a prescription for antibiotics may be equally good quality care.

Secondly, guidelines imply that one size should fit all. In some situations this is likely to be correct. For example, a breast lump in a woman 65 years old needs to be properly investigated in a specialist clinic until malignancy has been excluded. However, there will always be some people who do not fit the guidelines. General practitioners are experts at finding the right treatment for their patients. This involves taking account of their psychosocial factors and welding different pieces of information together to make a decision.[4] A woman might have a phobia of needles that would make fine-needle aspiration of her breast a serious problem; she may also have other more pressing and urgent medical or non-medical problems that assume a greater priority. Being sensitive to these issues may actually be a sign of very good quality care. Patients' views (if well informed) may be as important a factor in deciding what to do as the evidence on which guidelines are based.

E-mail: c.delmar@cgp.uq.edu.au

REFERENCES

1. Pit S, Cockburn J, Zorbas H. Investigation of a new breast symptom: an audit in general practice. Sydney: NHMRC National Breast Cancer Centre; 1999.
2. Bridges-Webb C, Butler J, Calcino G, Colmer P, Del Mar C, Dickinson J, et al. General practice in Australia: 1996. Canberra: General Practice Branch, Commonwealth Department of Health and Family Services; 1996.
3. Glasziou PP, Hayem M, Del Mar CB. Antibiotics for acute otitis media in children [review]. In: The Cochrane Library. Oxford: Update Software; Issue 2, 2000.
4. Stewart M. Healing partnerships between patients and family doctors: an aspect of quality of care. Working paper series #98-1. Ontario: Centre for Studies in Family Medicine, The University of Western Ontario; 1998.

FURTHER READING

Some guidelines can be accessed through the following web sites:

http://www.guideline.gov/ (US National Guidelines clearinghouse)

http://www.health.gov.au/ (Commonwealth Department of Health and Aged Care – a good starting point for several other sites)

http://www.nhmrc.health.gov.au/ (National Health and Medical Research Council)

http://www.healthinsite.gov.au/ (A federally-funded information site about health)

http://www.ctfphc.org/ (One of the best sites on preventive health care, from the Canadian Task Force)

http://www.tg.com.au (Therapeutic Guidelines) (available at cost)

(Note: Three members of the Australian Prescriber Executive Editorial Board, Doctors R.F.W. Moulds, J.W.G. Tiller and J.S. Dowden, are unpaid directors of Therapeutic Guidelines Ltd., a not-for-profit organisation.)

Letters

Letters, which may not necessarily be published in full, should be restricted to not more than 250 words. When relevant, comment on the letter is sought from the author. Due to production schedules, it is normally not possible to publish letters received in response to material appearing in a particular issue earlier than the second or third subsequent issue.

Prescribing by numbers: pharmacoeconomic consideration

Editor, – Referring to comments made by P. Neeskens (Aust Prescr 2000;23:115) on the usefulness of the number needed to treat (NNT), it is worth mentioning that the figures were misquoted. The original article by Eve Hurley (Aust Prescr 2000;23:38) stated that X = event rate control was 4.1% and that Y = event rate active (with gemfibrozil) was 2.7%. In Dr Neeskens' comments these two figures were transposed.

While it may be true that the NNT does not always give a feel of the relevance of an intervention, it certainly does provide a useful measure for comparing interventions when pharmacoeconomic evaluations are performed. From the Helsinki Heart study, it can be calculated that to treat the 71 men for 5 years with gemfibrozil just to prevent one event would cost: 220 (ZAR) x 12 (months) x 71 (men) x 5 (years) = 937 200 ZAR (South African Rands) in drug costs alone. This is equivalent to $220 000. If there is a cost-effective non-pharmacological intervention or an alternative drug that provides the same or similar relative risk reduction (of 34% as quoted) then the use of NNT will help in decision-making for policy-makers as well as clinicians.

N. Malangu
Lecturer
Medunsa School of Pharmacy
South Africa

Medications which may lower seizure threshold

Editor, – Amongst the medications which may lower seizure threshold (Aust Prescr 2001;24:8-9) two stimulant medicines are listed, namely dexamphetamine (uncommon) and methylphenidate (anecdotal reports).

I would like to add another anecdotal report regarding caffeine, a self-medication or perhaps a recreational drug. I have seen two patients within a year or two of each other, both middle-aged women, who gave me almost identical histories. They had each been investigated for the cause of major seizures, including inpatient EEG monitoring, without a cause being found or effective relief obtained. On questioning, they each admitted to being heavy drinkers of instant coffee, to the order of 40 cups a day. I advised both women to reduce their coffee consumption to normal levels, and neither of them has had any further seizures over 10 years.

Michael Grounds
General Practitioner
Bendigo, Vic.

Editor, – I found Professor Neil Buchanan's article 'Medications which may lower seizure threshold' (Aust Prescr 2001;24:8-9) very timely and useful. Over the last month, the Acute Pain Service at my hospital has come across three patients taking pethidine (for patient controlled

analgesia) who have exhibited signs of seizure activity (twitching, anxiety etc.). None actually fitted and none had a previous history of epilepsy.

We see this problem from time to time but not with this sort of frequency. Interestingly, at least two and possibly all of the patients were also on tramadol, a drug with mixed opioid agonist and serotonin/noradrenaline reuptake inhibitor activity. The product information for tramadol suggests that it should be included in Professor Buchanan's list, and perhaps particular caution is required when considering the combined use of tramadol with pethidine.

John Loadsman
Staff Specialist
Department of Anaesthetics
Royal Prince Alfred Hospital
Camperdown, NSW

Economy class syndrome

Editor, – There has recently been a multitude of communications in the media describing 'economy class' syndrome. I believe it is important to know that this disease is not exclusive and can also occur in upper class travellers. They also need prophylactic measures. Here is a brief case history:

A 72-year-old man in good health and without varicose veins flew business class to Sicily. He had a one hour stop in Bangkok and two hours in Rome. On descending in Rome, he felt a 'discomfort in his foot'. Some two days later, a Sicilian doctor diagnosed a deep vein thrombosis. The patient was given daily injections in his 'abdomen' for two weeks to 'thin the blood'. His symptoms soon subsided and on his return to Sydney two months later, no clinical signs remained and sonogram showed free venous flow in the leg.

This case history has justified my policy of handing my patients a small article on the venous circulation and thrombosis before their trip. I advise on hydration and mobilisation of legs, suggest anti-embolism stockings, particularly for women on oral contraceptives and/or hormone replacement therapy, and prescribe low-dose aspirin for two day before and a day after the trip.

George Weisz
Orthopaedic Surgeon
Bondi Junction, NSW

Drug treatment for opioid dependence

Editor, – The author of 'Drug treatment for opioid dependence' (Aust Prescr 2001;24:4-6) refers to the term dependence as if there is only one possible meaning. However, there are two forms of dependence. One is where the opioid receptors require an opioid to prevent withdrawal effects – *physical* dependence – and the other is a *psychological* dependence whereby illicit opioid users use opioids but are not physically dependent. It is acknowledged that most, if not all, physically dependent people would have been psychologically dependent at some stage and may still be so. Which group is the author referring to? Does the author imply that there are 70 000 heroin users that are physically dependent or are some of these users not physically but psychologically dependent?

Our research into methadone reveals a wide and unpredictable half-life ranging from as little as four hours to as long as four days. The author states that methadone for maintenance need only be given once a day. This does not correlate with the variable half-life of methadone and may be one of the reasons that methadone given once a day fails in about 15% of patients. If the half-life is short, it would be possible to treat that person with a large once-daily methadone dose but from a pharmacological perspective they may well do better with a smaller dose given more frequently, more in line with the half-life of methadone. From the practical perspective this equates to twice daily. This approach has been verified when using methadone for pain control.

Associate Professor D.A. Cherry and
Associate Professor G.K. Gourlay
Pain Management Unit
Flinders Medical Centre
Bedford Park, SA

Dr Alex Wodak, author of 'Drug treatment for opioid dependence', comments:

Professors Cherry and Gourlay argue that physical and psychological forms of drug dependence should be considered separately. While contemporary definitions of 'drug dependence' by reputable authorities abound, most now regard the physical and psychological components of drug dependence as inseparable. The operational definitions used today are mainly derived from the DSM-IV and ICD-10 classifications of diseases. The estimate of more than 70 000 severely dependent heroin users in Australia was based on a unitary rather than a dualistic notion of drug dependence.

The wide variation in methadone plasma half-life, rightly emphasised by Professors Cherry and Gourlay, seems more of a problem for analgesia than for the management of heroin dependence. Even if twice-daily administration was preferable for methadone treatment, the need for supervised administration for the vast majority makes this option logistically unfeasible. Twice-daily supervised methadone administration does have a role for a small minority. For the vast majority of heroin-dependent persons seeking help, methadone treatment achieves substantial benefits with few adverse effects.

Iodine deficiency

Editor, – I am an endocrine surgeon working with a diverse overseas-born population. I have been checking the iodine nutritional status of my goitre patients recently, as iodine deficiency may be more common in Australia than previously thought. Only two or three patients out of 54 tested with normal iodine levels on 24-hour urinary iodine testing. One notable exception was a patient with 45 times the normal daily excretion. On questioning, she had not had recent IV contrast media or amiodarone, but had consumed a herbal cough mixture. The contents of the medicine are unclear.

Iodine does not appear to be listed on the box. The dose of half to one tablespoon without reference to frequency or age concerns me. Prescribers (and patients) need to be aware that herbal remedies can be hazardous. Patients with pre-existing goitre can become thyrotoxic if exposed to even a modest supranormal iodine load. Those with thyroid cancer who are given iodine by well-meaning naturopaths may delay or reduce the effectiveness of radioactive iodine therapy.

Peter Campbell

Endocrine Surgeon

Liverpool, NSW

Bisphosphonates – clinical applications in osteoporosis

Editor, – At last some common sense seems to be finding its way into medical thinking. Professor John Marley assures us of what we have all known at the back of our minds: that efficacy is not the same as effectiveness (Aust Prescr 2000;23:114-5). We have heard so much about evidence-based medicine and Cochrane reviews that we have barely escaped the conclusion that evidence-based, statistically sanctified, Cochrane-metanalysed* medicine is the *only* proper kind for us to practise. In the real world we are not free, as trial-makers are, to exclude patients because of age or concurrently taken drugs or comorbidities, so we have to use a little of that ancient virtue intuition when grappling with many problems.

Another improvement is that we are being given absolute risks along with 'risk reduction ratios'. The latter, of course, are the selling ploys of the drug companies – they seem so persuasive! Without the corresponding absolute risks they are virtually meaningless, and no basis for clinical decisions. The derivative parameter 'number needed to treat' (NNT), admirably set out in the article on bisphosphonates (Aust Prescr 2000;23:133-6), is much more useful. However, there are grave ambiguities: is the NNT based on the number of people to whom the doctor says 'I intend to treat you with a daily dose of Bonehardna for five years', or the number who actually comply with the treatment regimen? And is it the lifetime NNT or does it apply to a time-span such as a year? These points need to be stated.

Lastly, I have struggled to find meaning in the sentence: 'Increases were 4.3% greater than placebo in the lumbar spine, 2.8% in the femoral neck ...' (p.134, col. 2). 4.3% of what? If the placebo produced 100 units of improvement, did the risedronate produce 104.3? This is what the words seem to mean (and again, in how much time?), but it is hardly a strong recommendation, since the placebo is likely to have produced a negative benefit. Or does it mean something else? If it does, why not say so?

Alasdair Livingston

Surgeon

Mitcham, SA

* I decline to use the horrible word 'meta-analysis'. The Greeks had no qualms about eliding two or more prefixes together, and if we borrow their language, nor should we.

Associate Professor Peter Ebeling, author of 'Bisphosphonates – clinical applications in osteoporosis', comments:

I would like to thank Dr Livingston for his comments on 'Bisphosphonates – clinical applications in osteoporosis'. I agree with Dr Livingston that the absolute risk of an outcome is more important than the relative risk reduction, particularly when considering an individual patient's treatment. The duration of treatment required to calculate the number needed to treat appears in the tables and is for five years' and three years' treatment with alendronate and risedronate, respectively, in women with postmenopausal osteoporosis and at least one baseline vertebral fracture. For osteoporotic women without vertebral fractures, the number needed to treat was calculated for only four years of treatment with alendronate – as the data for the risedronate hip fracture study[1] had not been published at the time of preparation of the manuscript.

Regarding the changes in bone density in the risedronate fracture study, the differences between the treatment and placebo groups represent changes from baseline at three years, expressed as a percentage. In the placebo group small significant increases or decreases in bone density from baseline were seen depending on the skeletal site measured. Thus, treatment with calcium 1000 mg per day +/– vitamin D in the placebo group for three years resulted in a 1.1% increase in spinal bone density, but did not prevent bone loss from femoral sites in postmenopausal women with osteoporosis.

REFERENCE

1. Hip Intervention Program Study Group. Effect of risedronate on the risk of hip fracture in elderly women. N Engl J Med 2001;344:333-40.

Stopping antidepressants

Editor, – The article 'Stopping antidepressants' (Aust Prescr 2001;24:13-5) brings together many practical discussion points for pharmacists to reinforce the medical practitioner's treatment. However, in listing the factors influencing the decision to stop treatment, a significant omission as a factor is the continuing presence or otherwise of the trigger(s) which contributed to the original depression.

John Williams

Pharmacist

Mosman, NSW

Professor Isaac Schweitzer and Kay Maguire, authors of 'Stopping antidepressants', comment:

Mr Williams raises the role of triggers in precipitating and perpetuating a depressive disorder. This area remains somewhat controversial and each individual case must be considered in its overall context. Judgement is often required which can be difficult and complex. Did the depressive illness itself result in the difficult psychosocial situation of the patient or did psychosocial factors play a role in bringing on the illness? These are central questions which must be considered.

Prevention of endocarditis

Editor, – As a dentist, I am particularly concerned with guidelines for the prevention of endocarditis. The new Antibiotic Guidelines[1] differ from previous editions by giving only one set of recommendations for patients with cardiac lesions, which predispose them to infective endocarditis. These include congenital or rheumatic heart disease, a previous episode of endocarditis, and the presence of prosthetic heart valves. In previous editions there were guidelines for low-risk patients (those suffering from congenital or rheumatic heart disease) and for high-risk patients (those with prosthetic heart valves or a previous episode of endocarditis).[2] The prophylaxis for low-risk patients was 3 g oral amoxycillin given one hour before dental treatment. For high-risk patients this was supplemented with gentamicin 2 mg/kg.

In the new edition the dose of amoxycillin is reduced to 2 g and there is no additional drug for high-risk patients. I am unhappy about the omission of the category of high-risk patients because I am aware of three cases where oral amoxycillin failed to prevent the occurrence of endocarditis. A recent British paper[3] continues to advocate a supplementary antibiotic for high-risk patients.

The editors of the Antibiotic Guidelines do not explain these changes. They state 'Consensus is currently changing and these recommendations are based upon current international practice'. It would seem that on the whole the guidelines of the American Heart Association[4] were followed. Would it not be more logical to base the new recommendations on an analysis of case histories? One way of approaching this difficult subject would be by analysing instances where previous recommendations for prevention had failed. Unfortunately there is no central body responsible for listing such failures. The last such study[5] was published in 1982. We can only ascertain whether the prophylactic measures suggested by various authorities are effective or not, if records are kept.

It is unfortunate that guidelines for the prevention of endocarditis differ from country to country. I agree with the suggestion that we should have uniform guidelines throughout the world.[6]

E.H. Ehrmann

Senior Fellow

School of Dental Science

Faculty of Medicine, Dentistry and Health Science

University of Melbourne

Melbourne

REFERENCES

1. Writing Group for Therapeutic Guidelines: Antibiotic. Therapeutic Guidelines: Antibiotic. Version 11. Melbourne: Therapeutic Guidelines Limited; 2000.
2. Writing Group for Therapeutic Guidelines: Antibiotic. Therapeutic Guidelines: Antibiotic. Edition 10. Melbourne: Therapeutic Guidelines Limited; 1998.
3. Seymour RA, Lowry R, Whitworth JM, Martin MV. Infective endocarditis, dentistry and antibiotic prophylaxis; time for a rethink? Br Dent J 2000;189:610-6.
4. Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri P, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. JAMA 1997;277:1794-801.
5. Durack DT, Bisno AL, Kaplan EL. Analysis of 52 cases of apparent failure of endocarditis prophylaxis. Circulation 1982;66(Suppl II):102.
6. Durack DT. Prevention of infective endocarditis. N Engl J Med 1995;332:38-44.

Professor W. John Spicer, Chairman, and Dr David Looke, Member, Writing Group for Antibiotic Guidelines, comment:

We empathise with Dr Ehrmann's difficulties. These difficulties stem from one currently insuperable problem in writing guidelines for endocarditis prophylaxis; there are no accurate, quantitative data on:

- the risks of particular procedures
- the risks of particular cardiac lesions
- the results of particular antibiotic regimens.

The Antibiotic Guidelines have been evidence-based for over 20 years, but in endocarditis prophylaxis, the evidence is like the Dead Sea Scrolls. It is fragmentary, imperfect, capable of various interpretations, or (mainly) missing!

Another problem in countries like Australia is that it is difficult logically or medicolegally to differ from major overseas guidelines when there are no data to show whether the outcomes of a different Australian recommendation would be similar, better or worse.

To address Dr Ehrmann's specific difficulties:

1. There is no good evidence to continue the practice of low-risk/high-risk stratification.
2. Three grams of amoxycillin was recommended originally simply because of the availability of that formulation. Pharmacokinetic data show that 2 g is enough. Certainly, 3 g is too much for some patients to tolerate. Whether or not a second dose would prevent endocarditis not prevented by a single dose, is pure conjecture.
3. There is no good evidence that gentamicin is necessary or effective in prophylaxis (as distinct from treatment). We have therefore moved towards the American and British recommendations.

Dr Ehrmann's comments are welcome and constructive. In this area with so little hard evidence, opinion must be gathered, weighed and synthesised into coherent recommendations. Variation is acceptable if good reasons and particular circumstances exist. Compromise is inevitable, and disagreement predictable.

'Take as directed', whatever that means

Editor, – I refer to the article ' "Take as directed", whatever that means' (Aust Prescr 2000;23:103-4).

In South Australia 'that' means the prescription is invalid. Regulations under the Controlled Substances Act require that prescriptions be legible and include *specific* directions. In most instances the problem is resolved by reference to prescription records and discussion with the patient, to avoid forcing the patient to return to the doctor to have the prescription corrected.

Helen Hopkins' article omits mention of the positive contributions made by pharmacists in aiding compliance, mentioning only ' ... hesitating to communicate effectively with consumers about risks'. We may hesitate in some cases but we distribute the majority of Consumer Medicine Information and other printed and verbal information available from health professionals. Many pharmacists also print the indication on the label at the request of the patient, but this is often difficult when prescribers do not indicate that the tricyclic, for example, is for pain relief.

It would be interesting to know how many patients refuse to take medication after reading the Consumer Medicine Information – we suspect many – because the early information sheets often contained misleading information.

Finally, the term 'polypharmacy' is inappropriate because it is poly-prescribing that leads to the problems of multiple medication use, something today's pharmacists try to discourage.

Peter Bayly
Pharmacist
Wattle Park, SA

Book review

Australian Medicines Handbook Drug Choice Companion: Emergency and Primary Care

Adelaide: Australian Medicines Handbook; 2001. 176 pages.
Prices:
Drug Choice Companion $60
Drug Choice Companion + AMH Book $190
Drug Choice Companion + AMH Book + CD $212

(Reduced prices for students and members of the Royal Australian College of General Practitioners, the Pharmaceutical Society of Australia and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists)

Ann-Marie Crozier, Director, General Practice Casualty, Balmain Hospital, Sydney

This is an excellent book for the practical general practitioner who wants to quickly check prescribing of drugs for the emergency situation.

The handbook assumes a basic knowledge of diagnosis of emergencies and acute medicine. Each presentation, e.g. pneumonia, migraine, unstable angina, is covered by a single page which helps the reader rapidly access the information. Emergencies are listed in an index in the back of the book. The book uses a pragmatic style with the drug(s) to be prescribed written in bold at the top of the page (including adult and child doses). Dot points expand on the management of the presentation. A short list of references, with preference for Australian references, is to be found at the back. The handbook is 17 x 11 cm (smaller than a prescription pad) in size and therefore would fit easily in most general practitioners' emergency kits. Whilst the stated purpose of the book is for doctors working in regional and remote Australia, there is a wealth of concise and relevant information for urban practitioners.

A number of sources have contributed to the handbook including the Royal Australian College of General Practitioners, the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, and the Pharmaceutical Society of Australia. I note with interest that virtually all the general practitioners who have had input are from rural Australia including places like Tumut, Minlaton, King Island, Katherine, Wiluna and Thursday Island. Specialists throughout Australia and across a range of specialities have also been consulted.

The content of the protocols is based on evidence from resources such as *Australian Prescriber*, *Therapeutic Guidelines*, NHMRC guidelines, the *Medical Journal of Australia*, the Cochrane databases and emergency medicine texts, with a preference for Australian data where possible. The protocols are grouped according to organ systems. Drug choices in each protocol are ranked according to evidence about their efficacy, cost, tolerability and dosing schedule convenience. The dot points at the bottom of each page include advice on non-drug treatments and in some instances when not to use particular drugs.

The book is perhaps limited by its medication focus and its size. Conditions such as bradycardia, acute iritis and pericarditis do not appear. Emergencies where a drug focus is not paramount, such as burns, pneumothorax, barotrauma and heat stroke are not covered. This limits the book's potential as a complete emergency text and whilst this is not its stated aim, perhaps a greater coverage of emergencies and acute medicine would ensure that it could become the definitive emergency text for general practitioners. The index could be slightly expanded. For example, neither 'fit' nor 'convulsion' is listed whilst 'febrile convulsion' and 'status epilepticus' are. Tetanus prophylaxis is neither indexed nor addressed and again this may be beyond the scope of the book. Having said this, these minor negatives should not detract from the overall assessment which is that of a useful, concise and relevant emergency drug handbook.

I believe this is definitely a valuable addition to the working general practitioner's essential texts for the management of emergencies and acute medicine.