Fig 1

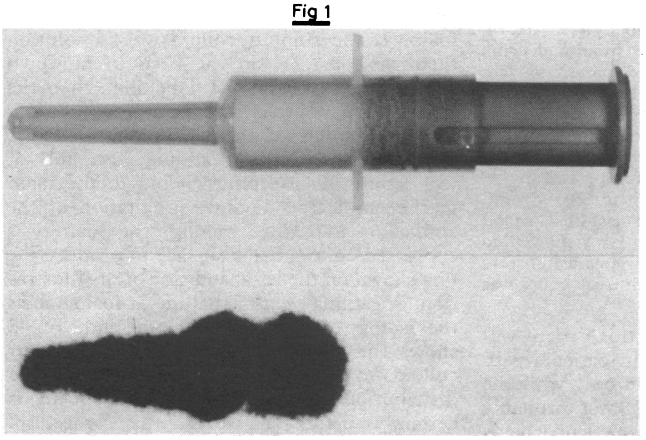

Fig 2

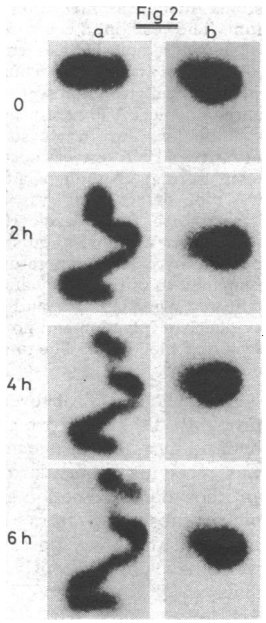

FIG 1—Gamma camera picture of the applicator containing foam mixed with technetium-99m sulphur colloid.

FIG 2—Posterior gamma camera pictures at 0, 2, 4, and 6 hours after introducing technetium-99m sulphur colloid alone (*a*) or mixed with 5 ml of foam (*b*) into the rectum.

0·9% sodium chloride to 5 ml of foam within the applicator through a needle of sufficient length to traverse the entire barrel of the applicator, so that the label could be distributed throughout the foam as the needle was withdrawn during injection. The mixture was then agitated by a series of to-and-fro and rotatory movements of the needle until a satisfactory mixing was obtained, as confirmed by a gamma camera picture of the applicator (fig 1). Gamma camera pictures of the foam after it has been expressed from the applicator suggested, if anything, that mixing had improved. This mixture remained stable as we described.

The study shown in fig 2, however, indicated that inadequate mixing of technetium-99m sulphur colloid and foam would underestimate rather than overestimate the extent of retrograde spread, and so cannot explain the disparity between our findings and those of Dr Hay and his colleagues.

The gamma camera pictures, from two studies in the same patient, show the effect of introducing technetium-99m sulphur colloid in 200 µl 0·9% sodium chloride into the rectum alone (fig 2a) or after mixing it with 5 ml of the 10% hydrocortisone foam (fig 2b). Clearly, the label remains in the rectum unless transported by the foam. This study also answers a question not raised by Dr Hay—namely, that artefactual results could be produced if the mixture dissociated and the label spread retrogradely without the foam or vice versa.

Assessing changes in the physical characteristics of the foam is more difficult. However, in our preliminary studies technetium-99m sulphur colloid did not obviously alter the integrity of the foam as assessed by volume changes of the foam when placed in glass tubes at 37°C, but discrete changes in its ability to spread over or adhere to mucosa cannot be excluded nor can they be measured easily. These observations would also apply to the technique used by Dr Hay and his colleagues.

Variations in technique are not the only variables and it may be that our patients differed in the activity and extent of disease factors known to affect the retrograde spread of aqueous enemas and supported by our findings with the foam enema.

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Genetic association with bladder cancer

SIR,—Your leading article (1 September, p 514) deals with an important new aspect of the pathogenesis of human environmental bladder cancer. It mentions some recent studies on the risk of developing bladder cancer associated with ABO antigens and HLA types. However, for a complete up-to-date assessment of the genetic influence on bladder cancer development a discussion of recent studies on the genetically determined susceptibility to human bladder carcinogens is needed.

It is well known that the susceptibility to arylamine bladder carcinogens in animals is species dependent. Recent studies have indicated that the liver *N*-acetyltransferase-deacetylase enzyme system is an important factor in the species-dependent susceptibility to arylamine bladder carcinogens. Thus species lacking the capacity for *N*-acetylation of arylamines develop bladder cancer after carcinogenic arylamine exposure, whereas species displaying a great capacity for *N*-acetylation do not develop bladder cancer. Liver *N*-acetyltransferase may thus be considered to provide a detoxifying step with respect to arylamine bladder carcinogenesis.

Human hepatic *N*-acetyltransferase is also genetically determined and subject to Mendelian genetic regulation as an autosomal recessive trait. In Copenhagen this results in an approximately 50:50 polymorphic distribution of individuals displaying respectively a rapid acetylator phenotype and a slow acetylator phenotype. In a population of patients with bladder cancer from Copenhagen 65% displayed the slow acetylator phenotype, indicating that slow acetylator individuals may be at higher risk to arylamine-induced bladder cancer. Thus also in human subjects susceptibility to arylamine bladder carcinogens is genetically determined and associated with the slow acetylator phenotype.

The future application of this finding is not a distant dream. It provides us with the possibility of identifying risk groups within a population, and especially within a population exposed to arylamine bladder carcinogens. After such identification it may then be possible to give guidance to individuals about avoiding exposure to these carcinogens.

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[1] Lower, G M, *et al*, *Environmental Health Perspectives*, 1979, **29**, 71.

Rosacea and mast cell stabilisers

SIR,—We were interested to read of the patient with ulcerative colitis who developed severe rosacea during treatment with sodium cromoglycate (3 November, p 1129). It was suggested that the patient should be given either tetracycline or metronidazole. During the last year three of our patients with colitis developed rosacea while receiving mast-cell stabilisers; two were treated with sodium cromoglycate, given as an oral preparation in one and by enema in the other; while a third patient was taking PRD-92 (Boehringer Ingelheim) which is a well-absorbed preparation that acts systemically. Withdrawal of the preparations was followed by a slow but marked improvement. All three patients had previously been unable to tolerate sulphasalazine.

We believe that rosacea is produced by mast-cell stabilisers in some patients; the side effect has not previously been recognised because much smaller doses have been used in patients with asthma. Treatment should include withdrawal of the drug and new cases should be reported to the Committee on Safety of Medicines.

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Oxamniquine and fever

SIR,—Drs G I Higashi and Z Farid (6 October, p 830) discuss the cause of fever resulting from the treatment of *Schistosoma mansoni* with oxamniquine and draw attention to its high frequency in Egyptian patients (40 out of 106) compared with patients in Brazil (17 out of 74).

What was not stated is that the Brazilian series were treated with a single divided (two sites) dose of 15 mg/kg body weight by intramuscular injection whereas, since the Egyptian strain of *S mansoni* is less susceptible to the drug, the dose was much greater in the Egyptian patients—20-30 mg/kg/day for three days—and treatment was given orally. Studies using comparable regimens of treatment would appear necessary before we consider

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differential metabolic mechanisms and production of pyrogenic metabolites.

Post-treatment fever has not been recorded in St Lucia, where the low-dose regimen (15 mg/kg in a single oral dose) gives satisfactory parasitological results and minimum side effects.

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Iatrogenic collapse

SIR,—I should like to comment on Dr Kathleen M Huntington's letter (20 October, p 1001) on her method of sedation for insertion of intrauterine contraceptive devices in nervous patients.

While vasovagal faints during this procedure are rare, profound respiratory depression following intravenous administration of pethidine 100 mg (perhaps more so with Phenergan (promethazine hydrochloride) 25 mg) is all too common.[1] It is certainly true that this is common practice in casualty departments and in wards for short procedures but these areas are better able to cope with the consequences. Intravenous pethidine must be considered in all cases to be a potential anaesthetic rather than an analgesic. As a minimum the patient must be starved and facilities for resuscitation, including effective suction and means for positive-pressure ventilation, should be readily to hand. Further, a narcotic antagonist such as naloxone (Narcan) should be instantly available.

The use of intravenous pethidine in ambulant patients is to be particularly deprecated, a large series[2] showing a 67% incidence of side effects (syncope, lightheadedness, subjective vertigo) in ambulant patients compared with only 26% in hospitalised patients. Finally, the choice of healthy young subjects is not in itself an absolute safety factor with this dosage.[3]

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[1] Goodman, L S, and Gilman, A, (editors), *The Pharmacological Basis of Therapeutics*, 2nd edn, p 264. New York, Macmillan, 1960.
[2] Batterman, R C, *Archives of Internal Medicine*, 1943, **71**, 345.
[3] Prescott, F, *et al*, *Lancet*, 1949, **1**, 340.

Hydrallazine as an aphrodisiac?

SIR,—Although antihypertensive drugs are known[1] to have deleterious effects on sexual function, as discussed in your recent leading article (13 October, p 883), data on the contrary effect are lacking. I wish to report an apparently beneficial effect on hydrallazine (1-hydrazinophthalazine) on sexual function.

A 55-year-old Englishman with essential hypertension of five years' duration had been treated for four years with oxprenolol 160 mg twice daily and hydrochlorothiazide 50 mg once daily without side effects. He developed podogra with a raised serum uric acid, which necessitated withdrawal of the thiazide. His blood pressure one month later was 160/110 mm Hg sitting and 170/114 mm Hg standing, and so hydrallazine 50 mg twice daily was added. This combination gave good blood pressure control and after three months the pressure was 132/92 mm Hg sitting and 132/100 mm Hg standing. He spontaneously volunteered that he had experienced a marked resurgence of sexual ability and had successful intercourse at least three times weekly. This change coincided with the initiation of hydrallazine treatment. He had not had intercourse for 15 years, either because he had not felt the desire to do so or because he failed to maintain an erection. Clinical examination showed normal secondary sexual characteristics and there were no signs of peripheral vascular disease. Blood glucose and the results of routine tests of hepatic and renal function were all normal. Autonomic function was normal as assessed clinically by sweating, sinus arrhythmia, and increase in heart rate on standing. In view of the marked beneficial effect on the patient and his marital relationship, it was felt unethical to test the matter further by hydrallazine withdrawal or placebo substitution.

The cardiovascular changes resulting from hydrallazine treatment even in combination with a beta-blocker may produce a marked reflex increase in sympathetic nervous activity.[2] This, together with the arteriolar vasodilating action, may be implicated in the mechanism of the observed effect. Of interest in this respect are the reports of priapism caused by hydrallazine and more recently (27 October, p 1039) by prazosin, which is a vasodilator and an α-adrenoceptor blocker. The patient described above had experienced no effect on sexual function after treatment with prazosin alone for one month after the initial diagnosis of his hypertension. It would be interesting to hear of any other patients who experienced aphrodisiac effects from hydrallazine because impotence is difficult to treat and can also result in lack of patient compliance with antihypertensive treatment.

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[1] Bulpitt, C J, and Dollery, C T, *British Medical Journal*, 1973, **3**, 485.
[2] Davies, I B, Sever, P S, and Rosenthal, T, *British Journal of Clinical Pharmacology*, 1979, **8**, 49.

Long-term urethral catheter drainage

SIR,—The article by Mr B G Ferrie and others (20 October, p 1046) draws renewed attention to the best method of prolonged drainage of the bladder as a necessity or as a convenience. They state that long-term urethral catheterisation is always to be regarded as second best, a statement with which I am in complete agreement; yet they advocate the same method in treating incontinence whatever its cause. In the case of spinal cord injuries it was the method used by Guttmann,[1] but it proved difficult to control the resulting urethral infection—which was inevitable even if the catheter was removed for 24 hours once a week.

A better alternative is a small, high suprapubic catheter (16 or 18 F), which I advocated in 1943[2 3]; it is inserted when the bladder is distended and should be left in situ for 10 days or more. By that time a track is formed along which a new catheter can be passed; it can be self-retaining or held in place by a stitch tied round it. This catheter can be changed as often or as seldom as the degree of infection indicates. The small skin incision is half way between the umbilicus and the symphisis and the oblique track gives a watertight route for it.

During the first world war some men with wounds of the cord or cauda equina had to be left in no man's land for up to three weeks. In these men the bladder became distended, and in some of them automatic micturition had occurred by the time they were rescued; they were not catheterised.[4]

I am grateful to Mr Ferrie and his colleagues for their paper; I still believe that the small, high suprapubic catheter would be easier, pleasanter, and less costly for the patients and those who look after them than the urethral catheter.

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[1] Guttmann, L, *Proceedings of the Royal Society of Medicine*, 1946, **40**, 225.
[2] Riches, E W, *British Journal of Surgery*, 1943, **31**, 135.
[3] Riches, E W, *Lancet*, 1943, **2**, 128.
[4] Vellacott, P N, and Webb-Johnson, A E, *Lancet*, 1919, **1**, 1733.

SIR,—I was interested to read the paper by Mr B G Ferrie and others on long-term urethral catheter drainage (27 October, p 1046). I applaud their assertion that the horrific bacteriological findings in the urine of those with long-term catheter drainage may normally be safely ignored. In my experience discontinuance of catheter drainage is required only in the following three problems: intolerable discomfort, including great difficulty and discomfort in passing the catheter; persistent leakage of urine around the catheter; and persistent haematuria.

I would, however, venture criticism regarding their remarks on the obsolescence of suprapubic catheters. A number of patients in the younger-chronic-sick ward attached to this hospital, mostly cases of multiple sclerosis, have been given suprapubic cystostomies for incontinence with conspicuous success. They were patients who for one reason or another had had problems with urethral catheters. Our urologist was at first reluctant to undertake the procedure, muttering something about putting the clock back 20 years. Now I believe, however, that he is reconciled, and the only obstruction to carrying out the operation on a much bigger scale and including geriatric patients would seem to be the work load it would impose on the urological units.

A De Pezza catheter is first inserted into the bladder, but after two or three weeks this is replaced by an ordinary Foley-type self-retaining catheter, size 28. The cystostomy opening closes tightly around the catheter and there is virtually no leakage. Replacement of catheters is much simpler and safer and for the patient less painful and less embarrassing than with urethral catheterisation. The first two patients to be so treated have had their catheters now for six and three years respectively; all patients have proved completely trouble free, with the exception of one man who has severe flexor spasms and gets occasional urethral leakage of urine.

If I were to suggest to any of these patients that they should return to the use of urethral catheter drainage I know what their response would be—"not Pygmalion likely."

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Blood donors and hepatitis

SIR,—The reply given to your questioner on the current regulations governing the acceptance of blood donors with a history of hepatitis (27 October, p 1047) is somewhat out of date.

Using sensitive techniques for the identification of the hepatitis B surface antigen,

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