posal[3] that the aldosteronism of progestational compounds is secondary to a natriuresis seems quite unlikely in these patients, often exhibiting a weight gain on these drugs.

Renin substrate is made by the liver.[19] Estrogens appear to increase or decrease the synthesis of various other proteins,[1] including a cortisol-binding globulin and an aldosterone-binding protein.[20] It therefore seems possible that the estrogens raise the serum renin substrate by stimulating hepatic biosynthesis. Renin substrate levels may be sharply reduced in patients with cirrhosis.[21] However, in one such patient, we produced a striking rise in angiotensinogen with oral contraceptives, possibly indicating a potentially adequate hepatic biosynthetic capacity. An alternate possibility to explain the angiotensinogenemia would be an effect of estrogens and progestogens on the kidney, since renal insufficiency and nephrectomy often produce sharp rises in renin substrate concentration.

Full understanding of the role of estrogenic and progestogenic steroids in the pathogenesis of various forms of hypertensive disease, especially the forms observed during pregnancy, will require further study. The observations reported here may be applicable to the study of hypertension in experimental models. Furthermore, they may be relevant to the use of female hormones in other clinical situations. Of note in this regard are the reports of strokes in young women using oral contraceptives[22] and of a significant incidence of cerebrovascular accidents in a large group of males[23] receiving estrogen treatment for prostatic carcinoma.

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