

## High blood pressure and oral contraceptives

Changes in plasma renin and renin substrate and in aldosterone excretion

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*A group of patients is described in whom the development or augmentation of hypertensive disease was associated with use of oral contraceptives. The experience suggests a causal role for these hormonal substances in certain susceptible individuals. Factors which might sensitize to the pressor effect of these drugs remain undefined. However, the effect may be related to marked associated changes observed in certain components of the renin-angiotensin-aldosterone hormonal interaction. The contraceptive medications consistently produced large sustained increases in plasma concentration of renin substrate. Less consistently, transient or sustained increases in plasma renin and in aldosterone were also observed. Parallel in vitro studies demonstrated that renin substrate is normally not present in excess because the contraceptive-induced increased substrate concentration was always accompanied by a significantly increased capacity for angiotensin formation when renin was added to the plasma. It seems possible that, in certain susceptible subjects, these induced hormonal changes, together with associated changes in sodium metabolism, could compromise the buffer capacity of the renin-angiotensin-aldosterone hormonal system, permitting exaggerated (pressor) responses to circulating renin when it is released by the normal physiologic stimuli. These observations also may be relevant to the use of female hormones in other clinical situations, and they may be applicable to the study of hypertension in experimental models.*

IN THIS communication we present studies stimulated by clinical observations in certain of our hypertensive patients which first suggested the possibility of a cause-and-effect relationship between the use of oral contraceptives and either the development or enhancement of high blood pressure.

At the outset it should be emphasized that because of the widespread use of these medications it seems very likely that in the large majority of those who take them they do not

induce hypertension. However, observations that we have made in 11 selected hypertensive patients suggest that in special circumstances these hormonal agents may become critically involved in the production of hypertensive disease. A preliminary report of these findings has been published.<sup>1</sup>

When clinical observations first suggested this relationship, it was decided to investigate concurrently the effects of these female hormonal substances on electrolyte metabolism and on the behavior of the renin-angiotensin-aldosterone hormonal interaction. This seemed appropriate because of the known relationship of this hormonal system to other forms of hypertensive disease and because previous work (Table I) had indicated that estrogens and progestogens can significantly

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*This work was supported by Grants  
HE-01275 and HE-05741 from the  
National Institutes of Health, United  
States Public Health Service.*