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Postadolescent acne in women

Increasing numbers of women worldwide continue to have acne after adolescence or may even develop it in their twenties to forties. It is important to recognise these patients because they may have underlying hormonal abnormalities and may benefit from hormonal therapy.

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Acne vulgaris is a common, self-limiting disorder affecting adolescents and teenagers. Acne may, however, continue or develop after the age of 20 years, and may even persist until menopause.

Women with acne fall into two subtypes: those with postadolescent acne that persists from teenage years into later life and those with late-onset acne who develop pimples at or after the age of 20 years and who have not had acne during their teens. It is important to recognise these patients as a distinct group because:

- the number of women affected worldwide is increasing
- the psychosocial effects of acne in this group may be profound and disproportionate to the severity of acne – many women find that their acne affects their working life or professional careers (such as when having to give office presentations or deal with clients)
- some women may have abnormal serum androgen levels that require further investigation
- these patients typically respond well to hormonal therapy alone or as an adjunct to other acne therapy, even in the presence of normal laboratory investigations.

Acne, hormones and the sebaceous gland

Acne is a complex multifactorial disorder. Its pathogenesis involves:

- abnormal keratinisation of the pilosebaceous opening
- increased sebum production by the sebaceous gland
- colonisation by *Propionibacterium acnes*
- inflammation.

Blockage of the sebaceous duct by abnormal

IN SUMMARY

- **Female postadolescent acne may continue past the teenage years or develop at or after the age of 20 years.**
- **Affected women may have normal or raised serum androgen levels.**
- **Polycystic ovary syndrome may be an underlying cause of female postadolescent acne.**
- **Assessment should include a menstrual history and examination for clinical signs of hyperandrogenism, such as hirsutism.**
- **Hormonal therapy (usually the combined oral contraceptive pill) is an effective adjunct in the management of these patients, including those with normal serum androgen profiles. Other antiandrogens, such as spironolactone or cyproterone acetate, may need to be taken in addition to the pill.**

Table 1. History checklist for postadolescent acne

- Age of onset of acne – during teens or later?
- Distribution of acne lesions – 'T zone' or 'hormonal' (affecting lower face and neck)?
- Duration of acne lesions – weeks rather than days
- Characteristics of acne lesions – recurrence in same area, tenderness, greasy skin
- Menstrual history – irregular periods, premenstrual exacerbation of acne
- Symptoms of hyperandrogenism – deepening voice, increased libido, hirsutism, male-pattern baldness
- Family history
- Lifestyle factors – make-up, sports headgear
- General medical history, including medication use – e.g. phenytoin, lithium

keratinisation produces a microscopic plug, the microcomedo. Colonisation of the pilosebaceous duct by the bacterium *P. acnes* contributes to an inflammatory response that manifests as papules, pustules and inflammatory cysts. Effective acne management involves targeting these steps; often combination therapy is used to target as many pathogenic factors as possible.

Sebaceous glands are found throughout the body and are present in greatest quantity and density on the face. They secrete sebum in response to androgenic stimulation. In general, patients with acne produce more sebum than those without acne, and sebum production is greater in those with more severe acne.

Under normal conditions, the ovaries contribute about 50% of the circulating androgens in women. Overproduction of androgens by the ovaries can occur in conditions such as polycystic ovary syndrome (PCOS) or ovarian tumours. The adrenal glands contribute the remaining 50% or so of circulating androgens in women. Stress may be a trigger by increasing adrenal androgen production that then stimulates increased sebum production.

Detailed discussion of PCOS and other hormonal causes of acne, such as ovarian tumours or congenital adrenal hyperplasia, are beyond the scope of this article, as is also steroid ingestion as a cause.

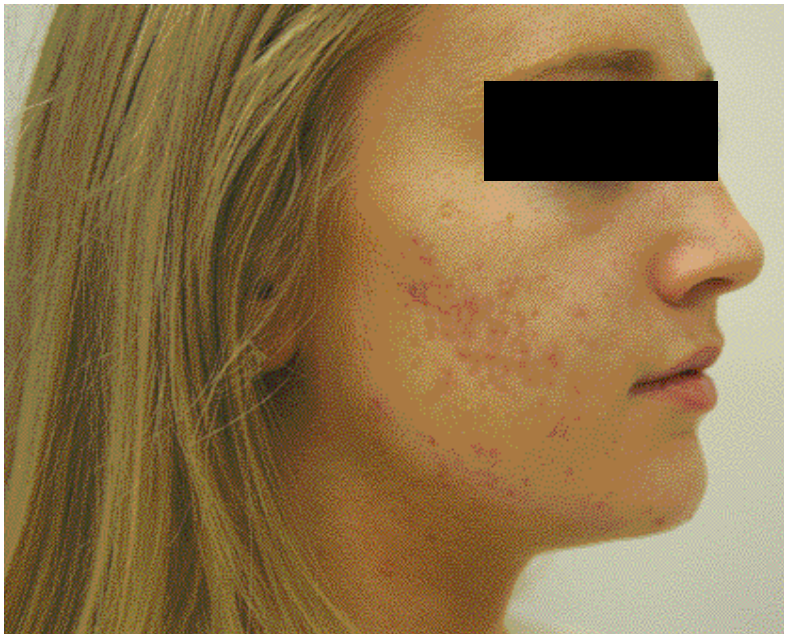

Figure 1. Postadolescent acne. In this patient the distribution of the lesions is similar to that in adolescent acne although the forehead and nose parts of the 'T zone' are relatively spared and most of the lesions are on the cheek.

Recognising postadolescent acne

History

The clinical history of a woman with acne should include enquiry about the factors discussed below and summarised in Table 1.

Age of onset

At what age did pimples start?

Some patients have acne that started with the onset of menstruation (i.e. when they were in their teens) while other patients develop acne when they are in their twenties or older.

Distribution of acne lesions

Where did the pimples start or spread to?

In some patients, the clinical pattern of postadolescent acne may look indistinguishable from teenage 'T zone' acne, which affects the forehead, nose and chin with or without upper chest and upper back involvement (Figure 1). In other patients, there is a more 'hormonal' distribution, with the lower third of the face being affected, particularly the lower cheeks, jawline, chin and neck (Figure 2). The trunk may also be affected and most patients will note seborrhoea or a greasy skin.

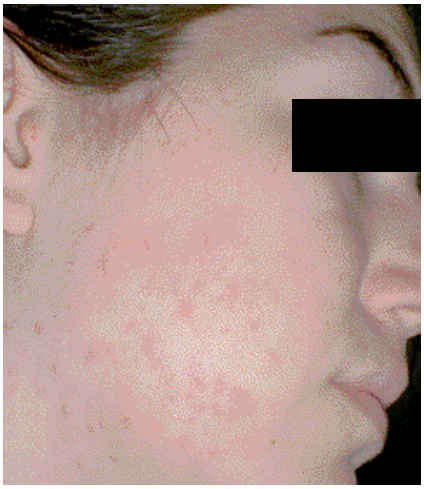

Figure 2. Postadolescent acne. Note the typical 'hormonal' distribution of lesions for late-onset acne: on the lower cheeks, jawline, chin and neck.

Duration of acne lesions

How long do the individual lesions last?

Patients may complain that their current acne lesions tend to last longer than lesions that occurred during adolescence – for weeks rather than days.

Characteristics of acne lesions

Do the pimples recur in the same area?
Are there any symptoms?

Patients often report that their pimples are tender or feel 'blind'. Some describe their face as hurting. The lesions may last for weeks, heal and then recur weeks or months later in the same area. There may be postinflammatory redness or pigmentation lasting for weeks or months as the lesions are resolving, and this is often very distressing for the patient. The inflammatory and chronic nature of these pimples may also lead to scarring (Figure 3).

Menstrual history

Is there any correlation of the pimples with the menstrual cycle?

It is common for the pimples to start a week prior to menses and continue for one to two weeks. Some patients will notice pimple activity at ovulation.

A careful menstrual history is important in the assessment of a woman who has late-onset acne. About 60 to 70% of women may complain of worsening of their acne on a cyclical basis, usually premenstrually. An irregular menstrual cycle may suggest underlying hyperandrogenism and the presence of PCOS. It may be worthwhile for the patient to chart her menstrual cycle because patients often assume their cycle is regular. Menstrual irregularity is defined as amenorrhoea for more than three months or irregularity of the menstrual cycle of greater than seven days from a standard 28-day cycle over three consecutive cycles.

Hyperandrogenism

Are there features of hyperandrogenism other than menstrual irregularity?

Features of hyperandrogenism other than menstrual irregularity may need specific enquiry; these features are listed in Table 2. Hirsutism may not be readily evident because patients may have had hair removed by a variety of means, such as waxing, electrolysis or laser. Mild hirsutism and irregular menstrual cycles have been reported in up to 29% and 14%, respectively, of these women.[1]

Obesity, hirsutism and irregular menstrual cycles are features of PCOS but are not always present in women with the syndrome. Data are conflicting regarding the number of women with postadolescent acne who have underlying PCOS; figures range between 10 and 50%.[2] Although it is beyond the scope of this article to discuss the diagnosis and management of PCOS, it should be noted that the diagnosis can be difficult in some cases because there are no universally accepted diagnostic criteria for PCOS.[3]

Family history

Do the patient's mother or sisters have acne?

One study has shown that 50% of patients had a first-degree relative who also had postadolescent acne.[1]

Lifestyle factors

Are there lifestyle factors that may promote or exacerbate acne?

Many patients report flares of acne when they are feeling increased stress. Creamy or 'greasy' cosmetics may promote plugging of the pilosebaceous follicle opening and are comedogenic. Some patients may be in occupations where heat may play a role, such as working in kitchens.

Friction or trauma due to occlusive headgear (such as worn in cycling, rollerblading or softball) may rupture existing comedones and bring about inflammatory lesions.

General medical history

What is the general health of the patient?

Certain drugs taken for coexisting medical problem may exacerbate acne. Phenytoin and lithium are examples.

Examination

Postadolescent acne may be clinically indistinguishable from adolescent acne. The examination should focus on:

- the distribution of lesions – lower cheeks, jawline, chin, neck, trunk
- the severity – nodules, cysts, scarring
- any psychological distress – how does the patient feel, does it stop her from doing any activity?
- features of hyperandrogenism – especially hirsutism or androgenic alopecia.

Late-onset acne typically localises to the lower third of the face, especially the lower cheeks, jawline, chin and neck. This is in contrast to adolescent acne, which is often midfacial in distribution – in the 'T zone' (i.e. forehead, nose and cheeks). Features of hyperandrogenism should be looked for (Table 2). Although there is often a typical 'hormonal' distribution, the pattern may be the same as teenage acne so the two types cannot always be differentiated by the distribution of the lesions.

Investigations

Although laboratory investigations are not

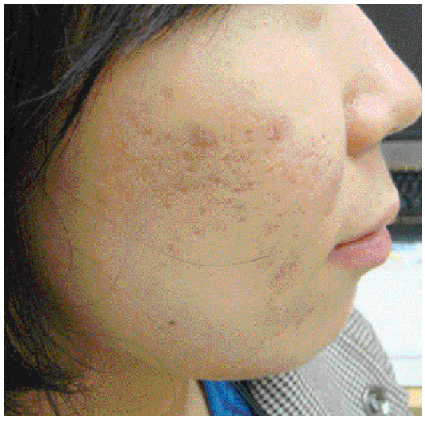

Figure 3. Acne scars from the inflammatory form of postadolescent acne.

indicated for most patients with pimples, hormonal investigations are appropriate for women with postadolescent acne, irregular menstrual cycles or evidence of androgenism such as hirsutism.

A basic screening test for androgenic abnormalities should include serum free testosterone, dehydroepiandrosterone sulfate (DHEA-S), sex-hormone binding globulin and the ratio of luteinising hormone (LH) to follicle-stimulating hormone (FSH). Elevated levels of free testosterone suggest hyperandrogenism but do not identify the source. Increased levels of DHEA-S suggest an adrenal cause and may be due to congenital adrenal hyperplasia or, rarely, an adrenal tumour. Elevated levels of testosterone with an increased LH to FSH ratio (greater than 2 to 3) are consistent with PCOS. The interpretation of serum androgen profiles is summarised in Table 3.

Frequently, both the ovaries and the adrenals are implicated in androgen overproduction in women with late-onset acne. Blood samples should be obtained in the early follicular phase (days one to seven) of the menstrual cycle where possible, and patients on oral contraceptives should discontinue their medication for one month before testing.

Depending on clinical circumstances, other investigations may be indicated. These include serum fasting glucose and lipids, prolactin, androstenedione and 17α-hydroxyprogesterone, and also pelvic ultrasound to detect polycystic ovaries. Patients with PCOS often have insulin resistance and are at increased risk of developing diabetes mellitus and cardiovascular disease. Referral to an endocrinologist or gynaecologist may be indicated. Patients may also benefit from weight reduction or possibly a low glycaemic index diet, and so a dietitian may also provide expert advice.

Compared with women of the same age without acne, women with postadolescent acne tend to have higher plasma levels of free androgens, often at high normal levels. It is important to appreciate, however, that the serum androgen measurements may be normal in many patients with postadolescent acne; this may reflect errors in sampling, contraceptive therapy or the end-organ response to androgens.

Sebaceous glands have a range of enzymes capable of metabolising androgens to more potent forms. For example, dihydroxytestosterone is converted to testosterone by type 1 5α-reductase in acne-prone follicles. The local concentrations of androgen levels due to metabolism and/or end-organ hyper-responsiveness may be more significant in regulating sebum production than are the levels of circulating androgens. This is important to explain to patients because they often cannot understand why hormonal treatments are prescribed in the presence of a 'normal' hormonal assay.

Table 2. Features of hyperandrogenism

- Male-pattern baldness
- Hirsutism
- Increased libido
- Acanthosis nigricans
- Deepening of the voice
- Menstrual irregularities
- Insulin resistance

Table 3. Guidelines for interpreting serum androgen profiles

Test result	Possible diagnosis
DHEA-S	
• Above 20 µmol/L	Adrenal tumour
• 10 to 20 µmol/L	Congenital adrenal hyperplasia
Total testosterone	
• 5 to 7 nmol/L	Ovarian tumour
• Mild elevations (below about 5 nmol/L)	Polycystic ovary syndrome
LH:FSH greater than 2 to 3	Polycystic ovary syndrome

ABBREVIATIONS: DHEA-S = dehydroepiandrosterone sulfate; LH:FSH = luteinising hormone to follicle-stimulating hormone ratio.

Management

General advice and counselling

Excessive washing and the use of antibacterial soaps and scrubs are not necessary for the cleansing of acne-affected skin, and may irritate the skin. Gentle cleansing using an oil-free soapless cleanser is appropriate, particularly for those women who have sensitive skin, while a foaming cleanser may be more appealing to those who have very oily skin. General measures include using oil-free sunscreens, make-up and moisturisers.

Educating and counselling patients regarding their acne is vital. Myths regarding acne (such as 'poor hygiene' as a cause) should be dispelled. Patient expectations about treatments should be clarified because it may take up to three months before significant improvements are observed. Patients may need reassurance because they may have had acne for a long time or be resistant to previously tried conventional treatments. They may therefore be quite frustrated by the time they seek your help. Encouragement during this period is helpful to promote compliance. Combination topical and oral therapy is often required.

Women with PCOS may have abnormal lipid profiles and are at increased risk of type 2 diabetes. Lifestyle modifications, including weight reduction measures and exercise, are recommended for these patients.[4] As previously mentioned, a team approach involving also a dietician, gynaecologist or endocrinologist may be required.

The therapeutic options for acne are summarised in Table 4.[5]

Topical agents

Topical salicylic acid (2% wash), glycolic acid, azelaic acid (15% gel) and benzoyl peroxide (2.5, 5 and 10% gels and 4, 5 and 10% creams) preparations are keratolytic and reduce comedone formation. (Glycolic acid is an alpha hydroxy acid [AHA] that has beneficial effects on oily skin and acne as well as on general skin condition. It is not TGA approved for use in treating acne but is contained, along with other AHAs, in many cosmetic products.)

The topical antibiotic preparations of use in the treatment of acne include clindamycin 1% lotion or gel and erythromycin 2% gel. Both these agents may be used in pregnant women, but as they may be secreted in breast milk their use should be avoided during lactation. They are particularly helpful in inflammatory acne. The newer combination therapies such as clindamycin 1% and benzoyl peroxide 5% may also be helpful.

Topical tretinoin, isotretinoin and tazarotene are vitamin A analogues (retinoids) that act mainly as keratolytic agents. Tretinoin is available as a 0.01% gel and as 0.025, 0.05 and 0.1% creams, isotretinoin as a 0.05% gel and tazarotene as a 0.1% cream. They should be applied at night. Patients should be advised about their side effects – irritation and photosensitivity (tazarotene has a higher irritant tendency than the others). These agents should be avoided in pregnancy.

Adapalene is a third-generation topical retinoid that is photostable and does not cause photosensitivity and therefore may be applied during the daytime; it is available as a 0.1% cream or gel. A combination topical retinoid treatment is available – adapalene 0.1% and benzoyl peroxide 2.5%; it should be applied once daily.

Systemic antibiotics

Oral antibiotic therapy is effective for inflammatory acne and suppresses acne until spontaneous clearing occurs. Doxycycline 50 to 100 mg daily and minocycline 50 to 100 mg daily are usually used as first-line antibiotics. Erythromycin 250 to 500 mg twice daily (or erythromycin ethyl succinate 400 to 800 mg twice daily) and trimethoprim 800 mg plus sulfamethoxazole 160 mg once or twice daily are considered second-line antibiotic choices.

Ideally, oral antibiotics should only be used for a maximum of three months at a time in order to minimise potential antibiotic resistance. If longer courses are required then the antibiotic should be used in combination with benzoyl peroxide or there should be a break of one to two weeks between three-month oral antibiotic courses during which benzoyl peroxide is used. Systemic antibiotics are, therefore, not an ideal option for long-term therapy, which is often needed for hormonal acne.

Table 4. Therapeutic options in postadolescent acne[5]

Topical agents

Keratolytics
- Azelaic acid 15% (gel)
- Benzoyl peroxide 2 to 10% (cream, gel)
- Glycolic acid
- Salicylic acid 2% (wash)

Topical antibiotics
- Clindamycin 1% (gel, lotion)
- Clindamycin 1% and benzoyl peroxide 5% combination (gel)
- Erythromycin 2% (gel)

Topical retinoids
- Adapalene 0.1% (cream, gel)
- Adapalene 0.1% and benzoyl peroxide 2.5% combination (gel)
- Isotretinoin 0.05% (gel)
- Tazarotene 0.1% (cream)
- Tretinoin 0.01% (gel), 0.025%, 0.05%, 0.1% (cream)

Oral agents

Systemic antibiotics

First line
- Doxycycline 50 to 100 mg daily
- Minocycline 50 to 100 mg daily (if doxycycline not tolerated)

Second line
- Erythromycin 250 to 500 mg twice daily
- Trimethoprim 800 mg plus sulfamethoxazole 160 mg, once or twice daily

Systemic retinoid
- Isotretinoin

Hormonal agents
- Combined oral contraceptives:
  - ethinyloestradiol/cyproterone acetate
  - ethinyloestradiol/desogestrel
  - ethinyloestradiol/dienogest
  - ethinyloestradiol/drospirenone
  - ethinyloestradiol/gestodene
- Cyproterone acetate
- Glucocorticoids:
  - dexamethasone
  - prednisolone
- Spironolactone

Oral isotretinoin

Women who have nodulocystic lesions or scarring acne should be referred to a dermatologist for treatment with oral isotretinoin. Oral isotretinoin reduces comedogenesis, reduces sebum secretion and is anti-inflammatory.

Counselling is essential with respect to contraception and the risk of birth defects while on systemic retinoid medication. Pretreatment investigations include serum lipid levels, a serum pregnancy test and liver function tests; liver function tests should be monitored during therapy.

Although patients with hormonal acne respond well to isotretinoin, they may relapse when their treatment courses are over because of the underlying hormonal stimulation of the oil glands. Although for some patients the use of low-dose or even intermittent oral isotretinoin will bring their pimples under control, oral isotretinoin should be considered a treatment option for refractory cases.

If acne tends to recur quickly after a course of isotretinoin then antiandrogen hormonal therapy such as the oral contraceptive should be considered as maintenance treatment.

Hormonal therapy

Hormonal therapy, usually with the oral contraceptive, is very effective in women who have postadolescent acne with or without elevated serum androgens.[6] Such therapy reduces sebum production by decreasing androgenic stimulation of the sebaceous gland. It may be used in combination with other antiacne therapies.

Hormonal therapy for postadolescent acne in women is indicated:

- in those with ovarian, adrenal or peripheral hyperandrogenism
- in those with PCOS
- for moderate to severe acne unresponsive to other therapy
- when there is relapse after multiple courses of antibiotics
- when there is quick relapse after a course of isotretinoin
- as an alternative to repeated courses of isotretinoin.

The therapeutic effect of hormonal therapy is slow, and patients should be warned not to expect noticeable improvement for three months. Therapy should be continued for at least 12 months. Relapses are not uncommon when hormonal therapy is ceased.

Combined oral contraceptives

The oestrogenic component of the combined oral contraceptive pill suppresses ovarian production of androgens and stimulates the production of sex-hormone binding globulin, thus reducing free testosterone levels. This has a benefit in acne because the oil glands are exposed to less androgenic stimulus.

Although all combined oral contraceptives are effective in acne because of the oestrogenic component, those containing androgenic progestins such as norgestrel and levonorgestrel are theoretically less effective.

Preparations containing low-androgenic progestins such as desogestrel or gestodene are considered helpful antiacne contraceptives. For many years, the 'gold standard' has been the combination of ethinyloestradiol 35 μg and cyproterone acetate 2 mg. However, other antiacne pills have been introduced recently, such as the combinations ethinyloestradiol 30 μg and dienogest 20 mg, ethinyloestradiol 30 μg and drospirenone 3 mg, and ethinyloestradiol 20 μg and drospirenone 3 mg.

Side effects of hormonal therapy include nausea, breast tenderness, weight gain and headache. A small increase in the risk of breast cancer has been suggested by epidemiological studies and this should be discussed with the patient, along with other relative contraindications.

Mention should also be made of the several long-term benefits of oral contraceptive therapy, which include reduced risks of ovarian and uterine cancers.[7]

Appropriate patient selection and counselling are required with the use of the oral contraceptive. (Although this article is about postadolescent acne, hormonal therapy is also appropriate for female adolescents with acne; however, oral contraceptive therapy should be avoided before puberty because of the risk of accelerated epiphyseal closure.)

The efficacy of oral contraceptives in acne is due largely to the oestrogenic component. Progestin-only pills and implants are therefore unsuitable as antiacne therapies, and some patients using these have noted a worsening of their acne. Patients should be warned that acne improvement may be slow (taking at least three months) and that treatment is long term (at least one year). Combination treatment may give improved efficacy: if the acne has not improved significantly after three to six months of oral contraceptive therapy then an androgen receptor antagonist such as cyproterone acetate or spironolactone can be added.

Cyproterone acetate

Cyproterone acetate is an antiandrogenic progestin that acts by both inhibiting ovulation and blocking the androgen receptor. The previously mentioned combination of cyproterone acetate 2 mg and ethinyloestradiol 35 μg is very effective for the treatment of acne in women with mild to moderate hyperandrogenism.

Cyproterone acetate is also available as a single agent in 10- and 50-mg tablets, and can be prescribed in addition to a combined oral contraceptive preparation containing it, or indeed any other combined oral contraceptive. The dose of cyproterone acetate can therefore be increased if the acne is unresponsive to an ethinyloestradiol and cyproterone acetate oral contraceptive. For example, 50 mg of cyproterone acetate may be added to the first 10 days of a cycle of a ethinyloestradiol 35 μg and cyproterone acetate 2 mg combined oral contraceptive (or other combined oral contraceptive), starting with the first active pill. Alternatively, 10 mg

of cyproterone acetate can be added to the first 15 days of the pill cycle. In postmenopausal women or those who have undergone hysterectomy, 50 mg of cyproterone acetate may be added to the entire active cycle (21 days) of therapy with an ethinyloestradiol and cyproterone acetate-containing oral contraceptive.

Improvement can be seen in 75 to 90% of women with acne who are treated with cyproterone acetate 50 to 100 mg per day. Oestrogen is necessary in these regimens because cyproterone acetate has strong antioestrogenic effects.

Side effects of cyproterone acetate therapy include menstrual abnormalities, breast tenderness and enlargement, mood changes, headache, nausea, melasma and fluid retention.

Glucocorticoids

If a woman's hyperandrogenism is due to an adrenal disorder, low-dose prednisolone (2.5 mg daily) or dexamethasone (0.25 mg daily) can be used to suppress adrenal production of androgens. Long-term use of these agents poses a risk of adrenal cortisol suppression, and patients should be monitored for this with periodic adrenocorticotropic hormone (ACTH) stimulation tests.

Spironolactone

Spironolactone is useful for women who are intolerant to oestrogens, have a contraindication to oestrogen therapy or do not wish to use oral contraceptives. Spironolactone acts as a competitive androgen receptor antagonist and as an inhibitor of 5α-reductase and is effective in doses of 50 to 200 mg daily. Using it as monotherapy at low doses of 25 to 50 mg may improve acne and not alter the menstrual cycle. If higher daily doses are required, it is often combined with the oral contraceptive so that the menstrual cycle is kept regular. Treatment may be prolonged (six months or more), but dosages may be reduced once an adequate clinical response is achieved.

Dose-dependent side effects of spironolactone therapy include menstrual irregularities, breast tenderness, hyperkalaemia, headache, dizziness, drowsiness and hypotension. Side effects may be minimised if therapy is started with a low dose of 25 to 50 mg daily. As an antiandrogen, spironolactone may cause feminisation of a male fetus, and therefore patients should not become pregnant while on the medication. Although monitoring of blood pressure and serum electrolytes may be required in some patients, most young, healthy patients show no abnormalities in their blood pressure and do not require laboratory tests.

Conclusion

Women with postadolescent acne are a relatively common presentation in general practice. Assessment of such patients should include identifying the presence of hyperandrogenism and possible underlying causes. Hormonal agents such as the combined oral contraceptive are effective treatments and may be combined with other acne therapies such as topical agents and/or oral antibiotics. MT

References

1. Goulden V, Clark SM, Cunliffe WJ. Post-adolescent acne: a review of clinical features. Br J Dermatol 1997; 136: 66-70.
2. Betti R, Bencini PL, Lodi A, Urbani CE, Chiarelli G, Crosti C. Incidence of polycystic ovaries in patients with late-onset or persistent acne: hormonal reports. Dermatologica 1990; 181: 109-111.
3. Legro RS. Polycystic ovary syndrome: the new millenium. Mol Cell Endocrinol 2001; 184: 87-93.
4. Norman RJ, Davies MJ, Lord J, Moran LJ. The role of lifestyle modification in polycystic ovary syndrome. Trends Endocrinol Metab 2002; 13: 251-257.
5. Dermatology Expert Group. Therapeutic guidelines: dermatology. Version 3. Melbourne: Therapeutic Guidelines Ltd; 2009.
6. Beylot C, Doutre MS, Beylot-Barry M. Oral contraceptives and cyproterone acetate in female acne treatment. Dermatology 1998; 196: 148-152.
7. Schlesselman JJ. Net effect of oral contraceptive use on the risk of cancer in women in the United States. Obstet Gynecol 1995; 85: 793-801.

Further reading

George R, Clarke S, Thiboutoto D. Hormonal therapy for acne. Semin Cutan Med Surg 2008; 27: 188-196.

Knaggs HE, Wood EJ, Rizer RL, Mills OH. Post-adolescent acne. Int J Cosmetic Sci 2004; 26: 129-138.

Williams C, Layton AM. Persistent acne in women. Am J Clin Dermatol 2006; 7: 281-290.

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