

Preference is given to letters commenting on contributions published recently in the *JRSM*. They should not exceed 300 words and should be typed double spaced

**The placebo effect and endogenous opioids**

Dr de Craen and colleagues (October 1999 *JRSM*, pp. 511–515) discuss the possible role of endogenous opioids in the placebo effect. I would like to elaborate on this issue.

An innovative study was conducted by Levine *et al.* about 20 years ago<sup>1</sup>. They hypothesized that endogenous endorphin might play a role in mediating placebo response. To test this hypothesis they studied the effect of naloxone, an opioid antagonist, on postoperative pain after extraction of impacted molars. Under double-blind, randomized conditions, patients received either naloxone or placebo several hours after surgery. Patients who were given naloxone reported significantly greater pain than those who received placebo. Patients given placebo as their first drug were divided into placebo responders, whose pain was reduced or unchanged, and non-responders, whose pain increased. Placebo non-responders had nearly the same postoperative pain levels as those who received naloxone. Naloxone given as a second drug did not increase pain levels in non-responders but did increase pain levels of placebo responders. Levine *et al.* concluded that endorphin release mediated placebo analgesia. The observations that people who are placebo responders get considerably more relief from pain with narcotic analgesics than do non-responders<sup>2,3</sup> and that placebo may partly reverse withdrawal symptoms in patients with opioid dependence<sup>4</sup> also support the theory that endogenous opioids are involved in the placebo effect. In 1997, I suggested that the interaction between the endogenous opioid system and different neurotransmitter systems in the brain mediates the placebo effect on mood and behaviour of healthy and sick people<sup>5</sup>. Further research is necessary to elucidate mechanisms of placebo effects.

The placebo effect is an impressive example of transformation of psychological effects into biological processes. The importance of the placebo effect should not be underestimated.

**Leo Sher**

National Institute of Mental Health, Building 10, Room 3S-231, 9000 Rockville Pike, Bethesda, Maryland 20892, USA

**REFERENCES**

- 1 Levine JD, Gordon NC, Fields HL. The mechanism of placebo analgesia. *Lancet* 1978;**ii**:654–7
- 2 Beecher HK. The powerful placebo. *JAMA* 1955;**159**:1602–6
- 3 Shapiro AK. Factors contributing to the placebo effect. *Am J Psychother* 1964;**18**:73–88
- 4 Leslie A. Ethics and practice of placebo therapy. *Am J Med* 1954;**16**: 854–62
- 5 Sher L. The placebo effect on mood and behavior: the role of the endogenous opioid system. *Med Hypotheses* 1997;**48**:347–9

**Clinical examination of the respiratory system**

The findings of Dr Bradding and Dr Cookson (December 1999 *JRSM*, pp. 632–634) show that the current situation is far from satisfactory, though I suspect it is much superior to that in the United States, where there is no teaching of cardiac auscultation in three-quarters of the internal medicine programmes<sup>1</sup>. However, Bradding and Cookson did not assess the teaching of the clinical signs of acute respiratory distress<sup>2</sup>; which in my opinion are of vital importance in intensive care when a patient is under consideration for mechanical ventilation, or is being weaned from the machine. Unfortunately the quantitative relationships between clinical signs and the underlying mechanical and physiological changes in acute respiratory failure are still largely unexplored, though recently intensivists in the USA have accepted the importance of clinical assessment in this context and lessened the strong emphasis on ‘the scientific approach’, in particular blood gas analysis. Sir William Osler’s (1849–1919) aphorism, ‘Don’t touch the patient, state first what you see!’, should surely continue to be taught even in the 21st century, whatever scientific advances are achieved.

**Alan Gilston**

20 Hocroft Avenue, London NW2 2EH, UK

**REFERENCES**

- 1 Mangione S, Neiman LZ, Gracely E, Kaye D. The teaching and practice of cardiac auscultation during internal medicine and cardiology training. *Ann Intern Med* 1993;**119**:47–54
- 2 Gilston A. Facial signs of respiratory distress after cardiac surgery: a plea for the clinical approach to mechanical ventilation. *Anaesthesia* 1976;**31**:385–97

It is frightening to realize that, even in this era of evidence-based medicine, it is still possible to take displeasure with an examination candidate on the basis of questionnaire responses which, at best, would only rate as level-5 evidence (i.e. expert opinion without explicit critical appraisal)<sup>1</sup>. The time is long overdue for clinical signs to be judged by sensitivity, specificity and predictive value rather than the fact that they have been faithfully handed down successive generations.

**O M P Jolobe**

3a Raynham Avenue, Didsbury, Manchester M20 6BW, UK

**REFERENCE**

- 1 American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Chronic Stable Angina). ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: executive summary and recommendations. *Circulation* 1999;**99**:2829–48

### Causes of impaired fetal growth

Professor Harding (December 1999 *JRSM*, pp. 612–615) states that ‘clinical trials to determine whether maternal folate supplementation will improve fetal growth, directly or indirectly, have not yet been reported’. She cannot be familiar with the studies reported by Baumslag *et al.*<sup>1</sup> in 1970, on prematurity and low birthweight infants. Whereas an oral folate supplement made no difference to birthweight in well nourished caucasians, in Bantu women birthweight increased from a mean of 2488 g in the absence of a supplement to 2824 g in those taking additional folate. These studies have been confirmed by others, and an Indian group<sup>2</sup>, in addition, noted a significant increase in placental weight from 456 g in a control group to 517 g in those getting the folate supplement.

#### I Chanarin

11 Fitzwilliam Avenue, Richmond, Surrey TW9 2DQ, UK

#### REFERENCES

- 1 Baumslag N, Edelstein T, Metz J. Reduction of incidence of prematurity by folic acid supplementation in pregnancy. *BMJ* 1970;i:16–17
- 2 Iyengar L, Rajalakshmi K. Effect of folic acid supplementation on birth weights of infants. *Am J Obstet Gynecol* 1975;122:332–6

### The health of the Cornish tin miner

Ms Proctor’s erudite and interesting history (November 1999 *JRSM*, pp. 596–599) covers the period from 1840 to 1914. J S Haldane travelled to Cornwall in 1904 believing that the miners’ breathlessness was due to lung disease and found that anaemia due to hookworm (*Ankylostoma duodenale*) was endemic in tin mines and a major cause of breathlessness due to the resulting anaemia. The reason why Cornish tin miners suffered so severely from hookworm while it was not found in coal mines was that the seams of tin run vertically while coal seams run horizontally. The tin miners could walk to the tin face while coal miners had to crawl to the coal face. It was therefore considered very unacceptable to defaecate in coal mines but allowable in tin mines, where the miners were able to move upright. Faeces containing the hookworm larvae were deposited on the ladder rungs from the feet of miners walking over the faeces of their colleagues. From the ladder, their hands came into contact with the larvae, which penetrated the skin, reached the lungs, climbed the respiratory tract and were then swallowed. The adult worm became attached to the upper part of the small bowel. Pulmonary tuberculosis was the great killer and later silicosis. In 1949, an experiment was started but quickly abandoned in the Geevor Tin mine to determine whether silicosis could be prevented by inhalation of aluminium dust, which was thought to compete for solubility with the silica dust. A group in one changing room inhaled aluminium dust with a group in

another changing room acting as control. Fifty years later, one does wonder whether there has been an increased incidence of Alzheimer’s disease in the area, due to absorption of aluminium.

#### P B S Fowler

152 Harley Street, London W1N 1HH, UK

### The sin of Onan

Dr Imogen Evans, in her review of *Ever Since Adam and Eve* (December 1999 *JRSM*, pp. 653–655), mistakenly identifies the ‘Sin of Onan’ as masturbation. In fact it is *coitus interruptus*:

‘But Onan knew that the offspring would not count as his; so whenever he lay with his brother’s wife, he spilled his seed on the ground so as not to raise up offspring for his brother. What he did was wicked in the Lord’s sight and the Lord took away his life also.’ (*Genesis* 38;9–10)

Whether or not masturbation was involved in the act, the spilling of his seed was his sin.

#### Mervyn Goodman

1 Hornby Lane, Calderstones, Liverpool L18 3HH, UK

### How do GPs respond to reports of abnormal chest X-rays?

Dr Lim and colleagues found that, although general practitioners responded appropriately to reports of abnormal chest X-rays, the delay before patients were seen in hospital could be excessive (September 1999 *JRSM*, pp. 446–449). They argue for direct referral from the radiology department to respiratory physicians. I am a retired radiologist who introduced open access for GPs in 1960. All patients whose radiography suggested the possibility of neoplasm were referred by me direct to the regional thoracic surgical unit, which was in the same hospital. This was welcomed by the GPs; there was only one dissenting voice (about 1985) and the objection was rapidly withdrawn. To illustrate what can be done, may I quote the case of a patient seen about 1972; seen by GP Monday am; at X-ray department Monday pm (no waiting list or appointment system); suspicious of neoplasm; tomographed (this was before computed tomography); confirm neoplasm definite; phone call to thoracic unit—patient added to that afternoon’s clinic; brought in following day (Tuesday), bronchoscoped—operable. Other tests (pulmonary function tests, diaphragm screening) on Wednesday; lobectomy on Thursday, 72 hours after consulting GP. This obviously was exceptional but I would have expected the time from doctor’s surgery to operation to be at most 3 weeks.

As a final note, the occasional case of active tuberculosis (3–4 a year) was likewise referred to the chest physicians at

another hospital and was seen by them within 48 hours. Much can be done by willing cooperation when the treatment lines are clearcut.

### J H E Carmichael

2 Woolton Hill Road, Liverpool L25 6HX, UK

### Systemic lupus with aneurysms

Dr Stratton and colleagues (December 1999 *JRSM*, pp.636–637) report a patient with systemic lupus erythematosus (SLE) who was found to have a systemic vasculitis and multiple abdominal aneurysms suggestive of polyarteritis nodosa, an infrequently reported occurrence<sup>1</sup>. In their review of the published work they may have overlooked additional neuro-radiological reports of possible associations between SLE, cerebral vasculitis and intracranial aneurysms that may be helpful in increasing our understanding of these conditions. Although a clinical diagnosis of SLE cerebral vasculitis is relatively common, true pathological or angiographic confirmation is rarely achieved. The incidence of subarachnoid haemorrhage secondary to rupture of a berry aneurysm has been considered to be raised in patients with SLE<sup>2–4</sup>. There are additional reports of cerebral aneurysms occurring at atypical sites in individuals with SLE<sup>5,6</sup> which may also be multiple. In particular Kelly described a ruptured fusiform aneurysm of a posterior communicating artery that was associated with a transmural angiitis, suggesting that these atypical aneurysms may be secondary to a vasculitis itself<sup>6</sup>. Indeed there are at least five reported cases of SLE cerebral vasculitis with fusiform aneurysms or arterial ectasia<sup>7,8</sup>. Dr Stratton's case report may represent a demonstration of the natural history of a small subgroup of patients with SLE, as they hypothesize, rather than an association between SLE and polyarteritis nodosa itself. The possible relationships between SLE, vasculitis and aneurysm development are intriguing but unresolved. Aggressive management of lupus vasculitis may itself reduce the incidence of these potentially fatal associations.

### Jonathan H Gillard

Department of Radiology, Addenbrooke's Hospital, Box 219, Hills Road, Cambridge CB2 2QQ, UK  
E-mail: jhg21@cam.ac.uk

### REFERENCES

- 1 D'Cruz D, Cervera R, Aydintug AO, Ahmet T, Font J, Hughes GRV. Systemic lupus erythematosus evolving into systemic vasculitis: a report of five cases. *Br J Rheumatol* 1993;**32**:154–7
- 2 Hashimoto N, Handa H, Taki W. Ruptured cerebral aneurysms in patients with systemic lupus erythematosus. *Surg Neurol* 1986;**26**:512–16
- 3 Asai A, Matsutani M, Kohno T, Fujimaki T, Takakura K. Multiple saccular cerebral aneurysms associated with systemic lupus erythematosus. Case report. *Neurol Med Chir (Tokyo)* 1989;**29**:245–7

- 4 Nagayama Y, Okamoto S, Konishi T, Suzuki H, Hamanaka H. Cerebral berry aneurysms and systemic lupus erythematosus. *Neuroradiology* 1991;**33**:466
- 5 Ferris EJ. Arteritis. In: Newton TH, Potts DG, eds. *Radiology of the Skull and Brain*, Vol. 2. St Louis: Mosby, 1974:2566–97
- 6 Kelly RE, Stokes N, Reyes P, Harik SI. Cerebral transmural angiitis and ruptured aneurysm. A complication of systemic lupus erythematosus. *Arch Neurol* 1980;**37**:526–7
- 7 Weiner DK, Allen NB. Large vessel vasculitis of the central nervous system in systemic lupus erythematosus: report and review of the literature. *J Rheumatol* 1991;**18**:748–51
- 8 Ferris EJ, Levine HL. Cerebral arteritis: classification. *Radiology* 1973;**109**:327–41

### Tyger tyger

Medical big game hunters wishing to bag other reports of tiger bite after reading that of Papadopoulos *et al.*<sup>1</sup> should not neglect to beat the leaves of the *Quarterly Journal of Medicine* wherein lies concealed a report<sup>2</sup> on a police inspector who, sent to shoot a troublesome tiger, was himself pounced upon by the beast from the thatched roof of a deserted hut. The man suffered severe mauling of the soft tissues of the back, followed by myoglobinuria and acute renal failure. His neck escaped injury and he made a good recovery. The tiger was shot. Subsequently, and not surprisingly, the patient changed his profession and emigrated to the West.

Younger colleagues should be cautioned against pursuing this topic. Attempts to frame its fearful symmetry will be professionally unrewarding, since the aetiological agent will soon be eradicated.

### Anand Date

Sultan Qaboos University, College of Medicine, PO Box 35 Al-Khod, Muscat-123, Oman  
E-mail: adate@squ.edu.om

### REFERENCES

- 1 Papadopoulos MC, Tubridy N, Wren D, Johnston FG. Neurological symptoms 27 years after tiger bite. *J R Soc Med* 1999;**92**:304–5
- 2 Date A, Raghavan R, John TJ, Richard J, Kirubakaran MG, Shastri JCM. Renal disease in adult Indians: a clinicopathological study of 2827 patients. *Quart J Med* 1987;**64**:729–37

### Multiple chemical sensitivity

There is a major illogicality underlying Steven Reid's discussion of multiple chemical sensitivity (MCS) (December 1999 *JRSM*, pp.616–19). On the one hand he acknowledges that association does not, of itself, imply causality, that not all MCS patients show psychological morbidity, and that they are more likely to have medically unexplained symptoms. But on the other hand he does not question the psychological aetiology of these symptoms and seems to reject out of hand the possibility that they could

have any other basis. In particular, he dismisses the contribution of environmental exposures to the aetiology, without examining the evidence in any adequate way. This is not an impartial review.

We would not dispute the assertion that the population of MCS patients includes a few whose primary pathology is psychiatric, but, in our experience of hundreds of cases, these form a very small minority, some of whom have been psychologically damaged by persistent medical refusal to listen to what they say<sup>1</sup>. Many MCS patients complain of disabling 'psychological' symptoms but most can avoid the symptoms once the incitants have been recognized<sup>2</sup>. Some with persistent mental health problems diagnosed by psychiatrists become well when the environmental origins are recognized. Rippere's description<sup>3</sup> of a youth with severe obsessions resistant to therapy over 17 years (including a 9-month admission to a London hospital), who was able to live a normal life after his environmental and food triggers were identified, should be prescribed reading for all psychiatrists.

We take issue with Dr Reid on several issues. He has clearly not observed the relief of patients when their symptoms are explained and can be avoided. We offered to cooperate on a randomized trial to demonstrate this some years ago<sup>4</sup>, but have had no takers among the psychiatric fraternity. He does not seem to be aware of the vast increase in indoor air pollution in the past 50 years, due to fuel saving measures and rising use of materials and household products which give off volatile organic compounds<sup>5</sup>. Is he aware of the steady increase in medically unexplained symptoms? Might not the increased exposures be relevant to the increase in symptoms? Is it not at least worthy of investigation?

We also take issue on the definition and prevalence of MCS. Cullen's definition was designed for industrial settings: the requirement for a specific exposure incident and exclusion of patients with measurable signs (such as bronchospasm) is inappropriate for patients in general and introduces a psychological bias. Recent American population studies put the prevalence of MCS considerably higher than his figure, between 16% and 34%<sup>4,6</sup>, showing no excess of higher social class. Reid does not refer to the major independent review of MCS commissioned by the State of New Jersey, which received a WHO award and was published in book form, updated recently<sup>6</sup>. Is he familiar with it?

Psychiatric diagnosis remains largely descriptive—of the clinical picture, of psychological stressors and, increasingly, of the biochemical effector mechanisms. Some psychiatrists are starting to look for an understanding which goes beyond this and is able to supply constructive aetiological insights. Environmental influences and nutrient deficits are two of the factors which can contribute to this project<sup>2</sup> but, sadly,

it will not happen until the possibility is taken seriously and the literature reviewed without a preset agenda.

**Honor Anthony**

**Jonathan Maberly**

Farfield House, North Street, Keighley BD21 3AA, UK

#### REFERENCES

- 1 Rippere V. The mental state of dismissed patients—an enquiry into dismissal injury. 4. Dismissal injury as a form of post traumatic stress disorder. *Newsletter Soc Environmental Ther* 1992;12:61–71
- 2 Anthony H, Birtwistle S, Eaton K, Maberly J. *Environmental Medicine in Clinical Practice*. Knighton: BSAENM, 1997
- 3 Rippere V. Can the taxpayer afford to have the medical profession go on ignoring clinical ecology? In: Hariman J, ed. *Does Psychotherapy Really Help People?* Illinois: Charles C. Thomas, 1984:183–99
- 4 Maberly DJ, Anthony HM. Psychology of multiple allergies [Letter]. *BMJ* 1993;307:1497
- 5 Eaton KK, Anthony HM, moderators. *Multiple Chemical Sensitivity: Recognition and Management. A Document on the Health Effects of Everyday Chemical Exposures and their Implications. Third Scientific Report from the British Society for Allergy Environmental and Nutritional Medicine*, BSAENM, PO Box 7, Knighton LD7 1WT (in press)
- 6 Ashford NA, Miller CS. *Chemical Exposures: Low Levels and High Stakes*. New York: Van Nostrand Reinhold, 1998

#### Attitudes to organ donation among South Asians in the UK

For the pilot phase of our study on death and bereavement customs amongst British Muslims, 25 Muslims attending a weekend parenting skills course held in London in the summer of 1998 completed a self-administered anonymous questionnaire. Two of the questions enquired about a 'willingness to donate organs after death' and a 'willingness to donate one's body to medical research.'

The mean age of respondents was 29.3 years (SD 7.4) and 18 (72%) were women. All were literate in English, with 23 educated to 'A-Level' or above. Almost half (12/25) indicated that they were unwilling to donate their organs after death, with a further 10 stating that they were unsure. Only 3 participants indicated that they would be willing to organ-donate. One person responded positively to the question of donating one's body to medical research, whilst the remaining 24 were either unsure (5/25) or unwilling (19/25).

Our pilot study, which is admittedly small, suggests significant reservations concerning the issue of organ and body donation even amongst young educated British Muslims. Although we did not enquire about the reasons underlying these responses, it is likely that religious considerations are an important determining factor<sup>1</sup>. Dr Ahmed and colleagues (December 1998, *JRSM*, p. 626) found that 16% of the 38 Muslims interviewed stated that they were 'unsure from a religious standpoint' about the acceptability of organ donation and transplantation. We

suspect that many of those who cited ‘personal feelings’ or ‘other’ factors had decided against carrying a donor card on the basis of religious considerations but were unwilling to discuss these beliefs in the context of a face-to-face interview. The suggestion that wider dissemination of the Muslim Law Council’s Fatwa should encourage a greater willingness to organ-donate is certainly reasonable, and the availability of the Fatwa on-line courtesy of the Department of Health should be helpful<sup>2</sup>. For those familiar with the nature of a Fatwa—as a religious edict that is not binding—it is however not surprising that there exists a range of views on the subject of organ donation amongst Muslims<sup>3</sup>. These views need to be respected wherever possible, whether or not they are in agreement with the particular Fatwa in question. A fuller study soliciting the views of a more representative sample of the British Muslim community is in progress and will be reported towards the end of this year.

**Aziz Sheikh**

Department of Primary Care and General Practice, Imperial College School of Medicine, London W2 1PG, UK

**Sangeeta Dhani**

GP Direct, Harrow, UK

**REFERENCES**

- 1 Sheikh A, Gatrads AR. Death and bereavement customs: a meditation and an exploration. In: Sheikh A, Gatrads AR, eds. *Caring for Muslim Patients: Exploring the Interface between Faith and Health*. Oxford: Radcliffe Medical Press (in press)
- 2 Muslim Law Council. *Muslim Fatwa on Organ Donation*. <http://www.worldserver.pipex.com/coi/depts/GDH/coi1568b.ok>
- 3 Sheikh A. Death and dying—a Muslim perspective. *J R Soc Med* 1998;91:138–40

**Correction**

**Severe parkinsonism secondary to carbon monoxide poisoning**

N D Gillespie, G Hallhead, Bill Mutch, P B James, M E T McMurdo

The authors wish to make clear that the image presented in this report (October 1999, *JRSM*, pp. 529–530) does not come from the patient discussed in the case history.

**This month in history**



**William Cheselden**

©Venita Jay

William Cheselden (1688–1752), the master lithotomist of all time, left an indelible mark in the annals of history on 27 March 1727. Initially a proponent of high or suprapubic lithotomy, Cheselden published a work entitled *Treatise on the High Operation for Stone* in 1723. His love of high lithotomy eventually soured, and he turned to the lateral perineal operation initiated by Jacques Beaulieu. His first encounter with this historic operation came in March 1727. He brought his surgical technique to a level of perfection that has never been excelled. In an era when anaesthesia was nonexistent, a surgeon’s speed was a prized asset. Cheselden is said to have accomplished a lateral lithotomy in forty-five seconds. Recounting his success with the operation, Cheselden wrote: ‘Publicly in St Thomas’s Hospital I have cut two hundred and thirteen; of the first fifty only three died; and of the second fifty, three; of the third fifty, eight; and of the last sixty-three, six.’ Besides his passion for lithotomy, Cheselden was fascinated with eye surgery. His love of anatomy found expression in several works including *Osteographia* (1733), which included beautiful illustrations by this master of British surgery.

**Venita Jay**