Multimodal Treatment of Acne, Acne Scars and Pigmentation

AvaT. Shamban, MD, FAAD[a,*], Vic A. Narurkar, MD, FAAD[b]

KEYWORDS

• Acne • Acne grading scale • Inflammatory acne
• Mulitmodal treatment • Photopneumatic
• Pigmentation • Scarring

Acne is a common skin disease that affects nearly 80% of adolescents and young adults aged 11 to 30 years.[1–4] Acne can present at any age, affecting 8% of adults aged 25 to 34 years and 3% of those aged 35 to 44 years.[4,5] Lesions appear primarily on the face, back, chest, and other areas with a high concentration of pilosebaceous glands.[6]

The development of inflammatory lesions often drives acne patients to seek treatment. If a lesion becomes severely inflamed it may leave a scar. (Scarring may also result in less severe cases of acne.)[6] Severe scarring caused by acne is associated with substantial physical and psychological distress, particularly in adolescents. Scarring may be permanent on the chest and back and on the face. Acne scars affect males and females of all ethnic backgrounds and facial scarring may occur in up to 95% of acne patients.[4]

The pilosebaceous unit (PSU) is the site at which acne originates on the skin. The PSU consists of sebaceous glands, a hair follicle with a canal lined with stratified squamous epithelial cells, and a rudimentary hair shaft. PSU growth and differentiation depend on androgens, growth factors, thyroid hormones, and other biologic factors.[4,7]

Sebum must be produced for acne to develop. Secreted by sebaceous glands, sebum consists of fatty acids that support colonization by *Propionibacterium acnes*, the bacterium associated with acne. Sebum production is increased by androgens and suppressed by isotretinoin.[8]

In normal skin, cells die and are replaced, and sebum sweeps desquamated epithelial cells up the follicular canal and toward the infundibulum, an opening at the top of the follicle. If the infundibulum becomes occluded, as in acne, sebum and dequamated cells accumulate in the canal, forming a medium for the growth of bacteria, triggering immune reactions and inflammation.[4,7]

In summary, 4 major factors contribute to the development of acne: (1) sebaceous gland hyperplasia and seborrhea; (2) altered growth and differentiation of hair follicular cells; (3) proliferation of *P acnes* in the affected follicle; and (4) inflammation with an immune response.[6] Sebaceous hyperplasia and altered follicular growth and differentiation together induce the development of microcomedones, the microscopic precursor to all acne lesions. The inflammatory cytokine interleukin 1α (IL-1α) may also be involved, as it has been shown to induce hyperkeratinization in vitro.[9,10] A microcomedone can become a noninflammatory comedo or, if it becomes inflamed, a pustule, papule, or nodule.[6,7,11]

THE ROLE OF ANDROGENS

In acne-prone children aged 7 to 8 years, androgens stimulate the sebaceous glands to enlarge, increasing (1) the number of lobules per gland, (2) the size of the sebaceous follicle, and (3) sebum secretion. The result is a microcomedo. Sebocyte differentiation is initiated when circulating androgens enter the cell and couple with the androgen receptor, which in turn initiates gene transcription and sebocyte differentiation and maturation. As

[a] Laser Institute for Derm and European Skin Care, #600-E, 2021 Santa Monica Boulevard, Santa Monica, CA 90404-2208, USA
[b] Ste 505, 2100 Webster Street, San Francisco, CA 94115-2381, USA
* Corresponding author.
E-mail address: avasham@aol.com (A.T. Shamban).

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differentiation progresses, the sebocyte ruptures and releases lipids into the sebaceous duct and follicle. At this sebhorrheic stage the follicle is ready for the development of a microcomedo.

Although androgens are stimulating sebocyte differentiation, keratinocytes in the hair follicle are hyperproliferating and accumulating rather than being shed as single cells into the lumen. They become densely packed among lipid droplets and monofilaments. As lipids, bacteria, and cell fragments accumulate in the hair follicle, comedogenesis occurs and an acne lesion appears on the skin.[6,7]

Although androgens play a role in acne, endocrine abnormalities are not detected in most acne patients[6,7,12] and a relationship between severity of acne and levels of circulating andogens has not been proven.[13] Endocrinologic testing in patients with acne is recommended only when evidence of hypergonadism is present.[12]

P ACNES

The microenvironment of the follicle is believed to be important in the pathogenesis of acne because it encourages the proliferation of *P acnes* into the follicular duct, resulting in an inflammatory papule or pustule. *P acnes* is a Gram-positive anaerobe whose role in acne is thought to be inflammatory rather than infectious. *P acnes* induces monocytes to produce tumor necrosis factor α (TNF-α), IL-1β, IL-8, and other proinflammatory cytokines by a mechanism thought to involve pattern recognition receptors such as the recently described toll-like receptors.[10] IL-8 and other chemotactic factors may also be important in attracting neutrophils to the PSU. *P acnes* also produces proteases, hyaluronidases, and lipases that contribute to tissue injury.[10]

Although the exact way in which *P acnes* colonizes the follicular duct is not known, reduction in *P acnes* is correlated with clinical improvement in acne. *P acnes* reduction is also associated with decreases in proinflammatory mediators.

INFLAMMATION

Severity of inflammation is associated with interactions between *P acnes* cells, antibodies, complement, and immune responses. CD4 lymphocytes and later, neutrophils, migrate to the follicular wall where they cause disruption, releasing corneocytes, lipids, and bacteria into the surrounding dermis. When this occurs, more inflammatory cytokines are recruited to the scene.[6,7,10] Recent evidence shows that sebocytes express neuropeptides, including substance P, which contributes to abnormal sebocyte differentiation, proliferation, and lipid synthesis.[6]

CLINICAL PRESENTATION

Patients with acne present with varying degrees of disease severity. Acne grading systems have been based on estimates of the types and number of lesions, the most frequently occurring lesion, and anatomic areas of involvement.[14] Comedones may be open (blackheads) or closed (whiteheads). Open comedones, which consist of sebum and desquamated keratinous cells and have a dilated opening, are slightly elevated or flat lesions 1 to 5 mm in diameter. They may resolve without treatment or become inflamed.[4] Closed comedones, which develop as follicles become occluded and sebum accumulates, present as firm, pale, slightly raised lesions 1 to 2 mm in diameter. Microcysts, or closed macrocomedones, may grow to 5 mm diameter. If the follicular sac of a closed comedone ruptures and discharges its contents into the upper layers of skin, an elevated, pus-containing lesion (pustule) develops, which may resolve without scarring. If the sebum and desquamated cells are released into the deeper dermal layers, raised solid lesions, or papules, develop, which require more time to resolve, and scarring often occurs. Nodules, which may become 10 mm in diameter, are deep-seated abscesses that occur in the most severe cases of acne.[4]

TREATMENT OF ACNE

The goals in treating acne are to relieve clinical symptoms and to prevent scarring. Since the extent and type of scarring are associated with the severity and longevity of acne before therapy is initiated[4]), dermatologists encourage patients to obtain early treatment.[8]

Treatment of acne should be aimed at the pathogenic causes and clinical symptoms. The following therapeutic goals have been recommended[4]:

1. reduce production of sebum
2. reverse hyperproliferation and normalize keratinization
3. resolve microcomedones and comedones
4. reduce colonization of *P acnes* and inflammation
5. prevent formation of microcomedones, comedones, and inflammatory lesions
6. resolve existing inflammatory lesions

An expert comittee[7] has recently updated the 2003 Evidence-Based Consensus Guidelines[6] of the Global Alliance to Improve Outcomes for the Treatment of Acne. The update is based on the greater understanding of acne pathogenesis since the guidelines were published.