The first patient described by Dr Philpot had ‘mild diabetes-related renal dysfunction and/or chronic low-grade hepatitis B’. If the patient had one relative contraindication (moderate renal impairment, GFR 30–60 mL/minute) our guidelines would recommend that low doses of metformin are appropriate (500–1000 mg/day). The situation should be reviewed regularly and metformin should be stopped if the patient were to develop an absolute contraindication. In the second case it appears that the patient might have moderate renal impairment (GFR 30–60 mL/minute) but no functional liver impairment. A metformin dose of 500–1000 mg/day would seem appropriate and might reduce the necessary insulin dose and improve glycaemic control.

**Letters**

**Insulins in 2002**

Editor, – Regarding insulin and metformin schedules – indeed one size does not fit all. Dr Pat Phillips’ excellent update ‘Insulins in 2002’ (Aust Prescr 2002;25:29–31) nicely highlights inter-individual insulin requirements (e.g. a predicted daily range of 39 to 78 units of insulin for a 78 kg man).

When metformin is factored into the equation, the considerations become even more complex, as when for example a patient has mild diabetes-related renal dysfunction and/or chronic low-grade hepatitis B, both of which are relative contraindications to the use of metformin.

I am also currently looking after a man in his 70s who is mildly overweight, with borderline urea and creatinine, chronic hepatitis B with a slightly raised GGT but normal ALT concentration. His insulin requirements exceed 100 units per day, but metformin is being withheld out of concern for potential adverse effects.

In view of the potential value of metformin with insulin, would Dr Phillips care to comment further on the nuances of this interesting combination of drugs?

Ross Philpot
Consultant Physician
Adelaide

Dr P. Phillips, the author of the article, comments:

Dr Philpot correctly points out the advantages of continuing metformin when starting insulin in patients with type 2 diabetes. Metformin has actions independent of insulin secretion (by reducing gluconeogenesis and insulin resistance) and it has benefits in controlling weight.

However, metformin can cause potentially life-threatening lactic acidosis in patients at risk of metformin accumulation (renal impairment), hypoxic challenges (respiratory or cardiac failure) or reduced lactate clearance (impaired liver function).

The first patient described by Dr Philpot had ‘mild diabetes-related renal dysfunction and/or chronic low-grade hepatitis B’. If the patient had one relative contraindication (moderate renal impairment, GFR 30–60 mL/minute) our guidelines would recommend that low doses of metformin are appropriate (500–1000 mg/day). The situation should be reviewed regularly and metformin should be stopped if the patient were to develop an absolute contraindication. In the second case it appears that the patient might have moderate renal impairment (GFR 30–60 mL/minute) but no functional liver impairment. A metformin dose of 500–1000 mg/day would seem appropriate and might reduce the necessary insulin dose and improve glycaemic control.

**The evidence-relevance gap**

Editor, – I was most impressed by the article ‘The evidence-relevance gap—the example of hormone replacement therapy’ (Aust Prescr 2002;25:60–2) in which Dr Neeskens gives a sensible and pragmatic approach to dealing with complex information thereby allowing the patient to put it in context for her situation. Too often we are confronted with population studies, but what do they mean to the individual person?

There are two other situations, one involving vast expense and the other some serious morbidity, which require similar scrutiny. The first involves the escalating use of ‘statins’ in the community at a cost which may result in limiting the ability of the Pharmaceutical Benefits Scheme to afford new drugs. Should we really be trying to reduce the cholesterol level to some magic number in every adult Australian, even those who are asymptomatic and without a relevant family history? And if so, for how long do we continue this therapy?

**Conflict of interest: none declared**
I frequently see patients in the 80–90 year-old age group presenting for surgery still religiously taking their prescribed statin. Is this necessary?

Secondly, the prescribing of warfarin with its dangerously low therapeutic index to prevent some perceived morbidity too often results in genuine catastrophes in the form of gastrointestinal or intracranial haemorrhage. Again, elderly patients present as emergencies requiring scarce blood products to reverse the coagulation defect before surgery can be performed. For how long do we keep prescribing this toxic drug? Presumably once patients have these major morbidities they are not started on warfarin again, so could it not be ceased before the disaster actually occurs?

Brian Duffy
Staff Specialist Anaesthetist
Queen Elizabeth Hospital
Woodville, SA

Editor, – Dr Neeskens is to be congratulated for his article ‘The evidence-relevance gap – the example of hormone replacement therapy’ (Aust Prescr 2002;25:60–2). I hope it will be a forerunner of articles testing the proposition that years of taking pharmaceuticals by basically well (i.e. symptomless people) is a good thing.

I know of no medicine that works which can be taken with impunity by everyone. We are all that little bit different.

The majority of trials are undertaken on people who have a problem (I include Framingham: it is surely not healthy to be under constant medical supervision). They are irrelevant to the majority.
B.W. Griffiths
Surgeon
Crescent Head, NSW

Editor’s note:
Dr Neeskens is currently preparing another article for Australian Prescriber.

Dental patients receiving warfarin therapy

Editor, – We refer to ‘Dental notes: Managing dental patients receiving warfarin therapy’ (Aust Prescr 2002;25:69). This commentary is unfortunate because it presents the historical approach to managing patients on warfarin therapy and does not reflect current best practice.

The key issue is the risk:benefit analysis of ceasing warfarin and risking thromboembolism, versus reducing it and risking local wound bleeding. Any logical analysis clearly comes down on the side that if warfarin is indicated and has been appropriately prescribed, then one should leave it alone. The real and potential risks such as stroke or myocardial infarction are clearly catastrophic events, whereas at worst local wound bleeding is messy and inconvenient.

There is an extensive body of research which shows that the appropriate management of patients on warfarin who require dentoalveolar surgery is as follows:

• **preoperative** – check INR the day before the procedure to ensure it is within the therapeutic range for the patient. If greater than 4.0, advise the patient’s physician and delay surgery until the INR is within the therapeutic range.

• **intraoperative** – the use of a local anaesthetic combined with a vasoconstrictor, plus a controlled, minimally traumatic surgical technique and local haemostatic methods are recommended. This includes irrigating the operative field with a 4.8% tranexamic acid solution. The sockets and mucoperiosteal flaps should then be sutured and oxidised cellulose gauze placed in the sockets.

• **postoperative** – the patients should be given a 4.8% tranexamic acid mouthwash with instructions to rinse with 10 mL of the solution for two minutes four times a day for 2–5 days.

There are some issues of supply, although most major hospitals on appropriate request from the patient’s pharmacy, are happy to supply tranexamic acid. The pharmacy of the Royal Adelaide Hospital is certainly willing and able to provide appropriate advice on this.

It is appropriate for the patient’s dentist and the treating general medical practitioner to review the patient’s anticoagulation therapy. In our studies, we found over one-third of patients on warfarin either no longer met the clinical indications for this therapy, or had an inappropriate dosage and thus either a sub-therapeutic INR or an INR above 4.

Alastair N. Goss
Professor
and
Glen Carter
Registrar
Oral & Maxillofacial Surgery Unit
The University of Adelaide

**FURTHER READING**


**Professor Woods and Professor Savage, authors of ‘Managing dental patients receiving warfarin therapy’, comment:**

We thank Professor Goss and Dr Carter for drawing attention to the management of minor oral surgery performed for patients taking warfarin. Certainly the procedure we recommend is based on the ‘historical’ approach, it is well tested, safe and effective. In this respect our recommendations are consistent with recommendations of Professor Goss and Dr Carter. Essentially, dental management of patients having warfarin therapy is a matter of co-operation between dentists and the physician managing the patient’s coagulation.
Notwithstanding this comment, the use of tranexamic acid as a mouthwash is a promising development. The technique has been tested with a number of favourable reports in the literature. The present position however, for most dentists treating patients taking warfarin, is that they have no ready access to a tranexamic acid mouthwash, there is no proprietary tranexamic mouthwash available.

For the present, the majority of dentists treating patients having warfarin therapy have no ready access to or assistance from a teaching hospital and will in practical terms, have to rely on the ‘historic’ advice in the Dental Notes.

**The heavy drinker in primary care**

**Editor,** – I refer to the article ‘The management of the heavy drinker in primary care’ (Aust Prescr 2002;25:70–3). This article is excellent in its succinct coverage of alcohol problems in general practice. However, I do feel that there is an underemphasis on the risk of acute thiamine deficiency even in the general practice population.

In our unit we have recently admitted two male patients with signs of Wernicke’s encephalopathy. These patients were both in their mid-forties and had no previous history of detoxification for alcohol dependence. Both patients had been transferred from other hospitals where they had been treated for alcohol withdrawal. The first patient had been a postoperative inpatient for five days before his transfer and had been treated for an acute confusional state with symptomatic medications. He improved within an hour of his first intramuscular injection of thiamine.

The second patient presented to a local hospital after having been hit by a car while intoxicated. Once he was medically stable he was transferred to our Drug and Alcohol Unit and was found to have a combination of confusion, ataxia, nystagmus as well as other cerebellar signs. He was so unwell he was transferred back to the local hospital but he recalls ‘waking up’ in the ambulance after a single 100 mg injection of thiamine.

The point is that this is an extremely serious but easily treatable condition. I would suggest that in Box 2 of Professor Whelan’s article the use of thiamine be reiterated and if there is any doubt whatsoever about oral absorption or nutritional status that intramuscular thiamine be given daily for at least three days.

Kevin McNamara
Director
Drug and Alcohol Unit
Palm Beach/Currumbin Hospital
Gold Coast, Qld

*Professor Greg Whelan, the author of the article, comments:* Dr McNamara rightly brings to our attention the importance of thiamine given prophylactically in the management of alcohol withdrawal.

The patients described by him are also seen in our hospital’s Accident and Emergency service. All patients admitted with a history of heavy alcohol consumption, whether in alcohol withdrawal or not, are given an intravenous ‘cocktail’ of glucose and multivitamins, including thiamine.

The article in *Australian Prescriber* is aimed at producing guidance for general practitioners who manage patients in primary care, not in hospital. As noted, these patients are given thiamine 100 mg. Our practice is to give this orally unless we are concerned about absorption.

**Medicinal mishaps**

**Editor,** – The case reported in ‘Medicinal mishaps’ (Aust Prescr 2002;25:73) highlights the importance of obtaining an accurate medication history as part of the hospital admission process. Frequently this is ‘easier said than done’. Obtaining an accurate medication history is often complex, time consuming and a fallible process. Reasons for this include:

- lack of patient knowledge of their medications
- lists from local doctors and patients that are out of date
- medication labels that are out of date or non specific (‘mdu’)
- transcription errors on residential care facility transfer letters
- neglecting to ask the patient what they are actually doing with their medications.

All patients should be encouraged to bring their medications to every hospital and clinic visit. Patients should be assisted by their pharmacist, local doctor or family member to maintain a current list if they are unable to remember their treatment themselves.

Glenn Valoppi
Pharmacy Resident
and
Simone Taylor
Senior Clinical Pharmacist
Emergency Medicine
Austin and Repatriation Medical Centre
Heidelberg, Vic.

**Discontinuation of naproxen suspension**

**Editor,** – Roche Products recently announced plans to discontinue production of naproxen suspension in Australia.¹ Their letter communicating these plans implies that rofecoxib suspension is a viable alternative. This is irresponsible, for several reasons, and demonstrates a clear lack of consideration of the best interests of children.

First, naproxen suspension is currently the most widely used non-steroidal anti-inflammatory drug (NSAID) in children with chronic arthropathies worldwide.² It has a well-established efficacy and safety profile in children. The liquid formulation also has a convenient dosage schedule (twice daily) and is affordable. The only other NSAID with demonstrated efficacy and safety in children currently available in liquid formulation in Australia is ibuprofen. However, its lower effectiveness, need for more frequent dosing and greater cost are disadvantages in chronic therapy. The discontinuation of naproxen suspension will therefore mean that children will be unfairly disadvantaged by having their already limited NSAID options even further restricted.

Second, children’s risk of significant gastropathy with NSAID therapy is negligible.³ There is therefore little rationale for considering a COX-2 inhibitor in the vast majority of children. Evaluable data regarding their safety/efficacy in children is

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¹ Editor, – I refer to the article ‘The management of the heavy drinker in primary care’ (Aust Prescr 2002;25:70–3). This article is excellent in its succinct coverage of alcohol problems in general practice. However, I do feel that there is an underemphasis on the risk of acute thiamine deficiency even in the general practice population.

² The heavy drinker in primary care

³ Discontinuation of naproxen suspension
Sensitivity and specificity – is your test reliable?

The reliability of a test depends on the sensitivity and specificity. You should ask ‘How am I using this test and how sensitive and specific is the test?’

The sensitivity of a test is defined as the proportion of people with disease who have a positive test. A test which is very sensitive will rarely miss people with the disease. It is important to choose a sensitive test if there are serious consequences for missing the disease. Treatable malignancies (in situ cancers or Hodgkin’s disease) should be found early – thus sensitive tests should be used in the diagnostic work-up.

The specificity of a test is defined as the proportion of people without the disease who have a negative test result. A specific test will have few false positive results – it will rarely misclassify people without the disease as being diseased. If a test is not specific, it may be necessary to order additional tests to confirm a diagnosis.

It is useful for clinicians to know the sensitivity and specificity of common tests to help in deciding which tests to use to ‘rule in’ or ‘rule out’ disease. However, predictive values are of more direct clinical usefulness, enabling the clinician to estimate the probability of disease given the test result. One problem is that predictive values are prevalence dependent, but the prevalence (likelihood) of disease can be increased by clinical signs, other tests and even clinical ‘intuition’.

Finally, clinical signs and judgement should never be ignored in the face of a technological test result. For example, if a suspicious breast lump remains palpable, a negative mammogram should be ignored. In such circumstances, clinical judgement should suggest biopsy, even though the test result was negative. Tests are to be used to assist clinicians, not to rule clinical decision-making.

REFERENCES