

## LETTERS

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## Depressed youth, suicidality and antidepressants

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**TO THE EDITOR:** Two recent items in the Journal might potentially lead to misinterpretation of the evidence on managing depression in young people.

The first was the book review entitled *Darker side of "wonder drugs"* by Jureidini<sup>1</sup> in which there was no disclosure that the author of the review is president of Healthy Skepticism, a body which has been quite strident in its opposition to antidepressant therapy. The second was the unattributed comment in the editorial by Rey and Dudley describing "parents who believe their children killed themselves because they were taking SSRIs [selective serotonin reuptake inhibitors]...",<sup>2</sup> which may imply subtly that this has occurred frequently.

In a review of the United Kingdom General Practice Research Database of more than three million people,<sup>3</sup> there were no suicides among the 6976 aged 10–19 years who had been prescribed one of two SSRIs or two tricyclic antidepressants; however, 15 people in that age group who had not received an antidepressant drug died by suicide. Furthermore, in a review of 14857 suicides in Sweden, of the 52 involving people under 15 years, no SSRIs were detected, and in the 15–19-years age group, those taking SSRIs had a lower relative risk of committing suicide than those taking other antidepressants.<sup>4</sup>

Clinicians with responsibility for children and adolescents can be reassured by these data, and also by the fact that the American Food and Drug Administration "black box" warning (their most potent warning) about antidepressants has recently been modified.<sup>5</sup> Furthermore, the American Academy of Child and Adolescent Psychiatry and the American Psychiatric Association have provided a new resource about the use of medication in treating childhood and adolescent depression,<sup>6</sup> which has been endorsed by over a dozen United States organisations comprising a "national coalition of concerned parents, providers, and professional associations". This should allay questions that have rightly been raised, but that have been answered in favour of the judicious use of antidepressants, along with other therapeutic measures for children and adolescents with severe depression.

In view of the strong association between child and adolescent mood disorders and suicide,<sup>7</sup> the above research findings and the recommendations of respected professional bodies raise the issue of potential legal action for not at least trialling antidepressant medication in young people with severe depression if non-pharmacological measures are ineffective.

**Competing interests:** I have received honoraria and research grants from a number of pharmaceutical companies for presentations and research on depression.

- 1 Jureidini JN. *Darker side of "wonder drugs"* [book review]. *Med J Aust* 2005; 182: 293.
- 2 Rey JM, Dudley JM. Depressed youth, suicidality and antidepressants. *Med J Aust* 2005; 182: 378–379.
- 3 Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *JAMA* 2004; 292: 338–343.
- 4 Isacson G, Holmgren P, Ahlner J. Selective serotonin reuptake inhibitor antidepressants and the risk of suicide: a controlled forensic database study of 14857 suicides. *Acta Psychiatr Scand* 2005; 111: 286–290.
- 5 Hanson E. AACAP/APA Press conference introduces new guides for educating parents, consumers about antidepressants. *Am Acad Child Adolesc Psychiatry News* 2005; 36: 60–61.
- 6 American Psychiatric Association and American Academy of Child and Adolescent Psychiatry. The use of medication in treating childhood and adolescent depression: information for patients and families. Available at: <http://www.parentsmedguide.org> (accessed May 2005).
- 7 Shaffer D, Gould MS, Fisher P, et al. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry* 1996; 53: 339–348.

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**TO THE EDITOR:** Rey and Dudley cite clinical experience as the basis of their recommendation of selective serotonin reuptake inhibitors (SSRIs) — chiefly fluoxetine — for youth with severe depression plus severe impairment or failure of non-drug therapy.<sup>1</sup> They do not discuss the evidence on efficacy because they claim that it is "ambiguous enough for scholars to be divided". It is true that industry-funded scholars are continuing to suggest that SSRIs (chiefly fluoxetine) provide a worthwhile benefit.<sup>2</sup> However, the evidence is unambiguous. The four published comparisons of fluoxetine versus placebo for children and adolescents have all been negative on their pre-specified primary endpoints.<sup>3,4</sup> A tiny average benefit is likely, but the magnitude of this benefit is unlikely to exceed the

magnitude of less frequent but more severe harms. Furthermore, the common clinical impression of worthwhile benefit is to be expected given the large average improvements seen in placebo groups.

Rey and Dudley speculate that psychosocial treatments may be less effective with uncooperative teenagers.<sup>1</sup> However, that group may also be at higher risk of the dangers of intermittent use of, and overdosing with, antidepressant drugs.

Rey and Dudley cite Timimi's critique of the concept of childhood depression<sup>5</sup> as supporting "treating depression primarily as a moral or social problem". However, Timimi did not even allude to depression as a moral problem, and advocated a multi-perspective approach that normalises emotional responses to adverse life experiences and includes interventions addressing biological factors, such as diet, exercise, and cognitive abilities. Rey and Dudley use a related straw-man argument in their final sentence when they suggest that the only alternatives to SSRIs are tricyclic antidepressants, victim blaming, and non-treatment.

Rey and Dudley deny being influenced by the gifts and funding that they have received from drug companies. There is compelling evidence that gifts and funding are effective, on average, for influencing beliefs, especially among people who have an illusion of invulnerability.<sup>6</sup> We are not aware of any way that any individual can know that he or she has not been influenced.

**Competing interests:** We are all office bearers in Healthy Skepticism, an international non-profit organisation whose main aim is to improve health by reducing harm from misleading drug promotion.

- 1 Rey JM, Dudley MJ. Depressed youth, suicidality and antidepressants. *Med J Aust* 2005; 182: 378–379.
- 2 March JS, for the TADS Group. Authors of TADS study reply to letter raising concerns. *BMJ* 2005; 330: 730–731.
- 3 Jureidini JN, Doecke CJ, Mansfield PR, et al. Efficacy and safety of antidepressants for children and adolescents. *BMJ* 2004; 328: 879–883.
- 4 Jureidini J, Tonkin A, Mansfield PR. TADS study raises concerns. *BMJ* 2004; 329: 1343–1344.
- 5 Timimi S. Rethinking childhood depression. *BMJ* 2004; 329: 1394–1396.
- 6 Katz D, Mansfield P, Goodman R, et al. Psychological aspects of gifts from drug companies. *JAMA* 2003; 290: 2404–2405.

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**IN REPLY:** The data available are inconclusive, but suggest that treatment with selective serotonin reuptake inhibitors (SSRIs) may increase the short-term (less than 14 weeks) risk of suicidal thoughts or self-harm in children and adolescents slightly, by about 2%. However, SSRI treatment may actually decrease the number of completed suicides,<sup>1</sup> as Goldney also highlights. To show whether SSRIs influence the risk of completed suicide, a rare event, requires a randomised trial including up to two million individuals.<sup>2</sup> This will not happen. Hence, clinicians must rely on accumulated data from experimental, epidemiological, and observational studies. Disagreements about interpretation will doubtless continue.

In response to Mansfield and colleagues, we personally know of media reports influencing some practitioners to revert to using tricyclic antidepressants, and child psychiatrists to avoid treating depressed adolescents. We do not shrink from our interpretation of the implications of Timimi's reconceptualisation of "depression" as "unhappiness". Regardless of how childhood depression is classified or named, we remain concerned that the impetus for clinicians to diagnose and treat it not be lost. Its social correlates include stigma and racism, which often involve seeing mental health problems as moral failures of character.

Our view is that fluoxetine shows a favourable harm-benefit profile in moderate to severe depression. According to the Treatment for Adolescents with Depression study,<sup>3</sup> which was not funded by drug companies, four children need to be treated with fluoxetine for one to show much or very much improvement attributable to medication. This compares with having to treat 21 children for one to display a widely defined harm-related event. The numbers improve further when fluoxetine is combined with cognitive behavioural therapy (3 and 50, respectively). Pending new studies, clinicians would be unwise to ignore these data when treating serious depression in young people, a recurring illness that produces much suffering, physical and psychosocial disability, and suicide (odds ratio estimates ranging from 11.0 to 27.0).<sup>4</sup> Our opinions are consistent with those of the recently released joint clinical guidance by the col-

leges of psychiatrists, general practitioners, and physicians.<sup>5</sup>

Mansfield and colleagues suggest that our editorial's content might have been influenced by drug company gifts. We provided the educated readers of the Journal with information to judge this for themselves.

**Competing interests:** Joseph Rey was a member of the advisory committee for Strattera (Eli Lilly) and Concerta (Janssen-Cilag) and was funded by Eli Lilly to attend an international conference. Michael Dudley attends Pfizer-sponsored peer review dinners, and has (before the recent debates about drug company gifts) received bags, pens, and a CD.

- 1 Isacson G, Holmgren P, Ahlner J. Selective serotonin reuptake inhibitor antidepressants and the risk of suicide: a controlled forensic database study of 14 857 suicides. *Acta Psychiatr Scand* 2005; 111: 286-290.
- 2 Gunnell D, Saperia J, Ashby D. Selective serotonin reuptake inhibitors (SSRIs) and suicide in adults: meta-analysis of drug company data from placebo controlled, randomised controlled trials submitted to the MHRA's safety review. *BMJ* 2005; 330: 385-388.
- 3 Treatment for Adolescents with Depression Study (TADS) Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression. *JAMA* 2004; 292: 807-820.
- 4 Beautrais A. Risk factors for suicide and attempted suicide among young people. *Aust N Z J Psychiatry* 2000; 34: 420-436.
- 5 Royal Australian and New Zealand College of Psychiatrists, Royal Australian College of General Practitioners and Royal Australasian College of Physicians. Clinical guidance on the use of antidepressant medications in children and adolescents. Available at: <http://www.ranzcp.org/publicarea/pracguid.asp> (accessed Jun 2005). □

#### Duncan Topliss

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**COMMENT:** Three essentially independent reviews of the use of selective serotonin reuptake inhibitor (SSRI) antidepressants in children and adolescents have been undertaken in Australia in the past 9 months.<sup>1-3</sup> The review by the Adverse Drug Reactions Advisory Committee<sup>1</sup> had input from representatives of the Royal Australian and New Zealand College of Psychiatrists and the Division of Paediatric and Child Health, Royal Australasian College of Physicians (RACP).

All three reviews noted the paucity of information to support the efficacy of these and other antidepressants in children and adolescents, and the frequent observation of increased suicidal thoughts and self-harm in clinical trials.

The colleges' review<sup>2</sup> and the National Prescribing Service Rational Assessment of

Drugs And Research (RADAR) review<sup>3</sup> support the ADRAC advice that:

Any use of SSRIs in children and adolescents with MDD [major depressive disorder] and other psychiatric conditions should be undertaken only within the context of comprehensive management of the patient. Management should include careful monitoring for the emergence of suicidal ideation and behaviour which may particularly develop early in therapy, or if therapy is interrupted or irregular because of poor compliance. Cognitive behaviour therapy, if it is available, may enhance the outcome in MDD.

An SSRI should be chosen for a child or adolescent with MDD or other psychiatric condition only after taking into account the recent evaluations of clinical trial data and the Australian product information. Prescribers should be aware that the marketers of fluvoxamine and sertraline (indicated for obsessive compulsive disorder) advise against their use in children and adolescents with MDD, and the marketers of citalopram, escitalopram, paroxetine, venlafaxine and fluoxetine warn or caution against their use in patients aged less than 18 years for any indication.

It is important to note that children and adolescents who are being treated for MDD with an SSRI should not have their medication ceased abruptly.

- 1 Adverse Drug Reactions Advisory Committee. Use of SSRI antidepressants in children and adolescents. *Aust Adverse Drug Reactions Bull* 2004; 23: 22. Available at: <http://www.tga.gov.au/adr.aadrb/aadr0412.pdf> (accessed Jul 2005).
- 2 Royal Australian and New Zealand College of Psychiatrists, Royal Australian College of General Practitioners and Royal Australasian College of Physicians. Clinical guidance on the use of antidepressant medications in children and adolescents. Available at: <http://www.ranzcp.org/publicarea/pracguid.asp> (accessed Jul 2005).
- 3 National Prescribing Service RADAR. Selective serotonin re-uptake inhibitors in child and adolescent depression. April 2005. Available at: <http://www.npsradar.org.au/npsradar/content/SSRIs.pdf> (accessed Jul 2005). □

## The crisis in mental health: the chariot needs one horseman

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**TO THE EDITOR:** The recent editorial by Andrews<sup>1</sup> quotes a report suggesting that the integration projects funded by the Australian Government produced substantial benefits to patient care at no extra cost. Working in an area in which one of these projects was funded, I suggest that such an inference is unwarranted, particularly as many patients report increased difficulty in accessing public mental health services.

The Illawarra, being geographically circumscribed and with a relatively small medical population, has always had a high degree of interaction between services, although it is true to say that these have somewhat declined in recent years with larger bureaucracies and increased privacy concerns. In my early days in the area, there was a monthly meeting involving police, Youth and Community Services, the Housing Commission, school counsellors, and hospital and community social and mental health workers to coordinate the management of problem families. Sadly, this no longer occurs.

Unfortunately, the major effect of the integration project was simply to add a management structure to the prior interaction, and not to significantly increase it. It seemed that the core issue was control and not service provision. Useful coordination projects, such as some commonality of core records, never seemed to happen, and with the passing of the project, things have, in fact, been worse, as fundamental community services such as the crisis team and chronic care components have been cut.

I have always been a strong supporter of a more integrated approach to care, but one that does not grow primarily from the workers involved in day-to-day clinical care and that addresses their needs is unlikely to be lasting and successful.

1 Andrews G. The crisis in mental health: the chariot needs one horseman. *Med J Aust* 2005; 182: 372-373. □

## Severe peanut allergy in Australian children

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**TO THE EDITOR:** Publicity such as that on the recently televised "Sunday" show (Channel 9) entitled "When food can be fatal" ([http://sunday.ninemsn.com.au/sunday/cover\\_stories/transcript\\_1770.asp](http://sunday.ninemsn.com.au/sunday/cover_stories/transcript_1770.asp)), which contained statements that "30 in every 1000 [3%] children in Australia are at risk of a severe allergic reaction [anaphylaxis] to a food", and a reference to a "tsunami of children" with serious allergies, provokes understandable concern and anxiety.

Some perspective on this issue is required. To determine the risk, it is essential to study a population-based cohort. Allergies to peanuts or tree-nuts are the most common cause of severe childhood food anaphylaxis and death.<sup>1</sup> What is the risk for Australian children of peanut-induced anaphylaxis that is likely to require adrenaline?

Of a population-based cohort of 456 Tasmanian children aged 7–8 years, none reacted to a peanut skin-prick test.<sup>2</sup> In the Australian Childhood Asthma Prevention Study (CAPS),<sup>3</sup> a high-risk cohort, 4.9% of 3 year olds were prick-test positive to peanut (unpublished data) using a liberal cut-off of  $\geq 2$  mm (for clinical testing the usual cut-off is  $\geq 3$  mm). Perhaps the most helpful information comes from a population-based study of 13 971 preschool children in the United Kingdom who were followed from birth to 6 years of age. Forty-nine (0.35%) children had an allergic reaction to peanut, of whom only two (0.014%) had what was described as anaphylaxis.<sup>4</sup> Thirty-six of the children underwent formal peanut challenge, 23 reacted and three had reactions for which adrenaline was given. Combining these three with the previous two gives a severe reaction rate requiring adrenaline of 0.036%. This suggests that, of the 49 children in the UK study who had an allergic reaction to peanut, only 10% were at risk of a severe

reaction requiring adrenaline. Only a third to a half of children with a positive peanut skin test will react if exposed.<sup>5</sup> Applying these considerations to Australian children indicates that the proportion at risk of a severe peanut reaction is only 0.25% ( $4.9\% \times 1/2 \times 5/49$ ) even in a high-risk cohort such as the CAPS. This would be substantially lower in a population-based cohort. For the cohort of 7–8-year-old Tasmanian children referred to above, the risk would be much less than 0.2%, considering none of 500 children was prick-test positive to peanut allergen. There has been a substantial increase in childhood food allergy in recent decades;<sup>5</sup> however, sensationalist statements and inaccurate figures are unlikely to be helpful in developing appropriate responses. The Australasian Society of Clinical Immunology and Allergy recently published guidelines for the prevention of food anaphylactic reactions,<sup>6</sup> and has other useful information for patients and medical practitioners on its website (<http://www.allergy.org.au/>).

1 Kemp A. EpiPen epidemic: suggestions for rational prescribing in childhood food allergy. *J Paediatr Child Health* 2003; 39: 372-375.

2 Ponsonby AL, Dwyer T, Kemp A, et al. A prospective study of the association between home gas appliance use during infancy and subsequent dust mite sensitization and lung function in childhood. *Clin Exp Allergy* 2001; 31: 1544-1552.

3 Peat JK, Mhrshahi S, Kemp AS, et al. Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. *J Allergy Clin Immunol* 2004; 114: 807-813.

4 Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003; 348: 977-985.

5 Grundy J, Matthews S, Bateman B, et al. Rising prevalence of allergy to peanut in children: data from two sequential cohorts. *J Allergy Clin Immunol* 2002; 110: 784-789.

6 ASCIA Guidelines for prevention of food anaphylactic reactions in schools, preschools and childcare centres. Available at: <http://www.allergy.org.au/pospapers/anaphylaxis.htm> (accessed Jul 2005). □

## Universal varicella vaccination

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**TO THE EDITOR:** Funding of universal varicella zoster vaccine (VZV) at ages 18 months and 10–13 years was recently announced in Australia. Health professionals should be aware of a number of related issues.

Varicella vaccination was recommended in the United States from 1996 for all chil-



dren aged 12–18 months, with catch-up vaccination to age 13 years. US surveillance shows:

- Decreased varicella mortality in all age groups except those aged  $\geq 50$  years (average varicella deaths per year: 145 in 1990–1994 versus 66 in 1999–2001).<sup>1</sup>
- Decreased varicella cases in all age groups, with a non-significant reduction in hospitalisations (average annual hospitalisations in three surveillance regions: 40 before vaccination versus 14 after vaccination).<sup>2</sup>

US data on herpes zoster have not yet been published.

There are concerns that, in the longer term, universal varicella vaccination may increase the incidence of adult varicella and herpes zoster, similar to the effect of pertussis vaccination on adult pertussis. Modelling in the United Kingdom predicted that universal infant vaccination would initially reduce varicella, but would result in increases in herpes zoster 5–10 years later and adult varicella 20–40 years later.<sup>3</sup> In contrast, modelling of adolescent vaccination predicted a small decrease in varicella, but no increase in later adult varicella.<sup>3</sup>

Varicella is generally perceived as a mild illness, while vaccination is largely valued for preventing serious, life-threatening conditions. Anecdotal reports of low levels of private purchase of VZV in Australia suggest it may not be a priority for some families. With 36% of general practitioners concerned about unknown side effects of VZV,<sup>4</sup> and public concern about vaccine adverse events in the face of low disease rates, the level of acceptance of universal varicella vaccination by providers and consumers is uncertain.

Alternatives to universal varicella vaccination were a high-risk strategy (vaccination of children with chronic illness and family members of high-risk individuals) or waiting until US disease patterns were established. These were real options as:

- A high-risk strategy may prevent up to 45% of paediatric hospitalisations.<sup>5</sup>
- Hospitalisation and herpes zoster contribute more to health costs than treatment in the community or acute varicella.<sup>5</sup>
- Natural infection, at the cost of disease, immunises most of the population.

Any increase in adult varicella and herpes zoster caused by varicella vaccination may be alleviated by booster doses, but the added cost, difficulty in reaching the target population, and potential impact on community confidence in vaccination may be

significant problems. The universal varicella vaccination program will test providers' and consumers' acceptance of vaccination against what is perceived as a mild illness.

**Competing interests:** I receive a research training scholarship from the National Health and Medical Research Council, and Wyeth Australia provides some project funding to my institution. These sources of support had no role in the preparation or submission of this letter.

- 1 Nguyen HQ, Jumaan AO, Seward JF. Decline in mortality due to varicella after implementation of varicella vaccination in the United States. *N Engl J Med* 2005; 352: 450–458.
- 2 Seward JF, Watson BM, Peterson CL, et al. Varicella disease after introduction of varicella vaccine in the United States, 1995–2000. *JAMA* 2002; 287: 606–611.
- 3 Brisson M, Edmunds WJ, Gay NJ. Varicella vaccination: impact of vaccine efficacy on the epidemiology of VZV. *J Med Virol* 2003; 70 Suppl 1: S31–S37.
- 4 Milledge JT, Cooper CD, Woolfenden SR. Barriers to immunization: attitudes of general practitioners to varicella, the disease and its vaccine. *J Paediatr Child Health* 2003; 39: 368–371.
- 5 Carapetis JR, Russell DMF, Curtis N. The burden and cost of hospitalised varicella and zoster in Australian children. *Vaccine* 2004; 23: 755–761. □

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**COMMENT:** Recently published data have added considerably to the evidence about the impact of varicella vaccination programs, and address many of the concerns raised by Mackenzie.

First, in the United States where universal varicella vaccination was recommended a decade ago, recent data show that — despite much slower implementation than is expected in Australia — varicella-related disease has declined by up to 90%, and hospitalisation rates and deaths from varicella by more than two-thirds, due to herd immunity.<sup>1,2</sup>

Second, data have now been published on the incidence of herpes zoster in areas of sentinel surveillance in the US, showing no change in age-specific rates to 2002.<sup>3</sup> Along with the success of a recent trial of high-dose varicella vaccine in reducing herpes zoster in older adults,<sup>4</sup> these data add to confidence that any increase in herpes zoster — as predicted in some models — will be detected and effectively combated by vaccinating people aged over 60 years. A substantial allowance for surveillance of both varicella and herpes zoster was included in the 2005 federal budget, to accompany the introduction of universal varicella vaccination in Australia.

Mackenzie is correct that varicella is perceived by some as a mild illness, but it is important for general practitioners to emphasise to patients that this is incorrect.<sup>5</sup> Each year in Australia, varicella causes around seven to eight deaths and more than 1500 hospitalisations,<sup>6</sup> many associated with serious complications, such as invasive bacterial infection, pneumonia, and encephalitis. Although complications are more likely in adults and immunocompromised patients, 42% of hospitalisations are in children aged 0–4 years,<sup>6</sup> most of whom are otherwise healthy.<sup>7</sup>

Patients can also be reassured about the safety of varicella vaccines, as clinical trials now date back 30 years, and more than 40 million doses of vaccine have been distributed in the US.

Mackenzie suggests alternatives to universal childhood varicella vaccination, such as vaccination of “high risk” patients and their families, or of adolescents alone. However, these programs would not prevent morbidity among otherwise healthy young children and older age groups, as they would be insufficient to generate herd immunity. Moreover, age-based vaccination strategies have been shown to be easier to implement than more targeted programs. In the absence of a publicly funded universal program, the private market could sustain modest varicella vaccination rates of around 40%–50% in Australia.<sup>8</sup> This would increase the number of adolescents and adults susceptible to varicella, because of reduced exposure to the virus and lack of vaccination; these groups also experience greater morbidity with infection than children.

A universal program vaccinating young children and adolescents against varicella offers the best current option to reduce morbidity and mortality from this disease in Australia. Ongoing surveillance of varicella and herpes zoster in Australia and elsewhere will reveal whether there is a need for further interventions, such as a second dose of varicella vaccine in children and high-dose varicella vaccine to prevent herpes zoster in older adults.

- 1 Davis MM, Patel MS, Gebremariam A. Decline in varicella-related hospitalizations and expenditures for children and adults after introduction of varicella vaccine in the United States. *Pediatrics* 2004; 114: 786–792.
- 2 Nguyen HQ, Jumaan AO, Seward JF. Decline in mortality due to varicella after implementation of varicella vaccination in the United States. *N Engl J Med* 2005; 352: 450–458.
- 3 Jumaan AO, Yu O, Jackson LA, et al. Incidence of herpes zoster, before and after varicella-vaccination-associated decreases in the incidence of varicella, 1992–2002. *J Infect Dis* 2005; 191: 2002–2007.

- 4 Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005; 352: 2271-2284.
- 5 Taylor JA, Newman RD. Parental attitudes toward varicella vaccination. The Puget Sound Pediatric Research Network. *Arch Pediatr Adolesc Med* 2000; 154: 302-306.
- 6 Brotherton J, McIntyre P, Puech M, et al. Vaccine preventable diseases and vaccination coverage in Australia 2001 to 2002. *Commun Dis Intell* 2004; 28 Suppl 2: vii-S116.
- 7 Carapetis JR, Russell DM, Curtis N. The burden and cost of hospitalised varicella and zoster in Australian children. *Vaccine* 2004; 23: 755-761.
- 8 Marshall H, Ryan P, Robertson D. Uptake of varicella vaccine — a cross sectional survey of parental attitudes to nationally recommended but unfunded varicella immunisation. *Vaccine* 2005. In press. □

## Potential pitfalls in the diagnosis of phaeochromocytoma

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**TO THE EDITOR:** The excellent report by Harding et al in the *Diagnostic Dilemmas* article in the Journal highlighted medications and conditions that may cause false positive results of biochemical tests for phaeochromocytoma.<sup>1</sup> Another group of patients, those with obstructive sleep

apnoea (OSA), may have raised urine noradrenaline levels in the absence of a phaeochromocytoma.

Of about 170 patients seen at a hypertension screening service at the Mater Adult Hospital between 1998 and 2000, six had elevated levels of urine noradrenaline and normetadrenaline up to twice the upper limit of the normal range on repeated testing. Five were obese and were proven to have significant OSA. All required at least three antihypertensive drugs for reasonable control of their blood pressure, and had normal suppression of catecholamines with clonidine.

A recent report described a series of five patients with OSA presenting as pseudo-phaeochromocytoma who had consistently elevated levels of noradrenaline on measurement of 24-hour urinary catecholamine levels; normetadrenaline levels were not measured.<sup>2</sup> Noradrenaline levels became normal in all five patients after treatment with continuous positive airway pressure, and blood pressure levels improved significantly. Excess urinary noradrenaline, rather than being adrenal in origin, was thought most likely to be due to increased neuronal release of noradrenaline from small arteries and arterioles as a result of sympathetic nerve activity and synaptic overflow.

In conclusion, OSA is an important reversible cause of elevated urine noradrena-

line and normetadrenaline levels in patients with resistant hypertension.

**Competing interests:** I have received speaker's fees from Eli Lilly.

- 1 Harding JL, Yeh MW, Robinson BG, et al. Potential pitfalls in the diagnosis of phaeochromocytoma. *Med J Aust* 2005; 182: 637-639.
- 2 Hoy LJ, Emery M, Wedzicha JA, et al. Obstructive sleep apnea presenting as pseudopheochromocytoma: a case report. *J Clin Endocrinol Metab* 2004; 89: 2033-2038. □

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**IN REPLY:** We thank Morton for his letter which highlights another group of patients in whom raised urinary noradrenaline levels exist in the absence of a phaeochromocytoma. His experience and our group of patients<sup>1</sup> should serve as a note of caution when making the diagnosis of phaeochromocytoma. A combination of positive results of biochemical tests, along with results of anatomical and functional imaging, should serve to minimise false positive diagnoses.

- 1 Harding JL, Yeh MW, Robinson BG, et al. Potential pitfalls in the diagnosis of phaeochromocytoma. *Med J Aust* 2005; 182: 637-639. □

## Postgraduate medical education: rethinking and integrating a complex landscape

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**TO THE EDITOR:** A great deal has been said and written in recent years about inadequate numbers in the medical workforce. As a result, many scientific and political articles about the need to increase the number of medical students and how to train them for the workforce have been written.<sup>1,2</sup>

Yet there has been little discussion of how those already trained and in the workforce should be retained, or of the rate of attrition of those in the workforce.

After 30 years as an anaesthetist, I can recall only one positive change in my conditions of work — the introduction of exhaust gas scavenging. All other changes have been negative: longer hours, greater stress (from multiple factors, such as increased complexity, day surgery and admission on day of surgery) and higher public expectations.

My motives in suggesting the need for such research are purely selfish — having recently retired, and enjoying the lack of stress, I wish to be sure there is an adequate workforce in my old age.

1 Dowton SB, Stokes M-L, Rawstron EJ, et al. Postgraduate medical education: rethinking and integrating a complex landscape. *Med J Aust* 2005; 182: 177-180.

2 Kluger MT, Townend K, Laidlaw T. Job satisfaction, stress and burnout in Australian specialist anaesthetists. *Anaesthesia* 2003; 58: 339-345. □