increased attention to dietary intake for prolonged periods may influence the patient's eating habits.¹

Clinical details of patients were not included because of limitations of space but they have been reported elsewhere.² None had an ileostomy or colostomy or had undergone recent surgery; their treatment and weight had remained constant in the preceding two months.

We agree with Mr Jourdan's observations that many thin patients with inactive Crohn's disease have healthy appetites, as shown in our study. This is in contrast to previous observations, in which inadequate oral intakes were thought to be the cause of weight loss, emaciation, and growth failure.^{3,4}

LAURA A JONES
A D HARRIES
R V HEATLEY
J RHODES

University Hospital of Wales,
Cardiff CF4 4XW

¹ Graham AM. Assessment of nutritional intake. *Proc Nutr Soc* 1982;41:343-8.

² Harries AD, Jones LA, Danis V, et al. Supplemented oral nutrition in Crohn's disease. A controlled trial. *Lancet* 1983;i:887-90.

³ Kirschner BS, Voinchet O, Rosenberg IH. Growth retardation in inflammatory bowel disease. *Gastroenterology* 1978;75:504-11.

⁴ Ketts DG, Grand RJ, Shen G, et al. Nutritional basis for growth failure in children and adolescents with Crohn's disease. *Gastroenterology* 1979;76:720-7.

Neutropenia due to β lactamine antibodies

SIR,—Dr B Rouveix and others (17 December, p 1832) described 13 patients with neutropenia occurring during treatment with β lactam antibiotics and, using a microagglutination technique, found leucoagglutinins in eight out of the nine patients tested.

We have studied one patient with penicillin induced neutropenia (who also had thrombocytopenia)¹ and two patients with cephalosporin induced neutropenia for platelet and granulocyte antibodies with the platelet² and granulocyte³ fluorescent antiglobulin technique, using cells fixed in paraformaldehyde. In each case a drug dependent IgG antibody was shown that reacted with the patient's granulocytes only in the presence of the drug. The patient with thrombocytopenia had a similar drug dependent platelet antibody.

There appear to be some important differences in the nature of the antibodies in the two studies. Whereas Dr Rouveix and others used only donor cells in their study, with appropriate controls to exclude reactions due to alloantibodies, we used the patient's own cells. The patient with penicillin induced thrombocytopenia and neutropenia was investigated four days after withdrawal of the drug, when the result of the direct antiglobulin test was positive, indicating in vivo sensitisation of the patient's cells. All three patients were studied a month after stopping the drug; the result of the direct test was negative and the drug dependence of the antibody could be shown with an indirect autoantiglobulin test—that is, patient's serum + patient's cells + drug. It appears that Dr Rouveix and others could find antibodies for only two days after withdrawing the drug, which probably reflects the relative insensitivity of their method.

It is suggested that the mechanism of neutropenia and thrombocytopenia is similar

to that seen in penicillin induced haemolytic anaemia, where the drug is adsorbed on to the cell surface and reacts with preformed penicillin antibody.⁴ Dr Rouveix and others, however, proposed that the neutropenia is due to circulating immune complexes, although their evidence for this is equivocal. They observed that the agglutinating activity of the serum was abolished or decreased by dialysis at low pH and restored by subsequent addition of the drug. They concluded that dialysis caused dissociation of the immune complexes, but their negative results after dialysis could also be explained by removal of the drug from the assay system.

M F MURPHY
R M MINCHINTON
P METCALFE
P GRINT
A H WATERS

Department of Haematology,
St Bartholomew's Hospital,
London EC1A 7BE

¹ Murphy MF, Riordan T, Minchinton RM, et al. Demonstration of an immune-mediated mechanism of penicillin-induced neutropenia and thrombocytopenia. *Br J Haematol* 1983;55:155-60.

² Borne AEG Kr von dem, Verheught FWA, Oosterhof F, Riesz E von, Brutel de la Riviere A, Engelfriet CP. A simple immunofluorescence test for the detection of platelet antibodies. *Br J Haematol* 1978;39:195-207.

³ Verheught FWA, Borne AEG Kr von dem, Decary F, Engelfriet CP. The detection of granulocyte alloantibodies with an indirect immunofluorescence test. *Br J Haematol* 1977;36:533-44.

⁴ Petz LD, Fudenberg HH. Coombs positive haemolytic anaemia caused by penicillin administration. *N Engl J Med* 1966;274:171-8.

Oxygen as a driving gas for nebulisers: safe or dangerous?

SIR,—As the patients studied by Dr K A Gunawardena and others (28 January, p 272) were relatively stable the mean rise in P_{CO_2} of 1.03 kPa (7.7 mm Hg) and its rapid return to the baseline value may give rise to a false sense of security in the "blue bloater" type of chronic bronchitic. The use of oxygen as a driving gas may be more dangerous in the acute situation,¹ and we report one such example.

A 58 year old smoker presented with a nine year history of shortness of breath, cough, and chronic production of sputum. Forced expiratory volume in one second was 0.35 l and forced vital capacity 1.1 l, improving to 0.45 and 1.65 respectively after inhaled terbutaline. Two weeks later he was admitted with an acute exacerbation, which responded to nebulised bronchodilators, antibiotics, and physiotherapy. Shortly before discharge blood gases on air were pH of 7.4, P_{CO_2} 5.95 kPa (44.7 mm Hg), and P_{O_2} 7.1 kPa (53.2 mm Hg).

Ten days later he was readmitted acutely short of breath and received 5 mg of salbutamol via a lifeline nebuliser driven by piped oxygen. This resulted in severe respiratory depression and a short grand mal seizure. Blood gases at this time showed a pH of 7.1, P_{CO_2} 14.7 kPa (110.7 mm Hg) and P_{O_2} 10.5 kPa (78.6 mm Hg). A doxapram infusion was started, and subsequent doses of salbutamol were delivered using compressed air as the driving gas. Four hours later blood gases on air showed a pH of 7.52, P_{CO_2} 5.5 kPa (41 mm Hg) and P_{O_2} 5.7 kPa (42.5 mm Hg). He made an uneventful recovery and his P_{CO_2} on discharge was 5.5 kPa (41 mm Hg) and P_{O_2} 7.9 kPa (59.3 mm Hg) breathing air.

The fact that the patients of Dr Gunawardena and others did not show worsening hypoxia during nebulisation with air means that it would be safer to use compressed air for all patients with chronic bronchitis who require

nebulised drugs. There is evidence that asthmatics have impaired CO_2 sensitivity during severe attacks,² but this is unlikely to be a clinical problem as the asthmatic with severe CO_2 retention and hypoxia is likely to need immediate artificial ventilation unless the response to initial treatment is dramatic.

J W HADFIELD
S J STINCHCOMBE
J R M BATEMAN

Derby City Hospital,
Derby DE3 3NE

¹ Sykes MK, McNicol MW, Campbell EJM. *Respiratory failure*. London: Blackwell Scientific Publications, 1976.

² Rebuck AS, Read J. Patterns of ventilatory response to carbon dioxide during recovery from severe asthma. *Clin Sci* 1971;41:13-21.

Can we still recommend meditation?

SIR,—Dr Peter Fenwick's leading article on meditation (12 November, p 1401) does not make it clear that almost all research on this subject has been conducted on the transcendental meditation technique taught by Maharishi Mahesh Yogi. There is no evidence that the effects can reliably or safely be generalised to other mental procedures.

Dr Fenwick omitted many important published findings, of which only a few can be mentioned here. For example, reductions in plasma cortisol and arterial blood lactate concentrations, redistribution of blood flow with increased cerebral and reduced hepatic blood flow, brief periods of suspension of respiratory excursions not followed by hyperventilation, reduced metabolism in resting forearm muscle, and decreased red cell glycolysis^{1,2} all clearly distinguish transcendental meditation from relaxation. Electroencephalographic phase coherence has been shown to be more sensitive than α power in discriminating between transcendental meditation and ordinary relaxation, and this increases longitudinally with regular practice.³

Even using less discriminative measures discussed in the article, transcendental meditation has been shown to be more effective than progressive relaxation in terms of stable and persistent physiological effect⁴ and in promoting sustained positive changes in personality variables. Also well documented are pronounced and sustained reductions in the use of cigarettes, alcohol, tranquillisers, antidepressants, hypnotics, and all major categories of non-prescribed drugs.⁵

Reductions in blood pressure,^{6,7} serum cholesterol concentration,⁷ and cigarette smoking indicate that transcendental meditation has an important contribution to make in the prevention of cardiovascular disease. Clinical studies have also reported improvements in asthma, angina pectoris, and sleep patterns. Reversal of biological aging has been shown using a standardised index of physiological age.⁸

In the management of psychiatric inpatients transcendental meditation was superior to progressive relaxation and α biofeedback.⁹ A large epidemiological study, conducted under the auspices of the National Health Board of Sweden, found not only no evidence that transcendental meditation was a significant cause of psychiatric morbidity but also that admission for psychiatric care was 150 to 200 times less common among the 35 000 individuals practising transcendental meditation in Sweden compared with the general population,

suggesting a major preventive influence from the technique.¹⁰

The suggestion that seizures might be intensified in epileptic subjects due to decreased alertness is not relevant to transcendental meditation as alertness is generally increased during this practice.^{1,2,3,11} It is the explicit policy of the organisation teaching transcendental meditation to emphasise that subjects seek and abide by the advice of their doctor in all matters relating to health.

Finally, it seems inappropriate to suggest the use of procedures that attempt to imitate certain aspects of transcendental meditation when these have been shown to have neither its excellent safety record nor its benefits. Such manipulation would not be considered proper in the case of pharmaceutical agents and may be equally irresponsible here.

R A CHALMERS

L J K DAVIS

B P RIGBY

British Association for the
Medical Application of
Transcendental Meditation,
Mentmore Towers,
Buckinghamshire LU7 0QH

¹ Jevning R, Wilson AF, Davidson JM. Adrenocortical activity during meditation. *Horm Behav* 1978;10:54-68.

² Jevning R, Wilson AF, Smith WR, Morton ME. Redistribution of blood flow in acute hypometabolic behavior. *Am J Physiol* 1978;235:R89-92.

³ Dillbeck MC, Bronson EC. Short-term longitudinal effects of the transcendental meditation technique on EEG power and coherence. *Int J Neurosci* 1981;14:147-51.

⁴ Throll DA. Transcendental meditation and progressive relaxation: their physiological effects. *J Clin Psychol* 1982;38:522-30.

⁵ Monahan RJ. Secondary prevention of drug dependence through the transcendental meditation program in metropolitan Philadelphia. *Int J Addict* 1977;12:729-54.

⁶ Wallace RK. Systolic blood pressure and long-term practice of the transcendental meditation and TM-Sidhi programme. *Psychosom Med* 1983;45:41-6.

⁷ Cooper M, Aygen M. Effect of meditation on serum cholesterol and blood pressure. *Journal of the Israeli Medical Association* 1978;95:1-2.

⁸ Wallace RK, Dillbeck M, Jacobs E, Harrington B. The effects of the transcendental meditation and TM-Sidhi program on the aging process. *Int J Neurosci* 1982;16:53-8.

⁹ Glueck BC, Stroebel CF. Biofeedback and meditation in the treatment of psychiatric illness. *Compr Psychiatry* 1975;16:303-21.

¹⁰ Ottoson JO. *Transcendental meditation*. Socialstyrelsen. Stockholm: National Health Board, 1973 (Report: No D:nr SN 3-9-1194/73.)

¹¹ Banquet JP, Sallhan M. EEG analysis of spontaneous and induced states of consciousness. *Rev Electroencephalogr Neuropsychol Clin* 1974;4:445-53.

*.*Dr Fenwick replies below.—ED, *BMJ*.

SIR,—Although most of the early work was done on transcendental meditation, a recent search of the published works on meditation since 1981 showed that about 57 studies were on transcendental meditation and 126 on other techniques of meditation and contemplation. Meditation in all its forms is now under scientific scrutiny.

It is not the role of a leading article to review individual papers. Nevertheless, a word on the scientific validity of some of the findings mentioned by Dr Chalmers and his colleagues is now in order. As regards the physiological changes found during transcendental meditation, much has been claimed on the basis of either inadequately controlled studies or minimal physiological differences. The interesting study on blood flow, lactates, etc, for example, used as a control non-meditators sitting with their eyes closed, although it has long been established that meditation is behaviourally different.¹ Even the authors note that their data "do not necessarily establish uniqueness of this behaviour [transcendental

meditation] in its effects on blood flow." Throll's study is certainly better controlled,² and further similar studies should succeed in showing that meditation is different physiologically from relaxation.

Although the results of the blood pressure study by Wallace are encouraging, they are still open to interpretation.³ Wallace himself points out that "long-term prospective studies using random assignment methods are obviously needed to fully answer these questions."⁴

The coherence work on meditation, which claims a fundamental change in brain rhythm, has a basic misunderstanding of what changes in coherence imply.⁴ Small shifts in the potential fields of different cerebral rhythms certainly produce pronounced changes in coherence value, but it is not known if these shifts are significant physiologically or can simply be related to differences in the difficulty of the task.⁵

The studies on drug consumption and personality changes have not yet distinguished between the effects of meditation and the expectations and culture of the meditating groups.⁶ Reductions in drug consumption are also recorded in other closeknit goal orientated groups of people who do not use transcendental meditation (as with Alcoholics Anonymous).⁷

The benefits of meditation are not, however, in dispute and those of us working with consciousness expanding techniques acknowledge the debt owed to the Maharishi Mahesh Yogi for providing a "pool" of meditating "guinea pigs" and for increasing public and scientific awareness of meditation.

PETER FENWICK

Institute of Psychiatry,
London SE5 8AF

¹ Jevning R, Wilson AF, Smith WR, Morton ME. Redistribution of blood flow in acute hypometabolic behavior. *Am J Physiol* 1978;235:R89-92.

² Throll DA. Transcendental meditation and progressive relaxation: their physiological effects. *J Clin Psychol* 1982;38:522-30.

³ Wallace RK. Systolic blood pressure and long-term practice of the transcendental meditation and TM-Sidhi programme. *Psychosom Med* 1983;45:41-6.

⁴ Dillbeck MC, Bronson EC. Short-term longitudinal effects of the transcendental meditation technique on EEG power and coherence. *Int J Neurosci* 1981;14:147-51.

⁵ Gevins AS, Doyle JC, Shaffer RE, Callaway E, Yeager C. Lateralized cognitive processes and the electroencephalogram. *Science* 1980;207:1005-8.

⁶ Monahan RJ. Secondary prevention of drug dependence through the transcendental meditation program in metropolitan Philadelphia. *Int J Addict* 1977;12:729-54.

⁷ Galanter M, Buckley P, Deutsch A, Rabkin R, Rabkin J. Large group influence for decreased drug use: findings from two contemporary religious sects. *Am J Drug Alcohol Abuse* 1980;7:291-304.

A question of confidence

SIR,—I support Dr Stephen Lock in his comments (14 January, p 123) on the high handed attitude of the General Medical Council in trying to censure him for allowing a member of our profession to mention a tragic episode in General Wingate's life.

I wonder, however, if Wingate's attempted suicide could be ascribed directly to cerebral malaria, as mentioned in the obituary tribute to Gladwin Buttle. Christopher Sykes's book, surely the most complete and best informed biography of Orde Wingate, implies poisoning by mepacrine (Atabrine),¹ and I believe that this was the main cause, although a malaria infection and mental depression must have formed a background to this episode.

Sykes's narrative can be summarised as

follows. On 16 June 1941 Wingate received an order to leave Ethiopia and to report to the general headquarters in Cairo. On 18 June he was in the first stages of malaria and was badly received by the headquarters staff. His report on the achievements of the Gideon Force and on the future of Ethiopia aroused hostile comments and his grievances were ignored. Wavell nearly put him under arrest for insubordination but was prepared to meet some of Wingate's justified demands. When three days later at Churchill's orders Wavell was replaced by Auchinleck as commander in chief, Wingate's illness was worse, but instead of reporting to the Royal Army Medical Corps hospital he consulted, on 27 June, a local civilian doctor, who gave him a large supply of mepacrine. This drug relieved Wingate's febrile symptoms and he continued to take it in excess. He became confused, fell into a state of deep depression, and had suicidal thoughts. On 4 July his temperature rose again, and in the afternoon of that day Wingate stabbed himself twice in the neck with a hunting knife. He was taken to the 15th general (Scottish) hospital, where his life was saved.

Toxic psychoses after mepacrine overdosage were not uncommon in the Army and Royal Air Force during the years 1941-4, when it was the main therapeutic and prophylactic antimalarial drug. Findlay stated that the proportion of officers who developed mepacrine psychoses in the Middle East was high.² The causes of these events may have been multifactorial and due to personality disorders, aggravated by disease and occurring a week or more after high dosage of mepacrine. In my own experience in west Africa the toxic effects of mepacrine were more frequent than it appeared from official reports. It was this high incidence of various side effects of mepacrine that led to its gradual withdrawal when other drugs were introduced.

L J BRUCE-CHWATT

Wellcome Museum of Medical Science,
London NW1 2BP

¹ Sykes CH. *Orde Wingate*. London: Collins, 1959:322-32.

² Findlay GM. *Recent advances in chemotherapy*. Vol 2. London: Churchill, 1951.

Reversal of insulin resistance in type I diabetes after treatment with continuous subcutaneous insulin infusion

SIR,—We were interested in the finding of Dr Ibe Lager and others (3 December, p 1661) of a reduction in insulin resistance in type I diabetics after treatment with continuous subcutaneous insulin infusion.

Dr Lager and colleagues suggested that during continuous subcutaneous insulin infusion a greater proportion of the daily insulin dose should be given as the preprandial component, thereby maintaining lower basal insulin concentrations than is possible with conventional injection treatment. The 40% of total dose used by Dr Lager and colleagues as a basal infusion compares with a mean (SD) of 58.8 (6.1)% in 20 diabetics whom we treated recently by continuous subcutaneous insulin infusion and in whom the mean daily plasma glucose concentration (hospital profiles) was 5.25 mmol/l (95 mg/100 ml). This value is considerably lower than the mean of 7.2 mmol/l (130 mg/100 ml) in the study by Dr Lager and colleagues, and perhaps their patients were