LETTERS TO THE EDITOR

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

Do infections prevent asthma?

The useful and thorough review by Professor Openshaw and Dr Walzl (October 1999 *JRSM*, pp. 495–499) raises questions whose answers may contribute to our understanding of the genesis not only of asthma but also of cot death and even cystic fibrosis. What it is that determines a tendency towards T1 rather than T2 responses or vice versa to antigen challenge is likely to be part of the answer, and particularly the role of mycobacteria (known to be adjuvants to some kinds of immune response) and smoking—an important association of respiratory illness in infancy and of cot death. Is it possible that some components of burned tobacco leaves directly affect the immune response in early life, even *in utero*; and what was it about certain measles and respiratory syncytial ss vaccines that seems to have exacerbated subsequent infection with these viruses? When I worked in Manchester/Salford (the latter once the chronic bronchitic centre of the world) I noticed that a very high proportion of older infants admitted with wheezing bronchitis were strongly sensitive to house-dust mite, exhibited considerable eosinophilia and came from districts where many of the houses had for a century been overcrowded with inadequate hygiene facilities—i.e. breeding grounds for house-dust mite. Not all these children became asthmatics. Another admitted with acute respiratory illness exhibited high fever, wheezing and a considerably raised polymorph count and some of them did go on to develop typical asthma. It would appear that inflammation of the lower respiratory tract in young children with relatively narrow airways causes wheezing from turbulent air flow resulting from a critical reduction in bore—whatever the type of inflammation. It is not safe to assume that relief of wheezing by pharmacological relaxation of what could be normal muscle tone in the airways necessarily means that it was caused by muscle spasm rather than the obstructive thickening of the lining so often found post mortem in asthma.

Developmental immunology is in its infancy and needs systematic exploration for which the opportunity is granted by the monitoring of immunization. It has already been shown that vulnerable babies over-react to such procedures in terms of cortisol production and temperature. Does BCG vaccination, for instance, modify the response to toxoid or live virus vaccines? Two of my own children became permanently 'allergic' to the plaster used to cover the site of smallpox vaccination. It is not only genetically determined immunodeficiency that deserves study; Dr Charles Janeway maintained that such deficiency artificially induced was actually protective against the encephalopathy caused by the lymphocytic choriomeningitis virus. If the gut flora affects immune responsiveness, a Gram-negative flora tending to switch on T1 responses, one might expect exclusive breast-feeding to have the reverse effect.

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Replacement of damaged neural cells

I was pleased to read Professor Eridani's account of stem cells (October 1999 *JRSM*, pp. 502–504). However, certain points require clarification. It is important to highlight the significance of stem cells in neural transplantation. As regards Parkinson's disease, approximately 200 patients have been transplanted world wide to date. The main factor hindering the widespread application of this treatment is the source of tissue—namely, primary fetal tissue obtained from elective abortions at 6 to 91 2 weeks after conception. For transplantation, 3–4 embryos are required for each side of the recipient. This procedure raises major ethical and technical difficulties and hence the search for alternative therapies. The availability of large quantities of stem cells that could be reliably transplanted and differentiate into the appropriate tissue without neoplastic transformation would circumvent this problem.

Professor Eridani presents cell therapy in the form of stem cells for the treatment of other neurodegenerative disorders, such as Alzheimer's disease. However, one needs to be cautious of the potential applications of cell therapy. Transplantation of primary fetal tissue into people with Parkinson's disease has been successful in alleviating some symptoms but does not seem to affect the clinical progression of the disease—i.e. transplanted cells do not even completely replace cell functions lost in the 'region of interest'. In Alzheimer's disease there is a more generalized loss of tissue throughout the brain, so that it is hard to envisage where one might place cells in patients' brains. Just replacing the brain cells may not be adequate; such cells would need to relearn the functions of the lost cells. In rats, functional outcome is improved following striatal lesions when the animals are taught to 'use the transplant'[1].

Finally, the use of human stem cells to augment the processes of regeneration/repair of the human nervous system is only one of many approaches under investigation. Other techniques include xenografting, transplantation of genetically modified cells, novel techniques of growth factor delivery and new surgical techniques such as ablation of the subthalamic nucleus. It is likely that a combination of the many techniques currently under investigation, perhaps with stem cells, will ultimately allow us to manipulate central nervous system regeneration.

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REFERENCE

1 Brasted PJ, Watts C, Robbins TW, Dunnett SB. Associative plasticity in striatal transplants. *Proc Nat Acad Sci, USA* 1999;**96**:10524–9

Placebo and placebo effects in medicine

The historical overview by Dr de Craen and colleagues (October 1999 *JRSM*, pp. 511–515) raises many interesting questions, not least whether there could be a therapeutic role for placebo outside clinical trials. In common with many other orthodox accounts of medical history, however, the review disregards salient information from unorthodox sources. I have undertaken a comprehensive literature review of 19th-century homoeopathic placebo research and everyday usage to clarify current beliefs and open up new areas for debate[1].

The earliest mention of nocebo—in Hahn's sense of patient expectations producing adverse effects from placebo[2] came as early as 1810[3]. Hahnemann had given placebo for a few days at the beginning of a course of treatment in chronic and non-urgent cases, before prescribing homoeopathically. Although this was initially as a washout for patients taking allopathic medication, he increasingly used placebo to derive psychological information about his patients. For instance, he states that hypersensitive patients who experience adverse effects from placebo are in fact revealing an important aspect of their condition—which has to be included when matching the 'totality of symptoms' to the materia medica.

Public discussion of this first seems to have occurred at the 1832 homoeopathic congress in Leipzig. The question was raised whether lactose placebos, commonly used in homoeopathy because indistinguishable from *verum*, could be intrinsically (i.e. chemically) harmful. The ensuing debate in the homoeopathic press makes it clear that nocebo effects were well known to homoeopaths at that time. Although it was felt that some cases could be attributed to carry-over effects of previously taken medicines and others to the natural course of disease, the general conclusion seems to have been that the patient's imagination was usually responsible[4].

If it is believed that recognition of pathophysiological responses to placebo could scarcely have been possible at a time when failure to bleed, cauterize and mercurialize were punishable offences in some quarters, the historical record now clearly suggests otherwise. However improbable it may seem, given their reputation as quacks, early homoeopaths regularly compared their medicines with a control treatment in everyday practice. This casts an intriguing light on a therapy which many doctors and scientists still feel able to dismiss as a placebo, in the face of meta-analyses of randomized placebo-controlled trials which demonstrate homoeopathy's superiority.[5,6]

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REFERENCES

1 Dean ME. A homoeopathic origin for placebo controls: 'An invaluable gift of God'. *Altern Ther Health Med* [in press]

2 Hahn RA. The nocebo phenomenon: concept, evidence and implications for public health. *Prev Med* 1997;**26**:607–11

3 Hahnemann S. *Organon der rationellen Heilkunde.* Dresden: Arnold, 1810

4 Peschier G. Sur le saccharum lactis. *Biblio Hom* 1835;**4**:273–80

5 Linde K, Clausius N, Ramirez G, *et al*. Are the effects of homoeopathy all placebo effects? A meta-analysis of randomized, placebo controlled trials. *Lancet* 1997;**350**:834–43

6 Vandenbroucke JP. Homoeopathy trials: going nowhere. *Lancet* 1997;**350**:824

Dr de Craen and colleagues refer to the ninth verse of *Psalm* cxiv, but this psalm only has eight verses. I presume the article should have referred to *Psalm* cxvi. The translation of this verse from the Hebrew is not 'I shall please the Lord in the land of the living' but 'I shall walk before the Lord in the land of the living'. The wailings of the hired mourners are not quite in accord with the Latin translation of this verse from the Hebrew, which is *ambulabo ad facies Domini in terris viventium*.

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Parkinsonism secondary to carbon monoxide poisoning

Dr Gillespie and colleagues (October 1999 *JRSM*, pp. 529–530) describe the not unusual occurrence of severe parkinsonism secondary to carbon monoxide poisoning in an 82-year-old patient. The interesting feature about this case is the cause of the carbon monoxide poisoning. Apparently, the gas fire was switched on but unlit. The room might have filled with methane and possibly suffocated the patient but carbon monoxide poisoning is only a hazard with natural gas if there is incomplete combustion. The point is important to emphasize since the common danger of carbon monoxide poisoning is a result of inadequately installed and faulty ventilation of gas appliances.

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Author's reply

The gas fire was the presumed source of carbon monoxide although without a full inspection of the patient's house we cannot exclude another source such as a boiler. The fire was reported as unlit but may have been releasing carbon monoxide while lit; the patient's carboxyhaemoglobin was very high.

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Management of acute bursitis

In his useful paper (October 1999 *JRSM*, pp. 516–521) Dr Stell reports good results from initial aspiration. Since all 47 cases were aspirated it is not possible to say whether the expectant treatment with antibiotics commonly given in general practice is as good. In my experience, most settled well without aspiration or any surgical intervention. Another study is needed to decide this and to see whether complications, such as occasional massive oedema of the forearm, are more common with or without aspiration.

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Unanswered questions about NICE

Dr Ellis's article (October 1999 *JRSM*, pp. 538–539) made me thankful that someone 'out there' appreciated the true position about NICE. For months and months I and many others have tried to bring the plight of multiple sclerosis (MS) sufferers to the attention of the Government, health authorities and the media, but alas the media in particular seem to have an embargo on the subject. I approached the Prime Minister on *Question Time* only to be told that he was not qualified to answer my question but I could write to him. Months later I got a reply which virtually said NICE were to issue guidelines. My question to the Prime Minister was (and this was in writing) 'Having regard to his manifesto could he say that NICE and other bodies will not be used to justify a refusal to fund treatment that a specialist has judged would be of benefit to a patient or to delay treatment that a specialist is satisfied is appropriate for his or her patient'? This has not been addressed. I have now learned that the decision on beta-interferon is likely to be delayed another eight or nine months.

We need someone like Dr Ellis behind us—MS sufferers and their carers are just getting nowhere.

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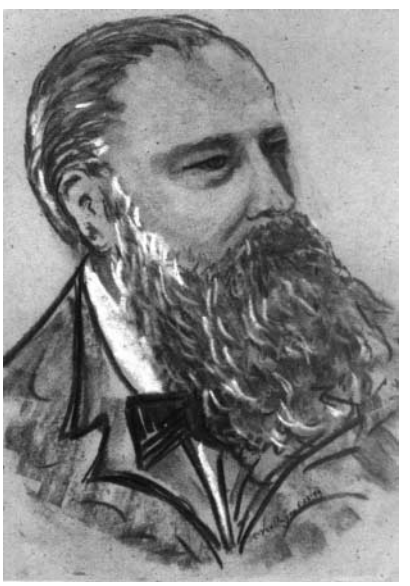

Theodor Billroth

This month in history

The titan of surgery, Theodor Billroth (1829–1894), made medical history on more than one occasion. On 29 January 1881, his claim to fame was the first successful gastrectomy for cancer of stomach. In 1879, Jules Péan had performed a gastric resection for pyloric cancer, but his patient died on the fifth postoperative day. Ludwig Rydigier attempted the second gastrectomy in history in November 1880, but his patient died 12 hours postoperatively. In 1880, at the Allgemeine Krankenhaus, Billroth and his assistants were busy refining the technique of gastric section in dogs. In January 1881, Thérèse Heller, aged 43, arrived at Billroth's door with a palpable tumour in the epigastrium and extremely wasted. On 29 January, the historic gastrectomy took place under chloroform anaesthesia and lasted one and a half hours. Pathological examination revealed an extensive cancer of the pylorus. While the operation itself was a success, the patient died four months later of metastatic disease.

Venita Jay