EFFECT OF SPIRONOLACTONE (S) ON ADRENAL AND GONADAL STEROIDS IN MAN.
A. A. Taylor, J. R. Mitchell, D. E. Rollins*, W. R. Snodgrass*, and F. C. Bartter**. NHLI, NIH, Bethesda, MD.

Gynecomastia, impotence, and irregular menses are frequently observed during therapy with S. Cytochrome P-450-dependent 17-hydroxylase and lyase activity in the adrenal and gonads are inhibited by S. To test the possibility that changes in the secretion of steroids synthesized via these enzymes cause the endocrine side-effects, plasma progesterone (P), 17-OH P, testosterone (T), estradiol (E), prolactin, FSH, LH (each determined by radioimmunoassay), and urinary 17OHCS and 17KS excretion were measured in 10 hypertensive patients before, during (2, 4, 8 and 12 wks), and after (2 and 4 wks) therapy with S at dosages ranging from 150 to 400 mg/day. In all patients, P and 17-OH P were 2-4x greater during S therapy than in the pre-or post-therapy periods. In contrast, T, E, FSH, LH, prolactin, 17OHCS, and 17KS did not change with S. In 2 menopausal women with undetectable E, S-induced changes in P and 17-OH P were not significantly different from those of other patients. Two of 6 men developed gynecomastia and 1 of 4 women had irregular menses. Patterns of plasma and urinary steroids in these patients were not different from those of patients without clinical side-effects. Conclusions: 1) Therapy with S inhibits 17-hydroxylase and lyase; this effect is reversed by stopping S; 2) Because S increases P and 17-OH P in patients with senescent ovaries, increased plasma concentrations of these steroids are probably of adrenal origin; 3) The clinical appearance of endocrine side-effects cannot be predicted by measurement of these steroid and pituitary hormones; 4) The development of endocrine side-effects during S therapy cannot be accounted for by changes in plasma concentrations of the hormones measured in this study.