travenous pyelography and micturition cystography. It is now our routine to wait until the patient has had a course of drug therapy and treatment with the alarm bell before arranging radiological investigations." They do not make other reference to "drug therapy," but 33% of their enuretic children were not cured by the electric alarm. They seem therefore to imply that a sizable proportion (? 33%) of enuretic children (ages unspecified) will require investigation by intravenous pyelography and voiding cystography. With this conclusion I must disagree.

Recognition of the very small minority of cases where enuresis is the symptom of an organic disease can be done by simple attention to a few salient points: (1) Excluding infection by examining the urine. (2) Excluding outflow tract obstruction and neurogenic bladder by checking the normality of the urinary stream and the absence of palpable bladder after voiding. (3) A careful history—for instance, periods of constant leaking of urine in a girl suggest an ectopic ureter.

Apart from the obvious undesirability of any non-essential pelvic radiology in children, past experience suggests that elaborate radiological investigations in enuretics are apt to prove positively misleading. For instance, no fewer than 61 of 135 (45%) enuretic children investigated by Fisher and Forsythe[1] by means of voiding cystography were considered to have "abnormalities of the urinary tract." Since all agree that the vast majority of enuretic children, whether treated or not, eventually lose the symptom, one is bound to conclude that the numerous radiological "abnormalities" which may be picked up will turn out to be no more than a large shoal of very red herrings.—I am, etc.,

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REFERENCE
1 Fisher, O. D. and Forsythe, W. I., 1954, *Archives of Disease in Childhood*, 1954, **29**, 460.

Mentally Subnormal Children

SIR,—Your leading article, Mentally Subnormal Children (17 January p. 130), brings out many of the problems that may arise following the transfer of responsibility for teaching the subnormal. The need for special teachers prepared to involve themselves with all subjects has been recognized by the National Society for Mentally Handicapped Children, which aims to establish a training school for teachers of the subnormal.

However, though some parents may feel their children would benefit from a more educational approach, thinking parents are much more concerned with the attitudes of staff to children. It is not so much a question of whether a particular child would benefit from academic education but of whether it is worth finding out. All too often doctors, social workers, and teachers make dogmatic assumptions that a child with such and such syndrome can under no circumstances have more than a fixed level of ability. Assumptions of this type have their basis in statistics derived from children who have vegetated in hospitals. There are no worthwhile statistics based on children who have been trained to the full extent of their capacity, so few have received such training.

Much more important than any change of departmental responsibility is an end to the present rigidity of mind among professional personnel. Since we have the initial responsibility it is for the medical profession to give a lead and admit that we cannot forecast except in the broadest terms what the ultimate attainment of any particular infant will be. If doctors spoke more of what will be possible and less of what will not, others might be encouraged to lift their sights higher.—I am, etc.,

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Transmission of Toxoplasmosis

SIR,—Your leading article on transmission of toxoplasmosis (17 January, p. 126) pays attention to the great discovery by Dr. W. M. Hutchison and his colleagues (p. 142). The last sentence of it asks, however, for some comment. It is stated that *Isospora hominis* is a rare human form of coccidiosis. If you mean the disease is rare, I agree, but if you mean the presence of sporocysts in the faeces then I would like to point out that we have examined 1, 820 newly joined Army recruits; 8% of these boys were found to be infected.[1]—I am, etc.,

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REFERENCE
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Diverticular Disease of Colon

SIR,—The recent article on the natural history of diverticular disease (13 December, p. 639) is welcome because it represents one of the largest series yet reported on this very common but poorly studied condition. Much of the voluminous literature on this subject is of little value because of the confusion engendered by the acceptance of assumptions long passed down through the literature without subjection to critical analysis.

The most misleading instance is where bowel symptoms present in patients found to have diverticula are assumed to be due to the diverticular disease. In a condition whose incidence approaches 50% of patients over the age of 50 years[1] it is essential that a control group also be studied. While there is sound evidence that diverticular disease is casually related to perforation and pericolic abscess, at present evidence is lacking that other symptoms, such as recurrent left iliac fossa pain and altered bowel habit, occur more frequently in patients with diverticular disease than in those with macroscopically normal colons. In fact, work in progress in this department suggests that the opposite is true.[2] These symptoms frequently persist after resection, particularly if they were present before surgery.[3] In this case the natural history of the disease can be validly assessed only in terms of conditions which are clearly related to the diverticular disease, such as proved inflammation, obstruction, and fistula.

A second assumption is that radiology is an accurate method of assessing the incidence and extent of the disease and its complications. Because of the capricious manner in which barium given by enema fills diverticula, this examination generally underestimates the incidence of the condition and may give a misleading picture of the extent of diverticula. Combined radiological and pathological studies[4 5] have shown that most of the signs usually regarded as indicating diverticulitis are not related to the presence of inflammatory disease.

A further misleading assumption is that surgical resection is a wholly successful method of treatment for diverticular disease, and that increased resort to "prophylactic" resection in relatively early cases can be justified. The results of Mr. Parks's investigation (Table VII) confirm those of many other studies that there is a remarkably small difference in the long-term results of groups treated conservatively or by surgery—particularly in relation to persistence of mild symptoms. Thus, although clinical experience shows that surgical excision is an effective and gratifying measure for patients with severe complicated disease, widespread application of "prophylactic" surgery for early disease will confer little benefit on the individual patient.—I am, etc.,

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Long-term Use of Depot Tetracosactrin

SIR,—Drs. B. L. J. Treadwell and P. M. Dennis (20 December, p. 720) referring to depot tetracosactrin (Synacthen) end with the comment that "its obliterative effect on the diurnal rhythm of cortisol production is a theoretical disadvantage in long-term therapy."

To date we have studied four patients who have been treated with 0·5 mg. depot tetracosactrin twice weekly for prolonged periods. It was found in all of these patients that after one year of treatment the plasma corticosteroid levels, measured by the Mattingly method,[1] showed a definite 24-hour rhythm by the third day after the last injection. This rhythm was even more conspicuous if the next injection of depot tetracosactrin was delayed several more days. Moreover, a good response in the plasma corticosteroids was demonstrated in all four subjects following insulin hypoglycaemia, and in three out of four subjects given lysine vasopressin. In two subjects plasma immunoreactive A.C.T.H. levels were determined;[2] one showed a definite 24-hour rhythm while in the second both morning and evening levels were below the limits of

sensitivity of the assay (30 picograms/ml.).

These results contrast with the failure of the plasma corticosteroid levels to respond to insulin or lysine vasopressin in a patient several months after the withdrawal of long-term prednisolone therapy given two to three times per day, in keeping with the findings of Livanou *et al.*[3]

The details of these cases will be published in due course. Meanwhile it is clear that the theoretical disadvantage of depot tetracosactrin referred to by Drs. Treadwell and Dennis is not a practical reality, at least when it is used in a dosage of 0·5 mg. intramuscularly twice weekly.—We are, etc.,

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1 Mattingly, D., *Journal of Clinical Pathology*, 1962, 15, 374.
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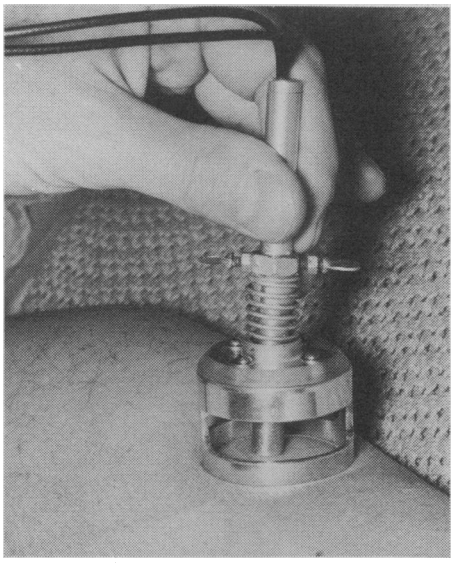
Ultrasonic Localization of Perforating Veins

SIR,—Many surgeons are unwilling to make long incisions through poor tissues of limbs which are the seat of severe post-phlebitic changes, because of the frequently encountered difficulties with healing. Yet few would disagree that the detection and obliteration of incompetent perforating veins is an important part of the ideal theoretical treatment. It is well known that incompetent perforating veins not dealt with during operations for varicose veins are a frequent cause of persistent symptoms and recurrent varices. Phlebography is an accepted but not frequently used method of detecting perforating veins.[1] A simply applied clinical test is described below.

The pencil probe of a Parkes model 802 Doppler blood flow velocity detector* is modified by the addition of an easily detachable spring-loaded device to compress the superficial veins in a 2 cm. radius around the tip of the probe (see Fig.). The theoretical considerations of the model 802 Doppler have previously been reported.[2] Probable sites of incompetent perforating veins are marked on the patient's leg by palpating for fascial defects as advocated by Fegan,[3] and the usual anatomical sites of perforators can also be marked. In cases without obvious varicose veins, or with gross fibrosis and oedema which make palpation difficult, the superficial veins can be detected with the Doppler and an examination carried out over their course.

The modified probe is placed vertically over the marked sites and depressed, compressing the superficial veins and bringing the probe itself into light contact with the skin, which is covered with coupling jelly. The examiner now regularly compresses and releases the calf with his free hand while manipulating the probe in various directions. If the probe is over an incompetent perforating vein a distinct to-and-fro motion of blood in the vein can be heard each time the calf is compressed and released. Noise, presumably from ultrasound reflected from moving tissue planes, is present, but is much coarser than the blowing sound produced by moving venous blood, and the two can be readily distinguished.

This procedure has been carried out on anaesthetized patients on the operating-table. The vessel can then be exposed through a small incision. Incompetence can be demonstrated by retrograde flow before ligation. Alternatively, compression sclerotherapy can be carried out with accurate placement of the sclerosant, the effectiveness of which can be checked at a subsequent examination.



The beam of ultrasound issuing from the tip of the probe is said to be only 1 mm. or so wide, and this allows accurate localization. The method does not demonstrate competent perforating veins, as blood flows only from superficial veins to deep veins and does not return. It is accurate in that false positive results do not occur if the ring is properly depressed and if bony prominences are take into account, though it cannot, of course, be claimed that no incompetent veins are missed.

This technique has been developed with the help of an Ernest Hart Award from the British Medical Association.

—I am, etc.,

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*Parkes Electronic Laboratory, Beaverton, Oregon. Available in Britain from Instrumentarium Ltd., 28 Manchester Street, London W.1.

Renin and Acute Renal Failure

SIR,—The article by Dr. J. J. Brown and his colleagues (31 January, p. 253) is a very interesting and detailed introduction to the proposition that renin may cause renal failure or contribute to it. We are, however, left in suspense with a hypothetical conclusion based on circumstantial evidence. One can try to prove the point experimentally, and there are several avenues open. In any such experiments it would be prudent to view with some deference the verbal and written diatribes of Homer Smith against using rabbits in any renal physiological experiment. I suggest, therefore, one should confine experiments to dogs and so avoid the conflicting results already existing in the literature.

Since renal failure in humans is usually the result of a sudden episode, any theoretical involvement of renin must surely require a sudden flooding of the outer renal circulation with very large quantities of this substance. If so, the amount of renin or angiotensin flooding the renal circulation must maintain exclusion of outer cortical flow for over 1½ hours if warm ischaemia is to cause tubule damage or frank acute tubular necrosis. Alternatively, a large dose of renin or angiotensin must be shown to be immediately and directly toxic to the tubule cells.

The Goldblatt clip on the renal artery experiment does not alter the renal distribution of blood, but reduces its perfusion pressure. At the same time the blood pressure rises, owing presumably to the release of excess renin/angiotensin. There is no evidence that this increased renin is vasoconstrictor to such an extent that the outer cortical vessels become excluded from perfusion. These vessels are still being perfused at a reduced pressure, and there is no evidence that the already reduced glomerular filtration rate leads to tubular damage.

A more physiological method of reducing renal blood flow and perfusion pressure involves Priscol (tolazine hydrochloride). Tolazine was used clinically as a peripheral vasodilator, but it is also a potent renal vasoconstrictor; 25 mg. injected intravenously will vasoconstrict the kidneys of a 22 kg. dog for up to 150 minutes.[1] This effect reduces blood flow and perfusion pressure but does not change distribution. The net effect should stimulate renin production, but no tubule damage has been observed, nor does outer cortical vasoconstriction progress with time. Ten minutes after an injection of tolazine the above vasoconstriction is established, as judged by Thorotrast (thorium dioxide) arteriograms. If now 0.05 mg. Hypertensin (angiotensin) is injected into the renal artery a profound reduction in blood flow occurs with no flow beyond the arcuates. The kidney responds within 15 seconds and becomes anuric. Normal and transplanted kidneys recover from this treatment in about 15 minutes, when urine production is resumed. No evidence of tubular or vascular damage followed the severe but temporary afferent vasoconstriction effected on three sucessive occasions within an hour.

How large a quantity of renin can suddenly be produced endogenously? Can it ever reach the levels of exogenous angiotensin injected in the above experiment? And if it did, would it not lead to its own shutdown, since the outer cortex is not being perfused at all during a period of 5-10 minutes?

There has been some difficulty in correlating blood pressure, plasma renin activity, and aldosterone secretion during rejection episodes in allotransplanted kidneys.[2 3] This is not surprising. Rejecting kidney allotransplants frequently provoke hypertension and I naively concluded that this was due to renin release from an ischaemic kidney by a Goldblatt effect.[1 4] Later on, Starzl[5] came to the same independent conclusion. The results of recent experiments have forced a change of opinion about the role of renin/angiotensin in the production of rejection hypertension.[6] Sometimes hypertension is not present during rejection, in both dogs and humans, and this is just as mysterious as when it is present, since ischaemic kidneys are common to both clinical situations. Perhaps a reasonable explanation is that outer cortical flow is completely excluded in those rejections presenting without hypertension.