



## Clearing Up Acne Treatment for the Primary Care Physician

A review of recent guidelines on the treatment of adolescent acne vulgaris

### ABSTRACT

Acne vulgaris is a common skin condition encountered in family practice and can cause significant distress during adolescence. Treatment options discussed include topical benzyl peroxide, topical retinoids, oral and topical antibiotics, hormonal therapy, and isotretinoin. The following review article provides up-to-date recommendations for treating mild to severe pediatric acne.

**KEYWORDS:** acne vulgaris, adolescence, treatment, pathogenesis



### Pathogenesis

The pathogenesis of acne involves four steps: (1) sebaceous hyperplasia and increased sebum production, caused by androgens. (2) alterations in follicular growth and differentiation leading to comedone formation. (3) colonization by *Propionibacterium acnes* (*P acnes*), which releases inflammatory mediators. (4) the immune response is mounted and inflammation occurs, which when severe can lead to scarring.<sup>1</sup>

### ABOUT THE AUTHORS

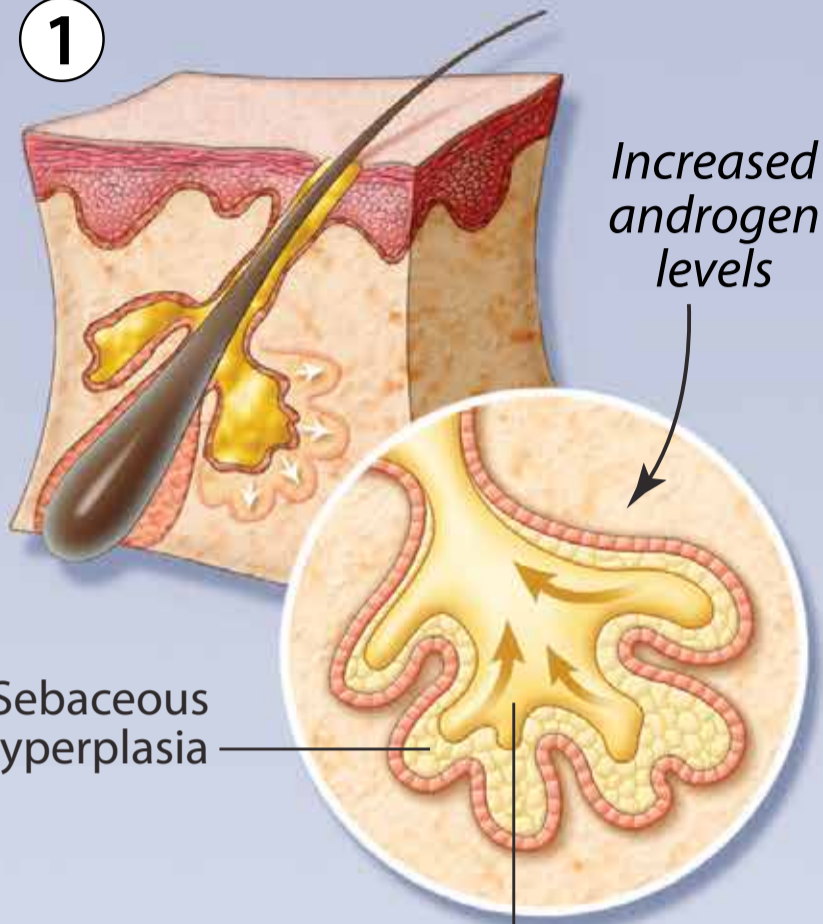
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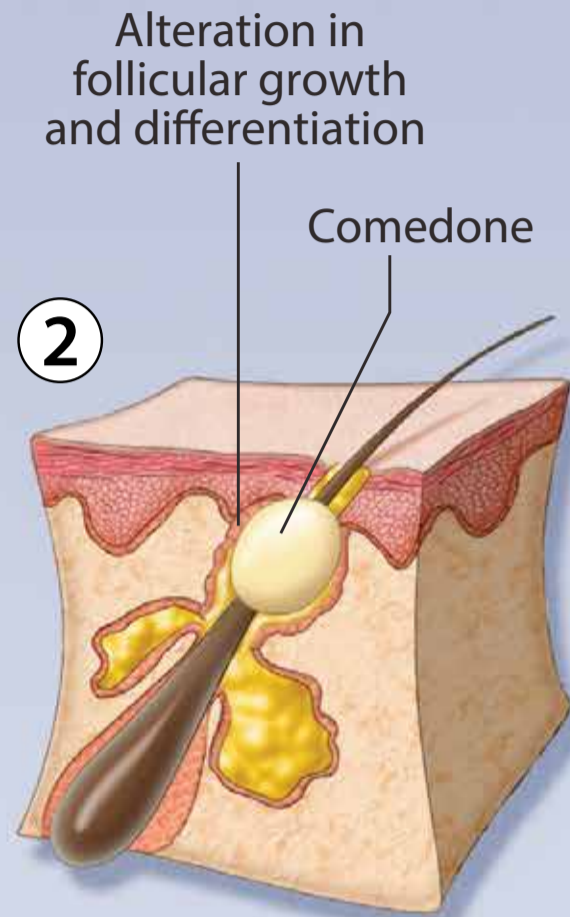


# Pathogenesis of Acne

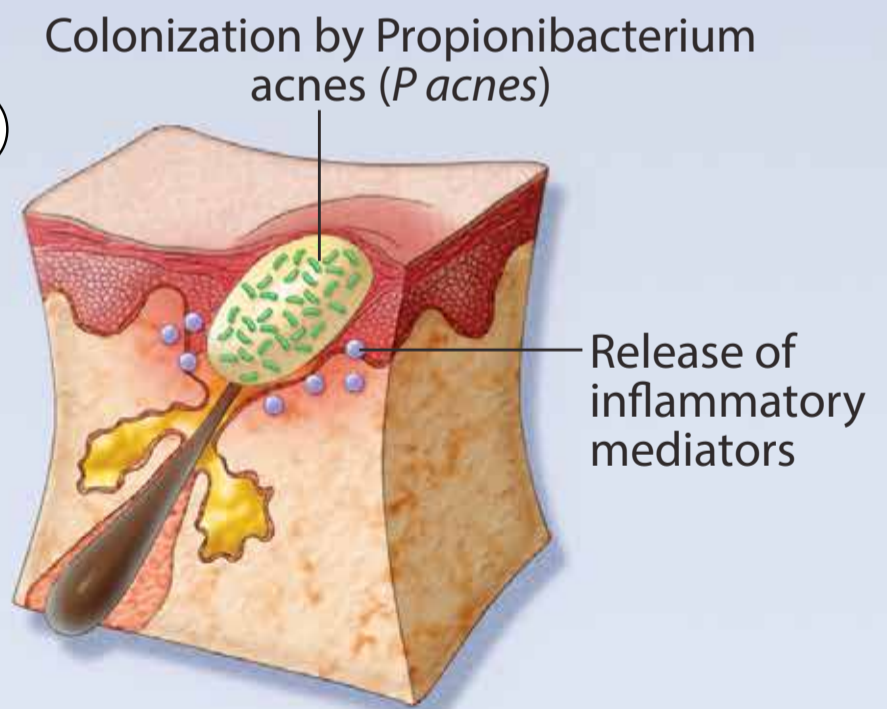
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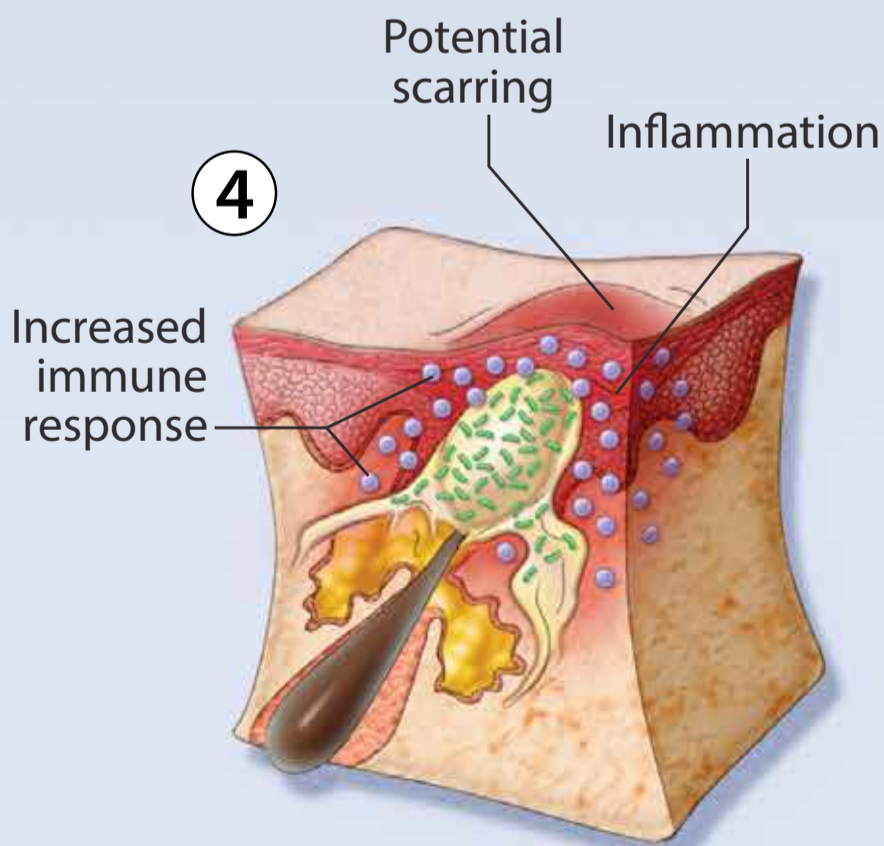
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## Differential Diagnosis & Classification

Comedones must be present for a diagnosis of acne. The differential diagnosis for acne in adolescence includes corticosteroid induced acne, folliculitis, keratosis pilaris, papular sarcoidosis, perioral dermatitis, pseudofolliculitis barbae, and tinea facie.<sup>2</sup>

Acne can be categorized according to age. Neonatal acne occurs up to six weeks of age. Infantile acne is from 6 weeks to one year of age. Mid-childhood acne occurs from 1 to 7 years of age. Preadolescent acne is from 7 to 12 years of age or until onset of menarche in girls. Adolescent acne is between 12 and 19 years of age or after menarche in girls.<sup>2</sup>

Acne may be classified as mild, moderate or severe based on the number and type of lesions involved as well as the total sur-

face area involved.<sup>2</sup> Acne morphology includes closed comedones (whiteheads), open comedones (blackheads), and inflammatory lesions, which include papules, nodules, and cyst-like lesions. The microcomedone is the precursor to both comedones and inflammatory lesions.<sup>3</sup> Secondary changes include post inflammatory hyperpigmentation, residual erythema, and scarring.<sup>2</sup>

## 6 Treatment Options

Acne therapy is targeted at treating as many pathogenic factors as possible.

1. Various over the counter products are available and are considered to be somewhat effective, particularly for mild acne. Salicylic acid and benzyl peroxide (BP) have been shown to be efficacious in clinical trials. BP is available in concentrations ranging from 2.5% to

**Comedonal Acne**



**Inflammatory Acne**



**Scarring Acne**





10%, which are all equally effective; however, skin irritation increases with concentration. Available formulations include ones that can be washed off and

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## Both topical and oral antibiotics work by inhibiting *P acnes* protein synthesis and decreasing inflammation.

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ones that are left on the skin.<sup>2</sup> BP has comedolytic, antibacterial, and anti-inflammatory properties. It acts at the pilosebaceous unit by generating free radicals that oxidize the cell wall of *P acnes*.<sup>4</sup> BP can be used as monotherapy or combination therapy for all types and severities of acne. Common side effects include dry skin, photosensitivity, and bleaching of hair, clothing, and towels that come in contact with BP.<sup>2</sup>

2. Topical retinoids desquamate the follicular epithelium preventing new microcomedone formation and clearing existing microcomedones. As well, some topical retinoids have anti-inflammatory activity. Three available topical retinoids are tretinoin, adapalene, and tazarotene. They can be prescribed in a variety of formulations and concentrations.<sup>1</sup> Topical reti-

noids can be used as monotherapy or combination therapy for all types and severities of acne in children and adolescents. They can cause skin irritation, which can be reduced by using a lower strength topical retinoid or regular use of a moisturizer.<sup>2</sup>

3. Both topical and oral antibiotics work by inhibiting *P acnes* protein synthesis and decreasing inflammation. The concern regarding their use to treat acne is the increase in *P acnes* resistance, which renders antibiotics less effective and may influence commensal bacteria in patients.<sup>5</sup> Topical antibiotics (clindamycin, erythromycin) are not recommended as monotherapy, but instead should be used with topical BP. Their onset of action is slow and there is greater likelihood of developing bacterial resistance if treatment is greater than a few weeks.<sup>2</sup> One study suggests a BP washout period after three months of topical antibiotics prior to further antimicrobial treatment.<sup>1</sup> Oral antibiotics are appropriate for moderate to severe acne. The most commonly used oral antibiotics for children older than eight years of age are tetracycline, doxycycline, and minocycline. Patients should be aware of adverse effects of oral antibiotics. The three previously



mentioned can cause staining of forming teeth enamel if given at less than eight years of age. Tetracycline may cause GI upset and a fixed drug eruption.

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## Topical fixed-dose combination therapies can be used for all types and severities of acne in children 9 years of age and older.

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tion.<sup>2</sup> Common side effects of doxycycline are photosensitivity and pill esophagitis.<sup>6,7</sup> Rare side effects of minocycline include drug hypersensitivity syndrome, Stevens-Johnson syndrome, and lupus-like syndrome.<sup>2,8,9</sup> For oral antibiotics, the maximal response may take three to six months. Prescribers should consider stopping oral antibiotics and maintaining topical therapy once inflammatory lesions are markedly decreased.<sup>1</sup> Ideally therapy should be limited to three to four months or the shortest possible duration to see a satisfactory response.<sup>10</sup>

4. Oral isotretinoin is used for severe acne. It targets all four factors in acne pathogenesis.<sup>1</sup> Common side effects include dry, chapped skin and lips, dry eyes, and myalgias. Some patients may experience a dose dependent and asymptomatic

increase in liver enzymes and triglycerides. Monthly lab work has traditionally been recommended for patients on the standard dose; however, current best evidence does not support this.<sup>11</sup> A major adverse effect is teratogenic potential. Female patients should have monthly pregnancy tests and be counselled to use two forms of birth control while on isotretinoin. Other more controversial adverse effects include skeletal issues, development of inflammatory bowel disease, and mood changes.<sup>12</sup>

5. Topical fixed-dose combination therapies can be used for all types and severities of acne in children 9 years of age and older. Examples include pairing BP with a topical antibiotic or a topical retinoid, or pairing a topical retinoid with a topical antibiotic.<sup>2</sup> Fixed combinations may be more expensive than each agent prescribed separately; however, they may be more convenient and thus have better adherence.<sup>13</sup>
6. Hormonal therapy targets suppression of ovarian androgen production and blocks androgen effects on sebaceous gland. Ortho Tri Cyclen, Estrostep, and Yaz are currently FDA approved for the treatment of acne, though others are efficacious and commonly used.



Common side effects include nausea/ vomiting, breast tenderness, headache, weight gain, and breakthrough bleeding. An uncommon but serious adverse effect is the risk of thromboembolism; prescribers should ask about family history and smoking.<sup>2</sup> Specific to the pediatric population is the concern over whether low doses of estrogen allow for enough estrogen for bone accrual given that peak bone mass accrual occurs during adolescence.<sup>14</sup>

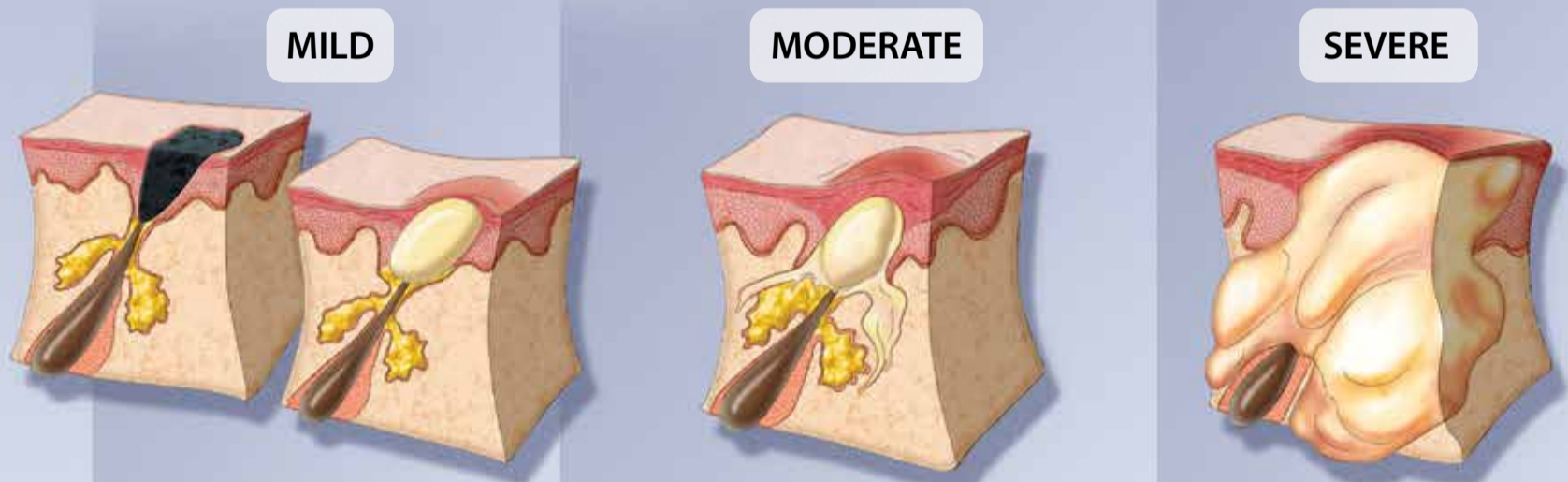
## Pediatric Acne Action Plan

Note that any acne treatment takes four to eight weeks before noticeable results are achieved.

### Mild Acne

- characteristics: comedonal or mixed comedonal and inflammatory
- initial treatment:
  - (1) BP OR topical retinoid
  - (2) topical combination therapy using BP AND antibiotic OR retinoid AND BP OR retinoid AND antibiotic

## Pediatric Acne Action Plan



	MILD	MODERATE	SEVERE
<b>Characteristics:</b>	Comedonal or mixed comedonal and inflammatory	Comedonal or mixed comedonal and inflammatory	Inflammatory/mixed and/or nodular lesions
<b>Initial Treatment:</b>	(1) BP <i>or</i> topical retinoid (2) Topical combination therapy using BP <i>and</i> antibiotic <i>or</i> retinoid <i>and</i> BP <i>or</i> retinoid <i>and</i> antibiotic <i>and</i> BP	(1) Topical combination therapy using retinoid <i>and</i> BP <i>or</i> retinoid <i>and</i> BP/antibiotic <i>or</i> retinoid/antibiotic + BP (2) Oral antibiotic + topical retinoid <i>and</i> BP <i>or</i> topical retinoid <i>and</i> antibiotic <i>and</i> BP	Combination therapy using oral antibiotic <i>and</i> topical retinoid <i>and</i> BP <i>and/or</i> topical antibiotic
<b>If Inadequate Response:</b>	First check adherence, then: (1) Add retinoid or BP if not already prescribed (2) Change topical retinoid concentration, type and/or formulation (3) Change topical combination therapy	First check adherence, then: (1) Change topical retinoid concentration, type, and/or formulation, and/or change topical combination therapy (2) Add or change oral antibiotic (3) Consider hormonal therapy in females (4) Consider isotretinoin (5) Consider dermatology referral	First check adherence, then: (1) Consider changing oral antibiotic (2) Consider oral isotretinoin (3) Consider hormonal therapy in females (4) Consider dermatology referral





## SUMMARY OF KEY POINTS

The differential diagnosis for acne in adolescence includes corticosteroid induced acne, folliculitis, keratosis pilaris, papular sarcoidosis, perioral dermatitis, pseudofolliculitis barbae, and tinea facie.

Acne may be classified as mild, moderate or severe based on the number and type of lesions involved as well as the total surface area involved.

Acne therapy is targeted at treating as many pathogenic factors as possible.

Topical fixed-dose combination therapies can be used for all types and severities of acne in children 9 years of age and older.

Both topical and oral antibiotics work by inhibiting *P acnes* protein synthesis and decreasing inflammation.

### AND BP

- if inadequate response: first check adherence, then
  - (1) add retinoid or BP if not already prescribed
  - (2) change topical retinoid concentration, type and/or formulation
  - (3) change topical combination therapy<sup>2</sup>

### Moderate Acne

- characteristics: comedonal or mixed comedonal and inflammatory
- initial treatment:
  - (1) topical combination therapy using retinoid AND BP OR retinoid AND BP/antibiotic OR retinoid/antibiotic + BP

- (2) oral antibiotic + topical retinoid AND BP OR topical retinoid AND antibiotic AND BP

- if inadequate response: first check adherence, then
  - (1) change topical retinoid concentration, type, and/or formulation, and/or change topical combination therapy
  - (2) add or change oral antibiotic
  - (3) consider hormonal therapy in females
  - (4) consider isotretinoin
  - (5) consider dermatology referral<sup>2</sup>

### Severe Acne

- characteristics: inflammatory/mixed and/or nodular lesions



## CLINICAL PEARLS

Do not be afraid of isotretinoin. It can be used first line in patients with severe nodular and/or inflammatory acne, acne conglobata, and recalcitrant acne.<sup>12</sup> It is the only treatment that targets all four pathogenic factors implicated in acne vulgaris and can permanently decrease acne.





## DID YOU KNOW?

### Just Acne?

Adolescents with acne reported social, psychological, and emotional symptoms similar to people with chronic medical conditions including asthma, epilepsy, diabetes, back pain and arthritis.<sup>15</sup>

- initial treatment: combination therapy using oral antibiotic AND topical retinoid AND BP AND/OR topical antibiotic
- if inadequate response: first check adherence, then
  - (1) consider changing oral antibiotic
  - (2) consider oral isotretinoin
  - (3) consider hormonal therapy in females
  - (4) consider dermatology referral<sup>2</sup>

## Conclusion

The pathogenesis of acne vulgaris appears to be similar across the ages. The above pediatric treatment approaches serve as a guide for the family physician to comfortably and successfully manage acne vulgaris.

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