incentive compared with working in a smaller town, where housing, education, and the cost of living are cheaper, while the quality of life and leisure is better. The medical students we are now teaching see this all too clearly and recognise that general practice offers greater life earnings and a better life style compared with hospital medicine.

In spite of appeals to the local area health authority they neither know nor want to know about the problem and are prepared, it would seem, to accept the lowering of surgical practice to that of a simple emergency service, with empty hospital beds and immensely long waiting lists.

We feel that the already lowered standard of surgery in this area will be reduced to a level where high-standard professional work is no longer possible.

We write this letter because we feel that neither the public nor even our general practitioner colleagues know the difficulties under which we work.

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Chairman,
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How effective is measles immunisation?

SIR,—Drs M D Coulter and B M Jones report the occurrence of measles in vaccinated children and ask, "How effective is measles immunisation?" (21 May, p 1347). The Medical Research Council Measles Vaccines Committee has now published three reports covering respectively the first six months, two years nine months, and four years nine months of their trial.¹⁻³ A report after 12 years of follow-up is shortly to be submitted for publication. The high protection rates observed in the early years have been well maintained over the 12-year period; throughout, about 10 times more cases of measles have occurred in unvaccinated as in vaccinated children.

The trial has established that a single dose of live attenuated measles vaccine given at 10 months or 2 years of age confers effective protection on about 90% of vaccinated children over a 12-year period.

C L MILLER
Secretary,
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¹ MRC Measles Vaccines Committee, *British Medical Journal*, 1966, 1, 447.

² MRC Measles Vaccines Committee, *British Medical Journal*, 1968, 2, 449.

³ MRC Measles Vaccines Committee, *Practitioner*, 1971, 206, 458.

Medical management of endometriosis

SIR,—In your leading article on this subject (7 May, p 1175) I feel that you are less than fair in your assessment of the effects of pseudo-pregnancy, particularly in your statement that its "beneficial effects . . . are often transient."

The paper by Andrews and Larsen that you cite¹ describes a uniquely unfavourable experience in this field, and our series of some 200 cases in Worcester has shown recurrence of symptoms after five years in no

more than 30%. In more than two-thirds of all cases freedom from symptoms has lasted much longer, in some cases as much as 17 years. The fact that in Andrews and Larsen's patients 19 out of 21 undergoing pelvic operation after pseudopregnancy showed active endometriosis is much less significant than your presentation would suggest. Surely these patients are a highly selected unfavourable group showing either persistent, recurrent, or new foci of endometriosis, which in our case material represents less than one-third of the total. Furthermore, even symptomatic relief for an average of 5½ years may be of value and may afford opportunities for pregnancy and at least the postponement of surgery to an age at which the patient may regard it as less of a disaster.

As regards danazol, it is perhaps unfortunate that you have concentrated entirely upon experience in the United States and that the not inconsiderable body of experience in Britain presented at a symposium at the Royal College of Physicians of London on 29 April was not available to you in time for the publication of your leading article. The findings presented were encouraging and suggest that your optimistic view of the value of danazol in endometriosis may well prove to be justified. In a small preliminary series treated in Worcester during the past three years results have been very good and the incidence of side effects lower than that with combined oestrogen-progestogen preparations. A further study now in progress with lower dosage will, it is hoped, still further reduce side effects while maintaining therapeutic effectiveness.

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¹ Andrews, W C, and Larsen, G D. *American Journal of Obstetrics and Gynecology*, 1974, 118, 643.

Potential of warfarin by azapropazone

SIR,—Recently in Portsmouth we have seen three instances of marked potentiation of warfarin action by azapropazone (Rheumox) which occurred in patients on long-term anticoagulant therapy who were treated for arthritic conditions. They had previously been well stabilised on moderate doses of warfarin. Within a few days of starting treatment with azapropazone all developed bruising and had British prothrombin ratios in the order of 15.0. One patient was taking only one capsule (300 mg) of azapropazone a day. Two of the patients had had cardiac valve replacement and may have had the added problem of mild liver dysfunction associated with chronic congestive heart failure. Their regular dose of warfarin was in the range of 5-10 mg a day, indicating that they were not unduly sensitive to the action of this drug.

Earlier suggestions that the administration of azapropazone to patients previously stabilised on warfarin resulted in an increase in prothrombin time led to an experiment at Bangor in which an attempt to reproduce this effect was conducted with two volunteer subjects. The first was stabilised on adjusted doses of warfarin until a plateau was reached after 12 days. Between day 12 and day 17 the prothrombin time was 23-24 s (twice the mean normal). On day 17 the subject started taking azapropazone 300 mg four times daily. After the first day the prothrombin time rose

to 28 s and the administration of warfarin was stopped. By day 20 the prothrombin time had increased to 48 s (four times normal). Vitamin K was administered and the prothrombin time returned to normal.

The second subject was stabilised at a prothrombin time 1.5 times the normal level of 12 s, the level after 14 days being 17 s. Azapropazone administration was started while the dose of warfarin was maintained at 3.5 mg daily. After two days the prothrombin time had risen to 22 s and by the third day of the combined regimen it had reached 24 seconds. The administration of warfarin was stopped while that of azapropazone was continued for a further two days. The prothrombin time reached a maximum of 30 s by the last day of azapropazone administration and then slowly declined.

On this evidence we feel it inadvisable to administer azapropazone to patients already taking warfarin. This caution should be extended to other oral anticoagulants until current studies produce further information.

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Laparoscopic surgery

SIR,—When first introduced laparoscopy was used with understandable caution in patients who had had previous lower abdominal surgery. It was felt by many that the risks of perforating bowel adherent to the parietal peritoneum precluded the procedure. However, concomitant pelvic adhesions could be present and the cause of infertility.

In 11 selected patients in whom retention of fertility was of great importance a laparoscopic assessment was done 7-10 days after earlier laparotomy had been performed for conditions such as ectopic pregnancy, pelvic sepsis, uteroplasty, or tuboplasty. Selection was based on the presence of persistent pain, pyrexia, or a pelvic mass indicating continuing pelvic pathology. In each case I found significant adhesions. These were all separated readily, but painstaking care was needed to ensure that separation occurred at the line of cleavage so that no damage was caused to the viscera. In three patients oozing persisted from the line of division. Although insufficient to warrant laparotomy, a Portovac drain was inserted and positive vacuum drainage instituted. A specimen of the fluid obtained was submitted for culture and sensitivities to antibiotics when relevant. More recently I have noted that this type of oozing is not seen when laparoscopy was undertaken at an earlier stage—6-7 days after the initial operation. The patients suffered minimum discomfort from this second procedure and all were discharged symptom-free within 24 h of laparoscopy.

These 11 cases were selected from a large and varied gynaecological practice over the past six months. In the first case the patient had had four laparotomies for recurrent

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.

E G SIMONS

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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.

M R SCOTT

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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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Peterborough Health District

Peterborough

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 ($P < 0.05$).