Steroid Hormones and Ageing

Von

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With 7 Figures

Advanced technics of steroid hormone analysis in body fluids coupled with a more detailed knowledge of steroid hormone metabolism permits at this time the formulation of a working hypothesis to explain the changes in steroid hormones in the ageing individual. In this review a brief summary of our present knowledge of steroid biosynthesis will be presented together with an analysis of the changes that are associated with the ageing process.

Steroid Biosynthesis

Acetate and cholesterol appear to be the primary precursors for steroid hormones in the gonads and adrenal [DORFMAN (1957)]. Cholesterol is most likely the important intermediate between acetate and the steroid hormones but a pathway from acetate to steroid hormones not involving cholesterol cannot be ruled out completely. Some evidence for this possibility comes from the studies of STONE and HECHTER (1954) as well as that of HEARD et al. (1956).

Androgens of the gonads, both testis and ovary, appear to be formed by a single mechanism involving the sequence cholesterol → pregnenolone → progesterone → 17-hydroxyprogesterone → Δ4-androstene-3,17-dione → testosterone [SLAUNWHITE and SAMUELS (1956); SAVARD et al. (1956, 1957); LYNN and BROWN (1956); SOLOMON et al. (1956); Fig. 1]. The adrenal can produce androgens by this pathway and most likely by a second which involves the direct splitting of cholesterol to the C19 androgen dehydroepiandrosterone (Fig. 2). This androgen can be oxidized to Δ4-androstene-3,17-dione which on 11β-hydroxylation results in the formation of 11β-hydroxy-Δ4-androstene-3,17-dione. Of importance is the fact that both dehydroepiandrosterone and the 11β-hydroxy androgen are specific adrenal products. On the other hand Δ4-androstene-3,17-dione is a common product of androgen biosynthesis in the gonad and adrenal.

The corticoids are also derived from cholesterol and a likely mechanism involves 20 and 22 hydroxylated derivatives of cholesterol as indicated in Fig. 3. One of these hydroxylated intermediates has in fact been demonstrated, the 20β-hydroxylated cholesterol by SOLOMON et al. (1956). The first C21 product is pregnenolone as is the case in the gonadal production of androgens. Pregnenolone is converted to progesterone by oxidation with 3β-ol-dehydrogenase. Progesterone is hydroxylated to form cortisol, corticosterone, and aldosterone.

The biosynthesis of estrogens appears to proceed mainly from androgens [BAGGETT et al. (1956) and HEARD et al. (1955)]. For this transformation two
Fig. 1. Biosynthesis of androgens in testis, ovary, and to some extent in the adrenal. Testosterone production by ovary and adrenal is probably extremely limited.

Fig. 2. Pathway of androgen production by adrenal.