predisposed subject in response to trauma of the skin. It grows outwards to a very large size in time and may become pedunculated. Hypertrophic scars in contrast are seldom of uniform consistency unless very small, may have hypovascular areas, may contract in parts, and do not form large lumps. It is these that may be provoked by wrongly placed incisions or infection or skin loss as described by your leader writer. In general they are more amenable to surgery and radiotherapy.—I am, etc.,

R. L. BATTEN.

Birmingham 15.

Estimating Plasma Antidiuretic Hormone Levels

SIR,—Estimation of plasma antidiuretic hormone (A.D.H.) levels has been hampered in the past because of lack of a sufficiently sensitive bioassay method. Using the modification described by Clarke *et al.*¹ of injection of 2.5% alcohol in normal saline by the intravenous route to replace the amount of urine passed every five minutes in fasted, alcohol-anaesthetized rats, I found it possible to estimate 0.1–0.25 μ U./ml. A.D.H.² Both the plasma samples and standard vasopressin solutions were injected by the intravenous route. Rats which were not fasted overnight were 4–10 times more sensitive, thus confirming some earlier observations that fasting reduces the sensitivity to A.D.H.³ Non-fasting rats were not routinely used in the present study due to their somewhat erratic response. The extreme sensitivity of the method made it possible to estimate the plasma A.D.H. level in all subjects by injecting plasma directly, without employing any concentrating technique. This is a distinct advantage, since all previous workers had to use tedious chemical extraction procedures to concentrate A.D.H. in order to assay it with relatively insensitive methods. Activity of plasma as well as vasopressin solutions was abolished by treating with freshly prepared 0.01 molar sodium thioglycollate solution for 1 hour.⁴ That the method is sensitive enough to detect small changes in A.D.H. in plasma was shown recently during a study of plasma A.D.H. levels before and during intermittent positive pressure breathing.⁵ Thus a slight fall in blood pressure in one case and haemorrhage of about 300 ml. without any fall in blood pressure in another were enough to raise the antidiuretic activity of plasma above the control samples from the same subjects.

Plasma A.D.H. levels were estimated in 20 normal men, 6 non-pregnant women, 5 pregnant women (seventh month of pregnancy, having oedema of legs), one case of severe eclamptic toxæmia (10 hours before, and 12 days after delivery), 10 patients with congestive heart failure, and 10 patients with nephrotic syndrome. Results are shown in the Table.

This appears to be the first measurement of circulating A.D.H. level in normal men, non-pregnant women, pregnant women, and also in patients with congestive heart failure, nephrotic syndrome, and eclampsia. The significantly lower plasma A.D.H. levels found in congestive heart failure and nephrotic syndrome fit in well with the observation of Strauss *et al.*⁷ that isotonic

Antidiuretic Hormone Levels in Human Plasma

Condition	No. of Subjects	A.D.H. Level in Micro Units per ml. $\pm$ S.E.M.*	Comments
Normal men	20	0.30 $\pm$ 0.01 (range 0.04–0.85)	A.D.H. levels in normal men, non-pregnant women and pregnant women are similar. The differences are not statistically significant. (P > 0.05)
Non-pregnant women	6	0.37 $\pm$ 0.06 (range 0.15–0.60)	
Pregnant women	5	0.30 $\pm$ 0.07 (range 0.12–0.50)	
Eclampsia	1	0.31 (10 hours before delivery 0.30 (12 days after delivery)	A.D.H. level was no higher than normal in the acute phase of eclampsia and remained the same after 12 days of delivery of a still-born foetus
Congestive heart failure patients	10	0.21 $\pm$ 0.05 (range 0.04–0.50)	Significantly lower than normal (P < 0.05)
Nephrotic syndrome patients	10	0.20 $\pm$ 0.05 (range 0.04–0.60)	Significantly lower than normal (P < 0.05)

Note * $\pm$ S.E.M. refers to standard error of the mean.
(1) Measurements of levels below 0.10 micro unit/ml. were made by using non-fasted rats for assay.
(2) Pregnant women from whom blood was collected showed oedema on legs.
(3) These results, except for the case of eclampsia have been reported in detail elsewhere.^{2, 6}

expansion of the extracellular fluid volume diminished A.D.H. secretion. The present study excludes increased secretion of A.D.H. as a cause of oedema in these conditions. Although observations on more patients will be needed, the failure to find a raised A.D.H. level in a patient with florid eclampsia is significant, and I think makes it very unlikely that increased secretion of A.D.H. plays any part in its causation.

Thus the availability of a sensitive method for bioassay of A.D.H. promises to be the start of a new phase in the study of its role in health and disease, and has already excluded its role in oedema of normal pregnancy, congestive heart failure, nephrotic syndrome, and in causation of eclampsia.—I am, etc.,

K. K. GUPTA.

Atkinson Morley's Hospital,
London S.W.20.

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- Gupta, K. K., Chaudhury, R. R., and Chhuttani, P. N., *Ind. J. med. Res.*, 1967, **55**, 643.
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Brescia-Cimino Shunts

SIR,—I was interested to read the paper by Dr. R. McMillan and Dr. D. B. Evans (28 September, p. 781) on their observation of circulatory overload in three patients with the Brescia-Cimino shunt. Because of clotting and infection with standard Scribner shunts we have of late increasingly used Brescia-Cimino shunt. While there is no doubt that patients with a Brescia-Cimino shunt should be observed carefully for evidence of cardiac overload, it is possible

that severe anaemia and hypertension may contribute significantly. The difficulty in obtaining a satisfactory flow rate in our experience during the early days of using this type of shunt was usually a technical problem. We found it possible to obtain a flow rate of 500–700 ml. per minute using a Baxter No. 14 gauge needle for the venous end and an intracath Bardic No. 14 gauge needle for the arterial end of the Brescia-Cimino shunt. The use of a Sarns blood pump (F.U.A. 14) of the roller type and a specially designed pump insert (Baxter) is desirable.

I would like to record two interesting observations which we have observed with the Brescia-Cimino shunt. One patient developed erythema of the skin surrounding a Brescia-Cimino shunt. This was followed gradually over a period of three months with soft-tissue swelling and increased warmth of the hand. The second patient suffered from bacteraemic shock due to severe pneumonia. It was observed that the hand containing the Brescia-Cimino shunt was warm compared to the extremities of the other limbs, which were cold. Thus it is important not to rely on the hand containing a Brescia-Cimino shunt for clinical manifestations of shock. Details of these cases will be published in a separate report.

I believe that a Brescia-Cimino shunt represents a major advance in the management of patients with chronic renal failure undergoing haemodialysis.—I am, etc.,

Y. K. SEEDAT.

Department of Medicine,
Royal Infirmary,
Manchester.

New Testing for the "Pill"?

SIR,—A number of my patients are women of child-bearing age who take oral contraceptives. I am sure that I am not the only physician who is concerned by the literature accumulating on the untoward and often conflicting, and as yet unknown, effects of long-term pill administration. Criticisms of the difficulty in arranging acceptable controls for the series of patients on the pill (21 September, p. 742) with increased headache reported by Dr. Ellen C. G. Grant (17 August, p. 402) do not invalidate the importance of the observed histological changes in the endometrium. The report of personality changes by workers from the Council for the Investigation of Fertility Control (28 September, p. 777) is equally disturbing, particularly as, according to a study just published in the *Lancet*,¹ it is suggested that there is a possible biochemical basis for these changes. In the daily press² I read the report of a coroner's inquest on a young woman bearing the headline: "Pill Danger Warning by Surgeon." The coroner very wisely stated that the association between her death and the pill could easily be a coincidence. However, an association between postoperative complications, including transient hypotension, and patients taking the pill, was reported earlier this year.³ Since the introduction of cortisone surgeons have been wary that patients on this type of medication may have postoperative difficulties. Does the pill—also a steroid—come in some way into this category?

The pill is now firmly established in our way of life and few would wish it to be withdrawn, but many would wish studies on it to be amplified. If side-effects are really end-