The problems of diurnal variability and laboratory variation in the measurement of plasma urate are real ones, as Mr Dunlop and Mr Davison clearly state. The former problem is not so important if blood is taken at a consistent time of day (in the morning in our study); and the latter problem can be reduced if repeated readings are demanded before a rise is accepted as real (three consecutive measurements in our study). By adopting these precautions we were able to identify a group with platelet count changes suggesting early consumption and consistent with the hypothesis that this is characteristic of the early onset of pre-eclampsia.

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JOHN BONNAR

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Rubella vaccination

SIR,—May I raise again the question of our policy on rubella vaccination?

The Department of Health and Social Security issued a circular letter CMO 76-4 in February 1976 reaffirming the policy of directing the immunisation programme at girls between their 11th and 14th birthdays and susceptible groups of women of child-bearing age. It was admitted that this policy had not resulted in any decrease in the incidence of congenital rubella. Recent serological surveys had shown that about 10% of young women were susceptible compared with about 20% before the vaccination programme began in September 1970; the acceptance rate of rubella immunisation was between 70 and 75% and no further significant reduction in the proportion of susceptible mothers was expected until the 1980s.

It is known that the protection afforded by rubella vaccination lasts for at least eight years and probably for very much longer. In view of this, should we not reconsider changing our policy and aim at the elimination of outbreaks of rubella by the routine vaccination of all children, boys as well as girls? Obviously the girls would still receive individual protection, and the growing practice of screening pregnant women for rubella antibodies and offering immunisation after delivery to those found to be susceptible could continue with advantage.

The Joint Committee on Vaccination and Immunisation should be asked to look at this again.

L A CRAWFORD

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Coronary heart disease and male sex hormones

SIR,—Several authors (25 February, p 472; 1 April, p 851) have recently presented indirect evidence suggesting that male sex hormones contribute to men's higher risk of coronary heart disease. However, several older investigations provide evidence against this hypothesis. Castration of teenage boys and young men apparently does not cause a significant difference in death rates from

cardiovascular disease.¹ Castration at older ages is not associated with any change in coronary atherosclerosis.² A comparison between young men who had recovered from a myocardial infarction and age-matched controls showed no significant differences in serum concentrations of testosterone or dihydrotestosterone.³ No consistent differences in the masculinity of body characteristics have been found in comparisons between young men who have coronary heart disease and controls^{3,4}; there were no significant differences in balding or in overall body hair, and observed differences in body form could for the most part be attributed to the greater obesity of the subjects with coronary heart disease. These observations suggest that male sex hormones are not a major cause of men's higher rates of coronary heart disease.

Other evidence indicates that major causes of men's elevated coronary heart disease mortality are men's higher rates of cigarette smoking and of the hard-driving coronary-prone behaviour pattern.^{5,6}

I L WALDRON

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¹ Hamilton, J B, and Mestler, G E, *Journal of Gerontology*, 1969, **24**, 395.

² London, W T, et al, *Annals of Internal Medicine*, 1961, **55**, 63.

³ Phillips, G B, *Lancet*, 1976, **2**, 14.

⁴ Gertler, M M, and White, P D, *Coronary Heart Disease in Young Adults*. Cambridge, Harvard University Press, 1954.

⁵ Waldron, I, *Social Science and Medicine*, 1976, **10**, 349.

⁶ Waldron, I, *New England Journal of Medicine*, 1978, **298**, 57.

Cetiprin (emepronium bromide) in patients with prostatism

SIR,—In the advertisement for Cetiprin (emepronium bromide) on the inside back cover of the *BMJ* dated 15 April the manufacturers, KabiVitrum, state under "contraindications and precautions": "Whilst emepronium bromide is indicated in the early stages of prostatic enlargement with urinary frequency, it is contra-indicated in later stages with flaccid bladder and large amounts of residual urine." In *MIMS* the contra-indications listed are advanced prostatic hypertrophy, with special precautions in patients with glaucoma and gastric retention.

I wonder if many urologists would recommend suppressing bladder activity in patients with prostatism. There is an obvious danger that the reduced bladder awareness and activity achieved by this form of treatment may well lead to increased residual urine. My own view is that emepronium should be prescribed only for patients who are not in danger of developing residual urine. I would hope that a warning to this effect may be included in subsequent advertisements.

ERIC GLEN

Urodynamic Service,
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Glasgow

*.*Mr Glen sent a copy of his letter to the manufacturers of Cetiprin, whose reply is printed below.—Ed, *BMJ*.

SIR,—Mr Glen rightly questions the use of emepronium bromide in patients with prostatic hypertrophy who are likely thereby to develop undesirable levels of residual urine. While we accept Mr Glen's comments as being con-

structive, it would, I feel, be wrong to regard prostatism, even in its earliest stages, as an absolute contraindication to emepronium therapy.

It is well known that even a small obstruction to the vesical outlet can increase bladder irritability, resulting in impaired control, frequency, and uninhibited bladder contractions. The balance between the degree of obstruction to the bladder outlet and the efficiency of the neuromuscular mechanism is important. Although large quantities of residual urine may be found in association with inefficient voiding contractions, it is possible that emepronium bromide can, by blocking involuntary uninhibited contractions and restoring normal detrusor-sphincter balance, improve bladder function and thereby reduce the amount of residual urine. I will be happy to refer Mr Glen to several urologists who hold this point of view.

ALLAN D LAUDER
Medical Director
KabiVitrum Ltd

London W5

Stricture of oesophagus associated with ankylosing spondylitis

SIR,—The letter from Mr A M Hay (4 May, p 1138) concerning a stricture of the oesophagus associated with ankylosing spondylitis is interesting but does not mention the association between spondylitis and Crohn's disease. The latter may present as dysphagia and strictures can develop.^{1,2} This may well have a bearing on this case.

A P WEETMAN

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¹ Gelfand, M D, and Krone, C L, *Gastroenterology*, 1968, **55**, 510.

² Dyer, N H, et al, *Gut*, 1969, **10**, 549.

Is pancreatic isotope scanning worth while?

SIR,—It was interesting to have comments from Dr H J Testa and his colleagues (18 March, p 720) on our paper (4 February, p 282) concerning isotope scanning of the pancreas since Manchester must be one of very few centres with an interest in pancreatic diseases still apparently relying on the technique; indeed, can they tell us of any other in Britain or overseas?

Their own data on 200 patients confirms everyone's experience that abnormal scans are meaningless; of 107 patients with abdominal scans, 49 proved to have no pancreatic disease. Thus only 93 (the normal scans) of all their 200 studies could be of any clinical value, even if they were all correct. The Manchester false-negative rate was certainly lower than ours, but even they were only able to detect 64% of patients with a normal pancreas, which seems rather poor for a screening test. Scans of all types are in demand if they are clinically useful; indeed many are requested even when they are not. Isotope scanning has been available for many years. From our own experience and the reported survey of nuclear medicine departments it is quite clear that pragmatic clinicians have now discarded the technique; it is just not worth asking for.

There is now no shortage of alternative diagnostic techniques for the pancreas. Most are complex and expensive, but grey-scale

ultrasonography is non-invasive, safe, and reasonably cheap. The results can be very accurate. In a recent prospective study of 124 patients¹ there were no false-normal reports. Ultrasound correctly identified all 33 patients with chronic pancreatic disease and correctly classified them as suffering from cancer or pancreatitis. There were four false-positive reports.

No doubt the results of ultrasonography and isotope scanning are both subject to the individual operator's expertise and experience. The crucial question for any promising diagnostic method is whether or not it is "exportable"—whether the same results can be obtained in less committed hands. The answer for isotope scanning is already clear; for ultrasonography we must wait a little longer.

PETER B COTTON

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¹ Lees, W R, *et al*, *Gut*. In press.

Psychiatric problems after mastectomy

SIR,—May I take issue with the choice of controls in the investigation reported by Dr G P Maguire and others (15 April, p 963)? The authors may be confusing the psychiatric effects of cancerophobia, those of mutilating surgery, and those of benign breast disease. Control groups should surely include, for example, women who have undergone other types of mutilating surgery (for example, limb amputation for benign lesions), those who have undergone mastectomy for benign lesions, as well as those who have experienced non-mutilating cancer surgery. If such obvious measures are not taken, surely one cannot disentangle the specific psychosocial blame attributable to mastectomy for neoplasm?

H G KINNELL

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Cimetidine and protective effect of mucus in gastric ulcer

SIR,—In a previous letter (18 March, p 718) we reported changes in gastric mucin after four weeks' treatment with cimetidine in patients with duodenal ulceration. Our data seemed to suggest that relapse of peptic ulceration after interruption of cimetidine treatment might be due to a reduced protective effect of gastric mucus. The present study was undertaken in order to determine whether in patients with gastric ulcer cimetidine could induce similar changes in gastric mucin.

Eight patients aged 34-62 years with endoscopically confirmed gastric ulcer were studied. Several gastric biopsy specimens were taken to exclude malignancy. Cimetidine was given at a dose of 1 g daily for four weeks. Gastric mucin fractions in fasting gastric juice were measured by Glass's method¹ before and after treatment, samples of gastric juice being obtained by gastric tube, left in situ for 30 minutes. Patients who showed no endoscopic evidence of healing at four weeks continued cimetidine treatment in full dosage for a further two weeks. Patients whose ulcers had healed were given a maintenance dose of 400 mg at bedtime.

The ratio of neutral glycoprotein-mucoprotease complex to acid mucoprotein complex was expressed as a "mucoprotective index" calculated from the formula $B \div (A+B) \times 100$, where A =

acid mucoprotein complex (g/l) and B = neutral glycoprotein-mucoprotease complex (g/l). No significant changes in mucoprotective index were found after cimetidine treatment ($P > 0.05$ by Student's *t* test). The mean values for the mucoprotective index were 41.7 ± 15.5 (SEM) before treatment and 29.2 ± 6.5 at four weeks.

The behaviour of gastric mucin in cimetidine-treated patients with gastric ulcer seems to be different from that previously found in duodenal ulcer. However, it must be pointed out that the initial values of the mucoprotective index in these patients were considerably lower than those observed in the patients with duodenal ulcer. Obviously it cannot be expected that cimetidine should worsen an already poorly protective gastric mucus. Nevertheless, it must be remembered that, in spite of the healing of gastric ulceration by cimetidine, the gastric mucosa is still subject to relapses because of the persisting lack of protective mechanisms. A possible rise in the potential difference across the gastric mucosa² does not mean that cimetidine has a protective effect on the gastric mucosal barrier.³

The unchanged poor quality of mucus in patients whose gastric ulcer has healed may possibly explain relapses when cimetidine is discontinued just as reduced mucoprotective function may explain relapses in patients with previous duodenal ulceration. The use of carbenoxolone as mucopoietic agent during or after cimetidine treatment could be helpful, and this is under investigation.

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A TITTOBELLO
A EVANGELISTA
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¹ Glass, G B J, *Annals of the New York Academy of Sciences*, 1967, **140**, 804.

² Ivey, K J, *et al*, *Lancet*, 1975, **2**, 1072.

³ Read, N W, and Levin, R J, *Lancet*, 1975, **2**, 1314.

Painful young bellies

SIR,—Your leading article (29 April, p 1090) omitted what in my experience is the commonest cause of abdominal pain in children and the commonest cause of unnecessary investigation and referral for unnecessary psychotherapy.

Injury to the abdominal wall during games and physical education is frequently seen by the general practitioner. The tender, painful lesion is usually palpable in the rectus abdominis or oblique muscles. It does not change in intensity when the child folds its arms across its chest and raises its shoulders off the couch. It is cured immediately by an injection of a mixture of triamcinolone acetonide and 2% lignocaine.¹

I H J BOURNE

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¹ Bourne, I H J, *British Medical Journal*, 1977, **2**, 1158.

SIR,—In your leading article on this subject (29 April, p 1090) there was no mention of the parasitic causes of abdominal pain.

In Africa, the Middle and Far East, and Eastern Europe, and to some extent in the rural areas of Northern Europe, *Ascaris lumbricoides* (the roundworm) is very well known to surgeons as a cause of abdominal pain. The worm measures 20-30 cm in length

and gives rise to colicky abdominal pain in young children because of the small lumen of their intestines. The pain may be acute or recurrent depending on the number of parasites eventually reaching the bowel. In adults it does not give rise to abdominal symptoms. The blood film shows eosinophilia. The plain abdominal x-ray is often unhelpful but barium studies may show the parasites. The stools will almost always contain the ova of the worms.

Surgeons in the endemic areas are very well aware of the problem and often the parasites are seen in the stool after the patients have been admitted for observation, with relief of symptoms.

In conclusion, I would stress that the investigation of a painful belly in a child is not complete unless the stools are examined microscopically.

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"Innovation in the Pharmaceutical Industry"

SIR,—Without wishing to come between David Schwartzmann and Professor M D Rawlins in their debate on the effects of increased regulatory demand on drug discovery (22 October, p 1076, and 8 April, p 919) I think the following is relevant to their discussion.

In recent years Parke Davis, Nicholas, and Twyford Laboratories have all closed down their research and development groups in Britain, with resulting redundancies of substantial numbers of scientists. Macfarlanes, Duncan Flockhart, British Drug Houses, Horlicks, Evans Medical, and Riker Laboratories have each terminated their individual research and development following take-overs; in certain cases major research groups were disbanded as a result.

This evidence supports David Schwartzmann's contention that the cost of drug development is now so great that pharmaceutical innovation is in danger of drying up.

J F CAVALLA

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Society for Drug Research

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Plasmapheresis

SIR,—In your leading article (22 April, p 1011) we were surprised to find no mention of plasmapheresis in hyperviscosity syndromes in patients with Waldenström's macroglobulinaemia and myeloma, particularly of the IgA type.

We would like to report our experience with plasmapheresis in a 47-year-old man who was admitted to hospital in January 1977 with pneumonia. Our investigations showed that he suffered from IgA myeloma with a plasma monoclonal IgA concentration of 61 g/l and 30% myeloma cells in the marrow. He was entered into the Medical Research Council trial for multiple myeloma and was selected at random to receive cyclophosphamide 1 g at 2-3-weekly intervals. In February 1977 he started complaining of blurring of vision, which worried him considerably. Plasma viscosity was found to be 0.4 Pa.s (4.4 cP) at 25°C. We therefore carried out plasmapheresis on six occasions over a