Acne and its management

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Abstract

Acne vulgaris is quite common during adolescence but also occurs in children, adults and pregnant women. It is a condition in which androgens are produced during puberty and induce hypertrophy of the sebaceous glands and the excess secretory rate in predisposed individuals, triggers acne. Sebum promotes the growth of a resident anaerobic bacterium on the skin, *Propionibacterium acnes* (*P. acnes*). Acne affects areas of the skin with large numbers of sebaceous glands. Treatment of acne can be done topically with retinoids, azelaic acid, benzoyl peroxide or topical antibacterials or systemically with oral antibacterials, hormonal therapies or isotretinoin. The pharmacist plays a particularly important role in educating patients about correct skin care products and medications used to treat acne, especially in women of child-bearing age.

Keywords: acne, acne vulgaris, azelaic acid, benzoyl peroxide, clindamycin, contraceptives, erythromycin, isotretinoin, oral, spironolactone, retinoids, teratogenicity, tetracycline

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Introduction

A literature review was undertaken using PubMed, Science Direct and internet sources to compile this article. Keywords such as "acne", "management of acne", "causes of acne", "*P. acnes*", "isotretinoin", "benzyl peroxide", "retinoids", "azelaic acid" and "acne vulgaris" were used as well as other articles selected and studied.

The role of the pharmacist in the management of acne cannot be underestimated. The role of the pharmacist not only commences when a prescription is received and needs to be dispensed, but also results in the supplying of advice to the patient as to when the medications(s) need to be taken; how they need to be taken; which side-effects can be expected and when referral is needed.

Acne is very common in adolescence and while it regresses in the late teens or early twenties, half of those affected continue to experience symptoms into adult life. Acne affects 80% of people at some point between 11 and 30 years of age. During adolescence, acne is more common in male than in female patients.[1] Acne affects areas of the skin with large numbers of sebaceous glands, especially in the face, neck, back and chest. It has a genetic component, which determines the rate of sebum production, particularly in response to androgens.

Sex hormones and metabolic hormones seem to play a role in the development and severity of acne. For example, elevated dehydroepiandrosterone (DHEAS), dihydrotestosterone (DHT), and insulin-like growth factor 1 (IGF-1) positively correlate with increasing acne lesion counts in women and androstenedione and DHEAS in men.[2]

The various hormones possibly implicated in acne and their proposed mechanisms are summarised below:[3]

- *Androgens* (testosterone, DHT, DHEAS) increase the size and secretion of sebaceous glands. Sources of circulating androgens include the adrenal glands, ovaries, or testes. Androgens can also be produced locally within the sebaceous gland; for example, testosterone can be converted to DHT by the type 1, 5-α-reductase of the sebaceous gland.
- *Oestrogens* counter the action of androgens by three potential mechanisms: direct opposition locally, inhibition of androgen production in the gonads via feedback loop, or by gene regulation.
- *Growth hormone* and *growth factors* – growth hormone stimulates production of growth factors such as IGF-1, both of which are secreted in high levels during puberty, when acne is at its peak incidence. In some tissues, possibly including sebaceous glands, the action of IGF-1 is influenced by androgens.
- *Melanocortins* (melanocyte-stimulating hormone, adrenocorticotrophic hormone [ACTH]) regulate sebum production.
- Through unknown mechanisms.

Androgens are produced during puberty and induce hypertrophy of the sebaceous glands and the excess secretory rate in predisposed individuals triggers acne, however, acne can also be triggered using anabolic steroids. A small number of other causes have been implicated in the pathogenesis of acne. These include cosmetic agents and hair pomades, medications (corticosteroids, lithium, iodides), hyperandrogenism and mechanical occlusion with headbands, shoulder pads and backpacks.[1] In women, acne can be a manifestation of polycystic ovarian syndrome, while smoking and a diet rich in dairy products or with a high glycaemic load, increase the risk for the development of acne.[4]

Increased sebum production in a response to androgenic stimulation distends the pilosebaceous glands. Proliferation of keratinocytes causes hyperkeratosis at the mount of the follicle, which blocks the duct and produces a small closed papule (comedo) called a whitehead. If this duct opens, compacted follicular cells and oxidised melanin at the tip give comedones the appearance of a blackhead.[5,6]

Sebum promotes the growth of a resident anaerobic bacterium

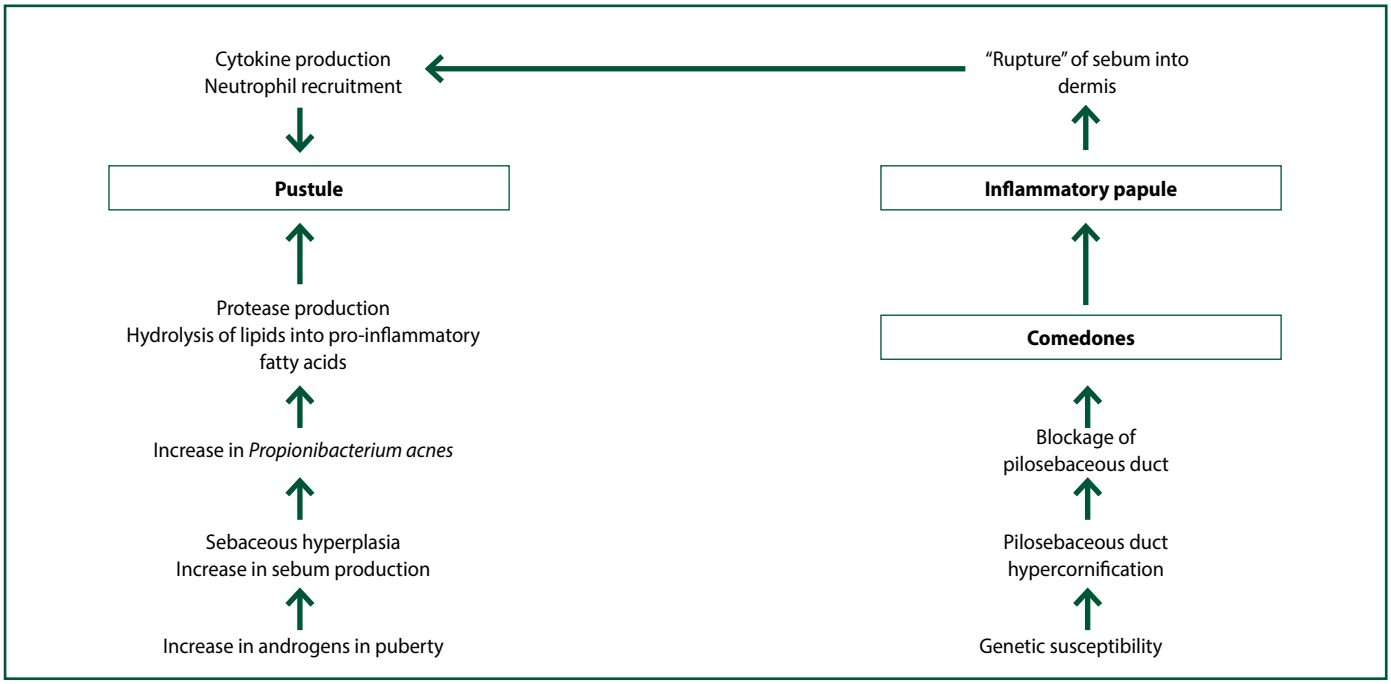

Figure 1: Pathophysiology of acne vulgaris[7]

on the skin, *Propionibacterium acnes* (*P. acnes*), which degrades triglycerides in sebum to free fatty acids and glycerol. *P. acnes* also release chemotactic factors and inflammatory mediators, which trigger an inflammatory response by activation of toll-like receptors and the induction of pro-inflammatory cytokines.[7] The combination of released mediators with the irritant free fatty acids produces inflammatory lesions (papules, pustules and nodules),[5,6] which coalesce to form multilocular cysts. These inflammatory lesions can scar, leaving permanent disfigurement. The pathophysiology of acne vulgaris can be seen in Figure 1. Release of elastase by activated neutrophils causes connective tissue damage and scarring. Post inflammatory hyperpigmentation is common in dark-skinned patients.

Mild acne is confined to the face and consists of papules and pustules with few inflammatory lesions. Moderate acne usually also involves the trunk and has increased numbers of inflammatory lesions, while severe acne presents with nodules and cysts which are widespread.[5]

Diagnosis is straight forward, and most patients will generally seek appropriate advice on correct product selection.

Acne exposome is defined as the sum of all environmental factors influencing the occurrence, duration and severity of acne. Exposome factors impact on the response and the frequency of relapse to treatments by interacting with the skin barrier, sebaceous gland, innate immunity, and cutaneous microbiota. They may be classified into the following six main categories: nutrition, psychological and lifestyle factors, occupational factors including cosmetics, as well as pollutants, medication and climatic factors.[8]

Nutrition

This first category is by far the most published acne exposome factor. Main food classes considered as triggering acne are dairy products (especially skim milk) and hyperglycaemic carbohydrates. An average regimen of dairy products has been reported impacting on acne, and one paper indicated that cow milk impacts on acne after drinking two glasses per day.[9,10]

Medication

The following androgenic progestins have been identified to cause or worsen acne: desogestrel and 3-cetodesogestrel, levonorgestrel, lynestrenol, norgestrienone, norethisterone, norgestrel, gestodene, norgestimate and etonogestrel. In contrast to this, chlormadinone acetate, dienogest, drospirenone and norgestimate oral contraceptive pills have been reported to be beneficial in the treatment of acne. Corticosteroids, halogens, isoniazid, lithium, vitamin B_{12}, immunosuppressants and certain anticancer agents and radiotherapy have been reported as causing acneiform eruptions.

Occupational factors, e.g. cosmetics; mechanical factors

The use of aggressive skin care regimens and inappropriate cosmetics may cause acne flare-ups. These products modify the skin barrier and the skin microbiota balance, especially in the sebaceous area, thus activating the innate immunity triggering inflammation.[8]

Mechanical factors comprising rubbing, scrubbing, the use of home devices or medical devices such as sonic brushes, derma rollers or micro needling systems may trigger acne flare-up.[11]

Pollutants, e.g. air, industrial and human-dependent pollutants

Air pollutants exert a harmful effect on the skin by increasing oxidative stress inducing severe alterations of the normal functions of lipids, deoxyribonucleic acid and/or proteins in the human skin.[12]

Acne has been frequently observed in industrial workers after

prolonged exposure to certain organic molecules, such as coal, tar, or crude oil.

Tobacco and cannabis use may be considered human-dependent pollutants which may play a role in acne.

Climatic conditions

Climatic conditions and seasonal variations resulting in a combination of heat, humidity and intensive ultra violet rays (UVR) may trigger inflammatory acne flare-up, which have been called acne tropicana, acne majorca or tropical acne.[13]

One of the major environmental factors affecting the skin is ultraviolet radiation. Both UVB and UVA have been reported to cause hyperplasia of the sebaceous gland, thickening of the stratum corneum, increase in sebum secretion and in the number of comedones.[14]

Psychosocial and lifestyle factors

Modern lifestyle, defined as stressful situations including urban noises, socioeconomic pressures and light exposure, may play a role in acne.[8]

Although acne is often considered a cosmetic problem, the condition can have a large impact on patients' psychosocial and physical well-being and may have a lifelong effect from disfiguring scars. The presence of acne correlates with various psychological factors such as depression, anxiety, anger, frustration, shame, low self-esteem, social isolation, and body dissatisfaction.

Patients with acne have been shown to have an increased risk of depression and suicide attempts, even when under treatment for depression. Among those with severe acne, the risk of suicidal ideation may be two to three times that of their unaffected peers. Behavioural signs such as poor eye contact, angry or negative verbalisation, poor self-care and personal hygiene, compulsive behaviours, or self-mutilating behaviours may also be considered a high risk. Patients with acne should be assessed for suicidal tendencies and depression, and anyone with concerning diagnosis should be appropriately referred.

Clinical features

Acne occurs in the face and upper trunk where the sebaceous glands are very dense, and the affected areas are greasy.

The five stages in the development of acne include the following:[15]

- Whiteheads
- Blackheads
- Papules
- Pustules

Table I: Global acne grading system[17]

Location (L)	Clinical assessment (A)	Local score	Global score
Forehead = 2	0 = no lesion	Local score = L times (x) A	0 = none
Right cheek = 2	1 = ≥ 1 comedon		1–18 = mild acne
Left cheek = 2	2 = ≥ 1 papule		19–30 = moderate acne
Nose = 1	3 = ≥ 1 pustule		31–38 = severe acne
Chin = 1	4 = ≥ 1 nodule		> 39 = very severe acne
Chest/upper back = 3			

Table II: South African grading severity,[18 adapted] symptoms and medication of choice

Grade	Symptoms/presentation	Medication of choice
Grade 1	Comedones only	Topical retinoids (adapalene, tretinoin or isotretinoin) **Alternatives:** Topical benzoyl peroxide, topical azelaic acid, comedo extraction for persistent, large comedones
Grade 2	Comedones + red papules	Topical retinoids plus antimicrobial preparations For superficial papules: Topical adapalene/benzoyl peroxide (BPO) combination product **Alternatives:** Topical retinoid at night, topical benzoyl peroxide in the morning; topical retinoid at night plus clindamycin/benzoyl peroxide combination product in the morning
Grade 3	Comedones + red papules + pustules	Method of choice: Topical retinoids plus oral cyclines **Alternatives:** Topical retinoids plus combined oral contraceptives containing cyproterone acetate for women Topical retinoids plus dapsone
Grade 4	Comedones + red papules + pustules + nodules/cysts/ conglobate lesions	Method of choice: Oral isotretinoin (OIT) as a full course **Alternatives:** Topical retinoids plus combined oral contraceptives containing cyproterone acetate, with added cyproterone acetate as 10 mg per day on days 5–19 of the menstrual cycle Topical retinoids plus dapsone 100 mg per day
Acne fulminans	The above + ulceration + fever and other synthetic symptoms	–

- Cystic acne

Whiteheads (closed comedones) are seen when sebum in the follicle increases leading to a dilatation on the opening of the sebaceous duct. Blackheads (open comedones) have a similar development as a whitehead but differs from it in that the opening of the dilated follicle is blocked by a mass of keratin. The black colour is not due to dirt, but due to the melanin in the keratin plug.

Papules develop from a whitehead. Two types are seen, namely: a non-inflammatory type, lasting for about two weeks and an inflammatory type. The inflamed papule is characterised by being slightly uncomfortable and the area of the skin is tender. Close examination reveals a slight inflammation in and around the lesion. These lesions may develop in pustules or resolve spontaneously over a period of two to three weeks.

Pustules develop when the epidermis is destroyed and an abscess forms within the follicle.

Cystic acne is when the contents of the comedone spreads into the surrounding tissue and into adjuvant follicles and may reach several centimetres in diameter. When aspirated with a large bore needle, viscous, creamy yellow material is drained. Cysts may be widespread and affect the face, back, chest, neck, and scalp.

Patients suffering from mild acne predominantly have open and closed comedones, white and blackheads, with a small number of active lesions normally confined to the face. An assessment on the degree of severity needs to be made and if referral is required. Generally, if there are widespread facial lesions as well as chest and back involvement, referral is advised. Referral is also indicative when there is moderate or severe acne, occupational acne, over-the-counter (OTC) treatment failure and rosacea.[16]

Table I gives the global acne grading system from which a global score can be calculated indicative of the severity of acne. Table II gives a South African grading severity classification and applicable treatment.

Management of acne

Non-pharmacological management

Non-pharmacological therapies are applied more often by health-care professionals such as pharmacists, general practitioners and dermatologists. The most applied non-pharmacological therapies include laser and light-based therapies, chemical peels, micro needling, (micro) derma abrasion and (mechanical) lesion removal. Non-pharmacological therapies are applied as independent therapies, in combination with conventional therapies or as maintenance therapy, especially in more persistent or chronic types of acne where long-term therapy is required.[19,20]

Light and laser treatments are a growing interest in new non-invasive therapies for acne. Light and laser therapies (photodynamic therapy, blue light, intense pulsed light) are commercially available, particularly in the private sector.[1] Intralesional corticosteroid injections, usually triamcinolone acetamide diluted to 5 mg/ml or less, can be used to flatten nodules or cysts within 48 to 72 hours.[1]

Pharmacological management

Acne should be treated actively to avoid unnecessary scaring and psychological distress. There are several effective anti-acne treatments on the market, with the choice of therapy dependent on the nature of the lesions and their severity.

Topical treatments

The ideal topical treatment is a combination of a keratolytic preparation and a topical antibacterial agent. Removal of the top layer of the skin leads to exposure of the follicle to become more aerobic (oxygenated) thus creating an environment that is no longer ideal for bacterial multiplication, especially *P. acnes*. Also, when the top layer of the skin is removed, the topical antibiotic can now penetrate the follicle and kill the bacteria involved.[15]

- *Retinoids* (e.g. isotretinoin and adapalene) are vitamin A derivatives with a keratolytic action that unblocks the pilosebaceous follicles and allows the flow of sebum to extrude the plug (comedolytic action). Topical retinoids can cause erythema and scaling, which can be minimised by starting on a low concentration. These preparations are used in a cream or gel formulation at concentrations of 0.025–2.5%. These preparations should be applied alone. Adapalene is an extensively modified retinoid and has a faster onset of action compared to that of isotretinoin and it produces less skin irritation.[18]
- *Azelaic acid* has antibacterial action against *P. acnes* and is effective against bacteria that have become resistant to erythromycin and tetracycline. It also inhibits keratinocyte division, which may reduce follicular plugging and prevent comedone development. The most frequent side-effects include local burning, scaling or itching, while hypopigmentation can become problematic in darker skin tones.
- *Benzoyl peroxide* has antibacterial activity against *P. acnes* by generating reactive oxygen species in the follicle and also exhibits weak anti-inflammatory and keratolytic actions. It can be fast acting, with a response rate as early as five days.[21] It is responsive when there are inflammatory lesions present. Benzoyl peroxide produces scaling and skin irritation, especially in high concentrations, although this may be transient. It can bleach clothing and hair and degrades isotretinoin (but not adapalene) and should be applied separately. Owing to its potential to cause erythema and irritation, concentrations of 10% should be avoided, since 5% and 10% concentrations seem to be equally efficacious.[16] Benzoyl peroxide prevents the resistance of *P. acnes* to antibiotic therapy and has moderate comedolytic and anti-inflammatory properties.
- *Topical antibacterials* (e.g. clindamycin and erythromycin) are less effective compared to oral antibacterials but have fewer side-effects. They possess weak anti-inflammatory and comedolytic action in addition to their direct action against *P. acnes*. Since bacterial resistance develops with regular use, they should be applied together with either benzoyl peroxide or a topical retinoid to improve antibacterial penetration into lesions, as well as for their synergistic actions on the lesions. Topical antibacterials should not be used for more than 12 weeks.

Systemic treatments

Oral antibacterials (especially lymecycline and doxycycline) have antibacterial action against *P. acnes* as well as anti-inflammatory action and are prescribed for inflammatory acne (papules/

pustules). Treatment should be given for no longer than 12 weeks and should be combined with a topical retinoid or benzyl peroxide to improve efficacy. Ciprofloxacin and trimethoprim can also be used, but their use is limited due to widespread tetracycline and erythromycin resistance. Oral antibiotics should not be prescribed for non-inflammatory acne and should be used in conjunction with a non-antibiotic topical agent, as this improves effectiveness and reduces bacterial resistance. Other antibiotics used include tetracycline and oxytetracycline. Table III lists oral antibiotic therapy for acne vulgaris.

Table III: Oral antibiotic therapy used for acne vulgaris[22]

Antibiotic, dose	Notes
Tetracycline, 250–500 mg twice daily	- Inexpensive - Contraindicated in pregnant women and in children under nine years of age - Chelated by antacids and milk - To be taken on an empty stomach
Minocycline, 50–200 mg daily	- Can be taken with food - Contraindicated in pregnant women or children under one year of age - Adverse effects: dizziness; pigment changes; hepatitis; lupus-like reactions
Doxycycline, 100–200 mg daily	- Can be taken with food - Acceptable for use in patients with renal failure - Contraindicated in pregnant women or in children under nine years of age - Adverse reactions: gastrointestinal upset; photosensitivity (greatest of all tetracyclines)
Erythromycin, 500 mg twice daily	- Safe in pregnant women and children - Adverse effect: may cause gastrointestinal upset - 42% may show resistance to *P. acnes*
Trimethoprim/ sulfamethoxazole 80/40 mg or 160/80 mg, four times per day	- Useful in patients resistant to other antibiotics - Adverse reactions: 3–4% of patients experience a rash; risk of serious skin reactions, such as Steven-Johnson syndrome

Table IV gives the main pathogenic factors in acne and their corresponding treatments.

The following illustrate some guidelines for acne treatment based on lesion type.[23]

There are three lesion types

- **Comedonal lesions –** prescribe one of the following:
  - Topical retinoid
  - Benzyl peroxide
  - Salicylic acid
  - Azelaic acid

  If results are unsatisfactory, increase strength or change medication
- **Mixed comedonal lesions and papulopustules** – prescribe one of the following:
  - Retinoid + topical antibiotic
  - Retinoid + benzyl peroxide
  - Retinoid + benzyl peroxide + topical antibiotic
  - Azelaic acid + benzyl peroxide
  - Azelaic acid + topical antibiotic

  If results are unsatisfactory, prescribe retinoid + course of oral antibiotics
- **Cystic lesions:**
  - Prescribe: Course of oral antibiotic + mixed comedonal-papulopustular topical therapy
  - If results are unsatisfactory, consider whether the patient is a candidate for oral isotretinoin therapy
  - If results are unsatisfactory, consider possible endocrinopathy – then either:
    - treat endocrinopathy, or
    - if no sign of endocrinopathy is found, consider repeat course of oral isotretinoin.

Hormonal therapies for acne include systemic medications with various mechanisms: androgen receptor blockers (e.g. spironolactone, cyproterone acetate, chlormadinone, and flutamide); adrenal androgen production blockers (e.g. glucocorticoids); or ovarian androgen production blockers. (e.g. gonadotropin-releasing agonists and oral contraceptives[24]).

Androgen receptor blockers

Spironolactone

Spironolactone is the most commonly utilised antiandrogen therapy in the United States.[25] Spironolactone blocks androgen

Table IV: Main pathogenic factors in acne and corresponding treatments[18]

Pathogenic factor	Relevant medication
Androgen stimulation of sebaceous glands	Cyproterone acetate, drosperinone
Hypersecretion of sebum	Oral isotretinoin
Hyperkeratosis and occlusion of the duct that drains sebum into the hair follicle	Topical retinoids
The formation of the invisible microcomedo	Topical retinoids
Inflammatory mediators (Interleukin 1 etc) released after stimulation of the toll-like receptor 2 by *P. acnes*	Topical retinoids and isotretinoin
Neutrophilic response to rupture of comedones and inflammation induced by free fatty acids in sebum	Oral cyclines, oral and topical dapsone, oral macrolides
Proliferation of *P. acnes*	Oral cyclines, oral macrolides, topical benzoyl peroxide
Inflammatory tissue damage by matric metalloproteinases	Oral cyclines

receptors and inhibits 5-α-reductase. Spironolactone may reduce the severity of acne when dosed 50–200 mg/day over a three-month period but generally, much lower doses are required to treat acne, such as 25–100 mg/day (25 mg/day, 25 mg, twice daily, or 50 mg twice daily), in contrast to the higher doses required to treat androgenetic alopecia or hirsutism.[25] Most acne patients experience clinically significant improvement with three months of therapy.[26]

Side-effects of spironolactone tend to be transient and include menstrual irregularities (in as many as half of treated patients). Usually, this is oligomenorrhoea or irregular menstrual bleeding but may, less often, manifest as hypermenorrhoea. Often, these side-effects resolve within two to three months of continued therapy.[26] Oral contraceptives may help decrease the side-effects such as dysmenorrhoea, irregular menses, and breast tenderness. These side-effects are dose-dependant and common with spironolactone use.[27] Additional side-effects include hyperkalaemia, nausea, dizziness, or polyuria (which may resolve in one to two weeks of continued therapy), and vertigo (which may necessitate discontinuation of therapy[26]). Pregnancy must be avoided as there is a risk of feminisation of the male foetus.

Cyproterone acetate

Cyproterone acetate, a progestational antiandrogen, is an androgen receptor blocker. It is available and widely used as part of a combination oral contraceptive pill (OCP).

Chlormadinone acetate

Chlormadinone acetate is a progesterone derivative, originally developed for progestin replacement therapy, but it is presently used in Europe as a component of combination OCPs, which contain ethinyloestradiol 0.03 mg and chlormadinone acetate 2 mg. Like cyproterone acetate, it blocks the androgen receptor of the pilosebaceous unit via competitive inhibition[28] as well as inhibits the endogenous secretion of gonadotropin.[29] Most common side-effects are similar to other combined OCPs and include headache in 24% of patients, breast tension in 19%, dysmenorrhoea in 10%, and nausea in 10%, although these are most often in the first three to four cycles of starting the medication.[28]

Flutamide

Flutamide is an androgen receptor blocker that is approved for the treatment of prostate cancer. Side-effects include dry skin in as many as 70% of treated patients; hot flushes and increased appetite in about a quarter of patients; headaches, fatigue, and nausea in > 10%; and, less often, dizziness, decreased libido, and breast discomfort.[29] Monthly liver function tests for the first four months of therapy are recommended, and periodically thereafter.

Adrenal androgen production blockers

In low doses, glucocorticoids suppress adrenal production of androgens and are prescribed in individuals with elevated serum DHEAS levels, which may be associated with 11- or 21-hydroylase deficiency. Prednisone 2.5 mg or 5 mg or dexamethasone 0.25–0.75 mg may be administered every day or every other day, at bedtime.[3] Adrenal suppression is possible, especially if dexamethasone is used, and can be screened with ACTH stimulation test, two to three months after starting therapy.[3,30] Duration of therapy is limited by the long-term side-effect of osteoporosis, and should therefore be limited to six months.[30]

Ovarian androgen production blockers

Gonadotropin-releasing hormone agonists block androgen production by the ovary via inhibition of the feedback loop that controls the pituitary's release of FSH and LH. Gonadotropin-releasing hormone agonists include buserelin, nafaelin, and leuprolide and may be used to treat acne in the presence or absence of endocrine abnormalities.[24] Side-effects may limit therapy and mimic menopause, with low oestrogen, headaches, and bone loss.[30] OCPs, with a combination of an oestrogen and progestin, are commonly used worldwide in the treatment of acne. The most commonly used oestrogen is ethinyloestradiol (EE).[29] Each generation of progestins has varying degrees of androgen cross-reactivity, with the potential to aggravate acne or worsen androgen-related conditions; however, the levels required to do so tend to be higher than those found in modern OCPs.[30] Second-generation progestins with low androgenic activity include ethynodiol diacetate, norethindrone, and levonorgestrel while third-generation progestins have the lowest of all androgenic activity, and include borgestimate, desogestrel, and gestodene. Drospirenone is derived from spironolactone, so its antiandrogenic and antimineralocorticoid can be used to improve acne and hirsutism, as well as mitigate the fluid retention associated with some OCPs due to oestrogen.[30]

Side-effects of OCPs include mood changes, decreased libido, headache, breast tenderness, and irregular menstrual bleeding (typically spotting between cycles).[31] Weight gain is often indicated as a side-effect of oral contraception and may deter women from starting the medication. Hormonal therapies (e.g. ethinyloestradiol or the antiandrogen cyproterone acetate) are useful in women who suffer from moderate to severe acne. They are prescribed in combination with a non-androgenic progestogen (e.g. norgestimate or desogestrel) as a combined oral contraceptive. Serum flow is decreased by 40%, but improvement can take as long as three to six months. Progestogen only contraceptives can exacerbate acne.

Isotretinoin

Isotretinoin is indicated for severe acne and gives an almost 100% probability of complete remission. High doses can produce prolonged remission. Side-effects include dry lips, nose and eyes, increased plasma triglycerides, photosensitivity, headaches and myalgia. It has also been reported and well publicised that cases of mood disorders are associated with isotretinoin. Teratogenesis is a problem and, although the half-life of the metabolites is less than two days, conception should be totally avoided during treatment and for one month after stopping treatment.[5] Treatment is usually deemed complete when a cumulative dose of 120–150 mg/kg has been reached. Isotretinoin therapy must be monitored carefully because adverse effects include potent teratogenicity, hypertriglyceridaemia and pancreatitis, hepatoxicity, blood dyscrasias, hyperostosis, premature epiphyseal closure and night blindness.[22] Patients should also be warned about suicidal tendencies and psychosis.[32]

Treatment of children and pregnant women

The treatment of acne in children is like that in adults. Topical therapies may be more irritating in children, initiation with low concentrations is recommended. Systemic treatments should be reserved for more extensive cases. Erythromycin is preferred over tetracyclines for children under nine years of age, because tetracyclines can affect growing cartilage and teeth. Although treatment with isotretinoin has numerous potential minor side-effects in patients of all ages, an uncommon complication in young patients is premature epiphyseal closure. This generally occurs when isotretinoin is administered in high doses, thus limiting long-term therapy. Selecting appropriate treatment in pregnant women can be challenging because many acne therapies are teratogenic; all topical and especially oral retinoids should be avoided. Oral therapies such as tetracyclines and antiandrogens are also contraindicated in pregnancy. Topical and oral treatment with erythromycin may be considered.

Topical antibiotic medications remain first-line agents for the treatment of patients with mild-to-moderate acne. For more severe cases, penicillin or cephalosporins are the most reasonable next step with macrolides as a second-line oral treatment option. Severe cases of nodulocystic acne or acne conglobata with severe psychosocial impact may require controlled courses of corticosteroid medications to ameliorate symptoms. Oral metronidazole represents a potential, alternative, third-line oral therapy that may be used, in combination with topical treatments and low doses of prednisone.[33]

The choice of treatment for acne is dependent on the severity of the presenting acne. Initially, management of non-inflammatory comedones should be with a topical treatment. Topical retinoids are increasingly used for all types of acne, except severe acne, or as maintenance treatment, with azelaic acid as an alternative option. For early inflammatory lesions, a topical antibacterial or benzoyl peroxide is recommended, as either single or combination agents. Oral antibiotics are useful for moderately severe acne, with oestrogen or antiandrogen therapy (as a combined oral contraceptive) as alternatives for women. Systemic treatment with isotretinoin is used in severe unresponsive acne but is also an option for moderately severe acne. The most common reason for treatment failure is a lack of adherence to the recommended treatment regimen.

Counselling

- Counsel the patients on the correct use of isotretinoin; inform the female patients that they should sign the form, of which a copy is placed in their patient file, stating that they will not become pregnant during the course of the treatment, and for one month thereafter. Inform them of the serious teratogenic effect of isotretinoin's use.
- Encourage sales of a sunblock (SPF 50) and lip balm when isotretinoin is prescribed. This will aid in protecting the skin against the sun and provide moisture to the dry lips.
- Encourage patients not to pick on their acne scars as this will lead to spreading of the acne. Also encourage patients to wash their hands when they touch the areas affected with acne.
- Advise patients to use topical antibacterials together with either benzoyl peroxide or topical isotretinoin as the antibacterial penetration thereof is increased.
- Enquire if the patient is taking any medications. This is to eliminate medicine causing acne-like skin eruptions. Medications implicated include the following: lithium, oral contraceptives (e.g. those that have high progestogen levels), phenytoin, azathioprine, and rifampicin. If the patient is using these treatments, additional counselling should be provided for management.
- Informing the patient that they should see a general improvement after eight to 12 weeks of treatment with simple anti-acne treatment and that should this fail, it is best for them to seek the assistance of a general practitioner or dermatologist.
- Educate the patient using benzyl peroxide about its side-effects of drying, burning and peeling of the skin and that they can stop the treatment for a day or two before starting it again. Patients should start treatment at the lowest concentration available, especially if they suffer from a sensitive or fair skin.
- Explain and educate the patient about the condition and state that the aim of the treatment is to be cosmetically advantageous as well as to prevent permanent scaring. Should diet be implicated, the necessary dietary changes need to be made and psychological factors need to be eliminated as far as possible.
- Explain to all women of childbearing age using acne treatments that:
  - All topical acne therapy should be stopped if pregnancy occurs.
  - Topical retinoids should not be prescribed to pregnant women, women wishing to become pregnant, or nursing women.
  - Oral tetracycline should not be taken by pregnant or nursing women. The only FDA-approved medication to treat acne during pregnancy is azelaic acid (category B) and should be used with caution in nursing women.
  - It is imperative for women who are starting oral isotretinoin (category X) to practice two forms of birth control, participate monthly in pregnancy tests, and not become pregnant for at least one month after cessation of therapy due to oral isotretinoin's known teratogenic effects.
- Explain to patients that they should apply basic skincare to manage their acne. The skin should be gently cleansed twice daily, and comedogenic creams and cosmetics should be avoided.
- Instruct patients to apply exceedingly small amounts of retinoids initially and that optimal response should occur after 12 weeks.
- Mention to the patient that when they are using benzoyl peroxide that they should take note that this medication has bleaching properties.
- Emphasise to the patient that when applying combination topical therapy, such as benzoyl peroxide and retinoids, that the combination of these medications is more effective than either therapy applied alone. However, these medications should be applied at separate times, as benzoyl peroxide may oxidise a retinoid, such as tretinoin, if applied simultaneously.[34]
- Educate and remind patients to avoid harsh washing of their

skin (avoid scrubs or exfoliating devices) as this may damage the natural skin barrier function. Cleansers with a pH of 5.5 should be favoured over traditional detergents (e.g. soaps) allowing for a gentle cleansing of the skin and for a reduction of the particle load on the skin in the evening. Optimal frequency of cleansing should be twice a day.

- Pharmacists can play an important role in the education of a patient suffering from acne as well as be a pillar of support for him/her. They can also refer patients to the relevant people/ instances that can aid in the alleviation of depression, suicide idealisation and low self-esteem.

Conclusion

Acne vulgaris is quite a common skin condition that can occur in children, adults and pregnant women. This condition is caused by an excess secretion of sebum that triggers acne. This promotes the growth of *P. acnes*. Treatment depends on the severity of the acne and can be done topically with retinoids, azelaic acid, benzoyl peroxide or topical antibacterials, or systemically with oral antibacterials, hormonal therapies or isotretinoin. The pharmacist plays an important role not only in the dispensing of acne medications, but also in the education of patients about correct skin care products and medications used, especially in women of childbearing age.

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