ovarian cyst formation. The first was performed in Northern Ireland when she was 16 years of age. She had had chronic pelvic pain since that time and a pelvic mass had re-formed on three occasions. The most recent "cyst" proved to be an inflammatory mass consisting of chronically infected omentum fixed to her remaining right tube and ovary. The omental mass was removed and the tube and ovary restored to an apparently normal condition. Within five days of operation a tender mass had re-formed. Laparoscopy on the eighth postoperative day confirmed that once more the omentum was matted around the tube and ovary. The tissues were all separated and dye studies showed that the tube was still patent. The patient was discharged the following day. She was seen recently, six months after discharge from hospital. She had been free of pain for the first time in 10 years and vaginal examination showed no obvious pathology. Marriage is contemplated and were she to conceive one would feel that a further advantage had been obtained.

It must be stressed that in each case post-operative problems were present, indicating persistent disease. Each time the laparoscopic procedure has relieved the patient of unpleasant symptoms; there have been no obvious repercussions and all remain symptom-free to the present time. The procedure requires great care and should, I feel, be practised only by surgeons with a wide experience of laparoscopic operating.

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Chasing the cause of Crohn's disease

SIR,—Your leading article (9 April, p 929) drew attention to two papers, one of which suggests that a common breakfast cereal, corn flakes,¹ and the other that food additives² may play a part in the aetiology of Crohn's disease.

We are presently following up two cases of Crohn's disease in children, one of which is undoubtedly aggravated, if not caused, by foods and the other by additives.

Case 1—This girl was first seen at the age of 9 as she had developed peritonitis due to multiple perforations associated with Crohn's disease of the small bowel. The lesion was removed surgically. The histological appearances were characteristic of Crohn's disease, many multinucleated giant cells being present.

After the operation she was asked to avoid cow's milk and dairy products and peanut butter—the latter because its ingestion was associated with diarrhoea. Four months later, on no medication, she was so well that she was allowed to take milk. Within a month she had to be readmitted to hospital as her diarrhoea, fever, and spells of abdominal pain had returned. On this occasion she was taken off all oral fluids and maintained on hyperalimentation. Her symptoms settled, and when all evidence of active disease had subsided she was once more allowed foods, but on this occasion she was offered the foods one at a time and any food which precipitated spells of abdominal pain or diarrhoea was excluded. On her restricted diet she remained symptom-free and gained weight. To remain well she has to avoid all milk and dairy products, ham, and bacon, as well as blueberries and cakes containing poppy seed. This child has at no time had steroids.

Case 2—This is a boy who first presented with diarrhoea associated with obvious blood loss when he was given cows' milk at the age of 6 months. He

reacted similarly to many other foods, soya included. Drugs, even aspirin, had to be avoided for they too caused a return of his bloody diarrhoea. For this reason he had to be brought up on a very restricted diet but remained relatively well until he was 13 years old, when he developed spells of abdominal pain and vomiting associated with fever and weight loss. Radiological studies indicated that he had linear ulcerations in the ascending colon, caecum, and distal 14 cm of the ileum, the last also having a cobblestone appearance. The sigmoid colon was normal. All oral foods and fluids were withheld and he was maintained on hyperalimentation alone. He received no steroid therapy. On this regimen his symptoms and fever settled and there was radiological evidence of recovery. When he was once more offered ordinary foods his symptoms gradually returned. He was therefore started on oral prednisone, but this was followed by an acute exacerbation of his pain and bloody diarrhoea and by radiological evidence of deterioration. He was therefore put back on hyperalimentation alone, and again his symptoms subsided completely. There was little doubt in our minds that "something" (in addition to foods) in the oral steroids (several preparations were tried), either lactose, starch, sugar, paraffin oil, or tartrazine, present in some of the preparations, aggravated his disease, for within 15–20 min of taking the preparation he would complain of an accentuation of his pain. As most foods, some more and some less, precipitated spells of abdominal pain and diarrhoea and as "something" in the oral steroid preparations also caused a return of his disease we decided to maintain him on long-acting corticotrophin (ACTH) and the foods that he best tolerated. On this regimen he is once more growing and developing normally and is symptom-free.

Two features in the above cases suggest that diet is related to the disease. Firstly, in each case the exclusion of all foods and fluids by mouth, with reliance on hyperalimentation alone, led to recovery; secondly, the reintroduction of a few selected foods in case 1, and of many more foods and additives in case 2, caused a relapse.

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¹ James, A H, *British Medical Journal*, 1977, **1**, 943.
² Martini, G A, and Brandes, J W, *Klinische Wochenschrift*, 1976, **54**, 367.

Absorption of lithium from controlled-release preparations

SIR,—Dr R P Hullin (21 May, p 1349) inadvertently gives the impression that all lithium carbonate tablets BP will necessarily have the same bioavailability; this is not so.

The disintegration test specified in the BP 1973 is not a measure of bioavailability; it is quite possible to manufacture tablets which comply with the specifications of the BP 1973, including disintegration, but produce lithium blood levels of a completely different pattern from those produced by the two products on the market. This is because the bioavailability of lithium is controlled by many factors in tablet formulation and manufacture which are not mentioned in the BP monograph and which are not controlled by the BP specification.

The bioavailability pattern of Camcolit 400 has been shown by Dr Hullin to be similar to that of Priadel and we agree with him that these two products are interchangeable; there seems little doubt that the Department of Health and Social Security will require any future products they licence to match the same pattern.^{1 2} However, there is, theoretically, nothing to stop a hospital pharmacy

producing tablets to the existing BP specification which could have a completely different pattern of bioavailability.

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¹ Stewart, A G, *Pharmaceutical Journal*, 1977, **218**, 254.
² Florence, A T, *Pharmaceutical Journal*, 1977, **218**, 255.

Efficacy of measles vaccination

SIR,—The letter from Drs M D Coulter and B M Jones (21 May, p 1347) stirred some distant memories.^{1 2} It also disturbed me a little that unvarnished "truth" has become a rare commodity in preventive medicine.

If a susceptible infant is actively immunised against measles there is, approximately, an 85% chance that he will escape measles infection in the next few years. Well over 90% of the herd will need to be immune if the virus is to be kept from gaining a toe-hold. Such an environment may be created in an isolated atoll in the Pacific. You could not hope for it in the mobile population of England.

The vaccine-produced immunity does wane as time goes by, while the potency of the vaccine is adversely affected by unfavourable storage conditions and by plunging the needle through skin to which is still clinging a viricidal cleansing agent.

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¹ Sanders, S S, *British Medical Journal*, 1973, **2**, 175.
² Anand, J K, *British Medical Journal*, 1973, **2**, 367.

Glucose-6-phosphate dehydrogenase deficiency and duodenal ulcer

SIR,—Since 1970 we have been studying the distribution of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency in Sardinian patients of the Ospedali Riuniti of Sassari. It is well known that the prevalence of the deficiency in Sardinia is very high¹ and is almost exclusively of the Mediterranean type—for example, it is found in about 8% of our patients, who come to us from the north-western part of the island.²

In the past 18 months we have been comparing the prevalence of G-6-PD deficiencies in 175 male patients suffering from duodenal ulcer, confirmed surgically, with that in an equal number of patients suffering from diseases other than duodenal ulcer. The two groups were matched for sex, age, and place of origin. The results are reported in the table, from which it will be seen that the prevalence of G-6-PD deficiency in patients with duodenal ulcer (14.85%) is double that in the controls (7.42%); this difference is statistically significant.

G-6-PD deficiency in male patients with duodenal ulcer and in controls

Group	No deficient	No non-deficient	Total
Duodenal ulcer . .	26	149	175
Controls . .	13	162	175
Total . .	39	311	350

χ^2 (with Yates's correction) = 4.15 (P < 0.05).

These data show that a high prevalence of G-6-PD deficiency in Sardinian men is associated with duodenal ulcer and suggests that this deficiency may be a cofactor in the pathogenesis of the disease. This association is difficult to interpret and in any case our findings should be compared with data from other countries where the prevalence of G-6-PD deficiency is similar to that found in Sardinia.

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¹ Siniscalco, M, *et al*, *Nature*, 1961, **190**, 1179.

² Addis, S, *Applicazioni Bio-mediche del Calcolo Elettronico*, 1971, **4**, 330.

Cranial arteritis

SIR,—Dr J W Paulley (21 May, p 1348) may well be right that loss of sight in cranial (giant-cell) is due to occlusion of the ophthalmic artery. Nevertheless, in 1943 Johnson *et al*¹ did describe "occlusion of the upper branches of the central retinal artery and vein" in one of their patients and in 1946 we² published the necropsy findings in another patient in whom "both optic nerves showed marked softening" and whose retinal arteries showed obliteration of the lumen by cellular fibrous tissue, with the characteristic histological findings on section. We also described the extensive large-artery involvement that may be found in temporal arteritis, as did Gilmour³ in 1941 and Sproul⁴ in 1942.

Dr R V H Jones (p 1355) is right in calling attention to the dramatic nature of headache encountered in elderly patients with temporal arteritis. Much of the early literature emphasised this, as we ourselves did in 1946. It has been our clinical practice over the past 30 years to regard such severe headaches in the elderly (in the absence of Paget's disease, bone secondaries, or hypertensive crises) as warranting the presumptive diagnosis of temporal arteritis. Descriptions such as those given by Dr Jones are characteristic.

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¹ Johnson, R H, Harley, R D, and Horton, B T, *American Journal of Ophthalmology*, 1943, **26**, 147.

² Cooke, W T, *et al*, *Quarterly Journal of Medicine*, 1946, **15**, 47.

³ Gilmour, J R, *Journal of Pathology and Bacteriology*, 1941, **53**, 263.

⁴ Sproul, E E, *New York State Journal of Medicine*, 1942, **42**, 345.

SIR,—My recent experience of temporal arteritis has been in line with that of Dr R V H Jones (21 May, p 1355), who has alerted us to the graphic language which may be used to describe the headache.

In 1974 a man attended me for the first time in 30 years (he had even failed to register under the NHS in 1948) complaining of a bad one-sided headache of recent onset. It was not difficult to judge that one attendance in 30 years for a modest complaint like headache indicated a more than ordinary headache. Biopsy confirmed arteritis. In March this year a man came to me complaining of severe headaches of recent onset with prostrating paroxysms of pain; previously he had never had headaches. Six months earlier he suffered a thrombotic glaucoma but did not seek

medical advice for 16 days, which indicates a stoic pain threshold. Biopsy confirmed the arteritis.

ALASTAIR A MCINNES

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Safety of children in cars

SIR,—To add a further point to recent correspondence (Dr A West, 2 April, p 908), I should like to point out that it is not just when hiring cars on the Continent that safety seats for children cannot be provided. My husband, 1-year-old daughter, and I return to England frequently and have made repeated efforts to hire a car with such a seat. My most recent inquiry was greeted by the, admittedly off the cuff, reply that it is illegal to hire a car with a baby seat. In my opinion it should be illegal not to provide such a seat if requested, as it is extremely dangerous to travel with an unrestrained 1-year-old, and frankly impossible unless there is an adult other than the driver in the car. I am at present in correspondence with some of the larger car hire companies regarding this subject but as yet have received no satisfactory answers.

M E M COCHRANE

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Very early recognition of coronary heart disease

SIR,—I think your leading article (21 May, p 1302) on this subject does a great service in emphasising the very poor predictive value of the recognised "risk factors" such as smoking, etc. This underlines how little we really know about the relevant predisposing mechanisms and their measurement. You also rightly question the value of early detection unless it can lead to useful action.

We shall never fully understand the predisposing mechanisms. Nevertheless, when 20 years ago the serum cholesterol was found to be often raised in coronary heart disease, it was a reasonable decision to deploy money and effort to try to correct this abnormal test. It was just bad luck that lowering the cholesterol does not seem to convey much clinical benefit except in gross hyperlipidaemia.

The search for further abnormal tests in people known to be at risk must go on. Such tests might, but not necessarily will, have prognostic value. If a test could be normalised therapeutically, this treatment stands a good chance of helping patients. If it helped patients we could then deduce more about the pathogenetic mechanisms.

There are a number of continuing studies searching prospectively and retrospectively for abnormal tests. One such test is the non-specific heparin thrombin clotting time, which may measure released platelet factor 4 and hence reflect platelet "activation." This test is abnormal in all the many groups so far studied of patients known to be at risk.^{1,2} It can be altered towards "supranormal" in healthy men by a change to a diet of unsaturated fat.³ In patients with gross vascular disease this and other tests can be normalised by treatment with clofibrate or an analogue,⁴ identified as ICI 55 897.⁵ This test then might be of individual prognostic value and

its correction might convey clinical benefit. This has yet to be determined.

You say, "Most previously fit patients who developed coronary heart disease . . . had no conventional risk factors . . ." and elsewhere you say, "Furthermore at present none of our more advanced tests . . . for thrombotic tendency . . . improve the specificity and sensitivity of the predictions." This view is too pessimistic. In so serious a disease even remote clues should be followed, but I submit, sir, that the approach outlined above and the further exploration of these kinds of test are most worthwhile.

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¹ O'Brien, J R, *et al*, *Thrombosis et Diathesis Haemorrhagica*, 1975, **34**, 483.

² Dana, B, *et al*, *American Journal of Cardiology*, 1976, **38**, 9.

³ O'Brien, J R, *et al*, *Lancet*, 1976, **2**, 995.

⁴ The First Florence Conference on Haemostasis and Thrombosis, 10-12 May, 1977. Abstracts, p 64.

⁵ Stone, M C, Thorp, J M, and Wain, J S, in *Lipids. Lipoproteins and Drugs*, p 151. Ed D Kritchevsky, R Paoletti, and W L Holmes. New York, Plenum Publishing Corporation, 1975.

Tourist hepatitis

SIR,—I was very interested to see the letter from Dr F W Best on the above subject (30 April, p 1158). There is little doubt that most physicians prescribe gammaglobulin for travellers on a very empirical basis. Many factors are involved, particularly the availability of the preparation (thus, for example, gammaglobulin is widely available in Canada and no prescription is needed). All biological preparations, especially immunisations, possess the potential to interfere with the "normal" immunological status of the recipient, and the indications for the administration of a particular product should never be immutable.

Although the noted adverse effects of gammaglobulin are relatively few, a "prospective" philosophy of adverse reactions may well be more significant as far as immunoglobulins are concerned, for modern methods of testing for immunological competence are relatively crude and presumably lack the sensitivity to detect subtle alterations in the immunological status of the recipient.

It would hardly seem justifiable to offer gammaglobulin to travellers on short trips to the tropics. Those who are spending a significant time in rural and high-risk tropical areas should be considered as candidates for gammaglobulin, also those with debilitating conditions. The preparation must be used with care in those with a history of repeated blood transfusions (antibodies to gammaglobulin may be present).

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Effects of tamoxifen in relation to breast cancer

SIR,—The letter by Dr E Ferrazzi and others (21 May, p 1351) concerning the oestrogenic effects of tamoxifen during the treatment of breast cancer deserves further comment. They make reference to the oestrogenic effects of tamoxifen in laboratory animals and suggest that mammary tumour regression in man