

## PLASMA TESTOSTERONE LEVELS AND ACNE

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**Abstract.** Plasma testosterone levels were determined by competitive protein binding or radioimmunoassay in 33 male and 31 female subjects with different types of acne of varying severity, and in 44 normal subjects (17 males, 27 females). Clinically, no signs of endocrinological disturbances were seen. In the males, no correlation was found between plasma testosterone levels and presence of acne. However, in the female group the plasma testosterone level was significantly elevated in patients with acne ( $P < 0.001$ ). In almost every second woman with acne the testosterone value exceeded 100 ng/100 ml of plasma, which is regarded the upper limit in females with the testosterone assay techniques used. The testosterone level did not correlate with type, distribution or severity of the disease.

Several clinical findings support the old assumption that acne vulgaris has an endocrinological basis. The onset of the disease occurs at puberty and it can be provoked by androgen administration. In most cases it is connected with seborrhea, and the sebaceous gland activity is primarily the result of androgenic stimulation. Thus, it has often been suggested that acne may be associated with excessive androgen production. Nevertheless, studies using methods previously employed for determination of plasma testosterone have failed to reveal any testosterone excess in acne. It was therefore considered worthwhile to determine the circulating testosterone levels by competitive protein-binding or RIA in a series of acne patients clinically classified according to prevailing type of lesion, distribution and severity of the disease.

### CLINICAL SERIES AND METHODS

The series consisted of 64 acne patients, 33 of whom were males (age 16-60) and 31 female (age 12-25). Of the males 12 had the papulopustular and 11 the cystic form of acne. The remaining 10 males have been classified as acne conglobata according to the criteria used by Berge & Gundersen (1), and they were summoned especially for this study. Of the

31 female patients 22 had the papulopustular and 9 the cystic form of acne.

Furthermore, with regard to the distribution of the lesions, the females exhibited less severe forms than the males. In 12 of the 31 females with acne vulgaris, the disease was limited to the face, whereas this was the case in only 2 of the 23 males. Severe forms affecting not only the face but also the entire back and buttocks were encountered in 6 males (acne conglobata patients excluded) and in 2 females. The patients did not exhibit clinical signs of endocrinological disturbance.

The 44 normal subjects (17 males, 27 females) consisted of healthy volunteers, mainly nurses, technicians and other hospital personnel without history and clinical signs of acne. In the female group the controls had a mean age somewhat higher than the acne patients, but the matching was considered satisfactory because there is no significant influence of increasing age on plasma testosterone levels in young women. The mean age of the male control group was intermediate to that of the acne vulgaris and acne conglobata patients.

Patients and controls who had used contraceptive pills during the 2 month period immediately prior to the study were excluded from the series. All internal medication was discontinued 3 days prior to the examination and no local treatment with steroids or antiandrogens was used.

For the determination of testosterone, one heparinized blood sample was collected in the morning from each patient and control who had fasted at rest. The blood was centrifuged within 30 min of withdrawal and either processed immediately or preserved at  $-20^{\circ}\text{C}$ . Testosterone was determined using a competitive protein-binding (CPB) technique (2, 3), using sex steroid-binding plasma protein derived from late twin pregnancy plasma (2). However, part of the material (both pathological and normal) was assayed using radioimmunoassay (RIA) which included exactly the same preparative steps as the CPB method with the exception of the precipitation of fatty material in cold methanol. In this case the quantitation was carried out using an anti-testosterone-3-oxime-BSA serum. Comparative experiments had shown a correlation coefficient of 0.95 for the two techniques both at high and low plasma testosterone levels (3). The techniques, though rapid and simple, show a reasonable degree of specificity (2). The sensitivity of the competitive protein binding technique is 11 ng/100 ml of plasma and is better in the case of the RIA technique.

Table I. Plasma testosterone levels, age and sex of 108 cases with and without acne

Sex	Group	No. of cases	Age		Plasma testosterone (ng/100 ml)	
			Range	Mean	Range	Mean $\pm$ S.D.
Male	Normal	17	19-43	31	417-1 787	763 $\pm$ 379
	A. vulgaris	23	16-26	20	215-1 990	641 $\pm$ 401
	A. conglobata	10	24-60	39	340-1 787	746 $\pm$ 442
Female	Normal	27	15-40	24	27-113	59 $\pm$ 18
	A. vulgaris	31	12-25	20	54-308	119 $\pm$ 62

## RESULTS

As can be seen from Table I there is no significant difference between the testosterone levels in male controls on the one hand and male acne vulgaris ( $P < 0.1$ ) or acne conglobata patients ( $P < 0.1$ ) on the other. Three acne vulgaris and 2 acne conglobata patients had levels higher than 960 ng/100 ml of plasma, as did 4 cases in the control group. Values lower than 300 ng/100 ml, considered to be the lower normal limit in adult males, were seen in 3 teenagers with acne vulgaris.

In the female group the plasma testosterone level was significantly elevated in patients with acne ( $P < 0.001$ ). Of the 31 female acne patients 14 showed values higher than 100 ng/100 ml of plasma, and in 4 patients the level exceeded 180 ng/100 ml. Of the 27 controls only one had a plasma testosterone value which slightly exceeded 100 ng/100 ml of plasma. The plasma testosterone level did not correlate to type, distribution, or severity of the disease.

## DISCUSSION

Since 1961 specific methods for measuring circulating testosterone have been available. However, these methods were tedious and costly and have therefore been applied to small series of acne patients only.

Using a comparatively insensitive double-isotope-derivative dilution technique and gas chromatography, Scoggins et al. (7) found no direct correlation in either sex between levels of plasma testosterone and the presence of acne vulgaris. Their series consisted of 7 male and 5 female patients.

Using enzymatic conversion of testosterone to estradiol, which was measured by a fluorimetric technique, Pochi et al. (6) found no elevation of plasma testosterone levels in a series of 42 male patients with acne. Neither could he find elevated testosterone levels in urine of the same patients, when

using a gas-liquid chromatographic technique. There was no direct correlation in these male subjects between hormone levels and severity of the disease either, a result which is supported by our study.

Recently, Mauvais-Jarvis et al. (5) studied females with acne. They found normal or slightly elevated plasma (6 subjects) and urinary (10 subjects) testosterone levels, but a significantly increased urinary excretion of androstenediol.

The introduction of CPB and RIA techniques for steroid analyses has permitted the study of larger series of patients. The results obtained with the two comparable techniques used in the present study, confirm as far as the male acne series is concerned earlier reports according to which no androgen excess is demonstrable in patients with this disease. However, the results of our female series indicate a plasma testosterone level above the normal in almost every second patient with acne. The difference between acne patients and controls was statistically significant. The slight difference in age distribution cannot explain the result and possibly increased androstenediol levels cannot be responsible for the difference because all androstenediols (and androstenediols) are excluded in the chromatographic step (2) of the methods.

In all the methods used, until now, for the determination of plasma testosterone, both free and protein-bound testosterone are extracted and measured together. It is generally accepted that of the two forms only the free is biologically active. Interpretation of plasma testosterone levels in relation to the influence of this steroid on acne development must take this fact into account. The role of androstenedione and dihydrotestosterone and other androgens known to circulate in plasma remains also to be investigated.

It has been stated (4) that female acne patients aged 30 years or more show a tendency to pubic hair growth of virile type. Therefore, it may be men-

tioned that none of those four females showing plasma testosterone levels above 180 ng/100 ml had evidence of virilism or hirsutism and all of them were under 30 years of age.

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