for this, especially in remote and rural areas not served adequately by doctors and pharmacists. The Society of Hospital Pharmacists[8] endorsed the need for special training if prescribing by pharmacists was to be extended to prescription drugs, and emphasised the need to separate wherever possible the prescribing and dispensing roles. Other health professionals (for example optometrists and physiotherapists) commonly have very limited prescribing needs and the convenience of patients must be one factor in deciding whether to extend their prescribing rights. With adequate training, supervision (where necessary) and regular evaluation, non-medical health professionals working with limited formularies should be capable of prescribing to an appropriately high standard.

Medical educators have belatedly awakened to the need to train students for the task of prescribing which, conservatively, will be undertaken at least 200 000 times in a general practitioner's career. The new computer-based prescribing curriculum assembled by the National Prescribing Service is being adopted by medical schools and has received positive support from teachers and senior medical students who have worked with it.[9] It may be useful for training other health professionals.

Any extension of prescribing must be evaluated using routinely generated data. In Australia, prescribing data are captured in pharmacists' computers, but only prescriptions for drugs listed on the Pharmaceutical Benefits Scheme are held in Commonwealth databases. This means that at least 20% of all prescriptions, whoever writes them, are not available for any form of evaluation. This has long been a major stumbling-block for the quality use of medicines. Our legislators appear powerless to take the simple steps needed to make complete, de-identified prescribing data available. This enabling step should be a prior requirement to any extension of prescribing rights.

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Conflict of interest: none declared

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.

Can we deny patients expensive drugs?

Editor, – We read with interest the editorial 'Can we deny patients expensive drugs?' (Aust Prescr 2006;29:146–8). We agree with many of the author's arguments, but take exception to the suggestion that Pharmaceutical Benefits Advisory Committee (PBAC) processes be bypassed for drugs targeting rare diseases and for which no PBAC submission has been made. The authors suggest that in such cases the Pharmaceutical Benefits Scheme (PBS) 'subsidise the use of these medicines for an indication after conventional therapies have proven ineffective'. We infer that such medicine be subsidised irrespective of costs. This implies society is willing to accept a higher cost per unit of health (for example a year of life) on the basis that the disease is rare. Some things need to be clarified; rare does not mean severe and expensive does not mean better. We acknowledge that efficiency should not be the only criteria in resource allocation decisions and that equity considerations need to be taken into account also. However, the fact that a person has a rare, as opposed to a common, condition is not a good moral basis for accepting higher opportunity costs. Such a system would send all the wrong signals to the research and development community. Locally, pharmaceutical companies would stop applying for PBS funding for drugs that target rare diseases. On a global

level, such a system signals our willingness to pay infinite amounts for uncertain benefits for rare conditions, at a time when we want more research and development in areas where we can make substantial gains in reducing the health burden.

Gisselle Gallego
Kees van Gool
Research Officers, Centre for Health Economics and Research Evaluation
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Sydney

Ms Karen Kaye, Ms Christine Lu and Professor Richard Day, authors of the editorial, comment:

We agree that PBAC processes should not be bypassed for medicines targeting rare diseases, but in fact this often happens in our current healthcare system. Expensive treatments for severe and rare diseases that are not PBS-subsidised are instead subsidised through supply by public hospitals. The problem with this process is that it is relatively *ad hoc* and decisions about patients' access to such medicines vary depending on the availability of local expertise and funding. It does not promote consistency or transparency in the decision process, does not guarantee equity of access to medicines for patients with the same condition in different parts of the country, and does not facilitate national monitoring of either costs or outcomes. The current system has not resulted in adequate research or PBS submissions to date and it will not in future unless hospitals refuse to supply these medicines. This is unlikely, especially when the disease is severe **and** there is evidence of clinical effectiveness **and** other therapeutic options have been tried and failed. Such a funding approach is ethically sound; a similar ethical approach forms the basis for the PBS 'rule of rescue' and Australia's Orphan drug program. Carefully monitored supply of expensive but effective medicines via a national system would at least facilitate collation of information to inform government, clinicians, industry and the public about use of these medicines (and associated costs and outcomes) and would help ensure equity of access. Provided supply continues to be reviewed on the basis of such information, there is likely to be benefit to both patients in need and society as a whole.

Should beta blockers remain first-line drugs for hypertension?

Editor, – It was disappointing to read that beta blockers have fallen from favour for the treatment of hypertension (Aust Prescr 2007;30:5–7), particularly at a time when their use as prophylaxis for myocardial ischaemia in the perioperative period is being encouraged.

Myocardial ischaemia related to surgical stress often occurs in patients with no history of coronary artery disease. It is also frequently silent, but causes significant cardiac morbidity and mortality.

Beta blockers are effective prophylaxis for high risk patients[1] and are recommended by the American College of Cardiology/American Heart Association guideline for perioperative cardiovascular evaluation for noncardiac surgery.[2]

The benefit and risk of prophylactic beta blockade in low to moderate risk patients is less clear. The POISE trial, which is currently recruiting 10 000 patients, should soon provide some definitive recommendations.[3]

Beta blockers may not be as effective at achieving target blood pressure as other classes of antihypertensive drugs. However, in the perioperative setting beta blockers should remain first-line therapy for blood pressure control, particularly when risk factors for ischaemic heart disease are present.

James French
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Dr Maros Elsik and Professor Henry Krum, authors of the article, comment:

In patients with cardiovascular comorbidities or complications as a result of hypertension, treatment needs to be individualised. In many such cases beta blockers are a reasonable option.

Their use in the perioperative setting, although not specifically discussed in our article, has been shown to improve cardiovascular outcomes mainly by reducing myocardial ischaemic events. This represents another situation where beta blockers should not necessarily be stopped or avoided.

Paracetamol

Editor, – Paracetamol is generally recommended as the first drug of choice in pain largely because of its safety profile and cost. But is it as safe as it seems?

The relative risk of upper gastrointestinal complications from paracetamol is 3.6 for doses greater than 2 g per day. This is compared to a relative risk of 2.4 for low to medium doses of non-steroidal anti-inflammatory drugs (NSAIDs) and 4.9 for high doses.[1]

The relative risk of hypertension with 0.5 g (or more) of paracetamol per day is 1.99 (1.39–2.85) in young women and 1.93 (1.30–2.88) in older women. For NSAIDs, the relative risk of hypertension is 1.60 (1.10–2.32) in young women and 1.78 (1.21–2.61) in older women.[2]

Should we be concerned at this data and is paracetamol a medication that should be taken without warnings being issued to the public?

David Vivian
Medical practitioner
Melbourne

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Expert comment:

Placebo-controlled trials show that paracetamol has no significant effect on the gastrointestinal tract.[1] By contrast, a case-control study on paracetamol reported that there was a dose-related increase in gastrointestinal adverse reactions.[2] We and several others concluded that the finding of gastrointestinal toxicity of paracetamol could be a biased result, a recognised hazard of case-control and observational studies especially when relative risks are low.[3,4,5] Furthermore, another case-control study found that upper gastrointestinal bleeding was not associated with paracetamol[6] indicating considerable uncertainty regarding paracetamol and gastrointestinal toxicity. Paracetamol may, however, cause upper gastrointestinal complaints such as dyspepsia[4], although this does not usually lead to cessation of treatment.

Regarding hypertension, controlled trials of paracetamol generally show no significant effect on blood pressure. Recent reviews recommend that paracetamol is suitable for use in patients 'who may be at increased risk for the blood pressure or fluid effects of NSAIDs'.[7] However, other studies report that the intake of paracetamol is associated with an increased incidence of hypertension.[8,9,10] This finding is not widely accepted and a comment published on one of the studies said, 'I await more compelling data prior to warning my patients that acetaminophen [paracetamol] may have adverse effects on blood pressure'.[11] Furthermore, an epidemiological study found no such association between paracetamol and blood pressure.[12] The reason that patients take regular doses of analgesics may be the confounding factor that explains the risk for increased blood pressure. This is a well known hazard associated with observational studies even when adjustments are made for possible confounding differences between exposed and non-exposed cohorts.[7]

For both questions on the adverse effects of paracetamol, the conclusion that more evidence is needed before changing clinical practice is still very reasonable.[11]

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Professor Graham has received funding from GlaxoSmithKline Australia for research on the mechanism of action of paracetamol. Professor Day has been a member of an advisory board for paracetamol (GlaxoSmithKline consumer) and is currently on an advisory board for over-the-counter ibuprofen (Reckitt Benckiser plc). Honoraria are deposited in audited trust funds of St Vincent's Hospital, Sydney.

New drugs – ziprasidone

Editor, – I would like to update the information in your New Drug comment on ziprasidone (Aust Prescr 2007;30:50–5). Much of the data on schizophrenia comes from a Cochrane review in 2000 which states that 'well planned, conducted and reported long-term randomised trials are needed if ziprasidone is to be accepted into everyday clinical use'. However, more recent studies published since 2000 were omitted from your comment.

Of these studies, a head-to-head trial found that ziprasidone (80–160 mg/day) had comparable efficacy to olanzapine (5–15 mg/day) with differences favouring ziprasidone in observed metabolic parameters.[1] These results are further supported by a 6-month double-blind extension of this study.[2]

Another head-to-head study of ziprasidone (80–160 mg/day) and haloperidol (5–15 mg/day) looking at relapse prevention found that both treatments were effective in reducing overall psychopathology, but ziprasidone was effective for negative symptoms and was better tolerated.[3]

An open-label study suggested that when outpatients who partially responded to conventional antipsychotics, risperidone or olanzapine were switched to ziprasidone their symptom-control was improved or maintained and the switch was well tolerated.[4]

A one-year study in patients with stable, chronic schizophrenia demonstrated that the probability of relapse was significantly lower in the ziprasidone-treated patients than those treated with placebo. In those patients who remained on treatment for at least six months, only 9% subsequently relapsed on ziprasidone compared to 42% on placebo (p=0.001).[5]

Regarding QT_c prolongation, your comment suggests that patients being initiated on ziprasidone may need a baseline ECG and one after starting treatment. This would be ideal practice for all patients receiving any antipsychotic medication and does not apply only to ziprasidone as implied. Prescribing information for ziprasidone states that 'experience with ziprasidone has not revealed an excess risk of mortality compared to other antipsychotic drugs or placebo'.[6] In patients treated with haloperidol, thioridazine, ziprasidone, quetiapine, olanzapine and risperidone, mean QT_c intervals did not exceed 500 milliseconds (the accepted level for clinical significance) in any patient taking any of the antipsychotics studied, in the absence or presence of metabolic inhibition.[7]

It is also important to note that there is six years experience with ziprasidone overseas and that the US prescribing information contains the same precautions as for other antipsychotic medications.

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Editorial Executive Committee comments:

It is appropriate that subsequent studies have addressed some of the issues identified by the Cochrane review. The studies cited by Dr Canny are not the only recent studies of ziprasidone. Different studies have reported advantages for other atypical antipsychotic drugs over ziprasidone.[8,9,10] One of the problems in assessing the evidence about antipsychotics is that most trials report outcomes which favour the drug produced by the company funding the trial.[11]

Schizophrenia is a chronic condition, but the head-to-head comparison with olanzapine only lasted six weeks. Although the trial was short, 49 of the 133 patients taking olanzapine and 66 of the 136 taking ziprasidone discontinued treatment.[1] Only 126 patients entered the six-month continuation study and by the end of the trial there were only 17 patients left taking ziprasidone and 21 patients taking olanzapine.[2]

Two of the trials discussed by Dr Canny[3,5] appear to have been included in the Cochrane review so their publication does not change our conclusions.

Another study quoted by Dr Canny pools data from three trials. This open-label switching study does not provide strong evidence for the efficacy and tolerability of ziprasidone.[4]

Ziprasidone seems to cause greater mean increases in QT_c intervals compared to olanzapine, haloperidol, quetiapine and risperidone.[1,2,3,7] Unlike other atypical antipsychotic drugs, the Australian prescribing information for ziprasidone includes a contraindication for patients who have a condition that potentially prolongs the QT_c interval.[6] We believe this is important information for prescribers and may help in treating patients with schizophrenia.

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Managing hepatitis C in the community

Editor, – We have recently been made aware of a dental note by Dr M McCullough of the Australian Dental Association in your journal (Aust Prescr 2006;29:52).

In the comment, Dr McCullough stated that, 'Dentists need to be aware that hepatitis C may be present in the saliva of infected patients. Our infection control practices therefore need to be exemplary to avoid spread of this, and other blood-borne viruses.'

We are perplexed by this comment on two levels. To the best of our knowledge, hepatitis C is a blood-borne virus and is not spread by saliva. We do not believe there has ever been a recorded case of such a transmission route. Secondly, to minimise the risks of transmission of a virus like hepatitis C between patient and health worker, adherence to standard infection control procedures is all that is required. We would be interested to know what 'exemplary' practices mean in this context, and how they differ from standard procedures.

Piergiorgio Moro
Community Development and Education Officer
Hepatitis C Council of Victoria
Melbourne

Dr M McCullough, author of the dental note, comments:

Firstly, I agree that hepatitis C is a blood-borne virus and there has not been a recorded case of spread via saliva. However, in my statement I did not say that it was spread by saliva, but that hepatitis C may be present in the saliva of infected patients. This was based on a recent literature search, which identified several articles on hepatitis C in saliva, and a review article.[1]

Secondly, the use of the term 'exemplary' was not in fact given a great deal of thought at the time. According to the Miriam-Webster dictionary, exemplary means 'deserving imitation because of excellence'. Standard infection control procedures used by Australian dentists are of course adequate to minimise the risks of transmission of a virus like hepatitis C. Furthermore, these standard procedures are at the level of international best practice and should be seen as excellent and deserving of imitation! The intention in the wording was not that we should undertake different procedures, but rather that we, as dentists, should be vigilant in adhering to these standard infection control procedures.

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