The sebaceous gland is a target of androgens, and hormonal influences play an important role in the multifactorial pathogenesis of acne. Testosterone and dihydrotestosterone are the two most potent androgens. Both in women and men there may be a hypersensitivity of the end organ to androgens due to an increase in the activity of the enzyme 5α-reductase type 1, which converts testosterone into active dihydrotestosterone. The production and the plasma transport of androgens may also be involved.

Ovarian androgens are produced in the thecal zone, which is stimulated by pituitary luteinizing hormone (LH). There is mostly androstenedione and little testosterone, corresponding to 50% of the circulating androgens. These levels are increased in some rare ovarian tumors, in hyperthecosis, and in the polycystic ovary syndrome (PCO). In the adrenal glands, two androgens are produced by the internal reticular zone. These are dehydroepiandrosterone (DHEA) and its sulfate (DHEA-S), which are then converted into androstenedione. These androgen precursors are increased in enzymatic defects on the cortisol metabolic pathway. Physical or psychological stress also leads to a simultaneous increase of cortisol and adrenal androgens.

Unlike estradiol and cortisol, ovarian and adrenal androgens are not specifically under negative feedback control by the pituitary gland hormones. The peripheral interconversion of ovarian and adrenal precursors in the liver, fat, and skin leads to transformation of low-potency androgens into progressively more potent androgens, from DHEA and DHEA-S to androstanedione and finally to testosterone. In plasma, more than 96% of circulating testosterone is bound to sex-hormone-binding globulin (SHBG), and there is only little free active testosterone. If SHBG decreases, the free active testosterone increases, leading to hyperandrogenism. Contraceptive pills with androgenic progestins are the most frequent cause of the decrease of SHBG.

Elevation of serum DHEA-S, testosterone, dihydrotestosterone, and other androgens (hyperandrogenism) has been linked to the development of acne. By means of radioimmunologic assays, some authors have shown that women with acne frequently have abnormal levels of circulating androgens, particularly in late-onset or persistent acne or in acne associated with hirsutism. However, most authors have not found abnormal levels of androgens. Generally, endocrinological studies are not warranted unless clinical manifestation reveals hyperandrogenic syndromes.

Prepubertal acne or acne in young adults may sometimes be a cutaneous marker of adrenal androgen excess, because an increase in DHEA-S and an incomplete enzymatic block due to a heterozygotic defect of 21-hydroxylase have been shown in premenarchal girls.

The prevalence of polycystic ovaries seems to be higher in women with acne. PCO and

The anatomic changes in the adrenal cortex from fetal life through maturation, i.e., adrenarche. Adrenal androgen production is high in fetal life and persists into the first year. Androgen levels are low in childhood until about the age of 8 years, when the zona reticularis appears. Shaded areas represent androgen-producing zones.
Development of the Adrenal Cortex

Fetal
High Androgens

Childhood
Low Androgens

Adult
High Androgens

Cholesterol

- StAR protein, cholesterol desmolase

Pregnenolone → 17-Hydroxypregnenolone → Dehydroepiandrosterone → Androstenediol

3β-Hydroxysteroiddehydrogenase

Pregnenolone

Progestrone

21-Hydroxylase

11-Desoxycorticosterone

11-Desoxycortisol

11β-Hydroxylase

Corticosterone

Cortisol

Aldosterone synthetase

Aldosterone

Cortison

17α-Hydroxylase

17-20-Lyase

17β-Hydroxysteroiddehydrogenase

11β-Hydroxysteroiddehydrogenase

StAR = Steroid acute regulatory protein

Source of Androgens in Women

Adrenal

Testosterone

Androstenedione

DHA

Ovary

DHEAS