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LETTERS

BAD MEDICINE: PAIN

Ignorance, opioids, and bliss

Spence says: "Pain clinics have pursued a hospital model of care for pain without fully appreciating the implications of generating a 'pain disability' and opioid dependence in the community."[1]

As a practising pain clinician for over 10 years, I have spent most of my time trying to keep patients out of hospitals and away from inappropriate surgery, as well as weaning them off the strong doses of opiates that colleagues, often faced with intense distress and anger (not pain), have prescribed. I have dealt with a host of patients in the community taking persistent and large doses of tramadol hydrochloride and codeine (the general practice drugs of pain dependence) who have been referred for non-specific pain symptoms and distress.

The risks of opioids have been highlighted in documents from the British Pain Society for over 10 years. Whose fault is it if GPs choose not to read them and to be duped by drug companies and a few of their invited speakers? It took 20 years for Spence's local health board to fund a pain management programme, and the lack of multidisciplinary resource in all the pain clinics in Scotland has been highlighted in four national reports. Spence and any of his GP colleagues who are really interested should audit the number of patients in their practices with repeat prescriptions of simple analgesia stronger than 8 mg codeine and get back to me. Then they can stop them all, if they are brave enough, and pay for the physiotherapists, psychologists, and administrative staff who are desperately needed in many pain clinics.

We have made the same mistakes as the Victorians, who took "tincture of opium for neurasthenia." As to who will help patients out of their mess, I think Spence may find that pain clinics have more of a role than he would give them credit for.

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Competing interests: MHB has occasionally spoken on behalf of pharmaceutical companies that market opioid analgesia but not for the past five years.

1 Spence D. Bad medicine: pain. *BMJ* 2010;340:b5683. (6 January.)

Cite this as: *BMJ* 2010;340:c458

Competing interests of professional societies

Spence highlights the vested interests of the huge "pain industry" following the revelation of the sum paid to the American Pain Society by Endo Pharmaceuticals.[1]

The US Institute of Medicine[2] has asked congress to require US companies to report payments not only to doctors but also to healthcare institutions, providers of continuing medical education, patient advocacy groups, and, interestingly, "professional societies." It recommends voluntary reporting until congress acts.

The institute also raised concerns about clinical practice guidelines, where "the risk of undue industry influence ... is significant." It recommends general exclusion of panel members with conflicts of interest and prohibition on direct funding from industry for guideline development. What chance of replicating this guidance in the United Kingdom, particularly by the British Pain Society?

The British Pain Society's guidelines on opioid prescription[3] are published without competing interest statements, though the issue was raised during consultation. The society's financial ties to the drug industry are so substantial that one manufacturer of analgesics advertising in the *BMJ* says that it has developed an educational programme "in collaboration with leading clinicians from the British Pain Society" which has been submitted for accreditation for continuing medical education.[4] The British Pain Society's policy is that participants declare competing interests to the society, but these declarations are not always published for all to see. They should be published, and any funding for the society in general, or guideline development in particular, should be declared.

None of the many pain society members responding to Spence raises the critical issue of pain societies and industry funding. This may be difficult now that specialist societies can support individual people for national excellence awards, but these issues must be addressed if the British Pain Society and its guidelines are to retain credibility.

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Competing interests: LA has been principal investigator for pan-European sponsored clinical trials by Janssen-Cilag. She has participated in several clinical trials sponsored by other pharmaceutical companies, and has also authored expert reports for regulatory purposes, lectured internationally, and participated in expert panels. She continues to provide paid consultancy services to the pharmaceutical industry. She is a shareholder in hd-clinical, an IT company providing internet solutions recognised by Connecting for Health by contract status and currently providing services in 110 trusts. EW provides writing, training, and consultancy services to several drug companies, including some that manufacture analgesics. She is chair of COPE, which recommends full disclosure of all competing interests on publications.

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Cite this as: *BMJ* 2010;340:c470

British Pain Society's policy on competing interests

The British Pain Society has a clear policy that any competing interests should be declared in its publications. The guidelines on the use of opioids for persistent pain to which Allan and Wager refer were first published in 2004. They have recently been revised in collaboration with the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of General Practitioners, and the Faculty of Addictions of the Royal College of Psychiatrists. The new guidance is in the final stages of publication and will be available on the websites of the respective organisations in February 2010. It contains a clear statement of competing interests from the authors.

The competing interests of council members of the British Pain Society are also freely available to any inquirer. The society's policy in this regard is under constant review. The society is always happy to discuss any specific concerns about its relationship with industry, or any other concerns, and follows a strict code of practice.

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Competing interests: JBH is immediate past president of the British Pain Society, board member of the Faculty of Pain Medicine, chair of advisory board and lecturer for Napp Pharmaceuticals, lecturer and principal investigator for Grunenthal, and lecturer for Pfizer.

The guidelines on the use of opioids for persistent pain to which Allan and Wager refer (previous letter) were first published in 2004.

Cite this as: *BMJ* 2010;340:c476

Risks of opioids are underplayed

In Australia the debate highlighted by Spence continues.[1] A draft national pain strategy has already been circulated for the national pain summit in Canberra on 11 March 2010.[2]

Leading participants include professional, consumer, and other organisations, all with varying potential conflicts of interest and standing to benefit from increased pain treatment. These groups include industry advocates and industry representative bodies.

Although a solitary addiction medicine doctor contributed to the draft strategy, the promotion of surveillance for opiate misuse and any advice on pain management in those with a history of substance use disorders were all but missing.

The role of addiction medicine doctors was confined to hospital care to minimise suffering and the duration of stay (goal 4). The only concern noted about long term opiate prescribing concerned "people with predominantly psychological factors contributing to the pain."

The pharmaceutical industry has been highly successful in increasing the indications for prescribing opiates outside cancer and decreasing prescribers' concerns.[3] Whereas doctors would prefer to see themselves as managing pain, they may well be gathering together a quite different population. Recent US findings show that half of the patients with a previous opiate disorder in 2001 were taking long term prescription opiates by 2005.[4]

We should not risk improving pain management by having a cavalier approach towards the risks entailed.

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Competing interests: SMH is a member of working groups looking at pharmaceuticals misuse for both the Alcohol and Drugs Council of Australia and the Royal Australasian College of Physicians.

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Cite this as: *BMJ* 2010;340:c464

THROMBOLYSIS IN STROKE

Example of a health divide?

We read with dismay Choi's personal view about the difference between stroke treatment in London teaching hospitals and in Greater Manchester.[1] In discussing the management of people with acute stroke in the hospital in which he works (Trafford General Hospital) he states that "the whole region is devoid of any concerted system to manage these patients." He also says that "many of the consultants express confusion about their local thrombolytic service even where it exists," and that if he had a stroke he would rather have one in London.

He is clearly unaware of the work of the Greater Manchester Association of Primary Care Trusts, which has jointly commissioned stroke services across the region. The Greater Manchester Cardiac and Stroke Network has established a stroke centre system where all acute hospitals (including Trafford General) are designated stroke centres, with two trusts designated primary stroke centre and one comprehensive stroke centre (Salford Royal Foundation Trust). The primary and comprehensive centres take all patients presenting within four hours of onset for immediate scanning and thrombolysis and other acute treatments where appropriate.

Patients from the Trafford region have been transferred by ambulance directly to the comprehensive stroke centre since 1 December 2008. All acute patients are reviewed on admission by a stroke consultant (available 24/7) with immediate scanning where appropriate. Around 10% of all admissions are now thrombolysed, which compares favourably with other centres in the UK; specifically 16% of all Trafford stroke admissions to our service were thrombolysed between December 2008 and June 2009. The network continues to work to raise awareness locally about stroke among the public and healthcare professionals, has regular thrombolysis training days for clinical staff, and monitors performance and outcome in stroke management across the region through a Network Clinical Governance Programme. Intra-arterial thrombolysis, thrombectomy, vertebral angioplasty, and hemicraniectomy are available and have been delivered for appropriate patients.

The network was awarded the *Health Service Journal* award for world class commissioning in 2009 for its work in acute stroke, and Greater Manchester is leading the way in delivering hyperacute stroke care. We continue to work towards our goal of equal access to high quality acute stroke care for all 3.2 million citizens of Greater Manchester.

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Competing interests: All authors are consultant stroke physicians in the comprehensive stroke centre in Greater Manchester and participate in the work of the Greater Manchester Cardiac and Stroke Network.

1 Choi H. Thrombolysis in acute ischaemic stroke: example of a health divide? *BMJ* 2010;340:c45. (6 January.)

Cite this as: *BMJ* 2010;340:c449

Author's reply

My article was written over a year and a half ago and accepted for publication before the thrombolytic service was formalised on 1 December 2008.[1] Since then, dramatic changes have been made to the regional thrombolytic service, as Tyrrell and others in the comprehensive stroke centre in Greater Manchester have rightly pointed out, and the fast track referral system to the comprehensive stroke centre is now well established as a result of the hard work of all involved at the Greater Manchester Stroke Network.

The matters discussed in the article reflected the regional challenges in introducing the thrombolytic service at the time of writing, and that time only. It was never my intention to offend anyone who is at the forefront of this great service.

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Competing interests: None declared.

1 Choi H. Thrombolysis in acute ischaemic stroke: example of a health divide? *BMJ* 2010;340:c45. (6 January.)

Cite this as: *BMJ* 2010;340:c452

Editor's note: This article was delayed pending legal and other editorial checks.

I'd rather have a stroke in the Netherlands

Choi proclaims that he would rather have a stroke in London,[1] but I was surprised about a door to computed tomography time of 40 minutes (and not even a needle time, which is what truly matters). In our hospital, the neurology registrar sees thrombolysis candidates as soon as they arrive (after having looked at medical information in the computerised records before arrival for exclusion criteria), the nurses do their bit, and after a quick history and examination the scan is performed, in less than 10 minutes. The nurses already have the drug ready when

the neurology registrar approves the scan (a radiologist is rarely needed to exclude blood or tumours) and thrombolysis is administered, sometimes within 20 minutes of arrival. Then angiography is performed, and if the patient does not recover and there is occlusion of the middle cerebral artery or basilar artery, intra-arterial thrombectomy or thrombolysis is considered, at all times of the day.

So, a door to computed tomography time of 40 minutes is better than nothing, but not something to be proud of. Time is brain. One thing is certain: I would rather have a stroke in the Netherlands than in London. I would at least know that all options had been considered.

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Competing interests: None declared.

1 Choi H. Thrombolysis in acute ischaemic stroke: example of a health divide? *BMJ* 2010;340:c45. (6 January.)

Cite this as: *BMJ* 2010;340:c454

It's more about the evidence

Choi laments that, "many clinicians were not familiar with the evidence base behind the benefits of thrombolysis. Without knowing the evidence you cannot wholeheartedly support the proposed service." I would have thought that with knowing the evidence you would be reluctant.

A more detailed analysis of the NINDS data clearly shows that the thrombolysis group had better outcomes.[1] However, there is essentially the same change in the National Institutes for Health stroke scale (NIHSS) score after intervention with either thrombolysis or placebo.[2] Thrombolysis made virtually no difference. The outcome differences resulted from unrelated factors, probably differences in stroke severity at recruitment. Also, no greater change was seen on the basis of time to treatment. The "time is brain" mantra was never suggested in the NINDS trial itself and is a myth. The reanalysis is imperfect, but only because the raw data are. The NIHSS score is not a clinical outcome but it is the only data collected at all time points of the trial. The conclusion that clinical outcome can be improved with no change in NIHSS score is unsupportable. It makes no sense. However, it is consistent with the overwhelming body of evidence from other controlled trials that thrombolysis makes little difference. Stroke physicians tend to ignore those trials.

Maybe some people benefit. But what is the cost of diverting fixed, and maybe declining, resources from interventions for stroke and other conditions where the benefit is clear and the evidence less conflicting?

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Competing interests: None declared.

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Cite this as: *BMJ* 2010;340:c455

Stroke and neurological illness: the real lottery

Stroke is only one of the neurological illnesses that Choi might best have in London.[1] London has four times as many neurologists per head of population than other parts of the country,[2] and patients covered by a London primary care trust are up to six times more likely to be seen in outpatients by a consultant neurologist than those living elsewhere.[3] This disparity comes after 10 years of neurology consultant expansion that has favoured specialist neurology centres rather than the district general hospitals around them. The introduction of the free market may have exacerbated this longstanding national lottery, with neurology provision reacting to demand rather than need. Manchester now has a wonderful stroke thrombolysis service, but many other parts of the country desperately need good thrombolysis and adequate inpatient and outpatient neurology opinion.

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Competing interests: None declared.

1 Choi H. Thrombolysis in acute ischaemic stroke: example of a health divide? *BMJ* 2010;340:c45. (6 January.)
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Cite this as: *BMJ* 2010;340:c457

PRIMARY CARE'S LOST CAUSE?

Not all those who wander are lost

Del Mar claims that primary care researchers once studied basic clinical problems and produced findings directly relevant to front line practitioners but have latterly drifted off course into the study of "processes."[1]

This analysis is superficial and suggests naiveté about who controls the agenda. The direction and underpinning values of primary care research in the UK over the past 40 years have been systematically studied by critical discourse analysis of key policy documents.[2] In short, primary care research is now almost

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exclusively led by politicians, civil servants, and a few senior decision makers within the profession. Research policy is currently powerfully shaped and constrained by talk of the knowledge based economy and the contribution of high technology innovation to UK plc. This discourse has repositioned the core business of primary care research as running a "population laboratory" for large scale epidemiological studies, preferably with a pharmacogenomic component. Such studies are important but they are not the whole story.

The days when general practice researchers explored clinical curiosities and local disease patterns using meticulous observation and kitchen table epidemiology are long gone, but not because we no longer turn out high calibre researchers. It is because the study of single diseases in small, stable, and ethnically homogeneous communities by single practitioners unburdened by the creeping institutionalisation and regulation of research belongs to a bygone era; epidemiology's unanswered questions demand large scale collaborative studies that can be undertaken only within a complex research infrastructure; and non-epidemiological questions relevant to primary care (for example, on the humanistic and social dimensions of illness and healing) are currently defined as a lesser form of science for which only B-list funding and publication outlets are available.[3]

If you don't water a plant, it will wither. Let's stop blaming the plant.

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Competing interests: None declared.

1 Del Mar C. Is primary care research a lost cause? *BMJ* 2009;339:b4810. (18 November.)
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Cite this as: *BMJ* 2010;340:c461

Not lost if it combines medical and social science approaches

Del Mar asks if primary care research is a lost cause.[1] Two institutional realities threaten it. Firstly, medical schools must search for large sums of research money to survive. This results in restructuring of research activity and the pursuit of high earning high technology activities, neither of which fits the preferred agendas of academic general practice.

Secondly, reordering general practice to promote incentivised public health interventions and allowing general practitioners to opt out of out of hours care has seriously compromised continuity and the primacy of patient agendas at general practice consultations.

By accepting these realities, academic general practice has risked losing its intellectual and research identity, and moved into evidence based research at the expense of work on the consultation, patient centredness, and holism, which del Mar—I think wrongly—suggests belongs to the past.

Del Mar referred to my work on prescribing for respiratory illness in the 1970s.[1] My first study was a randomised controlled trial that showed no benefit from antibiotic use in a normally healthy working age male population.[2] I have tried to find out why these findings have had so little effect in changing clinical practice. Work on the consultation and on patient centredness has helped most. I was recently invited to revisit another early study from the 1970s, and to comment on its relevance to modern clinical practice.[3] This has confirmed for me that for general practice research to contribute to the future of medicine in the way patients most need today, it must be through a combination of medical and social science approaches.

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Competing interests: None declared.

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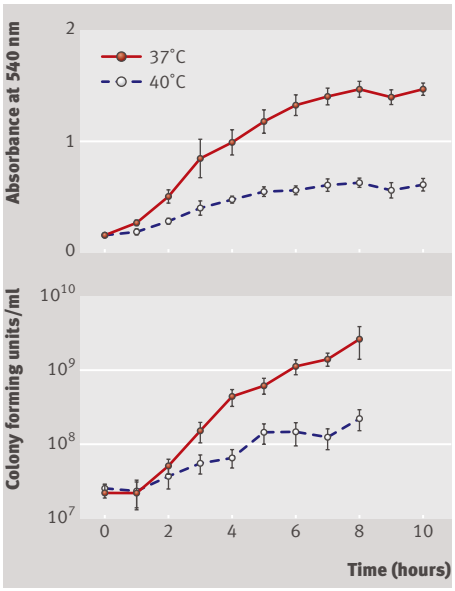
Cite this as: *BMJ* 2010;340:c462

FEVER AS NATURE'S ENGINE

Part of beneficial host response?

Fowler comments on the value of a raised temperature to combat flu.[1] Fever may also be necessary for optimal defence against bacterial infections.[2] We explored this possibility for meningococcal disease.



Growth of *Neisseria meningitidis* B in proteose peptone (top) and whole blood (bottom) at 37°C and 40°C. Data are means (SE) of five experiments

We diluted a suspension of an isolate of *Neisseria meningitidis* B to approximately 109 colony forming units/ml. We inoculated 500 µl suspension into supplemented proteose peptone 9.5 ml in duplicate and incubated one tube of each diluted suspension in a shaking water bath (120 rpm) at 37°C or 40°C. We measured optical density at 540 nm as an indicator of growth in a 100 µl sample every hour. We subsequently determined survival of *N meningitidis* in whole blood at different temperatures according to the method of Ison et al.[3]

The figure shows that growth in proteose peptone was retarded at 40°C compared with 37°C after 4 hours of incubation, corresponding to around the mid-log phase of growth (Student's paired *t* test, P=0.015). In addition, after 4 hours almost a log fewer bacteria were growing in whole blood incubated at 40°C compared with at 37°C (Student's paired *t* test, P=0.02).

Both experiments showed reduced meningococcal growth at higher temperatures, supporting the idea that fever is a beneficial host response.[4] Antipyretic treatment may be counterproductive. For example, controlling bacterial proliferation in early meningococcal disease may be critical since the bacterial load at presentation is a major determinant of clinical outcome.[5] Fever may have an important role in this process.

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Research at the Institute of Child Health and Great Ormond Street Hospital for Children National Health Service (NHS) Trust benefits from research and development funding received from the UK NHS Executive. CB was supported by the Medical Research Council of the United Kingdom, and was research assistant at both the Infectious Diseases and Microbiology Unit and the Immunobiology Unit at the Institute of Child Health.

Competing interests: None declared.

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Cite this as: *BMJ* 2010;340:c450

Or micro-organisms' adaptive response?

As a burns surgeon, I became interested in the treatment of fever in children after reading the clinical manual edited by El-Radhi et al.[1 2] The big question in burns care is whether the patient has sepsis or is just showing the signs of the inflammatory response to the burn with resetting of the hypothalamic set point. Most patients with burns die because of sepsis and the multiorgan failure it causes, while much morbidity is caused by wound and graft failure due to infection.

Considerable evidence in humans and other animals suggests that fever is a beneficial adaptive response. The alternative is that micro-organisms have evolved to deliberately raise the body temperature of their hosts to increase their survival and reproduction. If fever is nature's engine,[3] we should not try to reduce core body temperature but devote our energy to treating the cause of infection. Will the required trials to answer this very important question ever be organised?

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Competing interests: None declared.

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