of a return to Lane's technique and less reliance on antibiotics to cover simple lack of cleanliness in the theatres it will have done some good. If not I may feel safer, when my time comes, to have my prostate removed in the clean kitchen of my own home by a bald-headed surgeon. And that, sir, is not meant as a joke.

ROBERT BEWICK

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Inheritance of Marfan's syndrome

SIR,—Further to Dr J Burn's letter on the above subject (14 January, p 108) I should like to confirm the absence of mental handicap in Marfan's syndrome. I see the majority of the freshmen who come to this university each year, and over the past 15 years the incidence of this syndrome has been about 1 in 1500. The incidence in the general population is 1 in 20 000. QED.

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Smoking and asthma

SIR,—Dr F E de W Cayley (14 January, p 110) points out that giving up smoking may trigger the new appearance of type 1 hypersensitivity, and asks if we should encourage our asthmatic patients to smoke. It is true in our experience that type 1 hypersensitivity and cigarette smoking virtually exclude each other (though there may not be a direct causal link) and we frequently meet patients who had never had asthma until they stopped smoking.

We must not, however, advise our asthmatics to smoke since (a) given the choice one would rather have asthma than cancer and coronary disease, and (b) patients who become asthmatic on stopping smoking might not have developed allergic disease if they had never started smoking in the first place. One could easily postulate that the chronic immunosuppression of smoking¹ causes allergic sensitisation that only becomes manifest once the immunosuppression is removed.

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¹ Thomas, W, Holt, P G, and Keast, D, *Nature*, 1973, **243**, 240.

Carcinoma of the pancreas

SIR,—In your recent leading article on this subject (10 December, p 1497) no mention is made of the important problem of differentiating carcinoma from pancreatitis, which may often be extremely difficult and may delay the diagnosis of cancer.

We have shown that the estimation of lactoferrin, an iron-containing glycoprotein, by radioimmunoassay in pure pancreatic juice obtained endoscopically is a sensitive and apparently specific method for the differentiation of these two conditions.¹ We have now studied 20 patients with chronic pancreatitis, 10 patients with carcinoma of the pancreas, and 16 control subjects being investigated for suspected pancreatic disease and later found

to be normal. The median lactoferrin concentration in control subjects was 83 $\mu\text{g/l}$ (range 16–390); in patients with chronic pancreatitis 2240 $\mu\text{g/l}$ (range 870–11 400); and in patients with pancreatic cancer 105 $\mu\text{g/l}$ (range 10–387). In a single patient with both cancer and pancreatitis the lactoferrin level was 1300 $\mu\text{g/l}$. However, the combination of cancer and pancreatitis is rare.²

These results suggest that the measurement of lactoferrin in pure pancreatic juice may be a useful diagnostic aid in pancreatic disorders, particularly the differentiation between chronic pancreatitis and pancreatic cancer.

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¹ Fedail, S S, *et al*, *Gut*, 1977, **18**, A975.

² Robinson, A, Scott, J, and Rosenfeld, D D, *Radiology*, 1970, **94**, 289.

Vitamin D status in different subgroups of British Asians

SIR,—Dollery *et al*¹ suggested that the higher serum 25-hydroxycholecalciferol (25-OHD₃) concentrations of Goan Asians reported by Hunt *et al*² might result from induction of hepatic microsomes by meat and fish found in the diet of this community but absent from that of the groups with lower serum 25-OHD₃ values. Hunt *et al*³ subsequently reported a significant correlation between the serum 25-OHD₃ concentrations of the Asians originally surveyed and the percentage of protein derived from animal sources in the diet.

We decided to investigate in rats whether meat itself affects vitamin D metabolism. Three experiments were performed; in each of them groups of rats were given a meat or a vegetarian diet. In the meat diet the major protein source was boiled mutton; in the vegetarian diet it was wheat flour and cooked chickpeas. Apart from protein source the diets were designed to have similar percentages of energy from fat (34%), protein (12%), and carbohydrate (54%), polyunsaturated:saturated ratios, and fibre content. In composition they resembled the meat and vegetarian diets of the Ugandan Asians originally surveyed.⁴

In the first experiment two groups of 16 vitamin D-depleted rats fed on one of the two diets were injected subcutaneously with 25 μg of vitamin D₃. Three weeks later 10 rats were killed and their serum assayed for 25-OHD₃. For the second experiment two groups of 10 matched pairs of rats similarly depleted and fed were injected with 25 μg of 4-¹⁴C-cholecalciferol. Faeces were collected over five weeks and three-day collections were combusted and analysed for ¹⁴C content. The third experiment measured the rate of metabolism of drugs ("sleeping time") in rats fed the two diets. Sodium pentobarbitone and zoxazolamine were successively used since the enzymes involved in their metabolism show different responses to inducers.⁵

There was no significant difference between the serum 25-OHD₃ and faecal ¹⁴C excretion in rats fed the meat and vegetarian diets. Neither was there any significant difference in the sleeping time of rats on each diet after administration of the drugs.

Miranda and Webb⁶ reported that large differences in the level and quality of protein in the diet affect the toxicity of heptachlor in rats; however these variables were minimised in our study. Fraser *et al*⁷ presented evidence in humans that antipyrine half life is 50%

shorter in meat eaters than in vegetarians. They have also suggested¹ a specific induction of hepatic vitamin D-25-hydroxylase by meat rather than a general induction of metabolic enzymes similar to that thought to occur in osteomalacia induced by anticonvulsants. Our experiments did not confirm these suggestions, however. We found no evidence for induction of hepatic vitamin D-25-hydroxylase or increased metabolism and excretion of vitamin D when feeding meat. Neither was the rate of drug metabolism increased on the meat diet.

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¹ Dollery, C T, *et al*, *British Medical Journal*, 1977, **1**, 104.

² Hunt, S P, *et al*, *British Medical Journal*, 1976, **2**, 1351.

³ Hunt, S P, *et al*, *British Medical Journal*, 1977, **1**, 641.

⁴ Hunt, S P, *et al*, PhD thesis, University of London, 1977.

⁵ Conney, A H, *et al*, *Journal of Pharmacology and Experimental Therapeutics*, 1960, **130**, 1.

⁶ Miranda, C L, and Webb, R E, *Food and Cosmetics Toxicology*, 1973, **11**, 63.

⁷ Fraser, H S, *et al*, *Clinical Pharmacology and Therapeutics*. In press.

Fibrinolytic inhibitors for acute gastric haemorrhage

SIR,—I welcome your timely leading article (17 December, p 1565) on the use of fibrinolytic inhibitors in the treatment of acute gastric haemorrhage. It may be of interest to readers to know that this study of gastric bleeding, started in Manchester in the mid-'60s, was a clinical one. Previous to our publication the stomach had not been suspected as a site of fibrinolysis and the investigation antedated the modern discoveries of the production of vascular activator.

This clinical problem concerned the operative treatment of patients suffering from uncontrollable gastric haemorrhage in whom no ulcer was detectable before and after opening the stomach. A rather high partial gastrectomy was the routine procedure in these patients. I had for many years examined the removed portion of the stomach in the theatre when the specimen was fresh in order to try to identify gastric erosions. The mucosal surface was washed, dried with blotting paper, and carefully scanned with a magnifying glass. This procedure was not helpful. In the majority of cases no abnormality was found; in a few cases a suspicious area was found and marked by transfixion with thread, but in only one did the pathologist confirm the presence of an erosion.

The conclusion I drew from these observations was that a stomach could feel and look normal, at operation, from the outside and inside and yet be harbouring a potentially lethal haemorrhagic lesion—presumably multiple. The surgeon who has just completed a partial gastrectomy and finds what looks like a normal mucosa and no ulcer in the removed stomach is likely to be disappointed. On the other hand the surgeon may consider his operation to have been well judged if he finds a definite superficial ulcer. This is sometimes present high on the lesser curve. There appeared to be a degree of physiological confusion here because it is the normal-looking gastric mucosa which is killing the patient

and should be removed; the superficial ulcer (based on the subsequent pathological report) may be contributing little to the submucosal haemorrhage. These haemorrhages suggested a widespread pathological process in the stomach wall of unknown aetiology. Additional investigations were clearly required. The initial step in these further procedures was the aspiration of blood from the gastric veins and arteries at routine gastric operations. The laboratory testing of these specimens of blood was carried out by my colleagues at Withington Hospital and the first of our reports appeared in 1967.¹

H T Cox

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¹ Cox, H T, Poller, L, and Thomson, J M, *Lancet*, 1967, **1**, 1300.

"Squelch sign" in detection of small herniae

SIR,—It may sometimes be difficult to detect the presence of a small inguinal rupture, particularly if it is hard to be convinced of the presence of a cough impulse. The following method has been found to be valuable.

The patient is examined standing. If the clinician is right-handed he examines the patient while standing on his right. He places his hand flat over the patient's inguinal canal and applies pressure with a quick, jerky movement of the fingers (similar to that used in "dipping" to detect the presence of ascitic fluid). If a hernia is present the contents of the sac are felt sliding back into the abdominal cavity, producing a "squelching" sensation.

A similar sensation can sometimes be felt with a large lipoma of the cord. Nevertheless, when one is in any doubt about the presence of a hernia and a cough impulse cannot be elicited with certainty a positive "squelch sign" may be a useful aid to diagnosis.

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Papilloedema in patients taking perhexiline maleate

SIR,—We were interested in the report of "Raised intracranial pressure due to perhexiline maleate" by Dr W P Stephens and others (7 January, p 21), but we question the conclusion reached in their title. The three patients described had bilateral papilloedema; investigation excluded an intracranial mass or hydrocephalus and the fundal appearances improved when perhexiline was stopped. Measurement of cerebrospinal fluid (CSF) pressure was not made during the initial evaluation, but one man had a pressure of "130 mm Hg" (presumably 130 mm H₂O) six weeks after the perhexiline was stopped, when his fundi had returned to normal.

Papilloedema has been noted previously in three patients who presented with a peripheral neuropathy caused by perhexiline.¹ The CSF pressures were not included in this report, but a high CSF protein concentration was noted, up to 10 g/l. Although there was no clinical evidence for a neuropathy among Dr Stephens's patients, nerve conduction studies might have been revealing as one patient (case 3) complained of numbness and weakness of the limbs and all had ataxia of gait.

We recently investigated a 52-year-old man with a peripheral neuropathy and papilloedema; he had taken perhexiline maleate for one year. No structural intracranial lesion was defined and his CSF pressure was normal. The CSF protein level was elevated at 1.46 g/l. Four months after stopping perhexiline there had been substantial improvement in his neurological state and fundal appearances.

We feel that the cause of papilloedema in patients taking perhexiline needs to be identified for there is as yet no proof of elevated intracranial pressure. (We accept that intermittent pressure elevation might explain the findings in our patient.)

Papilloedema is sometimes seen in association with the Guillain-Barré syndrome. Abnormalities in CSF protein and changes in CSF pressure have been implicated in this context, but the mechanism for papilloedema remains unknown.^{2 3}

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¹ Bousser, M G, *et al*, *Coeur et Médecine Interne*, 1976, **15**, 181.

² Drew, A L, and Magee, K R, *Archives of Neurology and Psychiatry*, 1951, **66**, 744.

³ Morley, J B, and Reynolds, E H, *Brain*, 1966, **89**, 205.

Thyroid disease and asthma

SIR,—Your leading article (5 November, p 1173) omits discussion of the possibility that the link between these two types of disease might be the iodine contained in the medicines given to asthmatics.

The syndrome of iodine-induced thyrotoxicosis (Jod-Basedow) is well recognised. A recent review by Weaver *et al*¹ suggests that the increase in a variety of thyroidal abnormalities may be related to the iodine supplements added to our diet. Those who take large and continuing doses of potassium iodide, among them many asthmatics, are the more likely to show evidence of toxicity from this potentially harmful element.

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¹ Weaver, D K, Nishiyama, R H, and Batsakis, J G, *Annals of Clinical and Laboratory Science*, 1976, **6**, 545.

Pathogenesis of acute appendicitis

SIR,—I would like to endorse the findings of Mr L W L Horton (24-31 December, p 1672) with regard to the pathogenesis of acute appendicitis. At the suggestion of Mr Denis Burkitt we also have studied the histological findings in 30 consecutive cases of acute appendicitis. Appendices were opened longitudinally when fresh, as described by Mr Horton. In our series the inflammation was total or confined to the distal part of the appendix in 90% of cases. Inflammation of the proximal part of the appendix occurred in only one case.

Similarly, in our series, faecoliths were found in only 10% of cases, but an obstructed lumen due to faeculent or purulent material was found in 60%. These findings would tend

to confirm the low-fibre theory of obstruction causing acute appendicitis suggested by Mr Horton.

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Vasovagal shock after insertion of intrauterine device

SIR,—With reference to your expert's answer to a question on this subject (24-31 December, p 1645), while it is to be hoped that all clinicians will use care and gentleness when dealing with patients and while this approach would no doubt reduce patients' anxiety, it remains a fact that inhibition of cardiac action as a result of pelvic examination can at times be dangerous. This matter was dealt with by you in 1970 in a leading article¹ which was followed by a letter from me² pointing out the increased risk during the insertion of intrauterine devices.

To attempt to remove a device while a patient is suffering from vasovagal shock could result in more serious complications. The correct treatment is to inject atropine intravenously. (Unless premedication has included the use of atropine even light anaesthesia will not prevent this potentially fatal complication.) The value of the atropine administration can be confirmed by observing that the pulse rises to a normal value some 60 s after the injection. The answer to the question put to your expert should have been: "A syringe and solution of atropine suitable for intravenous administration." No clinic at which intrauterine contraceptives are inserted ought to be without this drug, and other resuscitation equipment should be available. As your expert writes, "Heaven forbid that any other resuscitative measures should need to be considered," but this cannot mean that the possibility is to be ignored.

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¹ *British Medical Journal*, 1970, **3**, 61.

² Menzies, D N, *British Medical Journal*, 1970, **3**, 221.

* * * Our expert replies: "What Mr Menzies suggests is sensible and reasonable, though what I recommended should really be enough. His suggestion that removal of the device might increase the shock is probably more theoretical than real."—ED, *BMJ*.

A case of self-diagnosis

SIR,—I read Dr Eoin O'Brien's article (24-31 December, p 1648) with enjoyment, but I suspect that he is mistaken in attributing his malaise to the Portuguese man-o-war *Physalia physalis*. Strong winds blow physalia from warmer waters to the south and west coasts of the British Isles by acting on its sail-like float. Although occasionally it arrives in great numbers,^{1 2} it makes little headway into the Irish Sea, where it is rare.³ I know of no records from the Irish shore as far north as the Martello Tower from which Buck Mulligan gazed out over this "snotgreen scrotum-tightening" sea.⁴ No unusual influx of physalia was reported in the British Isles in 1977 when, I presume, Dr O'Brien had his unpleasant experience. It is unlikely, therefore, that this species was present at the Forty Foot.