This report reflects the best available data at the time the report was prepared, but caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations set forth in this report.

Guidelines of care for acne vulgaris management

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Disclaimer: Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient.

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INTRODUCTION/METHODOLOGY

A work group of recognized experts was convened to determine the audience for the guidelines, define the scope of the guidelines, and identify nine clinical questions to structure the primary issues in diagnosis and management. Work group members were asked to complete a disclosure of commercial support, and this information will be in the acne technical report available on www.aad.org.

An evidence-based model was used and some evidence was obtained by a vendor using a search of MEDLINE and EMBASE databases spanning the years 1970 through 2006. Only English-language publications were reviewed.

The available evidence was evaluated using a unified system called the Strength of Recommendation Taxonomy (SORT) developed by editors of the US family medicine and primary care journals (ie, *American Family Physician*, *Family Medicine*, *Journal of Family Practice*, and *BMJ-USA*). This strategy was supported by a decision of the Clinical Guidelines Task Force in 2005 with some minor modifications for a consistent approach to rating the strength of the evidence of scientific studies.[1] Evidence was graded using a three-point scale based on the quality of methodology as follows:

- I. Good quality patient-oriented evidence.
- II. Limited quality patient-oriented evidence.
- III. Other evidence including consensus guidelines, extrapolations from bench research, opinion, or case studies.

Clinical recommendations were developed on the best available evidence tabled in the guidelines and explained further in the technical report. These are ranked as follows:

A. Recommendation based on consistent and good-quality patient-oriented evidence.
B. Recommendation based on inconsistent or limited quality patient-oriented evidence.
C. Recommendation based on consensus, opinion, or case studies.

These guidelines have been developed in accordance with the American Academy of Dermatology/American Academy of Dermatology Association "Administrative Regulations for Evidence-Based Clinical Practice Guidelines," which include the opportunity for review and comment by the entire AAD membership and final review and approval by the AAD Board of Directors.

Scope

These guidelines address the management of adolescent and adult patients presenting with acne but not the consequences of disease, including the scarring, post-inflammatory erythema, or post-inflammatory hyperpigmentation. The topic of light and laser therapy will be the subject of another guideline.

Definitions

Acne vulgaris is a chronic inflammatory dermatosis which is notable for open and/or closed comedones (blackheads and whiteheads) and inflammatory lesions including papules, pustules, or nodules.

Issues

The task force identified the following clinical issues relevant to the management of acne: grading and classification; the role of microbiologic and endocrine testing; and the efficacy and safety of various treatments, such as topical agents, systemic antibacterial agents, hormonal agents, isotretinoin, miscellaneous therapies, complementary/alternative therapies, and dietary restriction.

I. SYSTEMS FOR THE GRADING AND CLASSIFICATION OF ACNE

Table I shows the recommendations for a grading and classification system.

Recommendation

- Clinicians may find it helpful to use a consistent classification/grading scale (encompassing the numbers and types of acne lesions as well as disease severity) to facilitate therapeutic decisions and assess response to treatment.

DISCUSSION

The rating of disease severity is useful for the initial evaluation and management of acne, to aid in the selection of appropriate therapeutic agents, and to evaluate response to treatment.[2,3]

Several systems for grading acne exist; most employ lesion counting combined with some type of global assessment of severity (eg, mild, moderate, severe) that represents a synthesis of the number, size, and extent of lesions. However, there is no consensus on a single or best grading or classification system.[2-15]

II. MICROBIOLOGIC AND ENDOCRINOLOGIC TESTING

Microbiologic testing

Table II shows the recommendations for microbiologic testing.

Recommendations

- Routine microbiologic testing is unnecessary in the evaluation and management of patients with acne.

Table I. Recommendations for a grading and classification system

Recommendation	Strength of recommendation	Level of evidence	References
Grading/ classification system	B	II	2-5, 7, 11

Table II. Recommendations for microbiologic testing

Recommendation	Strength of recommendation	Level of evidence	References
Microbiologic testing	B	II	16-19

- Those who exhibit acne-like lesions suggestive of gram-negative folliculitis may benefit from microbiologic testing.

DISCUSSION

The prevalent bacterium implicated in the clinical course of acne is *Propionibacterium acnes (P acnes)*, a gram-positive anaerobe that normally inhabits the skin and is implicated in the inflammatory phase of acne.

Gram-negative folliculitis is typically characterized by pustules and/or nodules most commonly located in the perioral and nasal areas. Gram-negative folliculitis is caused by a variety of bacteria and is unresponsive to conventional antibiotic therapy for acne. Bacterial cultures, including antibacterial sensitivities, are usually of value in establishing the diagnosis and in determining therapy.[16-19]

Endocrinologic testing

Table III shows the recommendations for endocrinologic testing.

Recommendation

- Routine endocrinologic evaluation (eg, for androgen excess) is not indicated for the majority of patients with acne. Laboratory evaluation is indicated for patients who have acne and additional signs of androgen excess. In young children this may be manifested by body odor, axillary or pubic hair, and clitoromegaly. Adult women with symptoms of hyperandrogenism may present with recalcitrant or late-onset acne, infrequent menses, hirsutism, male or female pattern alopecia, infertility, acanthosis nigricans, and truncal obesity.

DISCUSSION

Although androgens play an important role in the pathogenesis of acne, most patients have normal hormone levels. Presently, there is little evidence from peer-reviewed literature indicating that routine endocrinologic testing has clinical value in the evaluation of patients with acne. Patients whose history or physical examination suggests hyperandrogenism may, however, benefit from such testing. In prepubertal children, the signs include acne, early-onset body odor, axillary or pubic hair, accelerated growth, advanced bone age, and genital maturation. After puberty, common virilizing signs and symptoms are infrequent menses, hirsutism, male or female pattern alopecia, infertility, polycystic ovaries, clitoromegaly, acanthosis nigricans, and truncal obesity.[20-24] In prepubertal children, a hand film for bone age is a practical screen prior to specific hormonal testing. Increased awareness of clinical signs of androgen excess will help identify those patients who may benefit from further evaluation and treatment by an endocrinologist or gynecologic endocrinologist. It is the opinion of the experts that the following laboratory tests may be helpful: free testosterone, dehydroepiandrosterone sulfate, leutinizing hormone, and follicule-stimulating hormone.

Table III. Recommedations for endocrinologic testing

Recommendation	Strength of recommendation	Level of evidence	References
Endocrinologic testing	A	I	20, 22

Table IV. Recommendations for topical therapy

Recommendation	Strength of recommendation	Level of evidence	References
Retinoids	A	I	25, 28, 38, 41
Benzoyl peroxide	A	I	42, 48, 50, 51
Antibiotics	A	I	52-58, 62, 65
Other agents	A	I	70, 72, 73, 75, 79

III. TOPICAL THERAPY

Recommendations for topical therapy are shown in Table IV.

Recommendations

- Topical therapy is a standard of care in acne treatment.
- Topical retinoids are important in acne treatment.
- Benzoyl peroxide and combinations with erythromycin or clindamycin are effective acne treatments.
- Topical antibiotics (eg, erythromycin and clindamycin) are effective acne treatments. However, the use of these agents alone can be associated with the development of bacterial resistance.

- Salicylic acid is moderately effective in the treatment of acne.
- Azelaic acid has been shown to be effective in clinical trials, but its clinical use, compared to other agents, has limited efficacy according to experts.
- Data from peer-reviewed literature regarding the efficacy of sulfur, resorcinol, sodium sulfacetamide, aluminum chloride, and zinc are limited.
- Employing multiple topical agents that affect different aspects of acne pathogenesis can be useful. However, it is the opinion of the work group that such agents not be applied simultaneously unless they are known to be compatible.

DISCUSSION

Topical retinoids

The effectiveness of topical retinoids in the treatment of acne is well documented.[25-41] These agents act to reduce obstruction within the follicle and therefore are useful in the management of both comedonal and inflammatory acne. There is no consensus about the relative efficacy of currently available topical retinoids (tretinoin, adapalene, tazarotene, and isotretinoin). The concentration and/or vehicle of any particular retinoid may impact tolerability.[33,35] Topical isotretinoin is not currently available in the United States.

Benzoyl peroxide

Benzoyl peroxide is a bactericidal agent that has proven effective in the treatment of acne. It is available in a variety of concentrations and vehicles; however, there is insufficient evidence to evaluate and compare the efficacy of these different formulations. It has the ability to prevent or eliminate the development of *P acnes* resistance.[42-51] Because of concerns of resistance, it is often used in the management of patients treated with oral or topical antibiotics.

Topical antibiotics

The value of topical antibiotics in the treatment of acne has been investigated in many clinical trials. Both erythromycin[52-58] and clindamycin[59-66] have been demonstrated to be effective and are well tolerated. Decreased sensitivity of *P acnes* to these antibiotics can limit the use of either drug as a single therapeutic agent.[58,61]

Combinations: Retinoids, benzoyl peroxide, and topical antibiotics

A combination of topical retinoids and topical erythromycin or clindamycin is more effective than either agent used alone.[67-71] Combining erythromycin or clindamycin with benzoyl peroxide eliminates or reduces bacterial resistance and enhances efficacy. The combinations are more effective than either of the individual components alone.[72-75]

Salicylic acid

Salicylic acid has been used for many years for the treatment of acne, although few well-designed trials of its safety and efficacy exist. Its comedolytic properties are considered less potent than topical retinoids. It often is used when patients cannot tolerate a topical retinoid because of skin irritation.[76]

Other topical agents

Azelaic acid has been reported to possess comedolytic and antibacterial properties. Data from clinical trials indicate that it is effective.[77-79] Although sulfur and resorcinol have been used for many years in the treatment of acne, evidence from peer-reviewed literature supporting their efficacy is lacking.[80] Aluminum chloride possesses antibacterial activity and, therefore, has been investigated in the treatment acne. Of two studies in the peer-reviewed literature, one found benefit[81] and one did not.[82] Topical zinc alone is ineffective.[83-85] There is some evidence to suggest efficacy for sodium sulfacetamide.[86-88]

IV. SYSTEMIC ANTIBIOTICS

The recommendations of systemic antibiotics are shown in Table V.

Recommendations

- Systemic antibiotics are a standard of care in the management of moderate and severe acne and treatment-resistant forms of inflammatory acne.
- Doxycycline and minocycline are more effective than tetracycline, and there is evidence that minocycline is superior to doxycycline in reducing *P acnes*.
- Although erythromycin is effective, use should be limited to those who cannot use the tetracyclines (ie, pregnant women or children under 8 years of age because of the potential for damage to the skeleton or teeth). The development of bacterial resistance is also common during erythromycin therapy.
- Trimethoprim-sulfamethoxazole and trimethoprim alone are also effective in instances where other antibiotics cannot be used.
- Bacterial resistance to antibiotics is an increasing problem.
- The incidence of significant adverse effects with antibiotic use is low. However, adverse effect profiles may be helpful for each systemic antibiotic used in the treatment of acne.

Table V. Recommendations for systemic antibiotics

Recommendation	Strength of recommendation	Level of evidence	References
Tetracyclines	A	I	90, 91, 95, 121
Macrolides	A	I	102, 108, 111, 115
Trimethoprim-sulfamethoxazole	A	I	117

Table VI. Recommendations for hormonal agents

Recommendation	Strength of recommendation	Level of evidence	References
Contraceptive agents	A	I	122-125
Spironolactone	B	II	132
Antiandrogens	B	II	134, 135
Oral corticosteroids	B	II	137

DISCUSSION

Antibiotics have been widely used for many years in the management of acne. There is evidence to support the use of tetracycline, doxycycline, minocycline, erythromycin, trimethoprim-sulfamethoxazole, trimethoprim, and azithromycin.[89-120] Studies do not exist for the use of ampicillin, amoxicillin, or cephalexin. However, any antibiotic which can reduce the *P acnes* population in vivo and interfere with the organism's ability to generate inflammatory agents should be effective. It is the opinion of the expert panel that while published data are conflicting, minocycline and doxycycline are more effective than tetracycline.[101,105]

A major problem affecting antibiotic therapy of acne has been bacterial resistance, which has been increasing.[18,121] For this reason, it is the opinion of the work group that patients with less severe forms of acne should not be treated with oral antibiotics, and where possible the duration of such therapy should be limited. Resistance has been seen with all antibiotics, but is most common with erythromycin.

The use of oral antibiotics for the treatment of acne may be associated with adverse effects. Vaginal candidiasis may complicate the use of all oral antibiotics.[102,103,107,108] Doxycycline can be associated with photosensitivity. Minocycline has been associated with pigment deposition in the skin, mucous membranes and teeth particularly among patients receiving long-term therapy and/or higher doses of the medication. Pigmentation occurs most often in acne scars, anterior shins, and mucous membranes. Autoimmune hepatitis, a systemic lupus erythematosus-like syndrome, and serum sickness-like reactions occur rarely with minocycline.[102,107]

V. HORMONAL AGENTS

Hormonal agent recommendations are shown in Table VI.

Recommendations

- Estrogen-containing oral contraceptives can be useful in the treatment of acne in some women.
- Oral antiandrogens, such as spironolactone and cyproterone acetate, can be useful in the treatment of acne. While flutamide can be effective, hepatic toxicity limits its use. There is no evidence to support the use of finasteride.
- There are limited data to support the effectiveness of oral corticosteroids in the treatment of acne. There is a consensus of expert opinion that oral corticosteroid therapy is of temporary benefit in patients who have severe inflammatory acne.
- In patients who have well-documented adrenal hyperandrogenism, low-dose oral corticosteroids may be useful in treatment of acne.

DISCUSSION

Oral contraceptives

There are clinical trials of estrogen-containing contraceptive agents for the treatment of acne.[122-125] Those currently approved by the US Food and Drug Administration (FDA) for the management of acne contain norgestimate with ethinyl estradiol (Ortho Tri-cyclen; Ortho-MacNeil Pharmaceutical, Inc, Raritan, NJ) and norethindrone acetate with ethinyl estradiol (Estrostep; Warner Chilcott, Rockaway, NJ).[122-128] There is good evidence and consensus opinion that other estrogen-containing oral contraceptives are also equally effective.[129,130] The effect on acne of other estrogen-containing contraceptives (eg, transdermal patches, vaginal rings) has not been studied.

Spironolactone

Spironolactone is an anti-androgen that exerts its effects by blocking androgen receptors at higher doses.[131] Dosages of 50 mg to 200 mg have been shown to be effective in acne. Spironolactone may cause hyperkalemia, particularly when higher doses are prescribed or when there is cardiac or renal compromise. It occasionally causes menstrual irregularity.[132,133]

Cyproterone acetate

Cyproterone combined with ethinyl estradiol (in the form of an oral contraceptive) has been found to

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