affect various components of this renal-adrenal hormonal system.[1-9]

### Methods and material

Eleven women with high blood pressure have been studied. Using previously defined criteria,[10] we classified 8 as having uncomplicated benign "essential" hypertension, 2 as renal hypertension, and one as advanced hypertension. Most of the patients were observed in the outpatient department, but 3 were admitted to the metabolism ward and studied under conditions of controlled electrolyte balance. In addition, the effects of oral contraceptives were evaluated further in metabolism ward studies of 2 fully informed normal male volunteers and in another male subject with uncomplicated essential hypertension.

Aldosterone secretion and excretion rates were measured by a double isotope dilution technique previously described.[10, 11] Blood samples for estimation of renin were taken at noon, when the patients had been ambulatory for about 4 hours. Renin activity, renin substrate concentration, and the rate of angiotensin formation in response to a fixed amount of exogenous renin were all measured by a modification of the method of Pickens and associates.[12] In our modification each incubation is carried out for 16 and for 24 hours in isotonic salt in the presence of EDTA and DFP. For studies designed to evaluate the capacity for angiotensin formation in a given plasma, a fixed amount of exogenous renin was added to the sample. In the earlier studies a final concentration of 0.0034 Goldblatt unit per milliliter of renin was employed in a 4 hour aqueous incubation.[1] In more recent studies (Fig. 6), 0.0017 Goldblatt unit per milliliter was employed with a one hour incubation in saline. Highly purified angiotensinase-free renin was prepared from human kidneys according to the method of Haas, Goldblatt, and Gipson.[13]

**Table I.** Oral contraceptives, hypertension, and abnormalities in the renin-angiotensin-aldosterone hormonal interaction

| *Elevated levels* | *Agent* | *Authors* |
|---|---|---|
| 1. Plasma angiotensinogen | Estrogen | Helmer and Griffith,[2] 1952 |
| 2. Aldosterone secretion | Progestogen, estrogen | Layne and associates,[3] 1962 |
| 3. Plasma renin | Pregnancy | Brown and associates,[5] 1963<br>Winer,[6] 1965<br>Genest and associates,[7] 1965 |
| 4. Plasma renin | Estrogen (large doses) | Crane and associates,[8] 1966 |
| 5. Blood pressure | Oral contraceptives | Laragh and associates,[1] 1967<br>Woods,[9] 1967 |
| 6. Plasma reactivity to renin | Oral contraceptives | Laragh and associates,[1] 1967 |

### Results

A summary of our previously reported observations[1] associating oral contraceptive therapy with changes in arterial blood pressure and with changes in the renin-angiotensin-aldosterone system is presented in Table II.

**Effects on arterial blood pressure (Table II).** Because of the frequent use of oral contraceptives and the high incidence of hypertensive disease in the population at large, the fact that hypertensive disease was first discovered in 6 of our patients receiving this treatment does not in itself imply any specific interrelationship. Furthermore, even the augmentation of pre-existing hypertension observed in 2 of 5 previously hypertensive patients could be a chance occurrence.

**Table II.** Oral contraceptives and high blood pressure*

1. 6 normotensive prior to medication
2. 5 hypertension known prior to medication
   2, hypertension augmented
   3, hypertension unchanged
3. 9 medication withdrawn
   3, normalized blood pressure
   3, improved
   3, unchanged
4. Reappearance of hypertension with restoration of treatment in each of two
5. Marked consistent elevation of angiotensinogen with increased plasma reactivity to renin
6. Less consistent or persistent increases in plasma renin levels and aldosterone secretion

*Findings in 11 patients presenting with hypertension.