LETTERS

Japanese encephalitis acquired near Port Moresby: implications for residents and travellers to Papua New Guinea

Joshua P Hanson,* Carmel T Taylor,† Ann R Richards,‡ Ina L Smith,§ Craig S Boutlis¶

*Registrar, ¶ Physician, Cairns Base Hospital, PO Box 902, Cairns, QLD 4870; † Scientist, § Research and Development Coordinator, Public Health Virology, Queensland Health Scientific Services; ‡ Public Health Nurse, Tropical Public Health Unit, Cairns, QLD.
joshua_hanson@health.qld.gov.au

To the Editor: The Japanese encephalitis flavivirus is the most common cause of encephalitis in Asia. Death occurs in 25% of clinical cases, and permanent neurological deficits occur in up to 50% of survivors.[1] Infection is transmitted from amplifying hosts (primarily waterbirds and pigs) by *Culex* mosquitoes. Although the virus has been isolated in the Western Province of Papua New Guinea,[2] and clinical cases have been described in the Western Province and suspected in the Milne Bay region,[3] to our knowledge cases have not been reported from around Port Moresby.

In January 2004, a 66-year-old man of European background was evacuated to our hospital with a 7-day history of fever and confusion. On examination, he had generalised upper motor neurone signs and a Glasgow coma score fluctuating between 6 and 10. Computed tomography and magnetic resonance imaging showed multiple non-specific white-matter lesions bilaterally. An electroencephalogram (EEG) demonstrated diffuse slowing in the delta to theta range in both hemispheres, with preserved response to painful stimulation. Lumbar puncture showed clear cerebrospinal fluid (CSF), with a leukocyte count of 65×10^6 cells/L (81% mononuclear) (reference range [RR], $< 5 \times 10^6$ cells/L), normal erythrocyte count, raised protein level of 0.79 g/L (RR, 150–500 mg/L); glucose level of 4.3 mmol/L (RR, 2.8–4.0 mmol/L) and negative bacterial and fungal cultures. The CSF was also negative for cryptococcal antigen and by polymerase chain reaction (PCR) testing for enterovirus and herpes simplex, Japanese encephalitis, Murray Valley encephalitis and Kunjin viruses.

Serological tests were negative for syphilis and human immunodeficiency virus infection. Paired sera from Days 2 and 19 of admission were tested in parallel against a panel of flaviviruses using a haemagglutination inhibition assay.[4] This showed fourfold rises in antibody titre against dengue virus serotypes 1, 3 and 4, and Japanese encephalitis, Murray Valley encephalitis, Kunjin, Alfuy and Kokobera viruses, and twofold rises in titre against dengue virus serotype 2 and Stratford virus. Overall, these results were diagnostic of recent flavivirus infection but were non-specific. IgM antibody responses to the same flaviviruses were measured in sera and CSF using an in-house enzyme-linked immunosorbent assay (ELISA), with strongest reactivity demonstrated to Japanese encephalitis virus (Box).

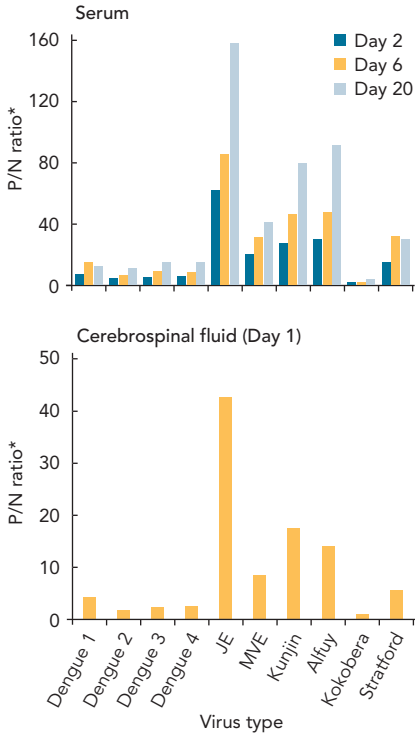
The patient had lived in Papua New Guinea since 1970, predominantly on a church-run farm at Bootless Bay, about 20 km from Port Moresby. He had not travelled outside this region in the month before his illness, and had no history of Japanese encephalitis vaccination or of dengue fever. The farm was situated about 150 metres from a piggery. The patient had no direct contact with this piggery. His accommodation was poorly screened against mosquitoes.

After 3 weeks of primarily supportive intensive care, the patient was discharged to a general ward. His neurological recovery was slow. After 5 months, he was able to walk with assistance and required a tracheostomy to protect his airway. He was judged likely to experience permanent neurological deficits.

The clinical, epidemiological, radiological, EEG and serological features of this case strongly support a diagnosis of Japanese encephalitis. Japanese encephalitis virus is difficult to detect in CSF by isolation or PCR because of neutralising antibodies and the limited duration of viraemia, which may have accounted for the negative PCR result in this case, despite the use of a highly sensitive method.[5]

This case highlights the desirability of further defining the epidemiology of Japanese encephalitis in the Port Moresby region, as well as reconsidering the current recommendation to vaccinate Australians only if they intend travelling to the Western Province of Papua New Guinea.[1]

IgM antibody levels, measured against a panel of flaviviruses by enzyme-linked immunosorbent assay (ELISA)



JE = Japanese encephalitis. MVE = Murray Valley encephalitis.
* IgM levels were measured as the P/N (positive/negative) ratio (ratio of the absorbance of the test sample to the absorbance of a negative control sample tested against the same antigen).

Acknowledgements: We thank Dr Jeffrey Hanna, (Tropical Public Health Unit, Cairns, QLD) for assisting in the preparation and review of this manuscript.

1 National Health and Medical Research Council. The Australian immunisation handbook. 8th ed. Canberra: Commonwealth of Australia, 2003: 175-182.
2 Johansen CA, van den Hurk AF, Ritchie SA, et al. Isolation of Japanese encephalitis virus from mosquitoes (Diptera: Culicidae) collected in the Western Province of Papua New Guinea, 1997-1998. *Am J Trop Med Hyg* 2000; 62: 631-638.
3 Mackenzie JS. Emerging viral diseases: an Australian perspective. *Emerg Infect Dis* 1999; 5: 1-8.
4 Clarke DH, Casals J. Techniques for hemagglutination and hemagglutination-inhibition with arthropod-borne viruses. *Am J Trop Med Hyg* 1958; 7: 561-573.
5 Pyke AT, Smith IL, van den Hurk AF, et al. Detection of Australasian Flavivirus encephalitic viruses using rapid fluorogenic TaqMan RT-PCR assays. *J Virol Methods* 2004; 117: 161-167. ❑

New recommendation on Japanese encephalitis vaccination for travellers to Papua New Guinea

George Rubin,* Jeanette Baird,† on behalf of the Australian Technical Advisory Group on Immunisation (ATAGI)

* Professor of Public Health, University of Sydney, NSW; † Director, Immunisation Section, Targeted Prevention Programs Branch, Department of Health and Ageing, MDP14, GPO Box 9848, Canberra, ACT 2601. jeanette.baird@health.gov.au

To the Editor: The Australian Technical Advisory Group on Immunisation (ATAGI) is responsible for maintaining and updating the *Australian immunisation handbook*, on behalf of the National Health and Medical Research Council (NHMRC).[1] At its 25th meeting, in April 2004, ATAGI discussed data (then unpublished) presented by Hanson and colleagues on evidence for the spread of Japanese encephalitis virus beyond the Western Province of Papua New Guinea to the Port Moresby region.[2] ATAGI believes it is probable the virus has spread to other parts of Papua New Guinea.

The current (8th) edition of *The Australian immunisation handbook* states on page 179: "Current understanding of the ecology of the JE [Japanese encephalitis] virus elsewhere in Papua New Guinea is fragmentary and unsubstantiated. Therefore no definitive recommendations about JE vaccination for travellers to other parts of Papua New Guinea can be made at the current time."

ATAGI agreed that the evidence provided by Hanson and colleagues was compelling, and sufficient to warrant expanding the current recommendation for Japanese encephalitis vaccination. ATAGI is proposing the recommendation be changed to include travellers staying more than one month in all parts of Papua New Guinea, not just those planning to stay in the Western Province.

A public consultation process to change this recommendation is being conducted as part of the requirements of the *NHMRC Act 1992*. A public consultation paper is available from the Immunise Australia Program website (www.immunise.health.gov.au). Submissions close on 17 September and can be directed to Ms Letitia Toms, Assistant Director, Immunisation Section, Department of Health and Ageing, MDP 14, GPO Box 9848, Canberra, ACT 2601 (letitia.toms@health.gov.au).

Acknowledgements: We thank Dr Jeffrey Hanna (Tropical Public Health Unit, Cairns, QLD) and Ms Letitia Toms (Department of Health and Ageing, Canberra, ACT) for their assistance in the preparation and review of this manuscript.

1 National Health and Medical Research Council. The Australian immunisation handbook. 8th edition. Canberra: Commonwealth of Australia, 2003.
2 Hanson JP, Taylor CT, Richards AR, et al. Japanese encephalitis acquired near Port Moresby: implications for vaccinating travellers to Papua New Guinea [letter]. *Med J Aust* 2004; 181: 282. ❑

Smoking cessation and elective surgery: the cleanest cut

Darryl J Hodgkinson

Director, Cosmetic and Restorative Surgery Clinic, Double Bay Day Surgery, 20 Manning Road, Double Bay, Sydney, NSW 2028.
dr_hodgkinson@bigpond.com

To the Editor: I would like to congratulate Peters et al on their strong stance against elective surgery in patients who smoke.[1] The plastic surgery community became aware in the last two decades of the problems of healing in smokers. When patients claimed that they gave up cigarette smoking before surgery, we often found that the serum cotinine levels on testing were elevated, indicating that they had not given up smoking.

Patients who are smokers and who develop a healing complication, in breast reduction, mastopexy, abdominoplasty or a facelift, often attribute the complication to the surgical technique rather than their own habit. Many of these patients have gone on to litigate successfully. Voracious plaintiff lawyers attribute only a small amount of blame to the patient whose smoking has, in fact, contributed significantly to their complication.

In our plastic surgery practice, we have a non-smoking policy, and my malpractice insurer will not cover me for patients on whom I operate and who develop a complication associated with smoking. Hence, all patients who are smokers who wish to have elective surgery are referred to a smoking-cessation program and have to have given up smoking for at least 2 to 4 weeks before surgery. I prefer not to operate on smokers at all, as serum cotinine tests often confirm that their cessation attempt has been incomplete.

In the United States, where patients pay for their own health insurance, their premiums are adjusted for lifestyle. In Virginia, in the 1990s, a "Healthy Virginian policy" existed where premiums were reduced for non-smokers. My suggestion would be that the Medicare levy also be either reduced for individuals who do not smoke or increased for those who do.

1 Peters MJ, Morgan LC, Gluch L. Smoking cessation and elective surgery: the cleanest cut [editorial]. *Med J Aust* 2004; 180: 317-318. ❑

Nicholas A Tonti-Filippini

Medical Ethicist, 15 Alburnum Crescent, Lower Templestowe, VIC 3107.
ntf-dsl@keypoint.com.au

To the Editor: Some time ago, I was approached by a general practitioner who had been trying for more than 12 months to arrange surgery for a patient who was suffering from intermittent claudication. The indications for surgery seemed compelling. The man was in great pain and disabled by the condition. The vascular unit at a major metropolitan hospital refused to operate on him while he remained a smoker. The man had been an alcoholic, but had managed to beat that addiction and had been "dry" for the entire 12 months.

With the patient's permission, and at the request of the GP, I contacted the surgeon. The surgeon explained to me that his refusal to provide elective surgery was on the grounds that the patient smoked, which would increase recovery time and the risk of complications. After discussion of the ethical and legal situation, an early appointment for surgery was arranged with the patient.

Peters and colleagues, authors of a recent editorial on smoking cessation and elective surgery,[1] would do well to attend to the terms of the Commonwealth *Disability Discrimination Act 1992*. It is unlawful for a person who provides services, or makes facilities available, to discriminate against another person on the grounds of the other person's disability.

It seems legitimate to consider the effects of smoking on success rates as part of deciding whether elective surgery is likely to be safe and effective for an individual patient. However, the editorial suggests that patients be denied surgery, such as joint reconstruction, as a resource-allocation decision, even if the surgery would be in their interests.

It is important that smoking is recognised as an addiction. Some groups, such as the mentally ill, are particularly prone to it. A study by the Harvard medical school found that people with mental illness are twice as likely to be smokers, and nearly 45% of all

smokers in the United States are people with a "mental disorder".[2] To the extent that it is an addiction, smoking needs to be considered as a medical condition in much the same way as alcoholism is referred to as a medical condition.

A doctor who did not provide a needed treatment to a smoker on the grounds that the patient was a smoker would be in violation of that person's fundamental human right to healthcare and his or her right not to be discriminated against because of a disability. In fact, the doctor would be in breach not only of the Hippocratic oath, but of the Australian Medical Association's *Code of Ethics 2004*,[3] which states "…refrain from denying treatment to your patient because of a judgement based on discrimination".

1 Peters MJ, Morgan LC, Gluch L. Smoking cessation and elective surgery: the cleanest cut [editorial]. *Med J Aust* 2004; 180: 317-318.

2 Lasser K, Boyd JW, Woolhandler S, et al. Smoking and mental illness: a population-based prevalence study. *JAMA* 2000; 284: 2606-2610.

3 Australian Medical Association Code of Ethics 2004. Available at: www.ama.com.au/web.nsf/doc/WEEN-5WW598 (accessed Aug 2004). ❑

Matthew J Peters,* Lucy C Morgan,† Laurence Gluch‡

*Head, Department of Thoracic Medicine, †Thoracic Physician, ‡ Surgeon, Department of Breast and Endocrine Surgery, Concord Repatriation General Hospital, Hospital Road, Concord, NSW 2137.
matthew.peters@cs.nsw.gov.au

IN REPLY: The rigid way in which Hodgkinson has addressed risk reduction in plastic surgery seems reasonable, as long as there is open disclosure and access to smoking-cessation services is assured.

It is an unfortunate fact that our healthcare system cannot provide everyone with what they want, or need, in a clinically appropriate timeframe. Resources are finite. In his own case example, and without considering the legal or ethical basis of his intervention, once Tonti-Filippini arranged for a patient at high risk of complications to have surgery, someone else was immediately prevented from having hospital care that was necessary for them. If complications developed, extending hospital stay, more than one patient might have been adversely affected.

Let me extend Tonti-Filippini's case a little and imagine that a similar patient with peripheral vascular disease who was moved further down the vascular surgery waiting list as a result of the smoker's surgery being expedited was an ex-smoker who had taken advice and ceased smoking to reduce risks and improve the surgical outcome. Then, in the period of surgical delay, the affected leg became acutely ischaemic and amputation (rather than vascular reconstruction) was required. Are there not ethical implications that follow? Reading more deeply into the Australian Medical Association's Code of Ethics, one finds that we should work to increase standards and the quality of and access to medical services in the community, and make available our special knowledge and skills to assist those responsible for allocating healthcare resources. These are important obligations.

Most smokers are addicted, and this is a medical problem that needs to be consistently identified and addressed; the issue of smokers with mental illness was highlighted in the editorial. If a clinical decision is made not to perform surgery in the context of

continued smoking, it is not made because the person is a smoker, or because they have an addiction, but because the ongoing smoking has major, adverse consequences that we are unwise to ignore. The distinction is subtle but important. ❑

Smoking and pregnancy

Jessica H Ford,* Annette J Dobson†

* Research Assistant, † Professor of Biostatistics, School of Population Health, University of Queensland, Herston Road, Herston, QLD 4006.
A.Dobson@sph.uq.edu.au

To the Editor: Helping pregnant women to stop smoking and not to resume after their baby is born is a key target for smoking prevention. Pregnancy (or trying to become pregnant) is a time when women are motivated to stop smoking for the sake of the baby and they are in contact with healthcare professionals who can help them do so.

We have calculated the impact of smoking during pregnancy in terms of deaths, hospital separations and costs to the healthcare system, and estimated the extent to which these effects could be reduced through interventions initiated by healthcare professionals as part of routine clinical contact.

We considered the following conditions: pre-eclampsia (which is less common among smokers), low birthweight (including hospital costs for the mother and the baby, and infant deaths), premature rupture of membrane, spontaneous abortion, ectopic pregnancy, placenta praevia (including infant death), and sudden infant death syndrome (SIDS). We used estimates of relative risks (RRs) for these conditions for women who smoke during pregnancy (or, for ectopic pregnancy, for women who might become pregnant) from meta-analyses.[1-3] We obtained data on deaths,[4] hospital separations,[5] and costs to the healthcare system[6] for 2001–02. The prevalence of smoking among pregnant women of all ages in New South Wales since 1994 has been in the range 17% to 22%.[7] The prevalence of smoking among all women of child-bearing age in 2001 was about 28%.[8] From these data, we calculated attributable fractions[1,2,9] for average values (using point estimates for RRs and 20% for prevalence of smoking in pregnancy) and extreme values (using the 95% confidence limits for RRs and 17% and 22% for smoking prevalence).

In summary, the average number of adverse events attributable to smoking each year in Australia are: infant deaths, 78 (extreme values, 66–87); hospital separations, 6890 (extreme values, 4130–9450); costs to the healthcare system, $23 million (extreme values, $16–$29 million).

A Cochrane review of behavioural (not pharmacological) interventions for stopping smoking in pregnancy showed an absolute reduction of 6% (95% CI, 4%–8%).[10] Thus, if the prevalence of smoking during pregnancy were reduced from 20% to 14%, we calculate that there would be 20 fewer infant deaths, 1600 fewer hospital separations, and a saving of $5 million to the Australian healthcare system per year. (Details of the calculations can be obtained from the authors.)

These gains could be realised by increasing community awareness of the risks of smoking in pregnancy and helping health

professionals to use smoking prevention strategies in their routine encounters with pregnant women.

Acknowledgement: This work was supported by a grant from the Medical Benefits Fund of Australia.

1 English DR, Holman CDJ, Milne E, et al. The quantification of drug caused morbidity and mortality in Australia. 1995 edition. Canberra: Commonwealth Department of Human Services and Health, 1995.
2 Ridolfo B, Stevenson C. The quantification of drug-caused mortality and morbidity in Australia, 1998. Canberra: Australian Institute of Health and Welfare, 2001. (AIHW Catalogue No. PHE 29; Drug Statistics Series No.7.)
3 Castles A, Adams EK, Melvin CL, et al. Effects of smoking during pregnancy: five meta analyses. *Am J Prev Med* 1999; 16: 208-215.
4 Australian Bureau of Statistics. Causes of death, Australia 2002. Canberra: ABS, 2002. (ABS Catalogue No. 3303.0.)
5 Australian Institute of Health and Welfare Interactive National Hospital Morbidity Data 2001–02. Canberra: Australian Institute of Health and Welfare. Available at: www.aihw.gov.au/cognos/cgi-bin/ppdscgi.exe?DC=Q&E=/AHS/principaldiagnosis0102 (accessed Jan 2004).
6 National Hospital Cost Data Collection. Round 6 (2001–02). Australian refined diagnosis related groups 4.2. Cost weights. Canberra: Commonwealth Department of Health and Ageing, 2002. Available at: www.health.gov.au/casemix/costing/graph_table/round6/Public_National_Cost_Weights_Round_6_estim.xls (accessed Apr 2004).
7 Centre for Epidemiology and Research, NSW Department of Health. New South Wales mothers and babies, 2001. *NSW Public Health Bull* 2002; 13 Suppl S-4: 1-124.
8 Australian Bureau of Statistics. National health survey 2001. Canberra: ABS, 2002 (ABS Catalogue No. 4364.0.)
9 Adams EK, Melvin CL. Costs of maternal conditions attributable to smoking during pregnancy. *Am J Prev Med* 1998; 15: 212-219.
10 Lumley J, Oliver S, Waters E. Interventions for promoting smoking cessation during pregnancy (Cochrane Review). In: The Cochrane Library, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd. ❑

Androgen deficiency and replacement therapy in men

Adam P Morton*

* Endocrinologist, Mater Hospital, South Brisbane, QLD 4101. Amorton@mater.org.au

To the Editor: I appreciated the recent comprehensive review of androgen deficiency and replacement therapy in men by Handelsman and Zajac.[1] I ask their opinion of the importance of obstructive sleep apnoea as a cause of secondary hypogonadism, and also of the safety of androgen replacement in men with hypogonadism who have obstructive sleep apnoea but are intolerant of continuous positive airway pressure (CPAP) treatment.

In my practice, obstructive sleep apnoea is one of the most common associations, if not indeed causes, of hypogonadotropic hypogonadism. Several studies have shown that obstructive sleep apnoea is associated with secondary hypogonadism, which is partly or completely reversed by both CPAP treatment and uvulopalatopharyngoplasty.[2-4] Secondary hypogonadism is also a feature of several conditions in which there is a high prevalence of obstructive sleep apnoea, including chronic spinal cord injury and cardiac failure. Of concern, studies have shown that androgen replacement may precipitate or worsen obstructive sleep apnoea.[5,6]

Similarly, a study of women with endogenous androgen excess caused by polycystic ovary syndrome found they were 30 times more likely to suffer from sleep-disordered breathing than control women.[7] A single case report describes resolution of obstructive sleep apnoea in a non-obese woman after removal of a benign testosterone-producing ovarian tumour.[8]

Thus, I would value Handelsman and Zajac's comments as to whether they consider obstructive sleep apnoea to be an important cause of secondary hypogonadism, and whether symptoms of this condition should be sought before initiating androgen replacement therapy.

1 Handelsman DJ, Zajac JD. Androgen deficiency and replacement therapy in men. *Med J Aust* 2004; 180: 529-535.
2 Luboshitzky R, Lavie L, Shen-Orr Z, Lavie P. Pituitary-gonadal function in men with obstructive sleep apnea. The effect of continuous positive airways pressure treatment. *Neuroendocrinol Lett* 2003; 24: 463-467.
3 Grunstein RR, Handelsman DJ, Lawrence SJ, et al. Neuroendocrine dysfunction in sleep apnea: reversal by continuous positive airways pressure therapy. *J Clin Endocrinol Metab* 1989; 68: 352-358.
4 Santamaria JD, Prior JC, Fleetham JA. Reversible reproductive dysfunction in men with obstructive sleep apnoea. *Clin Endocrinol* 1988; 28: 461-470.
5 Liu PY, Yee B, Wishart SM, et al. The short-term effects of high-dose testosterone on sleep, breathing, and function in older men. *J Clin Endocrinol Metab* 2003; 88: 3605-3613.
6 Matsumoto AM, Sandblom RE, Schoene RB, et al. Testosterone replacement in hypogonadal men: effects on obstructive sleep apnoea, respiratory drives, and sleep. *Clin Endocrinol* 1985; 22: 713-721.
7 Vgontzas AN, Legro RS, Bixler EO, et al. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. *J Clin Endocrinol Metab* 2001; 86: 517-520.
8 Dexter DD, Dovre EJ. Obstructive sleep apnea due to endogenous testosterone production in a woman. *Mayo Clin Proc* 1998; 73: 246-248. ❑

David J Handelsman,* Jeffrey D Zajac†

* Director, ANZAC Research Institute, Concord Hospital, Hospital Road, Concord, NSW 2139; † Head, Department of Medicine, Austin Hospital, Melbourne, VIC. djh@anzac.edu.au

In reply: We thank Morton for his thoughtful comment that, in addition to monitoring for obstructive sleep apnoea precipitated by testosterone therapy, it may be worthwhile screening for this condition before starting treatment. Symptoms to be sought include daytime sleepiness and partner reports of loud and irregular snoring, especially among overweight men with large collar size.

Obstructive sleep apnoea rises steeply in prevalence with age and causes mild hypogonadotropic hypogonadism, which is rectified by effective continuous positive airway pressure (CPAP) treatment.[1] Obesity, depression, cardiovascular disease and other conditions that become more common with age have similar effects. Together, they contribute to the lower blood testosterone levels found in unselected older men, in whom testosterone remains an unproven treatment.[2] This condition differs from classical hypogonadotropic hypogonadism caused by hypothalamic or pituitary disorders, which routinely requires lifelong testosterone replacement, and (occurring in a younger population) is rarely associated with obstructive sleep apnoea.

The prevalence of obstructive sleep apnoea precipitated by testosterone treatment remains unclear. A case precipitated by injectable testosterone has been reported,[3] while testosterone has potential adverse effects on sleep in older men.[4] Clinical experience suggests that, among younger hypogonadal men, obstructive sleep apnoea is a rare idiosyncratic reaction to testosterone, which, like polycythaemia, may be particularly related to supraphysiological blood testosterone levels. However, the prevalence may be higher among older men. Hence, we agree that pretreatment screening is wise (rather than proven) for older men starting testosterone treatment, but is not routinely necessary for young men with classical hypogonadism.

1 Grunstein RR, Handelsman DJ, Lawrence SJ, et al. Hypothalamic dysfunction in sleep apnea: reversal by nasal continuous positive airways pressure. *J Clin Endocrinol Metab* 1989; 68: 352-358.
2 Liverman CT, Blazer DG, editors. Testosterone and aging: clinical research directions. Washington, DC: Institute of Medicine, The National Academies Press, 2004.
3 Sandblom RE, Matsumoto AM, Scoene RB, et al. Obstructive sleep apnea induced by testosterone administration. *N Engl J Med* 1983; 308: 508-510.

4 Liu PY, Yee BJ, Wishart SM, et al. The short-term effects of high dose testosterone on sleep, breathing and function in older men. *J Clin Endocrinol Metab* 2003; 88: 3605-3613. ❑

Treatment of osteoporosis: why, whom, when and how to treat

B E Christopher Nordin,*
Allan G Need†
* Physician, Endocrine and Metabolic Unit, Royal Adelaide Hospital, Adelaide, SA;
† Head, Division of Clinical Biochemistry, Institute of Medical and Veterinary Science, Adelaide, SA.
christopher.nordin@imvs.sa.gov.au

To the Editor: The article by Seeman and Eisman on treatment of osteoporosis[1] not only neglects the pathogenesis and prevention of this condition, but also fails to appreciate the profound differences between the three main types of fragility fracture (peripheral non-hip, hip and spine).

To say that adults lose bone with age because the "volume of bone resorbed is greater than the volume replaced" is a spectacular but common tautology which simply describes what would be expected from an external negative calcium balance. The common postmenopausal bone loss can generally be accounted for by the rise in calcium requirement due to a fall in calcium absorption and rise in obligatory calcium excretion.[2-4] This can be corrected with hormones or compensated for with a calcium supplement, which is known to suppress bone resorption.[5] In 20 trials of calcium therapy completed up to 1997, the loss of bone in 855 postmenopausal women treated with calcium was 0.3% per annum, compared with 1.0% per annum in 635 untreated control women ($P < 0.001$).[6]

In older women, this relative calcium deficiency is complicated by a decline in vitamin D status caused by reduced exposure to sunlight and progressive thinning of the skin. It has been known for 30 years that vitamin D deficiency is common in patients with hip fracture,[7] for 20 years that this was also true in Australia,[8] and for 12 years that vitamin D with calcium can reduce the hip fracture rate by 43% in 18 months in women in residential care.[9]

When it comes to established osteoporosis (the combination of low bone density with fracture), treatment needs to distinguish between the three main types of fracture referred to above. In hip fractures, surely the first priority must be to give adequate vitamin D and calcium. Most non-hip peripheral fractures occur in women with bone densities in the normal range,[10] so the need for treatment is debatable unless bone turnover is very high.

Vertebral fractures are a different matter. Unlike peripheral fractures, they do not "heal" in the usual sense — the deformity remains and often causes local pain and mechanical dysfunction. The recurrence rate is very high, because all the vertebrae have much the same bone density, and the osteoporotic collapse of one indicates that the others are ready to follow. This condition is notoriously difficult to manage and should almost be regarded as a medical emergency that requires full investigation — not least to exclude myeloma — and rapid, effective treatment. It is in the secondary prevention of these fractures that the remedies advocated by Seeman and Eisman probably have their main role and are most cost-effective. In fact, although the authors place great emphasis on prevalent fracture as a risk factor for further fracture, the reference they quote deals with prevalent vertebral fracture, not with prevalent non-hip peripheral fracture, where the evidence of benefit from bisphosphonates and raloxifene is very much weaker.

We are arguing for much greater emphasis on the prevention of osteoporosis with adequate calcium after the menopause and adequate vitamin D in the elderly, and the use of appropriate investigation and selective treatment in the management of the condition when it is established.

Competing interests: A G N has received research funding from Eli Lilly, Merck Sharpe & Dohme and Roche Products, and travel assistance from Merck Sharp & Dohme.

1 Seeman E, Eisman JA. Treatment of osteoporosis: why, whom, when and how to treat. *Med J Aust* 2004; 180: 298-303.
2 Nordin BEC, Need AG, Morris HA, Horowitz M. Biochemical variables in pre- and postmenopausal women: reconciling the calcium and estrogen hypotheses. *Osteoporos Int* 2002; 13: 83-88.
3 Nordin BEC, Wishart JM, Clifton PM, et al. A longitudinal study of bone-related biochemical changes at the menopause. *Clin Endocrinol (Oxf)* 2004; 61: 123-130.
4 Human vitamin and mineral requirements. Report of a joint FAO/WHO expert consultation. Bangkok, Thailand. World Health Organization, Food and Agriculture Organization of the United Nations, Rome, 2002.
5 Scopacasa F, Horowitz M, Wishart J, et al. Calcium supplementation suppresses bone resorption in early postmenopausal women. *Calcif Tissue Int* 1998; 62: 8-12.
6 Nordin BEC. Calcium and osteoporosis. *Nutrition* 1997; 13: 664-686.
7 Aaron JE, Gallagher JC, Anderson J, et al. Frequency of osteomalacia and osteoporosis in fractures of the proximal femur. *Lancet* 1974; 2: 229-233.
8 Morris HA, Morrison GW, Burr M, et al. Vitamin D and femoral neck fractures in elderly South Australian women. *Med J Aust* 1984; 140: 519-521.
9 Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D_3 and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992; 327: 1637-1642.
10 Stone KL, Seeley DG, Lui L-Y, et al. BMD at multiple sites and risk of fracture of multiple types: long-term results from the Study of Osteoporotic Fractures. *J Bone Miner Res* 2003; 18: 1947-1954. ❑

Ego Seeman,* John A Eisman†
* Professor of Medicine and Endocrinologist, Austin Hospital, Studley Road, Heidelberg, VIC 3084.
† Professor of Medicine, and Director, Bone and Mineral Research Program, Garvan Institute of Medical Research, St Vincent's Hospital, Sydney, NSW.
egos@unimelb.edu.au

In reply: Our article concerned a discussion of evidence-based treatment for the *prevention of* osteoporotic *fractures*. Prevention of *osteoporosis per se* is important, but the approaches chosen must be evidence-based. Calcium supplementation may diminish, but not abolish, bone loss by reducing remodelling rate.[1] Any association of a lifelong diet high in calcium appears to be with peak bone mass, not rates of bone loss,[2] and may be attributable to differences in protein intake or physical activity. Despite opinion, meta-analysis of prospective, randomised, double-blind, placebo-controlled studies does not support a role for calcium supplementation in reducing fractures.[3]

Later rather than earlier intervention avoids needless exposure to treatment for large numbers of individuals at low *absolute* risk of fracture (ie, those who are unlikely to

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There should be no more than 5 references. The reference list should not include anything that has not been published or accepted for publication. Reference details must be complete, including: names and initials for up to 4 authors, or 3 authors et al if there are more than 4 (see mja.com.au/public/information/uniform.html#refs for how to cite references other than journal articles).

sustain a fracture even without treatment).[4] Vitamin D is of course indicated in vitamin D deficiency. However, there is no evidence for anti-fracture efficacy of vitamin D in ambulant community dwellers.[5]

Competing interests: E S has been paid to sit on medical advisory boards for Aventis, Eli Lilly, and Merck Sharp & Dohme; J A E has been a paid consultant for Aventis, Eli Lilly, Merck Sharp & Dohme, NPS (USA), Organon, Roche and Servier.

1 Dawson-Hughes B, Harris SS, Krall A, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age and older. *N Engl J Med* 1997; 337: 670-676.

2 Matkovic V, Kostial K, Simonovic I, et al. Bone status and fracture rates in two regions of Yugoslavia. *Am J Clin Nutrition* 1979; 32: 540-549.

3 Shea B, Wells G, Cranney A, et al. Osteoporosis Methodology Group; Osteoporosis Research Advisory Group. Calcium supplementation on bone loss in postmenopausal women. *Cochrane Database Syst Rev* 2004; 1: CD004526.

4 Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med* 1988; 318: 1728-1733.

5 Lips P, Graafmans WC, Ooms ME, et al. Vitamin D supplementation and fracture incidence in elderly people. *Ann Intern Med* 1996; 124: 400-406. ❑

Unexpected infant death: lessons from the Sally Clark case

John M N Hilton

Associate Professor, Department of Pathology, University of Sydney; and Consultant in Forensic Medicine, PO Box 45, Katoomba, NSW 2780.
kornhil@iinet.net.au

To the Editor: Byard's succinct dissertation on the Clark case[1] omits one crucial aspect in redressing this miscarriage of justice. Without the vigorous and persistent efforts of a vocal and well directed support group, which included Mrs Clark's legal team, their scientific and medical advisors, the Law Society of England, and her family, she would still be serving a life sentence in jail.

An Australian example of the effectiveness of such a support group in combating injustice is afforded by the Lindy Chamberlain case.[2]

Historically, Sir Arthur Conan Doyle spearheaded the efforts — sustained over nearly 20 years — to exonerate Oscar Slater,[3] an unfortunate German–Jewish immigrant to Glasgow who was condemned to death after a conviction for murder based largely on identification evidence given by one of the probable perpetrators. Slater was granted a reprieve from the death sentence at the last moment, only to serve some 17 years in a grim Scottish penitentiary. Less fortunate was Timothy Evans,[4] who was convicted and hanged for murdering his wife and daughter on the evidence of one of London's infamous mass murderers, John Christie. Evans was eventually pardoned — unfortunately, too late to save his life — largely thanks to a very active support group headed by the journalist Ludovic Kennedy.

In contrast, those who lack such a support group are exemplified by Ziggy Pohl,[5] who was convicted, despite rather than because of the evidence, of killing his wife in Queanbeyan, NSW. He served more than a decade in prison, only to have the true perpetrator confess after Pohl was released on parole.

Byard highlights evidentiary shortcomings in one recent English case. How many other people have suffered the ignominy, distress and dire consequences of unjust convictions because they lacked the support of an individual or a group prepared to question the propriety of the conviction process?

1 Byard R. Unexpected infant death: lessons from the Sally Clark case. *Med J Aust* 2004; 181: 52-54.

2 Royal Commission of Inquiry into the Chamberlain Convictions. Report by the Commissioner the Hon. Mr Justice T R Morling. Darwin: NT Government Printer, 1987.

3 Mortimer J, editor. Famous trials. London: Penguin, 1984: 78-132.

4 Kennedy L. 10 Rillington Place. London: HarperCollins, 1995.

5 Report of the inquiry held under s 475 of the Crimes Act 1900 into the conviction of Johann Ernst Ziegfried Pohl at the Central Criminal Court on 2nd November 1973 (McInerney J). Sydney: NSW Government Printer, 1992. ❑

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