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

Table VII. Isotretinoin recommendations

Recommendation	Strength of recommendation	Level of evidence	References
Isotretinoin	A	I	141, 148, 150-153, 155, 159, 161

be effective in the treatment of acne in females.[134-136] Higher doses have been found to be more effective than lower doses. Cyproterone/estrogen-containing oral contraceptives are not approved for use in the United States.

Flutamide

Flutamide, a non-steroidal antiandrogen approved for the management of prostatic hypertrophy or cancer and hirsutism, has had some success in the management of acne, but its use is limited because of the potential of hepatic failure.

Other antiandrogens

Finasteride and other compounds with possible antiandrogenic effects (eg, cimetidine and ketoconazole) have not been reported to be effective in acne.

Oral corticosteroids

Oral corticosteroids may have two modes of activity in the treatment of acne. One study demonstrated that low dose corticosteroids suppress adrenal activity in patients who have proven adrenal hyperactivity.[137] Expert opinion is that short-courses of higher dose oral corticosteroids may be beneficial in patients with highly inflammatory disease.

VI. ISOTRETINOIN

Isotretinoin recommendations are shown in Table VII.

Recommendations

- Oral isotretinoin is approved for the treatment of severe recalcitrant nodular acne.
- It is the unanimous opinion of the acne workgroup that oral isotretinoin is also useful for the management of lesser degrees of acne that are treatment-resistant or for the management of acne that is producing either physical or psychological scarring.
- Oral isotretinoin is a potent teratogen. Because of its teratogenicity and the potential for many other adverse effects, this drug should be prescribed only by those physicians knowledgeable in its appropriate administration and monitoring.
- Female patients of child-bearing potential must only be treated with oral isotretinoin if they are participating in the approved pregnancy prevention and management program (iPLEDGE; see below).
- Mood disorders, depression, suicidal ideation, and suicides have been reported in patients taking this drug. However, a causal relationship has not been established.

DISCUSSION

Indications

The approved indication for the use of oral isotretinoin has remained severe nodular treatment-resistant acne since the drug was introduced more than 20 years ago. However, it is the opinion of the expert work group that this drug is also indicated for all cases of acne that are either treatment-resistant or producing physical or psychological scarring.

Dosage

The approved dosage is 0.5 to 2.0 mg/kg/day. The drug is usually given over a 20-week course.[138-158] Drug absorption is greater when the drug is taken with food. The acne expert work group feels strongly that initial flaring can be minimized with a beginning dose of 0.5 mg/kg/day or less. Alternatively, lower doses can be used for longer time periods, with a total cumulative dose of 120 to 150 mg/kg.[138] In patients who have severely inflamed acne, even greater initial reduction of dose may be required. In the most severe cases of acne, consideration of pre-treatment with oral corticosteroids may also be appropriate.

Adverse effects

Isotretinoin, a vitamin A derivative, interacts with many of the biologic systems of the body, and consequently has a significant pattern of adverse effects. The pattern is similar to that seen in hypervitaminosis A. Side effects include those of the mucocutaneous, musculoskeletal, and ophthalmic systems, as well as headaches and central nervous system effects. Most of the adverse effects are temporary and resolve after the drug is discontinued.[139,141,143-145,149,152-158]

While hyperostosis, premature epiphyseal closure, and bone demineralization have been observed with prolonged use of higher dose retinoids, in the usual course of acne treatment these findings have not been identified. Therefore it is the unanimous opinion of the acne work group that routine screening for these issues is not required. Laboratory monitoring during therapy should include triglycerides, cholesterol, transaminase, and complete blood counts.[153,155,157,159]

Changes in mood, suicidal ideation, and suicide have been reported sporadically in patients taking

Table VIII. Recommendations for miscellaneous therapies

Recommendation	Strength of recommendation	Level of evidence	References
Intralesional steroids	C	III	168, 169
Chemical peels	C	III	170-172
Comedo removal	C	III	173

isotretinoin. While these events have been seen, a causal relationship has not been established. Nonetheless, there are instances in which withdrawal of isotretinoin has resulted in improved mood and reintroduction of isotretinoin has resulted in the return of mood changes. The symptoms mentioned are quite common in adolescents and young adults, the age range of patients who are likely to receive isotretinoin. Treatment of severe acne with isotretinoin is often associated with mood improvement. There is epidemiologic evidence that the incidence of these events is less in isotretinoin-treated patients than in an age-matched general population. There is also evidence that the risk of depressed mood is no greater during isotretinoin therapy than during therapy of an age-matched acne group treated with conservative therapy. Nonetheless, patients must be made aware of this possibility and treating physicians should monitor patients for psychiatric adverse effects.[159-165]

Some patients experience a relapse of acne after the first course of treatment with isotretinoin. The panel feels relapses are more common in younger adults or when lower doses are used.[147-149,151,166,167]

iPLEDGE

Because of the teratogenic effects of isotretinoin on the fetus, the FDA and the manufacturers have approved a new risk management program for isotretinoin.[154,155] Prescribers, patients, pharmacies, drug wholesalers, and manufacturers in the United States are required to register and comply with the iPLEDGE program. This program requires mandatory registration of all patients receiving this drug. Detailed information can be found on the iPLEDGE web site (www.ipledgeprogram.com).

VII. MISCELLANEOUS THERAPY

Recommendations for miscellaneous therapies are shown in Table VIII.

Recommendations

- Intralesional corticosteroid injections are effective in the treatment of individual acne nodules.
- There is limited evidence regarding the benefit of physical modalities including glycolic acid peels and salicylic acid peels.

Table IX. Recommendations for complementary therapies

Recommendation	Strength of recommendation	Level of evidence	References
Herbal agents	B	II	174-176
Psychological approaches	C	III	177
Hypnosis/biofeedback	B	II	178

Table X. Recommended dietary restrictions

Recommendation	Strength of recommendation	Level of evidence	References
Effect of diet	B	II	179, 180

DISCUSSION

Intralesional steroids

In the opinion of experts, the effect of intralesional injection with corticosteroids is a well established and recognized treatment for large inflammatory lesions. It has been found that patients receiving intralesional steroids for the treatment of cystic acne improved.[168] Systemic absorption of steroids may occur. Adrenal suppression was observed in one study.[169] The injection of intralesional steroids may be associated with local atrophy. Lowering the concentration and/or volume of steroid utilized may minimize these complications.

Chemical peels

Both glycolic acid-based and salicylic acid-based peeling preparations have been used in the treatment of acne. There is very little evidence from clinical trials published in the peer-reviewed literature supporting the efficacy of peeling regimens.[170-172] Further research on the use of peeling in the treatment of acne needs to be conducted in order to establish best practices for this modality.

Comedo removal

There is limited evidence published in peer-reviewed medical literature that addresses the efficacy of comedo removal for the treatment of acne, despite its long-standing clinical use.[173] It is, however, the opinion of the work group that comedo removal may be helpful in the management of comedones resistant to other therapies. Also, while it cannot affect the clinical course of the disease, it can improve the patient's appearance, which may positively impact compliance with the treatment program.

VIII. COMPLEMENTARY THERAPY

Complementary therapy recommendations are shown in Table IX.

Recommendation

- Herbal and alternative therapies have been used to treat acne. Although these products appear to be well tolerated, very limited data exist regarding the safety and efficacy of these agents.

DISCUSSION

A single clinical trial has demonstrated that topical tea tree oil is effective for the treatment of acne, although the onset of action is slower compared to other topical treatments.[174] Other herbal agents, such as topical and oral ayurvedic compounds, have been reported to have value in the treatment of acne.[175,176]

Psychological approaches/hypnosis/biofeedback

The psychological effects of acne may be profound, and it is the unanimous opinion of the expert workgroup that effective acne treatment can improve the emotional outlook of patients. There is weak evidence of the possible benefit of biofeedback-assisted relaxation and cognitive imagery.[177,178]

IX. DIETARY RESTRICTION

Recommended dietary restrictions are shown in Table X.

Recommendation

- Dietary restriction (either specific foods or food classes) has not been demonstrated to be of benefit in the treatment of acne.

DISCUSSION

There are few clinical studies available in the peer-reviewed literature that directly evaluate the effectiveness of dietary restriction or the consumption of specific foods or food groups to improve acne. Studies addressing the potential for particular foods to exacerbate acne have been conducted.[179,180] These studies fail to support a link between the consumption of chocolate or sugar and acne. Thus, no evidence exists on the role of diet in acne.

REFERENCES

1. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman JL, Ewigman B, et al. Simplifying the language of evidence to improve patient care: Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in medical literature. J Fam Pract 2004;53:111-20.
2. Lehmann HP, Robinson KA, Andrews JS, Holloway V, Goodman SN. Acne therapy: a methodologic review. J Am Acad Dermatol 2002;47:231-40.
3. Pochi PE, Shalita AR, Strauss JS, Webster SB, Cunliffe WJ, Katz HI, et al. Report of the Consensus Conference on Acne Classification. Washington, D.C., March 24 and 25, 1990. J Am Acad Dermatol 1991;24:495-500.
4. Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. Int J Dermatol 1997;36:416-8.
5. Allen BS, Smith JG Jr. Various parameters for grading acne vulgaris. Arch Dermatol 1982;118:23-5.
6. Lucky AW, Barber BL, Girman CJ, Williams J, Ratterman J, Waldstreicher J. A multirater validation study to assess the reliability of acne lesion counting. J Am Acad Dermatol 1996;35:559-65.
7. Cook CH, Centner RL, Michaels SE. An acne grading method using photographic standards. Arch Dermatol 1979;115:571-5.
8. Gibson JR, Harvey SG, Barth J, Darley CR, Reshad H, Burke CA. Assessing inflammatory acne vulgaris—correlation between clinical and photographic methods. Br J Dermatol 1984; 111(suppl 27):168-70.
9. Burke BM, Cunliffe WJ. The assessment of acne vulgaris—the Leeds technique. Br J Dermatol 1984;111:83-92.
10. Motley RJ, Finlay AY. Practical use of a disability index in the routine management of acne. Clin Exp Dermatol 1992;17: 1-3.
11. Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. Br J Dermatol 1995;132:942-9.
12. Martin AR, Lookingbill DP, Botek A, Light J, Thiboutot D, Girman CJ. Health-related quality of life among patients with facial acne—assessment of a new acne-specific questionnaire. Clin Exp Dermatol 2001;26:380-5.
13. Lasek RJ, Chren MM. Acne vulgaris and the quality of life of adult dermatology patients. Arch Dermatol 1998;134:454-8.
14. Mallon E, Newton JN, Klassen A, Stewart-Brown SL, Ryan TJ, Finlay AY. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. Br J Dermatol 1999;140:672-6.
15. Gupta MA, Johnson AM, Gupta AK. The development of an Acne Quality of Life scale: reliability, validity, and relation to subjective acne severity in mild to moderate acne vulgaris. Acta Derm Venereol 1998;78:451-6.
16. Cove JH, Cunliffe WJ, Holland KT. Acne vulgaris: is the bacterial population size significant? Br J Dermatol 1980; 102:277-80.
17. Bojar RA, Hittel N, Cunliffe WJ, Holland KT. Direct analysis of resistance in the cutaneous microflora during treatment of acne vulgaris with topical 1% nadifloxacin and 2% erythromycin. Drugs 1995;49(suppl 2):164-7.
18. Eady EA, Cove JH, Holland KT, Cunliffe WJ. Erythromycin resistant propionibacteria in antibiotic treated acne patients: association with therapeutic failure. Br J Dermatol 1989;121: 51-7.
19. Harkaway KS, McGinley KJ, Foglia AN, Lee WL, Fried F, Shalita AR, et al. Antibiotic resistance patterns in coagulase-negative staphylococci after treatment with topical erythromycin, benzoyl peroxide, and combination therapy. Br J Dermatol 1992;126:586-90.
20. Lawrence DM, Katz M, Robinson TW, Newman MC, McGarrigle HH, Shaw M, et al. Reduced sex hormone binding globulin and derived free testosterone levels in women with severe acne. Clin Endocrinol (Oxf) 1981;15:87-91.
21. Bunker CB, Newton JA, Kilborn J, Patel A, Conway GS, Jacobs HS, et al. Most women with acne have polycystic ovaries. Br J Dermatol 1989;121:675-80.
22. Lucky AW, Biro FM, Simbartl LA, Morrison JA, Sorg NW. Predictors of severity of acne vulgaris in young adolescent girls: results of a five-year longitudinal study. J Pediatr 1997; 130:30-9.

23. Timpatanapong P, Rojanasakul A. Hormonal profiles and prevalence of polycystic ovary syndrome in women with acne. J Dermatol 1997;24:223-9.
24. Lucky AW. Endocrine aspects of acne. Pediatr Clin North Am 1983;30:495-9.
25. Christiansen JV, Gadborg E, Ludvigsen K, Meier CH, Norholm A, Pedersen D, et al. Topical tretinoin, vitamin A acid (Airol) in acne vulgaris. A controlled clinical trial. Dermatologica 1974; 148:82-9.
26. Bradford LG, Montes LF. Topical application of vitamin A acid in acne vulgaris. South Med J 1974;67:683-7.
27. Krishnan G. Comparison of two concentrations of tretinoin solution in the topical treatment of acne vulgaris. Practitioner 1976;216:106-9.
28. Chalker DK, Lesher JL Jr, Smith JG Jr, Klauda HC, Pochi PE, Jacoby WS, et al. Efficacy of topical isotretinoin 0.05% gel in acne vulgaris: results of a multicenter, double-blind investigation. J Am Acad Dermatol 1987;17:251-4.
29. Shalita A, Weiss JS, Chalker DK, Ellis CN, Greenspan A, Katz HI, et al. A comparison of the efficacy and safety of adapalene gel 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris: a multicenter trial. J Am Acad Dermatol 1996;34: 482-5.
30. Clucas A, Verschoore M, Sorba V, Poncet M, Baker M, Czernielewski J. Adapalene 0.1% gel is better tolerated than tretinoin 0.025% gel in acne patients. J Am Acad Dermatol 1997;36:S116-8.
31. Cunliffe WJ, Caputo R, Dreno B, Forstrom L, Heenen M, Orfanos CE, et al. Clinical efficacy and safety comparison of adapalene gel and tretinoin gel in the treatment of acne vulgaris: Europe and U.S. multicenter trials. J Am Acad Dermatol 1997;36:S126-34.
32. Dunlap FE, Mills OH, Tuley MR, Baker MD, Plott RT. Adapalene 0.1% gel for the treatment of acne vulgaris: its superiority compared to tretinoin 0.025% cream in skin tolerance and patient preference. Br J Dermatol 1998;139(suppl 52):17-22.
33. Galvin SA, Gilbert R, Baker M, Guibal F, Tuley MR. Comparative tolerance of adapalene 0.1% gel and six different tretinoin formulations. Br J Dermatol 1998;139(suppl 52):34-40.
34. Grosshans E, Marks R, Mascaro JM, Torras H, Meynadier J, Alirezai M, et al. Evaluation of clinical efficacy and safety of adapalene 0.1% gel versus tretinoin 0.025% gel in the treatment of acne vulgaris, with particular reference to the onset of action and impact on quality of life. Br J Dermatol 1998;139(suppl 52):26-33.
35. Mills OH Jr, Berger RS. Irritation potential of a new topical tretinoin formulation and a commercially-available tretinoin formulation as measured by patch testing in human subjects. J Am Acad Dermatol 1998;38:S11-6.
36. Ioannides D, Rigopoulos D, Katsambas A. Topical adapalene gel 0.1% vs. isotretinoin gel 0.05% in the treatment of acne vulgaris: a randomized open-label clinical trial. Br J Dermatol 2002;147:523-7.
37. Kakita L. Tazarotene versus tretinoin or adapalene in the treatment of acne vulgaris. J Am Acad Dermatol 2000;43:S51-4.
38. Shalita AR, Chalker DK, Griffith RF, Herbert AA, Hickman JG, Maloney JM, et al. Tazarotene gel is safe and effective in the treatment of acne vulgaris: a multicenter, double-blind, vehicle-controlled study. Cutis 1999;63:349-54.
39. Ellis CN, Millikan LE, Smith EB, Chalker DM, Swinyer LJ, Katz IH, et al. Comparison of adapalene 0.1% solution and tretinoin 0.025% gel in the topical treatment of acne vulgaris. Br J Dermatol 1998;139(suppl 52):41-7.
40. Webster GF, Berson D, Stein LF, Fivenson DP, Tanghetti EA, Ling M. Efficacy and tolerability of once-daily tazarotene 0.1% gel versus once-daily tretinoin 0.025% gel in the treatment of facial acne vulgaris: a randomized trial. Cutis 2001; 67(Suppl 6):4-9.
41. Lucky AW, Cullen SI, Jarratt MT, Quigley JW. Comparative efficacy and safety of two 0.025% tretinoin gels: results from a multicenter double-blind, parallel study. J Am Acad Dermatol 1998;38:S17-23.
42. Belknap BS. Treatment of acne with 5% benzoyl peroxide gel or 0.05% retinoic acid cream. Cutis 1979;23:856-9.
43. Bucknall JH, Murdoch PN. Comparison of tretinoin solution and benzoyl peroxide lotion in the treatment of acne vulgaris. Curr Med Res Opin 1977;5:266-8.
44. Montes LF. Acne vulgaris: treatment with topical benzoyl peroxide acetone gel. Cutis 1977;19:681-5.
45. Hughes BR, Norris JF, Cunliffe WJ. A double-blind evaluation of topical isotretinoin 0.05%, benzoyl peroxide gel 5% and placebo in patients with acne. Clin Exp Dermatol 1992;17: 165-8.
46. Cunliffe WJ, Dodman B, Ead R. Benzoyl peroxide in acne. Practitioner 1978;220:479-82.
47. Fyrand O, Jakobsen HB. Water-based versus alcohol-based benzoyl peroxide preparations in the treatment of acne vulgaris. Dermatologica 1986;172:263-7.
48. Schutte H, Cunliffe WJ, Forster RA. The short-term effects of benzoyl peroxide lotion on the resolution of inflamed acne lesions. Br J Dermatol 1982;106:91-4.
49. Yong CC. Benzoyl peroxide gel therapy in acne in Singapore. Int J Dermatol 1979;18:485-8.
50. Smith EB, Padilla RS, McCabe JM, Becker LE. Benzoyl peroxide lotion (20 percent) in acne. Cutis 1980;25:90-2.
51. Mills OH Jr, Kligman AM, Pochi P, Comite H. Comparing 2.5%, 5%, and 10% benzoyl peroxide on inflammatory acne vulgaris. Int J Dermatol 1986;25:664-7.
52. Bernstein JE, Shalita AR. Topically applied erythromycin in inflammatory acne vulgaris. J Am Acad Dermatol 1980;2: 318-21.
53. Jones EL, Crumley AF. Topical erythromycin vs blank vehicle in a multiclinic acne study. Arch Dermatol 1981;117:551-3.
54. Prince RA, Busch DA, Hepler CD, Feldick HG. Clinical trial of topical erythromycin in inflammatory acne. Drug Intell Clin Pharm 1981;15:372-6.
55. Lesher JL Jr, Chalker DK, Smith JG Jr, Guenther LC, Ellis CN, Voorhees JJ, et al. An evaluation of a 2% erythromycin ointment in the topical therapy of acne vulgaris. J Am Acad Dermatol 1985;12:526-31.
56. Pochi PE, Bagatell FK, Ellis CN, Stoughton RB, Whitmore CG, Saatjian GD, et al. Erythromycin 2 percent gel in the treatment of acne vulgaris. Cutis 1988;41:132-6.
57. Dobson RL, Belknap BS. Topical erythromycin solution in acne. Results of a multiclinic trial. J Am Acad Dermatol 1980;3:478-82.
58. Mills O Jr, Thornsberry C, Cardin CW, Smiles KA, Leyden JJ. Bacterial resistance and therapeutic outcome following three months of topical acne therapy with 2% erythromycin gel versus its vehicle. Acta Derm Venereol 2002; 82:260-5.
59. Padilla RS, McCabe JM, Becker LE. Topical tetracycline hydrochloride vs. topical clindamycin phosphate in the treatment of acne: a comparative study. Int J Dermatol 1981;20:445-8.
60. Thomas DR, Raimer S, Smith EB. Comparison of topical erythromycin 1.5 percent solution versus topical clindamycin phosphate 1.0 percent solution in the treatment of acne vulgaris. Cutis 1982;29:624-5, 628-32.
61. Shalita AR, Smith EB, Bauer E. Topical erythromycin vs clindamycin therapy for acne. A multicenter, double-blind comparison. Arch Dermatol 1984;120:351-5.

62. Leyden JJ, Shalita AR, Saatjian GD, Sefton J. Erythromycin 2% gel in comparison with clindamycin phosphate 1% solution in acne vulgaris. J Am Acad Dermatol 1987;16:822-7.
63. McKenzie MW, Beck DC, Popovich NG. Topical clindamycin formulations for the treatment of acne vulgaris. An evaluation. Arch Dermatol 1981;117:630-4.
64. Kuhlman DS, Callen JP. A comparison of clindamycin phosphate 1 percent topical lotion and placebo in the treatment of acne vulgaris. Cutis 1986;38:203-6.
65. Becker LE, Bergstresser PR, Whiting DA, Clendenning WE, Dobson RL, Jordan WP, et al. Topical clindamycin therapy for acne vulgaris. A cooperative clinical study. Arch Dermatol 1981;117:482-5.
66. Ellis CN, Gammon WR, Stone DZ, Heezen-Wehner JL. A comparison of Cleocin T Solution, Cleocin T Gel, and placebo in the treatment of acne vulgaris. Cutis 1988;42: 245-7.
67. Glass D, Boorman GC, Stables GI, Cunliffe WJ, Goode K. A placebo-controlled clinical trial to compare a gel containing a combination of isotretinoin (0.05%) and erythromycin (2%) with gels containing isotretinoin (0.05%) or erythromycin (2%) alone in the topical treatment of acne vulgaris. Dermatology 1999;199:242-7.
68. Mills OH Jr, Kligman AM. Treatment of acne vulgaris with topically applied erythromycin and tretinoin. Acta Derm Venereol 1978;58:555-7.
69. Richter JR, Bousema MT, De Boulle KLV, Degreef HJ, Poli F. Efficacy of a fixed clindamycin phosphate 1.2%, tretinoin 0.025% gel formulation (Velac) in the topical control of facial acne lesions. J Dermatolog Treat 1998;9:81-90.
70. Zouboulis CC, Derumeaux L, Decroix J, Maciejewska-Udziela B, Cambazard F, Stuhlert A. A multicentre, single-blind, randomized comparison of a fixed clindamycin phosphate/ tretinoin gel formulation (Velac) applied once daily and a clindamycin lotion formulation (Dalacin T) applied twice daily in the topical treatment of acne vulgaris. Br J Dermatol 2000; 143:498-505.
71. Rietschel RL, Duncan SH. Clindamycin phosphate used in combination with tretinoin in the treatment of acne. Int J Dermatol 1983;22:41-3.
72. Chalker DK, Shalita A, Smith JG Jr, Swann RW. A double-blind study of the effectiveness of a 3% erythromycin and 5% benzoyl peroxide combination in the treatment of acne vulgaris. J Am Acad Dermatol 1983;9:933-6.
73. Tschen EH, Katz HI, Jones TM, Monroe EW, Kraus SJ, Connolly MA, et al. A combination benzoyl peroxide and clindamycin topical gel compared with benzoyl peroxide, clindamycin phosphate, and vehicle in the treatment of acne vulgaris. Cutis 2001;67:165-9.
74. Leyden JJ, Hickman JG, Jarratt MT, Stewart DM, Levy SF. The efficacy and safety of a combination benzoyl peroxide/ clindamycin topical gel compared with benzoyl peroxide alone and a benzoyl peroxide/erythromycin combination product. J Cutan Med Surg 2001;5:37-42.
75. Lookingbill DP, Chalker DK, Lindholm JS, Katz HI, Kempers SE, Huerter CJ, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. J Am Acad Dermatol 1997;37:590-5.
76. Shalita AR. Treatment of mild and moderate acne vulgaris with salicylic acid in an alcohol-detergent vehicle. Cutis 1981;28:556-8, 561.
77. Cunliffe WJ, Holland KT. Clinical and laboratory studies on treatment with 20% azelaic acid cream for acne. Acta Derm Venereol Suppl (Stockh) 1989;143:31-4.
78. Katsambas A, Graupe K, Stratigos J. Clinical studies of 20% azelaic acid cream in the treatment of acne vulgaris. Comparison with vehicle and topical tretinoin. Acta Derm Venereol Suppl (Stockh) 1989;143:35-9.
79. Hjorth N, Graupe K. Azelaic acid for the treatment of acne. A clinical comparison with oral tetracycline. Acta Derm Venereol Suppl (Stockh) 1989;143:45-8.
80. Elstein W. Topical deodorized polysulfides. Broadscope acne therapy. Cutis 1981;28:468-72.
81. Hurley HJ, Shelley WB. Special topical approach to the treatment of acne. Suppression of sweating with aluminum chloride in an anhydrous formulation. Cutis 1978;22: 696-703.
82. Hjorth N, Storm D, Dela K. Topical anhydrous aluminum chloride formulation in the treatment of acne vulgaris: a double-blind study. Cutis 1985;35:499-500.
83. Cochran RJ, Tucker SB, Flannigan SA. Topical zinc therapy for acne vulgaris. Int J Dermatol 1985;24:188-90.
84. Stainforth J, MacDonald-Hull S, Papworth-Smith JW, Eady EA. A single-blind comparison of topical erythromycin/zinc lotion and oral minocycline in the treatment of acne vulgaris. J Dermatolog Treat 1993;4:119-22.
85. Bojar RA, Eady EA, Jones CE, Cunliffe WJ, Holland KT. Inhibition of erythromycin-resistant propionibacteria on the skin of acne patients by topical erythromycin with and without zinc. Br J Dermatol 1994;130:329-36.
86. Thiboutot D. New treatments and therapeutic strategies for acne. Arch Fam Med 2000;9:179-87.
87. Lebrun CM. Rosac cream with sunscreens (sodium sulfacetamide 10% and sulfur 5%). Skinmed 2004;3:92.
88. Tarimci N, Sener S, Kilinc T. Topical sodium sulfacetamide/ sulfur lotion. J Clin Pharm Ther 1997;22:301.
89. Lane P, Williamson DM. Treatment of acne vulgaris with tetracycline hydrochloride: a double-blind trial with 51 patients. Br Med J 1969;2:76-9.
90. Smith JG Jr, Chalker DK, Wehr RF. The effectiveness of topical and oral tetracycline for acne. South Med J 1976;69: 695-7.
91. Gratton D, Raymond GP, Guertin-Larochelle S, Maddin SW, Leneck CM, Warner J, et al. Topical clindamycin versus systemic tetracycline in the treatment of acne. Results of a multiclinic trial. J Am Acad Dermatol 1982;7:50-3.
92. Katsambas A, Towarky AA, Stratigos J. Topical clindamycin phosphate compared with oral tetracycline in the treatment of acne vulgaris. Br J Dermatol 1987;116:387-91.
93. Braathen LR. Topical clindamycin versus oral tetracycline and placebo in acne vulgaris. Scand J Infect Dis Suppl 1984; 43:71-5.
94. Anderson RL, Cook CH, Smith DE. The effect of oral and topical tetracycline on acne severity and on surface lipid composition. J Invest Dermatol 1976;66:172-7.
95. Blaney DJ, Cook CH. Topical use of tetracycline in the treatment of acne: a double-blind study comparing topical and oral tetracycline therapy and placebo. Arch Dermatol 1976;112:971-3.
96. Rapaport M, Puhvel SM, Reisner RM. Evaluation of topical erythromycin and oral tetracycline in acne vulgaris. Cutis 1982;30:122-6, 130, 132-5.
97. Norris JF, Hughes BR, Basey AJ, Cunliffe WJ. A comparison of the effectiveness of topical tetracycline, benzoyl-peroxide gel and oral oxytetracycline in the treatment of acne. Clin Exp Dermatol 1991;16:31-3.
98. Sauer GC. Safety of long-term tetracycline therapy for acne. Arch Dermatol 1976;112:1603-5.
99. Baer RL, Leshaw SM, Shalita AR. High-dose tetracycline therapy in severe acne. Arch Dermatol 1976;112:479-81.

100. Plewig G, Petrozzi JW, Berendes U. Double-blind study of doxycycline in acne vulgaris. Arch Dermatol 1970;101:435-8.
101. Harrison PV. A comparison of doxycycline and minocycline in the treatment of acne vulgaris. Clin Exp Dermatol 1988; 13:242-4.
102. Skidmore R, Kovach R, Walker C, Thomas J, Bradshaw M, Leyden J, et al. Effects of subantimicrobial-dose doxycycline in the treatment of moderate acne. Arch Dermatol 2003; 139:459-64.
103. Hersle K, Gisslen H. Minocycline in acne vulgaris: a double-blind study. Curr Ther Res Clin Exp 1976;19:339-42.
104. Sheehan-Dare RA, Papworth-Smith J, Cunliffe WJ. A double-blind comparison of topical clindamycin and oral minocycline in the treatment of acne vulgaris. Acta Derm Venereol 1990;70:534-7.
105. Samuelson JS. An accurate photographic method for grading acne: initial use in a double-blind clinical comparison of minocycline and tetracycline. J Am Acad Dermatol 1985; 12:461-7.
106. Poliak SC, DiGiovanna JJ, Gross EG, Gantt G, Peck GL. Minocycline-associated tooth discoloration in young adults. JAMA 1985;254:2930-2.
107. Goulden V, Glass D, Cunliffe WJ. Safety of long-term high-dose minocycline in the treatment of acne. Br J Dermatol 1996;134:693-5.
108. Gammon WR, Meyer C, Lantis S, Shenefelt P, Reizner G, Cripps DJ. Comparative efficacy of oral erythromycin versus oral tetracycline in the treatment of acne vulgaris. A double-blind study. J Am Acad Dermatol 1986;14:183-6.
109. Al-Mishari MA. Clinical and bacteriological evaluation of tetracycline and erythromycin in acne vulgaris. Clin Ther 1987;9:273-80.
110. Parsad D, Pandhi R, Nagpal R, Negi KS. Azithromycin monthly pulse vs daily doxycycline in the treatment of acne vulgaris. J Dermatol 2001;28:1-4.
111. Christian GL, Krueger GG. Clindamycin vs placebo as adjunctive therapy in moderately severe acne. Arch Dermatol 1975; 111:997-1000.
112. Cunliffe WJ, Cotterill JA. Clindamycin as an alternative to tetracycline in severe acne vulgaris. Practitioner 1973;210: 698-700.
113. Poulos ET, Tedesco FJ. Acne vulgaris: double-blind trial comparing tetracycline and clindamycin. Arch Dermatol 1976;112:974-6.
114. Panzer JD, Poche W, Meek TJ, Derbes VJ, Atkinson W. Acne treatment: a comparative efficacy trial of clindamycin and tetracycline. Cutis 1977;19:109-11.
115. Stoughton RB, Cornell RC, Gange RW, Walter JF. Double-blind comparison of topical 1 percent clindamycin phosphate (Cleocin T) and oral tetracycline 500 mg/day in the treatment of acne vulgaris. Cutis 1980;26:424-5, 429.
116. Macdonald RH, Macconnell LE, Dunsmore IR. Trimethoprim-sulphamethoxazole versus placebo in acne vulgaris. Br J Clin Pract 1972;26:97-8.
117. Hersle K. Trimethoprim-sulphamethoxazole in acne vulgaris. A double-blind study. Dermatologica 1972;145:187-91.
118. Cotterill JA, Cunliffe WJ, Forster RA, Williamson DM, Bulusu L. A comparison of trimethoprim-sulphamethoxazole with oxytetracycline in acne vulgaris. Br J Dermatol 1971;84: 366-9.
119. Gibson JR, Darley CR, Harvey SG, Barth J. Oral trimethoprim versus oxytetracycline in the treatment of inflammatory acne vulgaris. Br J Dermatol 1982;107:221-4.
120. Bottomley WW, Cunliffe WJ. Oral trimethoprim as a third-line antibiotic in the management of acne vulgaris. Dermatology 1993;187:193-6.
121. Miller YW, Eady EA, Lacey RW, Cove JH, Joanes DN, Cunliffe WJ. Sequential antibiotic therapy for acne promotes the carriage of resistant staphylococci on the skin of contacts. J Antimicrob Chemother 1996;38:829-37.
122. Lucky AW, Henderson TA, Olson WH, Robisch DM, Lebwohl M, Swinyer LJ. Effectiveness of norgestimate and ethinyl estradiol in treating moderate acne vulgaris. J Am Acad Dermatol 1997;37:746-54.
123. Olson WH, Lippman JS, Robisch DM. The duration of response to norgestimate and ethinyl estradiol in the treatment of acne vulgaris. Int J Fertil Womens Med 1998;43: 286-90.
124. Thiboutot D, Archer DF, Lemay A, Washenik K, Roberts J, Harrison DD. A randomized, controlled trial of a low-dose contraceptive containing 20 microg of ethinyl estradiol and 100 microg of levonorgestrel for acne treatment. Fertil Steril 2001;76:461-8.
125. Leyden J, Shalita A, Hordinsky M, Swinyer L, Stanczyk FZ, Weber ME. Efficacy of a low-dose oral contraceptive containing 20 microg of ethinyl estradiol and 100 microg of levonorgestrel for the treatment of moderate acne: A randomized, placebo-controlled trial. J Am Acad Dermatol 2002;47:399-409.
126. Thorneycroft IH, Stanczyk FZ, Bradshaw KD, Ballagh SA, Nichols M, Weber ME. Effect of low-dose oral contraceptives on androgenic markers and acne. Contraception 1999;60: 255-62.
127. Worret I, Arp W, Zahradnik HP, Andreas JO, Binder N. Acne resolution rates: results of a single-blind, randomized, controlled, parallel phase III trial with EE/CMA (Belara) and EE/LNG (Microgynon). Dermatology 2001;203:38-44.
128. Rosen MP, Breitkopf DM, Nagamani M. A randomized controlled trial of second- versus third-generation oral contraceptives in the treatment of acne vulgaris. Am J Obstet Gynecol 2003;188:1158-60.
129. Thorneycroft H, Gollnick H, Schellschmidt I. Superiority of a combined contraceptive containing drospirenone to a triphasic preparation containing norgestimate in acne treatment. Cutis 2004;74:123-30.
130. Huber J, Walch K. Treating acne with oral contraceptives: use of lower doses. Contraception 2006;73:23-9.
131. Goodfellow A, Alaghband-Zadeh J, Carter G, Cream JJ, Holland S, Scully J, et al. Oral spironolactone improves acne vulgaris and reduces sebum excretion. Br J Dermatol 1984; 111:209-14.
132. Muhlemann MF, Carter GD, Cream JJ, Wise P. Oral spironolactone: an effective treatment for acne vulgaris in women. Br J Dermatol 1986;115:227-32.
133. Hatwal A, Bhatt RP, Agrawal JK, Singh G, Bajpai HS. Spironolactone and cimetidine in treatment of acne. Acta Derm Venereol 1988;68:84-7.
134. Greenwood R, Brummitt L, Burke B, Cunliffe WJ. Acne: double blind clinical and laboratory trial of tetracycline, oestrogen-cyproterone acetate, and combined treatment. Br Med J (Clin Res Ed) 1985;291:1231-5.
135. Miller JA, Wojnarowska FT, Dowd PM, Ashton RE, O'Brien TJ, Griffiths WA, et al. Anti-androgen treatment in women with acne: a controlled trial. Br J Dermatol 1986;114:705-16.
136. Fugere P, Percival-Smith RK, Lussier-Cacan S, Davignon J, Farquhar D. Cyproterone acetate/ethinyl estradiol in the treatment of acne. A comparative dose-response study of the estrogen component. Contraception 1990;42:225-34.
137. Nader S, Rodriguez-Rigau LJ, Smith KD, Steinberger E. Acne and hyperandrogenism: impact of lowering androgen levels with glucocorticoid treatment. J Am Acad Dermatol 1984; 11:256-9.

138. Amichai B, Shemer A, Grunwald MH. Low-dose isotretinoin in the treatment of acne vulgaris. J Am Acad Dermatol 2006; 54:644-6.
139. Goldstein JA, Socha-Szott A, Thomsen RJ, Pochi PE, Shalita AR, Strauss JS. Comparative effect of isotretinoin and etretinate on acne and sebaceous gland secretion. J Am Acad Dermatol 1982;6:760-5.
140. King K, Jones DH, Daltrey DC, Cunliffe WJ. A double-blind study of the effects of 13-cis-retinoic acid on acne, sebum excretion rate and microbial population. Br J Dermatol 1982;107:583-90.
141. Peck GL, Olsen TG, Butkus D, Pandya M, Arnaud-Battandier J, Gross EG, et al. Isotretinoin versus placebo in the treatment of cystic acne. A randomized double-blind study. J Am Acad Dermatol 1982;6:735-45.
142. Strauss JS, Stranieri AM. Changes in long-term sebum production from isotretinoin therapy. J Am Acad Dermatol 1982;6:751-6.
143. Jones DH, King K, Miller AJ, Cunliffe WJ. A dose-response study of l3-cis-retinoic acid in acne vulgaris. Br J Dermatol 1983;108:333-43.
144. Strauss JS, Rapini RP, Shalita AR, Konecky E, Pochi PE, Comite H, et al. Isotretinoin therapy for acne: results of a multicenter dose-response study. J Am Acad Dermatol 1984;10:490-6.
145. Lester RS, Schachter GD, Light MJ. Isotretinoin and tetracycline in the management of severe nodulocystic acne. Int J Dermatol 1985;24:252-7.
146. Chivot M, Midoun H. Isotretinoin and acne—a study of relapses. Dermatologica 1990;180:240-3.
147. Layton AM, Knaggs H, Taylor J, Cunliffe WJ. Isotretinoin for acne vulgaris—10 years later: a safe and successful treatment. Br J Dermatol 1993;129:292-6.
148. Lehucher-Ceyrac D, Weber-Buisset MJ. Isotretinoin and acne in practice: a prospective analysis of 188 cases over 9 years. Dermatology 1993;186:123-8.
149. Stainforth JM, Layton AM, Taylor JP, Cunliffe WJ. Isotretinoin for the treatment of acne vulgaris: which factors may predict the need for more than one course? Br J Dermatol 1993; 129:297-301.
150. Goulden V, Clark SM, McGeown C, Cunliffe WJ. Treatment of acne with intermittent isotretinoin. Br J Dermatol 1997;137: 106-8.
151. Strauss JS, Leyden JJ, Lucky AW, Lookingbill DP, Drake LA, Hanifin JM, et al. A randomized trial of the efficacy of a new micronized formulation versus a standard formulation of isotretinoin in patients with severe recalcitrant nodular acne. J Am Acad Dermatol 2001;45:187-95.
152. McElwee NE, Schumacher MC, Johnson SC, Weir TW, Greene SL, Scotvold MJ, et al. An observational study of isotretinoin recipients treated for acne in a health maintenance organization. Arch Dermatol 1991;127:341-6.
153. Strauss JS, Leyden JJ, Lucky AW, Lookingbill DP, Drake LA, Hanifin JM, et al. Safety of a new micronized formulation of isotretinoin in patients with severe recalcitrant nodular acne: A randomized trial comparing micronized isotretinoin with standard isotretinoin. J Am Acad Dermatol 2001;45: 196-207.
154. Lammer EJ, Chen DT, Hoar RM, Agnish ND, Benke PJ, Braun JT, et al. Retinoic acid embryopathy. N Engl J Med 1985; 313:837-41.
155. Dai WS, LaBraico JM, Stern RS. Epidemiology of isotretinoin exposure during pregnancy. J Am Acad Dermatol 1992;26: 599-606.
156. Zech LA, Gross EG, Peck GL, Brewer HB. Changes in plasma cholesterol and triglyceride levels after treatment with oral isotretinoin. A prospective study. Arch Dermatol 1983;119: 987-93.
157. Bershad S, Rubinstein A, Paterniti JR, Le NA, Poliak SC, Heller B, et al. Changes in plasma lipids and lipoproteins during isotretinoin therapy for acne. N Engl J Med 1985;313: 981-5.
158. Leachman SA, Insogna KL, Katz L, Ellison A, Milstone LM. Bone densities in patients receiving isotretinoin for cystic acne. Arch Dermatol 1999;135:961-5.
159. Goldsmith LA, Bolognia JL, Callen JP, Chen SC, Feldman SR, Lim HW, et al. American Academy of Dermatology Consensus Conference on the safe and optimal use of isotretinoin: summary and recommendations. J Am Acad Dermatol 2004;50:900-6. Erratum in J Am Acad Dermatol 2004;51:348.
160. Myhill JE, Leichtman SR, Burnett JW. Self-esteem and social assertiveness in patients receiving isotretinoin treatment for cystic acne. Cutis 1988;41:171-3.
161. Rubinow DR, Peck GL, Squillace KM, Gantt GG. Reduced anxiety and depression in cystic acne patients after successful treatment with oral isotretinoin. J Am Acad Dermatol 1987;17:25-32.
162. Hull SM, Cunliffe WJ, Hughes BR. Treatment of the depressed and dysmorphophobic acne patient. Clin Exp Dermatol 1991; 16:210-1.
163. Jick SS, Kremers HM, Vasilakis-Scaramozza C. Isotretinoin use and risk of depression, psychotic symptoms, suicide, and attempted suicide. Arch Dermatol 2000;136:1231-6.
164. Marqueling AL, Zane LT. Depression and suicidal behavior in acne patients treated with isotretinoin: a systematic review. Semin Cutan Med Surg 2005;24:92-102.
165. Chia CY, Lane W, Chibnall J, Allen A, Siegfried E. Isotretinoin therapy and mood changes in adolescents with moderate to severe acne: a cohort study. Arch Dermatol 2005;141: 557-60.
166. Lehucher-Ceyrac D, de La Salmoniere P, Chastang C, Morel P. Predictive factors for failure of isotretinoin treatment in acne patients: results from a cohort of 237 patients. Dermatology 1999;198:278-83.
167. White GM, Chen W, Yao J, Wolde-Tsadik G. Recurrence rates after the first course of isotretinoin. Arch Dermatol 1998;134: 376-8.
168. Levine RM, Rasmussen JE. Intralesional corticosteroids in the treatment of nodulocystic acne. Arch Dermatol 1983;119: 480-1.
169. Potter RA. Intralesional triamcinolone and adrenal suppression in acne vulgaris. J Invest Dermatol 1971;57: 364-70.
170. Kim SW, Moon SE, Kim JA, Eun HC. Glycolic acid versus Jessner's solution: which is better for facial acne patients? A randomized prospective clinical trial of split-face model therapy. Dermatol Surg 1999;25:270-3.
171. Wang CM, Huang CL, Hu CT, Chan HL. The effect of glycolic acid on the treatment of acne in Asian skin. Dermatol Surg 1997;23:23-9.
172. Grimes PE. The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. Dermatol Surg 1999;25: 18-22.
173. Pepall LM, Cosgrove MP, Cunliffe WJ. Ablation of whiteheads by cautery under topical anaesthesia. Br J Dermatol 1991;125: 256-9.
174. Bassett IB, Pannowitz DL, Barnetson RS. A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. Med J Aust 1990;153:455-8.
175. Paranjpe P, Kulkarni PH. Comparative efficacy of four Ayurvedic formulations in the treatment of acne vulgaris:

a double-blind randomised placebo-controlled clinical evaluation. J Ethnopharmacol 1995;49:127-32.
176. Lalla JK, Nandedkar SY, Paranjape MH, Talreja NB. Clinical trials of ayurvedic formulations in the treatment of acne vulgaris. J Ethnopharmacol 2001;78:99-102.
177. Ellerbroek WC. Hypotheses toward a unified field theory of human behavior with clinical application to acne vulgaris. Perspect Biol Med 1973;16:240-62.
178. Hughes H, Brown BW, Lawlis GF, Fulton JE Jr. Treatment of acne vulgaris by biofeedback relaxation and cognitive imagery. J Psychosom Res 1983;27:185-91.
179. Bett DG, Morland J, Yudkin J. Sugar consumption in acne vulgaris and seborrhoeic dermatitis. Br Med J 1967;3:153-5.
180. Fulton JE Jr, Plewig G, Kligman AM. Effect of chocolate on acne vulgaris. JAMA 1969;210:2071-4.

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