Inflation of a splint to 40 mm. Hg caused a marked reduction in blood flow in the limb in all subjects. Complete cessation of blood flow in the limb occurred in six subjects, and a reduction in blood flow to levels between 0.2 and 0.9 ml./100 ml. tissue/min. occurred in seven.

Inflation of a splint to 30 mm. Hg caused a similar but less pronounced reduction in blood flow.

Raising the limb above heart level, combined with splint-inflation, still further reduced the blood flow, resulting in complete cessation of the flow in five out of six subjects.

A theoretical explanation of these findings and some implications concerning the use of inflatable splints for the emergency treatment of fractures are discussed.

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Renin Secretion by the Denervated Kidney

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The mechanisms regulating renin secretion by the kidney are conjectural at present. The demonstration of renin in the cells of the juxtaglomerular apparatus (Edelman and Hartroft, 1961) and the anatomical evidence that these cells are innervated (Barajas, 1964) have led some investigators to suggest that the sympathetic nervous system may play a part in controlling the renin-angiotensin-aldosterone system (Wathen *et al.*, 1965; Gordon *et al.*, 1966).

In man the change of posture from the recumbent to the upright position is associated with an elevation of the peripheral venous renin activity (Conn *et al.*, 1965). This suggests increased renin secretion by the kidney.

We have studied three renal homograft recipients in order to observe the effect of renal denervation upon the postural renin response.

Methods

Case Material.—Two subjects who had previously donated a kidney served as normal controls. Three renal transplant recipients made up the experimental group (see Table I).

Procedure.—All of the patients were on an *ad lib.* salt intake before the study. Blood samples were drawn after each subject had been erect and active for four hours and again after four hours of recumbency. Peripheral venous renin activity was determined by Hickler's modification (Blaufox *et al.*, 1966) of the method of Boucher *et al.* (1964). This modification differs from the originally described method in so far as (1) after incubation the resin-containing peptide is washed and eluted by the batch method, no column being used, and (2) the elutions are collected in a cold flask and dried rapidly on a flash

evaporator. No acetic acid is used in the collection flask. The result is therefore a product which does not need sublimation before bioassay. The results of the investigation are given in Table II.

TABLE I.—Patient Data

Case No.	BUN	Cr _s	C _{cr}	U _{Na}	Urinalysis	Remarks
	(mg./100 ml.)		(ml./min.)	mEq/24 hr		
1	17	1.9	67	270	Negative	Identical twins; 10 months post-transplant
2	18	1.2	60	150		Brother donor; 2 months post-transplant
3	23	1.5	93	200		Brother donor; 11 months post-transplant; maintained on 500 mg. Aldomet* daily

BUN = Blood urea nitrogen. Cr_s = Serum creatinine. C_{cr} = Creatinine clearance. U_{Na} = Sodium output for the 24 hours preceding the study.

* Aldomet (methyl dopa).

TABLE II.—Results. Peripheral Venous Renin Activity Levels are Recorded as Nanograms Angiotensin II Evolved per 100 ml. Plasma per 3-hour Incubation

		Supine		Erect	
		B.P. (mm. Hg)	Renin (ng. A/100 ml.)	B.P. (mm. Hg)	Renin (ng. A/100 ml.)
Controls	A	134/88	123	118/80	292
	B	130/82	127	105/75	426
Patients	1	132/80	36	124/92	317
	2	130/85	342	136/90	677
	3	164/110	414	130/105	2,030

Ten recovery experiments with Hypertensin-Ciba (angiotensin amide) resulted in recovery of 76–100% of the known. Mean recovery in these experiments was 90% ± 7% (S.D.). Fifty duplicate samples resulted in a mean difference of 10.4% in reproducibility of the renin activity measured in peripheral venous blood.

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Discussion

The transplanted human kidney satisfies the criteria for denervation put forth by Quinby (1916) and emphasized by Bricker *et al.* (1958). Earlier reports have indicated that the sympathetic nervous system may play a part in the regulation of the secretion of renin by the cells of the juxtaglomerular apparatus. The renal nerves (Taquini *et al.*, 1964; Tobian *et al.*, 1965) and circulating catecholamines (Gordon *et al.*, 1966) have both been implicated as mediators of this regulatory mechanism. The present findings indicate that the normal "renin response" seen with postural change apparently remains intact after denervation of the kidney. Previous studies have cast doubt upon the contention that circulating catecholamines stimulate renin secretion. Laragh *et al.* (1960) were unable to demonstrate elevation of the aldosterone secretory rate with infusion of catecholamines. This is indirect evidence that renin secretion did not rise in his subjects. Wathen *et al.* (1965) were not able to stimulate renin release in dogs with intravenous catecholamine administration, though perfusion of catecholamines direct into the renal artery did increase renin secretion.

Studies performed upon persons with idiopathic orthostatic hypotension who do not display the normal orthostatic increase in sympathetic activity have suggested that low circulatory catecholamine levels do play a part in the abnormal renin secretory pattern seen in these patients (Gordon *et al.*, 1966). Hall and Hökfelt (1966) confirmed these findings; however, they could not reproduce this phenomenon in normal subjects given adrenergic blocking agents.

Conflicting experimental findings must leave the question of sympathetic mediation of the renin-angiotensin-aldosterone system an open one. Lewis *et al.* (1966) have previously shown that normal sodium-regulating mechanisms persist after human renal denervation and transplantation.

The present results support the concept that homeostatic mechanisms involving renin secretion are intact after renal denervation. While this finding does not disprove the existence of some association between the sympathetic nervous system

and the renin-angiotensin-aldosterone system, it suggests that other mechanisms are also operative.

Summary

Peripheral venous renin levels were measured in three homo-transplant patients in the upright and recumbent positions. The normal pattern of elevation of the renin level in the upright position and depression in the recumbent position was seen. It is concluded that a mechanism independent of the renal nerves is operative in regulating the postural change in renin secretion by the kidney.

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Low-dosage Oral Ethynodiol Diacetate Tablets for Long-term Contraception in Indian Women

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From field studies in Puerto Rico, Mexico, and Ceylon it has become evident that, contrary to all predictions by the experts, the poorly educated women of low socio-economic status accept oral contraception enthusiastically and successfully (Rice-Wray, 1957; Rice-Wray *et al.*, 1965; Chinnatamby, 1965; Rao, 1965). In that respect, as I reported earlier (Shah, 1965, 1966), Indian women belonging to this class of society are no different from their counterparts in other parts of the world. In fact, once these women know that an oral "pill" is available, it is difficult if not impossible to make them use any other method of birth-spacing.

Since the contraceptive efficiency of the various synthetic progestogens in different geographical populations is no longer in dispute, current research is directed towards finding an oral contraceptive that would have a low incidence of side-reactions

and a good cyclic control in each population, and towards assessment of the lowest effective dosage for each compound for successful contraception. Such low-dosage tablet, so far as developing countries like India are concerned, would have two added advantages: (1) reduce the cost of the pill, and (2) minimize its inhibiting effect on lactation in women in whom breast-feeding is a necessity for reasons of economy. The purpose of this paper is to report a few aspects arising out of our experience related to the administration of low-dosage ethynodiol diacetate in "combined" or "sequential" schedules for contraception in Indian women.

Present Series

A total of 380 fertile women aged 18 to 35, with an average age of 24.2 years, participated in the trial. Analysis of the data of these women indicated that 62% were illiterate or had had

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