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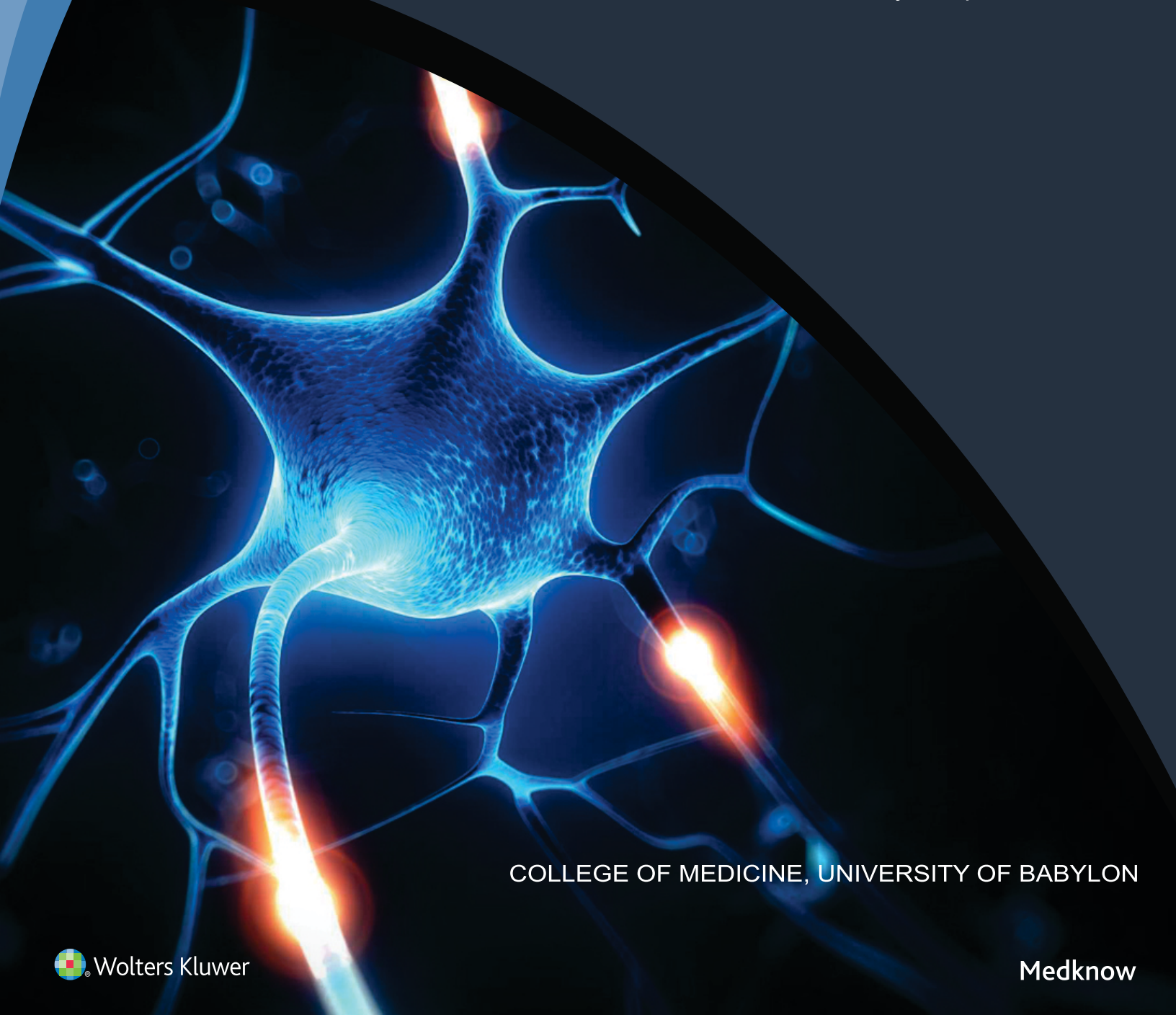

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Review Article

The Effect of Androgen Hormones in Acne Pathogenesis: A Review

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Abstract

At all ages (from birth to adulthood) large number of people may affect with acne, the disease with chronic inflammation of the pilosebaceous follicle. Although acne is a benign dermatological change, it has a massive effect and stays for a long time, with a defect in growth, self-confidence, and emotional stress. The interruption in observing the medical help aggravates the physical and psychological injuries; thus, it is related to elucidate the disease and to find the suitable treatment for it. In the skin, testosterone (T) and dihydrotestosterone (DHT) are synthesized and bind to the androgen receptor. Several revisions about acne sustenance the role of androgen hormones. There are two principles used for the treatment of acne rendering to the American Academy of Dermatology (ADD).

Keywords: Acne vulgaris, androgen, diagnosis, management, pathogenesis

Introduction

One of the communal dermatological complaints is acne vulgaris (AV), with pilosebaceous unit that origins inflammatory lesions (papules, pustules, and nodules), noninflammatory lesions (open and closed comedones), and variable grades of damaging. The prevalence of AV is approximately 85% and occurs frequently through puberty.[1]

Hormones control the constituents of sebocyte function.

Androgens bind to the nuclear androgen receptors (ARs) and disrupt the sebaceous gland function. Highest density of ARs is established in sebaceous glands.[2]

Reduced self-esteem, sadness, and nervousness are the important compliance to acne.[3]

Yentzer *et al.*[4] found that depression is reported in 8.8% of acne patients, and hopelessness in females is two times greater than in males (10.6% vs. 5.3%).

Acne Vulgaris

AV is a complex and common skin illness, affects approximately 85% of younger in the world, expresses in adolescence, and degenerates during puberty; however, several revisions submit that it may happen at any age of life.

According to typical faith, sebaceous gland hyperplasia may cause acne. in addition, follicular abnormality with keratinization, microbial hyper-colonization of the follicular canal, microbial hyper-colonization of the follicular canal, and increased inflammation could be the causes of the disease, as in Figure 1.[5]

Classification of Acne

A variety of lesions are present in people with acne. The comedone (KOM-e-do) is the basic acne lesion; it is simply an enlarged and plugged hair follicle. Closed comedone is the plugged follicle that yields a white bump named a whitehead.[6] Open comedone reaches the surface of the skin and opens; sometimes it is named blackhead. Exposed to air changes the sebum into black staining.

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Blackhead and whiteheads could stay on the skin for an extended period.[7]

Consequently, acne is categorized as the lesions in comidonica, popular–pustular, and nodular, according to severity into mild, moderate, moderate to severe, severe, and serious as in Table 1. These lesions are positioned mainly on chest, face, neck, and back.[8]

Acne Epidemiology

Worldwide the eighth most common skin sickness is AV with a prevalence approximately 9.38% (for all ages). In diverse nations and among diverse age groups, the occurrence of acne fluctuates with a range from 35% to 100% of adolescents at some point.[9]

Pathogenesis of Acne

Acne represents follicle disease. Pathologically, it comprises serum overproduction, disturbance in keratinization of follicular, creation of *Propionibacterium acnes*, and lastly the release of pro-inflammatory intermediaries to skin.[10] Although the first symptom of acne is the development of the microcomedones, the main causes for activating this reaction remain unknown. Individuals with acne have larger sebaceous glands stimulated during their teenage years. Dihydrotestosterone (DHT) was discriminating to face sebocytes.[11]

The activity of sebocytes was regulated by a number of pathways and hormones besides androgens, for example, substance P receptors, peroxisome proliferator-activated receptors, insulin-like growth factor, a-melanocyte-stimulating hormone, corticotropin-releasing hormone (CRH), ectopeptidases, and vitamin D.[12]

Larger comedones result during the failure to shed intra-follicular keratinocytes (sebum generation is abundant) and block the pilosebaceous units with keratolytic and sebum debris. In turn, this leads to an inflammatory response by persevering the follicle with the pathogenic *P. acnes*.[13] *Propionibacterium acnes* secreted lipase and protease enzymes that achieve to disturb and destroy the wall of the follicle and recruit inflammation and release chemical factors, as in Figure 1.[14]

Pro-vitamin D in the skin can be produced by the pilosebaceous unit. Polycystic ovary syndrome (PCOS) and insulin resistance may be linked with vitamin D deficiency.[15]

Several factors have a role in the pathogenesis of acne such as genetics (family history of severe acne), diet (e.g., dairy consumption and chocolate), and environmental factors (cosmetics, smoking, and occupational exposures).[3]

Androgens

The most important hormone that regulates sebum production is androgens.[17] At puberty (in both sexes), androgens (testosterone and DHT also with weaker androgens) motivate sebum production and the formation of acne. Dehydroepiandrosterone (DHEA) and androstenedione produce by the adrenal glands and ovaries. Adrenal glands produced DHEA, whereas the ovaries and adrenal glands secreted androstenedione in equal amounts. Of note, in infundibular sebocytes, the enzyme 5a-reductase may transform the testosterone to the 5–10 times more active DHT, as shown in Figure 2.[10]

Role of Androgens Levels in Acne

In the skin, testosterone (T) and DHT are produced and then bind with AR. Medical study demonstrated the androgen hormones role in pathogenesis of acne and refer to the onset of acne by flow of dihydroepiandrosterone sulfate (DHEA-S), administration with androgens

Table 1: Classification of acne[8]

	Injury type	Type of Acne	Degree	Gravity
Non inflammatory	Blackhead	Comedonica	I	Mild
Inflammatory	Pimple	Papular-pustular	II	Moderate
	Pustule			
	Nodule	Nodular	III	Moderate to Severe
	Cyst		IV or conglobata	Severe
	Scar		V or fulminant	Serious

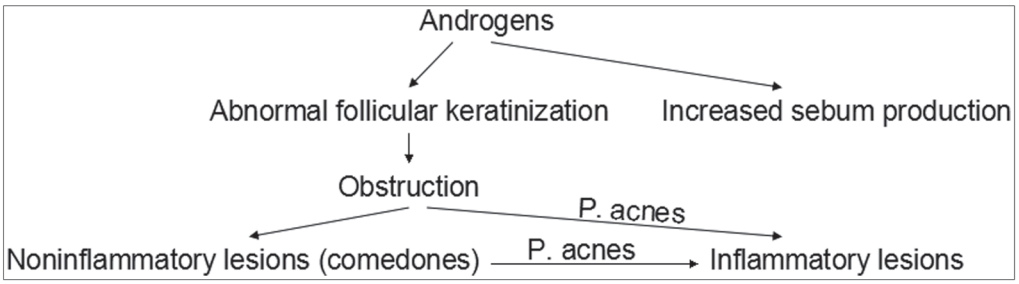

Figure 1: Mechanisms of acne pathogenesis[16]

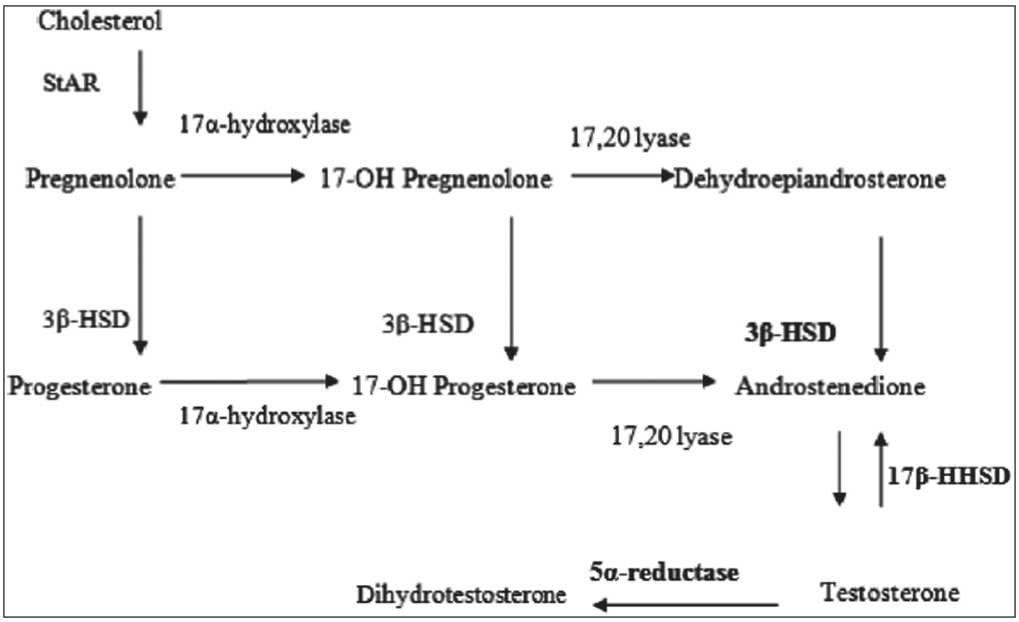

Figure 2: Steroidogenic pathway[18]

leading to acne and the treatment by blocking the androgen receptor.[19]

In both sexes, DHEA-S concentration is elevated, then DHEA-S is changed by dermal papilla and sebocytes into DHT and testosterone. Any defect in AR leads to acne.[20] Patients with CAH, Cushing syndrome, and PCOS have acne because they have higher levels of androgen. No relationship was observed between the severity of acne and hyperandrogenism. Roughly, elevated levels of DHEA-S were initiated. Androgen improved the sensitivity of receptors and the activity of 5α-reductase led to a higher level of DHT.[21]

Diagnosis

The AV diagnosed clinically, includes folliculitis, keratosis pilaris, perioral dermatitis, seborrheic dermatitis, and rosacea. Physical examination and history are beneficial to determine the main cause of the acne, like medication or hormonal abnormality leading to hyperandrogenism. Seborrhea, hirsutism, and androgenetic alopecia are the dermatological indexes of extra androgen. Adult women, especially women with new-onset of acne and further signs of elevated androgen (e.g., hirsutism and menstrual irregularities), must be verified for hyperandrogenism with the estimation of free and total testosterone in serum, DHEA, luteinizing, and follicle-stimulating hormone (FSH) levels. In pre-pubertal teenagers with acne, marks of elevated androgen comprise accelerated growth, pubic or axillary hair, body odor, and genital maturation.[22]

The laboratory checks for patients with hormonal acne includes:[10]

1. Testosterone: the elevations of testosterone greater than (<200 ng/dL) are indicative of benign ovarian or adrenal cause, although the level above this may be an indicator of ovarian or adrenal neoplasia.
2. Androstenedione: ovaries and adrenals secreted androstenedione in equal amounts. Due to the circadian rhythm, the best time to analyze androstenedione is in early morning.
3. DHEA: in adrenal tumors the levels of DHEA >8000 ng/dL and DHEA-S are elevated, although the DHEA-S levels of (4000–8000 ng/dL) point to benign adrenal hyperplasia.

Table 2: Management of acne vulgaris[23,24]

Type of Treatment	Mild Acne	Moderate Acne	Severe Acne
First-line medication	• Topical retinoid; or • Benzoyl peroxide; or • Topical combination therapy*	• Topical combination therapy*; or • Oral antibiotic, topical retinoid, and benzoyl peroxide; or • Oral antibiotic, topical retinoid, benzoyl peroxide, and topical antibiotic	• Oral antibiotic and topical combination therapy*; or • Oral isotretinoin
Alternative medication	• Add topical retinoid or benzoyl peroxide (in case one is not used already); or • Consider alternative retinoid; or • Consider topical dapsone	• Consider alternative combination therapy*; or • Consider change in oral antibiotic; or • Add combined oral contraceptive or oral spironolactone (female patients); or • Consider oral isotretinoin	• Consider change in oral antibiotic; or • Add combined oral contraceptive or oral spironolactone (female patients); or • Consider oral isotretinoin

Zaenglein *et al.*[24] modified the management of AV

4. Sex hormone-binding globulin (SHBG): if the level of SHBG is decreased, this is an indicative of elevated free unbound testosterone.
5. Prolactin: in hypothalamic or pituitary disease the level of prolactin elevated.
6. 17-Hydroxy progesterone: in congenital adrenal hyperplasia as a result of insufficiency or absence of 21α-hydroxylase lead to elevated 17-hydroxy progesterone (>200 ng/dL).
7. Luteinizing hormone: FSH ratio: when it increases above 2, it is a suggestive of PCOS.
8. Fasting and postprandial insulin: insulin levels should be checked for overweight and obese patients.
9. Serum cortisol: in adrenal neoplasia cortisol level elevated.

Management

Topical, systemic, and surgery are the suggested treatment for acne. The treatment of patients with acne is based on the injury and the patient's acceptability. To increase achievement of therapy, it required three types of treatment.

The first-line and alternative treatments in Table 2 are the two principles used for the treatment of AV according to the American Academy of Dermatology (ADD).[23,24]

Conclusion

Chronic inflammatory skin sickness affecting the pilosebaceous glands is AV. The main causes and treatment of the disease change according to the severity of the disease. Worldwide acne is the eighth most predominant illness. AV can affect the quality of life, self-confidence, and attitude of these patients. Disorder of androgens hormone is associated with AV.

In adolescence (in both sexes), sebum production and acne formation are stimulated by androgens. Testosterone and DHT with weaker androgens strong the secretion of sebum.

Mild-to-moderate acne is treated by topical therapies, whereas the treatment failed in a patient with limited education.

Ethical approval

Not applicable.

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Conflicts of interest

There are no conflicts of interest.

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