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# PHYSIOLOGY OF ANDROGENS, THEIR EFFECT ON SEBUM SECRETION AND ACNE EXACERBATION

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**Introductions:** Acne is considered the most common skin disease among teenagers and women aged 30 to 40. Due to insufficient understanding of the pathogenesis of this disease, many prescriptions are ineffective, but only worsen the condition of the patients' skin. Therefore, this issue should be investigated comprehensively, particularly in terms of the physiological effects of hormones.

**Purpose and task:** To study the mechanisms of action of androgens on targets in the sebaceous glands and to determine their relationship with the intensity of sebum secretion and exacerbation of acne.

**Materials and methods:** Comparative descriptive, induction, and deduction methods of analysis of scientific foreign literature were carried out.

**Results and discussion:** A correlation was established between the growth in the level of androgens and the intensity of sebum production, which is accompanied by the appearance of inflammation.

**Conclusions:** Considering the present disease through the prism of the pathophysiological cascade, it can be noted that even with normal levels of dihydrotestosterone in the blood, the cutaneous receptor can react overly through interrelated mechanisms.

Androgens — are a class of steroids that are responsible for the reproductive system; they play a powerful role not only in the reproductive system, but also outside it. Key metabolites play a crucial role in how skin functions normally and what goes wrong in skin conditions, including the control of the sebaceous glands activity. The dominant and most powerful androgens are testosterone, as well as 5α-dihydrotestosterone, which is formed by reducing testosterone in target organs,

thanks to the enzyme 5-alpha-reductase (5AP). Dihydrotestosterone (DHT) is considered the most dynamic, most vigorous metabolite in both men and women. If in the former, when DHT dominates, desensitization of the receptor most often occurs, then in the latter, the action of this mechanism is more intense, which means a much stronger skin response even with minimal fluctuations in this indicator. And due to the fact that the density of androgen receptors in sebocytes is maximum compared to other structures, they become a target even with moderate androgen stimulation and, as a result, extreme sebum secretion, which leads to an exacerbation of the course of acne. Normally, the cycle of keratinization of the skin takes from 26 to 28 days, androgens stimulate the proliferation of keratinocytes and control the process of differentiation of epitheliocytes. However, with high levels of DHT and existing hyperfunction, the rate of these processes declines, epidermal renewal is markedly slower, the stratum corneum increases, and hyperkeratosis appears. This mechanism is due to the fact that dihydrotestosterone, binding to the androgenic protein receptor (AR), reduces the activity of corneodesmosome-cleaving enzymes, which are responsible for the breakdown of desmoglein (mainly DSG1), thereby inhibiting the physiological exfoliation of dead skin cells. On top of that, this sets off a cascade of cellular signals deep in the skin, and the sebocyte starts to form more and more lipids than is normal. The composition of sebum also changes: the amount of palmitic, stearic, and oleic acids boosts tenfold. The unique sebum lipid-squalene — is oxidized to squalene peroxide and squalene monohydroperoxide, which causes the appearance of many comedones on the patient's skin. The altered skin microbiome and reduced immune response are ideal conditions for Propionibacterium acnes, now Cutibacterium acnes, to reproduce. This bacterium uses such a nutrient medium as a substrate, and the metabolic products of the bacterium (lipases and proteases) lead to the appearance of papules and pustules. Interestingly, when DHT levels are normal, squalene actually helps keep skin hydrated and supple, but the hyperandrogenic state of the skin itself turns this product into a factor that has comedogenic potential. Patients will complain of a chronic duration of rashes, a feeling of skin stickiness, subcutaneous rashes that do not go away for a long time, and post-acne. A woman's

skin needs special attention during ovulation and before menstruation, because during the release of the ovum, a large amount of testosterone is produced, which is a physiological mechanism associated with the peak of luteinizing hormone (LH). Considering that before the start of critical days, the level of estrogen and progesterone becomes lower, and the level of free male hormone and sensitivity to it is higher, rashes and corresponding skin reactions appear. Since the largest sebaceous glands are located in the T-zone (forehead, nose, chin), even with a slight variation and an increase in the androgenic signal, these areas will react the earliest of all. Currently, the first line in the treatment of acne is adapalene (Differin), benzoyl peroxide 2% and 5%, azelaic acid, as well as clindamycin phosphate as monotherapy or in combination with adapalene. These medications eliminate hyperkeratosis and combat the root cause of acne, caused by the bacterium Cutibacterium acnes. The most interesting from the point of view of the mechanism of work are means with adapalene and azelaic acid; in Ukraine, the latter is offered in the form of the drug «Skinoren». If adapalene normalizes the keratinization process and eliminates follicular hyperkeratosis, then azelaic acid acts simultaneously at several levels. This is supported by a 1991 study by Akamatsu and collaborators titled «Inhibitory effect of azelaic acid on neutrophil functions: a possible cause for its efficacy in treating pathogenetically unrelated diseases». (Akamatsu et al., 1991) Based on this, the ingredient is a relatively competitive inhibitor of 5α-reductase,(Schulte et al., 2015) and therefore has an antiandrogenic effect in sebocytes, and in addition, at the same time, minimizes the links of inflammation due to the inhibition of the production of reactive oxygen species (ROS) by neutrophils. Also among the recommendations for such patients are products with zinc and saw palmetto extract that work as natural blockers of androgen receptors. (Gupta, Charrette, 2017)

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