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Twenty-Four-Hour Mean Plasma Testosterone Concentration Declines with Age in Normal Premenopausal Women

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ABSTRACT

The 24-h mean plasma concentration of total testosterone (T) was measured in 33 healthy, regularly cycling, nonobese women between 21 and 51 yr of age. Percent free T was measured in 17 of them. Plasma dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) were measured in 24 of them, and the DHEA-to-T and DHEAS-to-T ratios were calculated. It was found that the concentration of total T showed a steep decline with age; the regression equation was: T (nanomoles per L) = $37.8 \times \text{age}^{-1.12}$ ($r = -0.54$; $P < 0.003$). According to this equation, the expected T concentration of a woman of 40 would be 0.61 nmol/L, about half that of a woman of 21 (1.3 nmol/L). The percent free T did not vary significantly with age, so free T concentration likewise showed a steep decline with age. The DHEA-to-T and DHEAS-to-T ratios were both age invariant, clearly because the levels of DHEA and DHEAS also decline steeply with age, as previously reported. (*J Clin Endocrinol Metab* **80:** 1429–1430, 1995)

STUDIES of plasma testosterone (T) levels in various pathological states in women, including obesity, have generally assumed tacitly that age is not a factor in these levels. However, in our studies of 24-hour mean plasma T levels in normal premenopausal women, we have now observed that there is a decline with age, such that the levels in women in their 40s are somewhat less than half those of women in their early 20s. Since plasma levels of the adrenal androgens dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) also decline with age (1), we also determined the effect of age of the DHEA-to-T and DHEAS-to-T ratios in most of the women studied. This paper reports details of these findings.

Subjects and Methods

Subjects

Thirty-three healthy, regularly cycling, nonobese women between 21 and 51 yr of age were recruited for this study. Women with any of the following were excluded: history of chronic or significant recent acute illness; ingestion of medications known or suspected to alter endocrine function; oral contraceptives or pregnancy within the preceding 6 months; obesity (>20% above ideal weight); significant hirsutism; and abnormal thyroid, kidney, or liver function. For purposes of standardization, all studies were done on days 4–6 of a menstrual cycle.

Twenty-four-hour mean plasma hormone concentrations

These were measured by sampling blood (from an indwelling venous catheter) every 20 min for 24 h, pooling aliquots of plasma from each sample, and determining the hormone content of each pool. Details of the 24-h blood-sampling technique have been previously reported from this laboratory (1).

Determination of plasma steroids

Total T was determined in all the subjects by the method of Boyar *et al.* (2), with modifications as described by Strain *et al.* (3). Free T was determined in 17 of them, by measuring plasma sex hormone-binding globulin, by the method of Kahn *et al.* (4), and plasma albumin, and by calculating the free T, as previously described (4). DHEA and DHEAS were determined in 24 of the subjects, as previously described (1).

Analysis of data

Regression equations for hyperbolic, logarithmic, power-function, and linear correlations between total plasma T and age were calculated by computer, using a curve-fitting program, and the equation showing the highest correlation coefficient was used for the analysis. Linear correlation coefficients between percent free T and age, DHEA-to-T ratio and age, and DHEAS-to-T ratio and age were calculated by Pearson's correlation coefficient.

Results

Figure 1 shows the decline of the 24-h mean plasma total T with age. The highest correlation coefficient was with a power function; the regression equation was T (nanomoles per L) = $37.8 \times \text{age}^{-1.12}$ ($r = -0.54$; $P < 0.003$). According to this equation, the expected T concentration of a woman of 40 yr would be 0.61 nmol/L, about half that of a woman of 21 yr (1.3 nmol/L). The percent free T did not vary significantly with age; the mean value was 1.8 + 0.4. The DHEA-to-T ratio (both measured in nanomoles per L) was age invariant, with a mean value of 20.7 ± 11.6 (Fig. 2). The DHEAS-to-T ratio (moles per L and nanomoles per L, for

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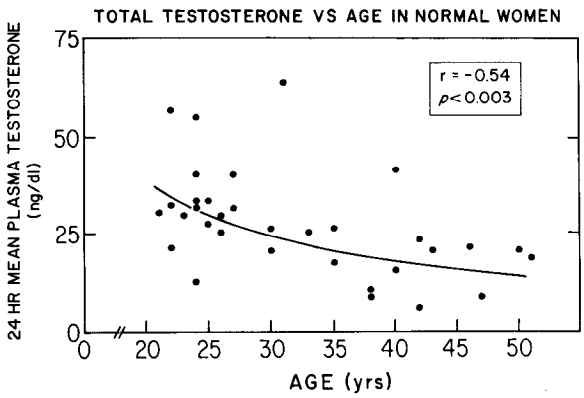

FIG. 1. Twenty-four-hour mean plasma total T *vs.* age in normal females. The regression equation was T (nanomoles per L) = 37.8 × age (years)$^{-1.12}$ (r = −0.54; $P < 0.003$).

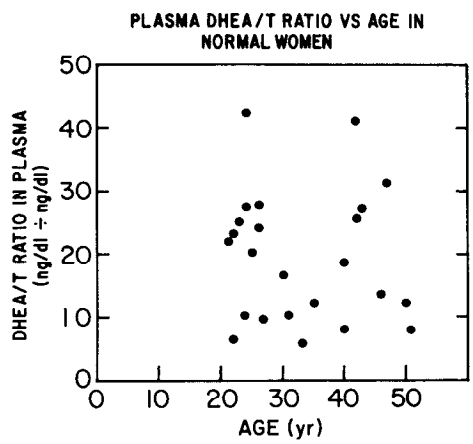

FIG. 2. DHEA-to-T ratio (both measured in nanomoles per L) was age invariant, with a mean value of 20.7 ± 11.6.

DHEAS and T, respectively) was age invariant, with a mean value of 3.0 ± 2.3 (Fig. 3).

Discussion

Our studies show that plasma total T declines steeply with age in normal premenopausal women; at age 40 yr, the level is about half what it is at age 21 yr. Since the percent free T does not vary significantly with age, free T likewise declines steeply with age. Although these findings have not been previously reported, they might well have been anticipated; since the great majority of circulating T in normal women is

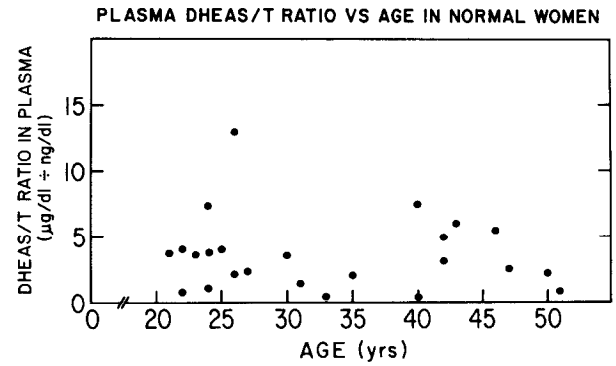

FIG. 3. DHEAS-to-T ratio (moles per L and nanomoles per L, respectively) was age invariant, with a mean value of 3.0 ± 2.3.

derived from metabolic transformation of the adrenal androgens DHEA and DHEAS, and since their levels are known to decline with age (1), one might expect the level of their metabolite T to decline too. What one could not guess is whether the DHEA-to-T and DHEAS-to-T ratios would be age invariant. The present study shows that they are.

An accurate knowledge of the values of plasma T concentration in normal women is essential for evaluation of possible abnormalities in pathological conditions, such as obesity. If age is a major factor, as our findings clearly demonstrate, it becomes essential, for the best interpretation, to compare the full age *vs.* concentration regression lines of an abnormal group with that of the normal population, or at least to have an age-matched control for each normal subject studied. It is to be hoped and expected that our current findings concerning the age variation of plasma T in normal women will improve the ability of researchers to evaluate abnormalities of T level in a variety of pathological conditions.

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