Acne

general principles of management

Today we are in a position to control and cure acne, a common and often socially incapacitating dermatological disorder.

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Acne is a common skin disorder, affecting over 90% of adolescents aged 16 to 18 years. Although it is predominantly a self-limiting complaint, even mild acne can have a devastating impact on self-esteem.[1,2] Today, acne is an eminently treatable disorder, and as doctors we have the means and medications to bring even the most severe types of acne under control before psychological and/or physical scarring can ensue.

Pathogenesis

At puberty, under the influence of androgenic hormones, the sebaceous glands enlarge and produce sebum, which maintains epidermal hydration and suppleness. Excessive sebum production is a prerequisite for the development of acne and may be caused by excessive androgen stimulation or increased reactivity of sebaceous glands to normal stimulation. The skin appears greasy, the pores large, and the scene is set for the development of acne.

Abnormal keratinisation of the follicular epithelium and subsequent desquamation causes obstruction of the pilosebaceous duct and the formation of a microcomedo, the precursor of acne lesions. If the obstruction occurs close to the skin surface, oxidation of the fatty material within the duct causes dark discolouration. This

IN SUMMARY

- **Acne affects over 90% of adolescents aged 16 to 19 years.**
- **Even mild acne can have a devasting impact on self-esteem.**
- **Acne is an eminently treatable disorder that can be well managed by the GP.**
- **The aim of treatment is to suppress and clear acne and to prevent scarring.**
- **The benefits of treatment may take two to three months to become evident.**
- **Topical, over-the-counter preparations are an essential part of therapy and may be all that is required in some cases.**
- **Fatty foods, dairy products and chocolate do not cause acne.**

Figure 1 (above). Papules, pustules and comedones.

Figure 2 (right). Severe papulopustular acne in a young woman. Although this is unsightly it is unlikely to scar.

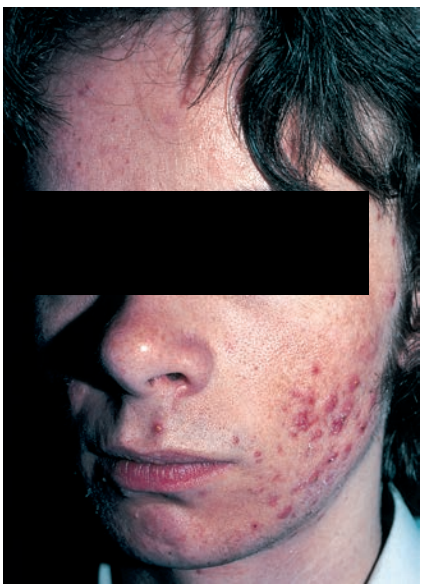

Figure 3 (left). Cystic acne carries an increased risk of scarring.

Figure 4 (above). Papules, pustules and cysts on the back.

is known as an open comedo or blackhead. If the blockage occurs lower down, no oxidation occurs and the lesion is known as a closed comedo (whitehead). Inflammatory lesions such as papules, pustules, cysts and nodules may supervene when there is overgrowth of *Proprionibacterium acnes* bacteria, which metabolise the sebum to produce fatty acids and other inflammatory by-products.

Although all adolescents and adults have the necessary factors for acne, most do not develop severe disease, indicating that other factors determine susceptibility. The familial association of severe acne and ongoing research suggest an inherited immune hyper-reactivity to *P. acnes* as the triggering factor.[3]

Clinical features

Acne vulgaris is most prevalent in adolescents. Although girls usually develop acne earlier, it is more common and severe in young men. It may worsen premenstrually, with excessive sweating or with stress.

Mild acne is characterised by comedones, papules and pustules (Figure 1). Although unsightly, this type of acne is usually associated with a low risk of scarring (Figure 2). Cysts and nodules, which are painful and situated more deeply in the dermis, are indicative of moderate to severe acne and an increased risk of scarring (Figures 3 and 4). Cystic acne must be recognised and treated aggressively to avoid permanent scarring.

The prevalence of acne declines after the teenage years, but up to 15% of males and 30% of females will continue to suffer with acne into their thirties.

A small (but significant) subset of women do not develop acne at puberty but present in their late twenties or early thirties with acne vulgaris. It may be triggered by pregnancy or cessation of the oral contraceptive pill, or it may occur spontaneously. Lesions are often confined to the lower cheeks, chin and jawline; they consist predominantly of papules and small, painful cysts, which may last for weeks. This type of acne may not appear to be severe on examination but characteristically causes small pitted scars and irregular skin texture around the mouth and chin (Figure 5). Premenstrual worsening is commonly reported. Up to 63% of women presenting in this way have elevated androgen levels and may have other signs of androgen excess such as menstrual irregularity, hirsutism and androgenic alopecia.[4] Where clinical signs of androgen excess are evident, a complete endocrine and gynaecological evaluation is warranted.

Some young women present with mild to nonexistent acne but numerous linear excoriations and hypopigmented scars (Figure 6). This variant of acne, known as acne excorie, occurs almost exclusively in young women who compulsively pick at and tamper with their skin. Invariably the acne is mild and it may be difficult to find a primary lesion,

Figure 5. Late onset acne with scars.

Figure 6. Acne excorie.

but scarring caused by picking is often severe and permanent. Aggressive therapy is warranted to suppress the acne completely, giving the young woman nothing to pick at. Severe or recalcitrant cases may require psychiatric assessment.

Management of acne

Acne is a physical and a psychological disorder. Even mild acne may undermine self-confidence, and the widely held community belief that acne is caused by poor hygiene and excessive consumption of fatty foods exacerbates the problem, implying that sufferers are responsible for their own disease. When medical treatment is sought, expectations may be unreasonable. The only prior contact the teenager may have had with the doctor is for treatment of minor infections, and the teenager may expect the medication prescribed for acne to work just as rapidly. It is important to address these issues and to dispel any myths.

The aim of treatment is to suppress and clear acne and to prevent scarring. The benefits of treatment may take two to three months to become evident and patients must understand it is likely to take six to eight months to achieve complete clearing. It is also important for patients to realise the ultimate goal is to prevent more acne, and it is therefore inappropriate to discontinue therapy as soon as the skin clears. Treatment is directed at overcoming the four factors contributing to the pathogenesis of acne:

- excessive sebum production
- abnormal keratinisation and blockage of the pilosebaceous duct
- overgrowth of *P. acnes*
- production of inflammatory by-products by *P. acnes*.

General principles of acne management are listed in Table 1.

Topical therapy

Topical comedolytics

Topical agents act as comedolytics to unblock the pilosebaceous duct or as antibacterial agents, or, in the case of benzoyl peroxide and azelaic acid, as both (Table 2). These products may be used alone in mild acne or in combination with systemic agents in more severe cases. Most are formulated in an alcohol or other drying base and are useful for drying out acute lesions, but ultimately they are meant to prevent new outbreaks and must subsequently be used throughout the acne prone area once or twice daily.

Benzoyl peroxide is both comedolytic and antibacterial. It can be purchased without prescription and is available as 2.5, 5 and 10% gels and creams. The weaker strength creams are used on the face, while the stronger preparations are ideal for use on the back. It is relatively

Table 1. General principles of acne management

Skin care

Gentle cleansing (e.g. with baby soap)
No toner, moisturiser or scrubs
No picking, squeezing or tampering with spots
Oil-free make-up permitted
Oil-free sunscreen

Diet

Balanced diet
No need to exclude particular foods, such as fats, dairy products or chocolate

Medical treatment

Topical keratolytics and antibiotics
Oral antibiotics
Antiandrogens
Isotretinoin

Reassurance

Acne is eminently treatable
Acne responds slowly (i.e. expected improvement is 40% after two months, 60% after four months and more than 80% after six months)

Table 2. Specific treatments of acne

Reduce sebum secretion
Topical
Isotretinoin
Oral
Oestrogen
Cyproterone acetate
Spironolactone
Isotretinoin

Reduce bacterial numbers
Topical
Mild soap
Benzoyl peroxide
Antibiotics
Azelaic acid
Oral
Antibiotics

Unblock pilosebaceous unit
Topical
Tretinoin
Isotretinoin
Adapalene
Salicylic acid
Glycolic acid
Azelaic acid
Benzoyl peroxide
Oral
Isotretinoin

Reduce inflammation
Topical
Salicylic acid
Adapalene
Azelaic acid
Oral
Antibiotics
Isotretinoin

Figure 7. Brown band discolouration of the teeth caused by tetracycline therapy during childhood.

PHOTOGRAPH COURTESY OF ROCHE PRODUCTS

Table 3. Isotretinoin therapy

Indications
Severe acne
Moderate acne unresponsive to conventional treatment
Significant risk of scarring
Acne associated with considerable depression
Rapid relapse after stopping antibiotics or antiandrogens

Some side effects (incidence)
Cheilitis (100%)
Facial dermatitis (95%)
Myalgia, arthralgia (60%)
Epistaxis (50%)
Conjunctivitis (40%)
Headaches (40%)
Eczema (20%)
Anorexia (10%)
Staphylococcal skin infections (6%)
Weight loss (1%)
Pyogenic granuloma (1%)

cheap, but it may bleach clothing. When used in combination with systemic antibiotics, daily use of benzoyl peroxide will also reduce the risk of antibiotic resistance developing.

Tretinoin or retinoic acid (a vitamin A derivative) is one of the most effective comedolytics available, but it is extremely irritating and may increase photosensitivity. Nearly all patients experience some mild facial erythema, desquamation and increased sensitivity one to two weeks after starting treatment. This reaction usually settles within two weeks and does not necessitate the discontinuation of treatment. Tretinoin increases the penetration of other topical agents and can therefore enhance the efficacy of topical antibiotics used concomitantly.

Topical isotretinoin (Isotrex Gel) and adapalene (Differin) are also vitamin A derivatives and are generally better tolerated and superior to tretinoin in the treatment of inflammatory acne. Topical use of isotretinoin may also reduce sebum production.[5]

All topical retinoids can cause photosensitivity and should be used at night and washed off in the morning. All are contraindicated during pregnancy because they are potentially teratogenic.

Topical antibiotics
Erythromycin and clindamycin are both available in topical form for the treatment of acne. Both should be used twice daily. The combination of topical antibiotics and tretinoin or benzoyl peroxide is more effective than either agent used alone and may reduce the risk of antibiotic resistance developing.[6] With increasing problems of antibiotic resistance in our community, the use of topical antibiotics alone or as the mainstay of treatment is rarely indicated.

Systemic therapy
Systemic therapy is used when acne is unresponsive to topical agents. Topical and oral agents are complementary, and the combination is most effective in moderate to severe acne. Systemic agents consist of antibiotics, antiandrogens and isotretinoin. Antibiotics reduce *P. acnes* within the sebaceous glands and reduce inflammation, whereas antiandrogens and isotretinoin have a direct inhibitory effect on sebaceous gland activity, reducing sebum production.

Oral antibiotics
The antibiotics most often used in acne are tetracycline, minocycline, doxycycline, trimethoprim–sulfamethoxazole and erythromycin. At appropriate doses,

antibiotics are both bactericidal and anti-inflammatory. Typically, antibiotics need to be taken for several weeks before a benefit is seen, and I normally advise patients to expect 40% improvement after two months, 60% clearing by four months and complete clearing by six to eight months. Failure to achieve this rate of improvement should be judged a therapeutic failure and the treatment should be altered.

Tetracyclines are given in a dose of 500 mg twice daily. They are inexpensive and generally effective. They must be taken on an empty stomach and cause gastrointestinal upset in many patients, resulting in poor compliance. Doxycycline (50 mg once or twice daily) and minocycline (50 mg twice daily) are used if the response to tetracycline is unsatisfactory. Both may be taken with food, reducing the risk of gastrointestinal upset and improving patient compliance. This group of antibiotics is contraindicated during pregnancy and in children younger than 12 years of age because they may stain unerupted permanent teeth (Figure 7).

Erythromycin (500 mg twice daily) is often used when tetracyclines are contraindicated. Although *P. acnes* tends to develop resistance to both tetracycline and erythromycin, resistance is more commonly associated with use of the latter.

Trimethoprim–sulfamethoxazole is highly effective for acne, but its use should be confined to those with more severe or unresponsive acne because of its potential for severe (though rare) side effects such as toxic epidermal necrolysis and bone marrow suppression.

Antiandrogens

Cyproterone acetate and spironolactone inhibit androgen stimulation of the sebaceous glands and hair follicles. They are of benefit in women with moderate to severe acne or persistent acne, hirsutism and/or androgenic alopecia. The therapeutic effect is relatively slow, requiring two to three months for noticeable improvement in the acne and six to nine months for complete clearing.

Cyproterone acetate is administered with ethinyloestradiol in a reverse sequential manner on days 5 to 14 of the menstrual cycle. It is available at a low dose (2 mg) in combination with oestrogen (Diane-35 ED, Brenda-35 ED) or separately at doses of 10 and 50 mg (Androcur, Cyprone, Procur). If acne is not significantly alleviated after three cycles of the cyproterone acetate–ethinyloestradiol combination, the dose of cyproterone acetate should be increased. Higher doses are generally necessary in the setting of hirsutism and androgenic alopecia.

Spironolactone (Aldactone, Spiractin) is a suitable alternative for women who cannot take oestrogen or oral contraceptives and whose acne is not severe enough to warrant isotretinoin; 100 to 200 mg is taken daily. During the initial weeks of treatment, spironolactone often has a diuretic effect and may cause hypotension. Other side effects include menstrual irregularity, breast tenderness, fatigue and hyperkalaemia.[7]

Antiandrogens can produce lasting improvement and are generally well tolerated by women. However, the success rate is lower and duration of treatment is longer than for isotretinoin. They are contraindicated in pregnancy because of the risk of feminisation of a male fetus.

Vitamin A derivatives

Isotretinoin is a synthetic vitamin A derivative that inhibits sebaceous gland activity and is comedolytic and anti-inflammatory.[8] In adequate doses, oral isotretinoin (Accure, Isohexal, Oratane, Roaccutane) can bring about long term remission of acne in 80% of patients. However, the dramatic therapeutic results seen with isotretinoin are in part counterbalanced by its side effects (Table 3).

Isotretinoin is teratogenic and pregnancy must be avoided throughout treatment and for one month after cessation of therapy. I always emphasise isotretinoin is believed to be teratogenic at every stage of fetal development. As a consequence, a serum pregnancy test is performed on all women of child-bearing age before therapy, which is initiated at the start of the next normal menstrual period.

Contraceptive measures should be discussed, even though the woman may not be in a sexual relationship when therapy with isotretinoin begins. Unlike vitamin A and etretinate, the other synthetic retinoid (which is used in the treatment of psoriasis and other disorders of keratinisation), isotretinoin is not stored within the liver and drug levels are usually undetectable two weeks after treatment ceases. Women wanting to conceive can do so as early as one month after completion of treatment.

Isotretinoin is metabolised by the liver and may cause mild liver dysfunction and elevation of hepatic enzymes. It may also cause hyperlipidaemia, which is dose related and reversible on cessation of treatment. The mechanism for this is an increased production of very low density lipoproteins, but small increases in triglyceride and cholesterol levels, and decreases in high density lipoprotein levels are also common.[9] Large increases in triglyceride levels have been recorded in individuals with pre-existing hypertriglyceridaemia.

Most dermatologists and physicians will recommend liver function tests and fasting lipid levels before starting treatment and repeat them after several weeks of treatment as a precautionary measure.

The average course of isotretinoin is five to six months. This medication is reserved for use in severe, treatment-resistant cystic acne and its prescription is limited to dermatologists and specialist physicians.

Conclusion

Today, we are in a position to control and cure acne, one of the most socially incapacitating and the most common of dermatological disorders. The medical practitioner must determine which therapeutic agents best suit the needs of the patient and must be prepared to change treatment that is not efficacious. MT

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