ACNE VULGARIS.
GRADES OF SEVERITY AND TREATMENT OPTIONS

W. K. Jacyh, MD
Department of Dermatology, University of Pretoria

Introduction

Acne is the most common skin condition treated by dermatologists. Acne is a polymorphic disease exhibiting a number of diverse lesions: comedones, papules, pustules, nodules, cysts, sinuses and scars. Despite this diversity, acne can be reduced to a two-stage sequence of events. Firstly an abnormal hypercornification and desquamation in the infundibular segment of the pilosebaceous unit (the infundibulum is the part of the hair follicle from the orifice of the sebaceous gland duct to the opening on the surface) leads to the formation of a comedo, initially without an inflammatory component; and later an inflammatory reaction results in disorganisation of the epithelial capsule.

AETIOLOGY

There are four major aetiological factors involved in the pathogenesis of acne:

- ductal hypercornification
- increased sebum production under androgen control
- abnormal microbial activity in the pilosebaceous duct (colonisation with Propionibacterium acnes)
- inflammation

Proliferation of P. acnes within the occluded environment of comedo is associated with release of neutrophil and lymphocyte chemo-attractants which leads to the accumulation of these cells within the follicular epithelium and perifollicular infiltrate. Propionibacterium acnes activates complement and stimulates the release of several cytokines (Interleukin-1, IL-8, TNF-α). The clinical presentation of acne in an individual patient reflects which of the above listed factors takes the upper hand. In some patients, non-inflammatory lesions in the form of closed and open comedones (white- and blackheads) predominate, in others, inflammatory lesions, papules, pustules, nodules, cysts, drainage sinuses form the picture. In the majority of patients, both types of lesions occur.

For treatment purposes, the classification of acne into mild, moderate and severe is sufficient. It is necessary to determine whether the condition is mainly comedonal, non-inflammatory or inflammatory, or a mixture of both types of lesions. Patients with mainly comedonal acne should be treated with a topical agent with significant comedolytic activity.

Retinoids, compounds chemically related to vitamin A normalise follicular hypercornification and loosen the comedones. They also have anti-inflammatory action. Retinoic acid (tretinoin) is the prototype retinoid. It is available in RSA as 0.05% cream and 0.025% gel. In the early stages of treatment with this agent skin irritation may occur. In some patients an eruption of pustules may appear within the first week of treatment. It reflects the elimination of previously invisible comedones. Patients should be informed that this is a favourable event.

Patients undergoing local treatment with retinoic acid should avoid prolonged sun exposure and no other topical treatment should simultaneously be

<table>
<thead>
<tr>
<th>Table 1: International Acne Treatment Algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I (Mild)</td>
</tr>
<tr>
<td>Topical Retinoids</td>
</tr>
<tr>
<td>Benzoyl peroxide or topical antibiotic</td>
</tr>
<tr>
<td>Oral antibiotic</td>
</tr>
<tr>
<td>Hormonal therapy</td>
</tr>
</tbody>
</table>

For treatment purposes, the classification of acne into mild, moderate and severe is sufficient. More elaborate scoring systems based on counting of different acne lesions are used for assessment of efficacy of medications in clinical trials requiring statistical validity. Acne is considered mild when there are mainly non-inflammatory lesions and only a few superficial inflammatory lesions. In severe acne, there are deep inflammatory lesions resulting in scarring. What lies between is called moderate acne. The therapeutic approach would depend on the type of the prevalent lesion, the extent of the involvement and the response to previous treatments.

Table 1 — International Acne Treatment Algorithm provides the recommendations for the treatment of acne depending on the severity. It is the consensus of opinions expressed during the 9th Congress of European Academy of Dermatology and Venereology in Geneva in 2002. Figures 1 to 3 demonstrate mild, moderate and severe acne.

MILD ACNE

In cases of mild acne, topical treatment is usually sufficient. It is necessary to
used. The response is usually slow and several weeks are needed for a marked improvement. Topical isotreinoin (0.05% gel, Isotrex) seems equal to retinoic acid in mild-to-moderate non-inflammatory acne and is less irritant. Retinoic acid should be applied once daily at bedtime; isotreinoin may be applied twice daily.

Adapalene (0.1% gel and cream, Differin) has been shown to have more pronounced anti-inflammatory action than retinoic acid. It appears to be better tolerated than retinoic acid. Adapalene should be applied once daily at bedtime.

Tazarotene (0.05% gel, Zorak), the newest of topical retinoids developed for the treatment of psoriasis, is also effective in acne but irritates the skin. The previous three retinoids appear superior in the management of acne.

In patients with predominance of inflammatory lesions, benzoyl peroxide and topical antibiotics are used. Benzoyl peroxide is used in both inflammatory lesions and comedones and has antimicrobial action. Propionibacterium acne does not become resistant to it. Benzoyl peroxide is available in two concentrations (5% and 10%) in various formulations. Benzoyl peroxide tends to irritate and dry the skin, particularly in fair-skinned individuals. It is advisable to start with a 5% concentration and to increase it to 10% if the response is not satisfactory. As benzoyl peroxide is available over the counter many patients have already tried it before consulting a physician.

Topical antibiotics act by suppressing P. acnes. Topical erythromycin and clindamycin are used in 1% to 4% solutions and lotions. Resistance of P. acnes to erythromycin has been reported from several countries (especially in those receiving oral erythromycin). Development of resistance can be lessened by concomitant use of benzoyl peroxide.

Preparations containing a combination of benzoyl peroxide and erythromycin (Benzamycin gel) and zinc acetate and erythromycin (Zineryt lotion) are available. Azelaic acid (15% cream, Skinoren) is of benefit in both inflammatory and comedonal acne. Azelaic acid works slowly and may irritate the skin.

**MODERATE ACNE**

In patients with moderate acne, topical treatment is aided by usage of systemic antibiotics and, in women, by hormonal therapy. For acne with a greater inflammatory component, it is prudent to also introduce benzoyl peroxide or topical antibiotics along with the topical retin-
resistance of P. acnes to erythromycin, time limit and not to linger on for many months. One has to be prescribed. Six months is my limit to prescribe antibiotics. Doxycycline and minocycline daily versus 1-2 g daily of tetracycline. Doxycycline and minocycline absorption is less affected by dairy products than absorption of tetracycline. However, minocycline is not any longer considered very safe. Side effects are not common but when they occur, some are serious - hepatitis, acute eosinophilic pneumonia, lupus erythematosus, hepato renal syndrome - all have been described. My choice is, at the moment, 100-200 mg of doxycycline and minocycline daily versus 1-2 g daily of tetracycline. Improvement in inflammatory lesions is usually noticed after 6 to 8 weeks and the dose may then be reduced. If there is no satisfactory effect within 4 to 6 months, another antibiotic may be tried or preferably isotretinoin prescribed. Six months is my limit to continue antibiotics. One has to have a time limit and not to linger on for many months.

Warn the patient about photosensitivity, particularly those on a dose above 1.0 g daily.

As there is growing evidence of greater clearance.

Who to treat with isotretinoin?

- Severe nodulocystic acne
- Moderate acne not responding after 4-5 months of oral antibiotics in adequate dose
- acne with marked scarring
- severe dysmorphophobia and depression resulting from acne

The standard dose is between 0.5 to 1.0 mg/kg/day. Doses higher than 1.0 mg/kg/day cause more adverse effects without real additional evidence of greater clearance.
Being a lipid soluble compound, isotretinoin is better absorbed when administered with food.

At the moment, I usually do not start the treatment at doses higher than 0.5 mg/kg/day, increasing the dose if needed. Starting with this lower dose minimises and even often prevents flares that not infrequently accompany the inception of treatment.

The cumulative dose is of paramount importance, much more than the daily dose. The cumulative total dose of 120 to 150 mg/kg is required. The minimum of 120 mg/kg can be obtained by either giving 1.0 mg/kg/day for 4 months or a lower dose for a longer period of time.

I attempt to give every patient this 120 mg/kg minimum. Financial constraints do not always make this feasible.

Extensive clinical experience confirms that adherence to the adequate cumulative dose provides a near complete clearance after a single course of therapy and prevents relapses in the vast majority of patients.

There are small subsets of patients responding slower or having more frequent recurrences. Very young men with predominantly truncal lesions and women with hormonal dysfunction may require greater cumulative doses obtained by lengthening the treatment period. Repeated courses of isotretinoin can be instituted. There are no hard data on the long-term safety of multiple courses. However, long term sequelae were not observed even when patients had as many as five courses of treatment. Slow response is often observed in patients with macrocomedones.

Patients with macrocomedones are also prone to initial therapy flares. It is important to examine the skin prior to treatment for the presence of macrocomedones (macro - a comedo bigger than 1 mm in diameter, mainly an open comedo).

If macrocomedones are present, it is recommended to start with a low dose of 0.25 mg/kg/day and to increase the dose slowly. Macrocomedones can be removed with light cautery preceded by 90 to 120 minutes of topical anaesthetic (EMLA). Side effects of isotretinoin, though numerous, are mostly trivial. Dryness of the face, lips, eyes and nares is experienced by all patients. In time these tend to lessen. Moisturisers should be used freely. Sunscreens are required throughout the treatment.

Teratogenicity of isotretinoin is well known and pregnancy must be avoided. A negative pregnancy test before prescribing isotretinoin is recommended. Sexually active women must use a reliable method of contraception during the treatment and for four weeks after its discontinuation.

There are three significant isotretinoin toxicities: triglyceride elevation, decreased night vision and pseudotumour cerebri. Mild elevation of triglycerides is common. Patients showing marked rise in triglycerides at the 4 to 8 week visit should have triglyceride assessment done every month during their course of isotretinoin.

Decreased night vision does occur. Alert the patient to this symptom.

SA Fam Pract 2003;45(9)
Pseudotumour cerebri or benign intracranial hypertension may be caused not only by isotretinoin but also by tetracyclines. Concurrent use of tetracyclines and isotretinoin is not recommended.

**Laboratory monitoring**
The manufacturer advises frequent laboratory testing. Most physicians perform pretreatment baseline tests and another test at 4 to 8 weeks. If values are normal further tests are not done.

Which tests? The utility of lipid assessment is clear. The rationale behind liver function testing is not so obvious. Transient and mild elevation of liver enzymes occurs during isotretinoin intake while the more severe signs of liver toxicity are exceedingly rare. In South Africa, isotretinoin is not recommended for patients with porphyria variegata (not uncommon in teenagers of Afrikaner lineage) though little is known about the effect of retinoids on liver function in these patients.

**Isotretinoids and depression**
This is the topic of hectic recent debate. Depression is not rare in teenagers and the question arises whether it is related to isotretinoin. When significant depression occurs in patients on isotretinoin, the drug should be discontinued.

**ACNE IN AFRICAN PATIENTS**
Acne appears to be more or less equally prevalent among patients of African and European descent. However, the clinical presentation and course and, most importantly, the long-term sequelae of acne can be different. In general, acne in Africans is milder, seldom with severe inflammatory, nodulocystic lesions, less often truncal.

**Figure 4:** Acne in an African patient. Mainly papular inflammatory lesions, postinflammatory hyperpigmentation.

**Figure 5:** Acne in an African patient. Postinflammatory hyperpigmentation prevails.

The most striking feature of acne in Africans is postinflammatory hyperpigmentation. These pigmentary changes often cause more concern than active acne lesions, and unlike European patients, Africans often seek dermatological care for this secondary problem. In general, the acne therapies effective in European patients are equally effective in African patients though few studies have been carried out in exclusively black populations.

The ideal acne treatment for African patients should specifically target the inflammatory process resulting in hyperpigmentation. The recent study conducted in South Africa demonstrating that 0.1% adapalene gel was effective in reducing both the active lesions and acne associated hyperpigmentation requires confirmation on larger clinical material.

**Figures 4 and 5** show the most common presentation of acne in African patients.

**References:**

**So precious, so scarce. Something everybody wants, but nobody has enough of.**

However, depending on how important it is for you, you will find the time to do certain things and neglect others. Basically, it boils down to your priorities.

As a general practitioner, what should then be important enough for you to spend your time on? Friends? Maybe. Family? Of course. Your patients? Without a doubt.

Because the Department of Family Medicine at the University of Pretoria understands the importance of time and the need for continuous education, we provide you with flexible learning possibilities. Through our distance-learning course, you will be able to study in your own time and at your own pace. Staying abreast of new developments in your profession is necessary and by following our flexible programme, you will not only be able to provide a better service to your patients and fulfil your CPD requirements, but you will save time too.

Enrol for our Postgraduate Diploma in Family Medicine