic subjects treated with HBO than in subjects who did not receive HBO [93]. Stone, in an observational, controlled study involving 469 diabetic patients with chronic lower-limb wounds, observed that 72% of the patients who received hyperbaric oxygen therapy avoided amputation, whereas only 53% of the patients treated without HBO did not undergo amputation [287].

Other authors conclude that HBO is effective as adjuvant therapy for chronic diabetic lesions [15, 34, 327].

In conclusion, the results of the main studies indicate that HBO can have a beneficial effect on diabetic wounds. However, all of the studies conclude that these results need to be confirmed by randomized, controlled trials. The only study with an acceptable level of evidence concerned topical "hyperbaric" oxygen therapy, which is not considered a true hyperbaric treatment [177]. The result of this study did not show it to have a significant effect [182]. The nature of diabetic lesions and the infectious complications observed most often point to a specific role for hyperbaric oxygen as an adjuvant treatment for chronic diabetic wounds.

3.3.7.2 Burns

While treating miners with severe burns who were also receiving HBO therapy for carbon monoxide poisoning, Ikeda and Wada observed a rapid improvement in the second-degree burns [152, 309]. This accidental discovery prompted numerous experimental studies involving animal models in Japan and the United States [120, 151, 166]. Hartwig and Kriste [140] and subsequently Wells and Hilton [317] confirmed these results, reporting beneficial effects by way of improved local microcirculation and a decrease in inflammation.

In their experimental studies, Korn and Saunders observed survival and rapid epithelialization of the tissues concerned and increased collagen synthesis [172, 268]. Although Waisbern *et al* [310], in 1982, did not report any effect (positive or negative) by HBO, numerous authors have reported an improvement in burns after treatment [119, 135, 230]. In an experimental study involving animals with second-degree burns, Shoshani *et al* did not find HBO therapy to have any particular benefit in relation to normobaric oxygen therapy. However, they point out that standardizing the protocols [277] could play a key role.

In a randomized, controlled trial involving 12 subjects, Niezgoda *et al* [226] reported that HBO was effective in decreasing edema and shortening healing time. Brannen *et al*, in a randomized, controlled trial involving 125 patients, found no significant difference between the burn patients who received HBO and those who did not [36].

As regards economics, the results of Cianci *et al*’s study indicate a decrease in the length of hospital stay and in the number of surgical interventions in burn patients [54, 55, 56].

Table 8: Studies of hyperbaric oxygen in the treatment of diabetic wounds

AUTHOR(S)	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Doctor *et al* 1992 [79]	Nonrandomized, controlled trial	To evaluate the effect of HBO as adjunctive therapy in the treatment of diabetic foot wounds.	Diabetic patients hospitalized for chronic foot wounds.	- 30 subjects. - Both groups received conventional traitement. - The experimental group also received, during a 2-week period, a 45-minute daily session of HBO at 3 ATA. - Clinical and bacteriological follow-up of wounds.	- A 70% decrease in the number of positive cultures in the HBO group but of only 40% in the control group. - There were significantly fewer amputations in the HBO group (2) than the control group (7). - No significant difference with regard to the length of hospital stay.
Faglia *et al* 1998 [93]	Observational, controlled study	To assess the impact of using HBO to reduce the number of amputations in diabetics.	Diabetic patients followed or hospitalized for leg ulcers between 1990 and 1993.	- 115 diabetic patients with leg ulcers. - All the patients received the treatments appropriate for their case (debridements, identification of microorganisms, general antibiotic therapy, then specific antibiotic therapy, depending on the nature of the microorganisms and their susceptibilities, etc.). - Group 1: 51 patients treated with HBO for 90 min at 2.5 ATA once a day, then at 2.2 to 2.4 ATA 5 days a week (32 ± 11 sessions). - Group 2: no HBO, 64 patients (excluded: patients who refused HBO, claustrophobia, contraindications to HBO).	- Group 1: 7 major amputations* (13.7%). - Group 2: 20 major amputations (31.3%). * (above or below the knee). There was a significant difference, which would need to be confirmed by randomized, controlled trials.
Stone 1995 [287]	Observational, controlled study	To evaluate the role of HBO in the treatment of diabetic foot wounds.	Diabetic patients referred because of lower-limb wounds.	- The study covered a period of 33 months and involved 469 patients. - 382 patients, 73 of whom were referred for amputation, received standard treatment (medical and surgical) . - 87 patients, 27 of whom were referred for amputation, received adjuvant HBO therapy (an average of 19 sessions).	- 72% of the patients in the HBO group avoided amputation vs. 53% in the non-HBO group.

Table 9: Studies of hyperbaric oxygen in the treatment of burns

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Niezgoda *et al* 1997 [226]	Randomized, double-blind, controlled trial	To confirm the positive effects of hyperbaric oxygen therapy on burns.	Healthy, nonsmoking volunteers with no contraindications to HBO and who underwent an HBO tolerance test (single exposure).	- 12 volunteers (5 women, 7 men). - A burn-type lesion was created on their forearm. - Two groups were formed within the 2 hours after exposure: the experimental group, which underwent HBO sessions (100% O_2 at 2.4 ATA), and the control group (8.75% O_2 at 2.4 ATA). - Two dives per day, for a total of 6 sessions. - Wounds assessed once a day.	As early as day 2, there was a significant difference in the reduction in the signs of inflammation (hypere-mia, edema) and in wound size (6.1 mm vs. 9.5 mm for the control group). No difference was observed for reepithelialization.
Brannen *et al* 1997 [36]	Randomized, controlled trial	To evaluate the effect of HBO in the treatment of burns.	Burn patients admitted to hospital within 24 hours of injury.	- 125 subjects matched by age, degree of burn and the presence or absence of airway lesions were assigned to two groups: experimental (n= 63) and control (n= 62). - 90 minutes of treatment twice a day for a minimum of 10 sessions and a maximum of one treatment per percent total body surface area burn. - Both groups received the same treatment, except for HBO in the experimental group.	No significant difference between the two groups.

In conclusion, demonstrating the efficacy of HBO in problem grafts has not yet moved beyond the experimental stage. However, given the positive results obtained in osteoradionecrosis and in tissue reconstruction in certain regions (e.g., the jaw) [10, 118, 157, 303], we can foresee the possibility of HBO playing a useful role in such cases.

3.3.7.3 Grafts

Tissue hypoxia is one of the classic problems in grafts (heterotopic and flaps). One of the consequences of grafts is the release of vasoactive substances that affect blood vessel viability, since they induce vasoconstriction and platelet aggregation, which result in vascular obstruction. The theory on which HBO utilization is based is that optimal healing can be achieved only with oxygen tensions two to three times greater than that required for normal cell activity (30 mm Hg) [150, 274].

Hyperoxygenation improves the effectiveness of blood and/or plasma through compromised blood vessels. The volume of oxygenated tissue is estimated to be 16 times normal. Also, there is an increase in new, mature vessels. The third effect of HBO is a decrease in edema and cell migration (polynuclears, macrophages). Numerous experimental studies carried out in animals [58, 122, 222] and subsequently in humans have examined the effects of HBO on grafts. Some authors, such as Perrins and Cantab [241], Bowersox *et al* [35] and subsequently Hill *et al* [143], conclude that HBO is effective in graft take. Other authors report HBO applications in post-radiation therapy grafts and better outcomes [7, 106, 118, 122, 157, 303].

3.3.7.4 Leg ulcers

The efficacy of hyperbaric oxygen in the treatment of leg ulcers derives from the fact that HBO shortens healing time by activating the different processes involved in tissue repair (angiogenesis, collagen synthesis, etc.). In one of their studies, Kindwall *et al* explain the mechanisms of action of HBO in the treatment of lesions. The main effects are a decrease in white blood cell adherence to capillary walls, the cessation of lipid peroxide production and the stimulation of blood capillary formation and collagen synthesis [168].

Leg ulcers are seldom due to a single cause. In most cases, they are of multifactorial origin, and a holistic approach is often necessary. It is in this connection that the use of HBO as adjuvant therapy for leg ulcers in general and for chronic venous ulcers (varicose or CVUs) is often reported in the literature [9, 127, 297].

The best available evidence is provided by Hammarlund et *al'*s double-blind, controlled trial [127]. After four weeks of treatment, the investigators observed a significant difference in ulcer size reduction between the HBO-treated patients (22% reduction) and the control group subjects (4% reduction).

According to McEwen *et al*, the use of HBO in treatment protocols applied at the national level can reduce the cost of treating leg ulcers by one half [203]. The authors conclude that using hyperbaric oxygen therapy as an adjuvant in the treatment of CVUs is cost-effective. They also think that not using HBO is due to insufficient resources and to physicians' ignorance of its potential benefits. Richmond *et al* state that HBO could be useful in the treatment of certain types of ulcers due to hemoglobinopathies [261].

In conclusion, we see that the only available rigorous study on the treatment of chronic leg ulcers with hyperbaric oxygen concludes that such therapy is effective as an adjuvant to the conventional treatments. This demonstration, coupled with that of the mechanisms of action of HBO in the treatment of lesions, would provide a sufficient level of evidence for justifying the use of HBO in the treatment of this chronic condition.

3.3.8 Other medical conditions

3.3.8.1 Tissue ischemias

This section deals with three types of ischemia:

- Traumatic ischemias (crush injuries)
- Cerebral ischemias
- Myocardial ischemia.

3.3.8.1.1 Traumatic ischemias

A certain number of authors have studied the effect of HBO therapy on traumatic war injuries. They state that HBO has a beneficial effect on certain severe injuries, such as crush injuries with or without fractures, vascular injuries and the compartment syndrome [251, 254].

In a randomized, double-blind, controlled trial, Bouachour *et al* observed complete wound healing in 17 of the 18 subjects in the experimental group versus 10 of the 18 subjects in the control group. According to the authors, HBO therapy is very useful in managing grade III lower-limb traumatic injuries (more extensive, with bone and artery involvement) in individuals over the age of 40 [33].

The studies and clinical experience are, for now, insufficient for drawing any conclusions.

Table 10: Study of hyperbaric oxygen in the treatment of leg ulcers

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Hammarlund *et al* 1994 [127]	Randomized, double-blind, controlled trial	To evaluate the effect of hyperbaric oxygen therapy in the treatment of chronic nondiabetic leg ulcers.	Patients with chronic nondiabetic leg ulcers with no associated vessel disease.	- 16 subjects. - Experimental group: n=8; HBO for 90 min at 2.5 ATA 5 days/week. - Control group: n=8; air for 90 min at 2.5 ATA 5 days/week. - Duration of treatment: 6 weeks (30 sessions). - Wound size measured at 0, 2, 4, 6 and 18 weeks.	There was a significant difference at week 4 of treatment: 22% reduction in wound size in the HBO group vs. 3.7% in the control group.

3.3.8.1.2 Cerebral ischemias

In the United States, severe head injuries are one of the leading causes of death among people aged 2 to 42 [108]. The theoretical benefits of hyperbaric oxygen therapy have spurred research into its potential use in cerebral ischemic diseases and their sequelae [58, 305]. In one of these studies, Holbach *et al* recommend the systematic use of HBO in the treatment of severe brain lesions [146, 147]. It should be pointed out that, in their study, the severity of the injuries is not very clearly indicated, and the methodology was flawed (selection bias).

The results of the study by Rockswold *et al* [263] are similar to those obtained by Holbach *et al* and include a 17% mortality rate in the HBO-treated group (84 subjects) versus 32% in the control group (84 subjects). The mortality rate was 50% lower in the patients with Glasgow scores of 4 to 6. However, functional recovery was poor because of the severity of the injuries and/or the adverse effects of the hyperbaric oxygen therapy (free radicals, peroxidation). The authors conclude that hyperbaric oxygen therapy requires a more extensive evaluation in order to determine the treatment frequency and duration. Numerous studies of the use of HBO in combination with antiperoxidants are currently under way [125, 126].

With regard to the evaluation of hyperbaric oxygen therapy in cerebral ischemias, mention should be made of a randomized, double-blind, controlled study conducted by Nighoghossian *et al* [228]. They compared two groups of patients who experienced a stroke and presented within 24 hours of its onset and who were treated with HBO (at 1.5 and 1.2 ATA). The authors conclude that HBO is safe in acute cerebral ischemia and that larger and more-thorough studies would be needed to assess the efficacy of this therapy.

Other authors [66, 236] advocate HBO as a possible therapy in certain cerebral ischemic diseases. In fact, seemingly encouraging results have prompted some authors to investigate the effect of HBO in the treatment of the sequelae of cerebral hypoxia (cerebral palsy).

Experimentally, the studies basically examine the safety of HBO in such diseases and on the metabolic changes induced by HBO in the brain [65, 233, 252]. In their study on the treatment, with HBO, of induced global cerebral ischemia in rabbits, Mink and Dutka report a decrease in cerebral blood flow, which, however, had no effect on evoked potential recovery. They observed few positive effects and describe the limitations of the treatment [208]. Omae *et al*, in their study on the effect of HBO on cerebral blood flow, report a reduction in CBF during HBO exposure at pressures greater than or equal to 2 ATA [233].

Table 11: Study of hyperbaric oxygen in the treatment of severe traumatic injuries

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Bouachour *et al* 1996 [33]	Randomized, double-blind, controlled trial	To evaluate the effect of HBO therapy on severe traumatic injuries of the lower limbs (crush injuries).	- Patients with grade II or III* lower-limb injuries, surgical management within 6 hours after the injury and no history of peripheral vascular disorders. - Patients with associated diseases (neurological, pulmonary, ENT) or contraindications to HBO were excluded. Pregnant women were excluded as well. *Grade II: injury larger than 1 cm without extensive loss of tissue. *Grade III: more extensive injury (periosteal stripping and bony exposure).	- 36 subjects. - Experimental group: standard therapy + HBO (90 min of 100% O_2 at 2.5 ATA twice daily for 6 days). - Control group: standard therapy + ambient air (90 min at 1.1 ATA twice daily for 6 days).	- Complete healing in 17 of the 18 patients in the experimental group vs. 10 of the 18 in the control group. - New surgical procedures were required in 1 patient in the experimental group vs. 6 in the control group. - Subjects over the age of 40 (grade III lesions): healing in 7 in the experimental group vs. 3 in the control group.

Neubauer and James recommend HBO as an adjuvant for the recovery of cerebral cellular activity and therefore for improving the disability due to secondary muscle spasticity [224]. Their work is based on pathophysiology and the results of a new imaging technology (single-positron emission computerized tomography, or SPECT) that demonstrated the existence of a zone of nerve cell inactivity, dubbed the "penumbral zone", in which the blood vessels are damaged and where the blood flow is extremely reduced. This causes nerve cell activity to stop, although these cells are not destroyed.

In cerebral palsy or cerebral vascular insufficiency syndrome, management involves antiepileptic treatment, if there are epileptic seizures, functional reeducation, fitting with a prosthesis, functional surgery and speech therapy. The experimental use of HBO therapy in certain types of facial palsy and in certain traumatic sports accidents (severe muscle elongation) has led to increased interest in this technology. In a pilot study, an MRI (magnetic resonance imaging) evaluation of eight patients who experienced motor functional recovery of the upper limb after post-cerebral ischemia hemiparesis or hemiplegia led Cao *et al* to hypothesize that an "uncrossed motor neural pathway" can be accessed to compensate for the functional impairment of the damaged nervous system.

Most studies are still in the experimental stage. The future of this type of therapy will depend on the development of our knowledge of the observed physiological mechanisms in what is referred to as the "penumbral zone" [138, 207, 280]. Further experimental work with animal models for studying the functional recovery of nerve cells is still needed [23, 85, 173, 208, 217, 288, 289].

An unpublished analysis (1989) of a series of cases in Brazil (Machado), which certain proponents of the use of HBO in the treatment of cerebral palsy base themselves on, revealed a 50% in reduction in spasticity in 218 out of 230 patients with cerebral palsy. They underwent 20 1- to 2-hour sessions of hyperbaric oxygen therapy at 1.5 ATA. The improvement was assessed by means of a home-made grid. However, it should be noted that no objective criteria were used to assess the efficacy of the treatment.

A randomized, double-blind, prospective, controlled, multicentre study was just completed in Québec, the main objective of which was to assess the efficacy of HBO in the treatment of cerebral palsy*. Nearly 200 children between the ages of 3 and 12 took part in the study. The results showed an improvement in the same proportion of the children in the experimental group (100% oxygen in a pressurized chamber at 1.75 ATA) as in the placebo group (regular air at 1.3 ATA). Although the investigators conclude that HBO does not have any effect, other possible interpretations are suggested and raise questions about the factors for improvement, hence the need for further research.

In conclusion, there are presently no sufficiently rigorous scientific data from which it can be concluded that hyperbaric oxygen has a beneficial effect on the evolution of cerebral ischemias [306]. Consequently, its use in such cases cannot be justified.

3.3.8.1.3 Myocardial ischemia

Over the past few years, and in line with the use of HBO as a means of intensive oxygenation for revitalizing ischemic tissues, experimental studies have been carried out on animals with myocardial ischemia. The encouraging results of the experimental study by Thomas *et al* [295] have contributed to the increased interest in this subject.

The investigators reported that combined HBO and tissue plasminogen activator treatment resulted in a 96.9% restoration of enzyme activity. Treatment with tissue plasminogen activator alone restored 48.9% of the enzyme activity.

Shandling *et al* conducted a randomized pilot study involving 66 patients with myocardial infarctions (MIs), 43 with inferior MIs and 23 with anterior MIs. The experimental group received a similar treatment, i.e., tissue plasminogen activator in combination with HBO [273]. The authors report a 35% decrease in the CPK (creatine phosphokinase) level, earlier resolution of ST-segment elevation and faster pain relief in the subjects who received HBO in relation to the control group. However, their conclusions only concern the feasibility and safety of HBO therapy in MIs. Because of the sample size and possible selection bias in the HBO group (unstable angina), no conclusions can be drawn as to the efficacy of the treatment in combination with HBO.

In conclusion, the level of evidence regarding the efficacy of HBO in the treatment of myocardial ischemia is presently insufficient for justifying its use in this disease.

3.3.8.2 Amenias

The use of HBO in anemias has usually occurred in experimental settings [155, 248]. Some authors, such as Ludwig [187], have recommended its use in cases of exceptional blood loss [30, 133], in post-radiation therapy anemia and in complications of hemoglobinopathies (sickling crises during drepanocytosis, thalassemia major) [76, 106, 109, 111, 261, 311].

In their uncontrolled observational study (case series), Mazin *et al* observed a decrease in mortality in those patients on hemodialysis (patients with renal failure) who received adjuvant HBO therapy [202].

Hyperbaric oxygen is used in certain specific anemias, but such use is rare and occurs most often in an experimental context. The level of

* Personal communication from the principal investigator in the study, Jean-Paul Collet, M.D., director of the Randomized Clinical Trials Unit, Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, May 26, 2000.

Table 12: Studies of hyperbaric oxygen in the treatment of cerebral ischemias

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Nighoghossian *et al* 1995 [228]	Randomized double-blind, controlled trial	To outline the practical aspects and safety of HBO and to evaluate its effect on long-term disability.	- Patients who had had a stroke within the previous 24 hours. - Age 20 to 75. - Orgogozo scale score of less than 80.	- 34 patients (17 and 17), monoplace chamber. - HBO group: 40 min at 1.5 ATA, 10 sessions. - Control group: 1.2 ATA. - Standard treatment for both groups.	- No significant difference between the two groups.
Rockswold *et al* 1992 [263]	Randomized, controlled trial	To determine if HBO can be beneficial in severely brain-injured patients.	Patients admitted for severe head injuries with a Glasgow score of 9 or less as determined 6 to 24 hours after hospital admission.	- 168 patients (84 and 84) followed for 12 months. - Same medical/surgical treatment and follow-up for both groups. - Monoplace chamber. - 100% HBO: 60-min session at 1.5 ATA every 8 hours for 2 weeks (or until the patient was diagnosed brain dead or regained consciousness).	Mortality - HBO group: 17% - Control group: 32%. Morbidity after 12 months - No difference. *Note*: There were differences between the HBO group and the control group with regard to the Glasgow score distribution.
Holbach *et al* 1979 [146]	Case series	To study the effect of HBO in combination with an extra-intracranial bypass in patients with chronic cerebral ischemia.	Patients with post-cerebral ischemia neurological impairment.	- 35 patients with chronic cerebral ischemia secondary to internal carotid artery thrombosis (more than 10 weeks). - HBO for all the patients: daily treatment (10 to 15 sessions at 1.5 ATA). - 21 of the 35 patients underwent an extra-intracranial (EIC) anastomosis. - Investigation before, during and after the sessions and 6 weeks after the end of treatment.	- 15 patients experienced significant improvement in cerebral function and a resumption of electrical activity after the end of HBO treatment. - The EIC anastomosis improved this activity. - 14 treated patients showed little or no improvement in cerebral function or cerebral electrical activity. - An EIC anastomosis was performed on 6 patients in whom HBO was considered ineffective. Even though angiograms showed a 30 to 40% increase in temporal vascularization, there was little postsurgical improvement. - 1 death.
Cordoba-Cabeza *et al* 1998 [66]	Case series	To evaluate the efficacy of HBO in cerebral palsy due to severe brain injuries.	Hospitalized children with cerebral palsy due to severe brain injuries (severe asphyxia, cerebral infections, traumatic craniocerebral injuries, vascular occlusion due to a sickling crisis) between September 1994 and September 1995.	- 14 patients with cerebral palsy (5 due to severe asphyxia, 7 to cerebral infections, 1 to head injury and 1 to vascular occlusion secondary to a sickling crisis). - 20 sessions of HBO.	"Encouraging results" for all the HBO-treated patients.

evidence regarding the efficacy of HBO in the treatment of specific anemias is presently insufficient for justifying its use for these conditions.

3.3.8.3 Migraines

The pathophysiology of certain migraine conditions, the still-moderate efficacy of the treatments, and the potential effects attributed to hyperbaric oxygen therapy have prompted nume-rous studies in this area. HBO was used in the rapid treatment of acute migraine attacks, then as prophylactic treatment [86]. The efficacy of increasing the blood oxygen level is based on the metabolic changes and vasoconstriction induced by HBO.

Myers *et al* report better results in migraine attack prevention in patients treated with HBO 218]. They hypothesize that hyperbaric oxygen could have a beneficial effect through the increase in the rate of energy production and metabolic reactions induced by oxygen-dependent neurotransmitters.

Following a prospective trial involving 14 chronic migraine sufferers (Bing-Horton syndrome), Di Sabato *et al* hypothesized that pain relief is due to the action of hyperbaric oxygen on the serotonergic system [78].

The results, published in 1998, obtained by Wilson *et al* [321] in their randomized, double-blind, controlled study involving eight women suffering from migraine with aura suggest that hyperbaric oxygen therapy reduces migraine pain.

The rare studies of the use of HBO to treat chronic migraine attacks (in particular, Bing-Horton syndrome) show that hyperbaric oxygen exhibits a certain degree of efficacy in this group of medical conditions. However, the study samples were small and the methodologies were fair to poor.

In its latest report (1997) on migraine pathology, the Canadian Medical Association [45] makes no mention of HBO as a nonpharmacologic treatment for migraine.

In conclusion, the level of evidence concerning the efficacy of HBO in the treatment of migraine is presently insufficient for justifying its use in this disorder.

3.3.8.4 Facial palsies: Bell's palsy

Sixty-six percent of unilateral facial palsies are of unknown origin and are presently placed under the heading of "Bell's palsy". More and more, the different studies of Bell's palsy tend to suggest that this disease is of viral origin [3].

Some studies have involved a controlled evaluation of conventional, corticosteroid-based therapies (prednisone) and alternative treatments. In a randomized, controlled study, Racic *et al* followed 79 patients with Bell's palsy who were treated with prednisone or subjected to hyperbaric oxygen. Based on nine months of follow-up and the encouraging results obtained in these patients, the authors state that HBO could have a beneficial effect in the treatment of Bell's palsy and suggest that it could be an alternative to corticosteroid treatment [253].

In conclusion, the use of hyperbaric oxygen therapy in the treatment of facial palsies is still in the research stage. The level of the available evidence is insufficient for justifying its use in these disorders.

Malignant diseases

3.3.8.5.1 Cancer of the uterine cervix

Fletcher *et al* [101] conducted a study in which they followed 233 patients with cancer of the uterine cervix (stage IIb to IVa) treated with radiation therapy. Of them, 109 additionally recei-ceived hyperbaric oxygen therapy. The

Table 13: Studies of hyperbaric oxygen in the treatment of myocardial ischemia

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Shandling *et al* 1997 [273]	Randomized, controlled trial	Study of the feasibility and safety of HBO therapy in patients with an MI.	- A diagnosis of MI with ST-segment elevation on two ECGs and angina pain lasting more than 20 min but less than 6 hours that was not relieved by taking nitroglycerine. - Receiving rTPA as a thrombolytic agent. - Exclusion criteria: other cardiac abnormalities, recent surgery, lung disease, complete class III or class IV MI (Killip), a contraindication to HBO.	- 66 patients (34 in the HBO group and 32 in the control group). - Both groups: thrombolytic therapy in combination with a platelet antiaggregation agent. - 60 min of HBO at 2 ATA for the experimental group. - Monitoring.	- Significant difference in the time to pain relief and in the time for the ST-segment and laboratory values to return to normal.

Table 14: Studies of hyperbaric oxygen in the treatment of anemias

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Mazin *et al* 1992 [202]	Case series	To evaluate the efficacy of HBO in posthemorrhagic tissue hypoxia or in cases of inadequate or no hematopoiesis.	Patients with renal failure on hemodialysis.	- 48 patients treated with HBO (1.5 to 2.2 ATA for 60 to 90 min after a session of hemodialysis). - Duration of treatment: 5 to 10 sessions.	29% decrease in mortality in these patients.

results did not show hyperbaric oxygen therapy (before radiation therapy) to have any benefit in these patients or for these stages of the disease.

Watson *et al* report the results of a randomized, controlled trial conducted at four radiation therapy centres in the United Kingdom which involved 320 patients with stage II to IVa cervical cancer. Patient selection was done in a similar manner at all four centres. The results showed a significant improvement for locally advanced (stage III) tumors in the patients under 55 years of age [314].

3.3.8.5.2 Bladder cancer

Cade *et al* carried out a randomized, controlled trial involving 236 patients with bladder cancer [44]. The results reported by the four radiation therapy centres after six to seven years of treatment and more than 13 years of follow-up showed no significant improvement with the use of HBO as an adjuvant treatment.

3.3.8.5.3 Other malignant diseases

In a certain number of studies, HBO was used as an adjuvant to chemotherapy or radiation therapy for squamous cell carcinoma of the head or neck [179, 271] or to treat necrotic complications of radiation therapy [180, 271, 272]. Although the results concerning the treatment of such complications are fairly well documented, the facilitating role of HBO in cancer therapy (chemotherapy) is still, for the most part, in the experimental stage [159].

Table 15: Studies of hyperbaric oxygen in the treatment of migraine

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Wilson *et al* 1998 [321]	Randomized, double-blind, controlled trial	To evaluate the effect of HBO on migraine with aura.	- Patients with a diagnosis of migraine confirmed by a neurologist at least 18 months prior to study entry. - Migraine attacks occurring regularly without any apparent triggers. - Exclusion criteria: contraindications to HBO, pregnancy, associated diseases and fewer than 2 migraine attacks per month.	- Monoplace chamber. - 8 women with migraines with aura. - Treatment within 2 hours of the onset of a migraine attack. - Group A: phase 1: HBO (100% at 2.4 ATA for a maximum of 60 min); phase 2: NBO (1.1 ATA, ambient air). - Group B: phase 1: NBO (1.1 ATA, ambient air); phase 2: HBO (100% at 2.4 ATA for a maximum of 60 min). - A pre- and posttreatment evaluation (clinical, al-gometry, VAS*) was performed on each subject. *Visual analog scale	- From a clinical standpoint (palpation), there was a significant difference in the scores, regardless of the type of treatment. - The objective measurement of pain (dolorimetry) showed an increase in pain thresholds, with no difference between the two treatments. - As for the VAS (patient responses), the subjects experienced greater improvement during treatment with HBO.
Myers and Myers 1995 [218]	Randomized, controlled trial	To compare the effects of hyperbaric oxygen with those of normobaric oxygen.	- Patients with migraine attacks.	- 20 subjects (14 women and 6 men). - Length of sessions: 40 min each. - Group 1 (n=10): 100% O_2 at 1 ATA. - Group 2 (n=10): 100% O_2 at 2 ATA. - All the patients who did not experience any improvement were given HBO.	- 9 patients in group 2 saw their symptoms disappear vs. 1 patient in group 1. - The other 9 patients in group 1 saw their symptoms disappear after one session of HBO (40 min).
Di Sabato *et al* 1997 [78]	Nonrandomized, controlled trial	To determine the effects of HBO on the serotoninergic system.	- Patients who had been suffering from chronic migraines (Bing-Horton) for at least 5 years (diagnosis according to IHS* criteria). - Exclusion criteria: failure to meet the above-mentioned criteria, contraindications or not agreeing to the treatment protocol. * International Headache Society.	- Multiplace chamber. - 14 subjects, 15 sessions. - Experimental group (n=10): HBO at 2.5 ATA, 100% O_2 for a maximum of 30 min. - Control group (n=4): NBO, ambient air. - Daily blood specimen at the same time, with test run on the sample immediately.	- Gradual decrease in the number of attacks in the subjects given HBO (as early as the start of treatment). - The number remained low during the first two weeks of treatment. - HBO had an effect on serotonin binding to cell receptors.

Table 16: Study of hyperbaric oxygen in the treatment of facial palsies

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Racic *et al* 1997 [253]	Randomized, controlled trial	Controlled study of the effects of HBO vs. Those of prednisone.	- Volunteer patients diagnosed with Bell's palsy within the previous week. - Moderate or severe type. - No contraindications to HBO.	- 79 patients. - HBO group (n=42): 100% O_2 at 2.8 ATA for 60 min twice a day, 5 days a week + placebo (30 sessions or until complete recovery. Followed for 9 months). - Control group (n=37): 7% O_2 at 2.8 ATA under the same conditions + prednisone.	- 95.2% of the subjects in the HBO group and 75.7% of those in the prednisone group recovered. The difference was significant for the moderate and severe cases. - The average duration of symptoms was 22 days in the HBO group and 34.4 in the control group.

The different published studies that have evaluated the efficacy of HBO in malignant diseases are rare and usually uncontrolled.

In conclusion, experimental data and the results of clinical trials do not show hyperbaric oxygen therapy to have any inherent efficacy as an adjuvant treatment for malignant tumors, but HBO could, in a certain number of cases, such as in post-radiation therapy tissue necrosis, promote the healing of irradiated tissues.

3.3.8.6 Ear/hearing disorders

In their analysis of over 50 studies involving more than 4,000 patients followed for traumatic or sudden hearing loss and treated with HBO as primary (18 patients) or adjuvant (4,109 patients) therapy, Lamm *et al* [176] conclude that HBO could have a beneficial effect in patients with idiopathic or traumatic hearing loss of less than three months' duration. Other studies advocate the use of HBO in certain chronic ear conditions [16, 161]. However, all of these studies are only case series.

In conclusion, since there are no rigorous scientific studies in this area, no conclusion can be drawn as to the efficacy of HBO in these disorders.

3.3.8.7 Other medical conditions

Despite euphoria [100] over the potential benefit of using HBO in *multiple sclerosis,* the results of the randomized, double-blind, controlled trials conducted by Confavreux *et al* [64], Harpur *et al* [132] and Wood *et al* [324] were all negative. In 1991, Kindwall *et al*, in a report concerning the follow-up of 312 patients at 22 institutions, confirmed that there is no significant improvement in the health of patients during oxygen therapy of limited duration [169]. However, Hafner recommends the use of HBO in the treatment of leg ulcers associated with multiple sclerosis [124]. According to a meta-analysis, performed by Kleijnen *et al*, of 14 randomized, controlled trials evaluating the efficacy of HBO in multiple sclerosis, seven studies concluded that this treatment is ineffective in this disease [170].

In conclusion, most results of studies with a valid or good methodology show that HBO is ineffective in the treatment of multiple sclerosis.

The literature contains a certain number of reports of unique or isolated cases in which the use of HBO as a last resort is purported to have yielded highly satisfactory results. One such case involved treating *quinine toxicity* with loss of vision (amaurosis). After HBO therapy (100% O_2 at 2.4 ATA for 90 minutes) within 17 hours

Table 17: Studies of hyperbaric oxygen in the treatment of malignant diseases

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Cade *et al* 1978 [44]	Randomized, controlled trial	To evaluate the effects of HBO as an adjuvant to radiation therapy in the treatment of bladder cancer.	- Patients diagnosed with bladder cancer with no spread to other tissues or organs. - No contraindications to HBO.	- 236 patients (118 and 118). - Experimental group (HBO): 100% O_2 at 3 ATA. - Control group: air at 3 ATA.	- No significant difference between the HBO group and the control group.
Watson *et al* 1978 [314]	Randomized, controlled trial	To evaluate the effects of HBO as an adjuvant to radiation therapy in the treatment of cancer of the uterine cervix.	- Patients under the age of 75 with stage II to IVa (Stockholm) cervical cancer. - Histologic diagnosis. - Exclusion criterion: contra-indications to HBO.	- Radiation therapy for all the patients. - 320 patients (161 HBO, 159 air).	- Greater improvement in the patients under the age of 55 with a stage III tumor.
Fletcher *et al* 1977 [101]	Randomized, controlled trial	To evaluate the effects of HBO as an adjuvant to radiation therapy in the treatment of cancer of the uterine cervix.	- Patients under the age of 70 with stage Iib to IVa cervical cancer. - Followed for 6 years.	- 233 subjects (109 HBO, 124 air). - All the patients received radiation therapy. - HBO therapy at 3 ATA 20 minutes before radiation therapy.	- No significant difference between the two groups.

after ingesting quinine, the patient recovered all of his visual acuity less than 24 hours after treatment [322].

The use of HBO in *certain patients with acute renal failure* caused by different types of trauma (renal, obstetrical, urological, etc.) has been reported. In a study involving 183 patients with such symptoms who underwent hemodialysis, Mazin *et al* observed an improvement in their health, with a substantial decrease incom-plications [202].

The use of HBO in *cyanide poisoning* has been reported, but treatment in such cases is by chemical means (amyl nitrate). Normobaric oxygen is currently the standard therapy.

In *sports injuries*, a double-blind randomized, controlled trial involving 32 subjects with a twisted ankle did not show hyperbaric oxygen to confer any benefit [25, 32].

The use of HBO in *autoimmune diseases* (e.g., Crohn's disease [178]) is very sparingly documented.

3.4 SUMMARY OF STUDIES OF THE EFFICACY OF HBO

In general, there have been few or even no randomized, controlled trials (RCTs) of the efficacy of hyperbaric oxygen in the different medical conditions discussed. The absence of RCTs is sometimes due to the very nature of the condition. For example, in the case of carbon monoxide poisoning or decompression sickness, such studies can be difficult to carry out. Administering placebo treatment to a group of subjects could be difficult to justify from an ethical standpoint when HBO is already recognized by clinicians as the treatment of choice for both of these conditions.

Based on the state of scientific knowledge and the expert opinions expressed in the literature,

Table 18: Studies of hyperbaric oxygen in the treatment of ear/hearing disorders

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Kau *et al* 1997 [161]	Case series	To evaluate the efficacy of HBO in chronic cochlear disorders (inner ear).	- Patients with chronic inner- ear disorders with hearing loss that had not responded to standard treatment. - Study duration: 18 months.	- 359 patients followed for 18 months.	There was a substantial recovery of hearing in the patients who had had symptoms for less than 3 months.
Lamm *et al* 1998 [176]	Case series	To compare the effects of HBO therapy with those of pharmacologic treatment with steroidal and nonsteroidal drugs.	- 4,109 patients with traumatic (acoustic) or sudden hearing loss (of more than 2 weeks' but less than 6 weeks' duration) who had undergone conventional therapy.	- HBO as second-line treatment.	- 50% of the patients showed a hearing gain of more than 20 dB in at least three frequencies. - 33% experienced a gain of 10 to 20 dB. - 13% showed no improvement. - 81.3% reported a decrease in tinnitus intensity.

Table 19: Studies of hyperbaric oxygen in the treatment of multiple sclerosis

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Kleijnen *et al* 1995 [170]	Systematic review	To evaluate the efficacy of HBO in patients with multiple sclerosis (MS).	- Patients with progressive or stable MS. - Explicit, appropriate criteria.	- Systematic review of 14 RCTs. - At least 50 subjects in each group. - Double-blinding.	- Methodologically, the studies were of adequate or good quality. - 7 studies yielded results showing that HBO is ineffective in MS. - The adverse effects of HBO were minor (auditory, ophthalmic).
Confavreux *et al* 1986 [64]	Randomized, double-blind, controlled trial	To evaluate the effect of HBO as a treatment for MS.	- MS with no progressive flare-ups in over 6 months. - Permanent disability of 3 to 8 on the Kurtzke scale. - No specific change in treatment in the previous 3 months. - Agree to be followed for 13 months. - No contraindications.	- 17 patients. - HBO group (n=8): exposed to 100% O_2 in a monoplace chamber for 90 minutes at 1.5 ATA 5 days a week. - Placebo group (n=9): same conditions but at 0.1 to 0.2 ATA. - Duration of treatment: 4 weeks. - Evaluation performed on the first day of the week and on day 26 (current medications, flare-ups, adverse effects and examination to assess neurological disability [Kurtzke]).	- 1 patient in the placebo group stopped showing up for her appointments after the treatment. - No significant difference between the two groups.

Table 19 (Cont'd): Studies of hyperbaric oxygen in the treatment of multiple sclerosis

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Harpur *et al* 1986 [132]	Randomized, double-blind, controlled trial	To evaluate the potential effects of HBO in the treatment of MS.	- A diagnosis of MS based on Poser's criteria; stable and having had no flare-ups for at least 3 months. - Kurtzke score of 3 to 7.5 inclusive. - No contraindications to HBO. - Patients had to agree to adhere to the protocol.	- 82 patients assigned in equal numbers to 2 groups. - Clinical, functional and radiologic (MRI) evaluation. - Treatment in a multiplace chamber. - HBO group: 90 minutes of 100% O_2 at 1.75 ATA daily for 20 consecutive days and 7 booster treatments (2 sessions after 1 month, then 1 session a month). - Same for control group; 12.5% O_2 at 1.75 ATA.	- 2 tympanostomies were necessary. - At the midpoint and at the end of treatment, there was no significant difference in the functional, clinical or radiologic (MRI) scores.
Wood *et al* 1985 [324]	Randomized, double-blind, controlled trial	To evaluate the role of HBO in the treatment of MS.	- Diagnosis of MS (Schumacher's criteria). - No contraindica-tions.	- 44 patients with a Kurtzke score of 3 to 8. - Multiplace chamber. - Treatment: 90 minutes 5 days a week for 4 weeks. - HBO group (n=21): 100% O_2 at 2 ATA. - Control group (n=23): 10% at 2 ATA.	- 3 subjects in the control group were removed from the study because of complications due to the hyperbaric conditions. - Improvement in 8/21 in the HBO group vs. 7/20 in the control group. - No significant difference.

Table 20: Studies of hyperbaric oxygen in the treatment of various medical conditions

AUTHORS	TYPE OF STUDY	OBJECTIVE	INCLUSION CRITERIA	METHODS	RESULTS
Borromeo *et al* 1997 [32]	Randomized, controlled trial	To evaluate the efficacy of HBO in functional recovery after a sprained ankle.	- Individuals presenting with a sprained ankle within 72 hours of its occurrence. - No pharmacologic treatment. - Exclusion criteria: fractures, contraindications to HBO.	- 32 subjects. - HBO group (n=16): 1 90-minute and 2 60-minute sessions of 100% O_2 at 2 ATA. - Control group (n=16): 1.1 ATA and sessions as above.	No significant difference between the two groups.
Lavy *et al* 1994 [178]	Case follow-up	To evaluate the effect of HBO on patients with Crohn's disease.	- Signs of perianal Crohn's disease.	- 10 patients followed for 18 months. - 20 90-minute sessions of HBO at 2.5 ATA.	- 7 patients experienced healing after 3 sessions. - 2 showed no improvement. - No recurrences after 18 months.

we established four groups of medical conditions with regard to the efficacy of HBO:

a) Medical conditions where the effect of hyperbaric oxygen is recognized by specialists, even though the available scientific data do not provide an adequate level of evidence:

- Carbon monoxide poisoning
- Decompression sickness
- Gas embolism
- Gas gangrene

b) Medical conditions where the use of hyperbaric oxygen yields encouraging results. The clinical studies involve methodologies providing a fair to good level of scientific evidence:

- Post-radiation therapy injuries (osteoradionecrosis and soft-tension lesions)
- Refractory tissue or bony necrosis due to a single microorganism or a mixed population of microorganisms (aerobic or anaerobic)
- Diabetic foot
- Chronic leg ulcers
- Severe burns which are refractory to treatment and/or which compromise graft take.

The efficacy of HBO in problem grafts has not yet been demonstrated. However, given the positive results obtained in osteoradionecrosis and tissue reconstruction, we can foresee the possibility of HBO playing a useful role in such cases.

c) Medical conditions treated in experimental studies or pilot projects, but whose results have thus far not demonstrated the efficacy of hyperbaric oxygen therapy:

- Cerebral ischemias
- Traumatic ischemias
- Myocardial ischemia
- Anemias
- Migraines
- Facial palsies
- Malignant diseases
- Ear/hearing disorders.

d) Medical conditions where, from the scientific evidence, it can be concluded that hyperbaric oxygen therapy does not result in any significant improvement:

- Multiple sclerosis

Based on these different observations and in light of the current knowledge regarding this technology, *CETS* concludes that there is sufficient evidence to support the use of hyperbaric oxygen in the treatment of the following medical conditions:

- Carbon monoxide poisoning
- Decompression sickness
- Gas embolism
- Gas gangrene
- Refractory tissue or bony necrosis due to a single microorganism or a mixed population of microorganisms (aerobic or anaerobic)
- Post-radiation therapy injuries: osteoradionecrosis and soft-ten sion lesions
- Chronic tissue lesions associated with chronic critical ischemia: diabetic foot, chronic leg ulcers

  Severe burns which are refractory to treatment and/or which compromise graft take

4. ADVERSE EFFECTS AND COMPLICATIONS OF HYPERBARIC OXYGEN

The clinical applications of HBO require special equipment, including a monoplace or multiplace hyperbaric chamber, plus special training for the team in charge of this technology. The clinical use of HBO requires special knowledge of the benefits, risks, adverse effects and exact indications, and a team that is experienced in intensive care and that has the capacity and the ability to manage the complications.

HBO is a therapy that requires continual, close supervision and monitoring before, during and after its administration. Whatever the target pathology, a potential candidate for HBO therapy must meet strict physiological and psychological criteria (even though they have not yet been standardized). Furthermore, the procedure requires a technically and professionally competent environment.

Like any other health technology, hyperbaric oxygen therapy has certain temporary and sometimes severe adverse effects that are more or less foreseeable but which are practically always due to improper use.

One of the complications reported most often in the literature, ear problems, is not rare. Middle ear barotrauma is at the top of the list. It occurs most often in patients who are no longer able to control the pressure in their middle ear [26, 298]. The results of studies of tympanostomy devices installed to prevent this type of problem are unconvincing [57]. Pulmonary barotrauma rarely occurs.

Impaired visual acuity in the form of myopia or hyperopia due to hyperbaric oxygen therapy has been reported, most often in the context of prolonged treatment. These symptoms are generally transient, but studies specifically concerning these complications are very few in number [189, 264, 266].

Although the neurological origin of oxygen toxicity to the central nervous system and the mechanisms involved have only been partially elucidated, free radicals (superoxide ions, etc.) seem to play a key role in the formation of lipid peroxides [50, 318]. Pablos *et al* observed increased levels of peroxidation reaction products (lipids) in rats subjected to 100% O_2 at 4 ATA for 90 minutes [234].

Experimental studies have revealed that HBO has negative effects at the molecular level [284]. One study carried out on rat polymorphonuclear leukocytes showed a decrease in their adherence properties following exposure to hyperbaric oxygen [51].

One potential complication, interactions when HBO is administered concurrently with certain drugs, has been investigated [69, 102, 206]. It will be noted that most of these studies were been carried out under normal therapeutic conditions [206].

Special precautions should be taken in divers with a history of pulmonary barotrauma who require further sessions of hyperbaric oxygen therapy [49].

The diversity in the treatment protocols has led to a certain number of controversies over the currently accepted indications [37].

5. SAFETY MESURES WHEN USING HYPERBARIC OXYGEN

Whatever type of therapeutic chamber is used, it is important to bear in mind that every technology, even though it may be promising, involves risks. Supervision and regular, continual and close monitoring are required at all times. The last accident, which occurred in Milan (1997), serves as a reminder (see section below concerning hyperbaric incidents and accidents).

The use of hyperbaric oxygen and therefore of hyperbaric chambers poses a risk not only to the patients being treated, but also to the personnel both inside and outside the chambers. Apart from the recommended safety instructions for using hyperbaric chambers, some countries, such as France, have adopted legislation and regulations. In Québec, the *Commission de la Santé et la Sécurité au Travail* recommends applying the Canadian Standards Association (CSA) [46] standard for the use of hyperbaric facilities (see Appendix 3). The *Association des physiciens et ingénieurs biomédicaux du Québec* places hyperbaric chambers in the category of equipment posing a level 1A risk ("equipment used for resuscitating patients or for critical monitoring or which could injure a patient in the event of a breakdown or malfunction") [12].

5.1 INCIDENTS AND ACCIDENTS

A recent tally of the incidents and accidents that have occurred in the past 73 years shows that more than 61% of the 99 accidents occurred under hyperbaric conditions (Appendix D). Thirty-six percent of the events involved multiplace chambers, 25% involved monoplace chambers, and 31% of the accidents were due to support system defects. Fire was involved in 67% of the cases, pressure in 22% [275].

The latest report by the Undersea and Hyperbaric Medical Society's safety committee (1998) indicates 76 fatalities and 23 injured during hyperbaric treatment [75]. The last recorded accident occurred at the Galeazzi Orthopedic Institute in Milan, where ten patients and a nurse died in a multiplace hyperbaric chamber fire. The accident was reportedly due to a hazardous object having been brought into the chamber (according to the expert report submitted at the last meeting of the European Diving Technological Committee, the object in question was a catalytic-type chemical heater) [185]. Turning on the device and its exposure to oxygen escaping from the patient's mask is what triggered the fire. The increase in the oxygen concentration (bothered by the heat, the other patients removed their masks), together with a nonfunctioning fire control system (water tanks empty), contributed to the spread of the fire.

5.2 SAFETY MESURES WHEN USING HYPERBARIC OXYGEN

HBO therapy is a special technology because of the diversity of its indications, the treatment protocols and the conditions of utilization. Furthermore, it exposes the treatment staff to certain risks, such as decompression sickness, nitrogen narcosis and barotrauma.

Safety is of utmost importance in hyperbaric oxygen therapy, and it should be given even greater attention when a chronic medical condition is being treated. In such cases, HBO is used not to save the patient's life, but rather to cure or prevent severe lesions. It is recommended but not indispensable. Therefore, these patients should not be exposed to additional risks.

In addition to the safety measures that apply to the equipment, the gas (oxygen) used, given its properties, and the activities of the staff using them, the management of patients with chronic medical conditions should include the following [160, 315]:

- Any contraindication should be ruled out (clinical examination and thorough investigation).
- Complete information on HBO, training on the safety rules (clothing, etc.) and training on the treatment (placement of mask, mobility, etc.) should be provided.
- A minimum of clinical monitoring (ECG, blood pressure) must be provided throughout the treatment.
- Patient management and patient comfort measures must be effective before, during and after the treatment. In some medical conditions, treatment continuity must be possible, e.g., in the case of resuscitation patients, for whom respiratory assistance, drainage or other interventions need to be continued when they are placed in a hyperbaric chamber.
- Measuring the actual physiological effect of the hyperbaric oxygen therapy on the patient is desirable (transcutaneous PO_2 determinations).

5.2.1 Equipment

The many accidents and deaths that occurred between 1962 and 1970 led to the establishment of standards in the United States and subsequently to the use of safety codes (National Fire Protection Association [NFPA]) [6, 220, 238, 239, 260].

- Chamber components: The constituent materials of hyperbaric chambers must meet flammability standards (UIC standards). These standards concern the framework, paint, coverings and bedding.
- Electrical circuits: The electrical current inside chambers is low. A system for indicating insulation faults in the electrical circuits is required.
- The electrical devices used must not generate any sparks (low voltage, special materials, ground, etc.).
- The equipment used (structural or monitoring) must be water-resistant and nonexplosive (not generate any sparks) and meet specific specifications (e.g., the equipment must have been tested at 10 ATA and with 100% O_2) [238, 315].
- The ventilation system must permit the rapid evacuation of any excess gases (oxygen, carbon dioxide) inside the chamber.
- A working pressurized fire control system is required. The system must be operable from both inside and outside the chamber. A tank and gate valve maintenance and inspection log must be kept up to date. Noncompliance with these basic rules can result in serious accidents.

5.2.2 Treatment and monitoring

- The air in hyperbaric chambers must meet well-established purity specifications. The oxygen concentration inside a hyperbaric chamber must not exceed 23.6% (NFPA Code 99) [220].
- Oxygen must be breathed through airtight equipment (no leakage of oxygen inside the chamber), and the expired gases must be evacuated outside the chamber.

- The oxygen concentration inside the different compartments of the chamber must be measurable at all times. The analyzer must be maintained and inspected on a regular basis.

- It is also advisable to monitor the CO_2 concentration.

- It is preferable to be able to check peripheral oxygen delivery in the patient: transcutaneous oxygen pressure measurements performed while the patient is breathing hyperbaric oxygen, using miniaturized, thermoregulated Clark-type polarographic electrodes placed simultaneously on the reference site (subclavian region) and on the diseased area. This procedure has proven to be a simple, reliable, noninvasive means of monitoring the treatment.

5.2.3 Training

Hyperbaric oxygen therapy requires willingness, energy and a great deal of discipline on the part of the people involved. Training in this type of technology concerns the personnel in charge of the treatment as well as the patients. Despite strict and usually well-defined chamber utilization rules at treatment centres, instructing patients and treatment personnel to abide by the safety rules is of utmost importance.

5.2.3.1 Patients

Informing and educating patients with regard to the safety measures required during treatment in a hyperbaric chamber is essential to preventing chamber accidents. A large number of the accidents reported in the literature were due to bringing risk-posing personal items inside the hyperbaric chamber (toys, prohibited products and materials).

Treatment team

The medical staff must have the necessary competence to act urgently in sometimes very difficult working conditions and be able to perform therapeutic procedures that are as diverse as they are specific to the different medical conditions for which it is responsible. Multidisciplinary management is often necessary both in emergency and in elective cases. Some conditions require advanced, specialized training on the part of the treatment personnel (e.g., complex resuscitation cases). The personnel must also be able to manage patients who might have strong, negative psychological reactions to feeling trapped in the chamber. Lastly, errors in interpreting certain changes in test results can undermine the quality of treatment (e.g., SaO_2).

5.2.3.3 Technical team

- The personnel in charge of operating and maintaining the equipment must be extremely vigilant and prevent the situation where inspections become mere routine checks (see Milan accident of 1997).

- The operators must have training in controlling the operation of the different systems (determination of oxygen concentration inside the chamber, etc.) and know what to do in case of a malfunction or an incident. They must be familiar with the physical and physiological principles of diving in a hyperbaric chamber.

The obligation to apply the Canadian Standards Association standard for hyperbaric facilities (Z275.1-93) may be an important factor in the safe management of hyperbaric oxygen therapy (see the table of contents of the standard and the section on the personnel's responsibilities in Appendix C).

6. ESTIMATE OF THE DEMAND FOR HBO THERAPY IN QUÉBEC

6.1 CURRENT CAPACITY FOR HYPERBARIC MEDICAL SERVICES IN QUÉBEC

In Québec, until quite recently, hyperbaric medical services were available only at the *Hôpital du Sacré-Coeur de Montréal*, which has had a 7-person multiplace hyperbaric chamber since 1982. A team of pneumologists is responsible for its operation. Since it was put into service, the chamber has been used to treat more than 1,500 patients, 80% of whom for carbon monoxide poisoning. In 1997, 170 patients were treated in the chamber, including 141 cases of carbon monoxide poisoning (83%) from all regions of Québec (see Appendix E).

In 1997, these 170 patients generated a total of 550 visits. Cases of carbon monoxide poisoning generally require only one visit. The approximately 400 other visits (75%) were by about 30 patients with other, nonemergency conditions. For example, the ten or so patients with osteoradionecrosis treated each year with HBO account for more than 40% of the chamber's utilization time.

For 17 years, the *Hôpital du Sacré-Coeur de Montréal* was the only hospital-based referral centre for the emergency treatment of carbon monoxide poisoning and underwater diving accidents occurring anywhere in Québec.

A project in the form of a partnership between the *Centre hospitalier régional de Rimouski* and the *Institut Maritime du Québec* was instituted in May 1998, its purpose being to serve the Lower St. Lawrence, the Gaspé Peninsula and the Magdeleine Islands, and the North Shore. Accessibility to the *Institut Maritime du Québec*'s multiplace chamber is mainly for the purpose of reducing the time it takes to transport patients requiring emergency treatment for gas embolism, decompression sickness and carbon monoxide poisoning. A few treatments have also been administered for elective cases (recurrent wounds, osteoradionecrosis, gas gangrene), but this is a marginal practice (personal communication with Dr. Maxime Amar, *Centre médical*, *Institut Maritime du Québec*).

Since January 24, 2000, the Hôtel-Dieu de Lévis's Department of Emergency Medicine has been providing emergency hyperbaric medical treatment, by means of a monoplace chamber, to patients from the Québec City and Chaudière-Appalaches areas* with carbon monoxide poisoning, cerebral gas embolism (postoperative or upon central catheter placement) or decompression sickness (underwater diving). This development is part of a broader project to institute a hyperbaric medicine unit that can provide services on an outpatient basis. The project has already been submitted to the regional and ministerial authorities. About 15 monoplace chambers for treating work accidents are in operation in the industrial sector. Also, the Seagram Sport Centre at McGill University has a duoplace chamber. Lastly, a private multiplace chamber was recently put into service in Longueuil within the context of a research pro-ject, and development projects at private clinics are under way as well.

6.2 MODEL OF THE POTENTIAL DEMAND FOR HBO THERAPY

The potential demand for hyperbaric oxygen therapy in Québec was estimated by the method proposed by Persels [243]. First, the provincial database, MED-ÉCHO, was consulted to determine the number of hospitalization cases associated with the medical conditions for which

* Hôtel-Dieu de Lévis press release. Consulted on May 3, 2000 and available electronically at: http://www.hdl.qc.ca/fr/comm_presse.htm.

HBO is indicated. Given the accuracy limits of the ICD-9 method of classification used in this hospital discharge database, certain medical conditions could not be identified. They were excluded from the calculations.

The calculations therefore concerned the number of hospitalizations observed for the following conditions:

- Carbon monoxide poisoning
- Gas embolism
- Maxillary osteoradionecrosis
- Leg ulcers
- Gas gangrene
- Diabetic lesions
- Decompression sickness

Next, the following formula was used for each condition, with modulators specific to each one:

$T_i = P_i\,(C_{Op,i})\,(C_{HBO,i})\,(C_{Tx,i})$

where:

T_i = Total number of potential treatments (1 treatment = 1 visit, or dive) associated with the medical condition in question.

P_i = Total number of hospitalizations for the condition, based on the corresponding ICD-9 codes.

$C_{Op,i}$ = Coefficient accounting for the cases that were never hospitalized but which were treated on an outpatient basis only.

$C_{HBO,i}$ = Percentage of patients whose situation warrants HBO therapy.

$C_{Tx,i}$ = Average number of treatments necessary to complete therapy for the condition in question.

The coefficients used (see Table 22) are based on data reported in two retrospective studies: Workman *et al* [325] and Marroni *et al* [190]. Data from Alberta were consulted as well [210].

The results are presented separately for eastern and western Québec. Eastern Québec consists of:

- The Lower St. Lawrence
- Saguenay-Lac Saint-Jean
- Québec City
- Mauricie and Central Québec
- Abitibi-Témiscamingue
- The North Shore
- Northern Québec
- The Gaspé Peninsula and the Magdeleine Islands
- Chaudière-Appalaches

Western Québec consists of:

- The Eastern Townships
- Montréal Urban Community
- The Outaouais
- Laval
- Lanaudière
- The Laurentians
- Monteregia

The data taken from the MED-ÉCHO database are for the year 1996-1997. Table 21 shows the number of hospitalization cases for the medical conditions for which the corresponding ICD-9 code has been assigned as a main or secondary diagnosis.

Table 22 shows, for each condition, the potential number of HBO treatments per year in Québec as calculated according to the method proposed by Persels [243]. The data are presented separately for eastern and western Québec. In the first set of calculations, we took into account only the number of hospitalization cases for which the condition in question (e.g., leg ulcers) was the main diagnosis (*Main diagnosis only*). In the second set, we took into account all the hospitalization cases, including those for which the condition figured among the "secondary diagnoses" (*All diagnoses*).

Table 21: Number of hospitalization cases in Québec in 1996-1997 for seven medical conditions for which HBO is indicated

Medical Condition	Eastern Québec			Western Québec			Province		
	Main diagnosis	Secondary diagnoses	Total	Main diagnosis	Secondary diagnoses	Total	Main diagnosis	Secondary diagnoses	Total
CO poisoning	30	28	58	50	27	77	80	55	135
Gas embolism	1	2	3	1	3	4	2	5	7
Maxillary osteoradionecrosis	104	88	192	79	95	174	183	183	366
Leg ulcers	110	291	401	293	903	1,196	403	1,194	1,597
Gas gangrene	1	26	27	3	19	22	4	45	49
Diabetic lesions	221	501	722	478	1,193	1,671	699	1,694	2,393
Decompression sickness	2	0	2	1	0	1	3	0	3
TOTAL	**469**	**936**	**1,405**	**905**	**2,240**	**3,145**	**1,374**	**3,176**	**4,550**

We used the MED-ÉCHO hospital discharge database to estimate the potential demand for two reasons. First, it is the only provincial database complete enough to provide the necessary data by patient's region of origin and by medical condition. Second, we hypothesized that, for most of the medical conditions for which HBO is indicated, the patients must, at some point during their long series of care episodes, have spent at least one night in hospital during the previous 12 months. If the severity of their condition warranted a series of HBO treatments, it is reasonable to maintain that they spent at least one night in hospital because of their illness. Such is the case with carbon monoxide poisoning, gas embolism, leg ulcers, gas gangrene and decompression sickness.

As for osteoradionecrosis and diabetic lesions, the calculations were adjusted to take into account the patients who would have been treated solely on an outpatient basis and who would not have been admitted to hospital for their illness during the previous 12 months. The estimated number of treatments for cases of osteoradionecrosis and diabetic lesions was therefore adjusted upwards by a factor of 40% and 50%, respectively.

Table 22: Potential number of HBO treatments per year for eastern and western Québec, based on the method proposed by Persels [243]

Medical condition	$C_{Op,I}$	$C_{HBO,I}$	$C_{Tx,i}$	TOTAL NUMBER OF TREATMENTS					
				Eastern Québec		Western Québec		Province	
				Main diagnosis only	All Diagnoses	Main diagnosis only	All diagnoses	Main diagnosis only	All diagnoses
CO poisoning	1	0.6	2	36	70	60	92	96	162
Gas embolism	1	1.0	2	2	6	2	8	4	14
Maxillary osteoradionecrosis	1.4	0.4	40	2,330	4,301	1,770	3,898	4,099	8,198
Leg ulcers	1	0.3	20	660	2,406	1,758	7,176	2,418	9,582
Gas gangrene	1	1.0	7	7	189	21	154	28	343
Diabetic lesions	1.5	0.3	40	3,978	12,996	8,604	30,078	12,582	43,074
Decompression sickness	1	1.00	1	2	2	1	1	3	3
TOTAL				**7,015**	**19,970**	**12,216**	**41,407**	**19,230**	**61,376**

$C_{Op,i}$ = Coefficient accounting for the cases that were never hospitalized but which were treated on an outpatient basis only.
$C_{HBO,i}$ = Percentage of patients whose condition warrants HBO therapy.
$C_{Tx,i}$ = Average number of treatments necessary to complete therapy for the medical condition in question.

Using this approach, we estimate the potential number of HBO treatments in Québec at approximately 20,000 a year, if only the main diagnoses are considered, or at about 61,000, if all the secondary diagnoses are factored in as well. Patients in eastern Québec would account for about a third of these treatments.

Most of the HBO treatments would be for "non-emergency" conditions, namely, maxillary osteo-radionecrosis, leg ulcers and diabetic lesions. The large number of treatments required in each case (up to 40) explains the large figures. It should be borne in mind that, in all three cases, HBO is an adjuvant treatment that is still seldom used on a systematic basis in Québec.

The above estimate of the potential number of treatments does not take into account the distances that patients would have to travel in order to be treated. When it comes to treating an emergency case of carbon monoxide poisoning or decompression sickness, which require only one or two dives, the decision to transport the patient, whose life is in danger, even over a long distance, is automatic. It is not when it comes to undertaking a series of 40 daily treatments for the purpose of improving healing and the quality of life of a patient with maxillary osteoradionecrosis, for example. In such cases, the distance to the place of treatment is an important factor.

This is why Persels recommends another method of estimating the potential demand, one that takes into account the population density around the planned hyperbaric medical centre [243]. He suggests one treatment/day/100,000 population within a 50-km radius as a good estimate of the potential demand. This distance implies that the patient will be able to make it to the centre for his or her daily treatment.

Based on this method, the Greater Montréal Area (population of about 3 million, including Laval and part of Monteregia) would generate a demand of 7,500 treatments a year (250 work days). For example, to meet this demand, there would need to be in Montréal one multiplace chamber capable of treating ten patients at a time 250 days a year at the rate of three dives a day.

The same calculation for the Québec City and Chaudière-Appalaches areas (population of 1 million) yields a demand of 2,500 treatments per year, which would require a chamber capable of treating five patients at a time at the rate of two dives a day.

If we use the "medical condition" method of calculation for the Montréal and Québec City and Chaudière-Appalaches areas, we obtain, respectively, 19,228 and 7,520 treatments a year (see Tables F.2 and F.3 in Appendix F).

We therefore estimate that the potential demand for HBO treatments in the Montréal area could range from about 7,500 to 19,200 a year, while that for the Québec City area would be between 2,500 and 7,500 a year.

The same calculation could be made for each of the province's large cities. However, some authors maintain that a population of one million within a 50-km radius is the minimum for maintaining a hyperbaric centre [243]. The Greater Montréal and Québec City Areas would therefore be the only ones whose population densities could justify the creation of a hyperbaric medical centre.

Whatever method of calculation is used, we note a large gap between the potential demand for HBO in Québec and the current supply.

6.3 ADDITIONAL NEED FOR HBO SERVICES

The gap between the supply and potential demand can be explained in several ways. First, thus far, HBO has been reserved almost exclusively for the treatment of carbon monoxide poisoning and decompression sickness, two conditions for which it is the treatment of choice. For the other conditions, HBO is used less frequently because of structural capacities and even human reasons (need for a multidisciplinary team, knowledge of the technology). Apart from these reasons, two other factors limit the routine use of this resource: the lack of available facilities and skepticism on the part of some practitioners with regard to the efficacy of the technology. This skepticism is kept alive by a scientific literature that is not always unanimous and which is based on often uncontrolled studies.

Table 23: Summary of the current supply of and potential demand for HBO treatments

	Current supply (T/year)	Potential of the existing hyperbaric chamber (T/year)	Potential demand according to the population method[3] (T/year)	Potential demand according to the medical condition method[4] (T/year)
Montréal area	900[1]	5,250[2]	7,500	19,200
Québec City area	--	--	2,500	7,500

1 Current number of treatments in the hyperbaric chamber at the *Hôpital du Sacré-Cœur de Montréal* (HSC).
2 Potential number of treatments in the *Hôpital du Sacré-Cœur de Montréal*'s chamber if operated at full capacity by a multidisciplinary team (7 patients at a time, 3 dives/day, 250 days/year).
3 Estimate based on the criterion of 1 treatment/day/100,000 population within a 50-km radius.
4 Estimate based on the following formula: $T = \sum T_i = \sum P_i\ (C_{Op,i})\ (C_{HBO,i})\ (C_{Tx,i})$
where:
T_i = The total number of potential treatments (1 treatment = one patient diving in the chamber once).
P_i = Total number of hospitalizations for each medical condition, based on the corresponding ICD-9 codes.
$C_{Op,i}$ = Coefficient accounting for the cases that were never hospitalized but which were treated on an outpatient basis only.
$C_{HBO,i}$ = Percentage of patients whose condition warrants HBO therapy.
$C_{Tx,i}$ = Average number of treatments necessary to complete therapy for the medical condition in question.

Table 23 summarizes the situation regarding the current supply of HBO treatments in the health-care system and the potential demand in the Greater Montréal and Québec City Areas.

Only the figures for the Greater Montréal and Québec City Areas are provided, because they are the only ones that meet the recognized criterion of a population large enough to sustain a hyperbaric centre, i.e., one million people within a 50-km radius. This does not necessarily rule out the possibility of developing hyperbaric medicine in other regional centres in Québec.

Given the available data, *CETS* believes that the potential demand for HBO treatments in the Québec City area is large enough to justify the installation of a hyperbaric chamber. If a decision were made to operate a multiplace chamber, it would be preferable to install a monoplace chamber as well in order to deal with the arrival of emergency cases (e.g., carbon monoxide poisoning) without having to interrupt treatments in progress in the multiplace chamber.

As for the Greater Montréal Area, assuming that the *Hôpital du Sacré-Coeur de Montréal*'s hyperbaric chamber can operate at full capacity with a multidisciplinary mode of organization, the estimate of the potential need might warrant the addition of hyperbaric chambers. The number and type of additional facilities would depend on the rate at which the potential demand materializes and on the institutions' and professionals' interest in using this therapy.

Whenever develops in the future, *CETS* believes that a monoplace chamber should be added at the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre in order to deal with emergency cases without having to interrupt treatments in progress in the multiplace chamber.

In short, there is a potential demand that could justify installing more hyperbaric chambers in Québec. However, it should be stressed that numerous conditions must be met in order to efficiently operate a hyperbaric centre. Compliance with safety standards, staff training, the availability of a multidisciplinary team willing to manage patients with various medical conditions are basic conditions that must be met before putting new chambers into service. The mode of organization necessary for operating a hyperbaric chamber in such a way as to be able to meet the potential demand determined above would require a great deal of cooperation and synchronization. Québec has not yet put in place such organizational mechanics. Furthermore, the increased supply of HBO treatments will have an economic impact, which will have to be factored into the decision. That impact is the subject of the next chapter.

7. COSTS

7.1 UNIT COST PER TREATMENT

7.1.1 Two Canadian experiences

A recent study conducted by a group in Hamilton, Ontario [73], estimated the cost of a treatment in a hyperbaric chamber at $350. This estimate included the capital and operating costs, the physician's fees and the expenses assumed by the patients.

The Hamilton team has two monoplace chambers operated by a single, full-time technician. Four dives can be done in the chamber in eight hours, i.e., eight patients (treatments) per day, for a maximum output of 2,000 treatments a year. Yet, only 750 are done. This underutilization is apparently due to the fact that the hyperbaric medical team has not developed the multidisciplinarity for and the systematic approach to all the recognized indications (personal communication from Dr. Mario Côté, Hôtel-Dieu de Lévis). Since the operating cost consists largely of staff salaries, it can be argued that the figure of $350 per treatment could be substantially lower if the centre was operated at full capacity.

An Alberta report based on the operating budgets of the hyperbaric centre at Edmonton's Misericordia Hospital estimates the cost of a dive at $220, excluding the capital costs and the expenses incurred by the patients [210]. The Misericordia Hospital has two monoplace chambers and treats eight patients per day as well. Thanks to a multidisciplinary approach to hyperbaric medicine, about 1,600 treatments are administered each year, which is close to the full capacity of 2,000. It is therefore not surprising that the per-treatment cost is lower than that in Hamilton, since, once again, the operating cost consists mainly of salaries. The cost for oxygen, mechanics, electricity, laundry and maintenance of the room are relatively minor compared to the salaries (personal communication from Dr. Mario Côté, 1999).

7.1.2 Unit cost in Québec, based on the current mode of operation

The Hôpital du Sacré-Coeur de Montréal estimated the cost of operating the chamber at $250 per dive, which does not include the physician's fees (personal communication from Dr. Mario Dugas, pneumologist, Hôpital du Sacré-Coeur de Montréal, 1999).

As for the fees in question, the RAMQ's fee schedule provides for the following reimbursements [259]:

Treatment in hyperbaric chamber (including, if necessary, close supervision of patient after he leaves chamber) (physician with patient in chamber)

- *1st hour:* *$240.00*
- *For each additional patient treated at the same time:* *$70.00*
- *Each quarter hour or fraction thereof after 1st hour:* *$40.00*
- *For each additional patient treated at the same time:* *$10.00*

Supervision (patient in chamber – physician outside)

- *1st hour:* *$120.00*
- *For each additional patient treated at the same time:* *$35.00*

Table 24: Physician's fee ($) per patient according to different hyperbaric chamber utilization scenarios (for a 90-minute dive)

	Physician with the patient in the chamber					Physician outside the chamber				
Number of patients	1st hour	30 add. min.	Total/ patient	Total	Cost/ Patient	1st hour	30 add. Min.	Total/ Patient	Total	Cost/ Patient
1	240	80	320	320	320.00	120	40	160	160	160.00
2	70	20	90	410	205.00	35	10	45	205	102.50
3	70	20	90	500	166.00	35	10	45	250	83.33
4	70	20	90	590	147.50	35	10	45	295	73.75
5	70	20	90	680	136.00	35	10	45	340	68.00
6	70	20	90	770	128.33	35	10	45	385	64.17
7	70	20	90	840	120.00	35	10	45	430	61.43
Average					**175.00**					**87.59**

- *Each quarter hour or fraction thereof after 1st hour:* *$20.00*
- *For each additional patient treated at the same time:* *$5.00*

To calculate the average fee per patient, we must construct different scenarios concerning the use of the chamber, based on the number of patients treated in it at the same time.

Table 24 shows a few of these scenarios, which are based on the assumption that a dive lasts an average of 90 minutes.

The average fee per patient could thus vary from $61 to $320. Assuming that the most common scenario is presently to treat three patients at a time with the physician inside the chamber, we arrive at a per-patient fee of $83. Currently, the cost of an HBO treatment at the Hôpital du Sacré-Coeur de Montréal would therefore be $333/patient ($250 + $83). This unit cost will be used later in a status quo scenario in order to calculate hospital cost/benefit ratios for HBO treatment.

These data illustrate one of the economic aspects of choosing the type of HBO facility: monoplace, duoplace or multiplace chambers. The example also shows the effect of the number of patients treated at the same time in a chamber on achieving full output and therefore the lowest possible unit cost. However, full utilization implies putting in place a multidisciplinary team capable of treating all the recognized indications for HBO therapy.

Table 25 shows the maximum output for three types of facilities: two monoplace chambers, one duoplace chamber and one 7-person multiplace chamber (inspired by a presentation made to *CETS* by Dr. Mario Côté, Hôtel-Dieu de Lévis, January 1999).

7.1.3 Unit cost in Québec, based on the full-capacity scenario

The current annual operating budget for the Hôpital du Sacré-Coeur de Montréal's hyperbaric centre is $230,000. About 900 treatments are done there each year, for a per-treatment cost of $250. The multiplace chamber can accommodate seven patients at a time and allows for three di-

Table 25: Output of three types of hyperbaric facilities

Parameter	2 monoplace chambers	Duoplace chamber	Multiplace chamber (7-person)
Dives/day	4	3	3
Patients/day	8	6	21
Treatments/year (250 days)	2,000	1,500	5,250
Personnel	1	1	4

ves a day over an 8-hour period, for a maximum capacity of 5,250 treatments a year (250 work days).

To achieve this output, the annual operating budget would have to be approximately $400,000 to $500,000. In addition to the variable costs, such as the oxygen, technical equipment and electricity, this budget would mainly cover the operating technician's salary and the salaries of three full-time nurses (personal communication from Dr. Mario Côté, Hôtel-Dieu de Lévis).

If we use the upper limit of this operating budget, that is, $500,000, and assume that a new multidisciplinary mode of organization would make it possible to treat all of the recognized indications for HBO, the Hôpital du Sacré-Coeur de Montréal's hyperbaric centre could provide 5,250 treatments a year at a cost of $95 each, excluding the cost of the physician's supervision. Based on the calculations in the preceding section, this supply of 5,250 treatments a year would still be less than the potential demand, which could vary between 7,500 and 19,200 for the Greater Montréal Area.

In these optimal operating conditions, the per-treatment cost would therefore be $95 + $61.43 (physician's fee for overseeing seven patients at a time; see Table 24) or $156.43. This unit cost will be used later in a full-capacity scenario in order to calculate hospital cost/benefit ratios for HBO treatments.

7.2 COST OF FACILITIES

In 1993, a monoplace chamber cost between $75,000 and $85,000 US, a multiplace chamber between $300,000 and $2.5 million US [243]. The renovation costs for installing the chamber must be included as well. Persels [243] estimates these costs at $100 US per square foot. A multiplace chamber may take up to 4,500 square feet. The cost of purchasing and installing a 10-person multiplace chamber in Québec has been estimated at $2 million (personal communication from Dr. Mario Côté, Hôtel-Dieu de Lévis, 1999).

7.3 HOSPITAL COST/BENEFIT RATIO AND ECONOMIC IMPACT

We attempted to estimate the cost-benefit ratio for an increased supply of HBO services in Québec and the economic impact of different implementation scenarios.

The cost-benefit ratio for oxygen therapy in Québec was determined from the standpoint of the hospital system. The costs taken into consideration were those generated by HBO therapy, including physicians' fees. The benefits were calculated in terms of the expected reduction in the lengths of stay for patients with the medical conditions considered.

Two of the benefits of HBO that were not taken into account in this analysis were the lives that HBO can save when potentially fatal conditions, such as carbon monoxide poisoning, are treated and the improvement in the quality of life of patients with chronic, painful and debilitating conditions. The cost savings resulting from treatments provided on an outpatient basis were not taken into account either.

7.3.1 Hospitalization costs associated with the conditions for which HBO is indicated

We estimated that the hospitalization costs associated with seven of the main conditions for which HBO is indicated were $36.2 million for the entire province in 1996-1997 (see Table F.1 in Appendix F for details of the calculations). The vast proportion of these costs (97%) were due to the numerous hospitalizations of patients with diabetic lesions (n = 2,393) or leg ulcers (n = 1,597), together with the relatively long mean lengths of stay: 16.8 days for leg ulcers and 21.5 days for diabetic lesions.

These costs are estimated at $14.8 million for the Greater Montreal Area and at $4.4 million for the Greater Québec City Area (see Tables F.2 and F.3 in Appendix F for details of the calculations).

7.3.2 Estimate of the costs for meeting the potential demand

Two scenarios were used to estimate the costs for meeting the potential demand for HBO treatments. The first, the status quo scenario, is based on the current output of the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre and yields a per-treatment cost of $333. The other, the full-capacity scenario, assumes optimum output by the centre and yields a per-treatment cost of $156, as calculated above. The calculations of these unit costs are shown in Section 7.1.

To meet the entire potential demand for HBO treatments as estimated in Chapter 6, the operating cost would be $20.4 million per year in the status quo scenario and $9.6 million in the full-capacity scenario. Table F.1 (Appendix F) shows the cost breakdown for the seven medical conditions in question.

These estimates pertain to the entire province. This assumes that all patients have access to a hyperbaric chamber within an hour's drive from their homes. The large number of treatments that would be administered to nonemergency cases (osteoradionecrosis, diabetic lesions, etc.) include up to 40 daily visits to the hyperbaric chamber. It is therefore not realistic to consider all the cases in the same manner, as if a hyperbaric chamber were available to everyone within a 50-km radius. Although based on actual data, these calculations have little pragmatic value.

Tables F.2 and F.3 (Appendix F) show the same calculations as for the entire province but for the Greater Montreal Area and the Greater Québec City Area, respectively. The HBO treatment costs for meeting the entire demand in the Montreal area would be $6.4 million annually in the status quo scenario and $3 million in the full-capacity scenario.

It should be noted that these calculations were made using the number of treatments estimated with the medical condition method. It was seen in Chapter 6 that this method estimated the number of treatments for the Greater Montreal Area at 19,200, nearly three times the number estimated by the “population" method (T = 7,500). If the costs in the full-capacity scenario are applied to the estimate of 7,500 treatments, we obtain an annual operating cost of $1.2 million. This figure is approximately the same as the operating cost for two 7-person multiplace chambers (like the one at Sacré-Coeur) operated at full capacity (2 x $500,000).

As for the Greater Québec City Area, the HBO treatment costs for meeting the entire demand would be $2.5 million annually in the status quo scenario and $1.2 million in the full-capacity scenario, once again, based on the number of treatments estimated with the medical condition method.

As estimated by the medical condition method, the number of annual treatments for the Greater

Québec City Area was 7,500, exactly three times the number estimated with the population method (T = 2,500). If the costs in the full-capacity scenario are applied to the estimate of 2,500 treatments, we obtain an annual operating cost of $390,000. This figure is slightly less than the cost of operating a 7-person multiplace chamber like the one at Sacré-Coeur operated at full capacity (between $400,000 and $500,000).

7.3.3 Estimate of the hospital cost/benefit ratio

Despite the fact that HBO is scientifically recognized as an effective adjuvant treatment for the medical conditions in question, there are no stu-dies from which we could quantify the possible reductions in hospital stays thanks to HBO therapy.

We therefore attempted to estimate the percent reduction in the lengths of hospital stay that HBO treatments would have to result in so that their costs would be offset by the hospitalization cost savings achieved. Details of the calculations are presented in Appendix F.

For the Montréal area. In the full-capacity scenario, the HBO treatments would have to result in a reduction of at least 20% in the mean lengths of hospital stay to yield a favourable hospital cost/benefit ratio. In the status quo scenario, a 43% reduction would be necessary (see Figure F.2 in Appendix F).

For example, if it is assumed that the HBO treatments would result in a 50% reduction in the lengths of stay, the hospital cost/benefit ratio would be positive, with annual savings of $4.5 million in the full-capacity scenario and $1 million in the status quo scenario.

For the Québec City area. In the full-capacity scenario, the HBO treatments would have to result in a reduction of at least 26% in the mean lengths of hospital stay to yield a positive hospital cost/benefit ratio. In the status quo scenario, a 57% reduction would be necessary (see Figure F.3 in Appendix F).

For example, if it is assumed that the HBO treatments would result in a 50% reduction in the lengths of stay, the hospital cost/benefit ratio would be positive, with annual savings of $1.1 million in the full-capacity scenario and an annual "loss" of $1 million in the status quo scenario.

Obviously, HBO therapy provides benefits other than reducing the lengths of hospital stay: a reduction in the risk of amputation in the case of diabetic foot, an improvement in the patients' quality of life, a reduction in the outpatient care required for wounds refractory to the usual treatments, and so on. However, we do not have the necessary Québec data to determine these benefits with any accuracy.

It should be borne in mind that this exercise does, of course, underestimate the actual cost/benefit ratio, since the analysis is limited to the hospital cost/benefit ratio.

8. CONCLUSIONS

HBO therapy has reportedly been tried out on nearly 130 medical conditions, but very few of them have been the subject of randomized, controlled, prospective trials. Based on an exhaustive review of the available scientific literature and on the opinions of expert organizations, *CETS* concludes that hyperbaric oxygen therapy is recommended in the following medical conditions:

- Carbon monoxide poisoning
- Decompression sickness
- Gas embolism
- Gas gangrene
- Refractory tissue or bony necrosis due to a single microorganism or a mixed population of microorganisms (aerobic or anaerobic)
- Post-radiation therapy tissue damage: osteoradionecrosis and soft-tissue damage
- Chronic tissue lesions associated with chronic critical ischemia: diabetic foot, chronic leg ulcers
- Severe burns which are refractory to treatment and/or which compromise graft take.

As for cerebral ischemias, no clinical studies have evaluated the beneficial effect of hyperbaric oxygen on their evolution. In this regard, the randomized, double-blind, prospective, multi-centre clinical study that was just conducted by Québec researchers provides the first rigorous data on this application. The results showed an improvement in an equal proportion of children in the experimental group and in the placebo group, which would mean that hyperbaric oxygen has no effect. However, this interpretation raises some questions as to the factors for improvement and could point to the need for further research.

Like any other health technology, hyperbaric oxygen therapy has certain temporary and sometimes severe adverse effects that are more or less foreseeable but which are practically always due to improper use. Middle ear barotrauma heads the list of complications. Pulmonary barotrauma is a more rare occurrence. Impaired visual acuity in the form of myopia or hyperopia due to hyperbaric oxygen therapy has been reported, most often in the context of prolonged treatment. These symptoms are generally transient, but studies specifically concerning these complications are few in number. A few experimental studies (involving animals and in specific study conditions) report oxygen toxicity to certain organs, especially the central nervous system. The origin and mechanisms of this toxicity remain poorly elucidated.

HBO is a treatment that requires continual, close monitoring before, during and after administration. Regardless of the medical condition to be treated, a potential candidate for HBO therapy must meet strict physiological and psychological criteria (even if they have not yet been standardized). Furthermore, this procedure requires a professionally and technically competent environment.

The safety measures pertain to the equipment and its maintenance, the conditions for operating a chamber, and training of both the treatment team, the technical team and the patients. *CETS* believes that all hyperbaric medical centres (private and public) operating in Québec should be subject to the Canadian Standards Association (CSA) standard for the use of hyperbaric facilities (Z275.1-93).

On the basis only of the medical conditions for which HBO therapy is recognized as being effective, *CETS* considers that the potential demand in the Greater Québec City area justifies the installation of a hyperbaric chamber. If a decision were made to operate a multiplace chamber, it would be advisable to install a monoplace chamber along with it.

As for the Greater Montréal Area, the potential demand could justify the addition of hyperbaric chambers. This assessment assumes that the multiplace chamber at the Hôpital du Sacré-Coeur can operate at full capacity, with a multi-disciplinary mode of organization. The number of treatments per year could, in effect, increase from 900 to 5,200.

The number and type of additional facilities will depend on the pace at which the potential demand materializes and on institutions' and professionals' interest in using this therapy. Whatever develops in the future, *CETS* believes that a monoplace chamber should be added at the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre in order to deal with emergency cases without having to interrupt treatments in progress in the multiplace chamber.

Adding these resources could have a significant economic impact. The operating budget for a multiplace chamber is approximately $500,000 a year. The cost of purchasing and installing a new multiplace chamber varies from $1.5 to $2 million.

These costs would very likely be offset by a reduction in the lengths of stay in a proportion that has yet to be determined, at least for chronic cases that require hospitalization. As an illustration, we estimated that for the Montréal area, the break-even point for HBO therapy would require about a 20% reduction in the lengths of stay. In other words, the addition of HBO therapy would have to result in a length-of-stay reduction of 20% in order for the benefits (in terms of hospitalization costs only) to equal the cost of the treatments. For the Québec City area, the break-even point would require a 26% reduction.

Studies should be undertaken in Québec to determine the extent of these reductions and to assess the impact, on resources, of the therapeutic benefit that hyperbaric oxygen therapy might have for patients treated mainly on an outpatient basis.

Lastly, adding hyperbaric chambers does not merely involve adding new facilities. To make the most of their full potential, steps must be taken to ensure:

1) the presence of a multidisciplinary team that includes specialists from all the areas in which HBO therapy can be of benefit;
2) the presence or permanent medical supervision;
3) compliance with safety standards, such as that issued by the CSA.

APPENDIX A: MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

APPENDIX A:

MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

MEDICAL CONDITION	PHYSIOPATHOGENESIS	MECHANISM(S) INVOLVED	DESIRED EFFECT(S)
Carbon monoxide poisoning	- Since CO binds to Hb with an affinity more than 200 times greater than O_2, hemoglobin becomes unavailable for tissue oxygen transport [61, 245]. - Binding to cytochrome a3 blocks (mitochondria) phosphorylation reactions and therefore energy production [60, 191, 290].	- Effect of oxygen on the hemoglobin dissociation curve by the administration of pure O_2. Hyperbaric conditions result in faster dissociation of the CO-Hb bond (half-life of 90 min in ambient air, 35 min at 2 ATA and 22 min at 3 ATA) [235]. - Dissociation of the CO-cytochrome a3 bond results in a decrease in pH and activation of mitochondrial metabolism [292]. - Decrease in leukocyte adherence to the vascular endothelium and in vascular lesions due to metabolites released by leukocytes [293].	- Faster elimination of CO from the blood and tissues. - Limiting of cerebral edema. - Facilitate the resumption of cellular enzyme activity.
Gas embolism	- The supersaturation of gas results in the formation of gas bubbles [84]. - The surfaces of the gas bubbles are recognized as foreign bodies and cause activation of the formed elements of the blood, especially platelets [19, 22, 244, 283]. Vascular endothelial lesions contribute, via the triggering of procoagulant activity (activation of coagulation factors: Factor X), to platelet aggregation [265, 286]. - Activation of the complement system (C5a) results in inflammatory reactions (edema, shock) and polymorphonuclear neutrophil activation [21, 285].	- Hyperbaric conditions (Henry's law). - Tissue oxygenation. - Alpha-adrenergic agent.	- Decrease in embolism size. - Limiting of edema and the spread of cerebral edema. - Elimination of inert gases.

APPENDIX A (Cont'd):
MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

MEDICAL CONDITION	PHYSIOPATHOGENESIS	MECHANISM(S) INVOLVED	DESIRED EFFECT(S)
Decompression sickness	- Symptoms of decompression sickness are always associated with a decrease, usually sudden, in the ambient pressure. - The inability of the body to eliminate the excess inert gas causes gas bubbles to form in the veins, tissues and, more rarely, arteries. This usually occurs when breathing a mixture of gases (nitrogen-helium). The presence of these gas bubbles prevents the elimination of gas by the tissues. - The formation of gas bubbles usually causes endothelial wall lesions and vascular obstruction and can cause pulmonary circulatory arrest and perivascular and peribronchiolar edema. - In addition to the physical problems, the gas bubbles result in the release of fat molecules and even fat embolisms. - The other manifestations are similar to those observed in pulmonary embolism.	- Hyperbaric conditions (Henry's law). - Tissue oxygenation. - Alpha-adrenergic agent.	- Gas re-solution. - Improved blood flow. - A decrease in the inflammatory processes.
Gas gangrene	- Microbial proliferation (*Clostridium*) [142]. - Production of toxins (alpha-toxins, etc.). - Edema. - Tissue necrosis. - Gas production.	- Antibacterial effect [13, 14, 142]. - Formation of free oxygen radicals toxic to anaerobes. - Stimulation of cellular immune defenses (polymorphonuclear neutrophils, macrophages). - Alpha-adrenergic effect. - Healing effect: stimulation of fibroblast formation and collagen synthesis. - Increase in the efficacy of certain anti-biotics (oxygen-dependent intracellular transport).	- Cessation of microbial proliferation and the production of toxins. - A decrease in edema. - Tissue regeneration.

APPENDIX A (Cont'd):
MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

MEDICAL CONDITION	PHYSIOPATHOGENESIS	MECHANISM(S) INVOLVED	DESIRED EFFECT(S)
Infectious diseases characterized by tissue necrosis (other than gas gangrene)	- Microbial proliferation (anaerobes). - Edema. - Tissue necrosis.	- Increase in tissue oxygen tension. - Antibacterial effect - Stimulation of oxygen-dependent phagocytic functions [18].	- To decrease edema. - To improve vascular circulation. - To assist cellular defenses.
Post-radiation therapy tissue necrosis (osteoradionecrosis)	- Acute destruction (tissues and vessels). - Atypical cell regeneration and persistence of necrotic tissue. - Parenchymal degeneration and chronic tissue necrosis.	- Antiischemic effect: delivery of oxygen to the injured tissues. - Healing effect: stimulation of angiogenesis and improvement in fibroblast formation and collagen synthesis [167, 168, 193, 194].	- A decrease in chronic tissue hypoxia, which is responsible for healing failure. - Regeneration of healthy tissues, which can lead to healing.
Diabetic lesions: diabetic foot	- Micro- and macroangiopathies---→Ischemia. - Diabetic arteriosclerosis. - Diabetic polyneuritis -------------→Lesions. - Chronic infections-----------------→Ulcers.	- Increase in the oxygen tension in ischemic tissues [94]. - Cytolytic effect on anaerobes and stimulation of cellular defense functions. - Stimulation of fibroblast growth and collagen synthesis [105].	- A decrease in chronic tissue hypoxia, which is responsible for healing failure. - Decrease in the infection. - Regeneration of healthy tissues, which can lead to healing.
Burns	- Inflammation. - Edema (numerous factors are involved in endothelial destruction and increased vascular patency [12]). - Ischemia, thrombosis and tissue necrosis.	- Alpha-adrenergic effect [112, 183]. - Increase in tissue oxygen tension. - Stimulation of angiogenesis. - Stimulation of epithelialization and collagen synthesis.	- A decrease in edema. - Improved local microcirculation. - Stimulation of healing.
Grafts (compromised)	- Inflammation. - Edema. - Microthrombi, occlusion and ischemia.	- Increase in tissue oxygenation (> 16x). - Stimulation of' angiogenesis [171, 281]. - Effect on edema [241]. - Stimulation of epithelialization and collagen synthesis.	- A decrease in edema. - Improved microcirculation. - Graft take. - Improved healing.

APPENDIX A (Cont'd):
MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

MEDICAL CONDITION	PHYSIOPATHOGENESIS	MECHANISM(S) INVOLVED	DESIRED EFFECT(S)
Leg ulcers	- Micro- and macroangiopathies ---→ Ischemia. - Chronic infections -----------------→ Ulcers [95, 96].	- Decrease in leukocyte adherence to vascular walls. - Cessation of lipid peroxide production. - Antibacterial action. - Stimulation of epithelialization and collagen synthesis [282].	- Revitalization of injured tissues. - Revascularization. - Activation of healing.
Traumatic ischemias	- Vascular lesions and/or ruptures (arterial). - Vascular thrombosis --→ Ischemia [121]. - Edema, tissue compression, bone damage. - Ischemia. - Tissue necrosis. - Infection.	- Alpha-adrenergic role. - Improvement in in situ tissue oxygenation. - Stimulation of cellular immune defenses. - Activation of fibroblast formation and collagen synthesis.	- Reduction in posttraumatic ischemia. - Prevention of risk of infection. - Faster healing. - Prevention of amputation.
Cerebral ischemias	- Destruction of nerve cells due to hypoxia. - Formation of umbral and preumbral zones.	- Oxygenation of preumbral cells (*theory of inactive or dormant cells*).	- Reduction of penumbral zone (pren-umbra). - Recovery of functional activity of certain nerve cells.
Myocardial ischemia	- Atherosclerosis, coronary insufficiency. - Myocardial ischemia.	- Antiischemic effect. - Effect on microcirculation?	- Tissue revitalization?
Anemias	- Hemoglobinopathies. - Bleeding. - Post-radiation therapy.	- Offsetting of the loss of hemoglobin with hyperbaric oxygen.	- Decrease in tissue hypoxia.
Migraines	- Various?	- Effect of HBO on neurotransmitters.	- Increase in neurotransmitter-induced metabolic reactions.
Facial palsies	- Various	- Tissue oxygenation.	- Decrease in pain due to inflammatory reactions or in hypoxia.
Malignant diseases	- Various.	- Tissue oxygenation. - Potentiation of chemotherapy.	
Ear/hearing disorders	- Various.	- Tissue oxygenation.	- Decrease in pain.

APPENDIX A (Cont'd):
MEDICAL CONDITIONS AND HYPERBARIC OXYGEN THERAPY

MEDICAL CONDITION	PHYSIOPATHOGENESIS	MECHANISM(S) INVOLVED	DESIRED EFFECT(S)
Multiple sclerosis	- ?	- Tissue oxygenation?	- Recovery of nerve cell functions?
Acute renal failure	- Various.	- Tissue oxygenation?	
Malignant external otitis	- Infectious.	- Antiinfective action?	
Cyanide poisoning	- Binding with hemoglobin.	- Dissociation of cyanide-Hb bonds?	
Sports injuries (e.g., sprained ankle)	- Various.	- Antiinflammatory and antiedemic.	
Autoimmune diseases (e.g., Crohn's disease)	- Various.	- Tissue regeneration?	

APPENDIX B: THE DIFFERENT STAGES IN THE EVOLUTION OF OSTEORADIONECROSIS ACCORDING TO MARX *ET AL*'S CLASSIFICATION [192]

APPENDIX B:

THE DIFFERENT STAGES IN THE EVOLUTION OF OSTEORADIONECROSIS ACCORDING TO MARX *ET AL*'S CLASSIFICATION [192].

Summary

STAGE I

This stage includes all patients with osteoradionecrosis, except those with cutaneous fistulas, pathologic fractures or in whom there is radiographic evidence of bone resorption. These three categories of patients are classified as stage III cases.

Stage I patients undergo 30 sessions of hyperbaric oxygen therapy. In this stage, no other treatment or surgical removal of bone is undertaken. After these 30 sessions, depending on the objective signs of improvement in the lesion, the patient undergoes ten additional sessions of hyperbaric oxygen therapy or is otherwise considered a stage II case.

STAGE II

After a surgical assessment of the bone involvement (superficial or cortical), a sequestrectomy and limited tissue repair are performed. If the healing occurs without complications, a series of ten sessions of hyperbaric oxygen therapy is started. If there is no improvement, the patient advances to stage III.

STAGE III

After 30 sessions of hyperbaric oxygen therapy, plastic surgery is performed (debridements, closure, jaw fixation, etc.). More complicated cases advance to stage III-R.

STAGE III-R

Stage III-R patients are the most complex cases. The earlier tissue repair and tissue reconstruction are performed, the better the outcome. Treatment of these patients requires a certain number of conditions (asepsis and rigorous sterilization) and includes bone reconstruction, grafts and sessions of hyperbaric oxygen therapy.

APPENDIX C: STANDARD Z275.1-93 – HYPERBARIC FACILITIES – CANADIAN STANDARDS ASSOCIATION (CSA)

APPENDIX C: STANDARD Z275.1-93 – HYPERBARIC FACILITIES CANADIAN STANDARDS ASSOCIATION (CSA)

C.1 TABLE OF CONTENTS

Provided below, by way of an overview of CSA standard Z275.1-93, entitled “Hyperbaric Facilities – Occupational Health and Safety” (December 1993), is an abridged version of its table of contents. Sections that are not relevant to this report have been omitted.

C.2 Full text of Appendix D – Administration of Standard Z275.1-93

Appendix D: Administration

Notes:

1. *This Appendix is not a mandatory part of this Standard.*
2. *The following is a suggested administrative guideline for hyperbaric installations.*

D1 Responsibilities

D1.1 Responsibility of Safe Conditions and Practices

The establishment and continuation of safe practices, the maintenance and repair of equipment, the appointment of hyperbaric team, and the safe operation of the hyperbaric facility shall be the joint responsibility of the employer or governing body of a health care facility, its administrators, and all personnel using or operating the facility.

D1.2 Safety Director

A safety director shall be appointed by the employer or governing body of the health care facility. The safety director shall be responsible for the inspection and maintenance of the hyperbaric equipment; shall establish and maintain safe operating procedures, emergency procedures, and maintenance routines; and shall ensure that all personnel operating hyperbaric equipment and attending patients in the facility are appropriately qualified to perform their duties.

D1.3 Medical Director

A medical director shall be appointed by the employer or governing body of the heath care facility. The medical director shall be responsible for all medical aspects of the exposure of people to hyperbaric conditions and in concert with the safety director, shall ensure that safe practices and procedures are employed. The medical director shall also be responsible for the occupational heath and safety of personnel associated with hyperbaric facility. The medical director shall ensure there are other qualified physicians to attend to chamber operations in his or her place.

D1.4 Chamber operator

D1.4.1

During the operation of the chamber(s), one person shall be designated as the chamber operator. The chamber operator shall be responsible for the safe operation of the chamber according to established operating procedures.

D1.4.2

The chamber operator shall ensure the completion of written records documenting:

a) the purpose of the hyperbaric exposure;

b) the names and roles of personnel;

c) the names of persons exposed to pressure;

d) the pressure-time profile of the exposures; and

e) any equipment faults detected before, during, or after the hyperbaric exposure.

D1.4.3

A qualified back-up chamber operator shall be available at all times.

D1.5 Chamber attendant

During the operation of the chamber when people are exposed to pressure, one person shall be designated as the chamber attendant. The attendant shall be directly responsible to the chamber operator. The attendant shall accompany the persons being put under pressure in the chamber, ensure that the exposure is conducted safely and without harm to occupants, and shall be able to immediately intervene in an appropriate manner if necessary.

D1.6 Hyperbaric Team in Health Care Facilities

D1.6.1 Multiplace Chamber Hyperbaric Team

As a minimum in a multiplace chamber facility, a hyperbaric team shall consist of two chamber operators, an attendant and a physician who shall be immediately available within the health care facility during any hyperbaric exposure.

D1.6.2 Monoplace Chamber Hyperbaric Team

As a minimum in a monoplace chamber facility, a hyperbaric team shall consist of a chamber operator, a qualified back-up person, and a physician who shall be immediately available within the health care facility during any hyperbaric exposure.

D1.7 Hyperbaric Team in Occupational Diving and Compressed Air Work

As a minimum, a hyperbaric team shall consist of a supervisor and a chamber operator, both of whom shall be capable of operating the chamber and shall be present during a hyperbaric exposure. A physician shall be available for consultation, as required by CSA Standard Z275.2, during diving operations and as required by CSA Standard CSA Z275.3 during compressed air work operations.

D2 Qualifications of Personnel

D2.1 Safety Director

The safety director shall be knowledgeable, by training or experience, in the operation, maintenance, and repair of all the mechanical, electrical, liquid, and gas systems comprising the hyperbaric facility and shall be acceptable to the regulatory authority.

Note. *While not necessarily one of the chamber operators, it is suggested that the safety director be the senior of the chamber operators and a certified hyperbaric technologist or equivalent.*

APPENDIX D: STATISTICS ON HYPERBARIC CHAMBER INCIDENTS AND ACCIDENTS

Table D.1: Breakdown, by cause and type of system, of the outcomes of hyperbaric chamber incidents and accidents that occurred between 1923 and 1997

BREAKDOWN	OUTCOME		
	Injury	Death	Total number of victims
BY CAUSE			
FIRE	22	96	118
PRESSURE	22	8	30
OTHER	2	6	8
TOTAL	46	110	156
BY TYPE OF SYSTEM			
MULTIPLACE	16	81	97
MONOPLACE	11	18	29
BELL	1	5	6
OTHER	18	6	24
TOTAL	46	110	156

Source: *UHMS Chamber experience and mishap report 1998* [75]

APPENDIX E: NUMBER OF PATIENTS TREATED AT THE HÔPITAL DU SACRÉ-CŒUR DE MONTRÉAL'S HYPERBARIC MEDICAL CENTRE

Table E.1: Breakdown of the number of patients treated and of the number of cases of carbon monoxide poisoning by region of origin, Hôpital du Sacré-Cœur de Montréal, 1997

Patients' region of origin		Total number of patients treated	Cases of carbon monoxide poisoning
01 Lower St. Lawrence		5	5
02 Saguenay-Lac Saint-Jean		11	11
03 Québec City		13	10
04 Mauricie and Central Québec		13	12
05 Eastern Townships		8	7
06 Montréal Urban Community		22	11
07 Ottawa Valley		2	2
08 Abitibi-Témiscamingue		5	3
09 North Shore		3	3
10 Northern Québec		1	1
11 Gaspé Peninsula and the Magdeleine Islands		1	0
12 Chaudière-Appalaches		5	5
13 Laval		15	15
14 Lanaudière		19	18
15 Laurentians		22	19
16 Monteregia		23	17
17 Nunavik		0	0
18 Cree Territories and James Bay		0	0
Outside the Province	Ontario	1	1
	United States	1	1
TOTAL		**170**	**141**

* **Source**: Written communication from Dr. Mario Dugas, pneumologist, Hôpital du Sacré-Cœur de Montréal, Montréal, Québec.

APPENDIX F: ESTIMATE OF THE HOSPITAL COST/BENEFIT RATIO

APPENDIX F: ESTIMATE OF THE HOSPITAL COST/BENEFIT RATIO

F.1 Estimate for Québec

The cost/benefit ratio for hyperbaric oxygen therapy in Québec was determined from a hospital system perspective. The costs taken into account were those generated by HBO treatments, including physicians' fees. The benefits were calculated in terms of the reduction in the lengths of stay for patients with the medical conditions of interest. Two of the benefits of HBO that were not taken into account in this analysis were the lives that can be saved with HBO when potentially fatal conditions, such as carbon monoxide poisoning, are treated and the improvement in the quality of life of patients with chronic, painful and debilitating conditions. Furthermore, the cost savings generated by treatments provided outside hospitals were not taken into account.

Two scenarios were used to estimate the costs involved in meeting the potential demand. One of them, the status quo scenario, is based on the current output of the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre and yields a per-treatment cost of $333, based on its present value. The other, the full-capacity scenario, assumes that the hyperbaric centre operates at full capacity and yields a per-treatment cost of $156, based on the calculation made in Section 7.1.1.

The calculations were made for the entire province, then separately for the Greater Montréal and Greater Québec City Areas.

Economic impact in meeting the potential demand for the entire province

To meet the entire potential demand for HBO treatments as estimated in Chapter 6, the annual operating costs would be $20.4 million in the status quo scenario and $9.6 million in the full-capacity scenario. One can appreciate the difference between these figures and the costs associated with the current supply, which amount to the $230,000 operating budget of the Hôpital du Sacré-Coeur de Montréal's hyperbaric medical centre. Table F.1 shows the cost breakdown for the seven medical conditions for which HBO therapy is indicated as the main treatment or as an adjuvant treatment.

Estimate of benefits expressed in terms of the reduction in hospitalization costs

Table F.1 also shows the hospitalization costs for these seven medical conditions as calculated from the number of cases and the mean lengths of stay according to the MED-ÉCHO administrative database and assuming a per-diem hospitalization cost of $450. The total is $36.2 million. It is difficult to quantify, for each condition, the extent to which HBO treatments would reduce the lengths of stay, but the experience of a group of Italian researchers is interesting in this regard.

Marroni et al [190] calculated the hospital cost/benefit ratio of the hyperbaric treatments provided in a region of Italy for five of the most common indications, namely, decompression sickness and gas embolism, carbon monoxide poisoning, gas gangrene, necrotizing soft-tissue infections and problem wounds, and diabetic lesions. The authors compared the costs that would be generated if all eligible patients received HBO treatments with the savings ensuing from the reduction in the lengths of stay resulting from these treatments.

Table F.1: Hospitalization and HBO treatment costs for seven medical conditions. Scenario: All patients have timely access to a hyperbaric chamber
Entire province, 1996-1997

Medical condition	Hospitalization			HBO		
	Mean stay	Numbe r	Cost[1]	Number of treatments[2]	Cost[3] Status quo	Cost[4] Full capacity
CO poisoning	4.9	135	$297,675	162	$53,946	$25,272
Gas embolism	6.8	7	$12,240	14	$4,662	$2,184
Decompressio n sickness	2.9	3	$3,915	3	$999	$468
Maxillary osteoradionecrosis	2.3	366	$378,810	8,198	$2,729,934	$1,278,888
Leg ulcers	16.8	1,597	$12,073,320	9,582	$3,190,806	$1,494,792
Gas gangrene	15.2	49	$335,160	343	$114,219	$53,508
Diabetic lesions	21.5	2,393	$23,152,275	43,074	$14,343,642	$6,719,544
TOTAL		**4,550**	**$36,253,395**	**61,376**	**$20,438,208**	**$9,574,656**

[1] At $450/day.
[2] See Table 22 for details of the calculation.
[3] **Status quo scenario**: $333/90-minute treatment (3 patients at a time in the chamber; the physician monitors them from outside the chamber).
[4] **Full-capacity scenario:** $156/90-minute treatment (7 patients at a time in the chamber; the physician monitors them from outside the chamber).

The authors used hospitalization data from the region of Friuli-Venezia-Giulia and the model proposed by Persels, which was mentioned earlier. The average cost of a session of hyperbaric treatment was estimated at 120 euros (about $180) and that of a day of hospitalization at 300 euros (about $450).

Marroni *et al*'s analysis suggests potential net annual savings of approximately $7.8 million euros (about $11.8 million) if hyperbaric chamber treatments were provided systematically to the 575 patients with the five medical conditions of interest. These savings would result from a reduction of more than 30,000 of the 40,000 days of hospitalization per year usually due to the five conditions in question. The tables in Section F.2 show the data from this study.

If we apply this 75% reduction figure to the 80,500 days of hospitalization noted in Québec, we would obtain a reduction of 60,000 days of hospitalization, for hospitalization costs savings of $27 million, if all the eligible patients in the province received HBO treatments. Upon subtracting the $20 million that these treatments would cost (see Table 6.1, status quo scenario), we obtain potential annual savings of $7 million. In the full-capacity scenario, the potential savings would be $18 million.

The 75% reduction in the mean lengths of stay was not demonstrated convincingly in the Italian study. The authors merely give the lengths of stay without explaining the protocol used to compare the two situations (with and without HBO). Nothing indicated that such results would be achieved in Québec.

Based on our estimates, the HBO treatments would have to result in a reduction of at least 58% in the mean lengths of hospital stay for the seven medical conditions concerned in order for the $20 million they would cost per year in the status quo scenario to yield a positive hospital cost/benefit ratio (see Figure F.1). In the full-capacity scenario, the HBO treatments would have to result in a 28% reduction in the mean lengths of hospital stay to yield a positive ratio. In both cases, these reductions have yet to be demonstrated.

These data do not take into account the improvement in the patients' quality of life.

Economic impact for the Montréal and Québec City areas

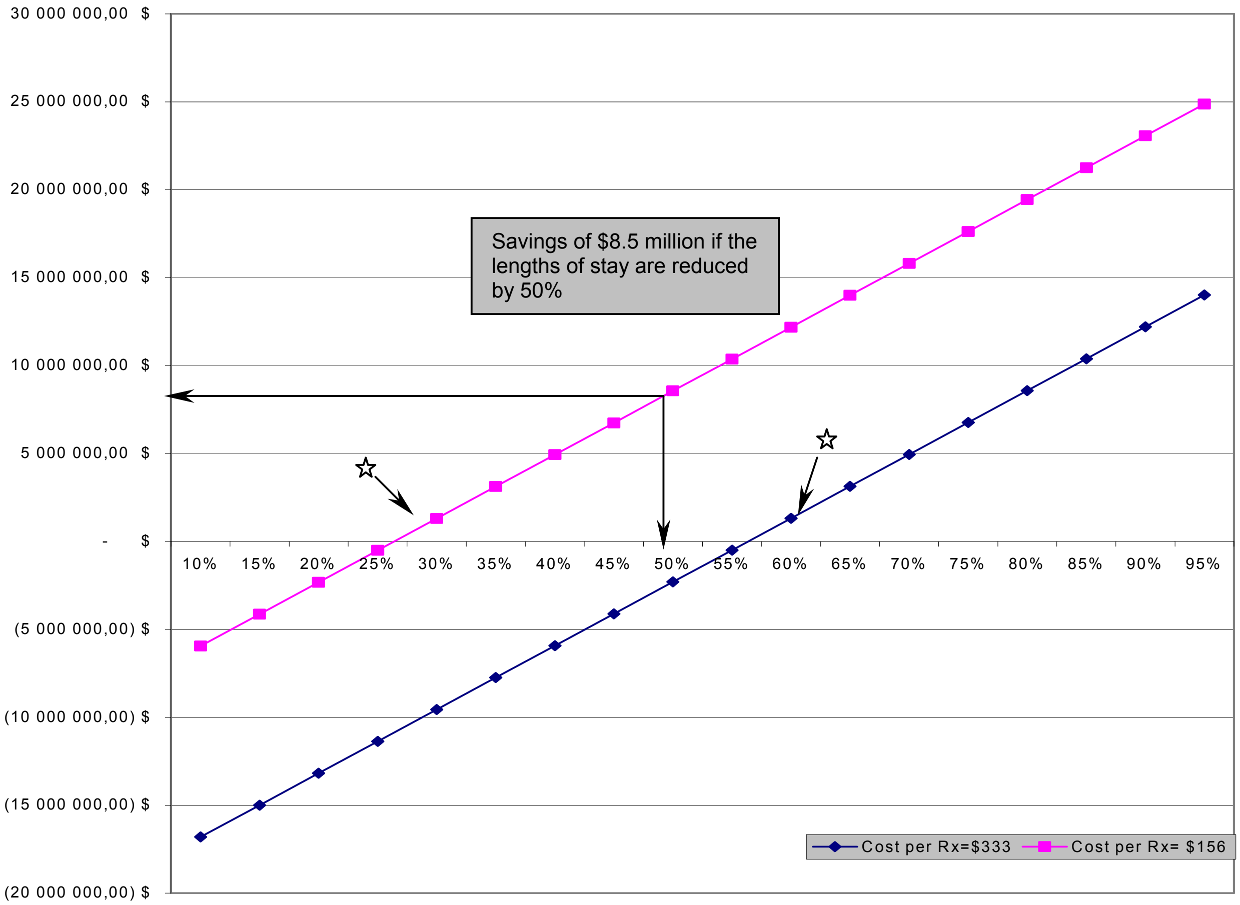
The data presented above pertain to the entire province. This assumes that all the patients would have access to a hyperbaric chamber within an hour's drive from their homes. The many treatments that would be provided to the nonemergency cases (osteoradionecrosis, diabetic lesions, etc.) involve up to 40 daily visits in a hyperbaric chamber. It is therefore not realistic to consider all these cases in the same manner, as if a hyperbaric chamber were available for everyone within a 50-km radius.

Using the criterion recognized in the literature, i.e., that a population of at least one million people within a 50-km radius is needed to support a hyperbaric medical centre, we redid the calculations for the only two areas that meet this criterion—the Greater Montreal Area and the Greater Québec City Area.

Tables F.2 and F.3 show the same calculations as for the entire province but for the Montréal and Québec City areas, respectively. The HBO treatment costs that would be incurred in meeting the potential demand in the Montréal area would be $6.4 million a year in the status quo scenario and $3 million in the full-capacity scenario.

As for the Québec City area, the annual hospitalization costs associated with the medical conditions in question would be $4.4 million. The HBO treatment costs that would be incurred in meeting the potential demand would be $2.5 million a year in the status quo scenario and $1.2 million in the full-capacity scenario. The number of annual treatments for the Greater Québec City Area estimated by the medical condition method was 7,500, exactly three times the number estimated with the population method (T = 2,500). If we apply the full-capacity scenario cost figures to the estimate of 2,500 treatments, we obtain an annual operating cost of $390,000. This figure is slightly less than the cost of operating a 7-person multiplace chamber, like the one at the Hôpital du Sacré-Coeur de Montréal, at full capacity (between $400,000 to $500,000)

Figure F.1: Hospital cost/benefit ratio by percent reduction in the lengths of stay achieved with hyperbaric oxygen therapy (entire province)



The x-axis represents the percent reduction in the lengths of stay achieved with hyperbaric oxygen therapy.
The y-axis represents the savings in hospitalization costs (benefits) minus the costs of HBO therapy (costs).

- The total hospitalization costs associated with the medical conditions of interest are estimated at $36.2 million.
- The total cost of HBO treatments that would be incurred in meeting the potential demand is estimated at $20.4 million in the status quo scenario (per-treatment cost of $333) and at $9.6 million in the full-capacity scenario (per-treatment cost of $156).

- **Examples if the per-treatment cost is $156**
    - If the HBO treatments result in a 50% reduction in the lengths of hospital stay, the cost/benefit ratio will be positive, with annual savings of $8.5 million.
    - If the HBO treatments result in a reduction in the length of hospital stay of only 20%, the cost/benefit ratio will be negative, with additional expenses of $4.1 million in a year.

☆ **The break-even point requires a reduction of 58% in the lengths of stay in the status quo scenario and of 28% in the full-capacity scenario.**

Table F.2: Hospitalization and HBO treatment costs for seven medical conditions
Scenario: Limited access to a hyperbaric chamber
Greater Montreal Area, 1996-1997

Medical condition	Hospitalization			HBO		
	Mean stay	Numbe r	Cost[2]	Number of treatments[3]	Cost[4] Status quo	Cost[5] Full capacity
CO poisoning[1]	5.2	77	$180,180	92	$30,636	$14,352
Gas embolism	6.8	4	$12,240	8	$2,664	$1,248
Decompression sickness	2.9	1	$1,305	1	$333	$156
Maxillary osteoradionecrosis	2.0	63	$56,700	1,411	$469,863	$220,116
Leg ulcers	21.1	667	$6,333,165	4,002	$1,332,666	$624,312
Gas gangrene	17.0	10	$76,500	70	$23,310	$10,920
Diabetic lesions	24.0	758	$8,186,400	13,644	$4,543,452	$2,128,464
TOTAL		**1,580**	**$14,846,490**	**19,228**	**$6,402,924**	**$2,999,568**

1 Includes all cases in western Québec.
2 At $450/day.
3 See Table 22 for the coefficients used in the calculations.
4 **Status quo scenario**: $333/90-minute treatment (3 patients at a time in the chamber, with the physician monitoring them from outside the chamber).
5 **Full-capacity scenario:** $156/90-minute treatment (7 patients at a time in the chamber, with the physician monitoring them from outside the chamber).

Hospital cost/benefit ratio

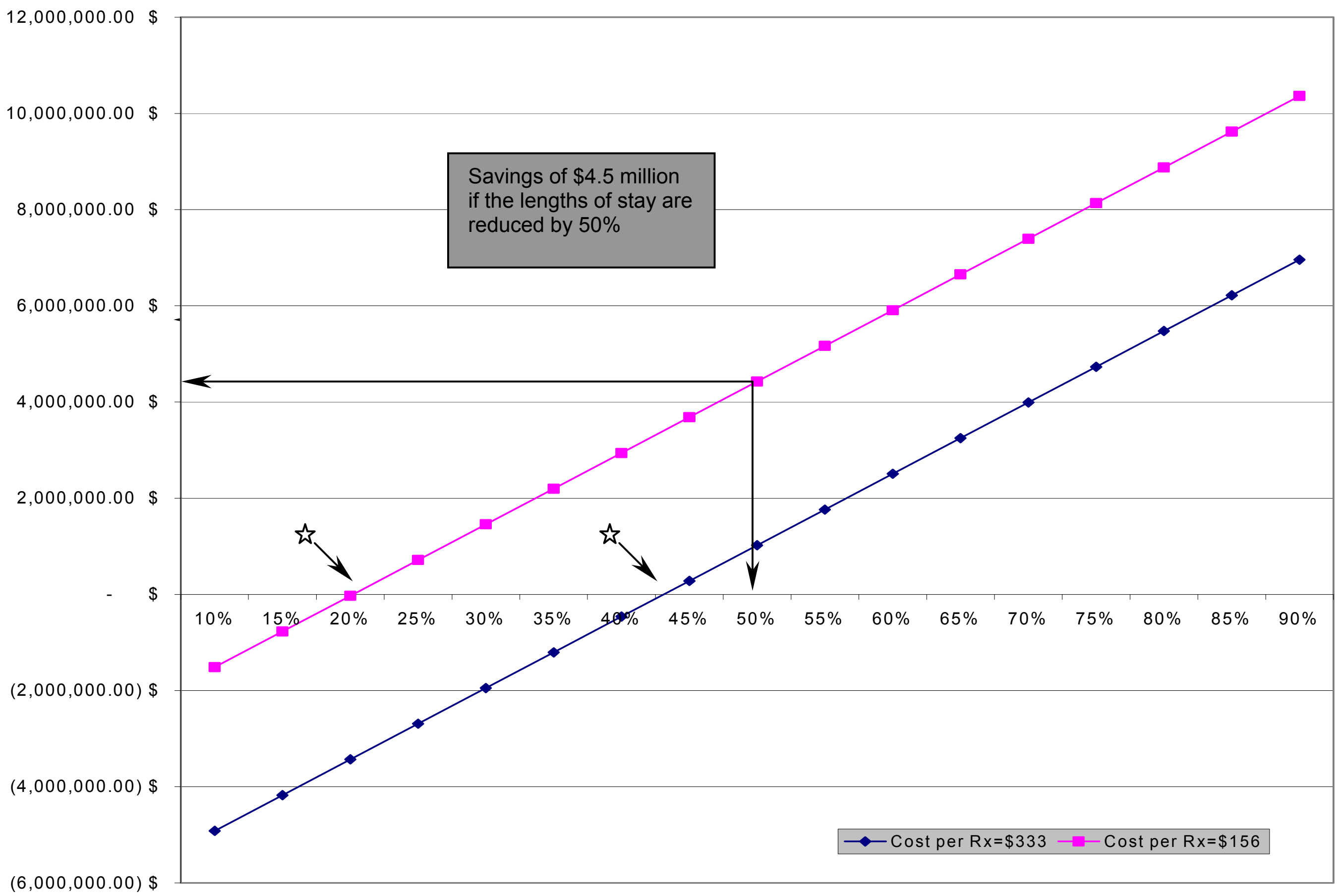
Figures F.2 and F.3 show the hospital cost/benefit ratios for HBO treatments in the Montréal and Québec City areas, respectively.

For the Greater Montréal Area, in the status quo scenario, the HBO treatments would have to result in a reduction of at least 43% in the mean lengths of hospital stay to yield a favourable cost/benefit ratio. In the full-capacity scenario, a 20% reduction would be necessary (see Figure F.2).

For the Greater Québec City Area, in the status quo scenario, the HBO treatments would have to result in a reduction of at least 57% in the mean lengths of hospital stay for the medical conditions concerned to yield a favourable cost/benefit ratio. In the full-capacity scenario, a 26% reduction would be necessary (see Figure F.3).

These reductions have yet to be demonstrated.

Figure F.2: Hospital cost/benefit ratio by percent reduction in the lengths of stay achieved with hyperbaric oxygen therapy (Greater Montréal Area)



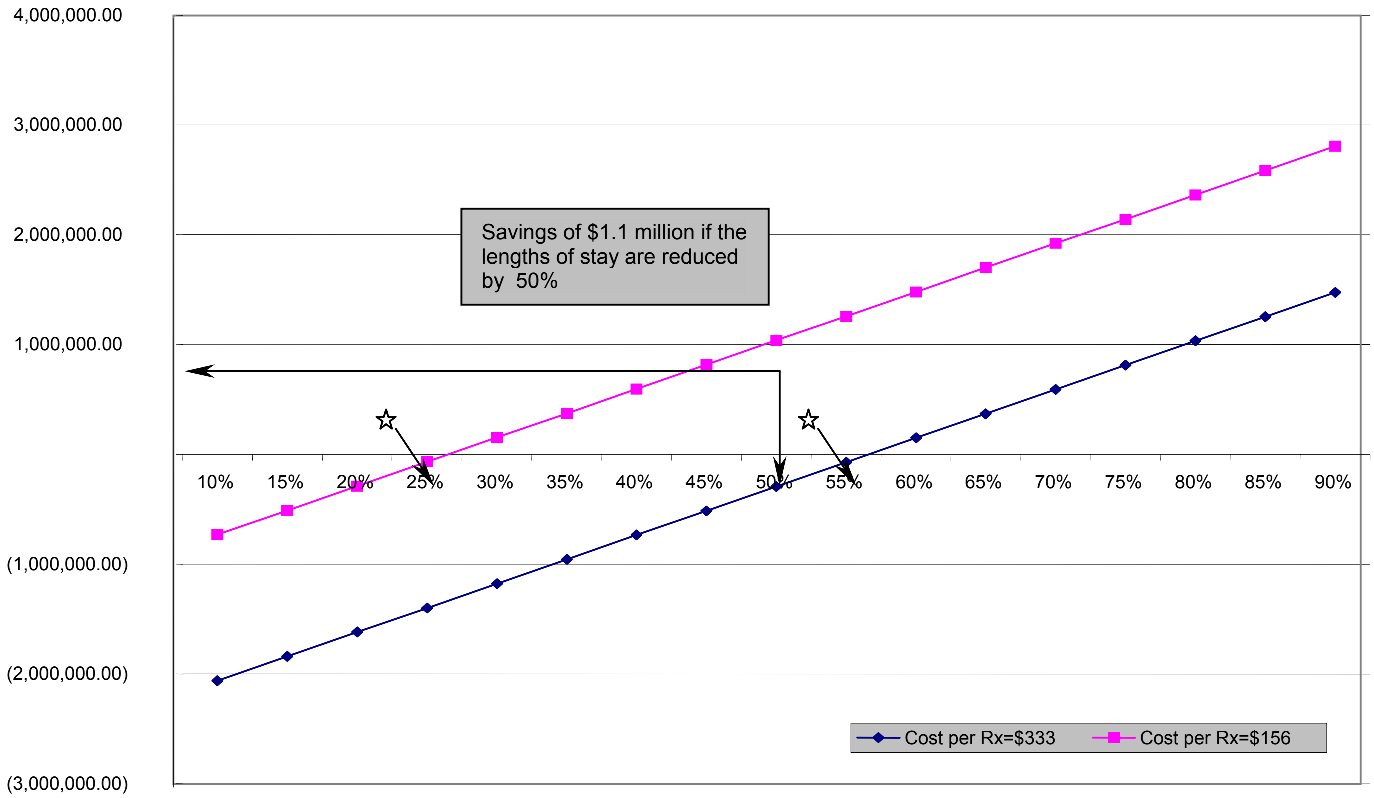
The x-axis repersents the percent reduction in the lengths of stay achieved with hyperbaric oxygen therapy.
The y-axis repersents the savings in hospitalization costs (benefits) minus the costs of HBO therapy (costs).

- The total hospitalization costs associated with the medical conditions of interest are estimated at $14.8 million.
- The total cost of HBO treatments that would be incurred in meeting the potential demand is estimated at $6.4 million in the status quo scenario (per-treatment cost of $333) and at $3.0 million in the full-capacity scenario (per-treatment cost of $156).

- **Examples if the per-treatment cost is $156**
  - If the HBO treatments result in a 50% reduction in the lengths of hospital stay, the cost/benefit ratio will be positive, with annual savings of $4.5 million.
  - If the HBO treatments result in a reduction in the lengths of hospital stay of only 20%, the cost/benefit ratio will be neutral.

☆ **The break-even point requires a reduction of 43% in the lengths of stay in the status quo scenario and of 20% in the full-capacity scenario.**

Figure F.3: Hospital cost/benefit ratio by percent reduction in the lengths of hospital stay achieved with hyperbaric oxygen therapy (Greater Québec City/Chaudière-Appalaches Areas)



The x-axis represents the percent reduction in the lengths of stay achieved with hyperbaric oxygen therapy.
The y-axis represents the savings in hospitalization costs (benefits) minus the costs of HBO therapy (costs).

- The total hospitalization costs associated with the medical conditions of interest are estimated at $4.4 million.
- The total cost of HBO treatments that would be incurred in meeting the potential demand is estimated at $2.5 million in the status quo scenario (per-treatment cost of $333) and at $1.2 million in the full-capacity scenario (per-treatment cost of $156).

- **Examples if the per-treatment cost is $156**
- If the HBO treatments result in a 50% reduction in the lengths of hospital stay, the cost/benefit ratio will be positive, with annual savings of $1.1 million.
- If the HBO treatments result in a reduction in the lengths of hospital stay of only 20%, the cost/benefit ratio will be negative, with additional expenses of $288,000 in a year.

☆ **The break-even point requires a reduction of 57% in the lengths of stay in the status quo scenario and of 26% in the full-capacity scenario.**

Table F.3: Hospitalization and HBO treatment costs for seven medical conditions Scenario: Limited access to a hyperbaric chamber Greater Québec City/Chaudière-Appalaches Areas, 1996-1997

Medical condition	Hospitalization			HBO		
	Mean stay	Numbe r	Cost[2]	Number of treatments[3]	Cost[4] Status quo	Cost[5] Full capacity
CO poisoning[1]	4.9	58	$127,890	70	$23,310	$10,920
Gas embolism	6.8	3	$9,180	6	$1,998	$936
Decompressio n sickness	2.2	2	$1,980	2	$666	312
Maxillary osteoradionecrosis	4.5	44	$89,100	986	$328,338	$153,754
Leg ulcers	17.1	170	$1,308,150	1,020	$339,660	$159,120
Gas gangrene	14.4	10	$64,800	70	$23,310	$10,920
Diabetic lesions	21.0	298	$2,816,00	5,364	$1,786,212	$836,784
TOTAL		**585**	**$4,417,100**	**7,517**	**$2,503 494**	**$1,172,808**

1 Includes all cases in eastern Québec.
2 At $450/day.
3 See Table 22 for the coefficients used in the calculations.
4 **Status quo scenario**: $333/90-minute treatment (3 patients at a time in the chamber; the physician monitors them from outside the chamber).
5 **Full-capacity scenario:** $156/90-minute treatment (7 patients at a time in the chamber; the physician monitors them from outside the chamber).

F.2 Details of the estimate in the Italian study by Marroni *et al*

Marroni *et al* [190] used the model proposed by Persels [243] to estimate the number of treatments required for each medical condition, including a coefficient accounting for patients who were not hospitalized but who were seen on an outpatient basis only.

The following tables show, for each condition, the mortality rate, the morbidity rate and the length of hospital stay for patients who received and those who did not receive HBO therapy. The per-patient cost incurred for the HBO treatments and the per-patient costs saved in terms of days of hospitalization are indicated as well.

Table F.4: Indices used by Marroni *et al* to calculate the potential number of HBO treatments [190]

Diagnosis	C_1	C_2	C_3
Decompression sickness	1	1	5
Gas embolism	1	1	5
CO poisoning	1	0.6	5
Gas gangrene	1	1	13
Necrotizing soft-tissue infections	1	0.5	30
Problem wounds	1.4	0.4	40
Diabetic gangrene	1.5	0.3	50

C_1: Coefficient taking nonhospitalized cases into account
C_2: Proportion of patients whose condition warrants HBO therapy
C_3: Average number of treatments required

Table F.5: Mortality, morbidity, hospitalization and cost data by medical condition and by use or nonuse of HBO therapy according to Marroni *et al*'s study

	Mortality	Morbidity	Hospitalization	HBO costs/patient (euros)	Cost savings/patient* (euros)
Decompression sickness and gas embolism					
HBO	< 1%	< 10%	10 days	600	-
No HBO	< 1%	> 80%	> 90 days		> 20,000
Carbon monoxide poisoning					
HBO	< 1.7%	4%	< 15 days	600	-
No HBO	< 7%	> 30%	> 30 days		> 20,000
Gas gangrene					
HBO	< 20%	< 15% (amputation)	< 7 days (acute) < 40 days (chronic)	1,560 3,600	-
No HBO	> 49%	> 60% (amputation)	> 15 days (acute) > 90 days (chronic)		> 20,000
Necrotizing soft-tissue infections					
HBO	< 20%	< 25%	< 15 days	3,600	-
No HBO	> 50%	> 60%	> 30 days		> 1,000
Problem wounds					
HBO	< 5% (amputation)	< 15% (amputation)	< 40 days	4,800	-
No HBO	> 15% (amputation)	> 90% (amputation)	> 100 days		> 13,000
Diabetic gangrene					
HBO	-%	< 5% (amputation)	< 60 days	6,000	-
No HBO	> 31% (amputation)	> 30% (amputation)	> 100 days		> 6,000

Source: Marroni *et al*, 1998 [190].
*By not providing HBO

Table F.6: Determination of the number of HBO treatments and the related costs for the region of Friuli-Venezia-Giulia according to Marroni *et al* (in euros)

Medical condition	Hospitalizations	Number of treatments (# of hosp. x C_1 x C_2 x C_3)		HBO costs (euros)
CO poisoning	11	11 x 1 x 0.6 x 5 =	33	3,960
Gas gangrene	37			
Acute		37 x 1 x 1 x 13 =	480	57,720
Chronic		37 x 1 x 1 x 30 =	1,110	133,200
Soft-tissue infections	184	184 x 1 x 0.5 x 30 =	2,760	331,200
Diabetic gangrene	54	54 x 1.5 x 0.3 x 50 =	1,215	145,800
Problem wounds	288	288 x 1.4 x 0.4 x 40 =	6,451	774,120
TOTAL	574		12,050	1,446,000

Source: Marroni *et al*, 1998 [190]

C_1: Coefficient taking nonhospitalized cases into account
C_2: Proportion of patients whose condition warrants HBO therapy
C_3: Average number of treatments required

Table F.7: Estimate of the total HBO costs and of the savings achieved by reducing the lengths of hospital stay, according to Marroni *et al*'s study (in euros)

Medical condition	HBO costs (a)	Cost savings from reduction of hospitalization (b)	Net savings (b-a)
CO poisoning	3,960	49,500	45,540
Gas gangrene			
Acute	57,720	77,000	19,280
Chronic	133,800	555,000	421,800
Soft-tissue infections	331,200	2,760,000	2,428,800
Diabetic gangrene	145,800	648,000	502,200
Problem wounds	774,120	5,184,000	4,409,880
TOTAL	1,446,000	9,273,500	7,827,500

Source: Marroni *et al*, 1998 [190]

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