from the preoperative day up to the seventh postoperative day with a Pitman ratemeter No 235. Readings as a percentage of heart count were recorded direct. Each patient's scans were analysed according to four different criteria (see below), all of which have been regarded as diagnostic by different authors. The last of these criteria has usually been used in combination with other criteria,¹ and others have used a 15% differential.² In each instance the scan was regarded as positive only if the criterion was met for 24 hours or more. Confirmation of a diagnostic count has not always formed part of the criteria; not to have done so here would have resulted in a higher number of positives, particularly when analysed by the first criterion, as shown.

Total patients screened	314
20% rise compared with preoperative count ³	73
20% difference between adjacent or opposite sites ¹⁻⁶	30
15% difference between adjacent or opposite sites ⁷	42
20% rise on previous day's count ¹	43

Much the highest number of positives is recorded when comparison is made with the preoperative count. Mr Roberts's suggestions for improved accuracy are desirable, but some of the attractions of the ratemeter compared with the scaler are then lost. Whether or not all these suggestions are followed, we think that only criteria which involve comparison on the same day should be used; in this way the effect of background, which forms an increasing proportion of the count, is minimised and the importance of daily variation in the magnitude of counts reduced. During the first few days, distribution of ¹²⁵I-fibrinogen between intravascular and extravascular spaces is changing and so is the geometry of counting—not only of the legs but of the precordium. We have found a general increase in later leg counts and think that the relative proportion of count formed by extravascular fibrinogen increases more in the legs than the precordium. We realise that the same percentage reading on one day may still represent a different magnitude of counts on another, but we think this is a further reason why comparison with a former count is best avoided. Although the risk of missing bilateral thromboses would seem to be greater if comparison with a former count is excluded, the diagnosis based on such criteria correlates well with phlebography.⁷

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- 1 Bonnar J, and Walsh, J. *Lancet*, 1972, 1, 614.
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Promiscuity and infertility

SIR,—With reference to your leading article (30 August, p 501) there may be other effects of promiscuity than that of venereal disease and subsequent infertility. Green-Armytage¹ reported in 1943 from the West London Hospital that a group of 20 recently married

women who did not use artificial contraception were observed over a period of two years and compared with a group of similar women for a similar period who used barrier methods. The 20 who did not use artificial contraception developed what Green-Armytage called full maturation of the uterus and a high proportion became pregnant, while the 20 who used barrier methods retained what he called a hypoplastic or premarital state of the uterus and five developed cervical erosions. I have looked through the *Index Medicus* and made other inquiries but have not been able to find reports of a confirmatory or conflicting nature. Would it not be possible to repeat the investigation using, at the end of two years for two such groups, assays of oestriol levels in the plasma and of macrophage and lymphocyte competence? The interpretation of such assays might be of interest.

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¹ Green-Armytage, V B. *Proceedings of the Royal Society of Medicine*, 1943, 35, 105.

Complications of central venous catheterisation

SIR,—The complications of central venous catheterisation are important, and Dr M J Greenall and his colleagues (14 June, p. 595) have raised some provocative technical points.

Radiographic visualisation of the catheter is essential as soon as practicable after insertion. Only radio-opaque catheters are acceptable. Nevertheless it is not possible always to x-ray a patient immediately after insertion of a central venous catheter and before its use for fluid infusion. The following technical points help to reduce the possibility of acute complications.

- (1) Advancement of a correctly placed catheter is gentle and easy.
- (2) Do not coil a long catheter up in the right atrium (or right ventricle!) by advancing it too far. Location of the tip in the ipsilateral innominate vein is preferable.
- (3) After insertion and before fixing the catheter attach a syringe containing isotonic saline, inject a millilitre or so to clear any clot, and aspirate blood into the syringe. Do not use undue force when aspirating. If the tip is lodged incorrectly or against the intima of a central vein excessive force is pointless and perhaps even harmful. Should gentle aspiration not produce free-flowing blood inject a little more saline, withdraw the catheter 2 cm, and repeat the aspiration test. Failure to obtain blood is a contraindication to further use of this catheter.

(4) Connect the intravenous drip and observe that it flows freely. The meniscus in the central venous pressure manometer tubing should fall freely to a "sensible" pressure. Erratic pressure measurements may be an early sign of an incorrectly placed catheter.¹

(5) Compress each side of the neck separately. A rise in the central venous pressure greater than 10 cm H₂O suggests the catheter tip is in the ipsilateral internal jugular vein.²

(6) Look at the meniscus and look for two distinct oscillatory patterns: (a) a larger amplitude respiratory oscillation, and (b) a smaller amplitude, higher frequency cardiac oscillation. If these are not both visible, do not infuse fluid nor take pressure readings until the aspiration test is successfully repeated.

A posteroanterior chest radiograph as suggested by Dr Greenall and his colleagues may be impracticable. Will the projection

on an anteroposterior chest film serve the same purpose? It is also impracticable that the arm should not be abducted beyond 90° in some patients requiring intensive nursing care and in certain postural requirements in the operating theatre. In infants wide arm abduction is commonplace.

Cannulation of the jugular³ or subclavian⁴ (or, less commonly, femoral) vein avoids a problem from shoulder movement, and, despite the risks^{5,7} and reasoned arguments for the use of the arm veins,⁸ other veins continue to serve a valuable purpose in experienced and careful hands.

The advice to use only electrolyte solution in the first 12 hours will not necessarily avoid serious consequences of accidental extravasation. On two occasions in my experience resuscitation using colloid infusion through an urgently cannulated subclavian vein was life-saving by the only adequate venous route obtainable.

One must question the wisdom of advising "routine" needle aspiration of the pericardial sac in a resuscitation programme for cardiac arrest in a patient with a central venous catheter in situ. A clinician experienced in this technique is rarely likely to be on the scene.

Withdrawal of an existing central venous catheter by 15 cm before its use in resuscitation can apply only to a arm (or leg) catheter if it is not to be pulled out altogether at an inconvenient moment for the patient.

This paper by Dr Greenall and his colleagues reminds us of two important but not widely appreciated facts. Firstly, cardiac tamponade and other major perforation complications can occur during the first minutes following the insertion of a central venous catheter by whatever route. Secondly, a high quality chest radiograph showing the catheter tip correctly and apparently safely placed, although essential, does not exclude the danger of a complication, immediate or delayed.

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Vaginal cytological examination in anorexia nervosa

SIR,—In connection with the interesting paper by Drs S J Nillius and L Wide (16 August, p 405) I should like to mention a very simple method of monitoring the effect of human chorionic gonadotrophin therapy in amenorrhoeic patients with anorexia nervosa—examination of the vaginal smear. It is easy to perform, quick, and completely harmless. The use of haematoxylin-Shorr staining is advisable.

Of five patients with anorexia nervosa examined before treatment the vaginal smear showed total hormonal ovarian insufficiency in four, while in the other five some oestrogenic effect was demonstrable. There was a

correlation between the vaginal hormonal state and the body weight. During treatment (which was nutritive, not hormonal) in all but one case there was a significant alteration in the vaginal hormonal cytological pattern in that appearance of a cyclic character could be demonstrated although menstruation had not yet returned.¹ We find this method very useful, particularly as it can be repeated frequently.

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¹ Bosze, P., and Oö, M., *Magyar Noorvosok Lapja*. In press.

Cryotherapy for piles

SIR,—In the past three years reports have appeared of the management of piles by cryotherapy, the claims being that treatment could be carried out in an outpatient department or consulting room; that, being painless, anaesthesia was unnecessary; that subsequent morbidity was minimal; and that complete symptomatic relief was almost invariable.^{1,2}

By courtesy of a grant from the East Anglian Regional Health Authority I have been able to test the effect of cryotherapy on piles. The apparatus is expensive—£600 or more. Liquid nitrogen is the cooling agent and at the probe tip a temperature of -180°C is achieved. Exposure of tissue to this temperature for about half a minute or less produces an inflammatory reaction but, usually, not necrosis. Exposure for long periods kills tissue and this is necessary to produce an appreciable effect on piles. A slough forms and is shed in due course, leaving an ulcer which heals by granulation and epithelialisation. An uninfected lesion on normal skin, about 1 cm diameter, was not completely healed until around the 56th day. In the anal canal infection always occurs and healing takes rather longer.

External piles can be treated by cryotherapy without anaesthesia. Freezing is followed by first a watery then a purulent discharge; the piles slough and become very smelly and rather tender. The patient is advised to have daily warm baths and wear an anal pad. After about six weeks the reaction has subsided and the external skin tags will have disappeared.

I have been unable adequately to expose internal piles for application of the probe without dilating the anal sphincter and inserting a speculum. For this day-case anaesthesia or very heavy sedation is necessary. Following application of the probe internal piles slough and are eventually shed. There is considerable discomfort, amounting frequently to pain. Patients remain in bed or away from work for from three to seven days. In all respects the clinical course is not dissimilar from that following spontaneous thrombosis of piles and the amount of analgesic sedation needed is comparable. After six weeks or so the end result is good and I have had no serious complications in 10 cases.

My impression from this investigation is that this is a cumbersome and expensive method of treatment. Pain, morbidity, and time incapacitated are no less, and in many cases longer, than can be achieved by other modern methods. For the conservationists this is manual dilatation of the anus.³ For

abolitionists like myself it is rubber-band ligation for small to moderate internal piles,⁴ while for internal piles which are either very large, covered with squamous metaplasia, or fibrosed by previous thrombosis a conservative excision using multiple transfixion ligatures for each pile is used.⁵ Careful use of these techniques and good judgment in the selection of method have produced results which, by all criteria, are equal to or better than those achieved by cryotherapy.

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Perforation of small intestine and Slow-K

SIR,—Dr B B Scott (13 September, p 649), commenting on our case report (26 July, p 206), draws attention to the often described ulcers of the small bowel which are believed to occur secondary to vascular disease.

Unfortunately our case report had to be pruned to meet the requirements for publication as a "short report" (4 October, p 6). Originally it included a longer report of the operative findings, including the facts that no arterial disease was apparent in the mesenteric vessels (which were easily inspected as there was little fat) and that histological examination showed no evidence of arteriolar disease, the factor cited in the sources quoted by Dr Scott. We note with interest that the authors of one of these papers¹ were attempting to cast doubt on what was to become a well-recognised association between enteric-coated potassium preparations and small-bowel ulceration.

We feel that in the absence of any other demonstrable intestinal disease in our patient, and bearing in mind the known risk of ulceration with Slow-K, the perforation we described was undoubtedly due to Slow-K.

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¹ Alexander, H. C., and Schwartz, G. F., *Gastroenterology*, 1966, 50, 224.

Prostaglandins and carcinoid tumours

SIR,—We read with great interest the case report by Dr J A Barrowman and others of high serum levels of prostaglandins in a case of thyroid medullary carcinoma (5 July, p 11). We have recently observed a patient who had a bronchial carcinoid tumour and very high levels of serum prostaglandins.

A 50-year-old woman had a bronchial carcinoid tumour with diffuse hepatic metastases and classical symptoms of the carcinoid syndrome. She had a permanent flush with exacerbations accompanied by profuse lacrimation and periorbital oedema. The biochemical findings were typical, with elevated serum serotonin ($3.7\text{ }\mu\text{mol}$ (0.65 mg)/l) and 5-hydroxyindole acetate in the urine ($502\text{ }\mu\text{mol}$ (96 mg)/24 h). The diarrhoea was watery in

consistency without increase in transit time, varied between 1 and 2 litres/day, and was not influenced by antiserotonin therapy (parachlorophenylalanine, cyproheptadin).

This watery diarrhoea precipitated a severe hypokalaemia with a plasma potassium level of only 1.8 mmol (mEq)/l. Levels of 3 mmol /l were never exceeded despite intravenous and oral potassium supplements of 250 mmol /day. The diarrhoea was associated with a low gastric acid secretion following pentagastrin stimulation.

There were two possible explanations for this syndrome: (1) An associated amine precursor uptake and decarboxylation tumour, but pancreatic angiography, thyroid scan, and estimation of different polypeptide hormones (vasoactive intestinal protein, thyrocalcitonin, gastrin, insulin) proved negative and no other associated tumour was found on thorough search at necropsy. (2) The secretion of a substance such as prostaglandins (PGs) by the tumour or its metastases. The plasma PG levels (in ng/l), which were measured by radioimmunoassay (Dr Dray), were as follows (normal ranges in parentheses): PGE, 18 (4.3 ± 1.4); PGE₂, 120 (4.5 ± 1); PGF₂, 86 (7.5 ± 2).

It appears from the above result and those of Sandler *et al*¹ that some carcinoid tumours secrete PGs as can other tumours such as medullary carcinoma of the thyroid.² This clinical syndrome—permanent flush, diarrhoea by hypersecretion, and gastric hypochlorhydria—is compatible with the known effect of these fatty acids.^{3,4}

It is worth mentioning that this clinical picture is particularly common in bronchial tumours.⁵ So it would appear to be worth while to estimate the plasma PG levels in cases of carcinoid tumour derived from the foregut and, when appropriate, to treat the profuse diarrhoea with PG inhibitors (indomethacin, aspirin).

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² Williams, E. D., Karim, S. M. M., and Sandler, M., *Lancet*, 1968, 1, 22.

³ Matuchansky, C., and Bernier, J. J., *Gastroenterology*, 1973, 64, 1111.

⁴ Milton-Thompson, G. J., *et al*, *Gut*, 1975, 16, 42.

⁵ Melmon, K. L., Sjoerdsma, A., and Mason, D. T., *American Journal of Medicine*, 1965, 39, 568.

Gentamicin nephrotoxicity in patients with renal allografts

SIR.—Mr J M Wellwood and his colleagues (2 August, p 278) suggest that gentamicin has deleterious effects on renal function in patients with renal allografts. We have found gentamicin to be of considerable value in the management of sepsis in the immunosuppressed renal transplant recipient and we would not wish its value to be undermined on scanty evidence. We agree that gentamicin causes ultrastructural changes in both mice and men and that urinary enzymes as studied by these authors are probably associated. However, we would challenge their view that gentamicin affects renal function significantly in any permanent way. An alternative cause—namely, transplant rejection—is discussed by the authors but they present no evidence to refute this possibility. This is surprising in view of their previous publication¹ in which they state that urinary N-acetyl D-glucosaminidase was abnormally high in 94% of transplant rejection episodes. In their present series the indication for gentamicin therapy in 8 of 19 cases was undiagnosed pyrexia—a phenomenon often