ORIGINAL PAPERS

EVIDENCE-BASED MEDICINE AND HYPERBARIC PRACTICE

Mike Bennett

Key Words
Evidence, hyperbaric oxygen, treatment.

Introduction

Evidence-based medicine (EBM) has been defined as "the conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients".[1] Despite recent enthusiasm expressed for the concept by many health care professionals, there has been a degree of criticism. There are those who feel the reference to evidence erodes clinical freedom and is designed by bean-counters to control medical expenditure. There are fears that EBM is "cookbook" medicine, requiring all individuals to receive the same diagnostic and therapeutic measures, regardless of individual needs. This is a grave misunderstanding. EBM requires the synthesis of best evidence and clinical expertise/experience in order to arrive at the best diagnostic and therapeutic approaches for each individual. Medical practitioners should see EBM as empowering and I hope this article will convey some of the sense of clinical enrichment.

The practice of EBM cannot spring into existence without effort. We need to train ourselves to ask appropriate questions, execute efficient searching techniques (in order to discover evidence and be sure we have the best), develop skills at critical appraisal of this evidence, grasp some basic clinical statistical methods (OH NO! Perhaps we should call this "rules of evidence") and relate our findings to individual patients. This paper is designed to introduce the concepts central to the practice of EBM and to use examples to show their relevance to hyperbaric practice. An excellent review of what constitutes EBM and why it is relevant to all of us was published in the Journal of the American Medical Association in 1992,[2] while another major resource of practical benefit is a pocket guide to teaching and practice of EBM by Sackett and others.[3] There are also a number of internet resources available. A short list of these appears in Table 1.

Asking good questions

The process of EBM begins with the identification of a clinical (or diagnostic, prognostic etc.) problem for which a practitioner feels there is no clearly defined and validated answer. From this realisation, often arrived at in the course of patient care, the practitioner must accurately define the problem before taking steps to discover an answer. One approach is to begin by asking structured clinical questions.

Clinical questioning is an important skill in itself. Sackett has defined a schema for building an "evidence-based" question, that is, one to which a focussed search is most easily applied. Bennett has discussed the application of this approach to facilitate critical appraisal within an anaesthetic journal club.[3,4] There are four major elements to such questions, all of which need careful consideration in order that the clinical problem, alternative therapies and outcomes of interest are clear to the searcher. Once a sufficiently focussed question is designed, it becomes much clearer to the searcher which citations represent possible

TABLE 1

SOME EBM RESOURCE SITES ON THE INTERNET

	Resource type		Address
1	Searching	PubMed gateway	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi
		Ovid gateway	http://medline.unsw.edu/ovidweb/login.htm
		DORCTIHM *	http://sesinfo/powweb/hyperbar.htm
		Cochrane	http://som.flinders.edu.au/fusa/cochrane/default.html
2	Critical appraisal	JAMA	http://www.acponline.org/journals/acpjc/
3	Rules of evidence	McMaster University	http://hiru.hirunet.mcmaster.ca/ebm/default.htm
		Stats gateway	http://uni.koeln.de/themen/Statistik/onlinebooks.html
4	General EBM	Oxford Centre for EBM	http://cebm.jr2.ox.ac.uk/
		Netting the evidence	http://www.shef.ac.uk/uni/academic/scharr/ir/netting.html

*Database of Randomised Controlled Trials in Hyperbaric Medicine- not yet active at time of writing (April 2000).

answers to the question and which are distractions from the clinical problem. An example question is worked through in Table 2, beginning, perhaps, from a discussion in any hyperbaric unit about whether HBO_2T works for carbon monoxide poisoning.

on internal and external validity. The most appropriate methodology will depend on the type of question asked. Most of the discussion which follows is primarily aimed at questions concerning a therapeutic intervention (does HBO_2T work for…?). Different methodologies are more

TABLE 2

BUILDING AN EVIDENCE-BASED QUESTION
(modified from Sackett et al.[3])

	1 Patient problem	**2 The intervention of interest (or cause/ prognostic factor etc)**	**3 Compared to…. (not always required)**	**4 Outcomes**
Tips	Need to define the patient of most interest	Be exact about the intervention	Often simply the main alternative	Focus on important outcomes of interest that seem relevant to the intervention
Example	"In adult patients with moderate to severe carbon monoxide poisoning…	...does the administration of hyperbaric oxygen (>1.5ATA for at least 1hr)	…compared to a regimen of normobaric oxygen for at least 2 hours…	...result in any demonstrable reduction in neurological or cardiovascular mortality or morbidity?

Searching for evidence

Once a question has been designed to the satisfaction of those interested in the outcome, the next step is an attempt to discover the evidence. It is important to develop a structured and practised approach to seeking evidence. While there is much scope for different approaches from individual searchers, there are some important elements that should not be overlooked. Table 3 (p 123) shows one search strategy that might be suitable in attempting to find evidence concerning an indication for HBO_2T. It is a modification of the protocol suggested by Andrew Booth from the School of Health and Related Research and available from the *Netting the Evidence* web site. [5]

Critical appraisal

Once a clinical problem has been defined and an efficient search conducted, the next requirement is for a means to determine which evidence is likely to be most reliable. Critical appraisal is the term given to the process of selecting the best articles of those retrieved and applying the rules of evidence to determine their applicability to an individual clinical situation.

Table 4 (page 125) is a methodological hierarchy suggested by the author. While there are many such schemes available from a variety of sources, most are very similar as there is broad agreement about the effect of methodology

appropriate for questions of diagnostic test evaluation (what does the $PtcO_2$ mean…?) or the definition of the magnitude of a health problem (how common are diabetic ulcers?, for example). For a detailed discussion of the role of trial design in the minimisation of bias in clinical trials, see Sackett et al.[3]

In general, the best available evidence of therapeutic efficacy is to be found through well conducted, large, multi-centre randomised controlled trials (RCTs) or meta-analysis of a number of smaller RCTs. The randomised and blinded trials so familiar to us now remain the only sure way of eliminating systematic bias from clinical inquiry. They do not, of course, eliminate the chance variations that may mislead us. Avoiding misinterpretation of random events as clinically meaningful is the purpose of statistical analysis and appropriate empowerment of well-designed trials.

Our search having identified a number of relevant articles, and the basic methodology of each identified, the most promising should be selected for further review. Each remaining article needs to be examined in more detail to identify any serious threats to internal or external validity. [Internal validity: are there any flaws in construction or execution of this trial that reduce the confidence we have in the results? External validity: are there elements in the patients studied or the trial execution that reduce our confidence that the results apply to our patient(s)?]. This can be a complex process and at the Prince of Wales, we have developed a critical appraisal sheet (Table 5 page 125)

TABLE 3

SEEKING THE EVIDENCE

ONE POSSIBLE PROTOCOL FOR DIVING AND HYBERBARIC MEDICINE

Step 1 MEDLINE Search

MEDLINE is still the best starting point for EBM queries in general. For therapy questions, however, the Cochrane Library has edged ahead as it now contains more controlled trials than MEDLINE.

There are two alternative methods of filtering the evidence from MEDLINE:

1 Conduct a search using two or three terms relevant to the question and then limit the retrieval set to **Review* in PT** (for reviews); **Clinical-Trial in PT** (for clinical trials); **/economics** subheading or **explode costs-and-cost-analysis** (for economic studies); **explode attitudes (**for patient, staff or carer perspectives). (**PT** is publication type)

2 Use the PubMed version of MEDLINE (the **Clinical queries** interface). Select the type of question that you require (e.g. diagnosis or therapy). Then indicate whether you wish to cast the methodological net wide (sensitivity) or to have a narrow focus (specificity).

If you retrieve little in the way of high quality evidence choose the most relevant looking reference and select **"See Related Articles" PubMed.**

Do not forget EMBASE, particularly for European Literature or articles on pharmaceuticals and CINAHL for the nursing literature and Consensus statements.

Step 2 Cochrane Library

This library gives access to all completed and proposed meta-analyses in a growing range of medical specialties. There are reviews of carbon monoxide poisoning and multiple sclerosis, for example. Perhaps even more useful, there is a searchable list of controlled trials and the Database of Abstracts of Reviews of Effectiveness [DARE], all searchable on the World Wide Web.

Step 3 Database of Randomised Controlled Trials in Hyperbaric Medicine (DORCTIHM)

This specifically diving and hyperbaric database is searchable and each trial included is summarised on a single page using the Critically Appraised Topic (CAT) software designed by Douglas Badenock in Oxford. The database is available from the authors and will soon be on the POWH departmental web site .[6]

Step 4 UHMS Committee Report

This regular publication appraises the evidence for the use of HBO_2T across a broad range of indications. It is becoming increasingly evidence-based rather than anecdotal.[7]

Step 5 Direct search of on-line or hard copy specialist journals

The key specialist journal, Undersea and Hyperbaric Medicine, is not available on-line, and so requires hand searching. The South Pacific Underwater Medicine Society (SPUMS) Journal has an on-line and downloadable index to over 2,400 articles published back to 1971 and can be found at: <http://www.spums.org.au/spums_journal_articles_database_.htm .>

Step 6 Pearling

This term refers to the practice of trawling the references of previously located articles for further relevant material.

TABLE 4

DESIGNATION OF LEVELS OF EVIDENCE

Evidence level	Description
I	Evidence obtained from a systematic review of all relevant randomised controlled trials or a single, well-designed, large, multi-centre randomised controlled trial.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies or interrupted time series with control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel contol group.
IV	Evidence obtained from case series, either post-treatment or pre- and post-treatment.
V	Evidence obtained from a single case report.
VI	Evidence based on expert opinion or qualitative review

to ensure we always examine the most important aspects of each paper.

One increasingly popular method of summarising the critical appraisal of an article is the use of the CATmaker software developed by Douglas Badenoch in Oxford.[8] Using this simple program, a one-page summary of the article is presented with a concise presentation of the important clinical findings. This summary constitutes a Critically Appraised Topic (CAT) and an example appears in Table 6 (page 127-128). With a little practice, these summaries can be produced in about 15 to 20 minutes. Once completed, such CATs can be reviewed when required in the light of new evidence. The Oxford Centre for Evidence-Based Medicine web site maintains a collection of these CATs in a 'CATbank'.[8]

More specifically, the Prince of Wales Hospital Hyperbaric Unit has developed a database as described above (DORCTHIM). In this searchable database, all trials are accompanied by a CAT. Any contributions to this collection are welcome.

Basic statistics or "rules of evidence"

Biostatistics are daunting for most clinicians. While we do not all have to achieve a detailed understanding of the subtleties of such mathematical gymnastics, it is not possible to take advantage of the evidence available without some general appreciation of basic statistical concepts. Trisha Greenhalgh has written a well-constructed summary in her two papers in the *How to read a paper* series in the BMJ in 1997.[9,10] This summary is designed specifically for those who feel totally at sea with statistical concepts. For those with a little more experience, she recommends the *Basic Statistics for Clinicians* series (4 papers) in the Canadian Medical Association Journal.[11]

Clinicians are most often interested in the impact on their patients of a proposed intervention. Three methods of measuring the effectiveness of interventions are in common use by EBM practitioners. Referring to the results of a 1996 study by Bouachour[12] on the treatment of crush injuries with HBO_2, Table 7 (p 128) shows three outcome columns:

1 Relative risk reduction (RRR).

The reduction in the incidence of an outcome relative to the incidence in the control group. This gives the reader a sense of the proportion of those who would have suffered an outcome, but will not now because of the new intervention. In this example, we estimate that 86% of those who suffer the outcome of failed wound healing would not have done if HBO_2T had been used. This is important, but without an estimate of absolute risk reduction (or increase), the total impact of the intervention cannot be gauged.

2 Absolute risk reduction (ARR).

The difference between the incidence of an outcome in the two groups. This gives the reader a direct sense of the absolute improvement likely. Here, the absolute increase in the risk of failed healing without HBO_2T is estimated at 38%, that is there will be 38% more cases of failed wound healing without HBO_2T. On its own, this information may not be useful, however. The importance of a 38% risk reduction may be very different if the incidence in the control group is 100% as opposed to the actual rate of 44.4%. In this example, the problem is all but eliminated by the institution of HBO_2T.

3 Number needed to treat (NNT).

The NNT is the reciprocal of the RRR. It is an estimate of the number of individuals who need to be treated with HBO_2T before one more person will achieve a good outcome. In this example, we only need to treat three cases of crush injury before we avoid a non-healing wound in one

TABLE 5

Prince of Wales Hospital Critical Appraisal Sheet

Important information that should be in the paper	**Potential related problems**	**Threats to the internal and external validity of the study**
	1.2 Is this question relevant to the clinical problem?	
2.1 What is the study type?	**2.2** Is the study type appropriate to the research question?	**2.3** If not, how useful are the results likely to be?
3.1a Define the population in which the authors nal are interested. Are the study subjects representative of this population?	**3.2a** Are there selection biases?	**3.3a** Any threat to external validity? Any threat to inter- validity?
3.1b If assigned to groups, how was this accomplished?	**3.2b** Was allocation random? Was allocation made after a decision to enter the trial?	**3.3b** Any threat to internal validity?
3.1c How many reached final follow-up?		**3.3c** Does this proportion threaten internal validity?
4.1 What is being studied (study factor)? How is it measured?	**4.2** Is there any likely measurement error (differential or non-differential)?	**4.3** Is there any likely important cause of bias? (Beware differential error with Case-Control Studies).
5.1 What outcomes are being assessed (outcome factors)?	**5.2** Any important outcomes missed? Any likely measurement error (differential or non-differential)?	**5.3** Do missed outcomes reduce the applicability of this study? Is there any likely source of bias?
6.1a What potential confounders are considered?	**6.2a** Any important confounders missing?	**6.3** How likely is confounding to be a significant source of bias?
6.1b How were they dealt with?	**6.2b** Were they dealt with adequately, or subject to measurement error?	
7.1a Is a point estimate of effect given?	**7.2a** Is it reasonable to accept these results are not due to chance?	**7.3** Is this study useful or inconclusive in answering the research question?
7.1b Are confidence intervals given? If not in a study with statistically non-significant findings, is power given?	**7.2b** Are the differences reported clinically significant? Was the sample size sufficient to detect a clinically significant difference?	
8.1 What are the authors conclusions?	**8.2** Have the authors correctly interpreted the results?	**8.3** Have the authors considered study limitations in their conclusions?

TABLE 6
EXAMPLE CAT (Critically Appraised Topic)

Hyperbaric oxygen did not reduce the number of patients with persistent deficit following carbon monoxide poisoning and was associated with a higher rate of delayed neurological sequelae.

Clinical Bottom Line

1 There was no benefit evident for hyperbaric oxygen in the prevention of persistent neurologic abnormality.
2 There were significantly fewer patients with delayed neurologic abnormality in the normobaric group.

Appraised by Mike Bennett, Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital, Sydney; Monday, 1 March 1999.

Clinical Scenario. A patient presented with acute carbon monoxide intoxication and we wondered if there was any demonstrable benefit in the administration of hyperbaric oxygen.

Three-part question. In patients with carbon monoxide poisoning, does the administration of hyperbaric oxygen, compared to normobaric oxygen, result in any improvement in the acute neurological state or the avoidance of late neurological deterioration?

Search Terms. Hyperbaric oxygenation, carbon monoxide

The Study. Double-blinded concealed randomised controlled trial with intention-to-treat.

Patients referred to a hyperbaric facility for the treatment of carbon monoxide poisoning- all grades of severity.

Control group (N = 87; 87 analysed): Normobaric oxygen at 1ATA for 72 hour with three periods of sham hyperbaric oxygen. Those with persistent symptoms or signs received three further daily sham treatments and a further 72 hours on oxygen.

Experimental group (N = 104; 104 analysed): Daily hyperbaric oxygen at 2.8 ATA for 60 minutes (total chamber time 100 minutes) for three days with normobaric oxygen between treatments. Treatment repeated for another three days if symptoms or signs persisted.

THE EVIDENCE

Outcome	Time to Outcome	Normobaric group	HBO group	Relative risk reduction	Absolute risk reduction	Number needed to treat
Persistent neurological sequelae	Discharge	0.68	0.74	-9%	-0.060	-17
95% CI:				-28% to 10%	-0.189 to 0.069	14 to INF 5 to INF
Delayed neurological sequelae	Unknown	0	0.048	INF	-0.048	-21
95% CI:					-0.089 to -0.007	-145 to -11
Complications of treatment	Discharge	0.01	0.09	-800%	-0.08	-13
95% CI:				-100% to -212%	-0.139 to -0.021	-47 to -7

Non-event outcomes	Time to outcome	Normobaric group	HBO group	P-value
Average number of neuropsychiatric tests abnormal	Discharge	2.7	3.4	0.02

Comments

1 Oxygen doses high in comparison to those generally administered.
2 Cluster randomisation accounted for differences in the final numbers and may introduce some bias.
3 Average delay to treatment was over 7 hours.
4 Minimal improvement in mini-mental state assessment before and after treatment in either group is puzzling.
5 No functional outcome other than mortality.
6 Follow-up at one month only 46%.

Expiry date. March 2000

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TABLE 7

RESULTS OF HBO_2T FOR CRUSH INJURIES
(from Bouachour et al.[12])

Outcome outcome	Time to group	Air group	HBO	RRR	ARR	NNR
Wound not healed	60 days	0.444	0.06	86%	0.384	3
95% CI:			29% to 100%	0.130 to 0.638	2 to 8	
Repeat surgical procedure	60 days	0.333	0.06	82%	0.273	4
95% CI:				9% to 100%	0.029 to 0.517	2 to 34

RRR = Relative risk reduction ARR = Absolute risk reduction NNT = Number needed to treat

person. Many clinicians find the NNT of most relevance when trying to assess the direct clinical impact of a therapy on their patients.

We might conclude, therefore, that the addition of HBO_2T in the treatment of lower limb crush injuries is justified by the impressive reduction in the incidence of non-healing wounds (86% reduction). We can expect to eliminate 38% of non-healing wounds following such injuries and this means we prevent one non-healing wound for every three patients we treat with HBOT.

Implementation of the conclusions

Without a doubt, implementation is the most difficult aspect in the practice of EBM. Appropriate strategies will vary with the individual situation, however it can be difficult to engage colleagues who have not participated in the process outlined above. It is our anecdotal experience that successful strategies arise from active participation by a significant proportion of clinicians. This is often relatively easy to achieve in a small area like a hyperbaric service. It has proved far more difficult in a large practice, such as a busy anaesthetic service, where it is difficult to marshal the majority of the faculty into one meeting.

There is no doubt that the pursuit of EBM is an active one. Colleagues will be engaged with the process when their own clinical questions are under discussion. At the Prince of Wales Hospital, we find it works best in a formal meeting, held regularly, with clinical problems working their way through the system described above, over a series of meetings. A suggested clinical problem will be worked into a formal question in one meeting, the search in answer to that question at the next, the critical appraisal of the chosen reference at the next and finally the CAT reviewed at the next. At each meeting, several different topics will be under discussion in order to maintain interest.

This process is outlined in more detail by both Sackett and Bennett.[3,4]

The most appropriate outcome is of course, better practice with improved outcomes for patients. The process described here is not foolproof and does not guarantee best practice. Each finding will require careful synthesis by the clinician into the overall situation of the individual patient. EBM provides systematic advice on existing evidence, only the clinician can actually treat the patient.

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Dr Mike Bennett, FANZCA, MM (Clin Epi) is Medical Director, Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital, High Street, Randwick, New South Wales 2031, Australia. Phone +61-2-9832-3883. Fax +61-2-9832-3882. E-mail m.bennet@unsw.edu.au .

A POSSIBLE CASE OF CEREBRAL ARTERIAL GAS EMBOLISM IN A BREATH-HOLD DIVER

David Williams

Key Words

Breath-hold diving, case report, decompression illness, cerebral arterial gas embolism

Introduction

Cerebral arterial gas embolism (CAGE) is second only to drowning as the most common cause of death in recreational SCUBA divers;[1] however, it is extremely rare in breath-hold divers unexposed to a compressed air source. The history of a possible case of CAGE in a previously healthy breath-hold diver is described here; and the differential diagnoses are discussed.

Clinical history

A fifteen year old male, from Munda in the Solomon Islands, made frequent repetitive breath-hold dives over a period of three and a half hours to spear fish. His maximum depth was approximately 8 m. On surfacing from his last dive, he developed a sudden severe headache, dizziness, blurred vision, and numbness and weakness of all four limbs. He was unable to stand or walk and had to be carried from the water by his father.

The symptoms persisted, and he was admitted to the Helena Goldie Hospital, Munda, the following day. He had no previous history of medical problems (specifically, no history of pulmonary or neurological illness), and had been completely well prior to and during his breath-hold dives. There was no history of exposure to a compressed air source, and he was the only person in the water at the time that the