

Acne: current treatment

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Acne is the most common skin disorder, affecting up to 85% of people at some stage in their life. Its peak occurrence is in adolescence but it can occur in infancy and in later adult life. Acne has a negative effect on emotional well-being and social function comparable with other 'serious' conditions such as asthma, epilepsy and arthritis. Early and correct treatment is important to prevent scarring.

Pathogenesis

Optimum treatment of acne requires an understanding of the pathogenesis.¹ Four main factors cause acne:

- androgen-induced seborrhoea
- comedone formation
- colonisation of the sebaceous duct with *Propionibacterium acnes*
- inflammation.

The sebaceous glands are predominantly stimulated by androgens. There is evidence that in most patients the seborrhoea of acne is due to an increased response of the sebaceous glands to normal plasma hormone levels. There is a correlation between acne severity and sebum excretion rate and some evidence that patients with very greasy skins may require higher doses of antibiotics and other therapy. Approximately 1–2% of women with acne may have significantly related polycystic ovary disease.² Anabolic steroid intake may cause androgen-mediated seborrhoea with associated acne. A recent publication suggests that acne may be linked to milk intake, with hormones and bioactive molecules in milk increasing seborrhoea.³

Abnormal proliferation and differentiation of ductal keratinocytes leads to formation of the primary acne lesion, the microcomedone, which is present in up to 30% of biopsies of normal looking

skin in acne prone areas and in 85% of early papules. Larger lesions are visible as closed or open comedones. (Comedones represent retention of hyperproliferating ductal corneocytes at the infra-infundibulum of the pilosebaceous unit; there are open comedones or 'black-heads' and closed comedones or 'white-heads'.) A significant inflammatory infiltrate is seen around follicles before any evidence of comedone formation; this inflammation may be an early trigger for comedone formation.⁴ Occlusion of the duct leads to enlargement of the sebaceous gland, leakage of sebum into the dermis and colonisation of the sebaceous gland with *Propionibacterium acnes*.

Acne assessment

Assessment of the extent and severity of the acne is important in selecting the most appropriate therapy. It also provides a way to monitor treatment response and measure patient satisfaction. The acne can be assessed visually, using a pictorial grading scheme such as the revised Leeds grading scheme.⁵ It is important to include all the various acne lesions – inflammatory papules, pustules, nodules and cysts, as well as the non-inflammatory lesions – and also record postinflammatory hyperpigmentation and scarring.

Acne can produce low self-esteem and depression and severely impact on the patient's quality of life. The psychosocial impact of acne does not always correlate well with clinical severity and can be difficult to quantify. Measurement using a psychological questionnaire such as APSEA (Assessment of Psycho/Social

Effects of Acne)⁶ should help to identify those patients who have a psychological impact from their disease higher than would be expected from clinical assessment of the disease. Measurement of sebum excretion rate may also be helpful both in identifying those patients with high sebum excretion levels and in monitoring progress with oral retinoids (Fig 1).

Treatment

Logical treatment of acne requires targeting the above aetiological factors by reducing:⁷

- sebaceous gland blockage with retinoids and benzoyl peroxide
- bacterial colonisation with antibiotics, benzoyl peroxide and azelaic acid
- seborrhoea by reducing either sebaceous gland size with isotretinoin or androgen drive by anti-androgens and oral contraceptives
- inflammation by retinoids, some antibiotics and, in severe cases, oral and topical steroids.

Acne is a chronic disorder and response to treatment is relatively slow. It is important to emphasise this to the patient. With most treatments little improvement is seen for 4 weeks after starting therapy.

Principles of treatment

- Mild acne: topical therapy.
- Moderate acne: oral antibiotics (or hormonal therapy) plus topical therapy.
- Severe acne: oral isotretinoin.

Key Points

Acne is a chronic disorder associated with significant psychosocial morbidity

Treatment should target as many aetiological factors as possible

Isotretinoin is indicated in severe and nodulocystic acne and should be considered at an early stage to prevent scarring

KEY WORDS: acne, comedore, isotretinoin, psychosocial morbidity, seborrhoea

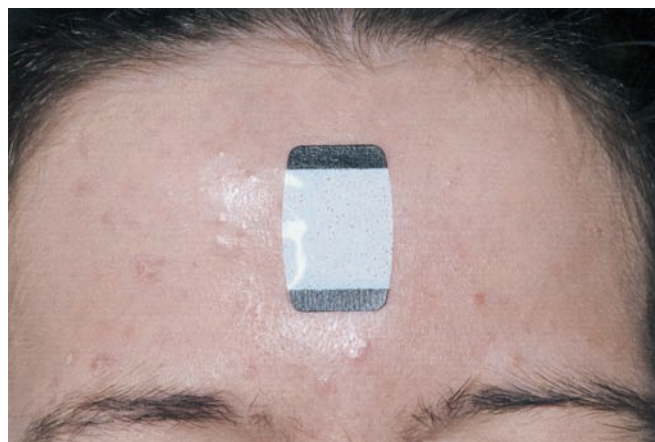


Fig 1. Measurement of sebum excretion rate.



Fig 2. Mild acne.

Mild acne (Fig 2)

Treatment with a topical retinoid will target comedogenesis. Newer topical retinoids such as adapalene have also been shown to have a number of direct effects on inflammatory pathways. Combination therapy with a topical antimicrobial agent such as benzoyl peroxide, clindamycin or erythromycin may be of additional benefit.⁷ Several combined proprietary preparations are available. Alternatively, benzoyl peroxide can usefully be given as a wash in the morning combined with a topical retinoid at night. Other available topical preparations are azelaic acid, which may reduce postinflammatory hyperpigmentation and can be useful in pigmented skin where this is often a problem, salicylic and nicotinic acid formulations.

Mild to moderate acne (Fig 3)

Oral antibiotics are usually necessary to control moderate acne, but topical treatment should be continued to target as many factors as possible. It is still debatable whether the main action of antibiotics in acne is anti-inflammatory or antibacterial.⁸ Non-antibacterial actions of antibiotics (eg bacterial lipase inhibition and anti-inflammatory immunomodulation) may be as important as their antibacterial action. Based on efficacy, safety and bacterial resistance, cyclines should be used in preference to other classes of antibiotics. Second-generation cyclines such as lymecycline and doxycy-



Fig 3. Moderate acne.

cline may have compliance advantages over tetracycline and both have a better side effect profile than minocycline.

Persistent acne after two or three adequate courses of antibiotics may be an indication for isotretinoin (see below) which has been shown to be a cost-effective alternative to long-term antibiotics and may reduce the incidence of bacterial resistance. Patients in whom there is significant psychological distress may also warrant isotretinoin therapy.

A treatment for women who require oral contraception or regulation of the menstrual cycle is hormone therapy with oestrogen and cyproterone acetate



Fig 4. Severe acne.

(which can be given as Dianette). Spironolactone is a further alternative for women; it improves acne because of its anti-androgen effect which reduces sebum excretion. Yasmin, a combined oral contraceptive pill containing drospirenone and which has spironolactone-like properties, may be of benefit in some patients.

Moderate to severe acne (Fig 4)

High-dose antibiotics such as minocycline 100 mg and trimethoprim 200–300 mg, both twice daily, may be of benefit in severe acne. If the acne is

nodulocystic, there is a significant risk of scarring and isotretinoin should be considered at an early stage.

Isotretinoin (13-*cis* retinoic acid), a naturally occurring dietary metabolite of vitamin A, has anti-inflammatory, regulatory and inhibitory effects on the sebaceous glands.⁹ It has been the gold standard of treatment of severe recalcitrant cystic acne for more than two decades. The potential side effects of isotretinoin will need to be discussed with the patient and also the expected treatment outcomes.

The patient should be examined carefully for the presence of macrocomedones. If present, it may be advisable to treat them with cautery or hyfrecation (treatment with a device similar to fine point cautery) prior to commencing treatment as isotretinoin can precipitate an acute flare of these lesions into new nodulocystic lesions.⁵

Dosage regimens vary. Most patients begin therapy at 0.5 mg/kg, increasing the dose after 4 weeks to 0.75–1 mg/kg if side effects are tolerated. Treatment is for 4–6 months, depending on the dose tolerated.

Acne fulminans and severely inflamed cystic acne. These conditions usually require initial treatment with oral steroids at a dose of 0.5–1 mg/kg/day for 2 weeks, reducing to zero over the next 4–6 weeks.¹⁰ In addition, individual cystic lesions may benefit from intralesional and/or potent topical steroids. Isotretinoin should be introduced gradually, starting at a low dose (eg 5–10 mg per day) (Figs 5 and 6).

Side effects of isotretinoin

Mucocutaneous side effects are predictable from the pharmacological effects of the drug and are common. These include cheilitis (dry lips), facial and irritant dermatitis, vestibulitis and blepharoconjunctivitis. They can be managed by changes in dose and are usually self-limiting. Side effects such as abnormal liver function tests and increase in triglyceride and cholesterol levels are less common. Other rare side



Fig 5. Nodulo-cystic acne before treatment.



Fig 6. After treatment with low dose isotretinoin and oral steroids.

effects, such as mood swings and depression, are much less predictable. There is some doubt about a definite causal relationship of these effects to the drug because patients with acne have a high incidence of psychosocial morbidity due to their disease. It is important to discuss the possibility of such side effects with the patient and to monitor carefully for them during treatment. It is also important to be realistic about the frequency of such reactions so that patients who will benefit from treatment with isotretinoin are not discouraged from taking it.

All doses of isotretinoin are teratogenic and women prescribed isotretinoin should use adequate contraceptive measures for a month before starting treatment, and continue them during treatment and for 6 weeks after stopping treatment. They should have a negative pregnancy test immediately before treatment, and under new regulations will require monthly pregnancy tests while taking the drug and 5 weeks after completing the course of treatment.

Treatment outcomes

Following isotretinoin therapy:

- two-thirds of patients will have a successful outcome, with complete

and permanent resolution of their acne

- 10–15% may have a minor degree of relapse, though often not for a year or longer
- about 10% will require further treatment, possibly with a further course of isotretinoin.

There is some suggestion that continuing with a topical retinoid after treatment may reduce relapse rates, but hard evidence for this is lacking.

Poor response to treatment

Compliance is probably a key factor in poor response to treatment. One study showed that compliance rates at 18 weeks were 38% with topical therapies and 45% with oral therapies. Problems commonly occur with antibiotic therapy where patients may need to take their tablets at an appropriate time with respect to food, and they may develop gastrointestinal symptoms and candidiasis. Side effects such as dryness and irritation, particularly with topical retinoids, may also be an issue. Applying retinoids as short contact for a few hours may be helpful. Resistance to *Propionibacterium acnes* may be implicated in treatment failure. Rarely, there is colonisation of the skin

with Gram-negative bacteria producing Gram-negative folliculitis, requiring treatment with trimethoprim or isotretinoin.

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