capsid antigen. The IgM titre was screened routinely at 1/8 but no further dilutions were assayed. The discrepancy in the titres reported from Manchester and Colindale on roughly contemporaneous samples can only be attributed to methodological differences.

Antibodies to cytomegalovirus were detected in the laboratory of Professor Harold Stern, St George's Hospital Medical School, using complement fixation as stated in our article. Numerous attempts were made to isolate this virus from the patient's urine but without success.

Because of limitations of space, we could only summarise the serological data in our article and we could not fully discuss the diagnostic possibilities. We agree that one cannot be dogmatic about the nature of this patient's illness. It is our belief that the most likely explanation is that she had a primary infection with EB virus to which she was unable to make an adequate immunological response. Indeed, the antibody titres to cytomegalovirus may be attributable to cross-reaction of antibody between this virus and EB virus.¹ However, we agree that we cannot exclude the possibility that this patient had a double infection with both viruses and that the impaired response to EB virus reflects the immunosuppression induced by cytomegalovirus.

A M DENMAN
HILLAS SMITH

Northwick Park Hospital
and Clinical Research Centre,
Harrow, Middx

¹ Horwitz, C A, *American Journal of Clinical Pathology*, 1977, **67**, 210.

1918 influenza epidemic

SIR,—Minerva (16 December, p 1722) says that there are few surviving medical witnesses of the 1918 influenza epidemic to remember any peculiarities of the disease.

I was serving in the RAMC at that time and was temporarily seconded to be medical officer to the First Reserve Brigade of the South African Infantry as two of its MOs had succumbed to the disease. I do not remember the "unique stench" mentioned in the American paper quoted, but I do recall vividly the curious violet cyanosis which often occurred quite soon after the onset of the attack. This was quite different from the bluish-grey of ordinary cyanosis and also from the pinkish hue of carbon monoxide poisoning. The phenomenon was so remarkable and widespread that a medical journal (I think the *BMJ*) sent an artist to make a watercolour sketch of one of our patients (colour-photography not having been invented). The picture was duly reproduced but the patient died the same evening and the artist a few days later.

The course of the disease could be extremely rapid. For example, it was quite common for two or three men to collapse during a morning route-march, to be carried back to barracks on stretchers, and to die before nightfall. I believe that every soldier who contracted influenza before he had been in Europe for three weeks died and that the South African expeditionary force lost more men from the disease than from wounds and gas poisoning combined. The tragedy was made worse by the fact that no available treatment appeared to have any beneficial effect, and also because most of the patients were of Boer descent and did not understand English.

Indeed, by a cruel irony, their fathers may well have fought *against* the British in the Boer War some 18 years before.

C LANGTON HEWER

London N6

Postoperative deep vein thrombosis in Nigerians on high-fibre diets

SIR,—It was with great interest that I read Mr U Osime's article (9 December, p 1607) and I would like to make a few comments.

Several years ago I visited Equatorial Africa and India with Mr Denis Burkitt and cross-questioned several hundred surgeons and doctors, and it is quite obvious that pulmonary embolism in these areas is very rare. Impressed by this fact, over five years ago we commenced giving bran routinely to our patients in one surgical ward—mainly urological. It was given preoperatively and post-operatively if the patients were able to take it. Since then we have had no case of pulmonary embolism and only one case of clinical deep vein thrombosis. Three other surgeons in different parts of the UK have had similar experience.

We conducted tests on 50 patients—the majority having had open prostatectomies—using ¹²⁵I-labelled fibrinogen. We found positive calf signs in 22%, but in the vast majority these were transient and reverted to normal in 48 hours. There was no case of clinical deep vein thrombosis. I would be interested to know how many of Mr Osime's were also transient in appearance.

Might it be that high-fibre diets alter fibrinolytic activity? If so, this could explain why the Nigerians rarely develop pulmonary embolism.

CONRAD LATTO

Royal Berkshire Hospital,
Reading

Dealing with residual bile duct stones

SIR,—Mr R Mason (23-30 December, p 1788) rightly points out the difficulties in wire basket extraction of gallstones via the T-tube track when the track is narrow or tortuous, and recommends a 12 French gauge or larger T-tube brought out directly lateral to the common bile duct.

A large T-tube should certainly be used and there is usually no difficulty in placing such a tube in the dilated common bile duct which has contained stones. The track closes equally promptly after removal of the tube whether 14 or 16 French gauge or smaller T-tubes are used. The largest steerable catheter for stone extraction (Medi-Tech Company, Watertown, Massachusetts 02172) is 13 French gauge and Burhenne recommends a minimum T-tube size of 14 French gauge.¹ If an 8, 10, or 12 French gauge T-tube has been used and stones are subsequently found then the T-tube may be removed and a guide wire inserted, over which successively larger catheters are passed to dilate the track up to 14 French gauge. This may be done immediately before a first attempt at stone extraction six weeks after operation.

I would caution surgeons against bringing the T-tube out too directly. Many patients undergoing cholecystectomy are very obese and the T-tube exit wound may move downwards several inches when the patient stands up a few days after operation. If the T-tube takes too direct a route to the skin it can be

pulled out of the common bile duct. I have heard of a case in California that had fatal results. The T-tube should therefore describe a smooth curve between the common duct and the skin wound.

R W MOTSON

The London Hospital,
London E1

¹ Burhenne, H J, in *Advances in Surgery*, vol 10, ed W P Longmire, p 121. Chicago, Year Book Medical Publishers, 1976.

Breathing and control of heart rate

SIR,—Your leading article (16 December, p 1663) entitled "Breathing and control of heart rate" comments on the physiological good sense of swallowing water to relieve faintness. Although this manoeuvre may stimulate respiration and thus relieve bradycardia it may also directly cause slowing of the heart.

The majority of reported cases of "deglutition syncope" appear to be associated with oesophageal abnormalities,¹ but even in people without oesophageal disease syncope may be so severe and repeated as to require insertion of a demand pacemaker.² In susceptible individuals a drink of cold water might therefore be an appropriate treatment for supraventricular tachyarrhythmias rather than for bradycardiac syncope.

Your leading article also draws attention to the complex interaction between lung inflation and bradycardia initiated by face immersion. This interaction has recently been clarified.³ Our results confirm that breath holding at inspiration leads to bradycardia, and show that face immersion has a marked effect only if performed at expiration. These findings explain why other works have not been able to demonstrate a consistent effect of lung volume on the diving response in man, since bradycardia is seen irrespective of face immersion at high lung volumes.

PETER OPENSHAW
Medical Student

Guy's Hospital,
London SE1

¹ Tomlinson, I W, and Fox, K M, *British Medical Journal*, 1975, **2**, 315.

² Wik, B, and Hillestad, L, *British Medical Journal*, 1975, **3**, 747.

³ Openshaw, P J M, and Woodroof, G M F, *Journal of Applied Physiology*, 1978, **45**, 783.

Polyunsaturated fatty acids and colchicine in multiple sclerosis

SIR,—We were interested to read the report by Dr D Bates and others (18 November, p 1390) on the use of polyunsaturated fatty acids (PUFA) supplementation in multiple sclerosis (MS). We think that it is important to point out that the evening primrose oil (Naudicelle) capsules used in this trial contained dyes including tartrazine and ponceau R. In unpublished studies we have shown that both these dyes block the conversion of PUFA to prostaglandins (PGs) and this effect of tartrazine has also been reported by others.¹ The importance of this lies in the fact that the major biological function of the PUFAs is to give rise to PGs.² The effect of PUFAs in suppressing experimental allergic encephalomyelitis in rats is completely abolished by inhibition of their conversion to PGs.³

In preparation for a double-blind placebo controlled trial we have for the past six months

been evaluating evening primrose oil in dye-free capsules in 14 patients with long-lasting MS, all of whom displayed pyramidal, cerebellar, and posterior column signs and symptoms. They were clinically relatively stable and no patient had had an obvious relapse in the year before starting evening primrose oil. They were assessed clinically using the Kurtzke disability score. Fine motor control was assessed using the B-M manual dexterity test, which involves putting small pins into holes in 60 seconds. Grip strength was assessed by a dynamometer. All the patients had had previous experience with the tests. Eight patients received four 0.6 ml evening primrose oil capsules/day while six received the same dose of the capsules plus 0.5 mg colchicine twice a day. Colchicine was given for two reasons¹: (a) it has proved successful in Behçet's syndrome,² a disease in which there may be MS-like neurological disorders; and (b) it appears to stimulate conversion of PUFAs to thromboxane A₂, a substance which may prevent accumulation of calcium in cells.⁴ Uncontrolled calcium entry may be a major factor in demyelination.⁷ The results were as follows:

Evening primrose oil alone—Five patients showed no change on the Kurtzke scale while three showed some improvement. There was no improvement in grip strength but there was a significant ($P < 0.05$) improvement in performance in the manual dexterity test.

Evening primrose oil plus colchicine—Four patients improved on the Kurtzke scale while two did not respond. Two of the patients regarded themselves as dramatically improved and one returned to work after being unemployed for eight years. In the manual dexterity test two patients who had been unable to insert pins at all for two years became able to insert some, and the overall improvement in the group was significant at the $P < 0.025$ level. Grip strength also improved but this improvement just failed to reach significance.

These results, we believe, justify a formal controlled trial and suggest that evening primrose oil packaged in dye-free capsules, especially when combined with colchicine, may be of value.

D F HORROBIN
T BOTEZ
M I BOTEZ

Clinical Research Institute
of Montreal,
Montreal, Quebec

- ¹ Cesarani, R, *et al*, *Prostaglandins and Medicine*, 1978, **1**, 499.
- ² Beerthuis, R K, *et al*, *Recente Travaux Chimie*, 1968, **87**, 461.
- ³ Mertin, J, and Stackpoole, A, *Prostaglandins and Medicine*, 1978, **1**, 283.
- ⁴ Horrobin, D F, *Prostaglandins: Physiology, Pharmacology and Clinical Significance*. Edinburgh, Churchill Livingstone, 1978.
- ⁵ Mizushima, Y, *et al*, *Lancet*, 1977, **2**, 1037.
- ⁶ Horrobin, D F, Oka, M, and Manku, M S, *European Journal of Rheumatology*. In press.
- ⁷ Schlaepfer, W W, *Nature*, 1977, **265**, 734.

Low-cholesterol diet in patients with gall stones taking chenodeoxycholic acid

SIR,—In a recent article (23 September 1978, p 851), Dr D P Maudgal and his colleagues concluded that a low-cholesterol diet resulted in an enhancement of the effect of chenodeoxycholic acid (CDCA) in patients with gall stones whose bile had already been rendered unsaturated by CDCA when taking a diet containing 600 mg cholesterol.

It should be noted that the difference obtained in the saturation index by the reduction of dietary cholesterol was very small (0.12 in experiment 1 and 0.05 in experiment 2) and we question whether these small differences are of any biological, as distinct from statistical, significance. There is certainly no evidence in the literature that the rate of gall-stone dissolution is related to the degree of lowering of the saturation index. The abstract

of Bell *et al*¹ cited by the authors states only that gall-stone dissolution in the rhesus monkey was associated with bile unsaturated with cholesterol. It is likely that the most important rate-limiting factor in dissolution may be the interfacial barriers² rather than the decrease of the saturation index.

We offer two other methodological criticisms of the paper. Firstly, the duration of "overnight fast" prior to bile sampling was not specified and yet it is critically important in studies where there is comparison of the saturation indices. A decrease in duration of fast from 16 to 9 hours, for example, can lower the index by as much as 0.36 in women and 0.19 in men.³ Secondly, the mean decrease in biliary saturation index of 0.12 in experiment 1 was produced in hospital on a 100 mg cholesterol diet, but a control group who entered hospital on a 600 mg cholesterol diet was not studied. There are many factors in the hospital environment, including the length of pretest fasting, which may have contributed to this change in saturation index.

In summary, we are not convinced that a low-cholesterol diet has been shown to have any place in the dissolution therapy for gall stones by CDCA.

JAMES MCK WATTS
ROGER H L DOWN
MALCOLM J WHITING

Department of Surgery,
Flinders Medical Centre,
Adelaide, South Australia

- ¹ Bell, G D, *et al*, *Gut*, 1972, **13**, 836.
- ² Molokhia, A M, *et al*, *Journal of Pharmaceutical Sciences*, 1977, **66**, 1101.
- ³ Williams, C N, *et al*, *American Journal of Digestive Diseases*, 1977, **22**, 189.

Vitamin E and malignant hyperthermia

SIR,—Last year (20 May, p 1345) I suggested that there might be an association between the consumption of excessive vitamin E and the development of malignant hyperthermia. The Malignant Hyperthermia Research Unit of the University of Leeds has now investigated the three children of the patient I previously described. Two of them have been proved by muscle biopsy to be susceptible to malignant hyperthermia.

It therefore seems likely that the episode of malignant hyperthermia I encountered was due to a genetically determined susceptibility, not to vitamin E.

PHILIP JAMES

Department of Anaesthetics,
Royal Isle of Wight County Hospital,
Ryde, IOW

Effect of propranolol on plasma concentrations of HDL apoprotein and lipid

SIR,—The provocative reports by Dr A Helgeland and others (5 August, p 403) and by Drs D Streja and D Mymin (25 November, p 1495) associating low concentrations of high-density lipoprotein (HDL) cholesterol with propranolol therapy are further supported by the longitudinal study of Dr N Tanaka and others on 10 subjects before and after propranolol therapy.¹ In that study subjects were normolipaeamic and on no other medication. They were maintained on a standard hospital diet and no weight changes were observed during the study. After control blood samples had been collected, 60 mg/day of propranolol was administered orally for seven weeks and

120 mg/day for the eighth and final week. Throughout the period of propranolol administration serial plasma samples demonstrated a persistent fall in both HDL apoprotein and lipid concentrations. At the end of eight weeks of therapy only three-quarters of the concentrations of plasma HDL apoprotein and lipid remained.

It has been suggested that the apoproteins of HDL may have a key role in bringing about the anti-atherogenic effect of HDL.² The study's demonstration of a significant fall with propranolol therapy in both plasma HDL apoprotein and HDL lipid content heightens concern about a non-beneficial effect of chronic propranolol therapy in hypertensive and coronary artery disease patients.

PHILIP HOOPER

Department of Medicine,
University of New Mexico
School of Medicine,
Albuquerque,
New Mexico, USA

- ¹ Tanaka, N, *et al*, *Metabolism*, 1976, **25**, 1071.
- ² Eaton, R P, *Journal of Chronic Diseases*, 1978, **31**, 131.

Cardiac arrhythmias and "epilepsy"

SIR,—You kindly published my comment on cardiac arrhythmias that can be confused with epilepsy (2 July, 1977, p 45). The long Q-T interval syndrome was mentioned as one of the possibilities, exemplified by the case history of a young woman. The patient died of ventricular fibrillation recently, at the age of 23, and the necropsy finding prompts me to correct my earlier report.

The pathologist found an extremely thin-walled right ventricle, almost devoid of heart muscle. A very small fibrotic area was seen in the left ventricle. The heart valves and the coronary arteries were intact. This unusual (congenital?) form of myocardiopathy is referred to as parchment heart¹ or *ventricule droit papyrace*² in the French literature. It can be regarded probably as a variant of endomyocardial fibrosis. Some of those patients who survive infancy are prone to have recurrent attacks of ventricular tachycardia. Only a few similar cases have been described.²⁻⁴

The prolongation of the Q-T interval was a secondary phenomenon in this case and due to the myocardiopathy. It might have had a contributory role, however, in the pathogenesis of ventricular tachycardia and fibrillation.

M WINTER

Municipal Hospital,
Hódmezővásárhely, Hungary

- ¹ Reeve, R, and MacDonald, P, *American Journal of Cardiology*, 1964, **17**, 715.
- ² Froment, R, *et al*, *Archives des Maladies du Cœur et des Vaisseaux*, 1968, **61**, 477.
- ³ Slama, R, *et al*, *Cœur et Médecine Interne*, 1969, **8**, 423.
- ⁴ Frank, R, *et al*, *Archives des Maladies du Cœur et des Vaisseaux*, 1978, **71**, 963.

Spontaneous pneumomediastinum complicating anorexia nervosa

SIR,—In their report of two cases of spontaneous pneumomediastinum complicating anorexia nervosa Drs Anita J Donley and T J Kemple (9 December, p 1604) found only one report of pneumomediastinum complicating starvation or wasting diseases.

We have recently managed a patient with spontaneous pneumomediastinum complicating severe hyperemesis gravidarum at 10