

## 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.

### Paracetamol

Editor, –The articles 'The vascular effects of COX-2 selective inhibitors' (Aust Prescr 2004;27:142–5) and 'Perioperative analgesia' (Aust Prescr 2004;27:152–4) advised physicians to opt for paracetamol as a first-line analgesic. Given that the major barrier to more widespread use of paracetamol is the need for at least four doses per day, is there any evidence regarding the benefits or otherwise of extended release paracetamol, and should these drugs be on the Pharmaceutical Benefits Scheme (PBS)?

Nicholas McLernon  
Resident Medical Officer, Obstetrics  
Osborne Park Hospital  
Osborne Park, WA

*Professor R.O. Day and Professor G.G. Graham, authors of 'The vascular effects of COX-2 selective inhibitors', comment:*

The idea of a sustained release paracetamol is very reasonable. The reduction in the number of daily doses would make long-term therapy with paracetamol more convenient. The problem is that the dose is large and the optimal sustained release tablet, say one that would last for 12 or even 24 hours, would be very large and too difficult to swallow. Cost-effectiveness would also need to be established for it to be subsidised by the PBS.

### The dwindling need for selective COX-2 inhibitors

Editor, – Regarding the article 'The vascular effects of COX-2 selective inhibitors' (Aust Prescr 2004;27:142–5), I agree that 'Low-dose aspirin or other anti-thrombotic treatment should be continued in patients receiving selective COX-2 inhibitors who are at risk of thrombosis'. However, one must ask why would we choose selective COX-2 inhibitors instead of conventional non-steroidal anti-inflammatory drugs (NSAIDs) for patients taking anti-platelet therapy?

In the CLASS study, patients who took celecoxib and aspirin (approximately 20% of nearly 8000 patients) had the same annualised incidence of symptomatic ulcers and upper gastrointestinal ulcer complications as patients taking aspirin with an NSAID (either ibuprofen 800 mg tds or diclofenac 75 mg bd).<sup>1</sup> The literature suggests that the principal 'advantage' of upper gastrointestinal safety is lost when a COX-2 inhibitor is co-prescribed with aspirin.

Published reports also show that patients taking COX-2 inhibitors appear to have only slightly fewer upper

gastrointestinal symptoms (such as dyspepsia) than patients treated with conventional NSAIDs.<sup>2</sup>

The COX-2 inhibitors have a substantial cost premium, but marginal safety advantages in some selected patients. With reference to your recent editorial 'Expensive new drugs – do we really need them?' (Aust Prescr 2004;27:136–7), the data would suggest that the COX-2 inhibitors are another example of expensive new drugs with an unclear cost-benefit value for the Pharmaceutical Benefits Scheme.

Paul Kubler  
Rheumatologist/Clinical pharmacologist  
Royal Brisbane Hospital & Royal Women's Hospital and  
Health Service Districts  
Brisbane

### References

1. Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis: the CLASS study: a randomised controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA 2000;284:1247-55.
2. Langman MJ, Jensen DM, Watson DJ, Harper SE, Zhao PL, Quan H, et al. Adverse upper gastrointestinal effects of rofecoxib compared with NSAIDs. JAMA 1999;282:1929-33.

*Professor R.O. Day and Professor G.G. Graham, authors of the article, comment:*

Dr Kubler is correct in stating that, in the CLASS study, patients treated with celecoxib and aspirin had the same incidence of upper gastrointestinal complications as patients receiving the non-selective non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac or ibuprofen. A similar result was found in the TARGET study of the COX-2 selective drug, lumiracoxib, versus naproxen or ibuprofen.<sup>1</sup> It has, however, been suggested that a selective COX-2 inhibitor and low-dose aspirin should be used with a gastroprotective drug, such as a proton pump inhibitor or misoprostol, in patients at high risk of gastrointestinal damage, although the value of such combinations is presently unknown.<sup>2</sup>

The comparative effects of the COX-2 selective drugs and the non-selective NSAIDs on dyspepsia is a more difficult question because many patients in clinical trials note that they have dyspepsia even when they are taking placebo. Consequently, the occurrence of dyspepsia during treatment with the COX-2 selective inhibitors can only be evaluated from controlled clinical trials when placebo was administered.

It is therefore of note that the incidence of dyspepsia and related effects during treatment with celecoxib was very similar to that recorded during dosage with placebo, but markedly lower than during treatment with naproxen.<sup>3</sup>

### References

1. Schnitzer TJ, Burmester GR, Mysler E, Hochberg MC, Doherty M, Ehsam E, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial. *Lancet* 2004;364:665-74.
2. Chan FK, Graham DY. Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications – review and recommendations based on risk assessment. *Aliment Pharmacol Ther* 2004;19:1051-61.
3. Bensen WG, Zhao SZ, Burke TA, Zabinski RA, Makuch RW, Maurath CJ, et al. Upper gastrointestinal tolerability of celecoxib, a specific COX-2 inhibitor, compared to naproxen and placebo. *J Rheumatol* 2000;27:1876-83.

### Rofecoxib withdrawal

Editor, –The article 'The vascular effects of COX-2 selective inhibitors' (*Aust Prescr* 2004;27:142–5) is now out of date. The COX-2 selective inhibitors including rofecoxib, celecoxib, meloxicam and diclofenac (diclofenac is about as selective as celecoxib) have never been shown to have an overall advantage over less selective anti-inflammatory drugs for any patient group.<sup>1</sup> There has never been a good justification for prescribing any of these drugs outside of a trial. The huge ongoing death toll could have been avoided in 1999–2001 but regulators, companies, patients' groups and educators have all done too little too late and many have pulled in the wrong direction. Our organisation, Healthy Skepticism, is one of the few who did warn against COX-2 selective inhibitors but we did not have the resources to get our message across.<sup>2,3</sup>

The root cause of this disaster is a vicious cycle of misleading drug promotion and inappropriate prescribing. We call for a Royal Commission to investigate major reforms that could avoid similar disasters in the future and dramatically improve medical research and health care.<sup>4</sup> The first step forward is to understand and accept that a major easily avoidable disaster has occurred. We urge *Australian Prescriber* to become part of the solution by publishing an article accurately summarising all the relevant evidence about COX-2 selective inhibitors.

Peter R. Mansfield

General practitioner and Research Fellow  
Department of General Practice  
University of Adelaide

Agnes Vitry

Senior Lecturer  
School of Pharmacy and Medical Sciences  
University of South Australia

### References

1. Mansfield PR, Vitry AI, Wright JM. Withdraw all COX-2-selective drugs. *Med J Aust* 2005;182:197. [http://www.mja.com.au/public/issues/182\\_04\\_210205/matters\\_arising\\_210205\\_fm-1.html](http://www.mja.com.au/public/issues/182_04_210205/matters_arising_210205_fm-1.html) [cited 2005 Mar 14]
2. Mansfield PR. Healthy Scepticism about Pfizer and Searle's promotion of celecoxib in Australia. *Healthy Skepticism International News* March/April 2000 Vol 18 No 3/4. <http://healthyskepticism.org/publications/editions/2000/IN0004.htm> [cited 2005 Mar 14]
3. James MJ, Cleland LG. Applying a research ethics committee approach to a medical practice controversy: the case of the selective COX-2 inhibitor rofecoxib. *J Med Ethics* 2004;30:182-4.
4. Sweet M. Doctors and drug companies are locked in 'vicious circle'. *Br Med J* 2004;329:998.

### Quality use of generic medicines

Editor, –The excellent editorial, 'Quality use of generic medicines' (*Aust Prescr* 2004;27:80–1) states 'confusion could be greatly reduced if generic names of the drugs were required to be **more prominent** [my emphasis] on the label than the 'brand' names'.

Recently, I was called to an elderly lady who had collapsed and was unable to get up from the floor. She was severely hypotensive because she had taken a double dose of enalapril, one that I had prescribed for her and one with a different brand name, prescribed by a locum doctor.

This is such an obvious danger that it needs to be confronted before more severe accidents and deaths occur.

How can the labelling requirement suggested in the *Australian Prescriber* editorial be brought about?

Peter Gould-Hurst  
General practitioner  
Campbelltown, SA

*Dr Leonie Hunt, Director, Drug Safety and Evaluation Branch, Therapeutic Goods Administration, comments:*

The issue of safe labelling of prescription medicines is under review in several areas. The Australian Pharmaceutical Advisory Committee (APAC) has a working party that is reviewing the issue of brand substitution generally. Looking at labelling specifically, the legal requirements for labelling of medicines are contained within both Australian government and state/territory legislation. The Therapeutic Goods Administration (TGA), through its Labelling Orders, regulates matters such as the minimum font size of lettering that may be used and essential information that must be included on labels for prescription medicines. The Labelling Order is currently under review.

The TGA has also been working with stakeholders from the health professions, industry and consumer groups to develop a Best Practice Labelling Guideline for Prescription Medicines.

The draft version of this document recommends equal prominence be given to the active ingredient or generic name and the brand name and makes recommendations on other aspects of label design to try to ensure that all relevant information is clearly presented to health professionals and consumers. This includes advice that both medicine names need to be displayed on at least three sides of the container for standard packaging.

### Signing the script

Editor, – I would like to commend Dr Nisselle and *Australian Prescriber* for the editorial 'Signing the script' (*Aust Prescr* 2004;27:108–9), which raised awareness of the responsibilities that medical practitioners assume when they prescribe on the Pharmaceutical Benefits Scheme (PBS). Unfortunately, the 1973 legislation Dr Nisselle quoted relates to Medicare rather than pharmaceutical benefits.

The relevant legislation is found in regulation 19B of the *National Health (Pharmaceutical Benefits) Regulations 1960*. This states that it is an offence to write a prescription bearing the letters 'PBS' when it is not a PBS prescription.

A prescriber who prescribes a medication under the PBS for a condition which falls outside the PBS indications may be committing a criminal offence under the *National Health Act 1953*. The relevant legislation is found in Paragraph 103(5)(g) of the *National Health Act 1953* and states that a person shall not:

by means of impersonation, a false or misleading statement or a fraudulent device, obtain, or by any of those means aid or abet another person to obtain, a pharmaceutical benefit or a payment in respect of the supply of a pharmaceutical benefit;

A prescriber acting in this manner may also be referred to a Professional Services Review Committee to determine whether or not they have engaged in inappropriate practice.

J. Trabinger  
Manager  
PBS Compliance Branch  
Health Insurance Commission  
Canberra

Editor, – Dr Nisselle reminds us that a judge can imprison us, under current legislation, for making therapeutically effective and cost-effective treatment decisions.<sup>1</sup> There are instances with 'SPs' where deeming that as '... criminal fraud' is both irrational and unacceptable.

Experienced professionals tend not to respond to threatening behaviour, even when it originates from official bodies that accord themselves the status of 'authorities'. Some categories of rules, and laws, can only ever aspire to be guidelines. The proportions that are neither enforced, nor

monitored, attest to that historical reality. The legislation has never been systematically enforced for many SPs during its 30-year existence. Draconian threats of imprisonment and fines are counter-productive and one suspects they have diminished respect for, and co-operation with, those 'authorities'. Few doctors in our town would be available for consultations if the regulations were enforced.

Education may change doctors' behaviour. Unfortunately the situation has evolved where an undue portion of doctors' knowledge about drugs emanates from drug companies. Authorities have lessened their funding and leadership roles; it might be preferable to balance the drug company billions spent on advertising with more non-partisan funding and leadership, rather than the threats in the legislation. Drug representatives take doctors to dinner, not to prison; they have (sadly) achieved greater influence over the profession.

Ken Gillman  
Consultant  
Pioneer Valley Private Hospital  
Mackay, Qld

### Reference

1. Gillman PK. Mirtazapine: not a dual action antidepressant? *Aust N Z J Psychiatry* 2004;38:266-7.

*Dr P. Nisselle, author of the article, comments:*

Though Dr Gillman may see the statutory sanctions as empty 'threats' (as, at least for 'SP' prescribing, they are rarely enforced), they are still law, and law made to place some discipline on the use of taxpayer funds. The PBS is the most rapidly growing component of the Commonwealth's funding of health care. While doctors hate the gate-keeper role that is thrust on them, for example, by restricted benefits, we also hate it when new medications are refused a PBS listing at all.

Those sections of the Act are to remind us of our responsibilities. We are not responsible for the Government's decision as to what drugs are, or are not, available under the PBS. Our responsibility is not to break the law. We give patients advice. If that advice is, that they take a medication which is not available to them as a PBS benefit, then we need to advise them of that fact and tell them of the cost. It is then a matter for them, whether they wish to pay that cost, or ask you to prescribe a cheaper alternative, or possibly be referred to an agency which will provide the medicine at no direct cost. It is not for us to make a social judgment that it is unfair for a particular patient to have to pay a full private fee for a particular medication and then, accordingly, ignore the law. If you feel strongly enough about it, lobby your local member, etc., to have the drug's classification changed. In the interim, don't 'bend' the law.

## The use of Latin

Editor, – Dr Nisselle's remarks on the legal significance of prescription writing are very much to the point (Aust Prescr 2004;27:108–9). I would like to take him up on the statement that 'prn' is an antiquated Latin abbreviation, when in the next column he uses an equally antiquated Latin term, 'mens rea', no less than three times. This term is one of a whole library of Latin terms used by the legal fraternity to befuddle the rest of the population. Why choose 'prn' when there are 'bd', 'tid', 'bid', 'ac', 'pc' and many other Latin abbreviations, some of which get more use than 'prn'. Used properly these abbreviations are very helpful in saving time and space.

In the 1950s there was an arrangement between Yugoslavia and the UK for reciprocal medical treatment of visitors. Inevitably, some British tourists fell sick and returned home with summaries of their treatment. These were written in Latin so I was able to translate the diagnosis and treatment. I would not have been capable of doing this if the summaries had been in one of the local languages.

I might add that I was not a Latin scholar, having as much trouble with 'ut' and the subjunctive as anyone. However, I think medicinal Latin was a very useful attribute and I do regret its loss.

L.A. Lees  
General practitioner  
Dapto, NSW

*Dr P. Nisselle, the author of the article, comments:*

Like Dr Lees, I have both nostalgic and practical reasons for personally wanting to retain Latin abbreviations in medicine. Nostalgic, because it reminds us of the history and traditions of medicine. Practical, because using shorthand saves a lot of time. But is it still safe? Dr Lees talks about being in practice in the 1950s. Many younger doctors and pharmacists have no knowledge of the abbreviations that were in common usage at that time. The lawyers have preserved Latin better than doctors. Phrases like 'mens rea' and 'res ipsa loquitur' are still in common use because they are still taught in law school. Latin remains alive in medicine, for example, in anatomy but even there, plain English is encroaching. *Materia Medica* is no longer taught. I doubt if any medical faculty in Australia still teaches Latin prescribing instructions in their pharmacology course.

In day-to-day office general practice, many general practitioners now use prescription writing software which is fast, efficient, safe and can be programmed to provide plain English, unambiguous instructions for taking each medication prescribed. Safety overcomes my nostalgia. If you know for certain to which pharmacist the patient will take your script, and if you know for certain that the particular pharmacist understands all the abbreviations you use, and

if you know that every doctor who subsequently will use the record you generate of that consultation understands Latin abbreviations, then you might choose to save time and use Latin-based shorthand like 'prn'. For me, there are too many 'ifs' in that statement. Safe prescribing requires clear, unambiguous instructions.

Editor, – I am saddened by the misuse of the Latin abbreviations 'tds' and 'tid' which today are almost universally used for 'three times daily'. In Latin (and in common usage through my career) 'tds' (*ter die sumendus*) translates as 'to be taken three times a day' (*sumendus* = to take). Hence 'tds' should be used for oral medications. 'tid' (*ter in die*) translates as 'three times daily' and should be used for external medications.

Unfortunately, the distinction has been blurred over the years and both abbreviations are now treated as equivalents. If we are to continue to use Latin abbreviations in the directions, we should use the correct terminology. Perhaps this shift in meaning has occurred because Latin is a subject that has been dropped from most schools and, I presume, the curriculum for medical and pharmacy students.

Peter Castellaro  
Pharmacist  
Clayfield, Qld

*John Youngman, Chair, Australian Council for Safety and Quality Working Party, Standard Medication Chart, comments:*

Medication errors are a significant cause of harm to patients. Standardisation of processes and their constituent components has been demonstrated to reduce medication errors. In April 2004 Australian health ministers agreed to support the introduction of the National Inpatient Medication Chart into public health facilities by mid-2006. The Australian Council for Safety and Quality in Health Care formed a working party to develop the chart which will be pilot tested in 30 public and private facilities. This national chart will build on the content and implementation of a standard chart used in Queensland public hospitals.

The National Inpatient Medication Chart is underpinned by a core set of principles and an agreed set of abbreviations, particularly focusing on the prescribing and administration of medicines in hospitals. Medication administration guidelines adopt 'mane' for morning, 'nocte' for night, 'bd' for twice a day, 'tds' for three times a day, 'qid' for four times a day, and for the administration of antibiotics '6 hrly' and '8 hrly'. Such standardisation will enable medical and nursing staff moving across facilities to use the same abbreviations and so reduce the likelihood of a misunderstanding or a mistake in the prescribing, dispensing and administration of medications to patients.

## Tramadol

Editor, – I read with interest the addition of tramadol to the already long list of medications that cause the syndrome of inappropriate antidiuretic hormone secretion (SIADH) (Aust Prescr 2004;27:97). The temporal relationship between serum sodium level and tramadol use appears to have secured the diagnosis.

While not so relevant to the elderly population, SIADH is essentially a diagnosis of exclusion where, in the presence of normovolaemia, other sinister (if not treatable) causes have been excluded.<sup>1</sup> It is important that readers should not get the impression that the diagnosis is based on solitary serum sodium and osmolality measurements. It is critical that, together with other osmotically active analytes, urinary sodium and urinary osmolality are measured in parallel in the overall assessment of hyponatraemia. This will assist in further understanding the pathophysiology which remains, as stated, hypothetical at this stage.

Huy A. Tran

Head, Department of Clinical Chemistry  
Hunter Area Pathology Service  
John Hunter Hospital  
Newcastle, NSW

## Reference

1. Robinson AG, Verbalis JG. Posterior pituitary gland. In: Larsen PR, Kronenberg HM, Melmed S, Polonsky KS, editors. *Williams textbook of endocrinology*. 10th ed. Philadelphia: W.B. Saunders; 2003. p. 281–329.

## Drugs and breastfeeding

Editor, – After reading the book review of 'Drugs and breastfeeding' (Aust Prescr 2004;27:154), I looked up the US product information for metronidazole in the 2000 Physicians' Desk Reference.

The information under Carcinogenicity states that pulmonary tumours were found in all six studies done in mice including one with dosing only every fourth week; there were also malignant tumours in the liver and malignant lymphomas. In rats, there were liver and mammary tumours. And finally, the drug is genotoxic – it damages the DNA directly.

Under the heading Nursing Mothers, it says, 'because of the potential for tumorigenicity shown for metronidazole in mouse and rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug'. It further states that, 'metronidazole is secreted in human milk in concentrations similar to those found in plasma'.

Based on this information, I take issue with the reviewer who says that, based on this book, she is reassured that metronidazole 'will do the baby no harm'. On the contrary, there is tremendous potential for harm and the US product

information actually says not to nurse when using metronidazole. So much for the usefulness of this book!

Elizabeth Barbehenn

Research analyst

Public Citizen's Health Research Group

Washington DC, USA

*Molika In, Pharmacy Department, The Royal Women's Hospital, Melbourne, comments:*

Prescribing for breastfeeding women is a potentially complex decision. Clinicians are often faced with a dilemma when reading product information, as these documents tend to recommend ceasing breastfeeding whenever medications are required. Weaning a baby may, however, not be practical and immediate treatment may be required. Various resources are available and should be used by clinicians in order to make informed decisions and weigh up the risks and benefits with breastfeeding women requiring treatment.

The product information for metronidazole clearly states a potential mutagenicity and carcinogenicity association in animals but not in humans. Several studies showed this association with short treatment courses of metronidazole as not statistically significant.<sup>1</sup> Also, the cytogenic effects occur only when there is a metabolic reduction of metronidazole, as in hypoxic tumour cells. Metronidazole has been used therapeutically for more than 40 years and its use in breastfeeding has been reviewed over two decades.<sup>2</sup>

Metronidazole is excreted in the breast milk, but very few cases of adverse effects have been reported and even then the correlation is questionable. Recent reports show no obvious adverse effects associated with mothers taking metronidazole while breastfeeding. Even more reassuring is the fact that the dose of metronidazole received by a breastfeeding infant is far lower than the dose used for treating neonates, infants or children.

Current literature and The Royal Women's Hospital Drugs and breastfeeding guide suggest the benefits of continuing breastfeeding outweigh the theoretical potential cancer risk posed by metronidazole.<sup>3,4</sup>

## References

1. Bendesky A, Menendez D, Ostrosky-Wegman P. Is metronidazole carcinogenic? *Mutat Res* 2002;511:133-44.
2. Drinkwater P. Metronidazole. *Aust N Z J Obstet Gynaecol* 1987;27:228-30.
3. Passmore CM, McElnay JC, Rainey EA, D'Arcy PF. Metronidazole excretion in human milk and its effect on the suckling neonate. *Br J Clin Pharmacol* 1988;26:45-51.
4. Bar-Oz B, Bulkowstein M, Benyamini L, Greenberg R, Soriano I, Zimmerman D, et al. Use of antibiotic and analgesic drugs during lactation. *Drug Saf* 2003;26:925-35.

A fuller list of references can be found with this article on the *Australian Prescriber* website [www.australianprescriber.com](http://www.australianprescriber.com)