Evaluation and Management of Acne

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INTRODUCTION

Acne vulgaris, commonly known as acne, is the most common skin condition affecting up to 95% of adolescents and young adults in the United States.1,2 It typically begins at puberty. It is estimated that acne affects 9.4% of the global population.3 Clinical presentations can vary drastically among patients, with mild to severe disease. Patients, particularly adolescents, may therefore experience significant social and emotional symptoms of embarrassment with associated psychological symptoms of depression or anxiety that affect social lives.4 Fortunately, there are several acne treatments available,1 but diagnosis and treatment guidelines are lacking and variations exist across specialties.4 This article reviews the epidemiology and pathophysiology and also discusses how primary care clinicians can appropriately diagnose patients with acne.

EPIDEMIOLOGY

Acne usually begins at puberty and affects adolescents of both genders. It is most common at ages 12 to 25 years.5 More than 85% of teenagers experience some

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KEYWORDS

- Acne - Evaluation - Management - Treatment - Retinoid - Sports medicine

KEY POINTS

- Acne vulgaris is a common disorder of the pilosebaceous follicles that affects adolescents and can persist into adulthood.
- The psychological and economic impact is significant and may prove challenging to address in the clinical setting.
- The diagnosis of acne vulgaris can be made from the patient’s history and physical examination and can be effectively treated in the primary care setting.
form of acne. Although acne tends to resolve before the age of 30 years, it may persist into adulthood. Prevalence studies in adults 20 years or older have shown that women were being affected at higher rates than men. It is a chronic disease that can persist for many years. There is limited amount of research about what specific factors predict whether it will last into adulthood.

PATHOPHYSIOLOGY

Acne vulgaris is a disease of pilosebaceous follicles. Studies indicate that pathogenesis of acne involves 4 main processes:

1. Androgen-induced increase in sebum production, usually around puberty
2. Altered keratinization of the sebaceous duct, leading to comedone formation
3. Inflammation around the sebaceous gland
4. Bacterial colonization of hair follicles on the face, neck, chest, and back by *Propionibacterium acnes*.

Current therapies target these 4 factors for acute control of flare-ups and long-term maintenance. The sequence of events and how these factors interact remain unclear, but there are various underlying causes of these changes. Increased androgen production leads to abnormal epithelial desquamation and follicular obstruction, which leads to the formation of the microcomedone, the precursor lesion in acne. Studies have shown that immune changes and inflammation may stimulate pilosebaceous vasculature before keratinization, which is led by CD4⁺ lymphocytes and macrophages. It has been hypothesized that interleukin (IL) 1a induces cytokines to activate local endothelial cells, which in turn upregulate inflammatory vascular makers such as E-selectin, vascular cell adhesion molecule 1, intercellular adhesion molecule 1, and HLA-DR around pilosebaceous follicles. This is due to a linoleic acid deficiency caused by excess sebum and agitation of barrier function within the follicle.

Comedones form as a result of increased cell division and cohesion of cells lining the follicular lumen. When cells accumulate abnormally, mix with sebum, and partially obstruct the follicular opening, they form a closed comedone, or whitehead. If the follicular opening is larger, keratin buildup becomes more visible and may darken to form an open comedone, or blackhead. *Propionibacterium acnes* colonizes different pilosebaceous units and leads to inflammation via the production of inflammatory mediators, activating toll-like receptor-2, which results in the production of proinflammatory cytokines such as IL-12 and IL-8, leading to the formation of inflammatory papules and pustules. Improved understanding of acne development suggests that acne is a disease consisting of a combination of the innate and adaptive immune systems, as well as inflammatory events. Treatment, therefore, targets both immune system activation and inflammatory pathways.

DIAGNOSIS

Acne is diagnosed by the identification of lesions on the skin on physical examination. However, before initiating treatment, it is important to assess and evaluate a patient by obtaining a standard history of present illness and review medications and prescriptions that the patient has been taking. Any hormonal influences caused by medications may affect natural hormonal processes, leading to possible acne. The patient should be assessed by asking about the duration of symptoms, locations on the body, variations of weather exposure, and stressors. In addition, any information regarding current treatments for acne and failures may be helpful in guiding treatment.
Additional information to obtain from women includes information about flare-ups that may occur with menstruation, menstruation history, pregnancy history, oral contraceptives, and cosmetics. Furthermore, family history regarding endocrine abnormalities, acne, polycystic ovarian syndrome, and skin disorders may also be important to evaluate.

On physical examination, useful clinical categorization of acne is based on predominate morphology: noninflammatory open or closed comedones (blackheads and whiteheads) to inflammatory lesions consisting of erythematos papules, pustules, or cystlike nodules.4

Severity can be classified as mild, moderate, or severe depending on the number of comedones or inflammatory lesions (Table 1).

There are many other conditions that can mimic acne, some of which contain the term acne in their nomenclature, but they lack the presence of comedones. Differential diagnoses include the following13:

- Keratosis pilaris
- Malaria
- Milia
- Rosacea
- Periorificial dermatitis
- Molluscum contagiosum
- Flat warts
- Infection
- Acne venenata
- Bilateral nevus comedonicus
- Tuberous sclerosis
- Demodicidosis
- Reaction to medication (corticosteroid, dactinomycin, lithium, phenytoin)

Table 1
Types and severity classifications of acne

<table>
<thead>
<tr>
<th>Types of Acne</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comedonal (noninflammatory)</td>
<td>Dilated hair follicles filled with keratin, sebum, and bacteria</td>
</tr>
<tr>
<td></td>
<td>Whitehead: closed comedone</td>
</tr>
<tr>
<td></td>
<td>Blackhead: open comedone with darkened mass of skin debris</td>
</tr>
<tr>
<td>Papulopustular (inflammatory)</td>
<td>Papule: pink/red inflammatory lesions 2–5 mm in diameter</td>
</tr>
<tr>
<td></td>
<td>Pustule: superficial papules with visible core of purulent material</td>
</tr>
<tr>
<td>Nodular (inflammatory) nodule</td>
<td>Solid, raised inflammatory lesions &gt;5 mm in diameter</td>
</tr>
</tbody>
</table>

Severity classifications:

- Mild
  - <20 comedones or <15 inflammatory lesions or <30 lesions total
- Moderate
  - 20–100 comedones or 15–50 inflammatory lesions or 30–125 lesions total
- Severe
  - >5 nodules or >50 total inflammatory lesions or >125 lesions total

- **Pseudofolliculitis barbae**
- In prepubertal children, consider
  - Cushing syndrome
  - Congenital adrenal hyperplasia
  - Premature adrenarche
  - Polycystic ovarian syndrome
  - Gonadal, adrenal, or ovarian tumor
  - Precocious puberty

Routine endocrinologic testing for androgen excess is not typically indicated but may have use for children who have signs of androgen excess (eg, body odor, axillary/pubic hair, infrequent menses, hirsutism).¹⁴

Acne lesions may vary widely and range from noninflammatory open or closed comedones to inflammatory lesions, which may include papules, pustules, or nodules. They are likely to occur on the face, neck, chest, and back, where sebaceous glands are more concentrated. Nodular acne is characterized by a predominance of large inflammatory nodules or pseudocysts and is often accompanied by scarring or the presence of sinus tracts when adjacent nodules coalesce.⁴

**TREATMENT**

There is no universal classification system for acne vulgaris because of the wide variety of presentations of the disease. Reduction in existing microcomedones and prevention of the formation of new ones is central to the management of all acne lesions.⁴ Treatment that targets both immune system activation and inflammatory pathways is, therefore, desirable.

**MANAGEMENT OF ACNE**

There are multiple modalities for the management of acne. Treatments are focused on several factors including
1. Normalization of keratin cells and sebum production to prevent pore blockage
2. Microbicidal activity
3. Hormonal therapy

**Table 2** summarizes the treatment of acne by type.

Before any pharmacologic intervention, the patient should be counseled regarding overscrubbing of the skin, as this behavior may dry and irritate the skin, thereby worsening acne. The patient should also be counseled against squeezing or picking comedones, as this promotes scar formation. Patients with acne should also be screened for depression as they are often disturbed by their body image.¹⁷

**TOPICAL RETINOIDS**

Topical retinoids are vitamin A analogs that normalize keratinization, which then leads to a reduction of follicular occlusion.¹³ In addition to treating active acne, retinoids may improve resolution of acne-related skin hyperpigmentation.¹⁵ They are used for the treatment of both noninflammatory and inflammatory acne and should be used as first-line treatments. They are considered the mainstay for maintenance therapy.

Patients should be counseled on evening applications, as retinoids are associated with sun sensitivity. Patients should also be counseled that they should apply small amounts of the medication and gradually increase until reaching the amount prescribed, as these cause irritation, dry skin, erythema, and flaking.
TOPICAL ANTIMICROBIALS

Topical antimicrobials decrease proinflammatory bacteria such as *P. acnes*. The most commonly used topical antimicrobial is benzyl peroxide. Other examples include erythromycin, clindamycin, sulfacetamide, and dapsone. Azelaic acid is a topical antimicrobial that naturally has mild anti-inflammatory properties that may help with acne-induced postinflammatory hyperpigmentation. Topical antimicrobials are generally prescribed in conjunction with topical retinoids. Similar to retinoids, topical antimicrobials may cause skin irritation or dry skin.

ORAL ANTIBIOTICS

The use of oral antibiotics should be limited to inflammatory acne and acne that involves the chest or back. Oral antibiotics are not indicated for long-term use. They are indicated in those with acne involving the chest or the back. Similar to retinoids, oral antibiotics may cause skin irritation or dry skin.

### Table 2
Methods of acne treatment by type

<table>
<thead>
<tr>
<th>Type</th>
<th>Mild Acne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comedonal</td>
<td>Mild Papular/Pustular</td>
</tr>
<tr>
<td>First line: topical retinoid</td>
<td>First line: topical retinoid and topical antimicrobial</td>
</tr>
<tr>
<td>Alternatives: topical retinoid or azelaic acid or salicylic acid</td>
<td>Alternatives: topical retinoid or azelaic acid or salicylic acid</td>
</tr>
<tr>
<td>Alternatives: none</td>
<td>Alternatives: none</td>
</tr>
<tr>
<td>Maintenance: topical retinoid</td>
<td>Maintenance: topical retinoid</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Moderate Acne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate Papular/Pustular</td>
<td>Nodular</td>
</tr>
<tr>
<td>First line: oral antibiotics and topical retinoid; may also consider the addition of benzoyl peroxide</td>
<td>First line: oral isotretinoin and topical retinoid; may also consider the addition of benzoyl peroxide and azelaic acid</td>
</tr>
<tr>
<td>Alternatives: topical retinoid or azelaic acid or salicylic acid</td>
<td>Oral isotretinoin or alternative oral antibiotic with a topical retinoid and benzoyl peroxide or azelaic acid</td>
</tr>
<tr>
<td>Alternatives for women: oral antiandrogen and a topical retinoid or azelaic acid, with or without an antimicrobial</td>
<td>Alternatives: oral antiandrogen with a topical retinoid with or without an oral antibiotic and with or without an alternative antimicrobial</td>
</tr>
<tr>
<td>Maintenance: topical retinoid</td>
<td>Maintenance: topical retinoid with or without benzoyl peroxide</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Severe Acne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular/Conglobate</td>
<td></td>
</tr>
<tr>
<td>First line: oral isotretinoin</td>
<td></td>
</tr>
<tr>
<td>Alternatives: high-dose oral antibiotic with a topical retinoid and benzoyl peroxide</td>
<td>Alternatives for women: high-dose oral antiandrogen with a topical retinoid, with or without a topical antimicrobial</td>
</tr>
<tr>
<td>Maintenance: topical retinoid with or without a benzoyl peroxide</td>
<td>Maintenance: topical retinoid with or without benzoyl peroxide</td>
</tr>
</tbody>
</table>

Data from Refs.9,13–16
resistance and only when absolutely necessary. Examples of commonly used antibiotics include macrolides, such as erythromycin, or tetracyclines, such as minocycline. Minocycline is most commonly prescribed as it induces more rapid improvement in inflammatory acne than tetracycline.\textsuperscript{16} Many oral antibiotics are also associated with photosensitivity.\textsuperscript{16}

**HORMONAL THERAPY AND ORAL CONTRACEPTIVES**

Patients who benefit from hormonal therapy are divided into 2 categories: (1) women with acne related to menses and (2) women with hyperandrogenism. The former may be treated with combined oral contraceptives that are approved by the US Food and Drug Administration for use in acne.\textsuperscript{18} Progestin-only pills may worsen acne. Women with hyperandrogenism may benefit from androgen-reducing medications and/or androgen receptor blockers. However, extreme caution should be used with these medications because of possible feminizing effects on a developing fetus.\textsuperscript{18}

**ORAL RETINOIDS**

Oral retinoids work by normalizing keratinization of cells, similar to topical retinoids. They have also been shown to induce apoptosis of sebaceous gland cells.\textsuperscript{19} Oral retinoids are effective for the treatment of severe, nodular acne. They may be used as monotherapy, under careful supervision. Only authorized physicians can prescribe oral retinoids. Women must be on active birth control when given oral retinoids, because of teratogenicity.\textsuperscript{9,13,18} Oral retinoids have also been linked to ulcerative colitis, depression, and suicidal ideation.\textsuperscript{19} These symptoms can also be associated with pseudotumor cerebri and hypervitaminosis A.\textsuperscript{19}

**TREATMENT OF ACNE MECHANICA (SPORTS-INDUCED ACNE)**

Acne mechanica is acne that is associated with athletes and is triggered by heat, friction, or pressure. It can occur anywhere on the body. It can appear as papules or pustules. Most cases respond well to topical benzyl peroxide and salicylic acid, along with improved hygiene.\textsuperscript{20}

**SUMMARY**

Acne vulgaris is a common disorder of the pilosebaceous follicles that affects adolescents and can persist into adulthood. The psychological and economic impact is significant and may prove challenging to address in the clinical setting. The diagnosis of acne vulgaris can be made from the patient’s history and physical examination. It can be effectively treated in the primary care setting.

**REFERENCES**