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ACNE

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Abstract: Acne is one of the most prevalent skin conditions affecting teenagers. It is a disease of the pilosebaceous unit. Blockage of sebaceous glands and colonisation with *Proionobacterium acnes* leads to acne. Grading the severity of acne helps to determine the appropriate treatment. Treatment of acne should be started as early as possible to minimise the risk of scarring and adverse psychological effects. It should be tailored to the individual patient, the type of acne, its severity, the patient's ability to use the treatment, and the psychological state. Topical agents are the mainstay for treatment of mild acne. Moderate acne is treated with oral antibiotics. Resistance to antibiotics may be reduced by subsequent use of non-antibiotic topical medications. Severe acne is treated with isotretinoin, and this can lead to permanent remission. With better education and care given by medical profession, acne treatment could be significantly improved.

Keywords: acne vulgaris, propionobacterium acnes, acne grading, acne treatment, acne psychological effects

Acne is one of the most prevalent skin conditions, affecting more than 85% of teenagers. It typically starts at puberty and resolves slowly as the person reaches 20, although some people continue to have acne into their 40s and 50s. It is seldom life threatening and is often dismissed as a self limiting condition. Little attention is given to it in either undergraduate or postgraduate education.[9]Despite its apparent cosmetic nature, its effects can go far deeper than the surface of the skin, and can place a heavy emotional and psychological burden on patients that may be far worse than the physical impact. The change in the skin's appearance may give rise to a changed body image that in turn is known to lead to anger, fear, shame, anxiety, depression, embarrassment, and bullying and stigmatisation within peer groups.Lack of confidence, social withdrawal, feelings of insecurity and inferiority, limited employment opportunities, functional and interpersonal difficulties at work, and suicidal tendencies have also been reported and attributed to the effects of acne.[9]The reduction in quality of life has been estimated to be as great as that associated with epilepsy, asthma, diabetes, or arthritis.

Aetiopathogenesis

Acne is a multifactorial disease: genetic factors, stress androgens, and excess sweating all influence its development and/or severity. Corticosteroids, oral contraceptives, iodides, bromides, lithium, and chemicals such as dioxins are known to induce acne eruptions, as are endocrine disorders such as Cushing's syndrome and polycystic ovary syndrome. It is often found that acne is worse in current smokers, but despite popular myth, diet, lack of exercise, lack of hygiene, greasy hair hanging over the face, and masturbation do not have any effect.

Acne is a disease of the pilosebaceous units in the skin. A changed keratinisation pattern in the hair follicle leads to blockage of sebum secretion. It is probable that hyperresponsiveness to the stimulation of sebocytes and follicular keratinocytes by

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androgens leads to the hyperplasia of sebaceous glands and seborrhea that characterise acne. The enlarged follicular lumen attributable to inspissated keratin and lipid debris forms a closed comedone (whitehead). When the follicle has a portal of entry at the skin, the semisolid mass protrudes forming a plug, producing an open comedone (blackhead).

Propionobacterium acnes colonises the follicular duct and proliferates, breaking down the sebum to triglycerides, irritants that probably contribute to the development of inflammation. When the follicular epithelium is invaded by lymphocytes it ruptures, releasing sebum, micro-organisms, and keratin into the dermis. Neutrophils, lymphocytes, and foreign body giant cells accumulate and produce the erythematous papules, pustules, and nodular swelling characteristic of inflammatory acne.

Clinical features

The clinical features of acne are a cluster of signs related to distended, inflamed, or scarred pilosebaceous units. Lesional polymorphism is the main feature, and is most commonly seen on the face, back, and the chest. Seborrhoea is the most frequently occurring feature. Distended pilosebaceous units can take the form of open or closed comedones, and the types of inflamed lesions exhibited are pustules, papules, nodules, and cysts. In more severe cases, multiple inflammatory papules and nodules fuse to form draining sinuses, which lead to chronic scarring and, rarely, malignant changes Post-inflammatory lesions may also occur and are represented by macular pigmentation and scars (hypertrophic, keloids, ice pick scars, depressed fibrotic and atrophic macules, perifollicular elastolysis).Post-inflammatory hyperpigmentation is commonly seen in pigmented skin.

Management of acne

Management should comprise safe treatment, reduction of the psychological burden through emotional and social support, and clarifying popular misconceptions about the disease.

Treatment should start as early as possible to minimise the risks of scarring or adverse psychological effects. It should be aimed at reducing non-inflammatory lesions that may be precursors to inflammatory lesions, improving existing inflammation, and lowering the *P acnes* population. Treatment must be tailored to the individual patient, the type of acne, its severity, the patient's ability to use the treatment, and their psychological state It is very important to emphasise to the patient from the outset that the treatment of acne is a long term affair. Advice on the use of cosmetics, moisturisers, sunscreens, and hair gels may be appropriate, as some formulations are greasy and could exacerbate existing acne or even cause acne-type lesions.

Treatment of mild acne

Topical preparations are the mainstay therapy, and their main action is the prevention of new lesions. Their effect is slow and treatment should be maintained to prevent recurrence. Topical agents are active only where and when they are applied, and should therefore be applied daily to all areas of the skin prone to acne.[1] Maintenance therapy is crucial to prevent recurrence.

The topical agents available are benzoyl peroxide, antibiotics, azelaic acid, or retinoids.

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Benzoyl peroxide is bactericidal for *P acne*s and improves both inflammatory and non-inflammatory lesions It is an oxidising agent that works by introducing oxygen into follicles, which then kills *P acnes*. Because of this mechanism of action, *P acnes* never develops resistance to benzoyl peroxide, however there can be adverse side effects such as irritant dermatitis and bleaching of hair, clothes, and linen.

Topical antibiotics such as clindamycin, tetracycline, and erythromycin are bacteriostatic for *P acnes* and are effective for mild to moderate inflammatory acne.

Topical retinoids such as tretinoin and adapalene correct abnormalities in follicular keratinocytes. They are effective in both the treatment of inflammatory lesions and in the prevention of the formation of comedones. They may also reduce inflammation by interfering with the interaction between toll-like receptor 2 and external products of *P acnes* on the surface of antigen presenting cells. In addition, topical retinoids improve the penetration of other topical medications and may also help to improve the hyperpigmentation that is left in dark skin types after the resolution of inflammatory lesion. The maximum therapeutic response to topical retinoids occurs over about 12 weeks. They may produce local irritation, increased sensitivity to sunlight, and exacerbation of inflammatory lesions.

Combined agents such as erythromycin/zinc, erythromycin/tretinoin, erythromycin/isotretinoin, erythromycin/benzoyl peroxide, and clindamycin/benzoyl peroxide are increasingly being used and are useful in reducing the development of antibacterial resistance in *P acnes*.

Most of these topical preparations are available in a variety of strengths and delivery systems. Drying agents (gels, washes, and solutions) are particularly suited to oily skin, whereas creams, lotions, and ointments are more suited to patients with dry, easily irritated skin.

Treatment of moderate acne

Oral antibiotics are the standard treatment for moderate acne and for cases where topical combinations are not tolerated or are ineffective. They have been shown to reduce the number of *P acnes* In addition to interfering with the growth and metabolism of propionobacteria, antibiotics have an anti-inflammatory activity by reducing and inhibiting cytokine production, affecting macrophage functions, and inhibiting neutrophil chemotaxis. The main systemic antibiotics used are erythromycin and different types of tetracyclines. They have a long history of verified efficacy in the management of inflammatory acne. Erythromycin (macrolide) should be reserved for cases where tetracyclines are not tolerated or are contraindicated: for example in pregnancy, when breast feeding, and in children below the age of 8–12 years.

First generation tetracyclines (tetracycline hydrochloride, oxytetracycline) or second generation tetracyclines (doxycycline, lymecycline, or minocycline) should be considered as first line oral antibiotic therapy. Tetracycline is inexpensive and is often effective in previously untreated cases, however gastrointestinal side effects and the need to take it on an empty stomach are disadvantageous.

One advantage of the second generation of tetracyclines relates to improved absorption that is unaffected by food. This may improve compliance when second generation tetracyclines are used, particularly for adolescents. Doxycycline is cleared by the liver, allowing this treatment to be used in patients with renal impairment.[51] Co-

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trimoxazole and trimethoprim have been used as third line agents in the treatment of acne when other systemic antibiotics are contraindicated or there is verified resistance to other agents.[51]

Table 1 outlines the optimum dose regimen, expense, incidence of bacterial resistance, and potential adverse effects. It is recommended to continue treatment for up to three months. If little response is seen after six weeks, the addition of a topical non-antibiotic medication or a switch to an alternative oral antibiotic should be considered.[52] After control of acne is achieved and maintained for at least two months, a reduction in the dose can be attempted. Eventual withdrawal is the goal, followed by long term topical therapy.

Table 1 Systemic antibiotics for the treatment of acne vulgaris (adapted from Layton)[51]

Drug	Dose	Comments regarding use	Incidence of acne resistance	Adverse effects
Oxytetracycline	500 mg twice daily	Inexpensive, take 30 minutes before food and not with milk	Moderate (20%)	Rare onycholysis, photosensitivity, benign intracranial hypertension
Erythromycin	500 mg twice daily	Inexpensive	High (>50%)	Gastrointestinal upset, nausea, diarrhoea all fairly common
Minocycline	100–200 mg daily	Expensive	Low (but has increased)	Headache (dose dependent), pigmentary changes, autoimmune hepatitis
Doxycycline	100–200 mg daily	Moderate cost	Moderate	Photosensitivity (dose dependent)
Lymecycline	300–600 mg daily	Moderate cost	As for tetracycline	Less than with minocycline
Trimethoprim	200–300 mg twice daily	Inexpensive	Low (12%)	Rare hepatic/renal toxicity, agranulocytosis.

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Resistance to antibiotics is a problem, and a large contributory factor has been their widespread inappropriate use (such as inadequate potency, inadequate duration of treatment, and/or poor compliance). This may cause therapeutic failure in some patients. However, as a result of a change in prescription policy the level of resistance has recently fallen. Guidelines for optimising oral antibiotic use and preventing the emergence of resistant strains is given in box 1. If resistance to tetracycline is suspected, switching to minocycline is recommended, as resistance to it is rare.

Box 1 Recommendations to limit antibacterial resistance of *P acnes* (adapted from Simpson, Tan, Cunliffe)[56,58,59]

- Avoid antibiotics if non-antibiotic agents such as benzoyl peroxide or retinoids are effective.
- Only continue antibiotics until the doctor and the patient agree there is no further improvement. Prescribe antibiotics for a maximum of six months.
- Use the same antibiotics if relapse occurs.
- Give antibiotics for a minimum of two months before changing because of poor therapeutic response.
- Avoid concomitant use of oral and topical antibiotics with chemically dissimilar properties to decrease development of resistance to both agents
- Use short intervening courses (5–7 days) of benzoyl peroxide to reduce/eliminate selected resistant propionobacteria.
- Use benzoyl peroxide in combination with topical and oral antibiotics. Use systemic isotretinoin if several antibiotics have been tried without success.
- Culture *P acnes* for antibiotic sensitivities.
- Educate patients on the importance of good adherence to the prescribed regimen and the importance of limiting exposure to antibiotics.

Hormonal therapy

This can be very effective in women irrespective of their serum androgen levels. Oral contraceptives may decrease free testosterone level, and the oestrogen component may decrease the production of ovarian androgens by suppressing the secretion of pituitary gonadotrophins. The adverse effects of oral contraceptives include nausea, breakthrough bleeding, weight gain, and breast tenderness. Available scientific

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evidence does not support the hypothesis that antibiotics lower the contraceptive efficacy of oral contraceptives. Anti-androgen therapy may be of use to treat acne in women, particularly those with deep seated nodules of the lower face and neck.A combination of cyproterone acetate and ethinyl oestradiol (Dianette) is often effective, but its effect may be delayed for three to six months.Side effects of cyproterone include menstrual abnormalities, breast tenderness, nausea, vomiting, fluid retention, headache, and melasma. Pregnancy should be avoided during therapy with cyproterone, because of potential for feminisation of the male fetus. Spironolactone in doses of 50–100 mg twice daily seems to reduce sebum production and improves acne. It acts as an androgen receptor blocker and inhibits 5-α reductase. There is a theoretical risk of carcinogenicity and is therefore used only rarely. The starting dose should be around 25–50 mg daily and, provided the patient does not experience breast tenderness or headaches, can be increased to the maximum of 200 mg. It can be combined with the oral contraceptive in sexually active women to avoid the risk of pregnancy and feminisation of the fetus.

Treatment of severe acne

Patients with severe acne that does not clear with combined oral and topical therapy are considered for treatment with oral isotretinoin.[1] Isotretinoin is a member of the retinoid class of compounds related to retinol (vitamin A). It is the only treatment that has an effect on all four of the major factors involved in the pathogenesis of acne and it is the only treatment that may lead to permanent remission.[11] It is also more cost effective than oral antibiotics. As it is a lipid soluble drug, its absorption is increased when given with food. Dose regimens vary from 0.1 mg/kg/day to 0.2 mg/kg/day. The recommended starting dose is 0.5 mg/kg/day, which is gradually increased according to side effects and clinical response. Box 2 shows indications for the use of isotretinoin.

Minor side effects of isotretinoin, such as dryness and soreness of eyes, skin, oral mucosa, nasal mucosa, muscle aches and pains, hypertriglyceridaemia, and impaired night vision are reversible upon reducing the dose or withdrawal of treatment. Mucocutaneous drying can be managed by emollients and false tears. Retinoid induced hyperlipidaemia occurs more frequently in patients with underlying predisposing factors such as obesity, alcoholism, diabetes, or familial hyperlipidaemia. Pre-treatment levels are not necessarily predictive of increased levels of triglycerides and cholesterol during retinoid treatment. The high levels can be managed at least partially by an appropriate diet and lipid lowering drugs.

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Table 2 Potential interactions of oral isotretinoin with other drugs (adapted from Layton)[51]

Drug	Effect
Alcohol	Heavy intake of alcohol reduces efficacy of oral isotretinoin and may increase risk of hepatotoxicity
Imidazole	Antifungal may increase blood levels of isotretinoin
Highly acidic drugs	Salicylic acid and indomethacin have a high affinity for albumin and may displace isotretinoin from leaving sites, leading to increase of drug concentration in the plasma.
Carbamazepine	Plasma level decrease when concurrent isotretinoin is taken
Oral tetracycline	Both isotretinoin and tetracycline can lead to raised intracranial pressure,
Vitamin A	Addictive toxic effects

Conclusions

Acne is an extremely common skin condition, and despite not directly endangering life it can have a devastating physical and psychological effect on the lives of vulnerable adolescents. Effective and safe treatments for acne are available, yet many do not consider it a problem worth treating. Treatment of acne should be started early to prevent scarring, and the most effective agent with the minimum risk of adverse effects should be chosen.There is widespread misjudgment of the condition in both the medical profession and the public. Dispelling misconceptions about acne, its causes, and availability and efficacy of treatment must start from medical school to prevent the continuing perpetration of misinformation throughout the community.The failure of patients to take medicine in a way that would lead to therapeutic benefit is an important problem Health education should ensure that patients have accurate information of the causes of acne and also that they have realistic expectations about the time frame and probable results of treatment. Better education and care given by medical staff and other professionals to patients is central to concordance, because it will allow them to treat themselves more effectively.

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