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Fungal endophthalmitis in intravenous drug users injecting buprenorphine contaminated with oral *Candida* species

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TO THE EDITOR: Within the last 12 months, four injecting drug users (IDUs) who had been injecting buprenorphine presented to the Royal Victorian Eye and Ear Hospital with endogenous fungal endophthalmitis (EFE) involving *Candida* species. All four patients admitted that they had diverted or obtained diverted sublingual buprenorphine from the oral cavity after it was dispensed. They had dissolved the remaining drug in water and injected it intravenously. We present an illustrative case.

A 28-year-old woman presented with a 4-week history of left eye pain and erythema. She had a 10-year history of intravenous drug use. Over the previous 6 months, she had been regularly injecting buprenorphine that was prescribed to a friend. The friend had been removing the partially dissolved buprenorphine from his mouth before giving it to our patient. On examination, the patient could only detect hand movement with her left eye. Fundoscopy showed vitritis with a "snow ball appearance" consistent with EFE.

Treatment involved vitrectomy, intravitreal amphotericin and oral fluconazole. *Candida albicans* was cultured from vitreal specimens. Her visual acuity had improved to 1/60 at the time of discharge.

Intravenous drug use is known to be a risk factor for EFE. *Candida* species are the usual causative organisms, but *Aspergillus* species have also been reported.¹ In the 1980s, there were many reports of candida endophthalmitis in injecting drug users associated with the use of "brown" (or Iranian) heroin. The "brown" heroin required an acidic substance, often lemon juice, as a solvent. Lemon juice was shown to be the source of the candida.² However, over the past 10 years, the heroin available in Australia has been water soluble, and sterile or tap water is usually used to dissolve the heroin before injection. None of the cases we report in this letter involved lemon juice

to dissolve heroin or buprenorphine before injection.

Buprenorphine has been available in Australia since 2001 for the treatment of opiate addiction. It is usually dispensed daily by pharmacies in a crushed tablet form. Pharmacists are required to watch patients place and dissolve the medication under the tongue before they leave the pharmacy.

Contamination of injected buprenorphine with orally derived *Candida* species presents a recently recognised cause of fungal endophthalmitis in injecting drug users.³ Doctors, pharmacists and drug users need to be aware of the risk of this sight-threatening complication.

Acknowledgements: We thank Dr Adam Jenney for his very helpful editing, Miss Rowena Fary for advice about buprenorphine dispensing and Dr CH Khong for assisting with clinical information about the patients.

- 1 Essman TF, Flynn HF, Smiddy WE, et al. Treatment outcomes in a 10-year study of fungal endophthalmitis. *Ophthalmic Surg Lasers* 1997; 28: 185-194.
- 2 Newton-John HF, Wise K, Looke DF. Role of the lemon in disseminated candidiasis of heroin abusers. *Med J Aust* 1984; 140: 780-781.
- 3 Cassoux N, Bodaghi B, Lenoang P, Edel Y. Presumed ocular candidiasis in drug misusers after intravenous use of oral high dose buprenorphine (Subutex). *Br J Ophthalmol* 2002; 86: 940-941. □

Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose

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TO THE EDITOR: Two aspects of the recent article by Kelly et al comparing intranasal with intramuscular naloxone in suspected opioid overdose¹ make their study difficult to interpret. The methods allowed for a great deal of bias. There was no attempt to blind evaluators to therapy, and knowing which therapy is to be used *a priori* may influence both therapy selection and perceived outcome.

The second flaw we noted was the use of the Glasgow Coma Scale (GCS) in a non-trauma patient.² An improvement in GCS score may represent increased wakefulness or even withdrawal. The use of the GCS does not make it possible to determine what

degree of improvement or worsening the therapy resulted in. In the opioid-intoxicated patient, the "alert/verbal/pain/unresponsive" (AVPU) scale is more appropriate.

We agree that the use of needles in a high-risk patient is dangerous. However, if these patients do not respond to painful stimuli, there should be no danger at all.

- 1 Kelly AM, Kerr D, Dietze P, et al. Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose. *Med J Aust* 2005; 182: 24-27.
- 2 Fulton JA, Greller HA, Hoffman RS. GCS and AVPU: the alphabet soup doesn't spell "C-O-M-A" in toxicology. *Ann Emerg Med* 2005; 45: 224-225; author reply 225. □

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IN REPLY: The prehospital setting for research poses challenges that require some flexibility in study design. While it would have been preferable to have used blinded naloxone and placebo solutions for both routes of administration in our study, financial and operational constraints made this impossible, so some bias in evaluations is possible. However, this is not necessarily in favour of the intranasal route, as before the study many paramedics were very sceptical about the intranasal naloxone preparation. Therapy selection was by random allocation in sealed envelopes as described in our article.

The Glasgow Coma Scale score was chosen as an outcome measure because it was the parameter used operationally for treatment and disposition decisions in the ambulance service within which our study was conducted. We acknowledge its limitations in non-trauma patients.

The potential for needlestick injury in this situation is real. Patients with opioid intoxication may be in cramped locations and may be irritable on waking, increasing the risks involved with handling a "sharp". Given the prevalence of blood-borne viruses in the injecting drug user population, strategies to reduce the risk of needlestick injury are highly desirable. Additionally, a strategy that has been suggested for preventing opioid-overdose-related deaths is to make naloxone more widely available in the community.¹ The intranasal formulation of naloxone may be appropriate for this, as it has significant advantages including reducing risks of

blood-borne virus transmission and minimising the requirement for training and the secure storage of syringes and needles.²

1 Dettmer K, Saunders B, Strang J. Take home naloxone and the prevention of deaths from opiate overdose: two pilot schemes. *BMJ* 2001; 322: 895-896.

2 Fry C, Dietze P, Crofts N. Naloxone distribution: remembering hepatitis C transmission as an issue. *Addiction* 2000; 95: 1865-1866. □

Evidence-based policy making?

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TO THE EDITOR: With increasing attention focused on the need for evidence-based policy making in recent years, researchers have come to the realisation that research has, in fact, little impact on policy making. The literature abounds with theories on how to improve the appropriate use of research evidence in policy decisions.

Researchers must shoulder a large proportion of the responsibility, having spent too much energy generating evidence and insufficient time “translating” this knowledge into a useful product for decision makers.¹ Further, the failure of the two communities to communicate has allowed researchers to follow their own agendas, rather than those of the potential users of their research.² Improved two-way communication between researchers and policy makers may improve the uptake of research evidence.³ This is best achieved by supporting policy makers to utilise evidence and researchers to become more policy-sensitive.

However, even when evidence has been “translated” and acknowledged, it is still subject to other forces. There are numerous

barriers to evidence-based policy making, not the least of which is politics.

For example, Stevenson recently highlighted the fact that young drivers are disproportionately represented in road trauma statistics.⁴ He presented data on a number of interventions that have successfully reduced fatal and injurious crashes involving young drivers. Similar data were presented by the NSW Government in its options paper on improving safety for young drivers, which was put out for community consultation in late 2004.⁵ So far, a policy decision has been made on only two out of 11 options. One decision, which prohibits provisional (P1) licence holders from driving high-performance cars, has, by the Government's own admission, no supporting evidence of effectiveness.⁵ The other decision places a limit of one passenger for 12 months for drivers who lose their provisional (P1 or P2) licence. However, this decision is a variant of a strategy that is supported by evidence, and consequently may have little or no effect.

Researchers need to be aware that social, electoral, ethical, cultural and economic factors have a powerful influence on policy.⁶ While the literature on evidence-based policy exhorts researchers and policy makers to work on bridging the gap between evidence and policy, the role of other key players (such as the public) has tended to be overlooked.⁷

As part of a National Health and Medical Research Council capacity-building grant in population health research, a consortium of academic institutions is working on enhancing the interface between injury research and policy and on promoting evidence-informed policy in injury prevention. (Members of the consortium are the NSW Injury Risk Management Research Centre, the School of Public Health and Community Medicine, and the Prince of Wales Medical Research Institute [all of the University of NSW]; and the Rehabilitation Studies Unit and George Institute for International

Health [of the University of Sydney]). The role of the public as an audience with which researchers might profitably interact to improve dissemination and uptake of evidence will be explored, as will the role of health journalists in facilitating this.

1 Choi BCK. Understanding the basic principles of knowledge translation. *J Epidemiol Community Health* 2005; 59: 93.

2 Hanney SR, Gonzalez-Block MA, Buxton MJ, Kogan M. The utilisation of health research in policy-making: concepts, examples and methods of assessment. *Health Res Policy Syst* [online journal] 2003; 1: 2. Available at: <http://www.health-policy-systems.com/content/1/1/2> (accessed Mar 2005).

3 Innvaer S, Gunn V, Trommald M, Oxman A. Health policy-makers' perceptions of their use of evidence: a systematic review. *J Health Serv Res Policy* 2002; 7: 239-244.

4 Stevenson MR. Steering in the right direction? Young drivers and road trauma. *Med J Aust* 2005; 182: 102-103.

5 NSW Roads and Traffic Authority. Improving safety for young drivers. An options paper for community comment. November 2004. Available at: <http://www.youngdrivers.com.au/home.html> (accessed Feb 2005).

6 Black N. Evidence based policy: proceed with care. *BMJ* 2001; 323: 275-278.

7 Lomas J. Improving research dissemination and uptake in the health sector: beyond the sound of one hand clapping. Hamilton, Ontario: McMaster University Centre for Health Economics and Policy Analysis, 1997. □

The Nobel Prize and mainstream medicine

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TO THE EDITOR: I am amazed by your assertion in your recent column in the Journal that many clinicians fail to equate advances in basic research to advances in clinical medicine.¹ I would therefore like to make some small contribution to your understanding of the work of Richard Axel and Linda Buck, 2004 Nobel laureates in Physiology or Medicine,² and why this was considered worthy of the Nobel Prize.

Our understanding of the nervous system is still very primitive, and their almost complete description of the functioning of the odorant system — a small part of the nervous system — has laid down many of the principles pertinent to the more complex fundamentals for understanding neuronal signalling and signal processing. This is essential to an understanding of neurological and psychiatric diseases. The odorant receptors are also G-coupled protein

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kinases, and this is one of the most frequently targeted groups of compounds for novel small-molecular therapies.

If anyone still believes that Nobel Prize-winning science, such as understanding neuronal circuitry, is irrelevant to clinical medicine, they might look at the 2003 recipients for the Nobel Prize in Physiology or Medicine, Paul Lauterbur and Peter Mansfield. They received the award for the discovery of magnetic resonance imaging, which clearly plays a role in "mainstream" medicine.

1 Van Der Weyden MB. The Nobel Prize and mainstream medicine [From the Editor's desk]. *Med J Aust* 2005; 182: 145.

2 Nobelprize.org. Available at: <http://nobelprize.org/> (accessed Mar 2005). □

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IN REPLY: I welcome Foote's comments, but, to the contrary, I find it entirely credible that many clinicians "fail to equate advances in basic research to advances in clinical medicine." The reasons are many, but include not only the tortuous language of research,^{1,2} but also the scepticism that inevitably follows research announcements of "cures" and "breakthroughs", which prove to be patently premature or just peter out.³

However, I am amazed that Foote appears to have missed the point of my column — the "narrowness of the Nobel awards for physiology or medicine" with their recent predominance of basic research.⁴

While it must be admitted that the Nobel Prize is increasingly awarded for what is undoubtedly outstanding basic research that has the potential to be of "greatest benefit for mankind", much of this potential remains unrealised. Indeed, it was the need for recognition of clinical and epidemiological research in the Nobel awards that moved the *Lancet*, in its *Paper of the year 2004*, to seek sponsorship for the clinical equivalent of the Lasker and Nobel awards.⁵

In summary, it is research's exclusivity, the rise of its false prophets, and the irrelevance of most recent Nobel Awards to everyday practice that fuel disinterest among clinicians.

1 Dixon B. Plain words please. *New Scientist* 1993; 137: 32-40.

2 Gutterman JU, Rosen RD, Butler WT, et al. Immunoglobulin of tumor cells and tumor-induced lymphocyte blastogenesis in human acute leukemia. *N Engl J Med* 1973; 288: 173-175.

3 Ooi ES, Chapman S. Analysis of newspaper reports of cancer breakthroughs: hope or hype. *Med J Aust* 2003; 179: 639-654.

4 Narrowness of Nobel awards for physiology or medicine [editorial]. *Lancet* 1999; 346: 1399.

5 Paper of the year 2004. *Lancet* 2004; 364: 2166. □

Continuous improvement and "Continuous Improvement"

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TO THE EDITOR: The personal perspective on continuous improvement outlined by Kilham succinctly documents the concerns surrounding the application of management tools to the practice of medicine.¹ As Kilham says, continuous improvement has been around for a long time and "flowed from a particular attitude . . . [that of] a mind open enough to recognise better ways of doing things, or ways of doing better things".¹

However, I would argue that even history-taking does need to continually improve to include various communication skills appropriate to individual patients. Continuous improvement in history-taking skills, to enable each patient to express their major concerns and to feel more in control of the consultation, has significantly reduced my feelings of frustration provoked by previous patients. Adherence to the strict script of history-taking taught to me in my undergraduate training seemed to provoke a rejection of the expert advice I was giving them.

Management does need to understand the importance of recognising good work already done and the current high achievements of medical practitioners. On the other hand, even the busiest of clinicians should understand the professional advantage of participation in a project to further improve or develop new ways of solving their patients' problems. There are multiple strategies needed for the effective "change from the existing entrenched structure and culture of patient care to one based on patient-

centred, evidence-based care".² However, management certainly needs to support the busy clinicians during the project. It is also better to avoid jargon and the constant renaming of programs. I would argue that the learning principle underlying the range of continuous improvement programs is the same. That principle is to question, accept challenges, explain, justify and seek further information as a continuous process.³

One essential feature of continuous improvement (whatever it is called) is that the practitioner needs to participate in the selection of the project for continuous improvement and the objective outcome measures that will prove the change to be advantageous or not advantageous. It is also important to recognise that successful continuous improvement programs in one context do not necessarily translate to another context.

I agree that management must accept the same standards and accountability demanded of clinicians. In addition, all clinicians should participate in continuous improvement projects as well as being assured that we currently practise medicine at a high standard.

1 Kilham HA. Continuous improvement and "Continuous Improvement". *Med J Aust* 2005; 182: 119.

2 Leigh JA, Long PW, Barraclough BH. The Clinical Support System Program: supporting system-wide improvement. *Med J Aust* 2004; 180 (10 Suppl): S101-S104.

3 Resnick LB, Williams Hall M. Learning organizations for sustainable education reform. *J Am Acad Arts Sci* 1998; 127: 89-118. □

Medical humanities: to cure sometimes, to relieve often, to comfort always

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TO THE EDITOR: Gordon, Director of the Centre for Medical Humanities at the University of Sydney, suggests that "the separation of clinical care from the 'human sciences' is a professional and social mistake", and that "the arts, humanities and social sciences act as a counterbalance to the relentless reductionism of the biomedical sciences".¹ Her university now offers a Masters in Medical Humanities and the opportunity to study subjects such as *Medicine and war* and *Medicine and music*.

Gordon suggests that study of the medical humanities could result in "a more insightful



view of the patient, the doctor and the health care system, and an enhanced capacity to cure, relieve and comfort", and that "history, philosophy and sociology warn that the person with the disease is all too easily reduced to the non-hygienic, non-rational, disordered 'other'", while "the growth of medicine as an economic and rational profession has paradoxically contributed to the social diminution of the body, the very object of its focus".¹

This warrants a response more elegant than the earthy Australian expletives that come to mind. That master of teasing irony, Jane Austen, makes gentle fun in *Emma* of educational establishments "which professed, in long sentences of refined nonsense, to combine liberal acquirements with elegant morality upon new principles and new systems".²

In an article entitled *Medicine and literature*, UK medical historian Neve argues "there are numerous difficulties tracing the connections between two vast areas of human effort that may not be easily twinned" and that "the desire to twin them may be an ambition more attractive to medical practitioners than to writers and artists".³ Doctors may yearn to counter a modern perception that they are mere technicians, some by seeking to reclaim a lost identity as the last of the humanists. Neve provocatively suggests that for many modern practitioners, often "their cases are routine, unglamorous, and socially explicable in matter-of-fact terms".³

Maybe the best approach to the humanities for anyone, including doctors, lies somewhere between the sermonising of Gordon and the temptations of escapist fantasy, such as those offered by the master of ceremonies in the movie *Cabaret* with his excuse that "life is disappointing, forget it".⁴

- 1 Gordon J. Medical humanities: to cure sometimes, to relieve often, to comfort always. *Med J Aust* 2005; 182: 5-8.
- 2 Austen J. *Emma*. New York: Signet Classic, 1986: 40-41.
- 3 Neve M. Medicine and literature. In: Bynum WF, Porter R, editors. *Companion encyclopedia of the history of medicine*. Vol 2. London: Routledge, 1993: 1520-1521.
- 4 *Cabaret*: original soundtrack recording. MCA Records CA, 1972. □

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IN REPLY: It may be possible to identify an approach that lies "somewhere between the sermonising of Gordon", as Coote puts it, and the world-weariness of the master of ceremonies at the Kit Kat Club. Research in the social sciences suggests that we derive more personal happiness from positive experiences, including our social and intellectual pursuits, than from material possessions. These findings are probably due to the fact that positive experiences generate pleasant memories and a richer sense of personal identity. Positive experiences also have greater social value than possessions, being more easily shared with others.

Thinking and talking about new ideas provides a great deal of pleasure and satisfaction for students in the medical humanities. While mere "cases" may be, as Coote quotes, "routine, unglamorous, and socially explicable in matter-of-fact terms", the doctor-patient relationship is not. Medicine provides a resource which can be used, as philosopher Martyn Evans has pointed out, to reflect on ourselves, express ourselves, develop ourselves, criticise ourselves and encounter ourselves.¹ To do these things, we need tools constructed by the arts and humanities, as well as the sciences. Coote's choice of reading material — the *Companion encyclopedia of the history of medicine*² — is a great place to begin.

- 1 Evans HM. Is medicine a "cultural good"? *Med J Aust* 2005; 182: 3-4.
- 2 Bynum WF, Porter R, editors. *Companion encyclopedia of the history of medicine*. London: Routledge, 1993. □

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