

after 6–12 weeks and at each follow-up visit. If muscle symptoms occur the CK should be measured. This advice was published before the finding that muscle damage can occur with a normal CK concentration, so the recommendations regarding statin withdrawal may be too conservative.

Controlled trials have shown that statins improve overall mortality and the incidence of all forms of cardiovascular disease in patients at increased risk of these diseases. Muscle damage must be placed in the context of the recognised benefits of statin therapy. Clinicians should be aware of the need for vigilance in the monitoring of symptoms. Patients should be advised to report any symptoms at the earliest stage in order to prevent the rare, but more serious, muscle complications of statin therapy.

In many cases (perhaps the majority), muscle symptoms will prove to be unrelated to statin therapy. In others, elevated CK concentrations may be the result of exercise or minor muscle damage from trauma. Statin withdrawal and rechallenge may also be subject to a pronounced placebo effect. There is also the potential to further reduce compliance if patients were to believe that any muscle ache or pain they experience may be

related to statin therapy. These considerations suggest that the management of statin muscle damage will not be straightforward until there is a specific diagnostic test available.

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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.

Preparing tranexamic acid 4.8% mouthwash

Editor, – The beneficial haemostatic effect of tranexamic acid 4.8% mouthwash has been demonstrated in oral anticoagulant treated patients undergoing minor oral surgery.^{1,2} However there is no proprietary product readily available to dental practitioners in private practice (*Aust Prescr* 2002;25:105–6). A practical solution to this problem is the use of Cyclokapron tablets dispersed in water. A crude mouthwash can be prepared by placing a tranexamic acid 500 mg tablet into 10–15 mL of water in a metric measure. The tablet will disperse in approximately 3–5 minutes on standing and quicker with intermittent swirling. Tranexamic acid is readily soluble in water³, however inactive tablet excipients will still be present after adequate mixing. The resulting slurry has little or no taste. Patients should be instructed to swirl the total preparation including the undissolved residue around the mouth for two minutes and then to expel. This is repeated four times a day for up to seven days.^{1,2} Although this method has not been formally validated, sufficient tranexamic acid should be present in the saliva to reduce fibrinolysis.⁴

Unfortunately the Pharmaceutical Benefits Scheme does not subsidise tranexamic acid 500 mg tablets when prescribed by a dental practitioner. However, they are available as a private dental prescription at a cost of around \$31 for a broken pack quantity of 20 tablets. For dental practitioners with no access or assistance from a public teaching hospital

this approach partly addresses the issue of having ready access to the mouthwash, although it will not be suitable for all patients.

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Asthma delivery devices

Editor, – Thank you for the review of asthma therapy delivery devices (*Aust Prescr* 2003;26:5–7). This article covered important common sense issues in asthma treatment delivery. As suggested by the author, practical issues of use and patient acceptability dominate the decision between a number of otherwise acceptable drug delivery methods. An additional practical issue, in the experience of many Top End practitioners, is that dry powder devices often do not

stay dry enough to function in tropical humid conditions, particularly if the users are not very careful to keep the cap screwed on tightly. For this reason dry powder inhalers are not recommended in the Central Australian Rural Practitioners Association Standard Treatment Manual¹ for use in the tropical Top End.

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Editor

Standard Treatment Manual for Health Workers, 4th edition.

REFERENCE

1. Central Australian Rural Practitioners Association. Standard treatment manual for health workers. 4th ed. Alice Springs: CARPA; 2003.

Tisseel Duo 500

Editor, – I wish to draw your attention to some inaccuracy in the new drug comment about Tisseel Duo 500 (Aust Prescr 2003;26:46).

The article commenced by correctly referring to Tisseel Duo 500 with regard to available sizes and approved indications. It then refers to the composition of the 'kit', referring to vials of thrombin, calcium chloride, fibrinolysis inhibitor etc. This description refers to the lyophilised kit form of Tisseel which required reconstitution. The kit was previously available in Australia under the Special Access Scheme of the Therapeutic Goods Administration, until the registered Tisseel Duo 500 became available. This kit was only viable for four hours following reconstitution. It is no longer available in Australia.

Tisseel Duo 500 is deep frozen fibrin sealant, in a preloaded double syringe delivered with the same Duploject device. It does not require reconstitution, only thawing and warming to 37°C. Once thawed, Tisseel Duo 500 is viable for 48 hours. The thawing process requires very little time once removed from the freezer, significantly less than an autologous cryoprecipitate preparation process.

With regards to viral safety, I can state that the previous formulation of the product has been used for 25 years in 50 countries around the world in over 8 million applications resulting in no reported transmissions of HIV, Hepatitis B or C and prion disease. This is due to the donor screening program, the double steam heat treated processing and PCR testing of the product during the manufacturing process.

There are numerous published articles about fibrin sealants available from our Medical Affairs department.

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Routine change of intravenous catheters

Editor, – In the article 'Controlling intravascular catheter infections' (Aust Prescr 2003;26:41–3), Table 2 states 'Routinely replace peripheral catheters within 48–72 hours...'.¹

The Centers for Disease Control in the USA found no evidence to support the routine changing of peripheral venous catheters. The 'Guidelines for the prevention of intravascular catheter-related infections' recommend: 'In adults replace catheter and rotate site no more frequently than every 72–96 hours. Replace catheters inserted under emergency basis and insert a new catheter at a different site within 48 hours. In pediatric patients, do not replace peripheral catheters unless clinically indicated.'¹

Hospital bureaucracies frequently mandate routine changing of peripheral catheters within 72 hours, at the cost of great discomfort to patients and effort by resident medical officers. Given that routine changing of central lines has been shown to be unnecessary, and the daily infection risk quoted for peripheral cannulae is much lower than for central lines, it is also implausible that any benefit from routine changing of peripheral lines has been missed.

It would seem beneficial for *Australian Prescriber* to acquaint its readers with the evidence and discourage them from continuing what seems to be an unnecessary as well as painful custom.

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REFERENCE

1. MMWR 2002 Aug 16;51:711. Appendix B.

Dr Peter Collignon and Dr Robert Horvath, the authors of the article, comment:

The guidelines of the Centers for Disease Control (CDC) do recommend changes of peripheral lines after 72–96 hours rather than our suggested 48–72 hours. Our concern is that the CDC based the guidelines on the incidence of 'phlebitis', not bacteraemia. As phlebitis is thought to be usually due to non-infective causes (e.g. irritation from drugs), we do not believe it is an appropriate surrogate marker for bacteraemia.

If one examines bacteraemia caused by catheters, it becomes clear that there are almost no cases with catheters that are in place for 24 hours or less and sepsis is very uncommon if the catheters are in place for less than 48 hours.^{1,2,3} The CDC guidelines still recommend routine replacement at 48 hours for 'emergency cannulas'. This is a vague definition and appears to take in our concerns.

In our experience children do not have peripheral cannulas for prolonged periods. Although there is no reason to believe that intravenous catheter sepsis will be different in children, we are unaware of any authority currently recommending routine replacement of peripheral catheters in children.

The problem with doing studies on peripheral catheter sepsis is the very low incidence of bacteraemia (about one episode for every 3000 catheters).⁴ A prospective randomised study would have to be extremely large and is therefore unlikely to be done. However, we believe that the evidence on bacteraemia (rather than phlebitis) strongly suggests that routine replacement of catheters at 48–72 hours will result in lower sepsis rates than replacement at later times.

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Correcting rheumatoid arthritis

Editor, – I wish to point out an error in ‘Disease modifying drugs in adult rheumatoid arthritis’ (*Aust Prescr* 2003;26:36–40). On page 38 the article says sulfasalazine contains acetylsalicylic acid and sulfapyridine. This should be 5-aminosalicylic acid and sulfapyridine.

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Your questions to the PBAC

Folinic acid, the PBAC and the TGA – approval confusion

Editor, – In December 2001 the Pharmaceutical Benefits Advisory Committee (PBAC) approved the listing of oxaliplatin as a pharmaceutical benefit. Oxaliplatin was listed as an authority item for use in metastatic colorectal cancer after failure of fluorouracil-based therapy in patients with a WHO performance status of two or less, to be used in combination with 5-fluorouracil and folinic acid.

Folinic acid is available in Australia in both oral and injectable forms. The indications approved by the Therapeutic Goods Administration (TGA) include megaloblastic anaemia due to folic acid deficiency and reducing the toxicity of folic acid antagonists.

The role of folinic acid in combination with 5-fluorouracil in colorectal disease is well documented. Its use in combination with oxaliplatin and 5-fluorouracil is also well documented. The folinic acid potentiates the antitumour activity of 5-fluorouracil by acting as a coenzyme.¹ However, the use of folinic acid for this indication has not been approved by the TGA.

How can oxaliplatin be approved by the PBAC for combination therapy with folinic acid in metastatic colorectal cancer when the folinic acid does not have an approved indication in this disease? On a separate note, why has the PBAC approved folinic acid in this combination, but not made it available as a pharmaceutical benefit?

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REFERENCE

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PBAC response:

The PBAC thanks Mr Siderov for drawing this apparent anomaly to its attention. Drugs cannot be listed as pharmaceutical benefits unless the Therapeutic Goods Administration (TGA) has approved the indication. Oxaliplatin has TGA approval for use in the treatment of advanced colorectal cancer, in combination with 5-fluorouracil and folinic acid, and the Pharmaceutical Benefits Scheme (PBS) restriction is consistent with this indication.

Under the Therapeutic Goods Act, the TGA cannot compel a manufacturer to apply for a registered indication, nor can the TGA apply a registered indication to a drug if not requested by the manufacturer. In this case the registration of an indication for combination therapy would need to be sought by the manufacturers of folinic acid, rather than the manufacturers of oxaliplatin. Although use of folinic acid can only be promoted by its sponsor for its approved indications, a medical practitioner is not prevented under the Therapeutic Goods Act from using a product for an unapproved indication.

The PBAC noted that the injectable form of calcium folinate (3 mg/mL) was deleted from the PBS on 1 May 2002 at the request of the sponsor. The Department of Health and Ageing is seeking alternative sources of supply of the injection.