In vitro models for evaluation of hyperbaric oxygen therapy in wound healing: a review
Jos Malda, Rebecca A Dawson, Evette Kairuz, Gemma Topping, Robert Long and Zee Upton

Key words
Human skin equivalent, models, hyperbaric oxygen, chronic wounds, research, review article

Abstract
Chronic ulcers are a major problem affecting a significant number of people around the world. The condition is difficult to heal and often leads to amputation. Hyperbaric oxygen (HBO) has been used clinically for the treatment of chronic ulcers and positive outcomes have been reported. However, owing to the lack of large randomised controlled trials and some conflicting data, controversy regarding the effectiveness of HBO in chronic wound healing persists. Besides randomised controlled clinical trials, in vitro studies hold promise in providing further insight into the role of HBO in wound healing and in aiding the establishment of a scientific foundation upon which more rational and efficacious HBO therapeutic regimes may be developed. The present article provides an overview of the available in vitro data on HBO with regards to wound healing. In particular, it focuses on experimental design issues and future opportunities using human skin equivalent models to study HBO-mediated wound healing.

Introduction
Chronic leg and foot ulcers are a significant cause of pain and impaired quality of life. Even small lesions may become a long-term problem, resulting in partial lower-limb amputation, and creating a sustained demand on healthcare systems. The associated loss of productivity and the requirement to provide support infrastructure places additional financial burden on the wider community.

Hyperbaric oxygen treatment (HBO) has been suggested as a potential wound healing therapy due to the hypoxic nature of the chronic wound and the requirement for oxygen during the wound healing process. Indeed, increased wound closure in response to HBO has been demonstrated using animal models and, importantly, clinical studies have demonstrated faster healing of chronic ulcers and a decreased risk of major amputation.

These outcomes have been used as the justification of Medicare coverage for the treatment of these conditions with HBO (item numbers 13015 and 13020) in Australia. However, due to the conflicting data and the lack of a large randomised controlled trial, controversy regarding the effectiveness and validation of treatment regimes of HBO for enhancing healing of chronic wounds still exists. Thus, its clinical application is the subject of great debate. In view of this, elucidation of the pathophysiological mechanisms underlying the demonstrated success of HBO will aid the further validation and hence full exploitation of the therapeutic potential of HBO therapy in wound healing.

Evaluation of HBO in vitro using human cell monolayers
Two-dimensional (2D) in vitro monolayer cultures of keratinocytes, fibroblasts, melanocytes and endothelial cells have been used to evaluate the effects of HBO. HBO has not been shown to affect keratinocyte proliferation, either positively or negatively, in two studies reported to date. In addition, differentiation appeared not to be significantly affected by HBO, as evaluated by means of the expression of late differentiation markers cytokeratin 10 and involukrin. Data reported on the effects of HBO on human fibroblast proliferation is conflicting. For example, Hehenberger et al and Tompach et al observed a dose-dependent effect on proliferation after 24 hours following a single hyperbaric treatment. In contrast, Piepmeier et al did not observe any effects with a single treatment and Dimitrijevich et al observed a mitogenic effect only after prolonged HBO exposure. Interestingly, these authors also demonstrated that collagen production by fibroblasts is inhibited by HBO treatment, contrary to the widely accepted belief that HBO aids wound healing by up-regulating collagen synthesis. Clearly, it is difficult to draw any hard conclusions based on the limited and contrasting data available, illustrating the need for more extensive in vitro studies.
keratinocyte culture medium for one to three days to allow cell expansion prior to subsequent culture at the air/liquid interface (Figures 1a and b). This model possesses significant advantages over other skin equivalents with scaffolds. Specifically, it is composed of a dermal matrix (with or without incorporated fibroblasts) and has an intact basement membrane, elements that have been shown to be important for the adherence of the epidermis to the dermis and for the differentiation of keratinocytes. Hence, the epidermis formed on these scaffolds has a high degree of similarity to the epidermis in vivo, with the main regions clearly visible: a rapidly proliferating basal layer, a differentiating supra-basal layer and an uppermost, stratified cornified layer (Figure 1c).

HSE models have been used as a testing and research platform for the cosmetic, pharmaceutical and chemical industries, as well as for the study of skin wound healing. For example, the HSE model based on the de-epidermised dermis has been used as a model for contraction, cell invasion and angiogenesis. In addition, it was used clinically as a skin replacement following release of contractures in previously burnt patients.

Using this particular HSE model, we have recently demonstrated that daily hyperbaric treatments (90 min, 100% oxygen at 243 kPa) accelerate the reconstruction of an epidermis compared with air treatments at 101.3 kPa (1 ATA) (Figure 2). Immunohistological characterization of the HSEs using various epidermal markers, including cytokeratins 1/10/11 (primary proteins of skin), revealed the earlier onset of epidermal differentiation within the HBO-treated constructs compared with air (Figures 2c and d). Moreover, the reconstructed epidermal layers in HBO-treated samples were significantly thicker at both Day 3 and Day 5 compared with the non-treated controls (Figure 3).

Additionally, after three days of culture at the air/liquid interface, the populated surface area of the dermal scaffolds, as visualized using 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT; stains living cells purple) staining (Figure 1b), was significantly greater (p < 0.05) for the HBO-treated samples than for the controls (mean ± SD, 0.46 ± 0.03 cm² and 0.58 ± 0.06 cm² for control and HBO, respectively) due to an increase in cell migration and proliferation. Although a difference was observed after five days, this was not significant. Thus, using the HSE model and employing a protocol similar to that used to treat chronic wounds clinically, we demonstrated that HBO stimulates the reconstruction of the epidermis. Moreover, we showed, for the first time, that these changes in epidermal formation are supported by differences in markers of proliferation, differentiation and basement membrane components.

**Experimental design issues for in vitro HBO treatment**

Although the HSE model offers numerous opportunities to
further dissect the role of HBO in the healing of chronic wounds, there are differences between the model and the in vivo situation that should be considered and will impact on the experimental design. The HSE is a simplified model and lacks both innervation and vascularisation. However, oxygen will directly diffuse into the culture medium and has been shown to result in a significant rise in the partial pressure of oxygen (pO₂) over a 90-minute treatment; these values correlate with the values observed in normal tissue at 100% O₂ inspired within the range of 101.3–253 kPa. The fall in tissue pO₂ observed after clinical HBO exposure, will be faster in vitro than in vivo and therefore the HSE model is a somewhat conservative indicator of the potential in vivo benefits of HBO therapy.

Rapid gas exchange can also influence the pH in the culture medium. Optimal growth of cells in vitro is dependent on maintaining a physiologic pH. Although the changes in the pH of the medium during a 90-minute HBO treatment were shown to be less than 0.10 pH units, depending on the conditions, pH changes can be significant and should thus be considered. The most commonly used culture systems employ incubation in a high carbon dioxide (CO₂) environment, typically 5%. Hence, bicarbonate has to be present in the medium at a concentration of about 25 mM to reach the physiologic pH of about 7.4. When handling cells for extended periods of time in the absence of high CO₂ concentrations, e.g., in hyperbaric oxygen conditions, bicarbonate is not an adequate buffer and the pH of the media can rise to non-physiological levels. Therefore, other buffers with appropriate pKa levels, such as HEPES (N-[2-Hydroxyethyl] piperazine-N’-[2-ethanesulfonic acid]) for example, could be used.

The control of temperature is an additional challenge, since changes in the temperature will affect the cellular responses, including proliferation. Thus, it is important to carefully control the temperature in order to obtain reliable outcomes. Hence, a monoplace or multiplace chamber is less suitable than a research or custom-designed hyperbaric chamber that allows the control of temperature via a water jacket.

Figure 2
(A, B) Hematoxylin and eosin staining and (C, D) expression of the differentiation marker cytokeratin 1/10/11 (K1/10/11) of cross-sections of reconstructed epidermis after 5 days of daily 90-minute treatments with air at 101.3 kPa (A, C) or 100% oxygen at 243 kPa (B, D)
Future opportunities using skin equivalent models in wound healing research

HSE models provide an exciting means to improve and extend our knowledge regarding the effects of HBO on biological processes during the healing of chronic ulcers. Clearly, to further resemble native skin, various additional types of cells can be incorporated into the HSE, including melanocytes and Langerhans cells in the epidermal compartment, and fibroblasts and endothelial cells in the dermal compartment. In addition, wounds can be created in the model and the healing response can be monitored. Figures 4a and b show the wounded HSE model immediately after burning with a heated metal rod after eight days' culture, and Figure 4c the subsequent migration of keratinocytes facilitating wound re-epithelialisation.

The model could be further improved to specifically mimic the in vivo chronic wound environment. Generally, this environment is of a hypoxic and highly proteolytic nature and diabetes is often an underlying cause of the condition. The hypoxic nature of chronic wounds in vivo can be reconstructed by culturing the HSEs in a low-oxygen environment using a low-oxygen cell culture incubator or chamber. Similarly, the proteolytic environment of the chronic wound could be simulated by bathing the wounds created in the HSE model in chronic wound exudate obtained from consenting patients suffering from non-healing wounds. In addition, hyperglycaemia, as seen in diabetes, can be reproduced in the in vitro models by the application of abnormally high levels of glucose (up to 100 mM). Subsequently, intermittent HBO treatments can be administered and changes in the healing response can be evaluated histologically, as well as genetically. In this respect, the current advances in proteomics and genomics are of particular interest and can be incorporated into the research approach.

Conclusions

HSE models have advanced our understanding of wound healing, as well as of basic skin biology. Such models provide a more physiological 3D in vitro model of human skin that allows the incorporation of various cell types and circumvents the disadvantages associated with 2D in vitro models. Moreover, HSEs can be wounded and the healing can be studied. In addition, cultures can be maintained in the presence of chronic wound fluid, high glucose or hypoxia, thus simulating to some extent the inhibiting chronic wound environment. HSEs are therefore a valuable tool in furthering our understanding of the effects of HBO and can aid the further establishment of a scientific foundation upon which more rational and efficacious HBO therapeutic regimes may be developed.

Acknowledgements

The authors thank Drs A Kane and P Richardson and their patients for their generous donation of time and skin samples. Thanks are also extended to Mr D Geyer and Dr C Hyde for technical assistance. This study was supported in part by the Diabetes Australia Research Trust and the Wesley Research Foundation, an IHBI Postdoctoral Fellowship (JM) and Tissue Repair and Regeneration Program funds. Ethics committee approval for these studies was obtained from Queensland University of Technology (ID#: 3673H), as well as from the collaborating hospitals (The Wesley Hospital, ID#: 2004/43, and the Princess Alexandra Hospital, ID#: RP 2004/086).

References

7. Hammarlund C, Sundberg T. Hyperbaric oxygen


Jos Malda PhD, Rebecca A Dawson, Evette Kairuz, Gemma Topping and Zee Upton,
Tissue Repair and Regeneration Program, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane
Robert Long, Medical Director, Wesley Centre for Hyperbaric Medicine, Brisbane, Australia

Address for correspondence:
Dr Jos Malda
Tissue Repair and Regeneration Program
Institute of Health and Biomedical Innovation
Queensland University of Technology
60 Musk Avenue, Kelvin Grove, Brisbane
Queensland 4059, Australia
Phone: +61-(0)-7-3138-6213
Fax: +61-(0)-7-3138-6030
E-mail: <jos@malda.nl>
Services to diving recognised by Australian government

John Maxwell Lippmann
Medal of the Order of Australia

For services to scuba diving safety, resuscitation and first aid and in particular the establishment of the Divers Alert Network Asia-Pacific

Brian Andrew Hills
Member of the Order of Australia (posthumous)

For service to medical research, particularly in the fields of respiratory physiology and decompression sickness as an educator and author

---

Dr David Smart, the Medical Co-Director of the Department of Diving and Hyperbaric Medicine at Royal Hobart Hospital, has been appointed Clinical Associate Professor in Diving, Hyperbaric and Emergency Medicine, Faculty of Health Sciences, University of Tasmania. He has been Clinical Senior Lecturer with the Faculty since 1994.
SPUMS notices and news

South Pacific Underwater Medicine Society
Diploma of Diving and Hyperbaric Medicine

Requirements for candidates

In order for the Diploma of Diving and Hyperbaric Medicine to be awarded by the Society, the candidate must comply with the following conditions:

1. The candidate must be medically qualified, and be a financial member of the Society of at least two years’ standing.
2. The candidate must supply evidence of satisfactory completion of an examined two-week full-time course in Diving and Hyperbaric Medicine at an approved Hyperbaric Medicine Unit.
3. The candidate must have completed the equivalent (as determined by the Education Officer) of at least six months’ full-time clinical training in an approved Hyperbaric Medicine Unit.
4. The candidate must submit a written proposal for research in a relevant area of underwater or hyperbaric medicine, and in a standard format, for approval by the Academic Board before commencing their research project.
5. The candidate must produce, to the satisfaction of the Academic Board, a written report on the approved research project, in the form of a scientific paper suitable for publication.

Additional information

The candidate must contact the Education Officer to advise of their intended candidacy, seek approval of their courses in Diving and Hyperbaric Medicine and training time in the intended Hyperbaric Medicine Unit, discuss the proposed subject matter of their research, and obtain instructions before submitting any written material or commencing a research project.

All research reports must clearly test a hypothesis. Original basic or clinical research is acceptable. Case series reports may be acceptable if thoroughly documented, subject to quantitative analysis, and the subject is extensively researched and discussed in detail. Reports of a single case are insufficient. Review articles may be acceptable if the world literature is thoroughly analysed and discussed, and the subject has not recently been similarly reviewed. Previously published material will not be considered.

It is expected that all research will be conducted in accordance with the joint NHMRC/AVCC statement and guidelines on research practice (available at http://www.health.gov.au/nhmrc/research/general/nhmrcavc.htm) or the equivalent requirement of the country in which the research is conducted. All research involving humans or animals must be accompanied by documented evidence of approval by an appropriate research ethics committee. It is expected that the research project and the written report will be primarily the work of the candidate.

The Academic Board reserves the right to modify any of these requirements from time to time. The Academic Board consists of:
Dr Fiona Sharp, Education Officer, Professor Des Gorman and Dr Chris Acott.

All enquiries should be addressed to the Education Officer:
Dr Fiona Sharp,
249c Nicholson Road
Shenton Park, WA 6008
Australia
E-mail: <sharpief@doctors.org.uk>

Key words
Qualifications, underwater medicine, hyperbaric oxygen, research

Minutes of the SPUMS Executive Committee Meeting held on 4 June 2006 at the Pearl South Pacific Hotel, Fiji

Opened: 1700 hr

Present: Drs C Acott (President, Education Officer), R Walker (Past-President), G Williams (Acting Treasurer), D Smart (ANZHMG Representative), M Davis (Editor), C Lee (Committee Member)

Apologies: Drs S Sharkey (Secretary), D Vote (Committee Member)

1 Minutes of the previous meeting
Dr Acott proposed that the minutes of the previous telephone conference of 12 March 2006 be accepted as a true record. Seconded by Dr R Walker.

2 Matters arising from the minutes
2.1 SPUMS Administrator
No further comment.
2.2 SPUMS Committee overseas representatives
No response from either. It was decided to remove their names from the Journal but still have them on the SPUMS website.
2.3 ANZCA SIG member on the SPUMS Educational Board
No response had been received from Dr Walker.

2.4 Constitutional amendments
2.4.1 Consumer Affairs were drafted by Dr Williams for presentation at the 2006 AGM.
2.4.2 Motion regarding the application of ‘model rules’ to the publishing of the SPUMS Committee meeting minutes has been drafted by Dr R Walker for presentation at the 2006 AGM.
2.4.3 Increase in subscription fees was drafted by Dr Williams for presentation at the 2006 AGM.
2.4.4 Motion regarding additional membership categories has been drafted by Dr R Walker for presentation at the 2006 AGM.
2.4.5 Nominations for the Education Officer and Public Officer have been received and are to be presented at the 2006 AGM.

2.5 Strategies for increasing the SPUMS Membership
No new ideas were discussed.

2.6 Welcome letter for new members
No further action discussed.

3 Annual Scientific Meetings
3.1 Concerned the Fiji meeting; no further action.
3.2 Concerned the Fiji meeting; no further action.
3.3 No difficulties were noted for the 2006 conference regarding payment of registration and travel fees.
3.4 Concerned the Fiji meeting; no further action.
3.5 Concerned the Fiji meeting; no further action.
3.6 Concerned the Fiji meeting; no further action.
3.7 Dr Davis reported that arrangements for the 2007 conference were progressing.
3.8 Dr Acott proposed that the 2008 meeting be held at either Kimbe or Alatou in PNG. The theme of the meeting will be “Treatment tables: physiology and why do they work”.

4 Journal report
Amalgamation of *Diving and Hyperbaric Medicine* and the EUBS newsletter was briefly discussed. No further conclusions were made.

5 Treasurer’s report
To be presented at the AGM.

6 Education Officer’s report
Dr Fiona Sharp has volunteered to be the new Education Officer. This will be announced at the AGM.

7 Other business
7.1 Complaint regarding the misconduct of a SPUMS member conducting diving medicals ongoing.
7.2 SPUMS underwriting of personal business equipment carried for purposes of the SPUMS meetings. The Committee agreed that this should be covered by SPUMS if insurance can’t be obtained.
7.3 Delegates wishing to attend the Cocktail Party and/or Gala Dinner and not the Scientific Meeting. This was discussed by the Committee and it was agreed that the full registration fee needs to be paid for any person attending these functions. It was also agreed that:
- no discount is to be given if a delegate is unable to attend either the Cocktail Party or the Gala Dinner;
- attending only the Gala Dinner purely in a social setting despite paying the registration fee for the rest of the conference is to be discouraged, but should be at the discretion of the conference convenor.

Closed: Not recorded

---

Further report on Australian and New Zealand Standards Occupational Diving Committee
Held on Monday 29 May 2006 at Standards Australia House, Sydney

**Australian And New Zealand Standard 2299.1 Occupational Diving Operations Part 1: Standard Operational Practice**

Some further modifications include:

**Breathing-air quality/hydrocarbon contamination**
The draft revision of AS/NZS 2299.1 has been modified to indicate that control of the pressure, moisture and temperature of the compressor and filter system was critical to filter operation.

Clauses 3.13 and 5.6.4 of the draft have been modified to address moisture level and hydrocarbon contamination issues, along with addition of a new clause 5.6.5.

**Table 4.2 Limits for repetitive dives**
These now maintain consistency with published DCIEM tables.

**Medical examination requirements**
The New Zealand diving medical certification system is different to that used in Australia. All divers (including recreational) undertake a comprehensive medical examination every five years and health screening (using a system of nurses or other trained personnel) is undertaken annually.

If any problems are detected during the intermediate screening, the diver is referred back to their physician. This system works well if divers are under the continuous supervision of a single physician or group of physicians using a centralised database, but becomes problematic if divers are geographically mobile. Clause 8.2 has now been modified in a manner that suits both countries. The separate page containing the medical fitness certificate at the end of Appendix N has also been improved so it has a specific title and identifies the Standard. There is still a requirement for annual medical assessments for professional divers.
The SPUMS website
www.spums.org.au

The SPUMS Committee recognises the need to stay in touch with our members. As we move yet further into the age of ‘instant communication’ the value of having an up-to-date and informative website becomes critical. It is now some 18 months since we upgraded our website and improvements and refinements will continue to be added to meet your needs.

Amongst the services now available, it is possible to join the Society and pay your annual membership subscription on-line. The Diving Doctor List is available to any casual site visitor and is used by many diving organisations to direct their prospective divers to their nearest diving doctor. Under the Information and Research section review articles and diving-related resources can be found. The SPUMS Medical can be downloaded from the web and used in your practice. Upcoming Australian and international diving and hyperbaric medicine conferences and courses are promulgated, and links to other diving organisations can be found.

The SPUMS Constitution and policy statements are published on the site, as are the requirements for the SPUMS Diploma of Diving and Hyperbaric Medicine and the Instructions to Authors for submission of articles to the journal.

The Committee is currently evaluating options to place a full set of journals (from 1971 onwards) onto the site. Electronic access to all past journals will provide a fabulous resource to prospective researchers or practitioners interested in updating their clinical knowledge. A number of further refinements are planned over the next year.

Please take the opportunity to regularly review the site. Any suggestions for improvements or additions are welcome and can be forwarded to the SPUMS Secretary.

Dive supervisor qualifications
Minor wording changes have occurred to ensure that the dive supervisor has training that is specific to the type of diving being conducted.

Proposed date for next SF-017 meeting
It is proposed to hold the next SF-017 meeting on Tuesday 20 March 2007 following a meeting of the Training Working Group on Monday 19 March. The venue proposed is Sydney.

Dr David Smart
SPUMS Representative, Australian Standards for Occupational Diving

Australian and New Zealand College of Anaesthetists Annual Scientific Meeting
Diving and Hyperbaric Medicine Special Interest Group – Concurrent session

Date: 28 May 2007
Time: 1530–1700 hr
Venue: Melbourne Exhibition and Convention Centre

Speakers:
Professor Bruce Spiess, Virginia, USA
Simon Mitchell, Auckland, New Zealand
Associate Professor David Smart, Hobart, Australia
Glen Hawkins, Sydney, Australia

Contact: <margaret.walker@dhhs.tas.gov.au>
Conference registration: <www.anzca2007asm.com>

SPUMS diplomates 2006
Congratulations go to Dr Andrew Fock, The Alfred Hospital, Melbourne, who was awarded his diploma in 2006. His thesis was entitled “Deep decompression stops”.

SPUMS Annual General Meeting 2007
The SPUMS AGM 2007 is to be held in the Marina Room, Oceans Resort, Tutukaka, Northland, New Zealand, at 1830 hr, Thursday 19 April 2007.

PLEASE NOTE THE CHANGED TIME AND DATE

Agenda

Apologies:
Minutes of the previous meeting:
Minutes of the previous meeting will be posted on the meeting notice board and appeared in Diving and Hyperbaric Medicine, 2006; 36(3): 162-6.

Matters arising from the minutes:
Annual reports:
President’s report
Secretary’s report
Education Officer’s report
Annual financial statement and Treasurer’s report

Subscription fees for 2007:
Treasurer to propose a motion

Election of office bearers:
Nil

Appointment of the Auditor:
Nil

Please take the opportunity to regularly review the site. Any suggestions for improvements or additions are welcome and can be forwarded to the SPUMS Secretary.

Robyn Walker
## Accepted Indications for Hyperbaric Oxygen Therapy

Revised and approved December 2006

<table>
<thead>
<tr>
<th>Broad indication</th>
<th>Specific indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bubble injury</td>
<td>Decompression illness</td>
</tr>
<tr>
<td></td>
<td>Arterial gas embolism</td>
</tr>
<tr>
<td></td>
<td>(diving/iatrogenic/misadventure)</td>
</tr>
<tr>
<td>Acute ischaemic conditions</td>
<td>Compromised flaps/grafts</td>
</tr>
<tr>
<td></td>
<td>Crush injury/compartment syndrome</td>
</tr>
<tr>
<td></td>
<td>Reperfusion injuries</td>
</tr>
<tr>
<td></td>
<td>Sudden sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td>Avascular bone necrosis</td>
</tr>
<tr>
<td>Infective conditions</td>
<td>Clostridial myonecrosis</td>
</tr>
<tr>
<td></td>
<td>Necrotizing fasciitis</td>
</tr>
<tr>
<td></td>
<td>Non-clostridial myonecrosis</td>
</tr>
<tr>
<td></td>
<td>Necrotizing cellulitis</td>
</tr>
<tr>
<td></td>
<td>Malignant otitis externa</td>
</tr>
<tr>
<td></td>
<td>Refractory mycoses</td>
</tr>
<tr>
<td></td>
<td>Refractory osteomyelitis</td>
</tr>
<tr>
<td></td>
<td>Intracranial abscess</td>
</tr>
<tr>
<td>Radiation tissue injury</td>
<td>Osteoradionecrosis</td>
</tr>
<tr>
<td></td>
<td>established</td>
</tr>
<tr>
<td></td>
<td>prophylactic</td>
</tr>
<tr>
<td></td>
<td>Soft tissue radiation injury</td>
</tr>
<tr>
<td></td>
<td>established</td>
</tr>
<tr>
<td></td>
<td>prophylactic</td>
</tr>
<tr>
<td>Problem wounds</td>
<td>Chronic ischaemic problem wounds</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
</tr>
<tr>
<td></td>
<td>ulcers/gangrene/post-surgical</td>
</tr>
<tr>
<td></td>
<td>Non-diabetic</td>
</tr>
<tr>
<td></td>
<td>pyoderma gangrenosum</td>
</tr>
<tr>
<td></td>
<td>refractory venous ulcers</td>
</tr>
<tr>
<td></td>
<td>post-surgical problem wounds</td>
</tr>
<tr>
<td>Toxic gas poisoning</td>
<td>Carbon monoxide poisoning (mod/severe)</td>
</tr>
<tr>
<td></td>
<td>Carbon monoxide poisoning delayed sequelae</td>
</tr>
<tr>
<td>Ocular ischaemic pathology</td>
<td>Cystoid macular oedema</td>
</tr>
<tr>
<td></td>
<td>Retinal artery/vein occlusion</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Thermal burns</td>
</tr>
<tr>
<td></td>
<td>Bells palsy</td>
</tr>
<tr>
<td></td>
<td>Frostbite</td>
</tr>
<tr>
<td>Adjuvant to radiotherapy</td>
<td>As adjunct to radiotherapy in treatment of solid tumours</td>
</tr>
</tbody>
</table>

### Notes

1. The purpose of this list is to document the conditions for which it is considered hyperbaric oxygen (HBO) therapy has sufficient evidence of treatment benefit. These recommendations are based on review of the literature and clinical experience. These conditions are limited to those where the evidence for the efficacy of HBO is at least as strong as currently accepted therapeutic alternatives.

2. This list is made available for the use of individual hyperbaric medicine facilities in formulating admission and discharge policies. The list constitutes recommendations only and does not mandate clinical practice.

3. It is proposed that this list be reviewed by a joint committee of members of the ANZHM and ANZCA SIG on a two-yearly basis. Submissions will be possible through these organisations and all available evidence at the disposal of this joint committee will be considered.

4. The ANZHM and ANZCA SIG support clinical research into the efficacy of HBO in these and other conditions. Patients with conditions other than those above should be regarded as experimental and treatment undertaken in that context. These organisations hold that such treatment should be administered with the approval of a local ethics committee and involve no charge for professional or facility services.