Letters

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. Letters are usually published together with their responses or comments in the same issue. The Editorial Executive Committee screens out discourteous, inaccurate or libellous statements and sub-edits letters before publication. The Committee's decision on publication is final.

H1N1 immunisation

Editor, – Having just read the interesting editorial 'H1N1 immunisation: too much too soon?' (Aust Prescr 2010;33:30–1) by Peter Collignon, it would be evident that considerable waste took place in the delivery of the vaccine to the patient. Not only in the use of multidose vials, but in the waste of the unused vials which now have to be discarded with the introduction of the new 2010 trivalent influenza vaccine. I wonder if details of the wastage and relevant costs are available.

I understand that CSL developed the swine flu vaccine and delivered the vials to the Commonwealth Health Department. Was CSL paid by the Government for the vaccines or did CSL bear the loss?

As Deputy Chair of the Return Unwanted Medicines Project, I would also be interested to know how the unused vaccine vials are to be destroyed – I hope it is in an environmentally responsible manner!

Ken Bickle
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Professor Peter Collignon, author of the editorial, comments:

I agree with Ken Bickle that considerable waste was associated with the H1N1 immunisation program. Full details are not readily available because of 'commercial in confidence' agreements. From media reports it appears that CSL received about $120 million from our Federal Government for 21 million vaccine doses.[1] An added potential cost to the Government is the indemnity CSL received for any serious adverse events resulting from the vaccine.

Only a quarter of these doses were distributed[1] and the vaccine was presented in multidose vials. Multidose vials result in much higher vaccine wastage compared to single-use preloaded syringes.[2] I suspect that 30% of the distributed vaccine doses were never administered. Additionally, most of the vaccine given was to those over 65 years.[3] This age group already had high levels of pre-existing immunity to H1N1 (swine flu) and thus vaccination was not likely to have been much benefit for them.

The World Health Organization has documented the major infection problems associated with unsafe injection practices.[4] This results in millions of viral and bacterial infections every year, especially in developing countries.[5] Multidose vials and immunisation practices may only be a small component of this problem, but this risk can be virtually eliminated with the use of preloaded single-use syringes for vaccination (which we use for seasonal flu vaccinations here). Using single-use preloaded syringes also results in considerably less wastage of vaccine.[2] This reduced wastage will usually more than compensate for their small additional cost (about 14 cents).[2]

Multidose vials may sometimes have a place for the delivery of inexpensive vaccines in countries with low resources and poor infrastructure.[2] They have no place in a country such as Australia.

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Editor, – I was disappointed to read the editorial on H1N1 vaccination (Aust Prescr 2010;33:30–1), especially when the National Prescribing Service states that the publication is evidence-based and peer reviewed.

In particular, the article states: 'In the past, many infections, such as *Staphylococcus aureus*, hepatitis B and HIV, have been caused by vaccination programs using multidose vials.[2]' From my limited research, I am not aware of **any** past documented infections associated with general practice vaccination programs in Australia (as we are predominately using for H1N1 vaccination), nor any documentation of hepatitis B or HIV infections from any vaccination programs. Reference two in the editorial does not back up his claim – it in fact refers to the author's own article which has no comment on transmission of disease from multidose vials.

In addition, I question the balance of the author when discussing influenza vaccination. He quoted only one

study that 'showed that the decrease in all-cause mortality attributable to seasonal influenza vaccine was 4.6%', without noting the limitations of this study, nor referring to the wide body of international evidence supporting influenza vaccination, including those referenced in the 9th edition of the Australian Immunisation Handbook.

Although it is fair to comment that we would benefit from more effective influenza vaccines, and that policy makers must carefully review pandemic planning, including the role of multidose vials, I do not believe that the debate is assisted by claims that are not correctly referenced, nor highlighting of single studies. I would also question whether this editorial is consistent with the National Prescribing Service's claim to 'provide accurate, balanced, evidence-based information'.

Greg Rowles
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Riddells Creek, Vic.

Professor Peter Collignon, author of the editorial, comments:

I agree with Dr Rowles that we need more effective influenza vaccines and a review of pandemic planning. I accept that it is best to reference primary sources rather than reviews. Unfortunately word and reference limitations in invited editorials make that difficult to do at times.

On the issue of efficacy, most studies on influenza vaccines have major biases.[1] Generally vaccination rates are lower in people who are most at risk of death and thus the benefits from influenza vaccination are likely overstated.[1,2] Morbidity and mortality are often lower in vaccinees, even before the start of the flu season, compared to controls. One of the few studies that have tried to untangle these biases was the one I quoted. This very large Californian study found a benefit for vaccination, but it was 10-fold less than previously attributed for influenza vaccination.[2]

Infection control guidelines recommend as best practice that single-dose vials are used wherever possible. There is extensive documentation on the transmission of many different viral and bacterial infections when multidose vials are used. This includes vaccination programs using multidose vials.[3–7]

In Australia we had the Bundaberg disaster in 1928. Diphtheria vaccine contaminated with *Staphylococcus aureus* from multidose vials caused the deaths of 12 children and resulted in a Royal Commission.[4] In Geelong in the late 1960s, two factory workers died from *Streptococcus pyogenes* following workplace flu vaccinations from multidose vials. The coroner subsequently recommended against the use of multidose vials.[5,6] More extensive references on this international problem have been discussed previously.[7]

Multidose vials are involved in the transmission of infectious organisms. I believe they should not be used in mass vaccination campaigns in Australia.

References

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Radiographic contrast media and metformin

Editor, – I write regarding the article dealing with radiographic contrast media (Aust Prescr 2010;33:19–22).

I have recently authored a systematic review relating to the safety of iodinated contrast in patients receiving metformin.[1] The review found no evidence to substantiate beliefs about the need to cease metformin in individuals with stable, normal renal function who were to have a 'normal' amount of intravenous iodinated contrast for an examination such as a CT scan. Despite a number of international guidelines having disparate recommendations about cessation of metformin, the Royal Australian and New Zealand College of Radiologists (RANZCR), the Royal College of Radiologists (RCR) and the European Society of Urogenital Radiology guidelines recommend that there is no need to stop metformin in these patients. The RANZCR recommendations are based on the extremely low risk of precipitation of contrast-induced nephropathy in this group. The Australian and RCR guidelines were modified along these lines in March and June 2009, respectively, soon after the systematic review was presented at the Radiological Society of North America meeting in December 2008.

Other work by Jeffrey Newhouse supports our findings that the risk of contrast-induced nephropathy has been exaggerated by research focusing on patients who have large volume, intra-arterial administration of iodinated media and by the lack of a genuine control group in many of the studies that have linked iodinated media to high rates of post-procedural contrast-induced nephropathy.

The advice by the radiologist to cease metformin, when this is not necessary, can have many unintended consequences such as the patient forgetting to recommence metformin. In addition, patients may visit their general practitioner for advice about when it is safe to recommence metformin, incurring costs to the health system.

The advice given in the *Australian Prescriber* article is entirely appropriate for patients who:

- are having large contrast volume, intra-arterial procedures (such as coronary angiography or interventional procedures) or
- are known to have abnormal or acutely deteriorating renal function.

However, this important distinction is not made clear in the article and general practitioners may interpret this advice to apply to their own practice context, which is largely CT scanning or other lower dose procedures associated with intravenous contrast media.

Stacy Goergen
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Reference

1. Goergen SK, Rumbold G, Compton G, Harris C. Systematic review of current guidelines, and their evidence base, on risk of lactic acidosis after administration of contrast medium for patients receiving metformin. Radiology 2010;254:261-9.

Professor Ken Thompson and Dr Dinesh Varma, authors of the article, comment:

When writing this article we were well aware of the RANZCR guidelines and the issues of how to handle a patient with type 2 diabetes taking metformin who requires a contrast CT.

The RANZCR guidelines agree that it is difficult to measure estimated glomerular filtration rate (e-GFR) in all patients in an outpatient setting, although this is our practice.

While it is true that there is little or no high level evidence to recommend stopping metformin in patients with normal, stable renal function receiving a moderate dose of contrast media, the general practitioner who requests the contrast examination has no control over the actual amount of contrast media the patient is given. This may vary for a wide variety of reasons. An extremely low risk is not the same as no risk.

We were also influenced by the drug manufacturer's information and decided to provide advice that is consistent with the packaging information. In our view, the risk that a patient who takes a drug every day will forget to recommence the drug is unlikely.

Iodine allergy

Editor, – We would like to thank Professor Katelaris and Dr Smith for their timely article on the misleading label of iodine allergy (Aust Prescr 2009;32:125–8). This, as the authors indicate, is a marked source of anxiety for patients who need contrast media scanning.

We have also noted similar anxieties in patients who are potential candidates for the use of radioactive iodine (I-131) for the treatment of hyperthyroidism and thyroid cancer.

For patients who have a history of seafood or contrast sensitivity we arrange intravenous access as a precaution. However, in over 3000 administrations of oral high-dose radioactive iodine for thyroid cancer, we have not encountered any significant allergic phenomena.

We therefore feel that patients with seafood or contrast allergy can be reassured that this will not occur with low- or high-dose radioactive iodine.

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Robin Mortimer AO
Senior Endocrinologist, Royal Brisbane and Women's Hospital, and Senior Director, Office of Health and Medical Research

Queensland Health

Aliskiren and angioedema

Editor, – Aliskiren is a novel antihypertensive drug that is an orally-active direct renin inhibitor (Aust Prescr 2009;32:132–5). Its action shares a common biological pathway with angiotensin-converting enzyme (ACE) inhibitors. However, it has been suggested in an article by Professor Duggan that some respiratory and vascular adverse events were less likely than with the older drugs (Aust Prescr 2009;32:135–8). The proposal was fairly reasonable based on the different molecular target of the two drug groups. However, postmarketing experience revealed cases of aliskiren-associated angioedema and drug regulators implemented labelling changes and safety advice.[1–3] Therefore, physicians should be vigilant for the first signs of angioedema in aliskiren users. The biological basis, exact frequency and risk factors of this potentially life-treating event are currently not well understood. Until evidence becomes available, aliskiren and probably other similar drugs should not be used in patients with previous episodes of ACE inhibitor-induced angioedema of any clinical presentation.

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References

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2. Tekturna (aliskiren) tablets. Safety labeling changes approved by FDA Center for Drug Evaluation and Research (CDER) – November 2009.
3. Aliskiren. New contraindication and warning. WHO Pharmaceuticals Newsletter 2009;2:1.

Associate Professor K Duggan, author of the article, comments:

The true incidence of adverse effects often only becomes apparent after the drug has been marketed and my article was prepared before marketing. *De novo* angioedema as an adverse effect of the angiotensin receptor antagonists only became apparent postmarketing and the same appears to be occurring with aliskiren. Contraindications to the use of aliskiren should now include angioedema occurring as a consequence of the use of other renin-angiotensin drugs. This scenario highlights the importance of practitioners notifying regulatory bodies of adverse effects not previously reported.

Prescription drug subsidies in Australia and New Zealand

Editor, – The recent editorial on 'Prescription drug subsidies in Australia and New Zealand' (Aust Prescr 2010;33:2–4) reveals striking differences between the two countries in expenditure on prescription drugs. This is attributed in part to the New Zealand policy of exclusive contracts for supply of off-patent medications being awarded through competitive tender. The cost savings are obvious enough, but an additional benefit of this system is to make the generic brand instantly recognisable both for prescribers and consumers. The proliferation of generic brands in Australia, by contrast, leads to a great deal of confusion for patients. This often dissuades doctors from prescribing generic brands, at great cost to the health system.

Lachlan Brown
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Editor, – The editorial by Steve Morgan and Katherine Boothe (Aust Prescr 2010;33:2–4) makes a number of concerning statements. The authors consider that Australia and New Zealand appear to be 'converging in their use of certain [pharmaceutical procurement] policy tools'.

The authors do not identify the major factor responsible for the success of the Pharmaceutical Management Agency of New Zealand (PHARMAC) in reducing prices paid for pharmaceuticals. PHARMAC is exempt from the entire portion of the New Zealand Commerce Act 1986 that deals with restrictive trade practices. The result is that PHARMAC is in a dominant position as a monopsony and is able to embark on negotiating tactics not allowed under World Trade Organization rules or national legislation in most other first world countries.

The authors have made comparisons of growth in costs between PHARMAC and OECD (Organisation for Economic Co-operation and Development) data. The conclusions drawn are unreliable as the reporting methods used to collect these data are not comparable over time (as stated by the OECD).[1]

Where the authors report 'conspicuously little evidence' of health outcomes related to pharmaceutical access being different between the countries, they indicate no attempt to identify differences in health outcomes. It would be imprudent to assume that the lack of epidemiological evidence to support worse health outcomes in New Zealand linked to pharmaceutical access vindicates the reduced access to medicines.

For these reasons, it is unlikely that Australia could or would choose to align itself more closely with the New Zealand methods of pharmaceuticals procurement.

Kevin Sheehy
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Editor, – Regarding your editorial on 'Prescription drug subsidies in Australia and New Zealand' (Aust Prescr 2010;33:2–4), there is a point which is not discussed which greatly reduces costs in New Zealand – that of bulk dispensing. New Zealand allows people with common chronic diseases to have three or six months supply of medicines dispensed at one time, as opposed to the monthly dispensing usual in Australia. This means that a New Zealander with say, high blood pressure, will pay two dispensing fees per year, whereas an Australian will likely pay 12 dispensing fees.

I understand the rationale behind monthly dispensing, but really, does a person who will be taking a drug for the rest of their lives need monthly intervention by a pharmacist, and does this happen in any but a small minority of cases? I have monthly prescriptions for blood pressure medication, and invariably I hand the repeat to an assistant, who hands it to a pharmacist, who types out a label saying 'Take one in the morning', passes it back to the assistant, who puts it in a bag and says to me '$33.30 please'.

Jonathan Rout
A concerned consumer
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