

That said, Medicines Australia is currently considering the establishment of a Clinical Trials Register, similar to those established in the USA, whereby healthcare professionals, and members of the general public, can be made aware of the existence of clinical trials in certain disease states. While the availability of the results of those trials, both positive and negative, is also a consideration, Medicines Australia concurs with Professor Eadie's statement that this could undermine the publication, by the principle investigator, of these results in scientific journals and the like. This is a matter that needs to be discussed with the scientific community.

On the broader issue of transparency of the Pharmaceutical Benefits Advisory Committee (PBAC), Medicines Australia

concur with comments of Dr John Hewson, who is also President of the Arthritis Foundation of Australia, who recently said in the Australian Financial Review, 'Our Pharmaceutical Benefits Advisory Committee process needs to be much more transparent as to why a drug is or is not recommended for listing.'

The decisions of the PBAC affect the quality of life of millions of Australians. Therefore it is clearly in the best interest of doctors, patients and the general public to ensure absolute transparency for the operations of the PBAC. This should include all aspects of its operations and include peer review.

And consistent with other government administrative actions, the decisions of the PBAC should be subject to appeal and review by the Administrative Appeals Tribunal.

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.

Warfarin and antiplatelet drugs

Editor, – We read with interest the article 'Warfarin, antiplatelet drugs and their interactions' (Aust Prescr 2002;25:81–5) and were disappointed that although the authors emphasise the risks of combining warfarin with aspirin, they fail to acknowledge the proven benefits of this combination in patients with prosthetic heart valves. A recent meta-analysis¹ showed that compared with anticoagulation alone, the addition of an antiplatelet drug reduced the risk of not only thromboembolic events (odds ratio 0.41, $p < 0.001$) but also total mortality (odds ratio 0.49, $p < 0.001$).

The old view that the combination is dangerous is still held by many doctors and pharmacists. We certainly agree with the authors' recommendation that with the combination, low-dose aspirin should be used and the INR 'kept at the lower end of the desired target', and that patients on the combination should be carefully monitored for possible bleeding complications, including gastrointestinal blood loss. However, the evidence that adding low-dose aspirin to warfarin reduces total mortality by 50% in these patients should not be ignored and needs wide dissemination.

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REFERENCE

1. Massel D, Little SH. Risks and benefits of adding anti-platelet therapy to warfarin among patients with prosthetic heart valves: a meta-analysis. *J Am Coll Cardiol* 2001;37:569-78.

Managing constipation in children

Editor, – It was pleasing to see the article 'Managing constipation in children' (Aust Prescr 2002;25:85–7) as it is such a common problem. It was particularly pleasing to see the prominence given to the emotional aspects.

However, the article needs several comments. The first is the strong recommendation for oral bowel cleansing solutions and rectal medications. Oral cleansing solutions have significant risks in the presence of faecal impaction. Rectal medications frequently interfere with emotional management.

The article deals with stimulant aperients in the same paragraph as stool softeners. The two have very different indications. Stimulants such as senna and phenolphthalein often cause significant pain or incontinence due to increased muscle activity. Furthermore, their long-term use damages the intramural ganglion cells of the colon.

Stool softening agents are usually all that is needed for children with constipation unless there is an underlying organic cause. The vast majority of children who have no abnormality of the colon (albeit with a secondary fissure) require nothing more than stool softening. Dietary means alone are rarely enough in the first instance, but are important in long-term management. Paraffin oil, either plain or as an emulsion, is the only agent that will soften inspissated faeces. It is not absorbed so is safe to give in large doses and for prolonged periods. It takes 5–10 days to soften old hard faeces, but it will eventually do so and thereby avoid any anal

manipulations or general anaesthetic to perform manual evacuation. It has a reputation for interfering with absorption of fat-soluble vitamins, but I am unable to find a reliable reference for this.

Apart from a small number of children with an organic cause or very resistant constipation, the majority of constipated children have a totally normal colon, so once sensation and motility are restored by getting rid of accumulated faeces, they will defecate quite satisfactorily if the stool is soft.

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Malaria prevention

Editor, – The article 'Malaria prevention in the expatriate and long-term traveller' (Aust Prescr 2002;25:66–9) was good but deficient in a few areas. I am a pharmacist living in a malaria endemic area of Nigeria. By virtue of this I am aware of other ways of managing malaria as we are faced with this terrible disease for a lifetime.

In the section on the malaria standby treatment regimens, attention was not drawn to the use of dihydroartemisinin – a novel drug developed from the malaria herb Qinghaosu in China. This drug happens to be the most effective and safest antimalarial compared to the others listed in the article. It has a very fast onset of action and adverse effects that are not debilitating.

I would emphasise the life cycle of the plasmodium parasite, as the dormant hypnozoites and gametocyte forms in the liver and blood respectively contribute significantly in reinfection and transmission of the diseases. The need for a radical cure when the expatriate or traveller returns home means there is a possible role for a drug like primaquine.

In conclusion, these aspects would definitely add the cherry on the cake and make the article well balanced.

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Dr Daniel O'Brien and Dr Beverley-Ann Biggs, authors of the article, comment:

We acknowledge the comments of Bangboye Raymond regarding our article 'Malaria prevention in the expatriate and long-term traveller'. Indeed dihydroartemisinin is used widely throughout malarial endemic countries as a safe and effective treatment for malaria. However, our paper was written for Australian health practitioners, and as this medication is not currently registered for use in Australia, it was not included.

We also agree that treatment of malaria due to *Plasmodium vivax* and *Plasmodium ovale* requires consideration of

eradication of the liver hypnozoites to reduce the chance of recurrent infection in those who have left the endemic area, and are unlikely to be re-exposed in the near future. However our article deals with emergency standby treatment for those developing malaria in endemic areas. Here there is little value in treatment with drugs such as primaquine due to the likelihood of reinfection.

Sensitivity and specificity – is your test reliable?

Editor, – The recent article on sensitivity and specificity (Aust Prescr 2002;25:107) is of concern in that it implies that sensitivity and specificity are invariant when applied to a particular disease state. This is not so. We give examples below.

Following occlusion of a coronary artery during myocardial infarction, cardiac troponin will be released. However, troponin is a protein and will not get into the circulation until some hours after the coronary occlusion has occurred. Thus samples collected early, say at two hours post-event, will have a poor diagnostic sensitivity for identifying myocardial infarction, while samples collected later, say at 12 hours post-infarction, will have a very high diagnostic sensitivity. These two clinical settings with very different sensitivities are not covered by the usual statement that 'cardiac troponin has a sensitivity for myocardial infarction approaching 100%'.

Consider the use of ferritin measurement to establish or exclude a diagnosis of iron-deficiency anaemia. A low ferritin concentration is considered to support the diagnosis of iron-deficiency anaemia. If samples are collected only in the general practice setting there will be very few 'false normal' results. If however, samples are collected in the acute hospital setting, where there is a relatively higher prevalence of liver disease with release of tissue ferritin, then there will be proportionately more people falsely identified as having 'normal' iron homeostasis. The apparent diagnostic sensitivity in these two populations, if compared to the best test available – bone marrow biopsy and quantitation of stored iron – would be quite different, because of the characteristics of the two populations.

Both of the examples above demonstrate that diagnostic sensitivity can vary for a particular disease state, and are one of the reasons why tests appear to perform differently in the reports in the literature. It is important to define very precisely the population that is being studied, when diagnostic sensitivity and specificity is being discussed.

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