

Clinical review

Acne

Sarah Purdy, David de Berker

Acne is an easily treated cause of disfigurement and psychological morbidity. It affects more than 80% of people at some point in their life,¹ up to 14% of whom consult their general practitioner (GP) and 0.3% a dermatologist. About 3.5 million consultations with GPs occur in the United Kingdom annually for acne.^{w1} Morbidity can be high and associated with disfigurement, pain, loss of confidence, and impairment of normal social and workplace function, with documented effects on quality of life including depression, dysmorphobia, and even suicide.^{w2 w3}

What are the clinical features of acne?

In most cases it is not difficult to diagnose acne. It comprises a combination of papules, pustules, blackheads and whiteheads (open and closed comedones), nodules, and scarring. Background redness and greasy skin, known as seborrhoea, usually occur. It is important to avoid confusion with other conditions such as acne rosacea (box 1). Treatment with systemic corticosteroids can cause steroid induced acne, and the use of anabolic steroids can cause “bodybuilders acne.” Potent topical steroid treatment can cause perioral or periorbital dermatitis with papules and pustules. Pustular drug eruptions and bacterial and fungal folliculitis can also resemble acne but can be distinguished by the absence of comedones.

Typically, acne persists over years. Nodules can be more painful, more unsightly, and carry a greater risk of scarring than more superficial disease. In acne conglobata, nodules are widespread with interconnecting channels containing haemorrhagic, purulent exudate. When this evolves rapidly with fever, arthritis, and neutrophilia it is called acne fulminans.

Postinflammatory pigmentation can last months and occasionally years, especially in patients with dark skin. The upper chest and shoulders may develop hypertrophic or keloid scarring for 12 months or more. Atrophic or “ice pick” scars are typically found on the face. Small depressions and mild discoloration may last for six to 12 months, but usually settle.

Grading of acne is useful for recording the progress of disease or making treatment decisions.² As a basic tool in clinical practice it is worth noting the presence or absence of the diagnostic components and their severity with a three point scale. Nodules, scarring (including keloids), and psychosocial burden are particularly important to note.

Summary points

Acne is a common condition that can have a profound effect on the physical, psychological, and social wellbeing of patients

In general, treatment should be assessed after six weeks and, if beneficial, should usually be continued for at least four to six months

Start with topical treatment for mild acne; progress to a topical antibiotic or combined preparation if resistant to over the counter products

For moderate acne that fails to respond to topical treatment, try an oral antibiotic—usually a once daily tetracycline (not minocycline) supplemented with a topical non-antibiotic (such as benzoyl peroxide) if needed

Consider an oral contraceptive in women—use a product that does not contain norethisterone

Refer patients with moderate to severe acne that fails to respond to preliminary treatment, or those who present with aggressive painful disfiguring acne, for consideration of isotretinoin

What is the pathophysiology?

Acne is an inflammatory disease of the pilosebaceous unit that is typically most active for two to three years in mid-adolescence. Box 2 shows relevant factors.

What genetic factors are involved?

A recent study found that twins with acne were significantly more likely to have a family history of at least one non-twin sibling with acne, one or both parents with acne, and at least one child with acne compared with twins without acne.³ The same study concluded that 81% of the variance in acne was attributable to genetics and only 19% to environmental or unique factors. For some women, acne is a manifestation of

Academic Unit of Primary Health Care, University of Bristol, Bristol BS6 6JL

Sarah Purdy
senior clinical research fellow and general practitioner

Bristol Dermatology Centre, Bristol Royal Infirmary, Bristol BS2 8HW
David de Berker
consultant dermatologist

Correspondence to: S Purdy
sarah.purdy@bristol.ac.uk

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Extra references are on bmj.com

Box 1 Differences between acne vulgaris and acne rosacea

Acne vulgaris

- Peak prevalence in mid to late teens
- Papules, pustules, comedones, and nodules
- Scarring
- Improves in sunshine
- Can affect chest and back

Acne rosacea

- Peak prevalence in patients aged 40-70
- Papules, pustules, redness, and blepharitis
- Soft tissue overgrowth in the form of rhinophyma
- May be exacerbated by sunshine
- Usually limited to the head

Box 2 Factors in the pathophysiology of acne

- Increased production of sebum manifested as greasy skin
- Proliferation of commensal bacteria, especially *Propionibacterium acnes*, in part connected with increased production of sebum
- Blockage of the follicular opening due to hyperkeratosis of epithelium in the follicular canal, which is the basis for comedone formation
- An inflammatory reaction to commensal bacteria and hyperkeratosis
- In women, increased androgen values may be relevant, especially in association with polycystic ovary disease

polycystic ovary syndrome and appears to be a polygenic disease closely allied to family history.⁴

Who gets acne and when do patients grow out of it?

In a sample of adolescents in New Zealand, acne was present in 91% of males and 79% of females.⁴ Up to

30% of teenagers have acne of sufficient severity to require medical treatment,⁵ and it is the presenting complaint in 3.1% of people aged 13-25 years attending GP surgeries.⁶ Peak incidence is at 17—most patients get better in their 20s, 10% (7-17%) have acne after 25,⁷ and a few (1% of men and 5% women) still get it in their 40s.⁸ In younger women, about 25% get acne around the time of their period.^{w5}

How should acne be managed?

The aim of treatment is to reduce the presence and impact of symptoms, including psychosocial sequelae.⁹ Treatment needs to be continued for at least six weeks before changing or adding other treatments.

Is it to do with diet?

Obesity, insulin resistance, hyperandrogenism, and acne may be associated. A common belief is that diet is important,^{w6} but in the few studies that have been undertaken, no specific foods (including fatty foods and chocolate) have been identified as causative factors.^{10 w7}

How should I treat it?

Topical treatments

Topical treatments are useful in mild to moderate acne (table 1). Treatment should be assessed after six weeks and, if beneficial, should usually be continued for at least four to six months.

Benzoyl peroxide is a cheap and effective treatment for acne. It has antimicrobial, anti-comedonal, and anti-inflammatory effects.⁵ A recent randomised controlled trial (RCT) found that it had similar effectiveness to oral oxytetracycline and minocycline in mild acne. It was unaffected by bacterial resistance and was the most cost effective treatment studied.¹³ Lower concentrations (2.5% and 5%) seem to be as effective as higher concentrations (10%), with less local irritation. It helps to start with a low strength and increase it gradually. Reducing frequency of application or temporarily discontinuing treatment helps with irritation.

Azelaic acid has similar properties to benzoyl peroxide. It also may cause irritation, which can be helped by reducing the frequency of application or temporarily discontinuing treatment.

Topical antibiotics

The topical antibiotics clindamycin and erythromycin are effective against inflammatory lesions; topical preparations of tetracycline are also effective (table 2).⁹ Topical antibacterials can produce mild irritation of the skin and on rare occasions cause sensitisation.

Topical retinoids

The topical retinoids—tretinoin, isotretinoin, and the retinoid like drug, adapalene—are useful in treating inflammatory and non-inflammatory lesions in mild to moderate acne (table 3).⁹ Several months of treatment may be needed to achieve an optimal response, and treatment should be continued until no new lesions develop.

Topical retinoids are contraindicated in pregnancy. Women of child bearing age should take adequate contraceptive precautions.

Table 1 Topical treatments for acne

| Drug | Effectiveness | Level of evidence | Side effects |
|------------------|---------------------------------------------------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Benzoyl peroxide | Reduces non-inflammatory and inflammatory lesions | 2 systematic reviews, ^{11 12} 1 randomised controlled trial ¹³ | Local irritation, itching, stinging, burning, dryness, scaling, and erythema. Bleaches hair and fabrics |
| Azelaic acid | Reduces non-inflammatory and inflammatory lesions | 2 randomised controlled trials ^{w19 w20} | Local irritation, itching, stinging, burning, scaling, and erythema. Photosensitisation |

Table 2 Topical antibiotics used in acne

| Drug | Effectiveness | Evidence | Side effects |
|-------------------------------------|---------------------------------------------------|---------------------------------------------|----------------------------------------------------|
| Clindamycin | Reduces inflammatory lesions | 2 systematic reviews ^{11 12} | Local irritation |
| Erythromycin | Reduces inflammatory lesions | 2 systematic reviews ^{11 12} | No important adverse effects reported |
| Erythromycin plus zinc | Reduces non-inflammatory and inflammatory lesions | 1 systematic review ¹² | Local irritation, visible on skin |
| Erythromycin plus benzoyl peroxide* | Reduces non-inflammatory and inflammatory lesions | 1 randomised controlled trial ¹³ | Local irritation, may bleach clothing |
| Tetracycline | Reduces severity of acne | 1 systematic review ¹² | Skin discoloration, fluorescence in disco lighting |

*Some experts do not recommend combinations of antibiotics and benzoyl peroxide as degradation of the antibiotic by the benzoyl peroxide makes them unstable.⁵

Sources and selection criteria

We updated and expanded a previous search (June 2005).⁹ We also searched the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, and Medline. We used the keywords acne together with diagnosis, microbiology, pathology, drug therapy, therapy, laser, phototherapy, blue light, scarring, isotretinoin, genetics, inheritance, and grading. We also searched our personal archives of references and consulted with colleagues who are experts in acne.

Topical combinations

A recent RCT found combinations of topical erythromycin and benzoyl peroxide generally as effective as oral oxytetracycline and minocycline in mild acne, without the systemic side effects or problem of tetracycline resistance (table 2).¹³ Other combinations of antibiotics and antibacterial agents exist, and combinations of topical retinoid and antibiotic are also available. Combination products may be more convenient for patients to use as they reduce the numbers of products and applications required and thus may increase compliance. However, they are generally more expensive than single products.

Oral antibiotics

Oral antibiotics are useful for treating inflammatory acne if topical treatment is not effective (table 4). Treatment for non-inflammatory lesions may also be required (for example, topical retinoids). Improvement usually occurs after about six weeks. Treatment should be reviewed every four to six months.

No oral antibiotic has been shown to be more effective than others,^{12 14} but not all will work equally well for individual patients. Clinical experience indicates that some patients respond better to one antibiotic than another, and alternatives should be tried if the response diminishes over time or no response is seen after six weeks. Given the adverse effects of minocycline it is best avoided.¹⁴

Table 3 Topical retinoids used in acne

| Drug | Effectiveness | Evidence | Side effects |
|--------------|---------------------------------------------------|----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tretinoin | Reduces non-inflammatory and inflammatory lesions | 1 systematic review ¹² | Local irritation, erythema, dryness, soreness, peeling, burning, and pruritis. Avoid in severe acne that affects large areas, broken or peeling skin, and mucous membranes. Avoid ultraviolet light exposure. Possibly teratogenic |
| Isotretinoin | Reduces non-inflammatory and inflammatory lesions | 1 systematic review ¹² | As above |
| Adapalene | Reduces non-inflammatory and inflammatory lesions | 1 randomised controlled trial ^{w21} | As above |

Antibacterial resistance

Recent research has shown an increase in the prevalence of resistance of *Propionibacterium acnes* to antibiotics over the past 15 years. One UK study showed that in 1991 34.5% of patients with acne had strains of *P acnes* resistant to one or more antibiotic, but by 1997 this had risen to 64%.^{w8} The clinical relevance of antibiotic resistance is not always clear.¹⁵ However, one recent study showed a link between resistance and reduced effectiveness of oral tetracyclines.¹³

Contraceptive pills and cyproterone acetate

A recent systematic review looked at the combined oral contraceptive pill for the treatment of facial acne in women.¹⁶ Use of the pill reduces inflammatory and non-inflammatory facial lesions, the severity of acne, and patient's self assessment of acne. No evidence is available on the effectiveness of the pill compared with other treatments for acne or on the comparative effectiveness of different contraceptive pills, including those containing cyproterone acetate (such as Dianette).¹⁶ A general rule is to avoid pills containing norethisterone because of its androgenic properties. Pills containing cyproterone acetate may carry a higher risk of venous thromboembolism.^{w9} A full discussion of the adverse effects of contraceptive pills is beyond the scope of this review.

Oral retinoids

Oral isotretinoin is a synthetic form of vitamin A. It is effective in severe acne when standard treatment has

Table 4 Oral antibiotics used for treating acne

| Drug | Effectiveness | Evidence for effectiveness v placebo | Evidence for effectiveness v other oral antibiotics | Side effects |
|-----------------|---------------------------------------------------|---------------------------------------|---------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Erythromycin | Little evidence, clinically beneficial | No RCTs* | =Doxycycline (1 RCT) ^{w22} ; =tetracycline (1 RCT) ^{w23} | Nausea, vomiting, and diarrhoea. May cause failure of oral contraceptives |
| Doxycycline | Reduces inflammatory and non-inflammatory lesions | 1 RCT ^{w24} | =Erythromycin (1 RCT) ^{w22} ; =oxytetracycline (1 RCT) ^{w25} | See footnote† |
| Lymecycline | Little research evidence, clinically beneficial | No RCTs* | =Minocycline (1 systematic review) ¹⁴ | See footnote† |
| Oxytetracycline | Little research evidence, clinically beneficial | No RCTs* | =Doxycycline (1 RCT) ^{w25} | See footnote† |
| Minocycline | Little research evidence, clinically beneficial | No RCTs ^{*14} | =Doxycycline, lymecycline, tetracycline (1 systematic review) ¹⁴ | Can cause irreversible pigmentation. Associated with a higher risk of liver damage and systemic lupus erythematosus than the other tetracyclines ^{†14} |
| Tetracycline | Reduces severity of acne | 2 systematic reviews ^{11 12} | =Minocycline (systematic review) ¹⁴ ; =erythromycin (1 RCT) ^{w23} | See footnote† |

RCT=randomised controlled trial.

*Evidence of effectiveness based on comparative or non-placebo controlled RCTs.

†Oral tetracyclines may harm developing bones and teeth and should not be taken in pregnancy or when breastfeeding. They should not be prescribed to children under 12. They may cause failure of oral contraceptives in the first few weeks of treatment. Other adverse effects include nausea, vomiting, diarrhoea, dysphagia, and oesophageal irritation. Rare side effects include hepatotoxicity, pancreatitis, blood disorders, photosensitivity and hypersensitivity reactions, and benign intracranial hypertension. Tetracyclines should be used with caution in patients with myasthenia gravis, hepatic problems, or renal impairment. Tetracyclines interact with a wide range of other drugs. Many indigestion remedies reduce the absorption of tetracyclines. Milk reduces the absorption of oxytetracycline and tetracycline.

Tips for non-specialists

- When a patient visits you about acne offer active treatment rather than advise them to “wait and see”
- Benzoyl peroxide is effective but must be used with care and understanding of the side effects—start with a low strength and increase the frequency of application and strength slowly
- When using oral antibiotics, use a generic once daily tetracycline (not minocycline) for six weeks in the first instance
- When referring to secondary care, make sure any details of mood problems, psychiatric history, or social isolation are included

Additional educational resources**Clinical resources:**

Harper JC, Fulton J Jr. Acne vulgaris. eMedicine (www.emedicine.com/DERM/topic2.htm)

Prodigy Knowledge (www.prodigy.nhs.uk/acne_vulgaris)—Guidance for doctors

Clinical Evidence (www.clinicalevidence.com/ceweb/conditions/skd/1714/1714.jsp)—Clinical evidence from systematic reviews on treatment for acne vulgaris

Skin Disorders Specialist Library (<http://www.library.nhs.uk/skin>)—Evidence based information on all aspects of skin disorders, including their treatment and management and the impact they have on patients

British Association of Dermatologists. Clinical guidelines. Advice on the safe introduction and continued use of isotretinoin in acne (www.bad.org.uk/healthcare/guidelines/acne.asp)

National Institute for Health and Clinical Excellence. Obsessive compulsive disorder: core interventions in the treatment of obsessive compulsive disorder and body dysmorphic disorder. NICE clinical guideline, November 2005 (www.nice.org.uk/page.aspx?o=cg31)

Information for patients

<http://www.bad.org.uk/patients/leaflets/acne.asp>

Prodigy Knowledge (www.prodigy.nhs.uk/patient_information/pils/by_condition/skin_and_nails)—Good patient information leaflets with a brief summary of the condition and treatment options

New Zealand Dermatological Society. (www.dermnet.org.nz/acne/acne-vulgaris.html)

NHS Best Treatments (www.besttreatments.co.uk/btuk/conditions/1000216872.jsp)

Acne Support Group (www.m2w3.com/acne/ and www.stopspots.org)

failed, especially when active scarring exists. Available trials indicate its superiority over standard oral antibiotic and combinations of an oral antibiotic and a topical agent, such as azelaic acid, in severe nodular acne.^{w10-w12} Benefits are not always permanent, however, and up to 20% of patients need further courses.^{w13}

The drug has important side effects including cracked lips, nose bleeds, dry skin, and deranged liver function and lipid values. It appears that isotretinoin can cause mood disturbance, and can rarely lead to suicidal behaviour. No studies incontrovertibly link the drug with detrimental mood disturbance or suicide, however, and some data suggest mood benefits for patients, possibly because of the improvement in their acne.^{w17-w14} Patients should be counselled about mood swings and closely monitored during treatment, particularly those living alone or with a history of depression or violent behaviour. In patients with psychiatric disease, particularly those taking lithium, it is advisable to consult the relevant clinician before starting treatment. Lithium aggravates acne and some

patients may stop the drug, exacerbating their mental health problems.

Another area of concern is teratogenesis. Complex prescribing regulations exist for women of child bearing potential in the UK. Patients must undergo a “pregnancy prevention programme” including two forms of contraception, monthly outpatient visits with pregnancy tests before dispensing treatment, and a pregnancy test after completing treatment.

Laser therapy and phototherapy of inflammatory acne

A range of laser or laser-like treatments, not available in the UK’s health service, have been trialled in inflammatory acne. Most trials are small and the duration of benefit is not clear.^{w15-w17} Rigorous trials of “blue light” are also lacking and low energy laser light sources have shown no benefit.^{w18}

How can I manage scarring?

The active management of scarring requires the acne to be under control, if not completely settled. In the short term, shallow depressions and alteration of pigment can be concealed and will diminish or settle completely in the following year. No RCTs have found evidence for the benefits of facial peels or abrasion. A Cochrane review did not support laser resurfacing as a form of treatment for scarring,¹⁸ but a substantial number of practitioners and patients feel these treatments are helpful. Side effects include infection, discoloration, and scarring. In laser treatment, peeling is achieved by a controlled laser burn to the superficial dermis. A variety of surgical techniques are available that may help focal deep scars.

What advice and counselling should be given?

Patients should understand how to use their treatment and be aware of potential adverse effects. This is particularly important for topical agents that have an exfoliant or inflammatory effect. The likely time scale for improvement and duration of treatment should be

A patient’s perspective

I was affected by acne for at least three years. I am now 16. My back was plagued with pustular, inflamed papules. This was a problem because when it came to carrying anything on my back—like a backpack—my back would sweat, itch, and eventually bleed so that my clothes became bloodstained. My general practitioner prescribed benzoyl benzoate and antibiotics. The benzoyl benzoate bleached my clothes to the extent that I got fed up with using it. The oxytetracycline required me to be starved and this proved too difficult to integrate into my lifestyle. I was given minocycline for one year which didn’t work. I was then referred to a dermatologist who prescribed Roaccutane for about six months. I had various side effects including a dry mouth and cracked lips. I got round these problems by drinking a lot and carrying a pot of Vaseline around with me. My acne didn’t improve noticeably during the treatment, but soon after finishing treatment my skin started to look healthier and less inflamed. One month on, my back has improved greatly and no new spots are appearing.

Box 3 Referral guidelines

Patients should be referred to a specialist service if they have:

- A severe variant such as fulminating acne with systemic symptoms (acne fulminans)—needs urgent referral
- Severe acne or painful, deep nodules or cysts (nodulocystic acne) and could benefit from oral isotretinoin—needs to be seen soon
- Severe social or psychological problems, including a morbid fear of deformity (dysmorphobia)—needs to be seen soon
- A risk of (or are developing) scarring, despite treatment in primary care
- Moderate acne that has failed to respond to treatment, which should include several courses of topical and systemic treatment over at least six months. Failure should be based upon a subjective assessment by the patient
- A suspected underlying endocrinological cause (such as polycystic ovary syndrome) that needs assessment

explained—at least six weeks, possibly longer. Although benefit is often seen sooner, it is important that late responders do not give up.

Clinicians, including specialist nurses, have an important role in counselling and supporting patients

Box 4 How should a GP treat acne?**General points**

- Ensure that the diagnosis is acne vulgaris
- Advise patients to avoid picking, which leads to trauma, secondary infection, and scarring
- Advise patients to wash to control greasy skin, but not to the level of causing irritation
- Advise patients to avoid comedogenic moisturisers
- Document severity to aid treatment decisions and monitor progress
- Treatment should be assessed after six weeks and, if beneficial, should usually be continued for at least four to six months

Mild acne

- Start with topical treatments, such as benzoyl peroxide
- Progress to topical antibiotics or a combined preparation if resistant to over the counter products

Moderate acne

Patients with moderate acne that fails to respond to topical treatment

- Oral antibiotics—usually once daily tetracycline (for example, lymecycline, not minocycline)
- If necessary supplement with a topical non-antibiotic, such as a topical retinoid
- Consider an oral contraceptive in women. Use a product that does not contain norethisterone, such as Yasmin or Dianette

Severe acne

Patients with moderate to severe acne that fails to respond to preliminary treatments, or those who present with aggressive, painful, disfiguring acne

- Refer for consideration of isotretinoin

with acne. Acne can affect employment prospects and social life, resulting in stress and other psychological effects.¹⁹ Acne usually develops in teenagers, so doctors should be sensitive to the health needs of this group and offer appropriate and accessible care. Sources of patient information and support include the Acne Support Group.

Referral for specialist care

Most patients with acne can be managed in primary care, but referral to a dermatologist is indicated in some situations. Consensus guidelines have been produced by the National Institute for Health and Clinical Excellence (box 3).²⁰

How should GPs treat acne?

Given the wide range of treatments available for acne and the current supporting evidence, how should a GP or other generalist clinician manage patients with acne? We have set out some guidance in box 4.

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