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Guidance on the diagnosis and clinical management of acne

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Summary

This article discusses the effects of acne (sometimes referred to as acne vulgaris), how to diagnose it confidently and how to distinguish it from rosacea, and the options available for treatment, especially in primary care. We also suggest when referral to dermatology should be considered, and try to anticipate some frequently asked questions.

Introduction

Acne is a very common chronic inflammatory disease of the pilosebaceous units, characterized by increased sebum production (seborrhoea) and by formation of comedones, erythematous papules and pustules, and less frequently, nodules, deep pustules and scarring. Acne usually begins in adolescence, and often resolves by the mid-20s.[1] Studies of schoolchildren from 1971 to 1989[2,3] showed a consistent level of maximum prevalence, approaching 100% for 16–17-year-old boys and 85–100% in 16-year-old girls. However, during this time there was a major reduction in acne severity. In a community-based study, the prevalence of significant acne was 56% in boys and 45% in girls aged between 14 and 16 years, the condition being moderate to severe in 11%.[3] A peak in prevalence and severity occurs at the ages of 14–17 years in girls (with 40% affected), and 16–19 years in boys (35% affected).[1] As these figures show, acne develops earlier in girls than in boys.[1,2] Acne usually resolves slowly between 20 and 25 years of age, but in 7–17% of individuals, clinical acne persists beyond the age of 25 years,[4] with physiological acne having a prevalence of 24% in women.[5] Late-onset acne (age > 25 years) occurs in 8% of patients with persistent acne, and at the age of 40 years, significant lesions are still present in 1% of men and 5% of women.[6]

Genetic factors influence susceptibility to acne, there being a high concordance between monozygotic twins.[7] Patients with persistent acne have a strong family history of persistent disease, in contrast to those with adolescent acne.[4] The four main factors involved in the aetiology of acne are seborrhoea, comedo formation (both early events), colonization of the pilosebaceous duct with *Propionibacterium acnes*, and inflammation.

Both male and female patients with acne excrete, on average, more sebum than normal individuals,[8] and the level of sebum excretion correlates with acne severity. Sebaceous activity is predominantly dependent on androgenic sex hormones but it is usually not necessary to investigate female patients for an endocrinopathy.[9] Ductal hypercornification can be seen histologically as microcomedones, and clinically as blackheads (open comedones), whiteheads (closed comedones) and other forms of comedones such as macrocomedones. A microcomedone or comedone is present in the majority of early inflamed papules. At an early stage of inflammation, inflammatory mediators move through the duct wall into the dermis, where there is a type IV immunological response. Rupture of the duct occurs as a later event.[10] Acne is not infectious, and the microenvironment produced by *P. acnes* in the pilosebaceous unit is probably more important for the

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development of acne lesions than the absolute numbers of bacteria.

Impact on quality of life

Questionnaire studies have shown that many patients with acne experience shame (70%), embarrassment and anxiety (63%), lack of confidence (67%), impaired social contact (57%), and a clinically significant problem with unemployment.[11–13] Severe acne may be related to increased anger and anxiety.[2] Comparisons with other chronic illnesses have shown that patients with acne have levels of social, psychological and emotional disability that are similar to those reported in asthma, epilepsy, diabetes or arthritis.[14,15] Stress may play a role in the exacerbation of acne, and acne itself induces stress. Picking of the lesions will aggravate the appearance, which can be a particular problem in young adolescent female patients who present with acne excoriée.[2]

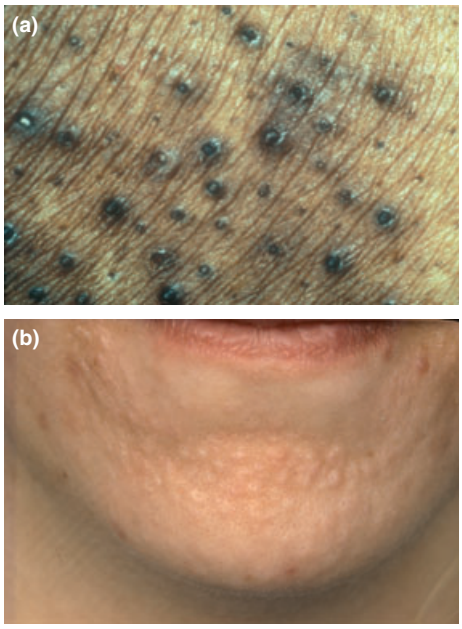

Figure 1 (a) Open comedones (blackheads) and (b) closed comedones (whiteheads) in acne.

Diagnosis

Acne is usually a straightforward clinical diagnosis. The condition mainly affects the face (99%) and, to a lesser extent, the back (60%) and chest (15%). Non-inflamed lesions (comedones) develop earlier than inflamed lesions in younger patients (Fig. 1). Inflammatory lesions may be superficial or deep, and many arise from noninflamed lesions.[2] The superficial lesions are usually papules and pustules, and the deep lesions are deep pustules and nodules (Fig. 2a). Acne 'cysts' are not true cysts because they are not lined with epithelium, and the term 'nodular acne' is preferred to 'nodulocystic acne'. Deep lesions are associated with scarring, but scarring can occur after superficial lesions in scar-prone individuals. Significant (socially noticeable) scarring occurs in 22% patients who attend dermatologists,[2] and the types of scars seen are ice-pick (Fig. 2b), depressed fibrotic, atrophic, hypertrophic or keloidal (Fig. 2c). Persistent postinflammatory hyperpigmention is a common feature in deeply pigmented skin, and may be more disabling than the original disorder (Fig. 2d).

Differential diagnosis

The differential diagnosis of acne includes rosacea, which usually occurs in older patients and lacks comedones, nodules, cysts or scarring. Occasionally patients may have both rosacea and acne. The presence of facial flushing, which is induced by heat, alcohol or spicy food, is a useful pointer towards a diagnosis of rosacea. Patients with rosacea may also have ocular involvement, and rarely have lesions on the trunk.

Perioral dermatitis, sometimes following the application of a potent topical corticosteroid to facial skin, is often dry with no comedones. Whiteheads may be confused with milia.

Folliculitis of the beard area or trunk should also be considered; the latter includes folliculitis due to *Pityrosporum* spp., and, uncommonly, due to Gram-negative organisms as a complication of acne treatment with antibiotics.[2]

Secondary comedones may be produced after exposure to dioxins (chloracne), pomades (pomade acne), topical corticosteroids and other drugs (e.g. phenytoin).

Treatment of acne in primary care

The first step in management should involve patient education, and a discussion about treatment aims and patient expectations. It can be useful to grade the acne severity on scale of 0–10 on the face, back and chest. In addition, a subjective assessment can be obtained by asking the patient to score their acne severity out of 10, where 10 out of 10 is as bad as it could be, and 0 out of 10 is no acne. Patients will vary enormously in their own assessment.

Choice of treatment is largely determined by the severity and extent of the disease, but may be modified

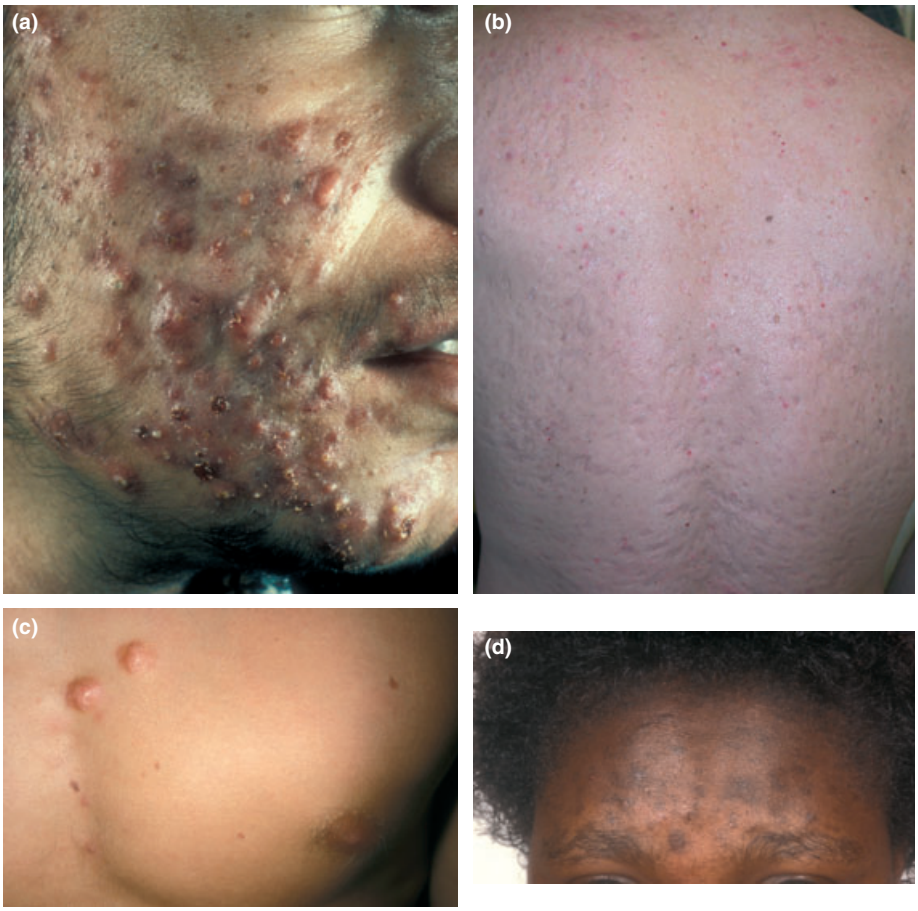

Figure 2 (a) Acne on the face with papules, pustules, nodules and scarring; (b) indented, angulated ('ice-pick') scars on the back from acne; (c) keloid scars from acne on the chest, a common site; (d) post-inflammatory hyperpigmentation from acne on the forehead of a woman of African origin.

by patient choice and cost. Patients with mild acne usually receive topical therapy, and patients with moderate acne receive both oral and topical therapies. Treatment choice will be influenced by the presence of scarring, the psychological effects of the disease, the success or failure of previous treatment, and sometimes a family history of persistent acne.

Topical therapies

The most widely used topical drugs are benzoyl peroxide, retinoids (e.g. adapalene, tretinoin), antibiotics and azelaic acid, either alone or in combination. Patients with predominantly inflamed lesions should receive topical benzoyl peroxide, antibiotics or azelaic acid. However, because of the central pathogenic role of microcomedones, a topical retinoid should be considered in most patients. Table 1 shows common topical therapies and their mode of action.

Benzoyl peroxide is supplied in concentrations of 2.5%, 5% and 10%, and is usually used in gel form. Topical antibiotics include clindamycin, erythromycin and tetracycline, used in concentrations of 1–4%, generally in a cream or lotion base. Combinations of antibiotics with benzoyl peroxide or zinc are reported to be more effective than single therapies.[2] Patients with predominantly non-inflamed lesions should receive topical retinoids as the first choice. Retinoic acid (tretinoin) is available in concentrations of 0.01–0.05% as a gel. A third-generation retinoid, adapalene, is claimed to have an improved risk:benefit ratio over tretinoin.[2]

Oral therapies

Oral treatments for acne include antibiotics (usually for at least 6 months), antiandrogens, and, in secondary care, isotretinoin and occasionally corticosteroids. There are several potential mechanisms of action for antibiotics in

Table 1 Topical treatments for acne.

Predominantly anticomedonal
Adapalene
Tretinoin
Isotretinoin
Azelaic acid
Predominantly antimicrobial
Benzoyl peroxide
Benzoyl peroxide/erythromycin
Benzoyl peroxide/clindamycin
Clindamycin
Erythromycin
Erythromycin/zinc
Tetracycline
Azelaic acid
Predominantly anti-inflammatory
Adapalene
Topical antibiotics
Nicotinamide

acne, including a direct effect in reducing inflammation. Tetracyclines are usually recommended, and include oxytetracycline, doxycycline and lymecycline. Minocycline, erythromycin and trimethoprim are considered to be second- or third-line treatments. The recommended dose of oxytetracycline is 500 mg twice daily, taken with water half an hour before food. Patient adherence may be improved with doxycycline 40–100 mg/day, lymecycline 408 mg/day or (later in a treatment plan because of expense and potential side-effects), minocycline 100 mg/day.

Oral antibiotic therapy is prescribed in combination with topical therapy for 6 months, with an expected improvement of 20% by 2 months and 80% by 6 months. The drug should be changed if there is no improvement after about 3 months. There is no logic to using a concurrent topical antibiotic in a patient being treated with an oral antibiotic for acne. In patients with nonresponding disease, minocycline is more effective than tetracycline,[16] and daily doses of doxycycline, lymecycline and minocycline are of similar efficacy, providing *P. acnes* is not resistant. Oral treatment is usually given to patients with moderate or moderate to severe acne, those with scarring or those prone to scarring or postinflammatory hyperpigmentation, and, on a carefully considered basis, to those with clinical depression or body dysmorphic disorder.

Anti-androgens are indicated usually when standard antibiotic regimens have failed, when concurrent control of acne and menstruation is required (e.g. as contraception), and when oral isotretinoin is inappropriate. Topical therapy is usually given at the same time. Anti-androgens decrease the testosterone drive to sebum excretion. The contraceptive pills Dianette® (co-cyprindiol) and Yasmin® (ethinylestradiol plus drospirenone) (both Bayer AG, Leverkusen, Germany) have been shown to improve acne,[17] their effects being slower than those of oral antibiotics, with maximum response at about 6 months. Dianette® is sometimes recommended by dermatologists in addition to an oral antibiotic and topical therapy; the absorption of the oral contraceptive is likely to be significantly impaired only if the antibiotic results in diarrhoea. There is a reasonable argument for using an anti-androgen with low oestrogen content to minimize the increased risk of deep vein thrombosis.[17]

Treatment options in secondary care

The most important treatment available in secondary care is oral isotretinoin. In the 1980s, this drug revolutionized the treatment of acne and remains the most clinically effective therapy, producing long-term remissions in many patients.[2] Isotretinoin significantly reduces elevated sebum production, comedogenesis, and surface and ductal colonization with *P. acnes*, and is also anti-inflammatory.

Oral isotretinoin is usually prescribed for patients with severe nodular acne or for those with persistent acne despite other treatments, because of the tendency to irreversible scarring.[2] It is important for the dermatologist to spend time discussing the likely outcome of treatment, including the side-effect profile of the drug, particularly the need for female patients of child-bearing age to avoid pregnancy when taking the drug and for a month after stopping it. The possible but unproven association between isotretinoin and suicidal depression should also be discussed, against the background of a significant prevalence of suicide in the UK and elsewhere among young men, with or without acne. About 50% of patients will notice an exacerbation of the acne in the first 2 weeks of isotretinoin therapy, and the response is usually gradual, with an excellent response after a dose equivalent to 1 mg/kg body weight per day for 4 months. Most patients are either effectively cured of their acne, with approximately 3 out of 10 requiring further treatment with, for example, a topical or oral antibiotic, and up to 2 out of 10 with severe nodular acne requiring a second course of isotretinoin. Recurrence after two courses of isotretinoin at 1 mg/kg body weight per day for 4–6 months may be followed by prescription of a lower dose of isotretinoin for a longer period, always under careful supervision. However, the recent trend for young women to take

intermittent small doses of isotretinoin for 'perfect skin' is to be discouraged, because of the teratogenic risks.

When to refer

Patients should be referred to a specialist under the following conditions:

- Diagnostic uncertainty.
- Failure to respond to topical treatments and oral antibiotics when given for sufficiently prolonged periods, usually 6 months.
- Nodular acne or any type of acne with a tendency to scarring.
- Moderately severe acne in patients with deeply pigmented skin, who are likely to develop postinflammatory hyperpigmentation.
- Major psychological component to the disorder.

Frequently asked questions

What is the role of diet in acne?

There is no convincing research evidence for a role of diet in either the aetiology or treatment of acne.

Is patient adherence a problem?

Yes. In one study, treatment adherence ('compliance') was < 40% after 18 weeks for both oral and topical therapies. Risk factors for poor adherence included young age, smoking and excessive alcohol use.[2] Adherence may be improved by educating patients about the chronic nature of acne and the slow response to treatment.

What about *P. acnes* resistance?

Resistance of *P. acnes* to antibiotics is commonest with erythromycin (with crossresistance to clindamycin). It occurs in about 20% of patients with acne on oxytetracycline or doxycycline, and is uncommon with minocycline. 24% of cases of resistant *P. acnes* are resistant to multiple drugs; however, microbiological resistance does not necessarily equate to clinical resistance, which will partly depend on drug concentration in the pilosebaceous duct.[2]

How can acne scarring be treated?

Treatment of acne scars should not be attempted until the acne is completely inactive. On the face, indented scars can be improved with laser resurfacing ('laserbrasion'), and individual scars may be excised. However, it is difficult to treat scarring on the back and chest. Acne keloid and hypertrophic scarring may soften and flatten after treatment with intralesional triamcinolone 10 mg/mL and/or silicone gel.

What about the treatment of active acne with lasers?

More research evidence is required before laser treatment of active acne is recommended routinely.

Further information

Further information and patient information leaflets are available on the website of the British Association of Dermatologists (http://www.bad.org.uk).

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