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Rebecca S Mason,* Terrence H Diamond†

* Associate Professor, Department of Physiology, University of Sydney, NSW 2006; † Senior Endocrinologist, Department of Endocrinology, St George Hospital, Kogarah, NSW.
rebeccam@physiol.usyd.edu.au

IN REPLY: Glendenning raises a number of interesting points, which require some clarification.

Are ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃) biologically equivalent?

The statement that ergocalciferol and cholecalciferol are bioequivalent in humans is made by most authoritative textbooks, based mainly on evidence from early studies of the antirachitic efficacy of ergocalciferol and cholecalciferol compounds, and contrasts with reduced efficacy of ergocalciferol in birds and monkeys.¹ Recent studies using more precise measurements have raised some doubts as to the absolute equivalency of ergo- and cholecalciferol, but the differences are marginal² and not universally found.³ There are few recent data on relevant biological endpoints. Serum concentrations of the active hormone, 1,25-dihydroxyvitamin D, were not different after administration of ergo- or cholecalciferol,² and increases in bone mineral density were greater after ergocalciferol therapy than after cholecalciferol in patients taking anticonvulsants.¹ In short, on current evidence, differences in biological activity between ergocalciferol and cholecalciferol are likely to be relatively minor.

Are there problems monitoring therapy?

25-Hydroxyvitamin D values may be used for monitoring treatment. The possibilities of impaired detection of the 25-hydroxy metabolite of ergocalciferol by some assays,² and perhaps a smaller rise in total 25-hydroxyvitamin D concentrations after low doses of ergocalciferol, should be borne in mind when monitoring therapy.

What is the current recommendation for vitamin D supplementation?

While the availability of larger dose sizes and/or cholecalciferol preparations would be helpful, 800 IU of ergocalciferol and 1 g of calcium for six months was shown to reduce secondary hyperparathyroidism in older patients,¹ and 600 IU/day (same for

ergo- and cholecalciferol) is the new recommended adequate intake for older patients with limited sun exposure.¹

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Confronting conflict of interest in research organisations: time for national action

Max Kamien

Professor, Department of General Practice, University of Western Australia, 328 Stirling Highway, Claremont, WA 6010. mkamien@cyllene.uwa.edu.au

TO THE EDITOR: A recent editorial in the *Journal* focused on the "blurring of research ideals and corporate interests".¹ But there are other funding and commissioning bodies, including government, whose wants or needs also have the potential to blur research ideals and exert control over what can be published. In recent times, those who pay the piper increasingly want to call the tune. Understandably, this is also an issue for research into Aboriginal ill health.^{2,3} Van Der Weyden's plea for the development of national guidelines on institutional conflict of interest should therefore be broadened to include all funding bodies.

One suggestion for inclusion in these guidelines, to enhance public interest in research, is an obligation for authors to state not only their sources of funding, but "the origin of the research question they are attempting to answer"⁴ and the person or group who initiated the funding of the project.

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Recent appearance of clindamycin resistance in community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) in south-east Queensland

Wendy J Munckhof,* Jacqueline Harper,†
Jacqueline Schooneveld,‡
Graeme R Nimmo[§]

* Specialist in Infectious Diseases and Microbiology, Ipswich Hospital, and Specialist in Infectious Diseases (corresponding author); † Chief Scientist; ‡ Scientist; § Director, Microbiology Department, Queensland Health Pathology Service, Princess Alexandra Hospital, Ipswich Rd, Woolloongabba, QLD 4102. wendy_munckhof@health.qld.gov.au

TO THE EDITOR: We report the appearance of erythromycin and inducible clindamycin resistance in the south-west Pacific strain of non-multiresistant methicillin-resistant *Staphylococcus aureus*, which has recently appeared in eastern Australia. Infections occur predominantly in Polynesian people and are usually community-acquired. Most strains belong to Western Samoan phage patterns (WSPP1 or WSPP2) and pulso-type A when typed by pulsed-field gel electrophoresis.^{1,2} These strains are resistant to all β -lactams, but are usually susceptible to erythromycin, clindamycin, gentamicin, tetracycline, trimethoprim-sulfamethoxazole and ciprofloxacin. Although most of these antibiotics would not be recommended for therapy,³ clindamycin has been recommended for non-parenteral treatment of soft-tissue and bone infections, as it is efficacious in treating similar infections caused by methicillin-susceptible *S. aureus*.⁴

Twenty isolates of community-acquired, non-multiresistant pulso-type A MRSA were collected from patients from southern Brisbane and Logan in 1997 and 1998.² A further 16 isolates were obtained from Ipswich patients between December 1998 and February 2001. We found that all 36



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isolates were susceptible *in vitro* to gentamicin, tetracycline, trimethoprim-sulfamethoxazole, ciprofloxacin, rifampicin, fusidic acid and vancomycin. However, two of the Ipswich isolates had erythromycin and inducible clindamycin resistance. When susceptibility testing was performed using standard disc methods, both isolates appeared resistant to erythromycin but susceptible to clindamycin. However, on testing for inducible macrolide resistance (MLSB phenotype) using a disc-approximation method, both showed inducible clindamycin resistance.⁵ These isolates were from superficial abscesses in Polynesian people with community-acquired infection. They were indistinguishable by pulsed-field gel electrophoresis, but there were no epidemiological links. As yet, we have found no community-acquired pulsed-field gel electrophoresis type A strains of MRSA with erythromycin resistance and constitutive (ie, non-inducible) clindamycin resistance.

Two other recent Australian studies found erythromycin resistance in 13 of 153 and three of 29 isolates of non-multiresistant MRSA, respectively.^{3,6} These studies did not report clindamycin susceptibilities, and it was not clear what proportion of the isolates belonged to phage patterns WSPP1 or WSPP2, or were community-acquired.

As clindamycin has been recommended as a therapeutic option for soft-tissue and bone infections caused by non-multiresistant MRSA, this finding of inducible clindamycin resistance has important implications. Microbiology laboratories should screen for inducible clindamycin resistance in erythromycin-resistant strains, and, if found, an alternative antibiotic should be used for treatment.⁷ Alternatively, rather than assessing inducible clindamycin resistance with a disc-approximation test, some laboratories may prefer to report all erythromycin-resistant strains as clindamycin-resistant. Also, given the increasing incidence of community-acquired MRSA infection in Australia, all suspected staphylococcal infections that are not responding to empiric therapy with β -lactam antibiotics should be swabbed for culture.

Acknowledgement: We thank the Ipswich Hospital Foundation for financial support.

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Time for a grant category for curiosity-based research

Gordon L Ada,* Frank Fenner†

*Professor and †Visiting Fellow, Division of Immunology and Cell Biology, The John Curtin School of Medical Research, Australian National University, GPO Box 334, Canberra, ACT 2601
gordon.ada@anu.edu.au

TO THE EDITOR: We strongly support the proposal¹ that it is time to create a special grant category for curiosity-based research proposals. Having been in biomedical research for over 50 years, we have experienced a period when most research was curiosity based. We can thus compare with the present situation — research aiming for a rapid, practical and commercial outcome has become almost a necessity for survival because of the increasingly severe reduction in government funding for universities and research institutes. We would like to illustrate the value of curiosity-based research with a few Australian examples from our own fields.

In 1946, one of us (F F) was working on the experimental epidemiology of the causative agent of infectious ectromelia of mice (related to vaccinia virus). A chance observation — that the mice which survived the infection developed a skin rash — led to further study of the virus as a model for smallpox, measles and chickenpox infections. Thus, unexpected discoveries were made about the way the virus spreads through the body during the incubation period of these diseases.²

In 1951, myxomatosis spread in rabbits in the Murray-Darling basin of south-eastern Australia. The virus was initially extremely virulent (99% fatal), but the rabbits slowly developed genetic resistance. One of us (F F) studied the virus for 15 years, and this work was acknowledged as the best example of the co-evolution of viral virulence and host resistance.³

In 1957, Macfarlane Burnet proposed the clonal selection theory of antibody formation — that individual B lymphocytes made antibody of a single specificity.⁴ This was one of the most original concepts ever proposed in biology and it took 10 years to be widely accepted. It has since led to the production of monoclonal antibodies,

which are used as basic reagents in research and diagnostic laboratories, and are now being used in immunotherapy.

In the 1970s, Peter Doherty and Rolf Zinkernagel studied the role of the newly discovered cytotoxic T cells (which could lyse virus-infected cells) to find out how T cells recognised the infected cells. They showed that killing was restricted by the major histocompatibility complex (MHC) and that its role was to signal “altered self” to the T cell.⁵ These studies led to the award of the Nobel Prize in 1996. Cytotoxic T cell activity has since been shown to be the main immune mechanism for controlling and clearing many intracellular infections. Induction of a strong cytotoxic T cell response is the mechanism of candidate vaccines currently being trialled against HIV-1.

In the late 1960s, one of us (G A), together with Chris Parish, showed that a bacterial protein, flagellin, induced antibody tolerance over a wide dose range. Parish was the first to show the inverse relationship between antibody and cell-mediated immune responses, which led others to describe two classes of helper T lymphocytes.⁶ These have been shown to be important in the development of allergy in infants, and offer the opportunity for immunotherapy to reduce the later incidence of allergy.

None of these research programs was initiated with a commercial goal in mind. Benjamin Franklin, when asked about the importance of some research, replied “Of what use is a baby?”.

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