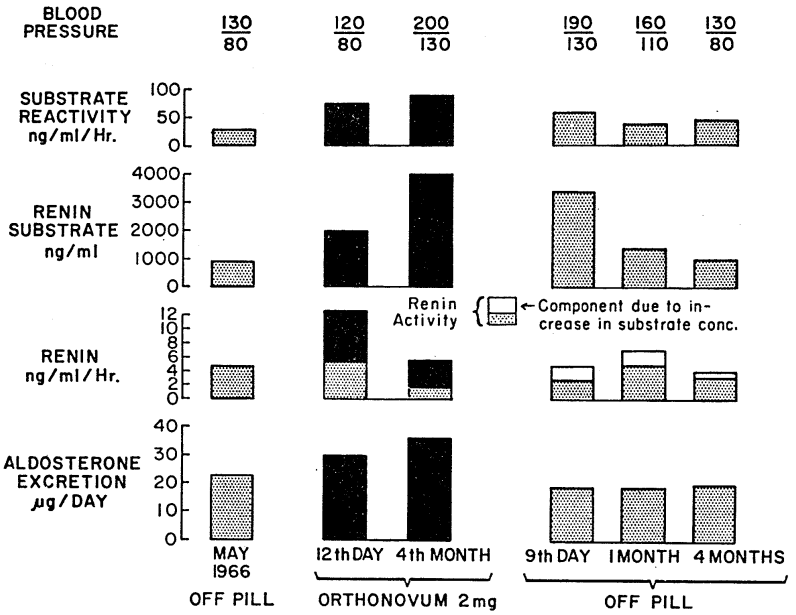

Fig. 2. Oral contraceptive hypertension in a 32-year-old woman in whom hypertension was first discovered after 3 years of oral contraceptive therapy with Enovid 5 mg. Hypertension disappeared after drug withdrawal. It reappeared, as shown here, when treatment was renewed, and then disappeared again after drug withdrawal. The onset and offset of hypertension was associated with concomitant increases and decreases in renin, aldosterone, renin substrate and reactivity to renin. The data illustrate that in this patient the observed increase in renin activity was largely due to an increase in renin substrate concentration.

treatment (Figs. 2 and 3). The time required for return of substrate levels to the normal range after drug withdrawal exhibited even more variation. Two to 4 weeks' time or even longer was often required for the return of substrate levels to a normal range (Fig. 1).

An attempt was made to determine which component of an oral contraceptive preparation was responsible for this biochemical effect (Fig. 5). The administration of norethynodrel produced significant, but smaller, increases in renin substrate than that observed with the use of either ethinyl estradiol or the combination pill. These results in 2 male subjects suggest that both components of the oral contraceptives can stimulate substrate formation with the predominant effect being referable to the estrogen. The stimulating effect of norethynodrel may derive from its estrogenic properties, since progesterone was found not to increase renin substrate in a previous report.[2]

Effects on the plasma reactivity to exogenous renin (Figs. 2 to 6). Because of the striking increases observed in renin substrate levels, a study was made to determine whether this abnormality might produce a change in the character or magnitude of the response to renin. This question was approached with an in vitro system in which the capacity to form angiotensin was measured after the addition of a fixed amount of renin to the individual plasma.

Significant increases in substrate reactivity were consistently observed. These increases were directly related to the corresponding induced rise in renin substrate concentration. Increased reactivity was produced as the substrate concentration increased to the region of 2,000 ng. per milliliter. Above this concentration further increases in substrate induced lesser increments in reactivity. In the one patient in whom substrate failed to increase significantly, no increase in reactivity to renin was produced.[1] These results suggest