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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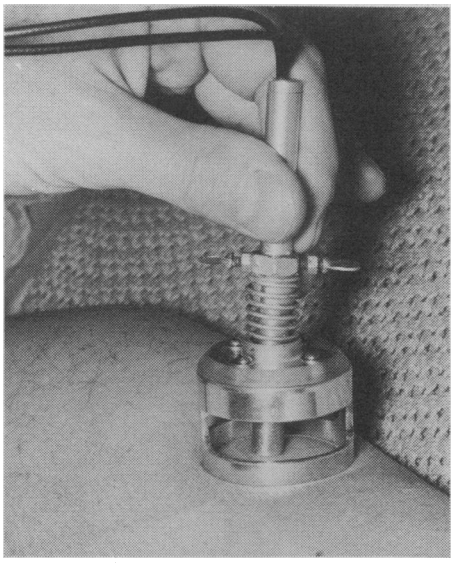
Ultrasonic Localization of Perforating Veins

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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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.