

THE NEW GENETICS: PRIVATE OR PUBLIC PROPERTY?

"We wish to suggest a structure for the salt deoxyribose nucleic acid [DNA]." So begins the report in *Nature* — 50 years ago this very week — on the greatest scientific discovery of the 20th century.

The celebrated issue of *Nature* featured not one, but three, reports on DNA: by Watson and Crick, by Wilkins, and by Franklin. Watson, Crick and Wilkins went on to receive the 1962 Nobel Prize for Physiology or Medicine. Rosalind Franklin died of cancer in 1958 — tragically, the Nobel Committee only honours the living.

Today, the new genetics is valued by both science and civil society. With the genetic gold promised by the Human Genome Project, disability, disease and even death may well exert diminished power over humankind.

But something sinister has accompanied the new genetics: the notion that outcomes of research are private property, and thus exploitable.

The DNA Nobel laureates worked in an atmosphere of shared access to information — an ethos untouched by the patenting of the intellectual property of seminal discoveries. Their universities were not overtly concerned with patents, exclusive commercial agreements, spin-off companies, royalty payments or access fees.

Things are different now. The US law academics, Rebecca Eisenberg and Richard Nelson, in *Public vs propriety science: a fruitful tension?* conclude that, "Public science . . . at its best, is a social commitment . . . It is a shared archive of an expanding knowledge base, a training ground for future researchers, and the germ from which future advances in human understanding will grow. Its social value does not depend on the ultimate profitability of the advances it spawns."

Some of our universities, research institutes, and researchers would beg to differ.

Martin B Van Der Weyden

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Magnesium infusion to treat Irukandji syndrome

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TO THE EDITOR: This is the first report of the use of magnesium sulfate to treat Irukandji syndrome.

A previously well 26-year-old commercial diver was stung on the neck by a jellyfish while collecting sea cucumbers in Barrier Reef waters off Townsville in February 2003. As is typical for an Irukandji syndrome, he was asymptomatic for about 30 minutes, after which he developed back and abdominal pain, nausea and headache.

He was retrieved from the scene by helicopter and arrived in the emergency department (ED) two hours after the onset of symptoms. On retrieval he had a blood pressure of 150/90 mmHg, agitation, marked diaphoresis, piloerection and some dyspnoea. A typical carybdeid jellyfish sting mark was present on the neck. The cardiac troponin I level was elevated from the time of admission.

En route and in the ED he was treated with intravenous morphine and diazepam. Skin scrapings were taken for nematocyst identification. After he had received 27.5 mg of morphine and 15 mg of diazepam, his pain settled somewhat, but abdominal discomfort, agitation and profuse diaphoresis persisted. Despite the dyspnoea, he showed no other overt clinical signs of cardiac failure.

Concern with the patient's increasing hypertension (170/100 mmHg five hours after envenomation) led to his being transferred to the high dependency unit (HDU) six hours after envenomation. It was decided to try a therapeutic trial of magnesium sulfate for this patient in an attempt to control the hypertension. This decision was taken on the basis of:

- the unsatisfactory results of measures taken thus far,
- the postulated hyperadrenergic basis of hypertension in Irukandji syndrome,
- the known 20%–30% fall in systemic vascular resistance associated with magnesium administration in hyperadrenergic states,¹ and
- considerable experience within the HDU with managing severe pre-eclampsia.

Intravenous magnesium sulfate was administered as a loading dose of 10 mmol followed by an infusion of 5 mmol per hour.

Sympathetic features and agitation resolved, and pain nearly completely resolved towards the end of the loading dose. Of note, an early reduction in the rate of magnesium sulfate infusion resulted in recrudescence of hypertension, back pain and piloerection. The infusion was uneventfully reduced to 3 mmol per hour at 11 hours after envenomation, and discontinued at 20 hours after envenomation. No adverse effects related to the magnesium infusion were noted. The patient subsequently remained well. The troponin I level rose to a peak of 6.4 µg/L, and an echocardiogram was normal at 20 hours after envenomation.

Irukandji syndrome is produced by carybdeid jellyfish envenomation² and has been shown (in animals) to be associated with dramatically elevated serum noradrenaline levels.³ Severe hypertension in Irukandji syndrome can be difficult to treat and has been associated with two deaths from intracranial haemorrhage. The origin of the extensive, severe pain associated with the syndrome is unknown. Postulated mechanisms include ischaemia from widespread small vessel vasoconstriction resulting from a hyperadrenergic state, and sodium channel opening in afferent pain fibres. Other mechanisms are equally likely. Induced catecholamine release or direct toxicity have been proposed as the cause of myocardial injury. This may produce overt, and occasionally severe, cardiac failure.

Magnesium decreases both catecholamine release and sympathetic terminal receptivity to catecholamines¹ via multiple sites of action, including most calcium channel subtypes (both at the cell membrane and intracellularly), as well as modifying other cation fluxes. It reduces catecholamine-induced myocardial necrosis in phaeochromocytoma (Professor M James, Department of Anaesthesia, University of Cape Town, personal communication) and is widely used in other hyperadrenergic states, such as phaeochromocytoma and pre-eclampsia.¹

The apparent efficacy of intravenous magnesium in our patient suggests the need to further investigate this therapy.

A larger case series, a multicentre randomised trial of magnesium sulfate administration in Irukandji syndrome and a dose-finding study are under way.

1. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth* 1999; 83: 302-320.
2. Bailey PM, Little M, Jelinek GA, Wilce JA. Jellyfish envenoming syndromes: unknown toxic mechanisms and unproven therapies. *Med J Aust* 2003; 178: 34-37.
3. Tibballs J, Hawden G, Winkel K. Mechanisms of cardiac failure in Irukandji syndrome and first aid therapy for stings [letter]. *Anaesth Intensive Care* 2001; 29: 552. □

Black cohosh and other herbal remedies associated with acute hepatitis

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TO THE EDITOR: We wish to comment on the article by Whiting and colleagues¹ on the proposed causal relationship between herbal remedies and severe acute hepatitis.

Investigators have found that reported adverse effects of herbal medicines are not, in fact, caused by herbs alleged to be in the product, but result from substitution or contamination of the declared ingredients, intentionally or by accident, with a more toxic herb, a poisonous metal or even a pharmaceutical compound.^{2,3}

In reports of adverse effects, there is often no effort to establish a positive identification of the herb involved or any adulterants. The attribution of tox-



icity to the wrong plant leads to inaccurate information being provided to patients, practitioners and regulators.⁴

A significant problem is the use of common names. As mentioned by Whiting and colleagues,¹ *Cimicifuga racemosa* (black cohosh) has at least 20 different common names, which can be very confusing. The most tragic example of such confusion is the fatal substitution of *Stephania tetrandra* by the toxic herb *Aristolochia fangchi* owing to the similarity of the common names of the two herbs.⁵

In recording and responding to adverse events involving herbs, certain key questions need to be asked by those reporting the event and, more crucially, by those subsequently citing the report. No details regarding verification of the herbal products taken by the individual patients were supplied by Whiting and colleagues.¹ Because of this failure to authenticate the plant compounds in the preparations, one cannot establish that the herbs were the cause of the hepatotoxicity. No information about plant parts used, solvent, concentration, manufacturing process or chemical analysis was supplied.

Although Whiting et al exclude other causes for hepatitis, external factors may have contributed to the reported liver reactions. Hepatitis for which no cause can be identified is not uncommon.⁶ In addition, absence of hepatitis B surface antigen does not exclude the possibility of hepatitis B virus infection.⁷

The correlation of the liver diseases with preparations of *Cimicifuga racemosa* is speculative, as viral causes were not definitively ruled out. Without further pathophysiological or biochemical investigation, no conclusion can be made as to the exact mechanism.

In a review of eight human studies on the effectiveness of an extract of black cohosh for alleviating menopausal symptoms, the authors concluded that black cohosh appears to be a safe, effective alternative to oestrogen replacement therapy for patients in whom oestrogen replacement therapy is refused or contraindicated.⁸

- Whiting PW, Clouston A, Kerlin P. Black cohosh and other herbal remedies associated with acute hepatitis. *Med J Aust* 2002; 177: 440-443.
- Ernst E, Pittler MH. Risks associated with herbal medicinal products. *Wien Med Wochenschr* 2002; 152: 183-189.
- Fugh-Berman A. Herb-drug interactions. *Lancet* 2000; 355: 134-138.

- Corrigan D. Adverse reports — some first principles. *Eur PhytoJournal* 2001; 1. Available at: <http://www.escop.com/epj2pdfs/corrigan.pdf> (accessed Mar 2003)
- Nortier JL, Martinez MC, Schmeiser HH, et al. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *N Engl J Med* 2000; 342: 1686-1692.
- Walker AM, Cavanaugh RJ. The occurrence of new hepatic disorders in a defined population. *Post Marketing Surveillance* 1992; 1: 107-111.
- Fasel-Felley J, Peitrequin R, Frei PC. Absence of circulating HBsAg in acute hepatitis B. *Infection* 1984; 12: 202-204.
- Lieberman S. A review of the effectiveness of *Cimicifuga racemosa* (black cohosh) for the symptoms of menopause. *J Womens Health* 1998; 7: 525-529. □

Hormone replacement therapy after a diagnosis of breast cancer: cancer recurrence and mortality

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TO THE EDITOR: We urge caution about the recently published findings of Durna and colleagues on use of hormone replacement therapy (HRT) by breast cancer patients.¹ They found no increase in risk of breast cancer recurrence or reduction in life expectancy in women using HRT after treatment for primary breast cancer, leading them to conclude that HRT seems a safe treatment for women with a history of breast cancer. We believe that their study has many limitations and consequently their conclusions are unfounded.

Durna's group conducted a retrospective, observational study using unmatched patient groups. The HRT group was statistically younger, with smaller tumours and fewer positive nodes, and thus had better prognosis. The authors discussed regression analyses for age of diagnosis and stage to reduce potential bias, but did not include these data.

The omission of tumour grade and receptor status in the analysis is an obvious flaw. The mean duration of HRT use was short compared with many previous studies (mean, 1 year). This is particularly important, as any risk is likely to be cumulative.² There were also statistically more women in the HRT group who had received HRT before diagnosis, and for a longer duration (mean, 6.5 years v 3 years). This too may bias results, as breast cancer

that develops after HRT has been suggested to carry a better prognosis.³ There was also no subgroup analysis of those who took concomitant tamoxifen.

Durna and colleagues also do not address the concerns raised by the Women's Health Initiative study, which showed an excess of cardiovascular and thromboembolic events in "healthy" women taking HRT.⁴ Many of these events occurred in the first years of HRT use, the time assessed in Durna's study. The risks of short-term HRT in breast cancer patients may be not only tumour-related, but may also include cardiac and thrombotic events, which were not specifically considered by Durna and colleagues.

Of additional concern is the extensive portrayal in some sections of the media that this study is conclusive regarding the risks of HRT use by women with breast cancer. The importance of correct media interpretation of studies is discussed in the accompanying editorial by Patel and colleagues.⁵ Despite this editorial and the inadequacies of Durna's study, the results of this study, released through the media, inaccurately suggested safety and even a possible benefit of HRT.⁶ This simply adds to the "HRT furore".

All studies addressing this issue to date have been small and non-randomised, often with no control group or unmatched groups.² Because of these limitations, no clear recommendation can be made about the safety of HRT in women with breast cancer. Until results are available from rigorous randomised controlled trials, such as the ongoing HABITS (Hormone Replacement Therapy After Breast Cancer — Is It Safe?) study (IBCSG 17-98), we should not be "advocating" HRT to breast cancer patients. For Durna's group to suggest otherwise is very premature. In addition, there are well studied, effective alternatives to HRT for treating menopausal symptoms in breast cancer patients (eg, venlafaxine),⁷ and these would seem the current safer option.

- Durna EM, Wren BG, Heller GZ, et al. Hormone replacement therapy after a diagnosis of breast cancer: cancer recurrence and mortality. *Med J Aust* 2002; 177: 347-351.
- Col NF, Hirota LK, Orr RK, et al. Hormone replacement therapy after breast cancer: a systematic review and quantitative assessment of risk. *J Clin Oncol* 2001; 19: 2357-2363.
- Nanda K, Bastian LA, Schulz K. Hormone replacement therapy and the risk of death from breast cancer: a systematic review. *Am J Obstet Gynecol* 2002; 186: 325-334.

- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002; 288: 321-333.
- Patel A, Norton R, MacMahon S. The HRT furore: getting the message right [editorial]. *Med J Aust* 2002; 177: 345-346.
- HRT after cancer can cut relapse risk: study. *Sydney Morning Herald* 2002; Oct 7.
- Burstein HJ, Winer EP. Primary care: primary care for survivors of breast cancer. *N Engl J Med* 2000; 343: 1086-1094. □

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IN REPLY: We feel that Hayes and colleagues repeat the editorial comments of Dixon¹ that accompanied our article.²

Our investigation, being retrospective, had biases and limitations normally associated with that type of study. In the third and fourth paragraphs of the discussion section of our article, we examined further the sources of bias and their impact.

Hayes and colleagues state that the omission of tumour grade and receptor status from our analysis is a flaw. We agree that including these variables would have made our study more complete, even if we doubt that this would have altered the conclusions. So many of these data were missing that statistical analysis would have been unreliable. As was stated in the methods section, the analysis was adjusted for the covariate HRT use before diagnosis. Tamoxifen use was very similar among HRT users and non-users (58% and 60%, respectively), and any bias introduced by this difference would be insignificant.

The scope of our article, as suggested by its title, was limited to the issue of cancer recurrence and mortality. We did not specifically investigate the impact of HRT on cardiovascular and thromboembolic events. Nonetheless, if cardiovascular disease had increased mortality, this would have been apparent as an increase in all-cause mortality.

We agree with Hayes and colleagues that it is vital that the media interpret studies correctly for the general public. We are disappointed that Hayes and

colleagues have misinterpreted our conclusion. Our article does *not* advocate HRT use by women with breast cancer.

We explicitly stated that “These results need to be confirmed in a randomised trial before HRT can be advocated for all women who have had breast cancer.” Furthermore, “...the observed association between HRT use and [reduced] risks of breast cancer recurrence and death cannot be inferred to be causal”.

We believe that we are justified in our conclusion that HRT use in women diagnosed with breast cancer is not associated with an increased risk of recurrence of breast cancer or a shortened life span. It is our clinical practice to use HRT only when alternative therapy fails.

- Dixon JM. Hormone replacement therapy: is it safe for breast cancer patients? [editorial]. *Med J Aust* 2002; 177: 340-341.
- Durna EM, Wren BG, Heller GZ, et al. Hormone replacement therapy after a diagnosis of breast cancer: cancer recurrence and mortality. *Med J Aust* 2002; 177: 347-351. □

Thalidomide and cancer?

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TO THE EDITOR: McBride reports that there were four deaths from cancer before the age of 40 years in a group of 480 thalidomide-affected people in the United Kingdom, an approximate cumulative mortality rate of 0.83%.¹ He compares this with the annual death rate in the under-40-years age group, and concludes that the rate is increased almost 100 times in those affected by thalidomide.

The correct comparison is with the cumulative mortality rate in the general population from birth to age 40. From 1999 UK statistics,² this is about 0.31% — that is, we would expect 1.48 deaths among 480 people. While the observed number of four is greater than this, it is only slightly greater, and the difference is not statistically significant (the mortality ratio is 2.7, with exact 95% confidence limits of 0.7 to 6.9, based on a Poisson distribution). McBride's conclusion is based on an inappropriate comparison.

A full analysis would use population death rates over the 40-year period and

take account of censoring, but that is unlikely to affect the result substantially.

- McBride W. Thalidomide and cancer [letter]. *Med J Aust* 2002; 177: 278.
- Quinn M, Babb P, Brock A, et al. Cancer trends in England and Wales 1950–1999. London: The Stationary Office, 2001. □

Low-molecular-weight heparins and heparinoids

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TO THE EDITOR: In a valuable review of low-molecular-weight heparins (LMWH), Eikelboom and Hankey¹ stray off the beaten path into the unwellcoming area of obstetric therapeutics — a notoriously hostile environment replete with traps and hazards. Their statement that “low-molecular-weight heparins are being used increasingly in pregnant women with prosthetic heart valves and for the prevention and treatment of venous thromboembolism” is contentious and requires considerable qualification.

The Journal has already published a position statement concerning the use of these heparins in pregnancy.² It clearly stated that the initial treatment for pulmonary embolism in pregnancy remains intravenous unfractionated heparin, because so far there are no trials of LMWH in pulmonary embolism in pregnancy. The guidelines of the American College of Chest Physicians do endorse the use of LMWH for this indication,³ but base that view on data in non-pregnant patients. We believe that, as yet, there is insufficient evidence to recommend LMWH for the initial management of pulmonary embolism in pregnancy, although, on theoretical grounds, the treatment seems attractive.

In anticoagulation therapy for artificial heart valves in pregnancy, there are serious problems. Unfortunately, the conscientious adviser must be very circumspect in counselling women with these prostheses. Pregnancy for these women presents significant risks. None of the heparins, unfractionated or low molecular weight, has been shown to protect reliably against

embolism from, or thrombosis of, these valves in pregnancy.

Whether LMWH is better than unfractionated heparin has not been established and awaits appropriate trials. Warfarin, which crosses the placenta, remains a valid, but worrying, choice in pregnancy for anticoagulation in patients with prosthetic heart valves. This drug provides optimal protection from valve thrombosis, but with the potential for teratogenicity in the first trimester and fetal (and maternal) haemorrhage later in pregnancy. Many experts use heparin and warfarin sequentially in this situation.³

Thus, anticoagulation therapy for pregnant women with serious medical problems remains, as always, perplexing, difficult and dangerous. While LMWH offer considerable promise and have undoubted utility in several areas, there are very compelling caveats about their current use for pulmonary embolism and prosthetic heart valves in pregnant women.

For these reasons and others, women with prosthetic heart valves planning pregnancy, as well as those already pregnant, should be counselled about these problems by a physician experienced in managing medical problems in pregnancy.

1. Eikelboom JW, Hankey GJ. Low molecular weight heparins and heparinoids. *Med J Aust* 2002; 177: 379-383.
2. Anticoagulation in pregnancy and the puerperium. *Med J Aust* 2001; 175: 258-263.
3. Ginsberg J, Greer I, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 2001; 119: 122S-131S. □

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TO THE EDITOR: The recent “*New Drugs, Old Drugs*” review of low molecular weight heparins (LMWH) and heparinoids¹ provides a timely reminder of the limitations of studies that support the use of these agents in preventing venous thromboembolism (VTE), particularly in orthopaedic surgery.

A new class of anticoagulants has recently been released in Australia and is being promoted as being more effective than LMWH in preventing VTE. However, while several randomised controlled trials suggest that fondaparinux reduces the risk of asymptomatic deep vein thrombosis (DVT) in

patients undergoing hip and knee replacement surgery,^{2,3} there is currently no evidence to suggest that it reduces the risk of symptomatic VTE.

Fondaparinux is a synthetic pentasaccharide that selectively binds to anti-thrombin III, enhancing the neutralisation of factor Xa and inhibiting generation of thrombin and subsequent clot formation.² Unlike LMWH, fondaparinux does not appear to affect platelet function, thus potentially reducing bleeding tendencies and avoiding the risk of immune-mediated thrombocytopenia.

The main problem facing researchers who study VTE prophylaxis in patients undergoing orthopaedic surgery is that, while asymptomatic DVT is common, symptomatic VTE is rare. The rate of fatal pulmonary embolism in patients undergoing hip replacement surgery is 0.1%–0.2% in those who receive no prophylaxis.⁴ Trials to demonstrate a reduction in symptomatic VTE are not performed because huge sample sizes are required to show a statistically significant difference in outcome (50 000 patients would need to be enrolled in a trial to show a reduction in the rate of fatal pulmonary embolism from 0.2% to 0.1% with 80% power). If such a difference could be shown, it would probably be clinically irrelevant to an orthopaedic surgeon performing 50 joint replacements a year.

Although asymptomatic DVT is used as a surrogate endpoint for trials that support VTE prophylaxis, the natural history of asymptomatic DVT is poorly documented. There is some evidence to suggest that asymptomatic DVT is not associated with an increased risk of subsequent chronic venous insufficiency,⁵ and the association between asymptomatic DVT and subsequent clot propagation and embolisation is not well established.

Further information on the natural history of asymptomatic DVT must be obtained before the clinical relevance of results from current studies of VTE prophylaxis can be determined. Until then, the clinical relevance of studies comparing the use of “new drugs” with “old drugs” in preventing VTE in orthopaedic surgery cannot be assessed.

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2. Bauer KA, Eriksson BI, Lassen MR, Turpie AGG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after elective major knee surgery. *N Engl J Med* 2001; 345: 1305-1310.

3. Eriksson BI, Bauer KA, Lassen MR, Turpie AGG. Postoperative fondaparinux versus preoperative enoxaparin for prevention of venous thromboembolism in elective hip-replacement surgery: a randomized double-blind comparison. *Lancet* 2002; 359: 1715-1720.
4. Murray DW, Britton AR, Bulstrode CJK. Thromboprophylaxis and death after total hip replacement. *J Bone Joint Surg Br* 1996; 78: 863-870.
5. Warwick D, Perez J, Vickery C, Bannister G. Does total hip arthroplasty predispose to chronic venous insufficiency? *J Arthroplasty* 1996; 11: 529-533. □

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IN REPLY: Walters and Graham question the role of low-molecular-weight heparin (LMWH) as a replacement for unfractionated heparin during pregnancy, and cite the lack of randomised comparisons to support their view that the standard initial treatment for pulmonary embolism during pregnancy remains intravenous unfractionated heparin. We do not deny the lack of clinical trials of LMWH in pregnancy; we were simply referring to the increased use of LMWH.^{1,2}

However, the lack of evidence of effectiveness does not equate with evidence of lack of effectiveness of LMWH in pregnancy. Clinical trials are needed to determine optimal anticoagulant strategies during pregnancy, particularly in patients with prosthetic heart valves. While awaiting the results of these trials, we believe that the major pharmacokinetic and safety advantages of LMWH over unfractionated heparin, coupled with an extensive body of evidence demonstrating their efficacy and safety in non-pregnant patients, should not be ignored in our pursuit of optimal anticoagulation therapies.

Williamson and Street question the validity of asymptomatic deep vein thrombosis as a surrogate for symptomatic venous thromboembolism in patients undergoing major orthopaedic surgery. Further, they cite a 0.1%–0.2% incidence of pulmonary embolism in patients undergoing hip replacement surgery without prophylaxis³ to support the conclusion that any effect of thromboprophylaxis on reducing symptomatic events is likely to be irrelevant for individual orthopaedic surgeons.

We believe that their argument is seriously flawed. Firstly, the “meta-analysis” they cite³ had major methodological limitations, as elegantly

highlighted by “Sherlock Holmes” in his critical appraisal of systematic reviews of surgical thromboprophylaxis.⁴ Secondly, rigorously conducted randomised trials and meta-analyses of randomised trials have demonstrated the efficacy of anti-thrombotic therapy for the prevention of both symptomatic and fatal venous thromboembolism in high-risk surgical patients, including lower-limb orthopaedic surgery.^{5,6} Thirdly, the clear correlation between reduction in asymptomatic and symptomatic venous thromboembolism in patients undergoing elective joint replacement surgery⁷ suggests that asymptomatic thrombosis detected by screening venography is a valid surrogate for symptomatic events. Fourthly, we agree that an individual orthopaedic surgeon performing 50 joint replacements per year may remain unaware of a small reduction in fatal pulmonary emboli in his or her own practice (eg, a 0.1% absolute risk reduction would be equivalent to preventing one death in 20 years of practice).

Yet, on a population basis, even a 0.1% absolute reduction (which is likely to be an underestimate — the PEP study showed a 0.3% absolute reduction in fatal pulmonary embolism with aspirin⁵) equates to 50 preventable deaths per year in Australia alone⁸ and many thousands worldwide.

There is now overwhelming evidence of the efficacy of thromboprophylaxis for preventing venous thromboembolism, including symptomatic and fatal pulmonary embolism, in high-risk surgical patients. With the rapid ageing of the Australian population and the expected increase in joint replacement surgery in coming years,⁹ the failure to use effective thromboprophylaxis in orthopaedic patients will likely result in a growing burden of preventable morbidity and mortality from venous thromboembolism.

1. Sanson BJ, Lensing AW, Prins MH, et al. Safety of low molecular weight heparin in pregnancy: a systematic review. *Thromb Haemost* 1999; 81: 668-672.
2. Ginsberg JS, Greer I, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 2001; 119: 122-131.
3. Murray DW, Britton AR, Bulstrode CJ. Thromboprophylaxis and death after total hip replacement. *J Bone Joint Surg Br* 1996; 78: 863-870.
4. Petticrew M, Kennedy SC. Detecting the effects of thromboprophylaxis: the case of the rogue reviews. *BMJ* 1997; 315: 665-668.
5. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. *Lancet* 2000; 355: 1295-1302.

6. Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med* 1988; 318: 1162-1173.
7. Eikelboom JW, Quinlan D, Douketis JD. Long-term LMWH to prevent VTE in high-risk orthopaedic patients: a meta-analysis. *Lancet* 2001; 358: 9-15.
8. Australian Orthopaedic Association National Joint Replacement Registry. Available at: http://www.dmac.adelaide.edu.au/aoanjrr/aoanjrrreport_2002.pdf (accessed 22 Feb 2003).
9. Sanders KM, Nicholson GC, Ugoni AM, et al. Health burden of hip and other fractures in Australia beyond 2000. Projections based on the Geelong Osteoporosis Study. *Med J Aust* 1999; 170: 467-470. □

Religion, spirituality and health

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TO THE EDITOR: Koenig's rebuttal of some of the conclusions I drew in my recent article was perhaps more vigorous than can be justified given recent changes in Australian culture and the paucity of practice-oriented research.^{1,2}

I accept that religious patients may be healthier in many respects, and being religious may help some patients cope with illness. However, it does not follow that having doctors in Australia enquire into their patients' religious beliefs almost as a matter of routine would be a cost-effective use of their time.

In hospitals, doctors are part of a team, and do not themselves have to identify religious concerns and mobilise spiritual resources. Nurses commonly ascertain whether patients are religious, identify concerns, and liaise with chaplains and pastoral workers. Chaplains themselves are highly regarded by all members of the healthcare team; they counsel and help patients cope with illness as part of their role, and are effective.³

For most Australians, religious affiliation is largely nominal. Consequently, only a minority of patients presenting to general practitioners are likely to have religious beliefs affecting their care. Rather than take a religious history routinely, it might be better if GPs were to enquire into religious beliefs when a patient or the family is known to be particularly religious or if the clinical situation warrants it.

Urging doctors to take a *religious* history ignores those patients who are not religious but who might have a spirituality that helps them cope with illness and

their particular needs.⁴ It also ignores changes which have occurred in Australian culture since the mid-1970s.⁵

Organised religion has declined, while spirituality has surged.⁵ Moreover, whereas Christians understand spirituality in terms of their relationship with God, in the wider community, spirituality needs no God association. It is often seen as a previously ignored aspect of being human, alongside physical, emotional and social aspects.⁵ It is increasingly regarded as the integrating holistic factor in life, associated with healing, therapy and well-being.

The healthcare system as a whole will need to consider the relevance of these cultural shifts and how it is going to respond. Medical professionals should keep this in mind when discussing the relevance for medical practice and how they will respond. Spirituality has already assumed greater prominence in the practice and education of nurses, psychologists and social workers, and medical professionals should take account of the skills and experience of these groups.

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3. Carey LB. The role of hospital chaplains: a research overview. *Ministry, Society and Theology* 1995; 9: 41-53.
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IN REPLY: Despite recent changes in Australian culture, Peach underestimates the importance of religious beliefs to older Australians likely to see physicians today.¹⁻³ As people age and experience negative life events, such as medical illness, longitudinal studies show that they become more and more religious.⁴

Given the potential impact that spiritual issues have on treatment decisions, the physician-patient relationship and medical outcomes, physicians cannot simply defer these issues to nurses or chaplains, nor do many physicians wish to do so.⁵ Deferring such issues could, in fact, be more costly than the few additional minutes necessary to take a

spiritual history, particularly in patients with serious or chronic medical illness.

For patients who are not religious, the doctor should enquire about secular beliefs that could influence medical decisions or that give the patient's life meaning and purpose in the context of their illness.

I do agree with Peach that physicians should always phrase enquiries in terms of "spirituality", allowing patients to determine for themselves what this involves — whether it be God, church, or the random forces of nature. Keeping the spiritual history "patient-centred" in this way ensures that no one is excluded and provides many additional safeguards.

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4. Wink P, Dillon M. Spiritual development across the adult life course: findings from a longitudinal study. *J Adult Dev* 2002; 9: 79-94.
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TO THE EDITOR: The recent articles about spirituality and health^{1,2} provide a welcome discussion about the very soul of medicine as well as the soul of the individual healthcare practitioner. If spirituality is "whatever is left over when the doctor, social worker, psychologist, community education officer or psychiatrist have had a go",³ then indeed spiritual questions should be left to the particular expert on that fragment of the person.

However, if spirituality is the integration of every aspect of the person, the plumbing of depth, the search and discovery of meaning and purpose, the exercise of compassion and love often in relation to the divine,⁴ then our whole practice of medicine needs to be spiritually conceived and executed, both for our patients and for ourselves. We need to pause and reflect on the quality of our care of ourselves as well as of our patients.⁵ We need to rescue healthcare delivery from the reductionism of a

mere science of "fixing bits" according to economic criteria. We need to deliver healthcare with humanity, compassion and wisdom. Some would include godliness. This is not an optional extra, but the core of true healthcare, in which each of us will need to freely contribute, without imperialism, from the depths of our own spiritual journey.

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5. Van der Weyden M. Taking time out [From the Editor's desk]. *Med J Aust* 2003; 178: 49. □

National ethics committee urgently needed

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TO THE EDITOR: I am happy to inform Whiteman and colleagues¹ that, should they wish to undertake a project in Australian general practices, the Royal Australian College of General Practitioners (RACGP) has one ethics committee which covers the whole of Australia. As a researcher, I have participated in many multicentre trials under the aegis of this committee over the past 8 years.

Details of the RACGP national ethics committee may be found at <http://www.racgp.org.au/document.asp?id=523>.

1. Whiteman DC, Webb PM, Purdie DM, Green AC. National ethics committee urgently needed [letter]. *Med J Aust* 2003; 178: 187. □

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