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REVIEW

Acne vulgaris and variants

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Acne vulgaris is a multifactorial, inflammatory disease of the pilosebaceous unit (comprising the hair follicle and sebaceous gland), primarily involving the face, chest, and back. It is a chronic disease with a potentially severe impact on the quality of life and self-image of all age groups affected. It has been associated with increased rates of anxiety, depression, and suicidal ideation. Therefore, clinicians must be well informed on the pathogenesis, clinical diagnosis, grading of severity, treatment algorithm, and pharmacology of the medications used for acne.

Keywords: acne vulgaris, common skin condition

Introduction

Acne vulgaris is a common skin condition that affects all skin types and ethnic groups. Although perceived to be a teenage disease, acne often persists into adulthood and can result in significant scarring.[1] The condition typically begins at puberty when sex hormones begin to be produced, with the prevalence of acne in boys increasing from 40% at age 12 years to 95% at age 16 years, and the prevalence increases similarly from 61% to 83% in girls.[2]

The presence of acne has an important impact on emotional functioning, social functioning, relationships, leisure activities, daily activities, sleep, school, and work, particularly in adolescents. Suicidal ideation has been documented in ~7.1% of affected individuals.[3,4] The negative impact on the quality of life further illustrates the importance of early and aggressive treatment.[1] The risk factors for acne include genetics, hyperandrogenism, polycystic ovarian syndrome, medications such as anti-epileptics, lithium, progesterone-only contraception, isoniazid, oral and topical corticosteroids, vitamin B_{12}, the application of oily products and a high glycaemic-index diet.[5,6]

Variants of acne vulgaris include acne fulminans, acne conglobata, acne excoriée, drug-induced acne, acne mechanica, pomade acne, occupational acne, chloracne, neonatal and infantile acne.[1]

Pathogenesis

The pathophysiology of acne is multifactorial and is still not well understood. It is a chronic inflammatory condition that usually occurs at the onset of puberty due to increased production of androgens by the adrenals and gonads and/or increased sensitivity of androgen receptors.

The main pathogenetic factors important for acne include:[7,8]

- Androgen stimulation of sebaceous glands
- Hypersecretion of sebum
- Hyperkeratosis and occlusion of the duct that drains sebum into the hair follicle
- The formation of the invisible microcomedo
- Inflammatory mediators (Interleukin 1, etc) released after stimulation of toll-like receptor 2 by Cutibacterium acnes (formerly Propionibacterium acnes)
- Neutrophilic response to rupture of comedones and inflammation induced by free fatty acids in sebum
- Proliferation of Cutibacterium acnes
- Inflammatory tissue damage by matrix metalloproteinases

Clinical presentation

Acne vulgaris affects areas with a high density of sebaceous glands, i.e. the face, chest, and back, and the skin lesions can be inflammatory or non-inflammatory. It is a clinical diagnosis. Non-inflammatory acne is characterised by both open (blackheads) and closed (whiteheads) comedone formation.[5] Melanin deposition and lipid oxidation within the debris is responsible for the black discolouration.

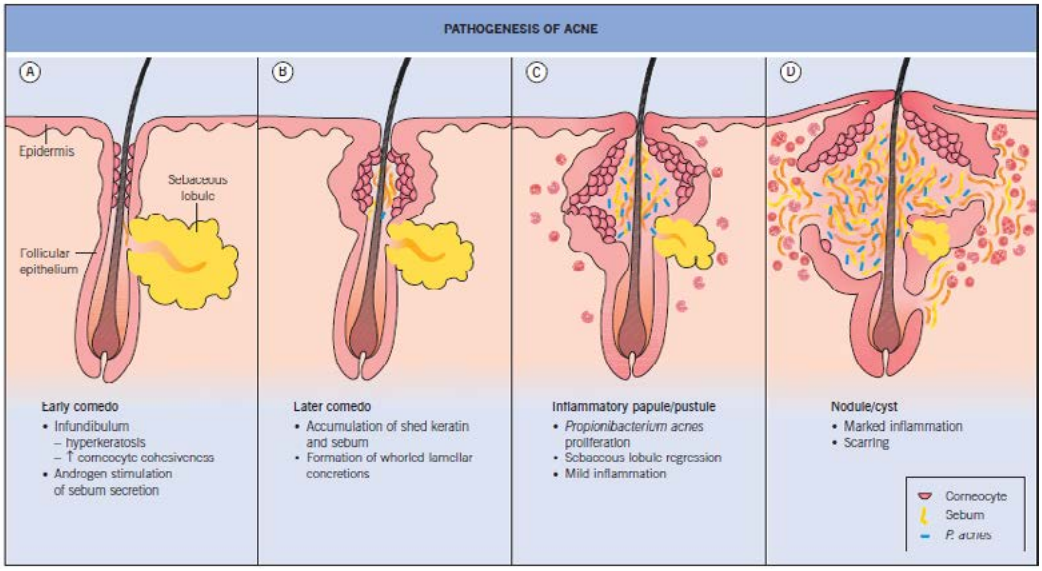
The inflammatory lesions of acne originate with comedo formation but then expand to form papules, pustules, nodules, and cysts of varying severity. As the severity of lesions progresses, nodules form and become markedly inflamed, indurated, and tender. The acne cysts are deeper and filled with a combination of pus and serosanguineous fluid. In patients with severe nodulocystic acne, these lesions may form massively inflamed complex plaques and sinus tracts.[7]

Acne can be clinically graded and classified to assess overall disease severity, help facilitate therapeutic decision-making, and assess and evaluate treatment response.[6]

Classified into:

- mild (comedones)
- moderate (papules/pustules)
- severe (nodules/cysts)

Pathogenesis of acne



Dermatology 2nd edition; Bolognia

Picture 1: Closed comedone (black arrow) and open comedone (blue arrow)

Courtesy of Dr AV Chateau

Picture 2: Papule

Picture 3: Pustule (black arrow) and nodule (blue arrow)

Grading:

- Grade 1 – Comedones only
- Grade 2 – Comedones + red papules
- Grade 3 – Comedones + red papules + pustules
- Grade 4 – Comedones + red papules + pustules + nodules / cysts / conglobata lesions

Complications

Scars are visible and persistent reminders of acne. This dreaded outcome can occur in all grades of acne. Early and appropriate treatment is best to minimise the potential for acne scarring. Scars form at the site of tissue injury and may be hypertrophic or atrophic. Atrophic scars are divided into three types: ice-pick, rolling, and boxcar.[1]

The scar: scar characteristics usually determine the treatment approach and may involve resurfacing, surgical revision, and dermal fillers. In many cases, topical retinoids are a useful adjunct to procedures in managing scarring.[1,2] Pigmentary complications are also of important cosmetic concern for all patients regardless

Picture 4: Types of acne scarring: Ice pick scarring (white arrow); boxcar (blue arrow); rolling (black arrow)

of skin colour, and inflammation is an important factor in post-acne hyperpigmentation.[9]

Management

There is currently vast literature and several guidelines for management of acne vulgaris (Table I).

Table I: Pathogenic factors in acne and relevant treatment

Pathogenic factor	Medication
Androgen stimulation of sebaceous glands	Cyproterone acetate
Hypersecretion of sebum	Oral isotretinoin
Hyperkeratosis and occlusion of the duct that drains sebum into the hair follicle	Topical retinoids
Formation of the invisible microcomedo	Topical retinoids
Inflammatory mediators released	Topical retinoids; oral isotretinoin
Neutrophilic response to rupture of comedones and inflammation	Oral cyclines; oral and topical dapsone; oral macrolides
Proliferation of *P. acnes* (Cutibacterium)	Oral cyclines; oral macrolides; topical benzoyl peroxide
Inflammatory tissue damage by metalloproteinases	Oral cyclines

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The treatment algorithm is stratified according to the grades of acne (Table II).

Indications to use of oral isotretinoin

- Grade 4 acne vulgaris (severe acne)
- Lesser grade of acne vulgaris that failed conventional treatment
- Lesser grade of acne vulgaris with significant scarring

Dosage

A full course of this drug is administered at 0,5–1,0 mg/kg per day until a total cumulative dose of 120 mg per kg is reached.

Table II: Treatment algorithm

Grading of acne vulgaris	Treatment
Grade 1 (mild acne)	**Topicals:** • Benzoyl peroxide (BPO) • Retinoids (adapalene, tretinoin) **Alternatives**: • Azelaic acid • Salicylic acid • Topical antibiotic (erythromycin, clindamycin, minocycline and dapsone) • Fixed-dose combinations (retinoids and BPO, retinoid and antibiotic, BPO and antibiotic) • Topical antiandrogen (clascoterone)
Grade 2 (mild – moderate acne)	**Topicals:** • BPO and retinoids • Retinoids and antibiotics **Systemics:** • Oral antibiotics – tetracycline, minocycline, lymecyline • Hormonal therapy – combined oral contraceptives –(oestrogen/progesterone) and spironolactone
Grade 3 (moderate acne)	**Topicals and systemics** • Retinoids and oral antibiotics • Retinoids and combined oral contraceptives ± BPO • Fixed dose topical combinations (combination of BPO, retinoids, or antibiotics) • Insufficient evidence to develop recommendations on use of oral azithromycin and trimethoprim/sulfamethoxazole for acne
Grade 4 (severe acne)	**Systemics:** • Oral retinoids (Isotretinoin 120 mg/kg) • Combined oral contraceptive (for females) **Alternative:** • Topical retinoids and combined oral contraceptives
Acne in pregnancy	**Topicals:** • Azelaic acid, BPO, erythromycin and clindamycin – limited expected systemic absorption • Salicylic acid (larger surface area), minocycline, dapsone, clascoterone – not recommended in pregnancy • Retinoids and minocycline – contraindicated **Systemics:** • Limited use of erythromycin and azithromycin • Retinoids – contraindicated • Tetracyclines – contraindicated
Childhood acne	**Topicals:** • Salicylic acid (0,5–2%) • Fixed dose combination (BPO 2, 5%/adapalene 1% gel; tretinoin 0, 1%/BPO 3% cream) • Dapsone 5% gel • Azelaic acid **Systemics:** • Tetracyclines – contraindicated below 9 years of age

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Laboratory monitoring during isotretinoin treatment

Includes – liver function test, fasting lipid profile and pregnancy test (if applicable).

Side effects of isotretinoin

- Teratogenicity (pregnancy test before initiation and effective contraception)
- Mucocutaneous side effect
- Photosensitivity

- Ocular complications
- Deranged liver enzymes and dyslipidaemia
- Raised intracranial pressure when combined with tetracyclines
- Myalgia and arthralgia
- Gastrointestinal side effects
- Mood disturbances

Maintenance treatment

Maintenance therapy is necessary post successful treatment of acne. A cure rate of 38% is seen in patients treated with oral isotretinoin. Maintenance should continue until a patient no longer develops new lesions. Topical retinoids are ideal for maintenance and are the only registered products for this indication as they eradicate inflammatory and non-inflammatory microcomedones. Topical retinoids can be combined with topical benzoyl peroxide (combination therapy) or as a single product (BPO in the morning and retinoids at night). Benzyl peroxide should not be used as monotherapy as it does not target the microcomedones and does not have non-inflammatory effects like retinoids. Azelaic acid can also be used if topical retinoids cannot be tolerated.[1,10]

Take home message

Acne vulgaris is not a self-limiting condition. Early and effective treatment can improve the patient's well-being and may prevent permanent scars or pigment changes.[1]

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