

**A Survey of the Knowledge of the Military and
Civilian Medical Practitioners in the Royal
Medical Service in the Kingdom of Bahrain
with regards to the Clinical Application of
Hyperbaric Oxygen Therapy**

Dr. AAM Abdulaal

Thesis presented in partial fulfillment of the degree
Master of Science (Baromedical Sciences)
at the University of Stellenbosch

Supervisor: Dr. WAJ Meintjes

March 2012

Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Date: T æ&@Á€FG

Verklaring

Deur hierdie tesis elektronies in te lewer, verklaar ek dat die geheel van die werk hierin vervat, my eie, oorspronklike werk is, dat ek die alleenouteur daarvan is (behalwe in die mate uitdruklik anders aangedui), dat reproduksie en publikasie daarvan deur die Universiteit van Stellenbosch nie derdepartyregte sal skend nie en dat ek dit nie vantevore, of in die geheel of gedeeltelik, ter verkryging van enige kwalifikasie aangebied het nie.

Datum: Tædø AGFG

Abstract

A survey was conducted between 3 August and 5 October 2011 to test and evaluate the knowledge and attitudes of the military and civilian medical practitioners at the royal medical Service in the kingdom of Bahrain with regards to the clinical application of hyperbaric oxygen therapy. The survey consisted of a questionnaire and a semi-structured interview in which a total of 93 (out of a possible 302) medical practitioners were included (13 participated in the interviews).

Similar to findings of previous studies, the knowledge of medical practitioners in Bahrain regarding hyperbaric oxygen therapy was low. Several practitioners were able to mention at least one indication for the therapy. No single factor had a statistically significant association with knowledge or the lack thereof. A large proportion of the participants had a positive attitude towards the use of hyperbaric oxygen therapy, felt that it is a valid treatment modality and they would refer their patients for such treatment. They would like to receive more information on hyperbaric oxygen therapy.

Educational interventions to address the knowledge gap would likely be effective, since most participants have a positive attitude towards the therapy and believe that it is cost-effective.

Acknowledgements

In the name of God, most grateful and mighty...

I would first like to thank God for giving me the strength to continue with my education and to finish my thesis. I would also like to thank the Director of the Bahrain Royal Medical Services, my supervisor, whose ongoing mentorship and ongoing support was much appreciated, and all the staff of the Bahrain Royal Medical Services who agreed to participate in this research project. I would also like to thank my family for their ongoing support and to everyone who has stood by me during this period.

Table of Contents

Declaration	2
Verklaring	2
Abstract	3
Acknowledgements	4
Table of Contents	5
List of and figures	8
List of Tables	8
Introduction	9
Literature review	9
Definition and description of hyperbaric oxygen therapy	9
The history of hyperbaric oxygen therapy	11
The UHMS-approved indications for hyperbaric oxygen therapy	12
Indications recommended by the European Committee for Hyperbaric Medicine	12
Description of the approved hyperbaric oxygen therapy indications	14
Decompression sickness	14
Carbon monoxide poisoning; cyanide poisoning	16
Air or gas embolism	17
Clostridial myositis and myonecrosis (gas gangrene)	18
Crush injuries, compartment syndromes and other acute traumatic peripheral ischaemias	19
Enhancement of healing in selected problem wounds	20
Exceptional blood loss anaemia	21
Intracranial abscesses	22
Compromised skin flaps and grafts	22
Necrotizing soft tissue infections	24
Refractory osteomyelitis	25
Delayed radiation injury (soft tissue and bony necrosis)	26

Thermal burns	27
Mechanisms of action of HBO	28
Hyperoxygenation	28
Stimulation of tissue growth and Angiogenesis	30
Fibroblast proliferation and collagen deposition	31
Effects on microorganisms and host immune response	31
Antibiotic activity enhancement	31
Vasoconstriction	32
Increased pressure and creation of gas gradients	32
Production of Nitric Oxide (NO)	32
Safety and the side-effects of HBO therapy	33
Pressure-related side effects.....	33
Oxygen toxicity	33
Reversible myopia.....	34
Irreversible cataracts	34
Previous similar studies on the subject	35
Study aim and objectives	35
Methodology.....	36
Review by Health Research Ethics Committees	36
Study design	36
Study Setting.....	36
Study participants.....	37
Inclusion criteria	37
Exclusion criteria	38
Sampling methods and sample size.....	38
Data sources and data collection	38
Data management and statistical analysis	39
Ethical aspects	39
Survey component results.....	40

Study participants.....	40
Descriptive data	41
Knowledge of hyperbaric oxygen therapy	42
Knowledge of contra-indications	44
Factors associated with knowledge of hyperbaric oxygen therapy.....	47
Lickert scale responses.....	47
Semi-structured interview component results.....	50
Study participants.....	50
Findings.....	50
Participants' knowledge of hyperbaric oxygen therapy indications within their field of work.....	50
Knowledge regarding the mechanisms of action of hyperbaric oxygen therapy.....	51
Knowledge regarding the levels of evidence existing for hyperbaric oxygen therapy	51
Referral of patients and including hyperbaric oxygen therapy in their practice.....	52
Discussion	53
Study participants.....	53
Participant knowledge of hyperbaric oxygen therapy	55
Lickert scale responses.....	57
Referral of patients	59
Conclusion	59
References	60
Addenda.....	72
Addendum 1: Stellenbosch University Health Research Ethics Committee Approval.	73
Addendum 2: Ethics approval letter from the Royal Medical Services of the Kingdom of Bahrain.....	74
Addendum 3: The research questionnaire	75
Addendum 4: Informed consent document for the research questionnaire	77
Addendum 5: Informed consent document for the structured interview	81
Addendum 6: Structured interview guidelines	86

List of and figures

Figure 1: A monoplace hyperbaric chamber.....	10
Figure 2: A multiplace hyperbaric chamber	10
Figure 4: Bar chart of the frequency by which each clinical department was represented in the survey	41
Figure 5: Bar chart of the number of participants at a specific level of appointment	42
Figure 6: Bar chart of the number of times a specific indication for hyperbaric oxygen therapy was mentioned by participants	43
Figure 7: Bar chart of the percentage of participants mentioning a specific indication who also considers the indication to fall within their specialty	44
Figure 8: Bar chart indicating the participants' responses to the Lickert scale statements.....	49

List of Tables

Table 1: The UHMS approved indications for hyperbaric oxygen therapy.....	12
Table 2: The ECHM accepted indications for hyperbaric oxygen therapy	13
Table 3: Theoretical arterial oxygen tension and blood oxygen content for different treatment protocols:.....	30
Table 4: Frequency table of contra-indications cited by study participants.....	46
Table 5: Factors associated with knowledge of more than 7 indications for hyperbaric oxygen therapy.....	47
Table 6: Mortality, morbidity, hospital stay and cost of HBO versus non-HBO in diabetic patients	58

Introduction

Although strong evidence has been growing recently to support the application of hyperbaric oxygen therapy (HBOT) in the treatment of acute and chronic diseases, the implementation of HBOT as an adjunctive therapy still seems to be limited. This may be due to the fact that very few academic programmes at medical schools contain elements of hyperbaric medicine and most medical practitioners have little or no knowledge about HBOT or its practice. Furthermore, because it has a high potential for monetary exploitation and unethical application, a high degree of medical skepticism has developed regarding its use^[1, 2].

Recognizing the need for an evidence-based approach to hyperbaric medicine practice, medical practitioners involved in hyperbaric medicine have conducted randomized trials to investigate the application of HBOT and a number of Cochrane reviews have subsequently been performed^[3-21]. The extent to which this information is known by clinicians is however unknown.

The primary investigator completed his postgraduate studies in hyperbaric medicine and is planning to open the first hyperbaric medical centre in the Kingdom of Bahrain. It is however important to establish the level of knowledge of this type of therapy amongst colleagues who would have to refer patients in future, as well as their attitudes towards this kind of therapy. This would identify possible knowledge gaps that could be addressed by means of continuous medical education events and provide valuable information regarding the future of this treatment modality within this setting.

Literature review

Definition and description of hyperbaric oxygen therapy

“HBOT is a treatment modality in which a patient breathes 100% oxygen while inside a treatment chamber at a pressure higher than sea level pressure” (101 kPa or one atmosphere)^[22, 23]. This then leads to specific therapeutic physiological effects.

Breathing 100% oxygen at one atmosphere (as commonly happens in many hospital situations) is not considered hyperbaric in nature or effect.

The treatment can be provided in either a monoplace hyperbaric chamber (where the chamber is usually compressed with 100% oxygen), which can accommodate one patient.

Figure 1: A monoplace hyperbaric chamber



A multiplace hyperbaric chamber could accommodate more than one person. Such a chamber is normally compressed with air and the oxygen is provided via an oxygen mask or head tent.

Figure 2: A multiplace hyperbaric chamber



The history of hyperbaric oxygen therapy

The alteration of atmospheric pressure in the treatment of certain medical conditions dates back more than 300 years. In 1664 Henshaw advocated treating acute and chronic diseases of all kinds by the modification of atmospheric pressure^[24]. The equipment used in this era (and the pressures at which the treatments were given) likely only had a placebo effect. In the 1870s, a French surgeon named Fontaine converted an early chamber into the first hyperbaric operating room^[25]. Several surgeons performed operations within hyperbaric chambers and reported favorable results^[26].

Lorraine-Smith recorded in 1899 that after providing 73% of oxygen at 101kPa of pressure, a fatal pneumonia developed in rats, thus reporting toxic effects of hyperbaric oxygen (HBO₂) on the lungs^[27]. In 1878 Paul Bert published a paper describing that breathing oxygen under pressure can cause a grand mal seizure and effect the central nervous system^[27, 28]. HBOT in clinical medicine started with Churchill-Davidson and Boerema in 1955 and 1956^[26, 29]. A growing concern in early 1960's by both hyperbaric and general physicians was that this treatment modality was being applied indiscriminately. There was also a lack of scientific approach in the implementation of HBOT and a lack of a regulatory body. Although HBO₂ is used in the treatment of decompression sickness, there used to be a schism between diving medicine and hyperbaric medicine and it required a crisis of funding being revoked due to indiscriminate and unscientific use. These concerns led to the establishment of a HBOT Committee, which produced its first critical work under Enrico Camporesi as editor – a critical appraisal of HBOT that became the template for the HBOT Committee Report of the Undersea Medical Society (UMS). The committee became an internationally recognized authority on accepted indications for hyperbaric oxygen therapy. They regularly update and publish a list of accepted indications and discriminate between those conditions that are approved for treatment and those that are supported by sound scientific theory but are still requiring research. The UMS is now known as the UHMS (Undersea and Hyperbaric Medical Society).

The UHMS-approved indications for hyperbaric oxygen therapy

The following indications (listed in Table 1) are approved uses of hyperbaric oxygen therapy as defined by the Hyperbaric Oxygen Therapy Committee^[22].

Table 1: The UHMS-approved indications for hyperbaric oxygen therapy

1	Air or gas embolism
2	Carbon monoxide poisoning; cyanide poisoning
3	Clostridial myositis and myonecrosis (gas gangrene)
4	Crush injuries, compartment syndromes and other acute traumatic peripheral ischaemias
5	Decompression sickness
6	Enhancement of healing in selected problem wounds
7	Exceptional blood loss anaemia
8	Intracranial abscess
9	Necrotizing soft tissue infections
10	Refractory osteomyelitis
11	Skin flaps and grafts (compromised)
12	Delayed radiation injury (soft tissue and bony necrosis)
13	Thermal burns
14	Acute retinal artery occlusion

The indications listed on this table are all considered (after review of the literature and evidence) to have sufficient evidence of benefit and enough information is available to indicate a cost-benefit ratio that is favourable, meaning that a treatment regime that excludes HBOT would be more expensive than one which includes HBOT.

Indications recommended by the European Committee for Hyperbaric Medicine

The European Committee for Hyperbaric Medicine (ECHM) evaluates the indications for inclusion in their list of “recommended indications” by means of conducting

consensus conferences, in which the indications to be recommended are agreed on by means of a consensus statement that is formulated^[30]. This is done by means of having experienced clinicians (who are considered experts in their field) present opposing views regarding the use of hyperbaric oxygen for a specific indication and then drafting a consensus statement afterwards. Table 2 (below) provides a list of indications recommended by the ECHM (with the levels of evidence presented)^[30].

Table 2: Accepted indications for HBO therapy (7th ECHM Consensus Conference, Lille 2004)

Condition	Accepted		
Level of Evidence*	A	B	C
Type I: Strongly Recommended <i>(The jury considers the implementation of the recommendation of critical importance for final outcome of the patient/ quality of practice/ future specific knowledge)</i>			
CO Poisoning		X	
Crush syndromes		X	
Prevention of osteoradionecrosis after dental extraction		X	
Osteoradionecrosis of the mandible		X	
Soft tissue radionecrosis (cystitis)		X	
Decompression accidents			X
Gas embolism			X
Anaerobic or mixed bacterial anaerobic infections			X
Type II: Recommended <i>(The jury considers the implementation of the recommendation as positively affecting final outcome of the patient/ quality of practice/ future specific knowledge)</i>			
Diabetic foot lesions		X	
Compressed skin grafts and musculocutaneous flaps			X
Osteoradionecrosis (other bones)			X
Radio-induced proctitis or enteritis			X
Radio-induced lesions of soft tissues			X
Surgery and implant in irradiated tissue (prophylaxis)			X

Sudden deafness			X
Ischaemic ulcers			X
Refractory chronic osteomyelitis			X
Neuroblastoma Stage IV			X
Type III: Optional <i>(The jury considers the implementation of the recommendation as an option)</i>			
Post anoxic encephalopathy			X
Larynx radionecrosis			X
Radio-induced CNS lesions			X
Post-vascular procedure reperfusion syndrome			X
Limb re-implantation			X
Burns > 20% of surface area and 2 nd degree			X
Acute ischemic ophthalmological disorders			X
Selected non-healing wounds			X
Pneumatosis cystoids intestinalis			X
<p>* The levels of evidence:</p> <p>A: Recommendation supported by level 1 evidence (at least 2 concordant, large, double-blind, controlled, randomized studies with little or no methodological bias).</p> <p>B: Recommendation supported by level 2 evidence (double-blind controlled, randomized studies but with methodological flaws; studies with only small samples, or only a single study).</p> <p>C: Recommendation supported only by level 3 evidence (consensus opinion of experts).</p>			

Description of the approved hyperbaric oxygen therapy indications

Decompression sickness

Decompression sickness (DCS) has many synonyms. These include Caisson's disease, the "bends," compressed air sickness, or diver's paralysis. DCS is a direct result of bubble formation within bodily tissues and the subsequent pathophysiologic changes induced by these bubbles. Although DCS may follow exposure to increased pressures, as in compressed gas or scuba diving, it can also follow rapid climbs in altitude or switches in breathing gas or the ambient (i.e. surrounding) gas medium during a hyperbaric exposure.. Because of its implications in operating jet aircraft and the space shuttle, DCS is a subject of research even in aerospace medicine^[31-33]. DCS has been reported to occur in auxiliary medical personnel who accompany

and treat patients within multi-place chambers^[34, 35]. After breathing compressed inert gases over a period of time, the partial pressures of the different gases reach new equilibriums within a person's tissues (in accordance with Henry's Law). In the case of nitrogen, for example, it is five times as soluble in fat as in air and becomes concentrated within fatty tissues, including the brain. Unless adequate time is allowed during decompression for their elimination, the gases previously dissolved in solution or in tissues may form bubbles. Since oxygen is rapidly consumed and nitrogen is basically inert, these bubbles are mainly composed of nitrogen. Because of the relatively poor circulation in fatty and cartilaginous tissues, a longer time is required for the elimination of gases from these tissues.

Although reductions in ambient pressure in a ratio of 2:1 were tolerated in Haldane's experiments with goats to a maximum of 606 kPa, this ratio was later found to be optimistic^[36, 37]. The true ratio is probably closer to 1.5:1^[37]. That is, DCS is unlikely when ascending from example a pressure of 303 kPa to 202 kPa but DCS may be expected if one ascends from 303 kPa to 101 kPa. Therefore, DCS is rare in dives of less than 202 kPa or climbs of less than 5,550 meters in unpressurised aircraft. It is possible to dive safely to depths greater than 202 kPa or to ascend to altitudes higher than 5,555 ft. To do so, however, requires a combination of ascent rates and pauses at certain depths or altitudes during ascent to allow excess inert gas to be eliminated before continuing decompression to the next level. In the case of compressed gas diving, this is called stage decompression. Decompression sickness can be prevented by adequate decompression times and performing decompression stops at appropriate depths for sufficient times, following different diving tables. It is important to realize that these diving tables (guidelines) are not completely safe and still have an associated decompression sickness incidence of between 1 and 5 percent^[38].

Hyperbaric oxygen ("recompression therapy") is recommended and approved for the treatment of DCS, based on the principle that it reduces the size of the bubbles which then move to smaller, more distal vessels. Recompression also hastens the dissolution and absorption of bubbles and eliminates inert gas more effectively by reducing the inspired inert gas partial pressure through the choice of therapeutic breathing gas - usually oxygen. Increased oxygen tensions help minimize ischemic

damage in the distal, hypoxic areas. In addition, by using 100% oxygen, nitrogen is removed from the bubbles and tissues at a faster rate (through counter diffusion).

The standard treatment for DCS is referred to as the “long oxygen table”, in which the patient is recompressed to an initial depth of 18m and breathes HBO_2 for 90 to 150 minutes, after which the pressure is slowly reduced over 30 minutes to a treatment depth of 9m and HBO_2 is provided for a further 150 to 300 minutes. The pressure is then again reduced slowly over 30 minutes until the ambient atmospheric pressure is reached. The oxygen is usually given for 25 minutes, followed by a 5 minute air break in repeated fashion. The total treatment usually lasts between 4 hours and 45 minutes, but can last up to 8 hours and 10 minutes in severe cases. If complete resolution of symptoms is not attained following the initial recompression, further recompression sessions could be provided (usually at a pressure of 240 kPa for 90 minutes) daily until no further improvement in symptoms is noted for two consecutive days.

Carbon monoxide poisoning; cyanide poisoning

Carbon monoxide (CO) poisoning is a complex event involving more than just the generation of carboxyhaemoglobin and the subsequent unavailability of haemoglobin to transport oxygen. CO is a systemic toxin capable of producing hypoxia at the cellular level in a number of ways. First, CO has an affinity for haemoglobin approximately 200 to 250 times greater than oxygen's^[39]. Therefore, even in environments containing only small quantities of CO, haemoglobin rapidly binds CO and becomes unavailable for the transportation of oxygen. CO also binds to other haeme pigments such as myoglobin. Second, once bound to haemoglobin, CO adversely affects the oxygen-haemoglobin dissociation curve, shifting it to the left. Oxygen already combined with haemoglobin becomes more firmly attached and a tissue oxygen tension much lower than normal is required before the oxygen is released, thus leading to tissue hypoxia. Lastly, once in the mitochondria, CO binds to the cytochrome oxidase enzymes responsible for cellular respiration, especially cytochrome a,a_3 ^[40], the terminal enzyme in the electron transport chain. This inhibits the final step in oxidative phosphorylation - the energy transfer from the

formation of metabolic water required for the production of ATP from ADP. The end result is oxygen becomes less available to meet the cell's metabolic needs and death by cellular anoxia results with the release of cytochrome C and large amounts of reactive oxygen species as the terminal events. . In fires there may be a complex mixture of fumes such as carbon monoxide, cyanide and other gases. Cyanide inhaled in this combination with carbon monoxide and smoke inhalation is a recommended indication for hyperbaric oxygen therapy, since it could be fatal as a result of cytotoxic hypoxia, which leads to organ dysfunction and possibly death^[41].

Hyperbaric oxygen therapy is approved and recommended for the treatment of selected cases of CO poisoning, based on the theoretical principles of action and the fact that previous studies have excluded patients who would “obviously” benefit from this treatment modality (in these studies they have received HBO and were thus excluded from analysis). There is still a lot of debate regarding the application of hyperbaric oxygen therapy in carbon monoxide poisoning^[42, 43].

Recently a number of randomized controlled trials on hyperbaric oxygen therapy for carbon monoxide poisoning were reviewed and published in the Cochrane database in which the reviewer concluded that “there is no evidence that unselected use of hyperbaric oxygen therapy in the treatment of acute CO poisoning reduces the frequency of neurological symptoms at one month. The available evidence from randomized controlled trials is thus still insufficient to provide clear guidelines for practice. Further research is needed to better define the role of hyperbaric oxygen therapy, if any, in the treatment of carbon monoxide poisoning. This research question is ideally suited to a multicentre, randomized, double-blind controlled trial”^[44].

Air or gas embolism

Arterial gas embolism is a major hazard of scuba diving (“diving air embolism”). Its exact incidence is hard to determine and many victims are probably recorded as drowning. As a diver begins to ascend, the volume of gas within the lung expands (in accordance with Boyle's Law). If the glottis is closed and a diver surfaces too

quickly, as in a panic situation, the only escape for the expanding air mass is through the thin alveolar walls. Because alveolar rupture requires only a pressure gradient of approximately 11 kPa air embolism can follow breath holding ascents after taking a full breath at depth from as shallow as 111 kPa (a depth of approximately 1 metre) to the surface^[45, 46]. Patients with localized areas of obstruction (asthma or secretions) are at risk to develop pulmonary over-distension even without breath holding. Air embolism is not restricted to divers. It has been reported in a number of other traumatic and surgical conditions including blast injuries or penetrating trauma such as gun shot or stab wounds^[47]. Gas may also enter the arterial circulation by shunting from the venous to the arterial systems. Because 30% of the population have a probe patent foramen ovale, air sometimes can pass directly from the right to left heart; therefore, arterial gas embolism can follow either decompression sickness or medical procedures which permit gas entry into the venous circulation (iatrogenic air embolism is nearly 200 times as common as diving air embolism, with at least 20,000 cases per year in the USA)^[48].

HBOT is approved and recommended for the treatment of air- or gas embolism based on the same principles as for DCS. There are two HBO regimens that are commonly used, depending on the facilities available: (1) either a brief period of compression in air or mixed gas at a depth equivalent to six times atmospheric pressure (606 kPa) followed by several hours in pure oxygen at 283kPa (e.g.: US Navy Treatment Table 6A), or (2) several hours compression in pure oxygen (e.g.: US Navy Treatment Table 6 or 9: at 283kPa or 253kPa respectively). Both approaches seem clinically comparable.

Clostridial myositis and myonecrosis (gas gangrene)

Gas gangrene is one of the most dreaded complications associated with open wounds, but it may also occur spontaneously in the presence of malignancy and as a complication of surgery. Untreated, it invariably results in death within 48 hours of the onset of symptoms. Originally associated with contaminated war wounds, gas gangrene now has become almost exclusively a disease of the civilian population. Hart estimates there are 1,000 to 3,000 annual cases of gas gangrene in the United

States^[49]. In a review of several published series, he found 49% of cases are posttraumatic, 35% postoperative, and 16% arise spontaneously^[49, 50]. The treatment of gas gangrene and other anaerobic infections began in Amsterdam in 1960

In the year 2000, Korhonen published an article on HBO₂ in acute necrotizing infections with special reference to the effects on tissue gas tensions, and showed that “HBOT resulted in a marked increase in tissue oxygenation in both healthy tissue and in the vicinity of infected tissue. The hyperoxygenated tissue zone surrounding the infected area may be of significance in preventing the extension of invading microorganisms^[52]. HBO₂ was also proven to inhibit alpha-toxin production, which has a direct link to patient morbidity and mortality^[53-55].

The UHMS Committee Report recommends HBO₂ at 253 kPa every 8 hours for the first day and then reduced to twice daily treatments until improvement occurs and no further myonecrosis is evident. Of course, by itself HBO is useless - it must be combined with aggressive debridement and meticulous haemostasis to be of therapeutic value. Surgery should be delayed until after the first HBO treatment. This allows for the administration of antibiotics, treatment of electrolyte and fluid imbalances, provides better surgical demarcation of necrotic tissue, and makes the patient less toxic and decreases the surgical risk.

Crush injuries, compartment syndromes and other acute traumatic peripheral ischaemias

A “crush injury” is the direct result of an injury where there is tissue destruction by high energy transfer to the tissue and or interruption of blood vessels, resulting in a vicious spiral which causes ischemia, hypoxia, edema, disturbed microcirculation, and leads to secondary ischemia in the border area of the tissue affected by primary trauma. There is thus usually a “gradient of injury” which contains the spectrum from dead (or necrotic) to living tissue of which the compromised (but not necrotic) component may vary significantly depending on the type of traumatic injury. The latter can include other forms of trauma and even frost bite, burns and a number of non-mechanical traumas. This is commonly complicated by stasis in the

microcirculation, reperfusion injury, and secondary infection, non-healing and non-union all potentially resulting in delayed loss of tissue. Garcia, *et al* published an evidenced based approach for the use of hyperbaric oxygen therapy in the management of crush injuries and traumatic ischaemias^[56]. They found that eight studies showed beneficial effects of hyperbaric oxygen therapy with only one reported major complication. From these eight studies however, only one was a randomized, double-blinded placebo-controlled study^[57], which indicated that hyperbaric oxygen therapy can be effectively applied for crush injuries.

The recommended regimen for the treatment of crush injuries is 100% oxygen at 202 kPa for 90 minutes, but it should be provided at 253 kPa if ischemia-reperfusion injury is present, and two 5 – 10 minute air breaks is required to reduce the risk of experiencing signs or symptoms of oxygen toxicity. The first treatment should be provided within eight hours following the injury and should be given twice a day for the first three days.

Enhancement of healing in selected problem wounds

Many case reports and case-series demonstrate the beneficial effects of hyperbaric oxygen therapy in diabetic foot ulcers. The first controlled trial of hyperbaric oxygen therapy in lower extremity wounds was published nearly 30 years ago^[58]. Since then there have been several prospective, randomized, controlled trials in non-healing diabetic foot ulcers^[59-64]. Outcome measures in these clinical trials vary from one study to another. The systematic review of some of these trials provides evidence that, for patients with diabetic ulcers resistant to standard care, hyperbaric oxygen therapy decrease the risk of major amputation^[19]. The findings that oxygen tensions around the ulcers are significantly raised following a course hyperbaric oxygen therapy supports a mechanism for this benefit. Transcutaneous oximetry is used as part of the assessment of problem wounds and provides an objective basis for decision-making^[65]. A Cochrane Review summarizes the evidence in RCT's of hyperbaric oxygen therapy for chronic diabetic ulcers: "There is a strong case for further large randomized trials of high methodological rigour in order to define the true extent of benefit from administration of hyperbaric oxygen therapy"^[66].

Hyperbaric oxygen therapy also showed to be beneficial in treating patients with other non diabetic wound ulcers^[67], although arterial ulcers seem to respond poorly and HBOT for venous stasis ulcers is usually not cost-effective.

Exceptional blood loss anaemia

Anemia is defined as a reduction in the amount of haemoglobin or the red blood cells which carry it. Anemia occurs whenever the haematopoietic equilibrium is disturbed by increased loss, reduced production or dysfunctional haemoglobin in red blood cells. Anemia may result from a variety of causes. For example, it may be hereditary, as in sickle cell anaemia; it may be metabolic, as in folate deficiency; it may be aplastic, as in drug-induced; anaemia's final common denominator is tissue hypoxia. Because the development of chronic anaemias allow sufficient time for the development of compensatory changes, affected individuals become capable of tolerating quite low haemoglobin levels. Because of religious convictions some patients (e.g. Jehovah's Witnesses) do not allow the transfusion of blood; in other cases, difficulties sometimes arise while attempting to successfully cross-match blood in a timely fashion. Uncommon blood types and certain haemolytic anaemias could also benefit from HBOT.. Hart *et al*/ reported on the use of hyperbaric oxygen therapy in treating 26 patients, of which 22 were Jehovah's Witnesses^[68]. They administered 202 kPa for 60 to 90 minutes until the patient's pulse decreased by one-third. They were removed from the chamber and closely observed until their pulse had nearly returned to pre-treatment levels. The process was then repeated. Initially treatments were needed every 3 to 4 hours, but after the first 24 hours the treatments could be spread out to every 8 to 12 hours. The total duration of hyperbaric oxygen therapy treatments depended on the severity of the blood loss as well as the patients underlying state. Hyperbaric oxygen therapy plays no role in the management of chronic anaemias.

The treatment regimens provided today involves a very detailed approach, using pulmonary wedge pressures, calculation of the oxygen debt, providing intensive medical care and titrating hyperbaric oxygen therapy (to address calculated oxygen debt) in accordance with strict protocols^[69].

Intracranial abscesses

Hyperbaric oxygen therapy is indicated as adjunctive therapy for intracranial abscesses in deep and dominant locations or in cases of multiple abscesses^[70]. Although most infections are anaerobic, aerobic infections also respond to HBO. It may also be used in situations where surgery is contraindicated and in patients showing no response to standard treatment. The development of perifocal edema around an intracranial abscess may progress to secondary hypoxic lesions in the surrounding brain tissues that can lead to a life-threatening situation and an increase in intra-cranial pressure. The effects of hyperbaric oxygen therapy on perifocal brain edema and the increased intra-cranial pressure has been well documented over 40 years ago in a series of studies performed by Miller *et al*^[71-74]. It was found that hyperbaric oxygen caused a 30% reduction of intracranial pressure and a 19% reduction of cerebral blood flow in the absence of changes in arterial PCO₂ or blood pressure, but only as long as administration of carbon dioxide caused an increase in both intracranial pressure and cerebral blood flow. When carbon dioxide failed to influence intracranial pressure or cerebral blood flow then hyperbaric oxygen had no effect.

Lampl and Frey have reported on a number of cases treated with HBOT, with excellent results^[75], leading to the inclusion of this indication to the UHMS and European list of indications. They also report in the dramatic reduction in mortality with the use of hyperbaric oxygen (mortality reduced from 19.2% to 3.1%^[75]).

HBO₂ is administered for intracranial abscesses at a pressure of 202 kPa to 253 kPa with a duration of 60-90 minutes per treatment and could be given twice per day depending on the condition of the patient.

Compromised skin flaps and grafts

Although hyperbaric oxygen therapy is not the first modality of treating routine complications of skin grafts, it is considered an appropriate adjunctive treatment modality in selected patients. In areas of impaired circulation, HBOT preserves tissue viability. Tissue oxygen tensions of 4-6 kPa (30 to 40 mmHg) are required for fibroblast regeneration and normal wound healing^[65, 76]. Collagen deposition serves

as a matrix to support new blood vessel growth (neovascularization). New capillary buds start to be noticeable within 5 to 10 days of daily hyperbaric oxygen therapy and a rich vascular bed is established within one month^[77]. In a compromised host or patient with marginal circulation, hyperbaric oxygen therapy will improve the granulation base and may permit "take" of a graft that would otherwise fail. HBOT is also useful in treating flaps which have a hypovascular base. Using animals, HBO₂ has been demonstrated to preserve flap length compared to non-treated control animals^[78]. HBOT may even have direct effects not dependent on the circulation. Using a pig model, Tan *et al*, raised skin flaps designed to become ischemic^[79]. After killing the pigs, their carcasses were placed in a chamber. The flaps still responded and became pink! They conclude that, in the absence of circulation, this could only be explained by the flaps' direct absorption of oxygen from the chamber air. Li *et al* experimented on auricular composite grafts in rabbits treated with HBOT^[80]. They suggest that HBOT enhanced graft survival, especially in the larger composite grafts.

In compromised flaps the contributing factors include hypoxia, edema, arterial vasospasm, arterial or venous occlusion, congestion and dehiscence or infection. Another factor of major importance is the so-called "reperfusion injury syndrome" when re-establishment of circulation follows prolonged tissular hypoxia as in complicated free flaps. Patient health factors like age, smoking, systemic disease and/or relative therapy may interfere with the flap prognosis. Clinical evaluation is of major importance and is tested according to the flap condition taking into account flaps characteristics like color, temperature, capillary fill and bleeding. The appearance of cyanotic colour in a graft is associated with delayed revascularization and hypoxia, white color with lack of blood supply and red color with presence of infection. Follow up of the flap "take" is critical for the first 48 hrs. Observation of the flap color may determine the leading factor of the complication. The primary cause of flap demise is not an inadequate arterial inflow but rather a venous insufficiency through a compromise venous outflow.

If a surgical flap is clinically edematous, with a deep purple or dark blue colour, (i.e. in total venous occlusion), capillary refill is missing and the flap temperature is low, then HBO₂ is recommended in the form of a twice-daily treatment at 202 kPa – 253 kPa for 90–120 minutes, reducing to once-daily when the graft or flap has stabilized.

A utilization review is recommended after 20 treatments, whether preparing a site for grafting, or maximizing survival of a new graft.

Necrotizing soft tissue infections

Aggressive and often fatal, necrotizing soft tissue infections involve subcutaneous tissues, fascia and, occasionally, muscles. They are almost always polymicrobial, involving multiple strains of gram-positive and gram-negative organisms. These are often synergistic infections caused by mixtures of aerobes, facultative aerobes, and anaerobes (the aerobes consume oxygen resulting in a reduced environment in which anaerobes thrive). Infections usually arise in ischemic areas, such as those existing as a consequence of trauma, peripheral vascular disease, burns, malignancy, foreign body introduction, or operative wounds. In addition, patients with altered host defence mechanisms, such as diabetics, are at increased risk. Enderteritis will occur, causing tissues to become hypoxic, hypovascular and hypocellular. Leukocytes may become sequestered in vessels, impairing local immunity, and incomplete substrate oxidation results in hydrogen and methane accumulation in the tissues. Tissue necrosis occurs, with purulent discharge and gas production, and reports of mortality range from 30% to 75%^[81]. A review of the available literature was done by Jallali in 2005 and concluded that there were “encouraging results” when adding hyperbaric oxygen therapy as an adjunct to the standard treatment^[82].

Conventional treatments may include surgical debridement with systemic antibiotics. In animal studies, hyperbaric oxygen therapy has a direct antibiotic effect, improving tissue oxygen tension, leukocyte function and bacterial clearance^[83]. Integrin inhibition decreases leukocyte adherence, reducing systemic toxicity. Hyperbaric oxygen therapy has been reported to reduce mortality by up to two-thirds^[84]. Hyperbaric oxygen therapy is particularly indicated in bacterial gangrene and non-clostridial myonecrosis (which have high mortality and morbidity), and in compromised or unresponsive hosts^[85].

The UHMS recommends twice-daily treatments for 90–120 min at 201–252 kPa, reduced to once daily when the patient's condition is stabilized^[86]. Further treatments may be given to reduce relapse, and a utilization review is recommended after 30 treatments^[86].

Refractory osteomyelitis

Osteomyelitis presents either with acute or chronic infection of bone and can be due to bacteria, mycobacteria, fungi, or (very rarely) viruses. Chronic and unresponsive bone infections are mainly caused by bacteria, which may remain dormant for years. Combined with antibiotics, debridement and removal of foreign material, hyperbaric oxygen therapy is recommended in localized and diffuse osteomyelitis, particularly with vascular or immune compromise^[87]. Hyperbaric oxygen therapy elevates plasma-based oxygenation and provides the level of hyperoxia required for collagen synthesis and angiogenesis, increasing vascularity and oxygenation^[40]. Leukocyte bacterial killing is enhanced, as is the efficiency of certain antibiotics, by maximizing oxygen dependent aminoglycoside transport across bacterial cell walls^[87]. Hyperbaric oxygen therapy eliminates anaerobes, promotes oxygen dependent osteoclastic resorption of infected bone^[88]. Oedema, inflammation and pressure are significantly reduced. Slack in 1965 was the first to use hyperbaric oxygen therapy in refractory osteomyelitis^[89], controlled animal studies confirmed its efficiency^[90, 91]. Davis *et al* reported the successful use of hyperbaric oxygen therapy in treating advanced malignant otitis externa, a progressive and potentially fatal form of refractory pseudomonas osteomyelitis of the ear canal and base of skull, usually affecting elderly diabetic patients^[92].

The severity of the disease forces the treatment regimen, but the UHMS recommends treatments generally for 90–120 min daily at 201 kPa – 252 kPa, in conjunction with debridement, antibiotics and nutritional support, and review is recommended after 40 treatments^[87].

Delayed radiation injury (soft tissue and bony necrosis)

Radiation can induce a non-healing, hypoxic wound which may occur in either soft tissue or bone. The radiation damages the cellular and vascular components of tissues resulting in a proliferative endarteritis. This results in a hypoxic, hypocellular and hypovascular tissue and a risk of non-healing following surgery^[93]. Successful treatment with hyperbaric oxygen therapy is documented in post-radiation damage, including chest wall necrosis, radiation-induced haemorrhagic cystitis, and central nervous system radiation damage^[94-96]. A recent trial, however, found little evidence for hyperbaric oxygen therapy in radiation-induced brachial plexopathy, though there were some improvements in warm sensory threshold and long-standing arm lymphoedema^[96].

HBO₂ increases vascular density and oxygenation in radiation-damaged tissue^[97]. It also increases tissue angiogenesis which increases circulation to the injured area. This increases oxygenation resulting in better wound repair by stimulating collagen deposition. Marx has shown that tissue oxygen levels in irradiated areas approach 80% of normal tissue levels within about approximately 20 hyperbaric oxygen therapy sessions. The benefits of HBOT are long lasting. In one study, three year follow-up revealed pO₂ levels that were still 80%-90% of those seen during the active treatment cycles which improved tissue oxygen gradients and angiogenesis and enhanced leukocyte bactericidal activity^[98]. This facilitates healing and may enable grafts to be placed. Mainous, reported a case of excellent improvement in mandibular healing with HBO₂ after radiotherapy^[99]. Marx reported in 1985 that prophylactic HBOT before tooth extractions in heavily irradiated mandibles prevented mandibular osteoradionecrosis more effectively than penicillin^[100]. HBOT given prophylactically prior to dental extraction is not 100% effective in preventing osteoradionecrosis. If given before dental extractions in high risk patients, 5% still develop osteoradionecrosis. However, where radionecrosis developed it was of a minor nature and readily managed by simple surgery. Untreated radionecrosis resulted in severe radionecrosis requiring sequestrectomies and resections of the mandibula. For comparisons sake, when only penicillin is given, 30% of patients develop osteoradionecrosis. Because it is much more economical to prevent osteoradionecrosis than to treat it, prophylactic HBOT is still recommended. The term "prophylactic" is misleading, however. Tissue for which HBO is provided in a

previously irradiated area prior to surgery contains late radiation tissue damage. The HBO is applied to reverse the radiation tissue damage so that the tissue can withstand the increased metabolic requirements of healing following surgery. It is important to state that this is not prophylactic in the true sense of the word. It is indeed therapeutic.

Neovius *et al* reported that patients with problem wounds following surgery and radiotherapy had complete healing after treatment with hyperbaric oxygen therapy and that hyperbaric oxygen therapy may reduce the incidence and progression of soft tissue radionecrosis, such as laryngeal radionecrosis^[101], although there is less support for this in the literature than for osteoradionecrosis. Marx showed that, in patients with previous radiation, “pre-operative hyperbaric oxygen therapy can reduce wound dehiscence and infections, and improve healing in soft tissue flaps, particularly in mandibular osteoradionecrosis, though randomized controlled trials are lacking”^[97].

Hyperbaric oxygen treatment for mandibular osteoradionecrosis is recommended by the UHMS to consist of 30 daily 90-minute sessions at 241 kPa, with surgical debridement in more advanced disease^[102]. Aitasalo *et al* proposed a lower number of treatments for cases that are treated early^[103, 104].

Thermal burns

The skin is the largest organ in the body and major burns to it result in multi-organ failure. Traditionally, the depth of a burn is classified as being either first, second or third degree. First degree burns, involving only the epidermis, are clinically manifested by localized erythema. Second degree burns extend into the underlying dermis and are marked by blisters, which often erode leaving behind red, moist and denuded skin. Because deeper elements of the dermis (the hair follicles and sweat glands) still contain epidermal tissue, second degree burns usually are capable of regenerating the epithelial layer, given enough time. Third degree burns are full thickness injuries in which the entire dermal layer of skin has been destroyed. These burns appear whitish and lack sensation. Re-epithelization is impossible and skin

grafts are needed to cover large areas. If a deep second degree burn becomes infected or desiccated, it can convert to a third degree burn. Initially, the greatest concerns in clinical management are hypovolaemia and the prevention of shock. Following a burn, initial vasoconstriction rapidly gives way to vasodilatation and stasis, the local capillaries become increasingly permeable, and plasma extravasates into the burned areas. A second concern in clinical management is the potential for infection. Most major burns are associated with a relative hypo immunity state, characterized by decreased levels of immunoglobulin and ineffective phagocytosis. Besides increasing local hypoxia, edema and changes in the microcirculation inhibit the ability of normal humeral and cellular immune elements from reaching the affected areas.

There is evidence that HBOT reduces polymorphonuclear killing ability^[105]. The hyperoxic environment results in vasoconstriction, decreases oedema, and increases collagen formation and angiogenesis. Phagocytic bacterial killing can be improved, and white cell endothelial adherence is inhibited, preventing capillary damage^[106]. Hyperbaric oxygen therapy maintains the microvascular integrity, and reduces infection^[107]. Hyperbaric oxygen therapy also decreases the healing time^[108], mortality and morbidity and hospitalization was reduced when compared to controls^[109]. The need for grafting is likewise dramatically reduced ^[108, 110]. However, other studies have showed no benefit from hyperbaric oxygen therapy in treating thermal burns^[111]. Concerns that hyperbaric oxygen therapy could worsen pulmonary damage in thermal burns are still unproven.

The UHMS recommends three sessions within 24 hours of injury and 90-minute treatments twice-daily thereafter, at 201 kPa – 241 kPa^[109].

Mechanisms of action of HBO

Hyperoxygenation

Most oxygen (19.4 ml/dL) is carried in the blood being bound to haemoglobin when breathing air at atmospheric pressure. A small amount of oxygen is carried in solution (in the plasma), and this portion will increase with an enlarged inspiratory

oxygen partial pressure due to Henry's Law, which will in turn increase tissue oxygenation. When breathing normobaric air, arterial oxygen tension is approximately 13.3 kPa (100 mmHg), and tissue oxygen tension approximately 55 kPa^[65]. However, breathing 100% oxygen at a pressure of 304 kPa can increase arterial oxygen tensions to 267 kPa (2200 mmHg)^[112, 113]. There is also a corresponding four-fold increase in the oxygen diffusion distance at the capillary arterial end and twofold increase at the venous end. This results in wound tissue oxygen tension increased up to 10 to 15 fold and a 68 ml/L of oxygen dissolved in plasma^[114] (compared to 3 ml/L at atmospheric pressure breathing air), which is sufficient to support resting tissues without a contribution from haemoglobin^[115].

The physiological significance of dissolved oxygen (and the ability to increase the fraction of dissolved oxygen) is profound. This is particularly true for respiration processes involved in wound healing, wound repair, processes involved in combating infections, nitric oxide functions, cytochrome P450 reactions, synthesis of neurotransmitters, etc. There is thus a physiological rationale for using HBO₂ in many conditions and it should not be seen as merely a means of providing more oxygen substrate. HBOT also mobilizes stem/ progenitor cells from bone marrow^[116].

All of these oxygen-dependent processes rely on the dissolved fraction of oxygen, since oxygen that is bound to hemoglobin is not available for any physiological processes. Hemoglobin-bound oxygen must first dissociate from hemoglobin (and dissolve into the plasma) in accordance with the oxy-hemoglobin dissociation curve and then further diffuse (from the plasma) into the extravascular, extracellular space until eventually ending up in the intracellular space, where it can diffuse into the mitochondria and other organelles which would then utilize the oxygen molecules in biochemical processes. Diffusion (and diffusion distance) is (amongst others, e.g. molecule size, type of tissues, membrane thickness, etc.) highly dependent upon the diffusion gradient that exists (diffusion takes place from a high gradient to a low gradient^[117]). This results in the effects of hyperbaric oxygen therapy described in previous studies, namely that even poorly perfused wounds can receive oxygen via hyperoxygenated plasma^[118].

Table 3: Theoretical arterial oxygen tension and blood oxygen content for different treatment protocols

Inhaled oxygen fraction	Absolute pressure	Arterial oxygen tension (mmHg)	Oxygen dissolved in plasma (mL per dL of blood)
0.21	101kPa (1 ATA)	100	0.31
1.0	101kPa (1 ATA)	660	2.0
1.0	202kPa (2 ATA)	1400	4.3
1.0	303kPa (3 ATA)	2200	6.8

Table 3 shows theoretical arterial oxygen tensions and the amount of oxygen dissolved in the blood for various hyperbaric therapy protocols as described by Thackham, et al^[112].

Stimulation of tissue growth and Angiogenesis

Oxygen is essential for angiogenesis and new blood vessel formation in wounds. Vascular endothelial growth factor (VEGF) is the most specific growth factor for neovascularization. Continuous hypoxia inhibits neovascularization, intermittent hyperoxia stimulate angiogenesis by satisfying metabolic needs and by enhancing VEGF production, therefore, maintenance of adequate tissue oxygen tension is critical to wound healing^[119, 120]. The process of angiogenesis requires approximately four weeks of hyperbaric oxygen therapy treatment sessions, but in essence reverse the micro-vasculopathic component of irradiated tissue or in the diabetic foot, resulting in steady increase in the tissue oxygen levels which is believed to be long-lasting^[121].

Fibroblast proliferation and collagen deposition

Fibroblasts are the major producers of collagen in the repair response. Collagen synthesis starts with hydroxylation of procollagen peptide chains by proline hydroxylase, one of the substrates for this process is molecular oxygen^[122], procollagen then cleaved and cross-linked to form mature collagen fibrils. Hydroxylation of proline and deposition is crucially dependent on molecular oxygen, oxygen tension also influence collagen cross linking and wound mechanical strength^[123].

Effects on microorganisms and host immune response

Wounds represent a break in immunity to bacterial infections. The more hypoxic a wound, the more vulnerable it is. Polymorphonuclear (PMN) leukocytes engulf or phagocytose bacteria and expose them to reactive oxygen species (ROS). ROS react with several bacterial molecules such as DNA, proteins and carbohydrates. It also destroys membrane lipids of organisms in a lipid peroxidation process (chain reaction). This process is modulated by NADPH oxidase (nicotinamide adenine dinucleotide phosphate-oxidase) or phox which is a phagocytic oxidase, in this process large amounts of molecular oxygen is consumed, as much as fifty-fold the baseline value, in what is termed the “oxidative or respiratory burst”^[124].

Antibiotic activity enhancement

Oxygen tensions play an important role in the outcome of infections. Oxygen is cidal or static for microorganisms that lack defenses against oxidants. In addition, hyperoxia potentiates (while anaerobiosis decreases) the activity of many antimicrobial agents. A series of studies have shown that increased tissue oxygen tensions reduce the minimum inhibitory concentrations and the minimum bactericidal concentration of *E. Coli*, *Enterobacter*, *Klebsiella*, and *Staphylococcus* against different aminoglycosides including: amikacin, gentamycin, and tobramycin^[125, 126].

Hyperbaric oxygen therapy, when combined with these antibiotics and surgery, is extremely useful as adjunctive therapy for treating tissue involving both anaerobic and aerobic bacteria in hypoxic wounds and tissues^[127].

Vasoconstriction

Exposure to oxygen at pressure results in a 20% reduction in blood flow in normal tissues (vasoconstriction). This effect is offset by the tenfold to fifteen fold increase in the oxygen content of plasma^[128]. This vasoconstriction may favorably affect the neurogenic edema that is seen in the feet of diabetic patients. Hyperoxia probably does not cause vasoconstriction in ischemic or hypoxic tissues, specifically in diabetics, this is due to calcification with non-compressibility of their peripheral blood vessels and auto-sympathectomy effects^[129].

Increased pressure and creation of gas gradients

The increased pressure at which HBOT is provided results in a compression of gas-spaces and a reduction in the volume of gases in accordance with Boyle's law. This effect is utilized in the treatment of decompression sickness and gas embolism. Breathing 100% oxygen during the treatment would also provide a gas gradient that is not only favourable for increasing oxygenation of tissues as described above, but also for the elimination of inert gases. Again, this effect explains why it is used in the treatment of decompression sickness.

Production of Nitric Oxide (NO)

HBO₂ induces the production of nitric oxide, which is known to be a key biological "messenger" and has a number of physiological effects. A study by Thom *et al* showed that one of the effects of this is the mobilization of stem cells from the bone marrow^[116].

Safety and the side-effects of HBO therapy

Hyperbaric oxygen therapy is considered to be a safe treatment modality if the necessary precautions are taken and patients are selected in accordance with the accepted international practice standards. The risks involved in the use of hyperbaric oxygen therapy are related to pressure changes and the toxic effects of oxygen.

Pressure-related side effects

Middle ear or sinus barotrauma

In the presence of abnormalities, hyperbaric oxygen therapy may affect gas spaces where the pressure cannot be equalized, like the ears and sinuses. Middle ear equalization problems are experienced as pain or discomfort during compression. Middle ear barotrauma incidence is about 2% and the majority of problems can be resolved with simple means and minor invasive procedures and termination of hyperbaric oxygen therapy rarely becomes necessary^[130]. Middle ear equalization problems usually are managed by slow decent rate, topical decongestants or insertion of tympanostomy tubes^[130].

Pulmonary overpressure with pneumothorax

Incidences of this side effect is very low in clinical practice; pulmonary barotrauma prevalence is reported to be 0.00045%^[131]. Careful patient evaluation and clinical examination to rule out predisposing factors is mandatory in all candidates for hyperbaric oxygen therapy.

Oxygen toxicity

Pulmonary oxygen toxicity is only seen during extended periods of treatment and when a very high number of hyperbaric oxygen therapy treatment sessions are

provided. Pulmonary oxygen toxicity from currently used wound-healing protocols is virtually unheard of^[132].

Central nervous system toxicity may present with transient visual changes, hearing changes, nausea, tingling sensation or dizziness and can also lead to grand mal seizures^[133]. Fever and certain medications can predispose one to this complication. Oxygen seizures are very rare, occurring 1 in 10,000 to 12,000 treatments^[134-136]. They are self-limited and treated by providing air (instead of oxygen) to breathe. Hyperbaric oxygen therapy may be reestablished after seizure activity has ceased^[137]. These seizures are not associated with any long-term neurological damage, although repeated excessive exposures (not standard hyperbaric protocols) may lead to disturbed carbon dioxide transport, accumulation of carbon dioxide and neurogenic pulmonary oedema^[138-140].

Reversible myopia

An additional minor side effect is a transient change in visual acuity that usually revert to baseline within few weeks to months after treatment^[141]. The rate of myopic change resulting from hyperbaric oxygen therapy has been reported to be approximately 0.25 diopter per week, with the changes being progressive during the period of the hyperbaric oxygen therapy^[130, 141, 142]. The hyperoxic myopia is generally attributed to oxidative changes causing an increase in the refractive power of the lens. As mentioned, this change is temporary and reversal of the myopic shift after discontinuation of the hyperbaric oxygen therapy normally takes place within 3 to 6 weeks^[130, 142].

Irreversible cataracts

There is no evidence that current protocols predispose to cataract formation^[142, 143]. The growth of preexisting nuclear cataracts may be stimulated by prolonged sessions of hyperbaric oxygen therapy, and new cataracts were found since patients who were exposed to high number of hyperbaric oxygen therapy treatments (>150

treatments). The nuclear cataracts were not reversible after such a high number of sessions^[142].

Previous similar studies on the subject

A number of previous studies have evaluated the knowledge and attitudes of health practitioners regarding the use of hyperbaric oxygen therapy and the incorporation thereof in their practice^[144-146]. Another survey is reported to evaluate the attitude of maxillofacial fellows regarding their attitudes regarding the performance of a national trial for hyperbaric oxygen therapy in radionecrosis of the jaw^[147]. These studies were all conducted on a targeted group of practitioners (e.g. wound care practitioners and maxillofacial fellows). The authors found that most respondents were unaware of the method of delivery of hyperbaric oxygen therapy and generally had a poor knowledge of the physical and physiological effects. Despite the relatively poor knowledge found in all these studies, the authors also report that most respondents had a positive attitude towards the use of hyperbaric oxygen therapy in their practice. Very few respondents have previously referred patients for hyperbaric oxygen therapy and on a national level it seems like those who have referred patients for hyperbaric oxygen therapy are clustered together (most likely in the vicinity of a hyperbaric facility). Younger respondents and those who had previously referred patients for HBOT were more likely to have a positive attitude towards the use of hyperbaric oxygen therapy.

No study regarding the use of hyperbaric oxygen therapy has ever been conducted in the Kingdom of Bahrain and there has indeed been no similar study published to describe the knowledge and attitudes of practitioners within any of the Middle Eastern countries.

Study aim and objectives

The main aim of this study is to assess the characteristics of medical practitioners, their working knowledge of and attitudes toward hyperbaric oxygen therapy within the Royal Medical Services of the Kingdom of Bahrain.

The following secondary objectives were also investigated during this study:

1. Estimating the proportion of practitioners with knowledge of internationally recommended and approved indications for hyperbaric oxygen therapy
2. Observing how many specialists know the indications for hyperbaric oxygen therapy within their field of specialization.
3. Evaluating whether medical practitioners have an understanding of the physiological principles explaining the effects of hyperbaric oxygen therapy
4. Evaluating the perception of hyperbaric oxygen therapy in medical and surgical specialties.

Methodology

Review by Health Research Ethics Committees

The study protocol was submitted for review by the Health Research Ethics Committee of the University of Stellenbosch and was approved on 14 July 2011, with reference number: N11/06/179. The Ethics Approval letter is attached as Addendum 1.

The protocol was also submitted for review by the Research Committee of the Royal Medical Services of the Kingdom of Bahrain, with approval received on 27 June 2011. The letter of approval is attached as Addendum 2.

Study design

A combined quantitative and qualitative cross-sectional study was performed to reach the aims and objectives of this study, using a research questionnaire and semi structured interview.

Study Setting

The study took place between 03 August 2011 and 05 October 2011 at the Royal Medical Services in The Kingdom of Bahrain including all the departments within the

military hospital and Sh. Mohammed Bin Khalifa Cardiac center, as well as all military camp clinics that fall under the Royal Medical Services.

There are approximately 300 medical practitioners who work in the royal medical services. Many of the practitioners are Bahraini citizens and there are also physicians employed from all over the world such as South Africa, India, Canada, United States of America, Pakistan, and others.

The Bahraini physicians typically completed their undergraduate medical training in the UK, Ireland, Bahrain, Kingdom of Saudi Arabia, and other European Countries. Most performed their postgraduate studies at North American universities (in Canada and the USA), while others studied in Germany and the UK and a few studied in South Africa. The non-Bahraini Physicians typically completed their undergraduate and postgraduate training in their native countries.

The Kingdom of Bahrain is a previous British colony, with English and Arabic as the main official languages used in the military and the Royal Medical Services. All medical practitioners are fluent in the English language. All the research instruments were provided in English only.

Study participants

A list of names of all the medical practitioners employed by the Royal Medical Services was obtained from the Human Resources Department. Each clinical department was visited and appointments were set up for completion of the questionnaires and conducting of the interviews. The military and civilian medical practitioners working in these departments were invited to take part in this study, provided that the inclusion and exclusion criteria were met.

Inclusion criteria

Potential participants were required to meet all the following criteria to be eligible to take part in the study.

- Be qualified medical practitioners
- Formally employed by the royal medical services
- Must be willing to give informed consent

Exclusion criteria

Potential participants presenting with any one of the following were not eligible for inclusion in the study:

- Persons not willing to provide informed consent
- Questionnaires that were illegible
- Medical practitioners who have undergone specialized training in hyperbaric or diving medicine.
- Medical practitioners who were on military deployments or on leave for duration beyond the study period.

Sampling methods and sample size

The sampling frame consisted of all the military and civilian medical practitioners in the Royal Medical Services. In order to properly evaluate the information, no sample was taken for the purpose of the written questionnaire.

For the purposes of the semi-structured interview, a purposive sample was taken to ensure representivity across the different departments. No sample size was determined for this part of the research project prior to initiation of the study and sampling continued until data saturation occurred.

Data sources and data collection

The primary investigator developed a questionnaire (see Addendum 3), with the assistance of his supervisor, which aimed to provide the details required to meet the aim and objectives of the study. Informed consent was obtained from all participants before they were requested to complete the questionnaire in a private and

confidential setting provided by the Royal Medical Services, which ensured that the process was not rushed and that participants had enough time to complete the questionnaire. The informed consent document is attached as Addendum 4.

A second informed consent document (see Addendum 5) was completed for each candidate participating in the semi-structured interview. The data was collected by means of a digital voice recording of the semi-structured interview, conducted by the primary investigator in accordance with pre-set question guidelines (see Addendum 6). These interviews also took place in a private and confidential setting provided by the Royal Medical Services.

Data management and statistical analysis

The findings of the survey were captured and stored in a Microsoft Excel spreadsheet. The data was analysed by means of 2x2 contingency tables and the associations were tested using the chi-squared test (with $\alpha=0.05$) or the Fisher's Exact test if individual cell frequency assumptions were not met. Odds ratios (with 95% confidence intervals) were used to evaluate possible factors associated with different levels of knowledge.

The transcriptions of the interviews were analysed to establish common themes, which was relatively easy, since the questions asked of participants already provided a thematic approach. The findings of the interviews are presented separately. Typical responses to the questions are quoted verbatim below.

Ethical aspects

The research protocol was approved by the Health Research Ethics Committee of Stellenbosch University, as well as the research committee of the Bahrain Defence Force Royal Medical Services. All participants were required to provide informed consent prior to participation in the study and separate consent was required for the qualitative component of the study.

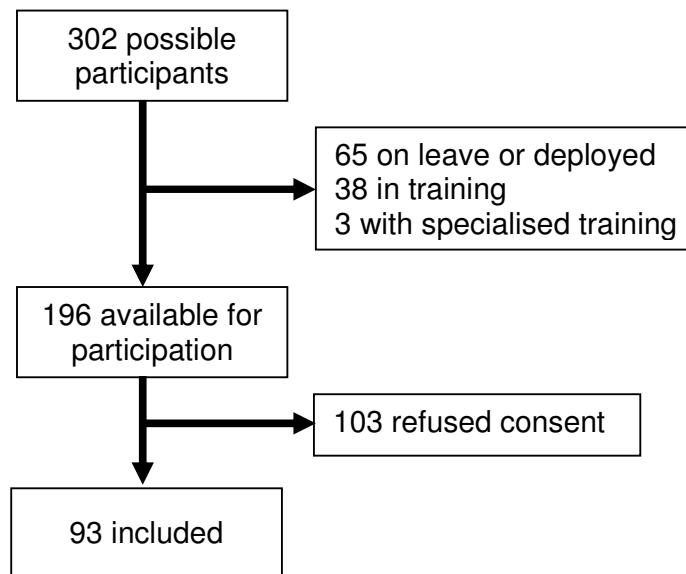
Survey component results

Study participants

A total of 302 medical practitioners are working for the Royal Medical Services of the Kingdom of Bahrain. 103 of these practitioners were not available for participation in the study (being deployed, on leave, on sick leave, etc.). Three medical practitioners were not eligible for inclusion due to previous specialized training in diving or hyperbaric medicine (including the primary investigator). Of the 196 being available for participation, 103 would not provide informed consent. A total of 93 medical practitioners participated in the research project. No questionnaires were illegible and all of them were included in the analysis.

Figure 1 provides the flow-diagram of the sampling frame, selection process and final sample obtained.

Figure 3: Flow-diagram of study participants

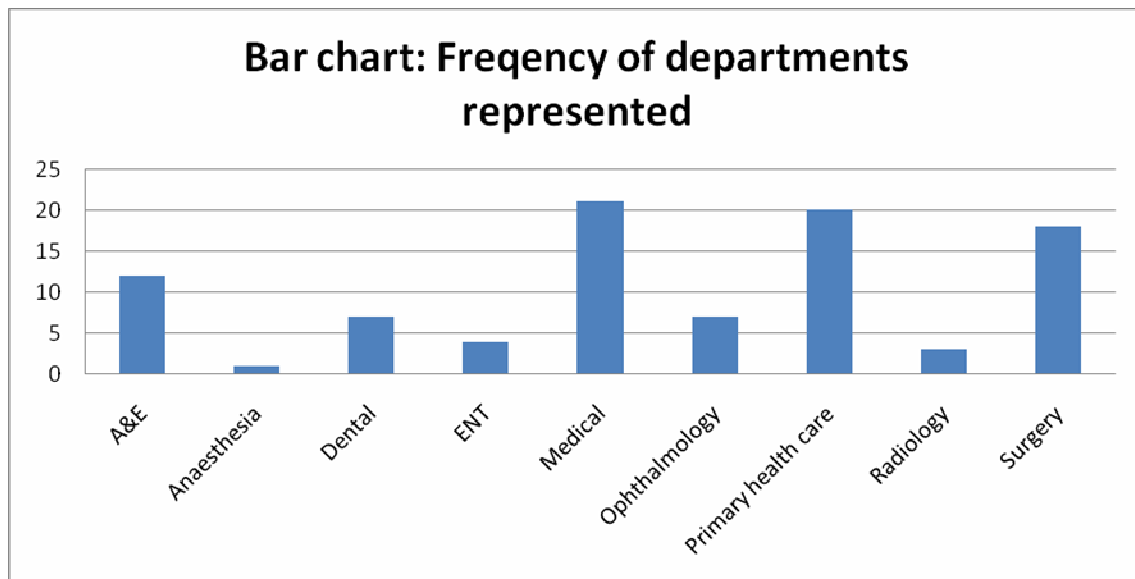


Descriptive data

A total of 93 medical practitioners, with a mean age of 38.8 (SD = 8.7) years, were included in the survey component of the study. Of all the participants in the survey, 77.4% were appointed as civilians within the Royal Medical Services, while 22.6% had appointments as military officers and 63.4% were registered as Bahraini nationals, while 36.6% were registered as international medical practitioners. The median year in which all participants obtained their primary medical degree was 1996 (range: 1974 – 2011) and for specialists this was 2004 (range: 1980 – 2011).

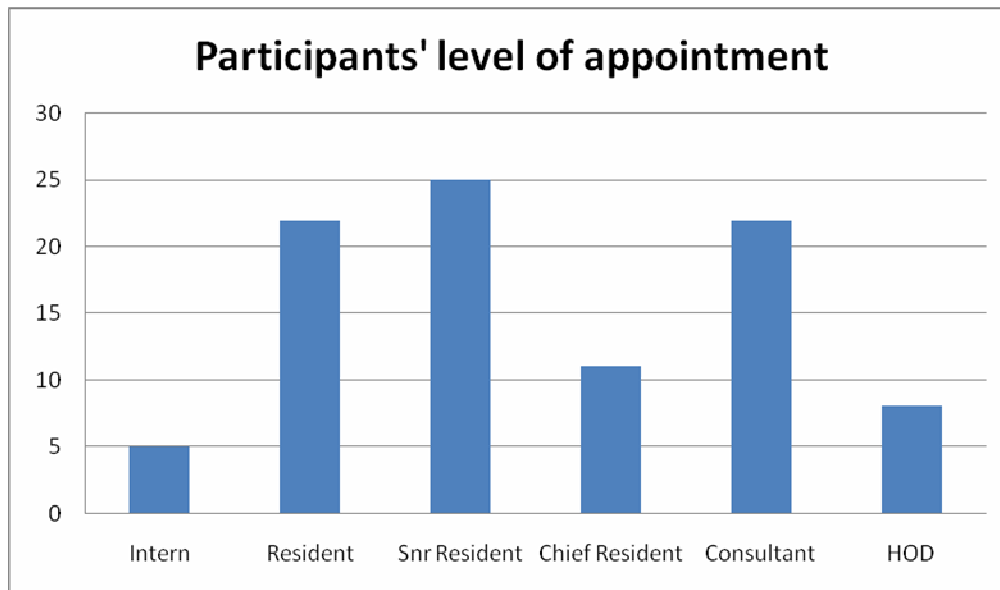
All departments, except Obstetrics & Gynaecology and Paediatrics were represented in the study. The average time that the medical practitioners had been employed in the specific department was 8.4 (SD = 7.8) years. Figure 4 indicates the frequency by which each department was represented in the survey questionnaire.

Figure 4:



The survey participants were representative of all the levels of seniority within the hospital, with a smaller proportion of chief residents participating. The number of participants at a specific level of appointment is displayed in Figure 5.

Figure 5

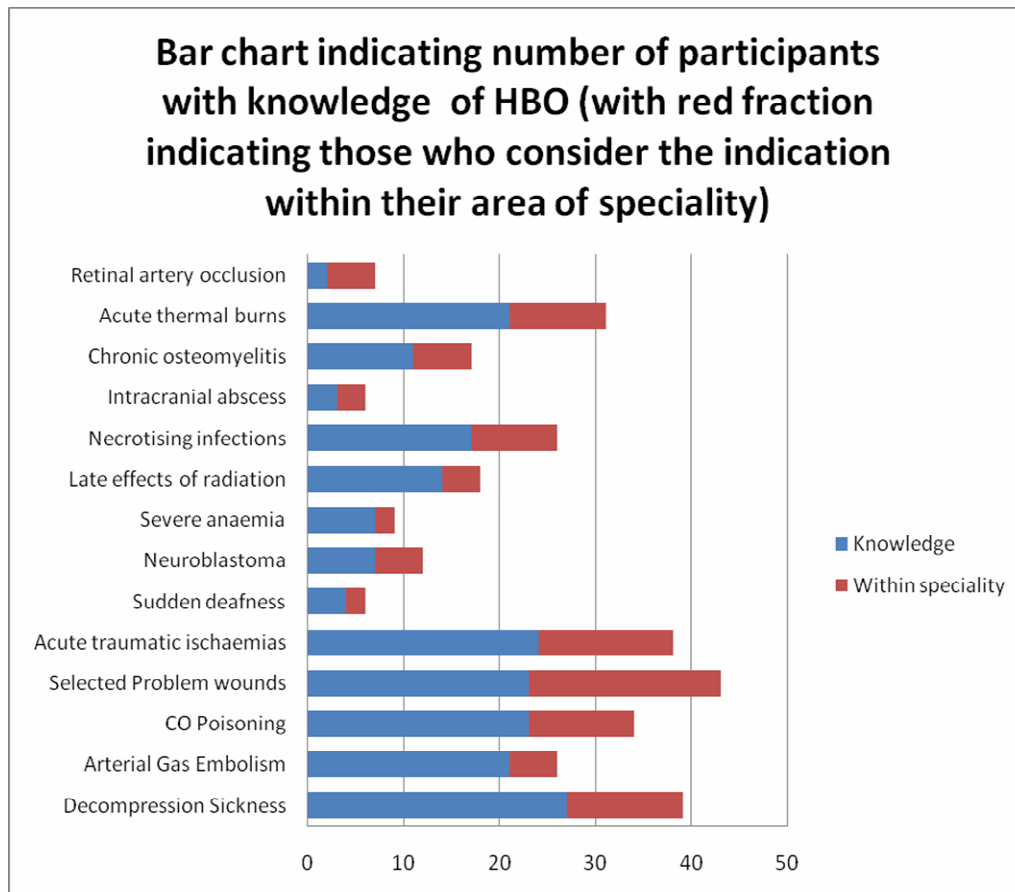


Knowledge of hyperbaric oxygen therapy

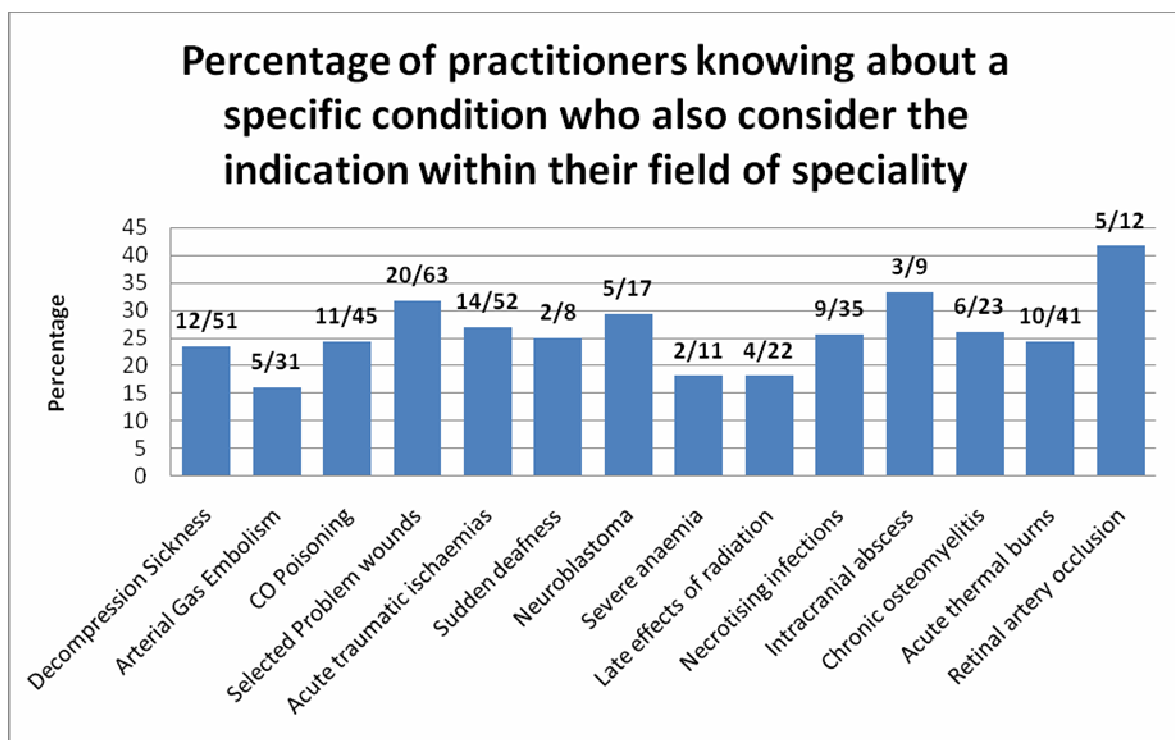
Participants who had never heard about hyperbaric oxygen therapy before comprised 11.8%. Of the 85 participants (88.2%) who had heard about this treatment modality before, 28 (32.9%) first heard about hyperbaric oxygen therapy during their undergraduate studies and 28 (32.9%) during their postgraduate studies. The rest of these participants had read about hyperbaric oxygen therapy in journal articles, textbooks or heard about this treatment modality during discussions with colleagues. The majority of these participants had not heard about hyperbaric oxygen therapy or read about it in a journal article in the previous calendar year (28.6% of those who previously had heard or read about hyperbaric oxygen therapy before indicated that they had heard or read about it more than 5 years ago).

When all the indications listed by an individual participant is considered, 82.8% (n=77) could correctly name only one indication. The most commonly cited indications were “problematic wounds” (n=43) and “decompression sickness” (n=39). 72% (n=67) could mention two indications; 53% (n=50), 39% (n=37), 25.8% (n=24), 20.4% (n=19), 15% (n=14) and 9.7% (n=9) could mention 3, 4, 5, 6, 7 and more than seven indications respectively. One person was able to mention all 14 indications listed by the UHMS and ECHM.

Figure 6 indicates the number of times a specific indication (as listed by the UHMS or ECHM) was mentioned by the study participants, as well as the number of times the participants indicated whether (although they knew that this was an indication for hyperbaric oxygen therapy) they considered such an indication as falling outside of their area of practice or specialisation (in blue) or within their area of specialisation (in red).



The percentages of practitioners who mentioned a specific indication for hyperbaric oxygen therapy, who also considered the specific indication to be within his or her discipline or area of speciality, is captured in Figure 7. The percentages were calculated by dividing the number of persons considering the indication to be within their area of speciality by the total number of persons who mentioned the condition to be an indication for hyperbaric oxygen therapy.



Knowledge of contra-indications

Thirty-six of the participants correctly mentioned a pneumothorax as a contra-indication for hyperbaric oxygen therapy. “Pregnancy” and “Chronic Obstructive Pulmonary Disease” (or emphysema) was cited by 16 and 12 participants respectively as contra-indications, while respiratory infections, claustrophobia, drugs

and barotrauma were cited less frequently. Table 4 provides the frequency by which contra-indications were cited.

**Table 4: Frequency table of contra-indications
cited by study participants**

Absolute contra-indications correctly identified	
Pneumothorax	36
Relative contra-indications correctly identified	
Pregnancy	16
COPD/ Emphysema	12
Respiratory infections	10
Claustrophobia	7
Fever	6
Medication	5
Barotrauma	5
Asthma	3
Chemotherapy	3
Malignancy	3
Chest surgery	2
Pulmonary Fibrosis	1
Oxygen toxicity	1
Unstable patient	1
Incorrectly cited "contra-indications"	
Glaucoma	1
Hypertension	1
Pulmonary embolism	1
Seizures	1
TM Perforation	1
Vessel injuries	1

Factors associated with knowledge of hyperbaric oxygen therapy

A good knowledge of hyperbaric oxygen therapy was defined by the primary investigator as being able to correctly mention more than seven of the indications listed by the UHMS and ECHM. Analyses were performed to see whether any factor is associated with such knowledge. Table 5 indicates the odds ratios (OR), with 95% confidence intervals (CI) and the p-values associated with participants knowing more than seven indications for hyperbaric oxygen therapy

Table 5: Factors associated with knowledge of more than 7 indications for HBO

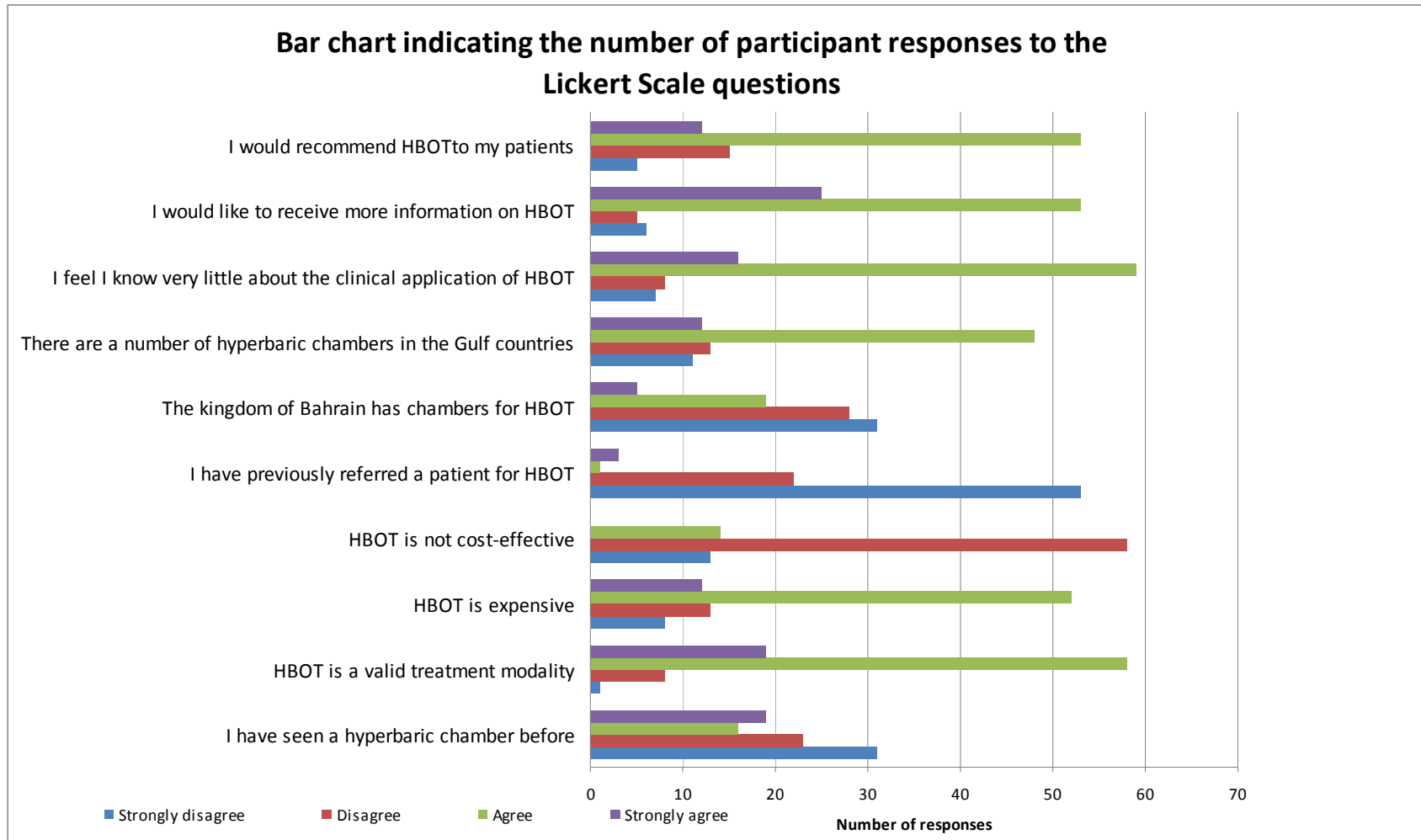
	OR	95% CI	p-value
Year of qualification after 1995	1	0.23 – 4.3	0.287
Year of specialist qualification after 1995	1.4	0.12 – 15.16	0.427
Age >40	0.98	0.25 – 3.93	0.27
Employment as a civilian medical practitioner	1.02	0.19 – 5.34	0.322
Registration as Bahraini vs. International	2.15	0.42 – 11.01	0.199
Specialists vs non-specialists	1.02	0.25 – 4.05	0.274
Heard of HBO during undergraduate training	2	0.49 – 8.09	0.176
Heard of HBO during postgraduate training	0.85	0.20 – 3.66	0.280
Read about HBO in journal articles	2.5	0.56 – 11.2	0.155

Lickert scale responses

The Lickert scale responses, testing participants' attitudes towards hyperbaric oxygen therapy yielded interesting results. Seventy five participants (80.6%) agreed (or strongly agreed) that they felt that they knew very little about hyperbaric oxygen

therapy. Despite this, 69.9% (n=65) still indicated that they would recommend hyperbaric oxygen therapy for their patients (although 75 participants, or 80.6%, indicated that they have never referred any of their patients for hyperbaric oxygen therapy. Most participants (n=78; 83.9%) indicated that they would like to receive more information on hyperbaric oxygen therapy. The participants indicated that hyperbaric oxygen therapy is expensive (n=65), but also that it is cost-effective (n=71) and that it is valid as a treatment modality (n=77). The frequency of a specific response to the Lickert scale statements (indicating whether the participant strongly agrees, agrees, disagrees or strongly disagrees with the statement) are depicted in Figure 8.

Figure 8: The frequency of participant responses to the Lickert scale statements



Semi-structured interview component results

Study participants

Participants involved in the semi-structured interview component of the study came from the same sampling frame as the participants completing the questionnaire. At the time of completion of the questionnaires, potential candidates were invited to participate in the interview component of the study, which was also conducted between August and October 2011. A purposive sample was taken to ensure a degree of representivity across the different disciplines.

Thirteen participants were interviewed, representing the Surgical, Ear-, Nose and Throat, Medical, Ophthalmology and Primary Health Care Departments. No participants from the Obstetrics and Gynaecology or the Paediatric departments were willing to participate in this component of the study.

Findings

Because the interview took place in a semi-structured manner, the specific themes to be investigated were already pre-selected. The following qualitative information was obtained from the participants:

Participants' knowledge of hyperbaric oxygen therapy indications within their field of work

Some of the specialist medical practitioners have previously been confronted with HBOT as a treatment modality, while some interviewees indicated that they have insufficient knowledge about HBOT and were not able to list specific indications for HBOT. Even some of the participants who were able to mention specific indications for HBOT (also within their speciality) were not able to explain or mention the physiological mechanisms of action of HBOT, neither how HBOT would interact to

address the pathophysiological mechanisms of the disease or how HBOT should be applied as an adjunctive treatment.

“My information or my knowledge ... is very small, so I cannot say or add more than these things, but I hope that it can be here or something that has been given for the doctors that's to... or some knowledge, so we can also help our patients or explain more specific for the patient that this thing can help in treatment”

Those who had previous knowledge about hyperbaric oxygen therapy, felt that it was a good treatment modality, some indicating that they had patients who went for treatment abroad (especially in Europe). These patients would return with information on hyperbaric oxygen therapy and for some practitioners this was a source of information regarding the use of hyperbaric oxygen therapy. This was most commonly mentioned for diabetic foot lesions.

“Many patients need this hyperbaric oxygen therapy concerned with patients with diabetic foot”

Knowledge regarding the mechanisms of action of hyperbaric oxygen therapy

The majority of the participants had no knowledge of the mechanisms of action of hyperbaric oxygen therapy and the majority responded to the question “Do you know the mechanisms of action of hyperbaric oxygen therapy” with a simple “no”.

Knowledge regarding the levels of evidence existing for hyperbaric oxygen therapy

A surprisingly large number of participants have read about the use of hyperbaric oxygen therapy in journal articles and in textbooks. However, the general knowledge of the existing literature supporting the use of hyperbaric oxygen therapy as adjunctive treatment modality was quite low.

“I,...I have read this in some of the studies and articles regarding this therapy and the amazing part of it – even from the first session, the patient could experience a change in his vision, which is really a promising result.”

“there is some research and research works have been done before and it gives evidence of the process of healing and improvement of the patients exposed to this hyperbaric oxygen”

“Yes, I read some articles about this type of medicine as well as in postgraduate internal medicine books”

Referral of patients and including hyperbaric oxygen therapy in their practice

A limited number of practitioners have referred patients for hyperbaric oxygen therapy. The main reason given for not referring a patient for hyperbaric oxygen therapy (and thus the main barrier mentioned by the participants to implementing hyperbaric oxygen therapy as part of their clinical practice) was the lack of availability of the chambers and equipment.

“We don’t have..., actually, in Bahrain we don’t have a chamber”

“Of course, we need actually a chamber – it is very important – especially in our speciality...”

“Actually it has not happened before, because I think that these machines are not available at our hospital...”

“I think the main barrier is the availability of these hyperbaric chambers”

Discussion

Study participants

A relatively small proportion of the possible number of participants in the sampling frame (93 of a possible 302) was included in the study.

A large number of potential participants (n=103) refused to participate. Specific reasons for their refusal to participate were not captured as part of this study, but informal discussions implicated a high workload (with insufficient time to participate) as a contributing factor. Another reason specifically mentioned by non-participants was a lack of knowledge regarding hyperbaric oxygen therapy and their perceived inability to contribute to the research. Others indicated that they do not want to participate because they felt that hyperbaric oxygen therapy did not have a place within their practice of medicine. This was specifically experienced within the paediatrics and Obstetrics & Gynaecology departments. The fact that these persons did not participate in the study may have biased the results of the study and explain why specific associations were not found to be statistically significant.

Non-participation for other reasons would likely result in less bias. Sixty-five participants were on leave or deployed during the time of the study, which unfortunately took place during a period in which the Kingdom of Bahrain suffered civil unrest, which resulted in a large number of the Royal Medical Services' medical practitioners being deployed around the country for months at a time. After the conflicts subsided, these practitioners took leave upon their return to their home bases. This further reduced the number of participants available for participation. Thirty-eight of the medical practitioners were enrolled for studies abroad and were also not available for participation. Another factor that influenced the availability of participants is the fact that the survey was conducted over the holy month of Ramadan, during which many medical practitioners were on leave. As mentioned, these factors are likely to only have a minor effect on the results, since military deployments, the taking of leave and religious background would not affect the outcomes investigated and would thus unlikely bias or confound the results.

Of the ninety-three medical practitioners participating in the survey, 77.4% were civilian and only 22.6% had a military appointment. This ratio shows only a minor difference from the ratio of persons appointed by the military health services (which is approximately 60% civilian). This is again most likely due to the fact that the military medical practitioners were required to assist during military deployments in the country, work in the military camps or be part of external military training exercises in support of the larger Royal Medical Services programme. The professional registrations of the medical practitioners (63.4% Bahraini and 36.6% with international registration), is representative of the registrations of medical practitioners in the Royal Medical Services.

No persons working within the department of Obstetrics and Gynaecology or the department of Paediatrics were willing to participate in the study. Practitioners within these specialities did not see a place for hyperbaric oxygen therapy within their field of practice. However, previous studies have indicated that carbon monoxide poisoning during pregnancy and in children may have devastating effects^[148]. Although there is some controversy in the literature^[44], the mechanisms of action underpinning the use of hyperbaric oxygen therapy in carbon monoxide poisoning would clearly favour the use of hyperbaric oxygen therapy within their fields. It should furthermore be noted that paediatric patients and pregnancy have been specific exclusion factors in studies examining the effect of hyperbaric oxygen therapy in carbon monoxide poisoning^[44], which means that an opinion cannot yet be formulated regarding this indication. Other indications that are approved by the Undersea and Hyperbaric Medical Society^[22] and/ or recommended by the European Committee for Hyperbaric Medicine^[30], for which adequate evidence exists, could also affect patients seen within these departments, e.g. crush injuries, necrotising infections, selected problem wounds, etc. However, since medical practitioners from other departments would also be involved in the treatment and management of these patients, the effect of these practitioners' non-participation is not likely to have a major effect on patient care, although it may have provided valuable information regarding the knowledge and attitudes of these medical practitioners.

Participants in the survey represented all levels of seniority. Even consultants and heads of department participated in the survey. This adds significant strength to the

study, since these senior personnel members are in decision-making positions and their knowledge and attitudes are likely to affect junior colleagues. Unfortunately not many senior residents participated in the survey. This is most likely due to their high workload (compared to other practitioners in the same department).

Participant knowledge of hyperbaric oxygen therapy

When considering the fact that there are (broadly speaking) 14 indications that are collectively approved by the Undersea and Hyperbaric Medical Society and the European Committee for Hyperbaric Medicine, the percentage of medical practitioners having a clear knowledge of the indications for this treatment modality is very low. Of the medical practitioners participating in the survey, 11.8% have never heard about hyperbaric oxygen therapy before. Most people were able to mention at least one indication, but this is to be expected in a military setting, where there is some knowledge regarding the treatment of decompression sickness in military divers. The fact that “selected problem wounds” were mentioned with a very high frequency is surprising. This was most commonly cited as “diabetic wounds” (and coded as “selected problem wounds” by the primary investigator, which is a very encouraging prospect, since there is some evidence that hyperbaric oxygen therapy is effective for selected patients with diabetic wounds^[19, 60, 63, 64] and Bahrain also has a very high prevalence of diabetes^[149, 150]. The one person who was able to mention all 14 indications for hyperbaric oxygen therapy has never received specialised training in hyperbaric medicine, but he has worked in a hospital (in Singapore) during his postgraduate training in which he had access to a hyperbaric facility and used to regularly refer patients for treatment.

The lack of availability of hyperbaric facilities in the Middle East and the fact that hyperbaric oxygen therapy as a treatment modality is not specifically included in most undergraduate and postgraduate training programmes would explain the very low level of knowledge about this treatment modality. These facts were confirmed during the structured interview component of this study and is consistent with other similar surveys performed^[146, 151].

Despite the lack of availability of treatment facilities, a high percentage of practitioners indicated that there had been some reference to the use of hyperbaric oxygen therapy in their undergraduate or postgraduate training. It was interesting to find a large number of participants (n=14) mentioning that they first heard about hyperbaric oxygen therapy in discussions with a colleague. Unfortunately most participants have not had any interaction with a hyperbaric medicine practitioner and they have not heard or read about it for at least the past five years.

Medical practitioners who participated in the survey displayed some knowledge of the hyperbaric oxygen therapy approved indications within their speciality, which is encouraging. The number of indications mentioned by individuals was also encouraging, but specifically also pointing to the effect of military training (where medical practitioners are exposed to military divers and associated decompression sickness and its treatment with hyperbaric oxygen therapy). Information about hyperbaric oxygen treatment was also likely obtained through specific training events and continued medical education that consists of lectures, books, journals or specific postgraduate training that the Royal Medical Services provide to the medical practitioners in their employ.

Even the rarely used and highly specific indications were mentioned by some medical practitioners participating in the survey, which is indicative of a high level of knowledge in some individuals. In the structured interview it became clear that some practitioners have previously worked in hospital settings where hyperbaric oxygen therapy was available as an adjunctive treatment.

A large number of participants in the survey were able to correctly mention the absolute and relative contra-indications for hyperbaric oxygen therapy. There were however a number of “contra-indications” mentioned that would not bar a person from treatment and which may in fact make the provision of hyperbaric oxygen therapy easier (e.g. perforation of the tympanic membranes).

A number of factors were identified to be associated with a high level of knowledge of the indications for hyperbaric oxygen therapy (defined as correctly mentioning

more than 7 of the approved indications). Participants who were able to mention more than seven indications were more likely to:

- have specialised after 1995
- hold a Bahraini medical registration rather than an international registration
- have heard about hyperbaric oxygen therapy during their undergraduate education. This could be explained by the fact that postgraduate studies are generally quite focussed on the specific medical field and it is thus unlikely that a broad, general approach to the use of various indications for hyperbaric oxygen therapy would be used. Postgraduate studies would thus likely be limited to indications specific to the area of speciality.
- have read about hyperbaric oxygen therapy in journal articles (likely indicative of continuing medical education).

None of these associations found during the study were statistically significant and these results should thus be interpreted with caution.

“Problematic wounds” mentioned as an indication for hyperbaric oxygen therapy was also the indication which most practitioners (who cited the indication) felt as falling within their area of specialisation.

Lickert scale responses

The Lickert scale data indicates that a large proportion (37.6%) of the participants have seen a hyperbaric chamber before and these participants were more likely to be employed as a military officer (Odds Ratio = 4.48; 95% CI = 1.6 – 12.7; $\text{Chi}^2 = 0.003$). This is to be expected, since they would be exposed to military divers and pilots as part of their work and have access to chambers as part of their military training.

Although a high proportion of participants felt that proving hyperbaric oxygen therapy is considered an expensive treatment modality, most still consider it to be cost-effective despite the expense and considered it to be a valid treatment modality. This is in line with economic studies performed on the application for hyperbaric oxygen therapy for a number of indications. An economical analysis by the

Canadian Agency for Drugs and Technologies in Health reviewing the use of adjunctive hyperbaric oxygen therapy for diabetic foot ulcers has come to the conclusion that hyperbaric oxygen therapy is more effective than standard care alone and reduces major lower extremity amputation rate from 32% to 11% with a decrease in the proportion of unhealed wounds and an acceptable 12 year cost outcome (19% reduction in overall health care costs) compared to standard care^[152]. Likewise, according to European data, the risk for major surgery and disability is considered 15 times higher in diabetics versus non-diabetics and increases with age or a history of previous amputation. Contra-lateral amputations are necessary in 50% of cases within 4 years of the initial intervention and ipsilateral re-amputations in about 27%. The use of adjunctive hyperbaric oxygen therapy can reduce the incidence of major surgery up to 82% as well as general morbidity, length of hospitalization and cost as demonstrated in the table 6 below^[153].

Table 6: Mortality, Morbidity, Hospital stay and cost of HBO versus non-HBO in diabetic patients

	Mortality	Morbidity	Hospital stay	HBO cost	Total cost
HBO	---%	5%	60 days	€ 3000	€ 36000
Non-HBO	31%	30%	100 days		€ 55000
Potential saving/pt					€ 19000/pt
Potential saving %					35%

An economical evaluation on demographic data of the Italian Ministry of Health on diabetic foot ulcers and diabetic foot lesions at risk for amputation, indicate a potential annual saving for the National Health Care system ranging between 58 and 69 million €, if hyperbaric oxygen therapy would be included as a standard adjunct in the treatment of the diabetic foot^[154]. It is not known to which extent this information, as well as data from other studies is known by the participants and it is possible that their perception of the cost-effectiveness of hyperbaric oxygen therapy for these indications is not based on the above facts.

All of the “UHMS-approved” indications for hyperbaric oxygen therapy are approved on specific criteria, one of which is the requirement for the hyperbaric oxygen should be cost-effective^[22]. In our study there was a strong association between

participants feeling that hyperbaric oxygen therapy is expensive and those feeling that it is cost-effective (Odds Ratio = 5.2), but this was not statistically significant (95% CI = 0.6 – 44.4; Fisher's exact = 0.069).

Referral of patients

Only 13.98% of participants indicated that they have previously referred a patient for hyperbaric oxygen therapy. It was quite surprising to see that practitioners who have not previously referred patients for hyperbaric oxygen therapy had no association with their agreement (or not) whether HBOT is “a valid treatment modality” ($p=0.2111$). Again, military participants were much more likely to have previously referred a patient for hyperbaric oxygen therapy than civilian participants (Odds Ratio = 7.6; 95%CI = 2.1 – 27.1; $p=0.0016$) and they were much less likely to feel that they have insufficient knowledge about hyperbaric oxygen therapy (Odds Ratio = 0.09; 95% CI = 0.02 – 0.3; $p<0.0001$). The perceived lack of availability of chambers within Bahrain (and other Middle Eastern countries) seems to be a major barrier to referral of patients, since patients would have to travel to Europe or elsewhere for therapy. A high percentage of practitioners indicated that they would refer their patients for hyperbaric oxygen therapy.

Conclusion

Although this study was restricted in terms of availability of personnel (due to civil unrest and religious commitments), some encouraging findings were elicited. There was a positive disposition toward the use of HBOT and there is also a good opportunity for knowledge intervention, since many practitioners indicated that they would like more information about HBOT. Similar to what has been found in previous studies, this study confirmed that medical practitioners generally have a poor level of knowledge of the indications for hyperbaric oxygen therapy, its mechanisms of action, as well as its side-effects and contra-indications. A visit to a hyperbaric facility and discussion of case-studies would likely have a positive impact on using adjunctive hyperbaric oxygen therapy in practice.

References

1. Leach RM, Rees PJ and Wilmshurst P. Hyperbaric oxygen therapy. *BMJ* 1998;1140-1143.
2. Gabb G and Robin ED. Hyperbaric oxygen. A therapy in search of diseases. *Chest*. 1987;92(6):1074-1082.
3. Bennett M and Heard R. Hyperbaric oxygen therapy for multiple sclerosis. *Cochrane Database Syst Rev*. 2004;(1):CD003057.
4. Bennett M, Jepson N and Lehm J. Hyperbaric oxygen therapy for acute coronary syndrome. *Cochrane Database Syst Rev*. 2005;(2):CD004818.
5. Bennett MH, Feldmeier J, Hampson N, Smee R and Milross C. Hyperbaric oxygen therapy for late radiation tissue injury. *Cochrane Database Syst Rev*. 2005;(3):CD005005.
6. Bennett MH, Kertesz T and Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2005;(1):CD004739.
7. Bennett MH, Kertesz T and Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev*. 2007;(1):CD004739.
8. Bennett MH, Lehm JP and Jepson N. Hyperbaric oxygen therapy for acute coronary syndrome. *Cochrane Database Syst Rev*. (8):CD004818.
9. Bennett MH, Stanford R and Turner R. Hyperbaric oxygen therapy for promoting fracture healing and treating fracture non-union. *Cochrane Database Syst Rev*. 2005;(1):CD004712.
10. Bennett MH, Trytko B and Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. *Cochrane Database Syst Rev*. 2004;(4):CD004609.
11. Bennett MH, Wasiak J, Schnabel A, Kranke P and French C. Hyperbaric oxygen therapy for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2005;(3):CD004954.
12. Buckley NA, Juurlink DN, Isbister G, Bennett MH and Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev*. (4):CD002041.

13. Coulthard P, Esposito M, Worthington HV and Jokstad A. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. *Cochrane Database Syst Rev*. 2002;(3):CD003603.
14. Coulthard P, Patel S, Grusovin GM, Worthington HV and Esposito M. Hyperbaric oxygen therapy for irradiated patients who require dental implants: a Cochrane review of randomised clinical trials. *Eur J Oral Implantol*. 2008;1(2):105-110.
15. Eskes A, Ubbink DT, Lubbers M, Lucas C and Vermeulen H. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. *Cochrane Database Syst Rev*. (10):CD008059.
16. Esposito M, Grusovin MG, Patel S, Worthington HV and Coulthard P. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. *Cochrane Database Syst Rev*. 2008;(1):CD003603.
17. Juurlink DN, Buckley NA, Stanbrook MB, et al. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev*. 2005;(1):CD002041.
18. Juurlink DN, Stanbrook MB and McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev*. 2000;(2):CD002041.
19. Kranke P, Bennett M, Roeckl-Wiedmann I and Debus S. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database Syst Rev*. 2004;(2):CD004123.
20. Phillips JS and Jones SE. Hyperbaric oxygen as an adjuvant treatment for malignant otitis externa. *Cochrane Database Syst Rev*. 2005;(2):CD004617.
21. Villanueva E, Bennett MH, Wasiak J and Lehm JP. Hyperbaric oxygen therapy for thermal burns. *Cochrane Database Syst Rev*. 2004;(3):CD004727.
22. Gesell LB. *Hyperbaric Oxygen Therapy Indications*. 12th ed. Durham, NC: UHMS, 2008.
23. Gesell LB. *Hyperbaric Oxygen Therapy Indications*. 12th Edition ed. Durham, North Carolina.: Undersea and Hyperbaric Medical Society, 2008.
24. Kindwall EP. A history of hyperbaric medicine. In: Kindwall EP, ed. *Hyperbaric Medicine Practice*. 3rd ed. Flagstaff, AZ: Best Publishing Company 2008:5-22.
25. Wattel F. A history of hyperbaric medicine. In: Matthieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht: Springer 2006:1-11.
26. Boerema I, Kroll JA, Meyne NG, et al. [High atmospheric pressure as an aid in heart surgery]. *Ned Tijdschr Geneesk*. 1957;101(31):1464-1469.

27. Lowry C. Oxygen Toxicity. In: Edmonds C, Lowry C, Pennefather J and Walker R, eds. *Diving and Subaquatic Medicine*. 4th ed. London: Arnold 2002:208-241.
28. Bert P. Translated text of "La pression barometrique". In: Hitchcock MA and Hitchcock FA, eds. *Barometric Pressure: Researches in experimental physiology*. Columbus, OH: College Book Company 1943.
29. Churchill-Davidson I, Sanger C and Thomlinson RH. High-pressure oxygen and radiotherapy. *Lancet*. 1955;268(6874):1091-1095.
30. Wattel F and Mathieu D. Methodology for assessing hyperbaric oxygen therapy in clinical practice. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht: Springer 2006:163-170.
31. Davis JC, Sheffield PJ, Schuknecht L, et al. Altitude decompression sickness: hyperbaric therapy results in 145 cases. *Aviat Space Environ Med*. 1977;48(8):722-730.
32. Lollis B. You're the flight surgeon: pulmonary decompression sickness. *Aviat Space Environ Med*. 2008;79(6):636-637.
33. Mooney RL. You're the flight surgeon: neurologic decompression sickness. *Aviat Space Environ Med*. 2008;79(5):539-540.
34. Risberg J, Englund M, Aanderud L, et al. Venous gas embolism in chamber attendants after hyperbaric exposure. *Undersea Hyperb Med*. 2004;31(4):417-429.
35. Correl B. Nurses death an accident. *The News Herald*. Wednesday, 24 July 1991.
36. Boycott DM, Damant GCC and Haldane JS. The prevention of compressed-air illness. *J Hyg*. 1908;8:342-443.
37. Walker R. Decompression sickness: history and physiology. In: Edmonds C, Lowry C, Pennefather J and Walker R, eds. *Diving and Subaquatic Medicine*. 4th ed. London: Arnold 2002:111-130.
38. Vann RD, Butler FK, Mitchell SJ and Moon RE. Decompression illness. *Lancet*. 2011;377(9760):153-164.
39. Fox HM. Carbon monoxide affinity of chlorocruorin and haemoglobin. *Nature*. 1948;162(4105):20.
40. Knighton DR, Silver IA and Hunt TK. Regulation of wound-healing angiogenesis-effect of oxygen gradients and inspired oxygen concentration. *Surgery*. 1981;90(2):262-270.

41. Lawson-Smith P, Jansen EC, Hilsted L and Hyldegaard O. Effect of hyperbaric oxygen therapy on whole blood cyanide concentrations in carbon monoxide intoxicated patients from fire accidents. *Scand J Trauma Resusc Emerg Med.* 2010;18:32.
42. Annane D, Chadda K, Gajdos P, et al. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. *Intensive Care Med.* 2011;37(3):486-492.
43. Birmingham CM and Hoffman RS. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. *Intensive Care Med.* 2011;37(7):1218; author reply 1219.
44. Buckley NA, Juurlink DN, Isbister G, Bennett MH and Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev.* 2011;(4).
45. Malhotra MS and Wright HC. The effects of a raised intrapulmonary pressure on the lungs of fresh unchilled cadavers. *J Pathol Bacteriol.* 1961;82:198-202.
46. Schaffer KE, Mc NW, Jr., Carey C and Liebow AA. Mechanisms in development of interstitial emphysema and air embolism on decompression from depth. *J Appl Physiol.* 1958;13(1):15-29.
47. Halpern P, Greenstein A, Melamed Y, et al. Arterial air embolism after penetrating lung injury. *Crit Care Med.* 1983;11(5):392-393.
48. Hodics T and Linfante I. Cerebral air embolism. *Neurology.* 2003;60(1):112.
49. Hart GB, Lamb RC and Strauss MB. Gas gangrene. *J Trauma.* 1983;23(11):991-1000.
50. Stevens DL, Bryant AE, Adams K and Mader JT. Evaluation of therapy with hyperbaric oxygen for experimental infection with *Clostridium perfringens*. *Clin Infect Dis.* 1993;17(2):231-237.
51. Brummelkamp WH, Boerema I and Hoogendyk L. Treatment of clostridial infections with hyperbaric oxygen drenching. A report on 26 cases. *Lancet.* 1963;1(7275):235-238.
52. Korhonen K. Hyperbaric oxygen therapy in acute necrotizing infections with a special reference to the effects on tissue gas tensions. *Ann Chir Gynaecol Suppl.* 2000;(214):7-36.
53. Fredette V. Effect of Hyperbaric Oxygen on Anaerobic Bacteria and Toxins. *Ann N Y Acad Sci.* 1965;117:700-705.

54. Van U. Inhibition of Toxin Production in *Clostridium Perfringens* in Vitro by Hyperbaric Oxygen. *Antonie Van Leeuwenhoek*. 1965;31:181-186.
55. Holland JA, Hill GB, Wolfe WG, et al. Experimental and clinical experience with hyperbaric oxygen in the treatment of clostridial myonecrosis. *Surgery*. 1975;77(1):75-85.
56. Garcia-Covarrubias L, McSwain NE, Jr., Van Meter K and Bell RM. Adjuvant hyperbaric oxygen therapy in the management of crush injury and traumatic ischemia: an evidence-based approach. *Am Surg*. 2005;71(2):144-151.
57. Bouachour G, Cronier P, Gouello JP, et al. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blind placebo-controlled clinical trial. *J Trauma*. 1996;41(2):333-339.
58. Baroni G, Porro T, Faglia E, et al. Hyperbaric oxygen in diabetic gangrene treatment. *Diabetes Care*. 1987;10(1):81-86.
59. Abidia A, Laden G, Kuhan G, et al. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. *Eur J Vasc Endovasc Surg*. 2003;25(6):513-518.
60. Doctor N, Pandya S and Supe A. Hyperbaric oxygen therapy in diabetic foot. *J Postgrad Med*. 1992;38(3):112-114, 111.
61. Duzgun AP, Satir HZ, Ozozan O, et al. Effect of hyperbaric oxygen therapy on healing of diabetic foot ulcers. *J Foot Ankle Surg*. 2008;47(6):515-519.
62. Faglia E, Favales F, Aldeghi A, et al. Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer. A randomized study. *Diabetes Care*. 1996;19(12):1338-1343.
63. Kalani M, Jorneskog G, Naderi N, Lind F and Brismar K. Hyperbaric oxygen (HBO) therapy in treatment of diabetic foot ulcers. Long-term follow-up. *J Diabetes Complications*. 2002;16(2):153-158.
64. Londahl M, Katzman P, Nilsson A and Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. *Diabetes Care*. 2010;33(5):998-1003.
65. Fife CE, Smart DR, Sheffield PJ, et al. Transcutaneous oximetry in clinical practice: consensus statements from an expert panel based on evidence. *Undersea Hyperb Med*. 2009;36(1):43-53.

66. Kranke P, Bennett MH, Debus SE, Roeckl-Wiedmann I and Schnabel A. Hyperbaric oxygen therapy for chronic wounds (Review). *Cochrane Database Syst Rev*. 2009;(3).
67. Hammarlund C and Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. *Plast Reconstr Surg*. 1994;93(4):829-833; discussion 834.
68. Hart GB, Lennon PA and Strauss MB. Hyperbaric oxygen in exceptional, acute bloodloss anemia. *J Hyperbaric Med*. 1987;2(4):205-210.
69. Bartlett B. HBO and exceptional blood loss anemia. In: Kindwall EP and Whelan HT, eds. *Hyperbaric Oxygen Practice*. 3rd ed. Flagstaff: Best Publishing Company 2008:793-834.
70. Hampson NP. Intracranial Abscess. In: Gesell LB, ed. *Hyperbaric Oxygen Therapy Indications*. 12th ed. Durham: Undersea and Hyperbaric Medical Society 2008:91-95.
71. Miller JD, Fitch W, Ledingham IM and Jennett WB. The effect of hyperbaric oxygen on experimentally increased intracranial pressure. *J Neurosurg*. 1970;33(3):287-296.
72. Miller JD and Ledingham IM. Reduction of raised intracranial pressure: hyperbaric oxygen versus hyperventilation. *Br J Surg*. 1969;56(8):630.
73. Miller JD and Ledingham IM. Reduction of increased intracranial pressure. Comparison between hyperbaric oxygen and hyperventilation. *Arch Neurol*. 1971;24(3):210-216.
74. Miller JD, Ledingham IM and Jennett WB. Effects of hyperbaric oxygen on intracranial pressure and cerebral blood flow in experimental cerebral oedema. *J Neurol Neurosurg Psychiatry*. 1970;33(6):745-755.
75. Lampl L and Frey G. Intra-cranial abscess. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht: Springer 2006:291-304.
76. Fife CE, Buyukcikir C, Otto GH, et al. The predictive value of transcutaneous oxygen tension measurement in diabetic lower extremity ulcers treated with hyperbaric oxygen therapy: a retrospective analysis of 1,144 patients. *Wound Repair Regen*. 2002;10(4):198-207.
77. Marx RE, Ehler WJ, Tayapongsak P and Pierce LW. Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg*. 1990;160(5):519-524.

78. Pellitteri PK, Kennedy TL and Youn BA. The influence of intensive hyperbaric oxygen therapy on skin flap survival in a swine model. *Arch Otolaryngol Head Neck Surg.* 1992;118(10):1050-1054.
79. Tan CM, Im MJ, Myers RA and Hoopes JE. Effects of hyperbaric oxygen and hyperbaric air on the survival of island skin flaps. *Plast Reconstr Surg.* 1984;73(1):27-30.
80. Li EN, Menon NG, Rodriguez ED, et al. The effect of hyperbaric oxygen therapy on composite graft survival. *Ann Plast Surg.* 2004;53(2):141-145.
81. Gill AL and Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. *Qjm.* 2004;97(7):385-395.
82. Jallali N, Withey S and Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. *Am J Surg.* 2005;189(4):462-466.
83. Mathieu D, Favory R, Cesari J-F and Wattel F. Necrotizing soft tissue infections. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht: Springer 2006:263-289.
84. Riseman JA, Zamboni WA, Curtis A, et al. Hyperbaric oxygen therapy for necrotizing fasciitis reduces mortality and the need for debridements. *Surgery.* 1990;108(5):847-850.
85. Hirn M, Niinikoski J and Lehtonen OP. Effect of hyperbaric oxygen and surgery on experimental multimicrobial gas gangrene. *Eur Surg Res.* 1993;25(5):265-269.
86. Jacoby I. Necrotizing soft-tissue infections. In: Gesell LB, ed. *Hyperbaric Oxygen Therapy Indications*. 12th ed. Durham, NC: Undersea and Hyperbaric Medical Society 2008:97-115.
87. Hart GB. Refractory Osteomyelitis. In: Gesell LB, ed. *Hyperbaric Oxygen Therapy Indications*. 12th ed. Durham, NC: Undersea and Hyperbaric Medical Society 2008:117-144.
88. Coulson DB, Ferguson AB, Jr. and Diehl RC, Jr. Effect of hyperbaric oxygen on the healing femur of the rat. *Surg Forum.* 1966;17:449-450.
89. Slack WK, Thomas DA and Perrins D. Hyperbaric Oxygenation Chronic Osteomyelitis. *Lancet.* 1965;1(7395):1093-1094.
90. Yablon IG and Cruess RL. The effect of hyperbaric oxygen on fracture healing in rats. *J Trauma.* 1968;8(2):186-202.

91. Niinikoski J, Penttinen R and Kulonen E. Effect of hyperbaric oxygenation on fracture healing in the rat: a biochemical study. *Calcif Tissue Res.* 1970;Suppl:115-116.
92. Davis JC, Gates GA, Lerner C, et al. Adjuvant hyperbaric oxygen in malignant external otitis. *Arch Otolaryngol Head Neck Surg.* 1992;118(1):89-93.
93. Delanian S and Lefaix JL. Current management for late normal tissue injury: radiation-induced fibrosis and necrosis. *Semin Radiat Oncol.* 2007;17(2):99-107.
94. Carl UM and Hartmann KA. Hyperbaric oxygen treatment for symptomatic breast edema after radiation therapy. *Undersea Hyperb Med.* 1998;25(4):233-234.
95. Feldmeier JJ and Hampson NB. A systematic review of the literature reporting the application of hyperbaric oxygen prevention and treatment of delayed radiation injuries: an evidence based approach. *Undersea Hyperb Med.* 2002;29(1):4-30.
96. Yarnold J. Double-blind randomised phase II study of hyperbaric oxygen in patients with radiation-induced brachial plexopathy. *Radiother Oncol.* 2005;77(3):327.
97. Marx RE and Ames JR. The use of hyperbaric oxygen therapy in bony reconstruction of the irradiated and tissue-deficient patient. *J Oral Maxillofac Surg.* 1982;40(7):412-420.
98. Greenwood TW and Gilchrist AG. Hyperbaric oxygen and wound healing in post-irradiation head and neck surgery. *Br J Surg.* 1973;60(5):394-397.
99. Mainous EG, Boyne PJ and Hart GB. Elimination of sequestrum and healing of osteoradionecrosis of the mandible after hyperbaric oxygen therapy: report of case. *J Oral Surg.* 1973;31(5):336-339.
100. Marx RE, Johnson RP and Kline SN. Prevention of osteoradionecrosis: a randomized prospective clinical trial of hyperbaric oxygen versus penicillin. *J Am Dent Assoc.* 1985;111(1):49-54.
101. Neovius EB, Lind MG and Lind FG. Hyperbaric oxygen therapy for wound complications after surgery in the irradiated head and neck: a review of the literature and a report of 15 consecutive patients. *Head Neck.* 1997;19(4):315-322.
102. Feldmeier JJ and Matthew WP. Delayed Radiation Injuries (Soft tissue And Bony Necrosis) In: Gesell LB, ed. *Hyperbaric Oxygen Indications*. 12th ed. Durham: Undersea and Hyperbaric Medical Society 2008:145-168.

103. Aitasalo K, Grenman R, Virolainen E, Niinikoski J and Klossner J. A modified protocol to treat early osteoradionecrosis of the mandible. *Undersea Hyperb Med.* 1995;22(2):161-170.
104. Aitasalo K, Niinikoski J, Grenman R and Virolainen E. A modified protocol for early treatment of osteomyelitis and osteoradionecrosis of the mandible. *Head Neck.* 1998;20(5):411-417.
105. Mader JT, Brown GL, Guckian JC, Wells CH and Reinartz JA. A mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. *J Infect Dis.* 1980;142(6):915-922.
106. Zamboni WA, Roth AC, Russell RC, et al. Morphologic analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg.* 1993;91(6):1110-1123.
107. Niccole MW, Thornton JW, Danet RT, Bartlett RH and Tavis MJ. Hyperbaric oxygen in burn management: a controlled study. *Surgery.* 1977;82(5):727-733.
108. Cianci P, Lueders HW, Lee H, et al. Adjunctive hyperbaric oxygen therapy reduces length of hospitalization in thermal burns. *J Burn Care Rehabil.* 1989;10(5):432-435.
109. Zamboni WA and C. B. Compromised Graft And Flaps. In: Gill AL, ed. *Hyperbaric oxygentherapy indication* 12 ed. Durham: Undersea and Hyperbaric Medical Society 2008:169-179.
110. Cianci P and Sato R. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns: a review. *Burns.* 1994;20(1):5-14.
111. Brannen AL, Still J, Haynes M, et al. A randomized prospective trial of hyperbaric oxygen in a referral burn center population. *Am Surg.* 1997;63(3):205-208.
112. Thackham JA, McElwain DL and Long RJ. The use of hyperbaric oxygen therapy to treat chronic wounds: A review. *Wound Repair Regen.* 2008;16(3):321-330.
113. Piantadosi CA. Physiology of hyperbaric hyperoxia. *Respir Care Clin N Am.* 1999;5(1):7-19, v.
114. Ratzenhofer-Komenda B, Favory R, Welslau W, Smolle-Juttner FM and Mathieu D. Physiological effects of hyperbaric oxygen on oxygen transport and tissue oxygen pressure. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine.* Dordrecht: Springer 2006:49-73.

115. Boerema I, Meyne NG, Brummelkamp WH, et al. Life without blood. *Ned Tijdschr Geneeskd*. 1960;104:949-954.
116. Thom SR, Bhople VM, Velazquez OC, et al. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol*. 2006;290(4):H1378-1386.
117. Wikipedia. Fick's laws of diffusion. [cited 24 November 2011]; Available from: http://en.wikipedia.org/wiki/Fick's_laws_of_diffusion
118. Sheffield PJ and Smith APS. Physiological and Pharmacological basis of hyperbaric oxygen therapy. In: Bakker DJ and Cramer FS, eds. *Hyperbaric Surgery*. Flagstaff, AZ: Best Publishing Company 2002:63-109.
119. Hopf HW, Gibson JJ, Angeles AP, et al. Hyperoxia and angiogenesis. *Wound Repair Regen*. 2005;13(6):558-564.
120. Sheikh AY, Gibson JJ, Rollins MD, et al. Effect of hyperoxia on vascular endothelial growth factor levels in a wound model. *Arch Surg*. 2000;135(11):1293-1297.
121. Cianci P and Hunt TK. Adjunctive hyperbaric oxygen therapy in the treatment of diabetic foot. In: Bowker JH and Pfeifer MA, eds. *Lenin and O'Neal's The Diabetic Foot*. 7th ed. Philadelphia: Elsevier 2008:339-360.
122. Hutton JJ, Tappel AC and Udenfriend S. Cofactor and substrate requirements of collagen proline hydroxylase. *Arch Biochem*. 1967;118:231-240.
123. Gimbel ML and Hunt TK. Wound healing and hyperbaric oxygen. In: Kindwall EP and Whelan HT, eds. *Hyperbaric Medicine Practice*. Flagstaff, AZ: Best Publishing Company 2008:317-353.
124. Hunt TK and Aslam RS. Oxygen 2002: wounds. *Undersea Hyperb Med*. 2004;31(1):147-153.
125. Thom SR, Lauermann MW and Hart GB. Intermittent hyperbaric oxygen therapy for reduction of mortality in experimental polymicrobial sepsis. *J Infect Dis*. 1986;154(3):504-510.
126. Park MK, Myers RA and Marzella L. Oxygen tensions and infections: modulation of microbial growth, activity of antimicrobial agents, and immunologic responses. *Clin Infect Dis*. 1992;14(3):720-740.
127. Mathieu D and Wattel F. Physiologic effects of hyperbaric oxygen on microorganisms and host defences against infection. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht, The Netherlands.: Springer 2006:103-116.

128. Bird AD and Telfer AB. Effect of Hyperbaric Oxygen on Limb Circulation. *Lancet*. 1965;1(7381):355-356.
129. Strauss MB and Miller SS. The role of hyperbaric oxygen in crush injury, skeletal muscle-compartment syndrome, and other acute ischemias. In: Kindwall EP and Whelan HT, eds. *Hyperbaric Medicine Practice*. 3rd Edition ed. Flagstaff, AZ: Best Publishing Company 2008:767.
130. Plafki C, Peters P, Almeling M, Welslau W and Busch R. Complications and side effects of hyperbaric oxygen therapy. *Aviat Space Environ Med*. 2000;71(2):119-124.
131. Toklu AS, Korpınar S, Erelel M, Uzun G and Yildiz S. Are pulmonary bleb and bullae a contraindication for hyperbaric oxygen treatment? *Respir Med*. 2008;102(8):1145-1147.
132. Pott F, Westergaard P, Mortensen J and Jansen EC. Hyperbaric oxygen treatment and pulmonary function. *Undersea Hyperb Med*. 1999;26(4):225-228.
133. Butler FK, Jr. and Thalmann ED. Central nervous system oxygen toxicity in closed circuit scuba divers II. *Undersea Biomed Res*. 1986;13(2):193-223.
134. Zwart BP. Two differences in hyperbaric exposure. *Undersea Hyperb Med*. 2004;31(2):187; author reply 191.
135. Yildiz S, Ay H and Qyrdedi T. Central nervous system oxygen toxicity during routine hyperbaric oxygen therapy. *Undersea Hyperb Med*. 2004;31(2):189-190.
136. Yildiz S, Aktas S, Cimsit M, Ay H and Togrol E. Seizure incidence in 80,000 patient treatments with hyperbaric oxygen. *Aviat Space Environ Med*. 2004;75(11):992-994.
137. Hampson N and Atik D. Central nervous system oxygen toxicity during routine hyperbaric oxygen therapy. *Undersea Hyperb Med*. 2003;30(2):147-153.
138. Bean JW and Rottschaefer G. Reflexogenic and central structures in oxygen poisoning. *J Physiol*. 1938;94(3):294-306.
139. Bean JW. Hyperbaric Oxygenation. Factors Influencing Clinical Oxygen Toxicity. *Ann N Y Acad Sci*. 1965;117:745-759.
140. Bean JW. Effects of high oxygen pressure on carbon dioxide transport, on blood and tissue acidity, and on oxygen consumption and pulmonary ventilation. *J Physiol*. 1931;72(1):27-48.

141. Kindwall EP. Contraindications and side effects to hyperbaric oxygen treatment. In: Kindwall EP and Whelan HT, eds. *Hyperbaric Medicine Practice*. Flagstaff, AZ: Best Publishing Company 2008:284.
142. Palmquist BM, Philipson B and Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. *Br J Ophthalmol*. 1984;68(2):113-117.
143. Butler FK, Jr. Diving and hyperbaric ophthalmology. *Surv Ophthalmol*. 1995;39(5):347-366.
144. Evans AW, Gill R, Valiulis AO, Lou W and Sosiak TS. Hyperbaric oxygen therapy and diabetic foot ulcers: knowledge and attitudes of Canadian primary care physicians. *Can Fam Physician*. 56(5):444-452.
145. Guo S, Counte MA, Schmitz H and Wu HS. Physician adoption of hyperbaric oxygen therapy in the treatment of chronic wounds. *Ostomy Wound Manage*. 2005;51(10):46-58.
146. Kanatas AN, Lowe D, Harrison J and Rogers SN. Survey of the use of hyperbaric oxygen by maxillofacial oncologists in the UK. *Br J Oral Maxillofac Surg*. 2005;43(3):219-225.
147. Rogers SN and Magennis P. Survey of fellows regarding a national study into treatment with hyperbaric oxygen. *Br J Oral Maxillofac Surg*. 2007;45(5):433-435.
148. Mathieu D and Mathieu-Nolf M. Oxygen therapy for CO poisoning: rationale and recommendations. *Przegl Lek*. 2005;62(6):436-437.
149. al-Mahroos F and McKeigue PM. High prevalence of diabetes in Bahrainis. Associations with ethnicity and raised plasma cholesterol. *Diabetes Care*. 1998;21(6):936-942.
150. Musaiger AO. Diabetes mellitus in Bahrain: an overview. *Diabet Med*. 1992;9(6):574-578.
151. Evans AW, Gill R, Valiulis AO, Lou W and Sosiak TS. Hyperbaric oxygen therapy and diabetic foot ulcers: knowledge and attitudes of Canadian primary care physicians. *Can Fam Physician*. 2010;56(5):444-452.
152. Chuck AW, Hailey D, Jacobs P and Perry DC. Cost-effectiveness and budget impact of adjunctive hyperbaric oxygen therapy for diabetic foot ulcers. *Int J Technol Assess Health Care*. 2008;24(2):178-183.
153. Marroni A, Longobardi P and Cali-Corleo R. Cost-effectiveness evaluation of hyperbaric oxygen therapy. In: Mathieu D, ed. *Handbook on Hyperbaric Medicine*. Dordrecht: Springer 2006:671-687.

154. Marroni A, Longobardi P and Cali-Corleo R. A cost-benefit evaluation of hyperbaric oxygen treatment of the diabetic foot. In: Marroni A, Mathieu D and Wattel F, eds. *The ECHM Collection*. Flagstaff, AZ: Best Publishing Company 2005:431-443.

Addenda

Addendum 1: Stellenbosch University Health Research Ethics Committee Approval.

Addendum 2: Ethics approval letter from the Royal Medical Services of the Kingdom of Bahrain.


Addendum 3: The research questionnaire

Addendum 4: Informed consent document for the research questionnaire

Addendum 5: Informed consent document for the structured interview

Addendum 6: Structured interview guidelines

Addendum 1: Stellenbosch University Health Research Ethics Committee Approval.



UNIVERSITEIT • STELLENBOSCH • UNIVERSITY
jou kennisvenoot • your knowledge partner

14 July 2011 **MAILED**

Dr A Abdulaal
C/O Dr Jack Meintjes
Department of Community Health
4th Floor
Teaching Block

Dear Dr Abdulaal

Survey for Knowledge of the Military and Civilian Medical Practitioners in the Royal Medical Service in the Kingdom of Bahrain with regards to the Clinical Application of Hyperbaric Oxygen Therapy.

ETHICS REFERENCE NO: N11/06/179

RE : APPROVAL

A panel of the Health Research Ethics Committee reviewed this project on 17 June 2011; the above project was approved on condition that further information is submitted.

This information was supplied and the project was finally approved on 8 July 2011 for a period of one year from this date. This project is therefore now registered and you can proceed with the work.


Please quote the above-mentioned project number in ALL future correspondence.

Please note that a progress report (obtainable on the website of our Division: www.sun.ac.za/rds) should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly and subjected to an external audit. Translations of the consent document in the languages applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239
The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).


Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 493 9907) and Dr Hélène Visser at City Health (Helene.Visser@capetown.gov.za Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

July 2011 14:26 Page 1 of 2



Fakulteit Gesondheidswetenskappe · Faculty of Health Sciences

Verbind tot Optimale Gesondheid · Committed to Optimal Health
Afdeling Navorsingsontwikkeling en -steun · Division of Research Development and Support
Postbus/PO Box 19063 · Tygerberg 7505 · Suid-Afrika/South Africa
Tel.: +27 21 938 9075 · Faks/Fax: +27 21 931 3362



Addendum 2: Ethics approval letter from the Royal Medical Services of the Kingdom of Bahrain.

Bahrain Defence Force
Royal Medical Services
P.O.Box 28743 – Rifaa, Kingdom of Bahrain
Tel : (+973) 17766666
Fax: (+973) 17669166



www.bdfmedical.org

قوة دفاع البحرين
قيادة الخدمات الطبية الملكية
ص.ب. ٢٨٧٤٣ – الرفاع – مملكة البحرين
هاتف : ١٧٧٦٦٦٦٦ (+٩٧٣)
فاكس : ١٧٦٦٩١٦٦ (+٩٧٣)

27.06.2011

Dr. Adel Abdul Aal
Royal Medical Service- Medical Battalion,
BDF Hospital

**RESEARCH PROPOSAL AT THE ROYAL MEDICAL SERVICES OF THE BAHRAIN
DEFENCE FORCE: Survey for the Knowledge of the Military and Civilian Medical
Practitioners in the Royal Medical Services in the Kingdom of Bahrain with regards to the
Clinical Application of Hyperbaric Oxygen Therapy: -**

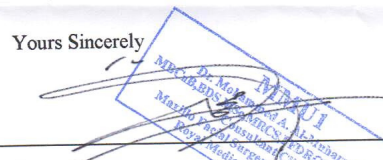
Dear Dr. Adel,

Thank you so much for submitting your request for ethical approval from the research committee of the Royal Medical Services of the Bahrain Defence Force.

It is with great pleasure to inform you that you have unanimous full ethical approval from the hospital research committee.

Many Thanks

Yours Sincerely


Mr. Mohammed A Al Muharrag
MBChB (Dnd.), BDS (Dnd.), MDSc (Dnd.), MRCS (Glas.), FFD RCS (Irel.), MFDS RCS (Eng.)
Chairman of the Research Committee
Consultant Oral & Maxillofacial Surgeon, Oral Physician
Royal Medical Services – Bahrain Defence Force



شهادة المجلس الاسترالي لمعايير الخدمات الطبية

ISO 9001
BUREAU VERITAS
Certification



شهادة الجودة العالمية الايزو ٩٠٠١

Addendum 3: The research questionnaire

The knowledge of medical practitioners in the Bahrain Defence Force about the clinical application of hyperbaric oxygen therapy

1. In which department are you currently working? _____
2. How long have you been working in this discipline? _____ months OR
_____ years
3. Which position do you currently hold in this department?
☐ Intern
☐ Resident
☐ Senior resident
☐ Chief resident
☐ Consultant
☐ Head of Department
4. State the year in which you have received your undergraduate medical degree
5. If you are a specialist, in which year did you qualify (as a specialist)?
6. What is your current age? _____ years
7. What is your current employment status in the BDF? ☐ Military medical practitioner
☐ Civilian medical practitioner
8. Which of the following describes your current registration best?
☐ Registered Bahraini medical practitioner
☐ International medical registration – working on contract with the BDF
9. Have you ever heard about the application of “hyperbaric medicine” before? ☐ Yes ☐ No
 - 9.1. If “yes”, please indicate where you first heard about hyperbaric medicine
☐ Undergraduate school
☐ Postgraduate school
☐ From colleagues
☐ From patients/ friends
☐ From books/ journals
☐ Other (specify) _____
 - 9.2. If you have read a book/ journal on hyperbaric medicine before, please indicate whether you are read it:
☐ In the last month
☐ In the last year
☐ In the last 5 years
☐ Longer than 5 years ago
 - 9.3. Book/ journal name: _____

10. Please list the internationally accepted indications for hyperbaric oxygen therapy you are aware of:

a.	<input type="checkbox"/>
b.	<input type="checkbox"/>
c.	<input type="checkbox"/>
d.	<input type="checkbox"/>
e.	<input type="checkbox"/>
f.	<input type="checkbox"/>
g.	<input type="checkbox"/>
h.	<input type="checkbox"/>
i.	<input type="checkbox"/>
j.	<input type="checkbox"/>
k.	<input type="checkbox"/>

11. Please indicate in the boxes on the right (above) which indications you consider to be within your field of speciality.

12. List the contra-indications for hyperbaric oxygen therapy you are aware of

13. Please complete the following table by indicating how you currently feel about the statements made.

	Strongly agree	agree	disagree	Strongly disagree
a. I have seen a hyperbaric chamber before	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Hyperbaric oxygen therapy is a valid treatment modality	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Hyperbaric oxygen therapy is expensive	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Hyperbaric oxygen therapy is not cost-effective	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. I have previously referred a patient for hyperbaric oxygen therapy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. The kingdom of Bahrain has chambers for hyperbaric oxygen therapy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. There are a number of hyperbaric oxygen therapy chambers in the Gulf countries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. I feel I know very little about the clinical application of hyperbaric oxygen therapy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. I would like to receive more information on hyperbaric oxygen therapy (e.g. lectures)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. I would recommend hyperbaric oxygen therapy to my patients	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Addendum 4: Informed consent document for the research questionnaire

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

Survey for the knowledge of the military and civilian medical practitioners in the Royal Medical Service in the kingdom of Bahrain with regards to the clinical application of hyperbaric oxygen therapy

REFERENCE NUMBER: N11/06/179

PRINCIPAL INVESTIGATOR: Dr ADEL ABDUL AAL

ADDRESS:

Royal Medical Services Hospital
Wali Al Ahed Highway
P. O. Box - 28743 , West Riffa
Kingdom of Bahrain.
Tel: (+973) 17766666 / 17766233
www.bdfmedical.org

CONTACT NUMBER: (+973) 39909993

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

And Also This study has been approved by the **Health Research Ethics Committee at the Royal Medical Services Hospital-Bahrain Defence Force** and will be conducted according to the ethical guidelines and principles of the

international Declaration of Helsinki, the Royal Medical Services Hospital Guidelines for Good Clinical Practice and the Research Ethics Committee (REC).

What is this research study all about?

- *The study will take place at the Royal Medical Services in The Kingdom of Bahrain. It will include all the departments within the military hospital and Sh. Mohammed Bin Khalifa Cardiac centre, as well as all military camp clinics that fall under the medical services.*
- *We are looking for all medical practitioners in the Royal Medical Services to be part of this study*
- *In this study we want to evaluate the knowledge of medical practitioners regarding hyperbaric oxygen therapy.*
- *If you agree to be part of this study, you will need to complete a questionnaire that will indicate your knowledge regarding the application of hyperbaric oxygen therapy in clinical practice.*
- *All the questionnaires are coded and no personal information will be written on it to ensure total confidentiality.*

Why have you been invited to participate?

- *You are a medical practitioner at the Royal Medical Services. In this study we want to evaluate the knowledge of medical practitioners in the Royal Medical Services regarding hyperbaric oxygen therapy.*

What will your responsibilities be?

- *If you agree to be part of this study, you will need to complete a questionnaire. This will take approximately 15 – 20 minutes.*

Will you benefit from taking part in this research?

- *You will not directly benefit from taking part in this study*

Are there in risks involved in your taking part in this research?

- *There is no risk for you while participating in this study. This study has no interventions – you only need to complete a questionnaire anonymously.*

If you do not agree to take part, what alternatives do you have?

- *If you do not want to be part of this study, you will NOT be affected in any way. Your participation is totally voluntary. You can withdraw from the study at any time. However, after you have returned your*

questionnaire, we will not be able to identify your questionnaire and you can thus not withdraw from the study at that time.

Who will have access to your questionnaire?

Only the primary investigator and the study supervisor will have access to the questionnaires. No personal information is available on the questionnaires and it is not possible to determine who has completed the questionnaires.

Will you be paid to take part in this study and are there any costs involved?

- *No, you will not be paid to take part in the study.*
- *There will be no costs involved for you, if you do take part.*

Is there any thing else that you should know or do?

- You can contact Dr Adel Abdul Aal at tel (+973)39909993 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee in South Africa at +27-21-938 9207 or the Ethics Committee in Bahrain at (+973) 17 766945 if you have any concerns or complaints that have not been adequately addressed by the study personnel.
- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I agree to take part in a research study entitled (Survey for the Knowledge of the Military and Civilian Medical Practitioners in the Royal Medical Service in the Kingdom of Bahrain with regards to the Clinical Application of Hyperbaric Oxygen Therapy).

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.

- I may choose to leave the study before handing in the questionnaire and will not be penalised or prejudiced in any way.

Signed at (*place*) on (*date*) 2011.

.....
Signature of participant

.....
Signature of witness

Declaration by investigator

I (*name*)declare that:

- I explained the information in this document to
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did not use a interpreter.

Signed at (*place*) on (*date*) 2011.

.....
Signature of investigator

.....
Signature of witness

Addendum 5: Informed consent document for the structured interview

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

Survey of the knowledge of the military and civilian medical practitioners in the Royal Medical Service in the kingdom of Bahrain with regards to the clinical application of hyperbaric oxygen therapy

REFERENCE NUMBER: N11/06/179

PRINCIPAL INVESTIGATOR: Dr ADEL ABDUL AAL

ADDRESS:

Royal Medical Services Hospital
Wali Al Ahed Highway
P. O. Box - 28743 , West Riffa
Kingdom of Bahrain.
Tel: (+973) 17766666 / 17766233
www.bdfmedical.org

CONTACT NUMBER: (+973) 39909993

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you initially agree to take part.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University in South Africa** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

And Also This study has been approved by the **Health Research Ethics Committee at the Royal Medical Services Hospital-Bahrain Defence Force** and

will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, the Royal Medical Services Hospital Guidelines for Good Clinical Practice and the Research Ethics Committee (REC).

What is this research study all about?

- *The study will take place at the Royal Medical Services in The kingdom of Bahrain in which it will include all the departments within the military hospital and Sh. Mohammed Bin Salman Cardiac center, also all-military camp clinics that fall under the medical services.*
- *We are looking for all medical practitioners in the Royal Medical Services to be part of this study*
- *In this study we want to evaluate the knowledge, experience and attitudes of the medical practitioners in Bahraini Royal Medical Services regarding hyperbaric oxygen therapy.*
- *The first part of the project involved the completion of a research questionnaire, but you are invited to take part in the second part of the research project, namely a semi-structured interview. This means that you will be asked a number of questions regarding the application of hyperbaric oxygen therapy.*
- *The interview will last for approximately 15 minutes.*
- *All the interviews will be recorded, so that your answers could be captured correctly. The interviews will be typed afterwards and your personal information will not be available in this format.*

Why have you been invited to participate?

- *You are a medical practitioner at the Royal Medical Services. In this study we want to evaluate the knowledge and attitudes of the medical practitioners in the Royal Medical services about hyperbaric oxygen therapy.*

What will your responsibilities be?

- *If you agree to be part of this study, you will be asked a number of questions regarding the use of hyperbaric oxygen therapy. You only have to answer these questions truthfully.*
- *You should not inform other colleagues about the content of the the semi-structured interview until such time as this study has been completed.*

Will you benefit from taking part in this research?

- *You will not benefit directly from taking part in this study. Your answers will however inform us of how practitioners feel about hyperbaric oxygen therapy.*

Are there in risks involved in your taking part in this research?

- *There is no risk for you while participating in this study. No interventions are tested – you only have to answer questions during an interview. The study is conducted totally anonymously.*

If you do not agree to take part, what alternatives do you have?

- *If you do not want to be part of this study, you will NOT affect you in any way. This study is totally voluntary. You can withdraw from the study even if you initially agreed to take part*

Who will have access to your semi-structured interview answers?

Only the primary investigator (who will conduct the interview) will know who have answered the questions. The interview will be typed afterwards and the digital files will be erased after it has been typed. These typed interviews (which contain no identifying information) will be stored in a secure cabinet for a period of 5 years, after which it will be destroyed. No person will thus know who has provided the answers to the questions during the interview.

Will you be paid to take part in this study and are there any costs involved?

- *No, you will not be paid to take part in the study.*
- *There will be no costs involved for you, if you do decide to take part.*

Is there any thing else that you should know or do?

- *You can contact Dr Adel Abdul Aal at tel (+973)39909993 if you have any further queries or encounter any problems.*
- *You can contact the Health Research Ethics Committee in South Africa at +27-21-938 9207 or the Ethics Committee in Bahrain at (+973) 17 766945 if you have any concerns or complaints that have not been adequately addressed by the study personnel.*
- *You will receive a copy of this information and consent form for your own records.*

Declaration by participant

By signing below, I agree to take part in this semi- structured interview about the research study entitled (Survey for the Knowledge of the Military and Civilian Medical Practitioners in the Royal Medical Service in the Kingdom of Bahrain with regards to the Clinical Application of Hyperbaric Oxygen Therapy).

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

Signed at (*place*) on (*date*) 2011.

.....
Signature of participant

.....
Signature of witness

Declaration by investigator

I (*name*)declare that:

- I explained the information in this document to
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above

- I did not use an interpreter.

Signed at (*place*) on (*date*) 2011.

.....
Signature of investigator

.....
Signature of witness

Addendum 6: Structured interview guidelines

Semi-structured interview

Thank you for agreeing to participate in this study on Hyperbaric Oxygen Therapy. This component of the study consists of a few questions we want you to answer truthfully. There are no “right” or “wrong” answers!

- 1- Do you know of specific indication(s) for the use of hyperbaric oxygen therapy within your specialty? (Specify)
- 2- (For these indications) Do you know the mechanism(s) of action or the “underlying physiological explanation” why HBO is used for these indications? (specify)
- 3- Do you give us an idea of the evidence that exists for these indications?
- 4- Have you ever referred patients for hyperbaric oxygen therapy?
 - a. If yes – give us more information
 - b. If no – any specific reason?
- 5- Have you read any journal article or a book on hyperbaric oxygen therapy? (give details: when last, which publication, etc.)
- 6- What do you consider to be the barriers (if any) to including hyperbaric oxygen therapy in your practice?
- 7- Which actions/ processes would promote the inclusion of hyperbaric oxygen therapy in your practice?
- 8- Do you have any specific opinion on hyperbaric oxygen therapy or anything else you would like to add?