the fact that death is usually due to acute arrhythmia rather than pump failure points to (fresh) ischaemia as the cause. Lowering of blood pressure may be the actual mechanism responsible for initiating this. However, increased blood viscosity and platelet adhesiveness could well raise the threshold of blood pressure which is operative.

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- ⁹ Royal College of Physicians, *Smoking or Health*. London, Pitman Medical, 1977.
- ¹⁰ Green, K G, *Principals and Problems of Controlled Clinical Trials in Cardiovascular Diseases*, ed J P Boissel and C R Klimt. Paris, INSERM.

Preventive genetic registers

SIR,—It was with great interest that I read the leading article (27 January, p 215) on registers for the prevention of genetic disease. You are clearly anxious that such a register should have an acceptable image, so that it will be widely used. I agree that such a register could be a valuable aid in reducing suffering associated with genetic disease, but feel that if suffering is to be genuinely reduced, rather than changed, certain questions must be taken into consideration.

You point out that discovering that one carries such a gene is distressing and that support should be available. The painful ramifications of discovering such a fact before or after one gets married, or of discovering, after one has had a handicapped child exactly which parent "caused" the disease are indeed distressing.

Not every carrier of genetic disease is destined to produce affected children, especially in a society where families are small; so a fair amount of this suffering would be needless, as also the suffering associated with having some healthy, and wanted, boy children aborted. I would like to think that the process suggested would not be initiated unless there was clear evidence that support was available to the person in question, or he or she had asked for it.

The other question concerns the freedom of the parents to decide whether or not to have a child, or an abortion. "There but for the grace of God go I" is not a phrase that comes easily to the mind of the common man. Already parents of handicapped children find themselves isolated from a rather critical society. This can only get worse if it becomes generally known that they could have found out and had the child aborted. It is one thing to worry about having to look after a handicapped child but quite another matter to discover that it is "me and him" against the rest of society, as so often happens. So people are being forced by social pressure to opt for sexing and abortion, while society leaves them to take the responsibility.

Finally, taking up the point that the frequency of these genes in the population would increase, I must ask what you mean by prevention. I thought that it had to do with the elimination of the cause of the disease, in this case a gene. Some responsible and intelligent

adults, faced with accurate information about their carrier status and appreciating the problems of carriers as well as affected children, will limit their families accordingly. Others, having had an affected child, feel little inclination to have more of the same. If nothing else were done, the gene frequency would decrease, and the small number of affected children born should be accepted by all as an inevitable, unalterable fact of life. What seems to be suggested here is that we solve our immediate problems regarding the care of children handicapped by hereditary disease by, quite literally, passing them on to our children.

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Severe hyponatraemia in hospital inpatients

SIR,—Dr P G E Kennedy and others (13 January, p 122), in replying to correspondence about their paper (4 November 1978, p 1251), criticise our letter of 9 December (p 1640). We gave three references¹⁻³ which cited evidence for water intoxication on the basis of appropriate biochemical tests. We feel it may be appropriate for us to quote from one of these references.³ "With euvoalaemia, hyponatraemia and hypertonic urine, inappropriate anti-diuretic hormone excess was diagnosed. The patient's fluids were restricted, but after 24 hours without improvement 5% saline and frusemide were given. This therapy resulted in dramatic improvement. Upon correction of the hyponatraemia the patient's electroencephalogram reverted to normal. Follow up one year later revealed a functional, active female with no neurological symptoms or signs." Dr Kennedy and his colleagues feel that management of this patient "may possibly have been a disadvantage." Clearly our objectives about patient management are different from theirs.

Kennedy *et al* in their paper of 4 November placed their diuretic-treated group of patients into the "depletional" group of hyponatraemia, but now in their letter of 13 January suggest that this may be "dilutional." They have no evidence to substantiate their placing this group of patients in either depletional or dilutional categories. They either disregard other mechanisms suggested (Dr C T G Flear *et al*, 9 December, p 1640) or do not consider other pathogenic mechanisms which may be involved.⁴

It has been suggested that serum sodium concentration is routinely measured in almost every hospital patient, being of value in only a minute proportion of these cases.⁵ It is not surprising therefore that hyponatraemia has been associated with a wide variety of clinical conditions. This is often difficult to interpret because in many instances it is multifactorial, and indeed the pathogenic mechanisms involved are not yet fully agreed on. We feel that this is often an epiphenomenon in otherwise ill patients. It is fortunate, however, that in many of these cases specific therapeutic intervention is rarely required. But when primary sodium and water disturbances do lead to encephalopathy then therapeutic measures may be undertaken only following appropriate biochemical tests on blood and urine.

From their selected group of hyponatraemic patients Kennedy *et al* still cannot justify their final conclusion that "Analysis of blood and

urine was of no value in distinguishing the different diagnostic groups in an emergency."

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Doctors, physiotherapists, and placebo pharmacology

SIR,—I appreciate the critical interest in my paper (23-30 December, p 1761). Some correspondents (3 February, p 341) wondered whether our seminar was very local and atypical of physiotherapists generally. The members came from all over London—all except two from different hospitals. I ask only the scientific status of travellers' tales for our findings, pending more careful and extensive explorations. We are convening another seminar with a different leader and recruits would be welcome. Inquiries should be sent to me please.

The paper was exceedingly condensed and meant chiefly to awaken doctors to the way they use physiotherapists. It would require a book to do justice to the subject and to the questions raised in letters. The book is written and awaits an imaginative publisher out to lose money.

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Cimetidine and duodenal ulcer

SIR,—We are appalled by the suggestion of Dr V W M Drury (10 February, p 410) that cimetidine should be used as a diagnostic rather than a therapeutic drug in the management of duodenal ulcer disease and symptomatic reflux oesophagitis. Many reports have shown that it is virtually impossible to diagnose accurately the cause of upper abdominal pain from the patient's history and physical signs, and cimetidine is not in any way a specific test, relieving as it does symptoms caused by duodenal ulcer, duodenitis, gastric ulcer, gastritis, and peptic oesophagitis. In addition, any form of treatment may have a placebo effect on abdominal pain, at least in the short term.

Much more dangerously, a number of cases have been reported¹⁻⁴ when carcinomatous or lymphomatous gastric ulceration has partially or totally healed endoscopically with complete symptomatic relief during cimetidine treatment, with consequent delay in appropriate surgical management. A patient whom we have recently seen serves to emphasise this point.

A 35-year-old man developed dyspeptic symptoms with epigastric pain as the principal complaint. Over 18 months he had three separate month-long courses of cimetidine with the first two providing complete symptomatic relief. He was investigated when the third course failed to relieve symptoms and was found to have a gastric lymphoma requiring extensive surgery and radiotherapy.

Unfortunately the course that Dr Drury has advocated is already being widely followed

in general practice, so that there are many cimetidine-treated patients in the community with undiagnosed or (if they come up to clinic during or shortly after a course of cimetidine) undiagnosable abdominal pain, some of whom may be harbouring palliated malignancy. It is necessary to emphasise, categorically, that it is in every patient's best interests to have a definitive diagnosis made before treatment with cimetidine is started. There is no doubt that the endoscopic and radiological facilities within the NHS are adequate to cope with the demand. A definitive diagnosis is all the more important since it is clear that prolonged, rather than short-term, cimetidine treatment is necessary for most of these patients with chronic duodenal ulcer disease who are suitable for medical treatment.

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¹ Ritchie, J A, and Truelove, S C, *British Medical Journal*, 1979, **1**, 376.

² Taylor, R H, et al, *Lancet*, 1978, **1**, 686.

³ Murray, C, et al, *Lancet*, 1978, **1**, 1092.

⁴ Minoli, G, Terruzzi, V, and Rossini, A, *Lancet*, 1978, **1**, 1092.

SIR,—As Dr Michael Drury (10 February, p 410) points out, the discussion about cimetidine by Dr J H Baron and others (20 January, p 169) has important implications. No one doubts that cimetidine presents a great advance in the treatment of duodenal ulcer and certain other disorders of the upper gastrointestinal tract, and the majority of patients with duodenal ulcer respond—at least in the short term—to such treatment.

The correlation between ulcer healing and remission of symptoms is known to be poor. Misiewicz¹ has reviewed this problem and concludes, "In the absence of endoscopic evidence, the presence or absence of symptoms cannot be assumed to indicate with certainty the presence or the absence of a peptic ulcer." A large multicentre trial on the treatment of duodenal ulceration with cimetidine, published after Misiewicz's review, shows that 22% of patients whose ulcers had been shown to have healed continued to have pain.² Further, ulcer healing rates in response to placebo may vary from 20% to 60%.³

Dr Drury suggests that a therapeutic trial, at least in younger patients with upper abdominal pain, should be carried out using cimetidine for one week as a first step in investigation. Many gastroenterologists would find it difficult to accept this proposition. I would suggest that, on the available evidence, it would be impossible to draw any firm diagnostic conclusions from such a therapeutic trial in any individual patient.

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¹ Misiewicz, J J, *Clinics in Gastroenterology*, 1978, **7**, 571.

² Gut, 1979, **20**, 68.

³ Langman, M J S, *Clinics in Gastroenterology*, **7**, 583.

Treatment of mastalgia with bromocriptine

SIR,—We read with interest the short report on the use of bromocriptine in mastalgia by Dr M Blichert-Toft and others (27 January, p 237). We would agree that patients with

mastalgia rarely have the full premenstrual tension syndrome. We have reviewed 83 patients with typical cyclical mastalgia using a detailed questionnaire and only six had more than four of the typical premenstrual symptoms described by Dalton.¹

We would also agree that bromocriptine improves breast pain, but only cyclical pain. Although the authors do not comment on the pain pattern, their table appears to show that women with non-cyclical ("constant") pain respond as well as those with cyclical pain. However, in our much larger controlled study using bromocriptine in mastalgia,² where the patients were divided into cyclical and non-cyclical groups defined according to previously published patterns,³ we have shown that only those women with cyclical mastalgia respond to the drug. A group of 11 women with non-cyclical pain failed to show any response to bromocriptine, while the 29 patients in the cyclical group responded in the manner described by Dr Blichert-Toft and his colleagues. We therefore advocate that patients with mastalgia should be divided into cyclical and non-cyclical groups as only the former are likely to respond to bromocriptine.

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¹ Dalton, K, *The Premenstrual Syndrome*. London, Heinemann, 1964.

² Mansel, R E, Preece, P E, and Hughes, L E, *British Journal of Surgery*, 1978, **65**, 724.

³ Preece, P E, et al, *Lancet*, 1976, **2**, 670.

Whooping-cough vaccination

SIR,—The recent controversy on whooping cough has centred entirely on the safety and efficacy of vaccines and has largely ignored the fact that by the time a child is old enough to be fully vaccinated he has little to fear from whooping cough. There is no dispute that the main brunt of the illness and practically all the mortality falls on infants in the first six months of life, so that even the revised "earlier age" schedules of vaccination fail to protect directly this vulnerable age group.

It is argued that vaccination reduces the incidence of whooping cough in older siblings, thus indirectly protecting the baby. However, the infant mortality in the last "well vaccinated" whooping cough outbreak was higher than in the present very much larger "unvaccinated" outbreak and this does not suggest that indirect protection is very effective.

The only other protective measure possible for the young infant is the use of antibiotic prophylaxis, and this of course depends on the prior occurrence of recognisable whooping cough in an older child in the family. During the present outbreak we have had the opportunity to confirm that erythromycin given for 14 days in a dose of 25 mg/kg/day is virtually fully effective in eradicating *Bordetella pertussis* from the upper respiratory tract. Therefore the simple prophylactic procedure is to treat the older child or children and the vulnerable baby with erythromycin for 14 days to eradicate the infection from the family.

This procedure has been recommended in the past by several authorities^{1, 2} and, although there are no controlled trials available, my own view from individual experiences is that it

works perfectly well. To quote a single example, a physician's 2-year-old child developed a febrile upper respiratory infection followed a week later by recognisable whooping, bacteriologically confirmed as whooping cough. A two weeks' course of erythromycin was given to this child and to the second child in the family, a 6-week-old baby, who would have had little chance of avoiding the disease. The baby snuffled for a day or two but otherwise remained in normal health.

In about half the infants admitted to this department during the present whooping-cough epidemic there was a history of a prior case in an older child, so that by applying prophylactic treatment it might be possible to halve the existing low mortality from the disease—surely a very worthwhile aim.

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¹ Warin, J F, and Ironside, A G, *Lecture Notes on the Infectious Diseases*, 2nd edn. Oxford, Blackwells, 1975.

² Arnell, G C, and McAllister, T A, *Practitioner*, 1977, **219**, 855.

Treatment of malaria

SIR,—I was interested in the article (10 February, p 385) on malaria in Birmingham and a London Teaching Hospital. I spent some ten years in Assam and Bangladesh and had an opportunity of seeing a great deal of malaria caused by both *Plasmodium vivax* and *P. falciparum*.

There are many interesting points raised by this article, but I want to raise only one. The authors indicate that their treatment for cerebral malaria was either intravenous quinine or chloroquine. In two of the cases thus treated there was a fatal outcome.

When I first arrived in Bangladesh there was a strong fear regarding the use of intravenous quinine for cerebral malaria. I had a bitter personal experience of a sudden death resulting from intravenous quinine given for cerebral malaria. However, having referred to Manson-Bahr's *Tropical Diseases*, I eventually laid down the following regimen for use in our hospital in cases of cerebral malaria. After confirmation of *P. falciparum* in the blood, the blood pressure and pulse were checked. The patient was then given 1 ml 1/1000 adrenaline over two minutes intramuscularly. A pause of five minutes was allowed for checking the pulse and blood pressure. Intravenous quinine dihydrochloride was given in a dose of 600 mg made up to 20 ml in distilled water and was instilled slowly over ten minutes. The usual result was the return to consciousness of the patient within five to ten minutes. It was then possible to continue oral medication.

It is not widely appreciated that the giving of intravenous quinine produces a form of Jarisch-Hexheimer reaction similar to that caused in former days by arsenic given for tertiary cerebral syphilis. The parasites in the cerebral capillaries are rapidly lysed and produce widespread infarcts. If adrenaline is given first, however, the parasites are driven out of the peripheral capillaries by the vasoconstrictive effect of the adrenaline, and the spleen also contracts, driving more of the parasites into the general circulation. If one gives the adrenaline five minutes to work then the peripheral capillaries are largely clear of the parasites and the quinine is allowed to