Letters

New Delhi metallo-beta-lactamase-producing Enterobacteriaceae in an Australian child who had not travelled overseas

To the Editor: The editorial by Looke and colleagues in the 18 March 2013 issue of the Journal highlighted the increasing threat of gram-negative resistance.[1] Since its description in 2009,[2] gram-negative bacteria carrying the gene for New Delhi metallo-beta-lactamase-1 (NDM-1) production have been observed globally. To date, a small number of cases have been reported in adults in Australia.[3-5] In all cases, patients travelled to the Indian subcontinent; many required hospitalisation for their infection. We report the first case of NDM-1-producing Enterobacteriaceae in a young infant who had not travelled outside Australia.

An Australian-born 3-week-old boy presented to hospital in 2013 with a 4-day history of cough, rhinorrhoea and vomiting. His mother had visited Pakistan and Afghanistan in 2011 and 2012, respectively. The mother had no relevant medical history and had not attended hospitals in either country. She had lived in Australia exclusively during pregnancy.

Culture of a clean-catch urine sample grew more than 10^8 colony-forming units (CFU) per litre of *Klebsiella pneumoniae* (amoxycillin resistant, otherwise susceptible). The child was diagnosed with a urinary tract infection and treated with ceftriaxone and gentamicin followed by oral combined trimethoprim and sulfamethoxazole (co-trimoxazole). The child's symptoms resolved and imaging showed no structural anomaly.

The child re-presented at 5 weeks of age with irritability and vomiting. A urine sample was taken, and the culture grew $>10^8$ CFU/L of *Enterobacter cloacae*. Susceptibility testing was performed using agar dilution, Vitek2 and Etests (bioMérieux). Using Clinical and Laboratory Standards Institute breakpoints, the isolate was resistant to all β-lactam antibiotics, including meropenem, aminoglycosides, quinolones, co-trimoxazole and nitrofurantoin. The minimum inhibitory concentrations to colistin, tigecycline and fosfomycin were <2 mg/L, <4 mg/L and <16 mg/L, respectively. Polymerase chain reaction-based investigation of β-lactamase production provided positive results for $bla_{\text{NDM-1}}$ and $bla_{\text{CTX-M}}$ genes. The child was successfully treated with oral fosfomycin (100 mg/kg/day).

This case highlights the emerging impact of NDM-1-producing bacteria. Given that the likely source was the mother or another household contact, this is an example of vertical or horizontal transmission in a country with low community prevalence of NDM-1-producing bacteria. In addition to an increased risk for patients previously receiving medical care overseas or returning from countries where there is a high risk of infection with gram-negative bacteria producing NDM-1, their children and household contacts are also at increased risk.

Christopher C Blyth Paediatric Infectious Diseases Physician and Clinical Microbiologist[1,2]

Lynette Pereira Microbiology Registrar[2]

Namraj Goire Senior Scientist[3]

1 School of Paediatrics and Child Health, University of Western Australia, Perth, WA.

2 PathWest Laboratory Medicine WA, Princess Margaret Hospital for Children, Perth, WA.

3 Department of Microbiology, PathWest Laboratory Medicine WA, QEII Medical Centre, Perth, WA.

Christopher.Blyth@uwa.edu.au

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> "The 'publish or perish' culture is perhaps one important factor cultivating this contamination of scientific literature"
>
> Xu et al

Caveat emptor: the corruption of open access scientific publishing

To the Editor: Since our publication in the Journal,[1] it would seem that a simple case report lead-authored by an intern has rendered him a virtual expert in the fields of infectious diseases, cell biology and cardiology, just to name a few. Or at least, one could be led to believe so with the sheer number of enticing invitations received in our corresponding author's inbox (about five per week), inviting his "eminent self" to write journal articles, sit on editorial boards, and speak at international cardiology conferences in far-reaching and exotic locations such as Guangzhou and Dubai.[2]

Such is how the rapidly expanding and controversial entity of "predatory publishing" is luring unsuspecting authors into submitting their research — either legitimate or decidedly sub-par — to a host of open access journals with more pecuniary than academic interest.[3] Once copyright is transferred, an invoice of thousands of dollars may be bestowed before publication can proceed. Jeffrey Beall, academic librarian and curator of a growing "black list" of these journals, lists 285 such publications

on his website, Scholarly Open Access (http://www.scholarlyoa.com), at last count. This contrasts a corresponding "white list" compiled by industry directories such as Open Access Scholarly Publishers Association and Directory of Open Access Journals.

The "publish or perish" culture is perhaps one important factor cultivating this contamination of scientific literature. Less scrupulous authors looking to "pad" their curriculum vitae may be drawn to the lacklustre peer review or disinterest in true scholarly value of these journals. An exposé recently published in *Science* documented a 70% acceptance rate of a spoof paper filled with methodological and ethical flaws, outlandish results and poor grammar, which was submitted to a sample of open access journals purporting peer review processes.[4] Disappointingly, this included 45% of journals on the putative "white list".

Despite these issues, many strongly believe that the revolution of open access publishing represents the future of academia and a necessary counterpoint to "luxury journals", by publishing work according to quality rather than arbitrary caps, and increasing the accessibility of scientific information worldwide.[5] In this context, we seek only to remind the open access consumer of the age-old adage, "caveat emptor".

Lileane Liang Xu Resident[1]

Anthony Minh Tien Chau Registrar[2]

1 Orthopaedics, Liverpool Hospital, Sydney, NSW.

2 Neurosurgery, Macquarie Neurosurgery, Sydney, NSW.

amtchau@gmail.com

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It's time for clinical guidelines to enter the digital age

To the Editor: We agree with Olver and Von Dincklage on the need to move towards digital guidelines.[1]

The National Stroke Foundation (NSF) has been developing guidelines for approval by the National Health and Medical Research Council (NHMRC) for the past 8 years. By the time a guideline has been developed, submitted to the NHMRC and then released (a process that takes about 2 years), there will be new evidence that will change some recommendations (eg, new evidence for blood pressure management in haemorrhagic stroke is not captured in current guidelines[2]).

While we are unaware of evidence that outdated guidelines are a barrier to the implementation of evidence-based care, clinicians express concern about guidelines that are not up-to-date and are likely to affect patient care.[3] We agree that better use of electronic platforms is both inevitable and beneficial for the reasons outlined by Olver and Von Dincklage.[1] Online platforms also provide the vehicle for international collaboration and sharing of information with other guideline developers, thus reducing the time and cost of guideline development while improving transparency and quality.

The NSF is using a staged approach to transition its guidelines onto a wiki-based platform. Initially, we will move the current NHMRC-approved guidelines into an online "document". Until NHMRC processes for approval of a wiki-based guideline are released, the entire guideline will need to be reviewed and approved by the NHMRC in the paper-based form, and then migrated to the online platform for implementation. This will be a costly and complex process, but it is necessary until a nationally accepted standard for developing online guidelines is released.

National standards specifically for digitally produced and maintained guidelines are urgently required.

Richard I Lindley Moran Foundation for Older Australians Professor of Geriatric Medicine[1]

Richard G Larkins President[2]

Erin Lalor Chief Executive Officer[2]

1 Sydney Medical School, Westmead Hospital, University of Sydney, Sydney, NSW.

2 National Stroke Foundation, Melbourne, VIC.

elalor@strokefoundation.com.au

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> "Changes in behavioural risk factors are effective in preventing both pre- and post-menopausal breast cancer, including in women at high genetic risk"
>
> Schultz

The utility of genetics in inherited cancer

To the Editor: In their perspective article, Winship and Tucker highlight the possibility of preventing genetic breast cancer, a triumph of modern medicine.[1] However less than 5% of breast cancer is caused by genetic mutation.[2] The vast majority of breast cancers are not genetic.

Compared with cases of breast cancer with genetic causes, many more cases have environmental causes, including lack of physical activity, overweight and obesity, and alcohol consumption. These are powerful effects: for example, cohort and case–control studies suggest that walking 3–4 hours per week may reduce the risk of breast cancer by around 30%.[3] Smoking is also an important cause of breast cancer, particularly smoking before a woman's first birth.[4]

Effective implementation of established health promotion strategies will prevent breast cancer.[3] Changes in behavioural risk factors are effective in preventing both pre- and postmenopausal breast cancer, including in women

at high genetic risk.[3] These strategies complement screening mammography and targeted strategies for the 1% of women at high risk.[3] Women should be informed that these common behavioural risk factors increase risk of breast cancer, in addition to their effects on other chronic diseases.[5] Population-based health promotion strategies should highlight reduction in breast cancer risk from healthy lifestyles.

Rosalie Schultz Senior Medical Officer

Regional Health Services Division, Central Australian Aboriginal Congress, Alice Springs, NT.

rosalieschultz20a@gmail.com

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Growing the clinical academic workforce: the case for structured academic training programs for junior doctors

To the Editor: In response to an emerging mismatch between supply and demand for academic clinicians,[1] several organisations have highlighted the potential value of an explicit clinical academic training pathway for Australian medical graduates.[1,2] An initiative of this nature would not only increase educational capacity, but would also help realise the aspirations of the McKeon Review of Health and Medical Research — to achieve and sustain health care excellence through training and retaining a world-class medical research workforce.[3]

While a longitudinal academic training program spanning different specialties is unlikely to eventuate in the short term, supporting prevocational trainees to undertake research and teaching activities is a critical first step. Interest in academic medicine wanes during the early postgraduate years, and targeted initiatives are needed to break down the barriers to clinical academic careers.[1,4]

An instructive example is the academic stream of the United Kingdom's Foundation Programme for medical graduates, which supports around 450 junior doctors per year to develop skills in research, teaching and leadership. Academic activities are "protected" and take place either concurrently or in sequence with clinical roles. A variety of projects (from lab-based research to health leadership initiatives) are on offer, and all participants have access to supervision, mentoring and academic infrastructure. The program was strongly commended in a recent evaluation report.[5]

The UK academic Foundation Programme provides a model that could be adapted for Australia. Although there are important barriers to reform (including geographical diversity in models of prevocational training; competing clinical service demands; suboptimal integration between universities, health services and funding partners; and resource constraints), the impending introduction of activity-based funding for teaching, training and research might provide an opportunity to tackle some of these problems. The success of the Australian General Practice Training program's academic rotation shows that these kinds of initiatives are feasible in the local context.

Patients, senior clinicians and trainees all stand to benefit from a stronger clinical academic workforce. Although there are other important barriers to the recruitment and retention of academic clinicians (including demands of clinical practice, job insecurity and pay inequity), supporting junior doctors to undertake academic activities is a strategy worthy of strong consideration.

"Patients, senior clinicians and trainees all stand to benefit from a stronger clinical academic workforce"

Eyre et al

Harris A Eyre PhD Candidate[1]

Rob D Mitchell Registrar[2]

William J Milford Senior Registrar[3]

1 Discipline of Psychiatry, University of Adelaide, Adelaide, SA.

2 Emergency Department, Townsville Hospital, Townsville, QLD.

3 Department of Obstetrics and Gynaecology, Mater Mother's Hospital, Brisbane, QLD.

harris.eyre@gmail.com

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Changes in alcohol consumption in pregnant Australian women between 2007 and 2011

To the Editor: I refer to the article by Cameron and colleagues.[1] As a member of successive Therapeutic Goods Administration Advisory Committees on Prescribing Medicines in Pregnancy (1989–2005), I thoroughly endorse the authors' concerns about the teratogenic effects of excessive alcohol consumption during pregnancy, and support wholeheartedly the advice that, ideally, avoiding alcohol during pregnancy is best.

However, I am concerned that, as stated in my submission to the National Health and Medical Research Council (NHMRC),[2] the current guidelines rely on poorly designed studies to support the implication that there are residual risks to the fetus from a pregnant woman consuming alcohol at a low level, by advising: "The risk to the fetus from low level drinking is likely to be low".[3] A large recent prospective cohort study conducted in the United Kingdom did not produce evidence of harm with low-level use.[4]

When women are provided with advice after intermittent low-level exposure to alcohol in pregnancy, they must also be given reassurance to avoid the prospect of unnecessary anxiety or contemplation of unwarranted termination.

Significantly, peak overseas health advisory groups, including the National Institute for Health and Care Excellence in the UK, and obstetric organisations in the United States and Canada have expressed concern about the potential for unwarranted terminations being contemplated by women following low-level alcohol use in pregnancy. The Society of Obstetricians and Gynaecologists of Canada have specifically published reassuring advice: "Health care

providers should advise women that low-level consumption of alcohol in early pregnancy is not an indication for termination of pregnancy".[5] The time is overdue for the NHMRC to provide a similar statement to provide greater reassurance to women who have consumed low levels of alcohol during pregnancy.

Ronald P Batagol Obstetric Drug Information Consultant

Melbourne, VIC.

healthy5555@hotmail.com

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Prevention of fetal alcohol spectrum disorders must include maternal treatment

To the Editor: There is an increased focus on fetal alcohol spectrum disorders (FASD) in Australia with population prevention strategies and innovative work to improve detection and diagnosis of FASD, particularly in Indigenous communities.[1] However, there has been insufficient focus on treatment for women with alcohol dependence, and this is where risk of harm is highest.

Despite evidence to suggest a decline in the number of Australian women drinking during pregnancy, the proportion drinking at high levels remains unchanged and treatment coverage for this group poor.[2] It is estimated that 3.7% of Australian women will meet the criteria for an alcohol use disorder in a given year,[3] yet only 8.5% will obtain any treatment.[4] Given that only a minority of these women will be pregnant, it suggests even poorer coverage for this group. Antenatal care is also compromised. Hospital data suggest that women with alcohol use disorders during pregnancy present late to antenatal care and are often unbooked at delivery.[5] Thus, targeted interventions and treatments are urgently required.

A lack of ambulatory services and dedicated detoxification facilities that will admit pregnant women, services that accommodate women with other children and the substantial stigma associated with alcohol use in pregnancy all remain significant barriers to treatment.

Unlike opioid substitution therapy, no pharmacological interventions, other than vitamins, are available for pregnant women who are alcohol dependent. Effective psychosocial approaches are also not routinely available. There is a need for high-quality intervention research.[5]

In addition to public health initiatives to prevent FASD, identification and treatment of alcohol dependence in pregnancy must be improved. Midwives, obstetricians and other professionals in primary and acute care need appropriate training in routine screening for alcohol use. Availability and access to services need to be improved, with clear pathways to care.

We know outcomes are far worse for women with alcohol dependence and their babies alike, with higher than expected rates of morbidity and mortality in both groups.[1] Alcohol dependence is a chronic relapsing disorder, and more needs to be done to treat women as a component of any effort to prevent FASD. Without this, prevention campaigns are neglecting one of the most vulnerable and high-risk groups in society; surely we can and must do much better than that.

> "When women are provided with advice after intermittent low-level exposure to alcohol in pregnancy, they must also be given reassurance"
>
> Batagol

Lucy Burns Associate Professor[1]

Courtney Breen Research Fellow[1]

Adrian J Dunlop Area Director of Drug and Alcohol Clinical Services[2]

1 National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW.

2 Hunter New England Local Health District, NSW Health, Newcastle, NSW.

l.burns@unsw.edu.au

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Pathways to enhancing the quality of stroke care through national data monitoring systems for hospitals

To the Editor: Stroke care can only benefit from an integrated system for monitoring the quality of hospital care. However, in Cadilhac and colleagues' article,[1] there appears a significant omission regarding the importance of correctly categorising stroke subtypes.

Categorising and including stroke subtypes is important, as the term stroke is poorly defined in the literature,[2] and the advent

of thrombolytic treatment has focused global research and public awareness campaigns on ischaemic events with the emphasis being on time to treatment and the provision of care within stroke units. The result of this has been a plethora of literature that identifies stroke solely with ischaemic events. The effect of this narrowed definition has been to focus attention and guidelines on ischaemic stroke, thereby disengaging other stroke subtypes that are generally not managed in mainstream stroke units, including haemorrhagic events and aneurysmal subarachnoid haemorrhage (aSAH), from being a "stroke".

To avoid the misrepresentation of stroke as primarily an ischaemic event, haemorrhagic events need to be acknowledged in the literature. A clear context statement or definition of stroke will remove the ambiguity from the inclusion or exclusion of haemorrhagic events, particularly aSAH, in research and more significantly, in national data monitoring systems.

While the paper highlights that "much can be gained from bringing together diverse groups with a vested interest in a single, clinical population", the population of haemorrhagic stroke patients must first be recognised and included.

Linda J Nichols Lecturer and Unit Coordinator, Neuroscience Nursing[1]

Lindsay Smith Lecturer[2]

Penny L Allen Research Fellow[3]

1 School of Health Sciences, University of Tasmania, Hobart, TAS.

2 School of Health Sciences, University of Tasmania, Launceston, TAS.

3 Rural Clinical School, University of Tasmania, Burnie, TAS.

linda.nichols@utas.edu.au

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In reply: We thank Nichols and colleagues for highlighting the heterogeneity of conditions underlying acute stroke, and the associated variability in risk factors, prognosis and management. The management of haemorrhagic forms of stroke, namely spontaneous intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH), has traditionally been focused on neurosurgical intervention to decompress the mass effect of the haematoma, relieve intracranial pressure, and reduce the risk of re-bleeding. The Australian Stroke Clinical Registry (AuSCR) and the National Stroke Foundation national audit include cases of ICH since care quality and outcomes may differ for patients with ICH compared with those with ischaemic stroke.[1] Since few ICH cases require neurosurgery,[2] evidence for better medical management of ICH is needed (eg, early intensive blood pressure lowering treatment).[3] Therefore, ICH must continue to be part of national monitoring of stroke care. Current national monitoring excludes cases of SAH since it remains firmly a "neurosurgical" condition. A separate national SAH registry to monitor process of care may be warranted, given that epidemiological data show stable rates and outcomes for the disease over recent decades.[4,5] Stroke is a complex disease for which continued efforts to monitor and improve care provide the best opportunity to improve outcomes.

Dominique A Cadilhac Head[1,2]

Craig S Anderson Senior Director,[3] and Professor[4]

1 Translational Public Health and Evaluation Unit, Stroke and Ageing Research, Southern Clinical School, Monash University, Melbourne, VIC.

2 Public Health, Stroke Division, Florey Institute of Neuroscience and Mental Health, Melbourne, VIC.

3 Neurological and Mental Health Division, The George Institute for Global Health, Sydney, NSW.

4 Stroke Medicine and Clinical Neuroscience, University of Sydney, Sydney, NSW.

dominique.cadilhac@monash.edu

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> A separate national subarachnoid haemorrhage registry to monitor process of care may be warranted
>
> Cadilhac et al

Proportionate research funding based on relative burden of conditions of communication and swallowing

To the Editor: Bourne and colleagues[1] describe an important disconnect between the relative burden of musculoskeletal conditions and investment in clinical research in Australia. A similar disproportionate allocation of funding is looming in conditions of communication and swallowing, which affect one in seven Australians.[2] These disorders typically concern vulnerable populations of early development and ageing, including those with autism, stroke and neurodegeneration.

To examine the alignment between disease burden and research investment, we conducted a database search of National Health and Medical Research Council (NHMRC) and Australian Research Council (ARC) funding over a 10-year period (2004–2013), focusing on grants for research into communication and swallowing disorders.[3] Grants included those for people support, projects, programs, and linkage and discovery. Of the 12 000 grants awarded by the NHMRC and ARC, 154 met the criteria for

communication and swallowing disorders. The monetary value of these grants totalled about $61 million (1.1% of all funding awarded). Funding for hearing impairment research (42%) represented the bulk of the grants, followed by funding for stuttering (17%), language (16%), speech (7%), literacy (3%) and swallowing (3%). Mixed-focus research accounted for 12% of funding.

In acknowledgement of the significant burden of communication and swallowing conditions in Australia, the federal government has initiated a Senate inquiry into the health, social and economic impact of these conditions.[4] The inquiry's remit is to investigate (i) the prevalence of communication and swallowing disorders; (ii) the availability, adequacy and projected demand of speech pathology services provided by all sectors (public and private); and (iii) the social and economic cost of failing to treat these conditions.

These data, along with studies by Bourne and colleagues[1] and Mitchell and colleagues,[5] signal the need for further consideration of the way in which medical and health dollars are allocated by Australia's premier funding agencies. The Senate inquiry may offer an opportunity to explore the role of proportionate research funding based on burden of disease within a group of disorders that are vastly underrepresented in the current grant environment.

Adam P Vogel Senior Research Fellow

Sarah E Plant Speech Pathologist

Speech Neuroscience Unit, University of Melbourne, Melbourne, VIC.

vogela@unimelb.edu.au

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> "conditions of communication and swallowing … affect one in seven Australians"
>
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