inhibitor and instead suggests that the increased reactivity to renin merely results from an increased substrate concentration.

Effects on endogenous plasma renin activity. Because of the consistently produced enhancement of plasma reactivity to renin, proper evaluation of the influence of oral contraceptive therapy on the true renin concentration requires that each measurement of endogenous renin activity be corrected by taking into account and correcting for the contribution of these alterations in reactivity (Figs. 1 to 5). Such data indicate that the observed apparent increases in endogenous renin activity resulted from either an increase in plasma reactivity or an increase in the true renin concentration or both (Fig. 3).

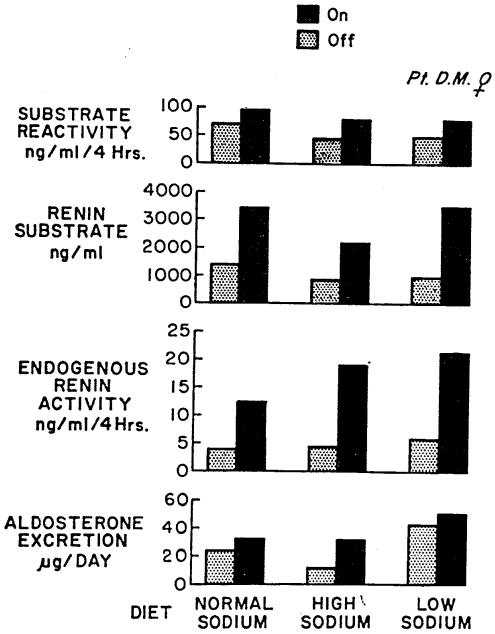

Fig. 4. The influence of changes in dietary salt intake on oral contraceptive induced abnormalities in the renin-angiotensin-aldosterone system. Data taken from a metabolism balance study of a 30-year-old woman who had been maintained on Enovid 2.5 mg. for 17 months and whose hypertension in the region of 160/110 was discovered shortly after starting the treatment. This patient exhibited persistent and significant increases in all of the measured components of the renin-angiotensin system. The abnormalities were apparent at all levels of sodium intake. The fluctuations of plasma renin levels with various regimens did not appear altogether appropriate.

With long-term administration of oral contraceptives, endogenous renin activity remained elevated in 4 patients, but in 5 others the values were normal.[1] Normalization of the endogenous renin activity levels in this situation suggests that true renin concentration actually may have been depressed below normal, with activity values being normal because of the raised substrate.

An example of a patient with persistently increased plasma renin levels is presented in Fig. 4. The data illustrate that the abnormality persists at all levels of sodium intake. The second pattern, i.e., the tendency for endogenous renin activity to return to normal after an initial rise, is illustrated by studies of 2 other hypertensive patients (Figs. 2 and 3) and of 2 normotensive males (Fig. 5).

Effects on aldosterone secretion or excretion. Abnormalities in aldosterone tended to be transient, and they were observed less consistently. In 4 of 8 hypertensive patients studied the levels remained elevated. However, in one the increase seemed referable to severe pre-existing hypertensive disease. In the other 3 (Figs. 2 to 4), the values were restored to normal by cessation of therapy. In 2 normal male subjects only transient increases in aldosterone excretion were induced in association with the transiently increased endogenous renin activity.

Comment

Because both hypertensive disease and the use of oral contraceptives are such common phenomena in the adult female premenopausal population, the development or enhancement of hypertension in subjects taking this medication could be mere coincidence. Notwithstanding this, in the present study considerable evidence has been advanced which suggests a cause-and-effect relationship between the use of this type of medication and the development or aggravation of high blood pressure in certain individuals who seem especially sensitive in this regard. Furthermore, these clinical observations are