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# Pediatric Acne Management: Optimizing Outcomes


## Faculty

*Lawrence F. Eichenfield, MD, Chair*
Clinical Professor of Pediatrics and Medicine (Dermatology)
Chief, Pediatric and Adolescent Dermatology
Rady Children's Hospital
University of California, San Diego
San Diego, California

*Hilary E. Baldwin, MD*
Associate Professor and Vice Chair
Department of Dermatology
SUNY Downstate
Brooklyn, New York

*Sheila Fallon Friedlander, MD*
Clinical Professor of Pediatrics and Medicine (Dermatology)
Rady Children's Hospital
University of California, San Diego
San Diego, California

*Anthony J. Mancini, MD*
Professor of Pediatrics and Dermatology
Northwestern University Feinberg School of Medicine
Head, Division of Pediatric Dermatology
Children's Memorial Hospital
Chicago, Illinois

*Albert C. Yan, MD*
Chief, Pediatric Dermatology
Children's Hospital of Philadelphia
Associate Professor, Pediatrics and Dermatology
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, Pennsylvania

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## TARGET AUDIENCE

The target audience for this educational supplement are dermatologists, pediatricians, and other health care professionals involved in the treatment of pediatric patients with acne.

## STATEMENT OF PROFESSIONAL PRACTICE GAP(S)

Although acne vulgaris is most commonly seen in adolescents and young adults (85% of individuals between 12 and 24 years of age develop acne), it may be seen at any age. The disease frequently is seen in preadolescents, and its occurrence in children as young as 7 years of age is not rare.

Untreated acne can leave permanent scars and, as such, create psychosocial issues for preadolescent, adolescent, young adult, and adult patients. Emerging therapies and regimens offer dermatologists a broader range of options to improve tolerability, sustain positive clinical outcomes, and effectively treat a diverse patient population. Treatment of acne depends on the type, extent, and severity of the condition. The current guidelines for acne management recommend the use of combination regimens in order to address multiple aspects of acne pathogenesis. For best outcomes, patient care should be individualized.

To achieve this goal of personalized therapy for patients of any age with acne, clinicians must stay informed about the proper use of existing therapies and the impending availability and anticipated appropriate use of emerging options. Furthermore, although randomized, controlled clinical trials of new and existing medications more frequently are including patients less than 12 years of age in study populations, to date all but a few prescription medications used to treat acne are approved by the FDA for use in patients as young as 12 years of age. It is important for clinicians to have the benefit of the opinions of experts to ensure that these medications are used appropriately and safely in younger pediatric patients.

This supplement addresses these needs and also provides an educational handout for the parents of younger pediatric patients to help families appropriately manage acne at home.

## LEARNING OBJECTIVES

Upon completion of this activity, participants should be better able to:

- Assess and classify acne vulgaris in pediatric patients, including preteen/preadolescent patients.
- Describe the topical and systemic medications available and suitable for use in pediatric patients with acne and note specifically which medications are indicated and contraindicated in pediatric patients less than 12 years of age.
- Discuss the evidence supporting how early treatment of acne changes the course of the disease in pediatric patients.
- Select the type of medication and route of delivery appropriate for individual patients, based on age, severity of disease, and other factors.
- Advise patients and their parents regarding the nature and management of the disease and on implementing strategies for coping with acne.

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# Introduction

Acne vulgaris is among the most common skin diseases, affecting almost all individuals by the time they reach adulthood. Acne is most commonly seen in patients between 12 and 17 years of age, but it may occur at any age, from birth through late adulthood. The articles in this supplement resulted from the meeting of a panel of experts convened during the Skin Disease Education Foundation's 35th Annual Hawaii Dermatology Seminar in March 2011. It was our goal to review the latest evidence and current expert opinions on the diagnosis and treatment of acne.

The authors involved in the development and writing of the following articles utilized the terminology proposed by the American Acne and Rosacea Society and the Acne Alliance of North American Pediatric Acne Guidelines Panel, not yet published, categorizing pediatric acne into four groups: *neonatal acne* (0-4 weeks of age), *infantile acne* (1 through 12 months of age), *mid-childhood acne* (≥1 through 6 years of age), and *preadolescent acne* (≥7 through 11 years of age). The presentation and differential diagnosis of each group is distinct, and these papers emphasize the spectrum of acne across the ages, the appropriate workup and management, and—with the limited database of therapy under age 12—the need to extrapolate from findings involving children 12 years of age and older.

While the term pediatric acne can be used variably, the expert panel emphasized acne and its differential diagnosis and treatment from birth up until adolescence. It is increasingly recognized that significant numbers of preadolescents have significant acne, and it is important to understand the epidemiology and presentations of acneiform conditions in the different pediatric age groups.

## The Need for Attention to Preadolescents

In 2010, this author served on a similar expert panel that met during the 34th Annual Hawaii Dermatology Seminar and developed a supplement titled "Facing the Challenge of Acne Vulgaris in Pediatric Patients."[1] In that supplement, the panel (Sheila Fallon Friedlander, MD, Joseph F. Fowler, Jr, MD, Richard G. Fried, MD, Moise L. Levy, MD, and Guy F. Webster, MD, in addition to this author) focused on current views of acne pathophysiology, the diagnosis and evaluation of the condition, and the medical and psychosocial impact of acne, including preadolescent patients in the spectrum of discussion.

One reason for the focus on preadolescent acne, in particular, in the recent panel discussion and current articles was the response of clinicians to the program evaluation question, "After participation in this activity, have you decided to change one or more aspects in the treatment of your patients?" A total of 407 out of 700 respondents (64.4%) answered in the affirmative. The verbatim statements regarding intended practice changes (a selected sample is shown in the Table) indicated that clinicians might benefit from more detailed attention to acne in the younger pediatric patient.

It is hoped that these papers combine the latest medical evidence with expert opinion in a useful and clinically practical way.

*Lawrence F. Eichenfield, MD, Chair*
Clinical Professor of Pediatrics and Medicine (Dermatology)
Chief, Pediatric and Adolescent Dermatology
Rady Children's Hospital, University of California, San Diego
San Diego, California

**Table. Intended Practice Changes: Selected Sample**

- Will not hesitate to treat younger patients [with acne]
- More confidence in prescribing acne medications to younger patients (8-11 y/o)
- Will consider psychological impact of acne and factor into treatment plan
- Start acne therapy at a younger age
- Use more topical retinoids; use them earlier
- Treat younger patients more aggressively
- More likely to use systemic therapy earlier
- Start retinoid therapy in less severe acne
- Be more proactive in treating acne
- I will address early acne in the younger age group

**Source:** Participant outcomes evaluations from Eichenfield LF[1].

### *Reference*

1. Eichenfield LF, Fowler JS, Fried RG, Friedlander SF, Levy ML, Webster GF: Facing the challenge of acne vulgaris in pediatric patients. Semin Cutan Med Surg 29:1-16, 2010 (2 suppl 1)

# Acne Life Cycle: The Spectrum of Pediatric Disease

Anthony J. Mancini, MD,* Hilary E. Baldwin, MD,† Lawrence F. Eichenfield, MD,‡
Sheila Fallon Friedlander, MD,§ and Albert C. Yan, MD¶

**Acne is no longer simply a diagnosis based on the appearance of characteristic lesions on the skin of adolescents. The presentation of acne differs across age groups, and the population of younger pediatric patients with acne continues to grow. This article addresses the changing epidemiology and demographics of acne, with specific emphasis on the 7- to 11-year-old acne patient population; the differences and similarities between pediatric acne and adolescent acne; age-based acne epidemiology; and current perspectives on acne etiology.**
**Semin Cutan Med Surg 30:S2-S5** 

In the past, one of the challenges in managing pediatric acne has been the lack of consensus on how to organize the discussion of the disease by age groups. Accumulating and recent evidence has led to growing consensus about age groupings and what to call them. Although this has not been a problem in the group of patients variously described as adolescents, teenagers, postadolescents, and young adults—generally considered as individuals between 12 and 18 years of age—the presentations, etiology, differential diagnosis, and management issues that affect pediatric patients less than 12 years of age are not so clear-cut. The goal of this article is to provide an overview of acne on the pediatric age spectrum, from birth through age 18 years.

*Professor of Pediatrics and Dermatology, Northwestern University's Feinberg School of Medicine, Head, Division of Pediatric Dermatology, Children's Memorial Hospital, Chicago, IL
†Associate Professor and Vice Chair, Department of Dermatology SUNY Downstate, Brooklyn, NY
‡Clinical Professor of Pediatrics and Medicine (Dermatology), Chief, Pediatric and Adolescent Dermatology, Children's Hospital San Diego, University of California, San Diego School of Medicine, San Diego, CA
§Clinical Professor of Pediatrics and Medicine, Dermatology, University of California, San Diego, Rady Childrens Hospital, San Diego, CA
¶Chief, Pediatric Dermatology, Children's Hospital of Philadelphia, Associate Professor, Pediatrics and Dermatology Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
Publication of this CME article was jointly sponsored by the University of Louisville Continuing Health Sciences Education and Skin Disease Education Foundation and supported by an educational grant from Johnson & Johnson Consumer & Personal Products Worldwide Division of Johnson & Johnson Consumer Companies, Inc.
Anthony J. Mancini, MD, FAAP, has served as a consultant for Galderma, Medicis, and Stiefel. He has also been a speaker for Galderma.
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Albert C. Yan, MD, has no relevant financial relationships with any commercial interests.
Corresponding author: Anthony J. Mancini, MD, Professor of Pediatrics and Dermatology, Northwestern University's Feinberg School of Medicine; Head, Division of Pediatric Dermatology; Director, Children's Memorial Hospital, Chicago, IL. E-mail: amancini@northwestern.edu

## Age-Based Epidemiology

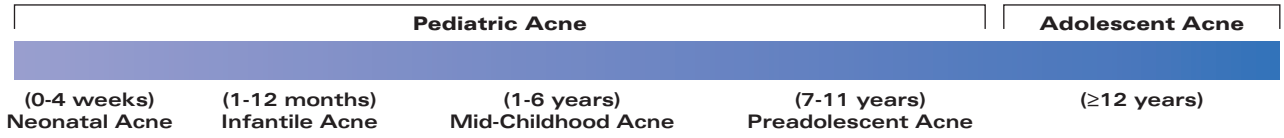
*Pediatric acne* is the term used to describe the presentation of disease from birth through 11 years of age; the term *adolescent acne* includes patients from age 12 to adulthood[1] (Figure). Under the designation of pediatric acne, four subgroups will be considered here: *neonatal acne* (0 through 4 weeks of age), *infantile acne* (1 through 12 months of age), *mid-childhood acne* (≥1 through 6 years of age), and *preadolescent acne* (≥7 through 11 years of age).[1]

### *Neonatal Acne and Infantile Acne*

Up to 20% of newborns present with neonatal acneiform eruptions. The characteristic lesions are erythematous papules and papulopustules, although some neonates may occasionally present with comedones. The lesions are typically located on the face, usually the cheeks, chin, eyelids, and forehead, although they sometimes extend to the scalp, neck, and upper chest. The condition, which appears more often in boys than in girls, is self-limited and usually mild. In most cases, the lesions resolve spontaneously within 1 to 3 months but, in some cases, may persist for longer, up to 12 months of age.[2] Neonatal acne is believed to be caused by stimulation of sebaceous glands by maternal androgens.

More recently, the term *neonatal cephalic pustulosis* (NCP) has been used by some to describe a similar process in newborns and young infants. This entity is considered synonymous with neonatal acne by some; however, others distinguish NCP as presenting with a larger number of inflammatory papules, a prominent pustular component, and the absence of comedones. NCP has been attributed to *Malassezia furfur* or *M. sympodialis* yeasts, and tends to respond well to topically applied azole antifungal agents.[3-5] The presence of comedones may actually represent early infantile acne, supporting the view of experts who

**Figure. Spectrum of Acne Vulgaris in Children and Adolescents**




suggest that neonatal acne and NCP are different terms for the same entity.

Infantile acne is also more common in boys than in girls. Although a prevalence has not been estimated by epidemiologic data, it is seen more rarely than is neonatal acne. The usual age of onset is between 3 and 6 months of age, but infantile acne may occur anywhere from 0 to 12 months of age (hence, the potential for overlap in the presentation of neonatal and infantile acne) and occasionally up to 16 months of age. The lesions of infantile acne typically involve the face, usually the cheeks. Unlike neonatal acne, infantile acne is usually a more inflammatory process, and patients may present with comedones, papules, and pustules, and also with occasional nodules and cysts.[6]

### *Mid-Childhood Acne*

In general, acne is very rare in children from 1 to 6 years of age. When it does occur, the term used to describe the condition is *mid-childhood acne*. The reason for the relatively rare occurrence of mid-childhood acne is that, normally, adrenal secretion virtually ceases after the first year of life until around 7 years of age, when an increase occurs in adrenal androgen production. Thus, in a child with mid-childhood acne, hyperandrogenism should be suspected and ruled out. The potential underlying causes include premature adrenarche, Cushing's syndrome, congenital adrenal hyperplasia, gonadal or adrenal tumors, and frank precocious puberty. Referral to a pediatric endocrinologist should be considered.

### *Preadolescent Acne*

Acne in a child between 7 and 11 years of age is termed *preadolescent* (or prepubertal) acne, referring to an age grouping rather than to a maturational stage. During these years, acne can appear as the first sign of impending pubertal maturation, before pubic hair or areolar development in girls and before pubic hair or testicular enlargement in boys. Most authors consider its appearance as a normal variant, without concerns for an underlying endocrinopathy. The typical presentation is comedonal lesions in the T zone of the face (across the forehead, on and near the nose, and on the chin), although inflammatory lesions also may appear.

As is well known, sebum production correlates with levels of dehydroepiandrosterone sulfate (DHEA-S) in preadolescent girls and boys, indicating that adrenal androgens are a major determinant of acne during this phase.

### *Adolescent Acne*

Acne vulgaris is one of the most common skin problems in the United States, affecting an estimated 15% of individuals of all ages and 85% of adolescents.[7]

## The Changing Demographics of Puberty and Acne Onset

trend for many years. In the 19th century, the average age of onset of puberty was 17 years. By the 1940s, the average age of puberty onset was about 13 years, which remained relatively unchanged for the next 3 to 4 decades. Since that time, the downward trend in age of onset of puberty has resumed, particularly with regard to breast development and menarche in girls.

Studies from the mid- to late 20th century indicate that breast and pubic hair development in American girls—especially African Americans—is occurring at younger ages.[8] As a result, regional definitions of precocious puberty have been revised. Puberty is considered to be precocious if it occurs before 6 years of age in African American girls, before 7 years of age in white girls in the United States, and before 8 years of age in European girls.[9]

A similar trend has not been apparent in boys. An expert panel, convened to analyze puberty timing data from 1940 to 1994,[10] evaluated the data for a secular trend (defined as a change in the distribution of an outcome in a population during a specified time frame). The majority of these experts agreed that sufficient data exist on earlier breast development and onset of menarche in girls to support a secular trend. However, they determined that there were not sufficient data to suggest a secular trend for an alteration of puberty timing in boys. The cutoff age for the consideration of precocious puberty in boys remains at 9 years.

Numerous hypotheses exist to explain the reasons for earlier puberty onset. The factors that are perhaps most frequently proposed include improved nutrition, obesity, and so-called *endocrine-disrupting chemicals,* which have been suspected as culprits in both early and delayed puberty. The chemicals implicated include polychlorinated biphenyls, polybrominated biphenyls, and phthalates.[11]

The trend toward earlier onset of acne has mirrored the downward trend in puberty timing, demonstrated by two seminal studies by Lucky and colleagues[12,13] that were published in the early 1990s. The first of these was the study of acne in adolescent boys 9 to 15 years of age.[12] These investigators found that the severity of acne correlated with pubertal maturation, and almost 50% of 10- and 11-year-old boys had more than 10 comedones (grade 2 or 3 comedonal acne) even before either testicular enlargement occurred or pubic hair developed. Mean acne scores correlated better with Tanner stage in pubic hair than with age. Inflammatory lesions were markedly less common during early pubertal development than were comedonal lesions. African American boys in this cohort who were in early stages of pubertal development had more comedones than did Caucasian boys.

In 1997, this group published a study of pubertal maturation and sex steroid hormones in relationship to acne in prepubertal girls.[13] The age range of the study population was 8.5 to 12.2 years. Lucky and colleagues found that 77.8% of the girls had some acne, of whom nearly half had only comedonal lesions. Acne increased with advancing maturity on examination, and DHEA-S levels were significantly higher in the prepubertal girls with acne.

No similar epidemiologic data have been published in the United States since these studies from Lucky's group, so it is not known if the epidemiology of acne has changed in this country in the intervening years. However, in 2008, a group of investigators from Taiwan[14] published data on the prevalence of skin diseases in a cohort of 3,200 children between 6 and 11 years of age. In that study, the overall prevalence of acne was 17%, and comedones were the earliest manifestation. Extrapolating from this study, it seems reasonable to suspect that a similar trend in younger American children might be occurring as well. The available data highlight the common occurrence of acne, primarily comedonal acne, in preadolescent patients.

## Current Perspectives of Acne Etiology[15-17]

The traditional four-factor cascade of events that have been identified in the etiology of acne vulgaris is familiar to most clinicians who see patients with acne: sebum overproduction, follicular hyperkeratosis, altered microbial flora and the role of *Propionibacterium acnes*, and immunologic/inflammatory processes. It is important to consider that the role of each of these factors may vary, depending on the age of onset of adrenarche—that is, the pathogenesis of disease in a 7- or 9-year-old patient may differ from that in a 15-year-old. In addition, the progression of acne varies from patient to patient, even among those at the same stage of maturational development, and the pathophysiology changes over time.

As new research information has become available regarding acne pathogenesis, the breadth, complexity, and interrelatedness of these four categories have become more fully appreciated and understood (Table).[15-17]

### *Sebum Overproduction*

It was once thought that the sebaceous gland's function was limited to the production of sebum. Androgens have long been implicated in the pathogenesis of acne and probably exert an effect primarily on the sebaceous glands by increasing the production of sebum.

However, more recent evidence demonstrates that these glands may have immunologic functions that play a role in the pathogenesis of acne. For example, sebocytes have been found to express functional receptors for neuropeptides, as well as toll-like receptors 2 and 4, and CD markers 1d and 14. Histamine-1 receptor has been demonstrated in these cells, and it has been shown that sebaceous glands produce inflammatory cytokines in the presence of *P. acnes*. Further, acetylcholine may modulate differentiation, sebum production, and composition. This neurotransmitter may act in a paracrine manner or may be stimulated in exogenous fashion by nicotine, which might suggest a role for the cholinergic system in acne and suggests that smoking may play an etiologic role in acne as well as other follicular disorders, such as hidradenitis suppurativa.[18]

**Table. Summary of Current Concepts in Acne Etiology[15-17]**

- Sebum overproduction
  - Sebaceous gland expresses functional receptors for neuropeptides
  - Sebaceous gland as "immunocompetent organ"
  - Toll-like receptor (TLR)-2 and TLR-4, CD1d and CD14 are expressed by sebocytes
  - May be activated by *Propionibacterium acnes*, with production of inflammatory cytokines
  - Histamine-1α receptor expressed in sebocytes
  - Acetylcholine may modulate differentiation and sebum production/composition
- Hyperkeratosis
  - Hyperkeratinization (retention hyperkeratosis), a crucial event in acne
  - Pathogenesis remains unclear
  - Interleukin (IL)-1 induces hyperkeratinization in vitro and in vivo
  - Increased dihydrotestosterone levels may stimulate hyperkeratinization
- Microbial flora
  - Significance of *P. acnes* still controversial
  - Part of resident microflora
  - Induces expression of antimicrobial peptides and proinflammatory cytokines
  - Activates TLR-2, which induces cytokine synthesis
- Immunoinflammatory mechanisms
  - Upregulated expression of multiple cytokines in presence of *P. acnes* and lipopolysaccharides
  - TLRs (transmembrane proteins serving as part of innate immune response) linked to acne inflammation
  - Reduction of anti-inflammatory IL-10 in patients with acne

### *Hyperkeratosis*

Hyperkeratosis or hyperkeratinization (also known as retention hyperkeratosis) is a crucial event in the development of acne lesions, but the pathogenesis remains unclear. Some recent research has shown that interleukin (IL)-1α induces hyperkeratinization, both in vitro and in vivo, and that increased levels of dihydrotestosterone also may stimulate its production.

### *Microbial Flora*

The significance of *P. acnes* is still somewhat controversial, with some arguing against its role in pathogenesis because the organism is part of the resident microflora. However, it has been shown that *P. acnes* can induce expression of antimicrobial peptides and proinflammatory cytokines and has an effect on toll-like receptor 2, leading to increased synthesis of cytokines.

### *Immunoinflammatory Mechanisms*

A great deal of research has focused on immunoinflammatory pathways of acne pathogenesis, including demonstration of the upregulation of multiple cytokines in the presence of both *P. acnes*, as previously mentioned, and lipopolysaccharides. Here again, toll-like receptors have been innately linked to acne inflammation. In addition, it has been shown that patients with acne tend to have reduced expression of anti-inflammatory cytokines, such as IL-10.

*continued on page 23*

# The Acne Continuum: An Age-Based Approach to Therapy

Sheila Fallon Friedlander, MD,* Hilary E. Baldwin, MD,† Anthony J. Mancini, MD,‡ Albert C. Yan, MD,§ and Lawrence F. Eichenfield, MD¶

**Acne vulgaris is classically considered a disease of adolescence. Although it most commonly occurs and has been best studied in that age group, it can develop at any time during childhood. It is important that health care practitioners recognize the manifestations of neonatal, infantile and childhood acne, as well as the differential diagnosis and best therapeutic approach in the younger child. Acneiform eruptions in infants and toddlers can occasionally be associated with scarring or with other significant disorders that may be life-threatening. In this article, the authors draw on their own clinical experience as well as the available literature to suggest an age-based approach to managing acne in children from the neonatal period through age 11 years.**
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*Clinical Professor of Pediatrics and Medicine, Dermatology, University of California, San Diego, Rady Childrens Hospital, San Diego, CA
†Associate Professor and Vice Chair, Department of Dermatology, SUNY Downstate, Brooklyn, NY
‡Professor of Pediatrics and Dermatology, Northwestern University's Feinberg School of Medicine, Head, Division of Pediatric Dermatology, Children's Memorial Hospital, Chicago, IL
§Chief, Pediatric Dermatology, Children's Hospital of Philadelphia, Associate Professor, Pediatrics and Dermatology Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
¶Clinical Professor of Pediatrics and Medicine (Dermatology), Chief, Pediatric and Adolescent Dermatology, Children's Hospital San Diego, University of California, San Diego School of Medicine, San Diego, CA
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Albert C. Yan, MD, has no relevant financial relationships with any commercial interests.
Corresponding author: Sheila Fallon Friedlander, MD, Clinical Professor of Pediatrics and Medicine (Dermatology), University of California San Diego. Rady Children's Hospital, San Diego, CA. E-mail: sfriedlander@chsd.org

Acne is an "equal opportunity" disorder, affecting not only the adolescent and middle-aged adult, but also children of all ages.[1] Clinical and epidemiologic studies over the past 2 decades have helped refine the diagnosis and treatment of acne in children less than 12 years of age. Studies documenting the changing demographics of acne in preadolescent children, as well as the nature of neonatal and infantile disease, have provided the information necessary to develop rational approaches to evaluation and treatment in our youngest patients.

## Neonatal Acne

The term *neonatal acne* has historically been used as an umbrella term to describe a variety of lesions occurring in newborns. One variant seen in neonates is characterized by comedonal or only mildly erythematous papular lesions (Figure 1), a distribution that may include the face, scalp, chest, and back, and a course lasting up to a year or more. In some patients, inflammatory and even nodulocystic lesions may appear and increase in severity with time. It is suggested that the term *infantile acne* be used to describe this condition, as it is not limited to the neonatal period; accordingly, it will be discussed under that heading, in the next section. More commonly seen in the neonatal period is a condition that has been called *neonatal cephalic pustulosis* (NCP). Inflammatory, often pustular lesions appear very early and tend to resolve spontaneously within the first 4 to 8 weeks of life. Male infants are affected five times more often than female infants and the lesions are characteristically limited to the face (Figure 2). It has been estimated that up to 20% of newborns experience this form of neonatal acne.[2]

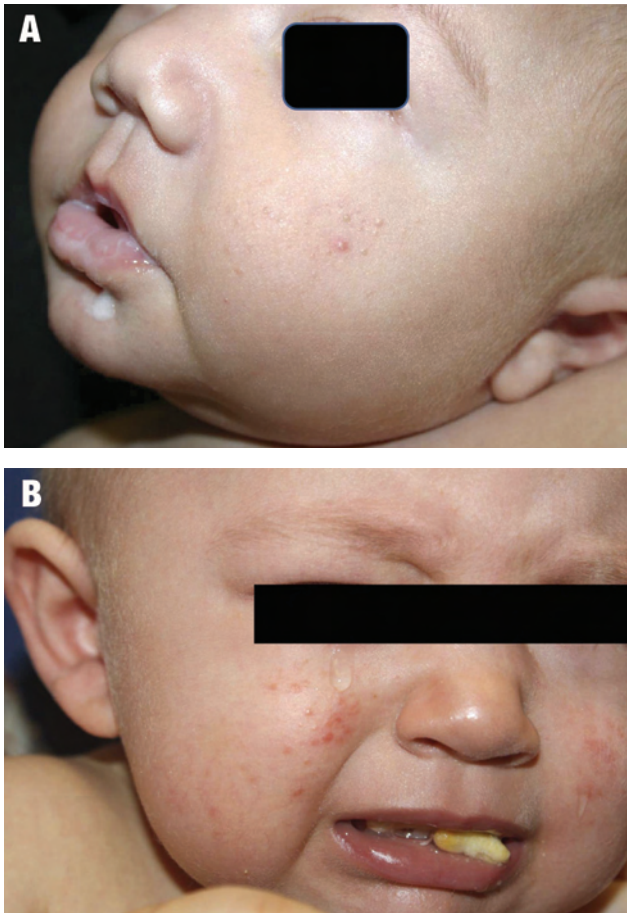


**Figure 1. Infantile Acne**
**A.** With Erythematous Papules and Comedones Present
**B.** With Comedones and Inflammatory Papules
Photos courtesy of Sheila Fallon Friedlander, MD.

Some evidence suggests that in a subset of patients, NCP may be associated with *Malassezia furfur* colonization. In one study published in 1996, a group of French investigators[3] sampled and examined smears from the faces and necks of 13 neonates. In 8 of the samples, neutrophils and *M. furfur* yeast were identified. The infants with positive smears were treated with topical ketoconazole 2% cream twice daily and the lesions resolved rapidly.

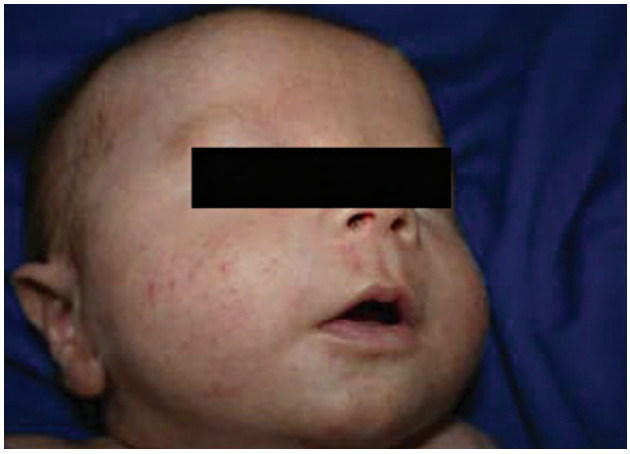

**Figure 2. Infant With Superficial Pustules of Neonatal Cephalic Pustulosis**

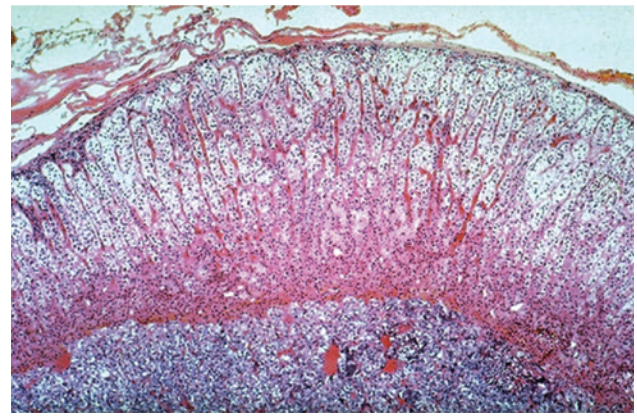

**Figure 3. Adrenal Gland Enlargement**
This photomicrograph demonstrates enlargement—suggesting hyperactivity—of the zona reticularis of the adrenal gland in a newborn. (elsevier.com)

However, subsequent studies of the possible correlation between *M. furfur* and pustular lesions in neonates have yielded conflicting results. Some have shown that not all patients with pustulosis have positive cultures, and some patients who are culture positive do not have any skin lesions. One explanation for these findings is that such outbreaks may represent a hypersensitivity reaction to the presence of *M. furfur* rather than a disease caused by an absolute increase in the number of organisms.[4-6]

It has been proposed that some cases of comedonal disease in neonates may, in fact, be a less inflammatory response to *M. furfur,* although this would not explain the clinical observation that comedonal disease tends to persist longer than the pustular condition. Until further research clarifies this issue, it seems reasonable to assume that there may be some overlap of conditions (NCP and infantile acne) in some patients, in whom the conditions may occur simultaneously. Once attributed to maternal placental androgens, the more recently accepted hypothesis for true neonatal acne is an increase in dehydroepiandrosterone (DHEA) production causes enlargement and, in some cases, hyperactivity of the fetal adrenal gland (Figure 3). An association with severe adolescent acne later in life has been suggested, but the data supporting such a link are not robust.[2]

## *Diagnosis and Treatment of Neonatal Acne*

The first goal in a neonate with pustular lesions is to rule out bacterial, viral, or fungal infections. The differential diagnosis includes erythema toxicum neonatorum (seen commonly in neonates, it usually disappears within the first week or two of life), milia, miliaria, sebaceous gland hyperplasia, and drug reaction (to either maternal medications or to topical or systemic drugs administered to the baby). In almost all cases, these other conditions can be ruled out based on the age of the patient, the distribution and morphology of the lesions, and results of laboratory evaluations. (Differential diagnosis is shown in Tables 1 and 2; features of neonatal vs those of infantile acne are listed in Table 3.)

**Table 1. Differential Diagnosis of Pediatric Acne in Patients ≤12 Years of Age[1]**

| Condition | Comment |
|---|---|
| Angiofibromas (adenoma sebaceum) | • Associated with tuberous sclerosis<br>• Mid-facial clustering of lesions, often in the alar creases<br>• Typically initially pink, then white<br>• Check for hypopigmented macules (ash-leaf spots); Wood's lamp examination may be helpful to demonstrate these macules<br>• Query regarding family history of angiofibromas, seizures, and hypopigmented spots<br>• Signs other than hypopigmented macules are usually not present in earlychildhood |
| Aseptic facial granuloma | • Usually an isolated, painless nodule on the cheek |
| Drug exposure | • Phenytoin and other anticonvulsants<br>• Lithium<br>• Isoniazid<br>• Corticosteroids (oral, topical, inhaled) |
| Eosinophilic pustular folliculitis | • Scalp lesions common |
| Erythema toxicum neonatorum | • Seen commonly in neonates<br>• Can be pustular<br>• Usually disappears within the first week of life |
| Hormonal pathology: adrenal disease (particularly congenital adrenal hyperplasia), adrenal tumors, true precocious puberty, premature adrenarche, gonadal tumors, early onset of polycystic ovarian syndrome | • Uncommon<br>• Must be ruled out when acneiform lesions occur in mid-childhood (1 through 6 years of age) |
| Infections | • Staphylococcal<br>• Pityrosporum folliculitis<br>• Herpes simplex<br>• Atypical mycobacteria<br>• *Candida* species |
| Keratosis pilaris | • Gray-white, hyperkeratotic, follicular papules<br>• Most commonly occur on the extensor surfaces of the upper arms, thighs, and cheeks<br>• Papules may occasionally be inflammatory |
| Milia | • Characteristically small (1 to 2 mm), white, globoid, noninflammatory papules<br>• Extremely common in newborns but may be seen in older children and adults |
| Miliaria | • Caused by sweat retention; often occurs in covered areas<br>• Common in first few weeks of life<br>• Fine vesicles, papules, or papulovesicles |
| Molluscum contagiosum | • Often looks like acne when inflamed<br>• In most patients, presents with classic umbilicated, pearly papules |
| Periorificial dermatitis | • Noncomedonal<br>• Classic distribution around mouth, eyes, and nose<br>• Does not respond to standard acne therapy<br>• May represent a juvenile form of acne rosacea |
| Pomade acne | • Form of occlusion folliculitis<br>• Question patient and/or parents about the use of hair styling or other cosmetic products on or near the face |
| Verrucae planae (flat warts) | • Koebner phenomenon (appearance of lesions along a site of trauma), when present, is a useful distinguishing feature<br>• Typically noninflammatory<br>• Common warts may be present elsewhere |

Significant hormonal abnormalities may rarely be a cause of lesions in this age group; a laboratory workup is not indicated unless height, weight, or maturational abnormalities are noted (this does not include neonatal gynecomastia, which is a normal variant).

Because NCP is self-limited and transient, treatment is not necessary. However, when parents are concerned and a discussion about the condition fails to reassure them, some providers prescribe topical ketoconazole 2% cream twice daily for 1 week. No clinical trials support such use of ketoconazole; however, its use is based on the clinical experience of the authors, which has shown that this therapy may sometimes be helpful.

**Table 2. Differential Diagnosis of Neonatal Acne[1]**

**More Common:**
- Drug reaction (to maternal medications or to topical or systemic drugs administered to the baby)
- Erythema toxicum neonatorum
- Milia
- Miliaria
- Sebaceous gland hyperplasia

**Less Common:**
- Viral, bacterial, fungal infection
- Endocrinopathy

If the lesions are still present after 4 weeks of age or if comedonal lesions are prominent, the patient may have infantile acne and may require more aggressive therapy over time. In cases in which comedones persist and the family desires treatment, topical benzoyl peroxide or a topical retinoid is appropriate. For persistent inflammatory disease, a topical antibiotic (clindamycin or erythromycin) should be added.

# Infantile Acne

Infantile acne, which—like neonatal acne—is more common in male infants, may be seen in children from birth to approximately 12 months of age. However, it more commonly presents after the neonatal period. The classic presentation is predominantly comedonal, but inflammatory lesions may be present (either inflammatory comedones or—particularly in young infants—concomitant pustular neonatal acne lesions). Infantile acne also may be nodular. The lesions most commonly appear on the face, but lesions also may be seen on the neck, back, and chest. Although infantile acne usually resolves by 1 year of age, the condition can persist for several months or even years.[7]

**Table 3. Neonatal vs Infantile Acne[1]**

| | Neonatal | Infantile |
|---|---|---|
| Onset | Often 2 to 3 weeks of age | Often 3 to 6 months of age |
| Lesions | Pustules; less likely, comedones | Comedones, pustules, cysts |
| Possible etiology | *Malassezia* species colonization (neonatal cephalic pustulosis) | Androgens may play a role |
| Course | Spontaneous resolution, usually by about 1 month of age | Can persist for months to years |
| Sequelae | None | Scarring possible with inflammatory disease; possible association with severe acne in adolescence |

## *Diagnosis and Treatment of Infantile Acne*

The more common conditions that should be considered in the differential diagnosis are listed in Table 1. The physical examination should always include assessment of growth and charting of the infant's height and weight. Blood pressure also should be measured and monitored to rule out corticosteroid or androgen-secreting disorders. Accelerated growth of hands and feet suggests the need for further workup. In addition, the clinician should be alert for androgen effects, such as odor, changes in areolae and testes, and the presence of axillary and/or genital hair. Children in whom these signs are noted should have a complete laboratory workup, as listed in Table 4.

Children whose clinical examination is within normal limits generally do not require further workup and may be treated with the standard regimens shown in Table 5. However, a high index of suspicion for underlying pathology must be maintained for acne that presents after the first year of life and before 6 to 7 years of age, and more aggressive evaluation is required in that age group (see the following section on "Mid-Childhood Acne"). Careful follow-up is mandatory and should include continued monitoring and charting of maturational milestones and observation for features of virilization. If the condition proves refractory to standard therapy or any evidence of virilization occurs, a complete laboratory workup and bone age assessment are appropriate.

**Table 4. Evaluation When Hyperandrogenism Is Suspected[1]**

- Family & drug exposure history
- Search for axillary, genital odor/hair
- Assess breast & testicular development
- Laboratory considerations:
  - Testosterone (free and total)
  - Dehydroepiandrosterone sulfate (DHEA-S)
  - Luteinizing hormone
  - Follicle-stimulating hormone
  - Prolactin
  - 17-Hydroxyprogesterone
  - Bone age

**Table 5. General Approach for Treating Acne**

- **Mild (comedonal or mixed comedonal and inflammatory lesions)**
  - Topical benzoyl peroxide or topical retinoid OR
  - Topical combination therapy (benzoyl peroxide plus retinoid, benzoyl peroxide plus topical antibiotic, or benzoyl peroxide plus both topical antibiotic and retinoid) OR
  - Topical sulfacetamide
  - Topical dapsone

*If response is inadequate*, consider adding a retinoid product to a regimen that does not already include it, changing the concentration and/or type of vehicle in the retinoid product, or changing to a combination product that has not been tried.

- **Moderate (combined comedonal and inflammatory)**
  - Add oral antibiotic (erythromycin, macrolide derivatives such as clarithromycin; in patients >8 years of age, doxycycline or minocycline)*
  - Increase strength of topical retinoid

*In older girls* who do not respond to other treatment, consider hormonal therapy with a combination oral contraceptive

- **Severe**
  - Combination topical therapy with retinoid and/or benzoyl peroxide and/or antibiotic AND
  - Oral antibiotic

If no response, switch to a different oral antibiotic and/or increase topical product strengths or combinations If no response, consider oral isotretinoin.

* Experience with other oral antibiotics has been reported, including trimethoprim-sulfamethoxazole and cephalexin. (Fenner JA, Wiss K, Levin NA. Oral cephalexin for acne vulgaris: Clinical experience with 93 patients. *Pediatr Dermatol.* 2008;25:179-183.)

Topical treatment is the initial therapy for significant, comedonal infantile acne, including benzoyl peroxide and tretinoin as monotherapy or combination therapy. If inflammatory lesions are present, topical antibiotics may be added to the therapeutic regimen. If necessary, systemic antibiotics can be added as well. Drugs in the tetracycline class should not be administered to children less than 8 years of age.

In severe, refractory cases involving large, nodular lesions, scarring is a potential long-term risk. In such cases, clinicians have used intralesional corticosteroids as well as low-dose systemic isotretinoin with good effect. A suggested dosage for isotretinoin is 0.2 to 1 mg/kg/day for 4 to 14 months. If isotretinoin is considered, the patient's family should be cautioned about possible adverse effects. Intralesional injection of a corticosteroid (1 to 2.5 mg/kg triamcinolone) is a nonsystemic alternative to manage nodules.

## Mid-Childhood Acne

The age range for mid-childhood acne is 1 to 7 years of age. The most common conditions to consider in the differential diagnosis (Table 1) are angiofibromas, keratosis pilaris, milia, miliaria, flat warts, molluscum contagiosum, pityrosporum folliculitis, and periorificial dermatitis. Also, certain medications to which children in this age group may be exposed may induce an acneiform eruption. These include anticonvulsants (such as phenytoin) and isoniazid, as well as topical, systemic, and inhaled corticosteroids.

Although underlying hormonal pathology occurs less commonly than do the dermatologic diseases mentioned above, such pathology should be seriously considered when children in this age group present with acneiform lesions. The possible hormonal conditions include adrenal disease (particularly congenital adrenal hyperplasia), adrenal tumors, true precocious puberty, premature adrenarche, gonadal tumors, and early onset of polycystic ovarian syndrome.

The clinician should ask about a family history of partial congenital adrenal hyperplasia. A careful review of medications should be performed. In addition, blood pressure should be measured. Unless medication reaction is identified as the cause, the patient should be assessed for abnormal maturation, as described above. A full hormonal laboratory workup and bone age assessment are indicated for any patient with mid-childhood acne.

## Preadolescent Acne

Many children between 7 and 11 years of age are in various stages of puberty, so the term *preadolescent* is now preferred when considering acne in children who are in this age range. The appearance of comedonal, only mildly inflammatory lesions in children in this age group represents what might be called *adrenal awakening* and is generally not a sign of worrisome pathology.

The seminal studies on this topic by Lucky and colleagues[8,9] showed that comedonal acne may be seen in children as young as 7 years of age and that girls are more likely to be affected than are boys in the preadolescent age group. The prevalence of comedonal acne among all children in the United States 11 years of age or younger is 47.3%. Comedonal acne is the most common form seen in the preadolescent age group, with a typical mid-face distribution. Other sites, such as the conchal bowl of the ears, also may be involved. Typically, the condition is mild in this age group. Severe comedonal disease in girls has been associated with severe acne in adolescence.

The dermatologic conditions and possible drug reactions that should be considered in the differential diagnosis are the same as for patients with mid-childhood acne (particularly including angiofibromas, keratosis pilaris, perioral dermatitis, and pityrosporum folliculitis).

In the absence of findings suggesting hyperandrogenism, a thorough physical examination and family history are sufficient to rule out other dermatologic conditions in the differential and establish the diagnosis of preadolescent acne.

Physical findings that suggest an underlying hormonal pathologic process as the cause of acneiform lesions in preadolescent patients include recalcitrant disease, significant and/or rapid development of pustular nodular lesions, and lack of response to standard acne therapy. Signs of abnormal hormonal stimulation also include signs of sexual development or virilization.[10,11] In such cases, further workup is indicated; laboratory tests should include those listed in Table 4. Bone age should also be evaluated. In addition, if Cushing's syndrome is suspected, adrenocorticotropic hormone stimulation testing can be considered.

Some clinicians recommend initial therapy with a benzoyl peroxide wash for patients with very mild comedonal acne, but all of the topical medications that are used for acne in patients 12 years of age or older also are appropriate for use in preadolescents. The efficacy and safety data on these younger patients are limited: tretinoin has been tested in children as young as 8 years of age,[11] and a benzoyl peroxide/adapalene combination topical agent has been tested in children as young as 10 years of age. Based on the large body of efficacy and safety data from older pediatric patients (ie, those from 12 through 17 years of age)—and, as extensive clinical experience has shown—it is reasonable to presume similar efficacy and safety in younger children. However, because preadolescent patients tend to produce less sebum than do older patients, their skin tends to be more sensitive. To improve tolerance, it is often helpful to initiate therapy with decreased frequency of application (for example, twice weekly or every other day), and application of smaller amounts of the medication. In addition, the daily application of a noncomedogenic moisturizer may be useful.

When necessary for the treatment of severe, nodulocystic acne in preadolescent patients, systemic agents—including oral isotretinoin—should be considered.

## Summary

Acne can occur at any time in life; cause for concern differs depending on age of presentation. Neonatal disease is often transient and may be related to pityrosporum disease. Acne that presents in the postneonatal period but before 1 year of age is usually defined as infantile disease and generally is not associated with underlying pathology. In contrast, disease that presents between 1 and 7 years of life is of more concern, and a full evaluation for possible underlying hormonal pathology is warranted. Children as young as 7 years of age can present with mild, usually comedonal disease, which most often is a normal physiologic occurrence.

Treatment at any age depends on the type and severity of involvement. Comedonal disease responds best to topical benzoyl peroxide and topical retinoid products; inflammatory disease usually benefits from the addition of topical or systemic antibiotics. Severe disease may warrant treatment with systemic isotretinoin, regardless of age. Families should always be counseled regarding the risks and benefits of any therapeutic option.

*references on page 20*

# The Effects of Culture, Skin Color, and Other Nonclinical Issues on Acne Treatment

Hilary E. Baldwin, MD,* Sheila Fallon Friedlander, MD,† Lawrence F. Eichenfield, MD,‡ Anthony J. Mancini, MD,§ and Albert C. Yan, MD¶

**The effective and safe treatment of acne vulgaris often is affected by individual patient characteristics, including skin color and cultural background. Skin of color is especially prone to hyperpigmentation, both from lesions and from irritating therapy. Clinicians also should be aware of cultural attitudes and folk remedies that may adversely affect dermatologic conditions such as acne.**
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Clinicians who treat patients with acne vulgaris must consider factors other than accurate diagnosis and the prescription of an appropriate treatment plan. Complicating the clinical picture in patients with acne vulgaris is the need to be aware of variations in skin color, culture, and attitudes of both patients and their parents.

*Associate Professor and Vice Chair, Department of Dermatology, SUNY Downstate, Brooklyn, NY
†Clinical Professor of Pediatrics and Medicine, Dermatology, University of California, San Diego, Rady Childrens Hospital, San Diego, CA
‡Clinical Professor of Pediatrics and Medicine (Dermatology), Chief, Pediatric and Adolescent Dermatology, Children's Hospital San Diego, University of California, San Diego School of Medicine, San Diego, CA
§Professor of Pediatrics and Dermatology, Northwestern University's Feinberg School of Medicine, Head, Division of Pediatric Dermatology, Children's Memorial Hospital, Chicago, IL
¶Chief, Pediatric Dermatology, Children's Hospital of Philadelphia, Associate Professor, Pediatrics and Dermatology Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
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Hilary E. Baldwin, MD, has served as a consultant and speaker for Allergan, Galderma, Medicis, and Onset. She has also been a speaker for GlaxoSmithKline and Ortho Dermatologics.
Sheila F. Friedlander, MD, has served on an advisory board for Galderma and Onset.
Lawrence F. Eichenfield, MD, has served as an investigator for Galderma, GlaxoSmithKline, Johnson & Johnson, Neutrogena, and Stiefel. He has also been consultant and/or served on the advisory board for Coria and Galderma, GlaxoSmithKline, Intendis, Medicis, Ortho Dermatologics, Stiefel, and Valeant.
Anthony J. Mancini, MD, FAAP, has served as a consultant for Galderma, Medicis, and Stiefel. He has also been a speaker for Galderma.
Albert C. Yan, MD, has no relevant financial relationships with any commercial interests.
Corresponding author: Hilary E. Baldwin, MD, Associate Professor and Vice Chair, Department of Dermatology, SUNY Downstate, Brooklyn, NY. E-mail: hilary.baldwin@downstate.edu

## Acne and Skin Color

There is little epidemiologic evidence demonstrating that acne occurs earlier, is more aggressive, or is more likely to persist longer in any particular ethnic group. An exception comes from Perkins and colleagues,[1] who reported that acne was more common in the darker-skinned individuals among the populations they studied (Caucasian, Asian, Continental Indian, and African American women).

A commonly cited study by Lucky and colleagues showed that pubertal maturation may occur earlier in African American girls, so acne vulgaris also may occur earlier.[2] However, the differences between racial groups in acne age of onset was not clearly seen when the data were controlled for pubertal development.

In addition, there is no evidence that acne therapy works more effectively in any particular ethnic group(s) than in others. What is seen more frequently in people of color than in Caucasians is postinflammatory hyperpigmentation (PIH). Scarring tendencies may differ and keloid formation is more likely in patients of color.

### *Postinflammatory Hyperpigmentation*

Manipulation of lesions is associated with an increase in PIH, underscoring the importance of early and effective therapy to eliminate acne lesions. The tendency to develop PIH appears to be genetically determined. It is not limited to cystic lesions, but is seen with lesions of all types.[3]

In a study of acne in African American women, Halder and colleagues[4] compared the clinical appearance of facial acne lesions of all types (comedones, papules, pustules, hyperpigmented macules, and depressed scars) with histologic findings of 3-mm punch biopsies. The investigators found that the degree of inflammation in all types of lesions was "marked and out of proportion" to their clinical appearance. This was not the case in light-skinned individuals. According to the authors, this suggests that acne vulgaris in African Americans is clinically and histopathologically different from the disease found in Caucasians, which may explain why hyperpigmentation and scarring is more common in darker-skinned persons.

No acne treatments have been identified as causal for PIH. However, the irritation associated with topical therapy can increase the risk of PIH in skin of color. To minimize irritation, treatment of patients with skin of color should be approached with this in mind. Specifically, acute irritation from topical benzoyl peroxide and retinoid preparations should be avoided, if possible. When initiating topical retinoid therapy, lower concentrations can be used, cream formulations rather than gels utilized, and applications decreased to every other day. The concentration of medication and frequency of application can be increased gradually, in a stepwise fashion. The need for a gentle introduction to topical care must be balanced with the knowledge that acne lesions themselves are a source of PIH.

When acne is severe, prompt clearing of lesions is necessary to avoid lesion-related PIH, so such a slow, stepwise approach to topical therapy may not be advisable as monotherapy. In such cases, it may be prudent to initiate oral therapy earlier than one might have ordinarily. Acne surgery is useful for eradicating closed and open comedones, but overly aggressive extraction can cause long-lasting PIH. In patients with skin of color, anecdotal experience shows that 1 month of treatment with topical retinoids prior to acne surgery is beneficial. Comedones are more easily extracted with less pigment-producing trauma.

Hyperpigmentation often is more of a problem for patients than is acne itself. Treatment options for PIH include hydroquinones, topical retinoids, and multiple types of cosmeceutical products.[5-7] Chemical peels[8] and laser and light therapy[9] can be effective but must be approached cautiously to avoid further hyperpigmentation and the possibility of scarring.

### *Preadolescent Patients*

It is common for preadolescents and early adolescent patients—particularly girls—to seek treatment for "blemishes" rather than acne itself. Many are noncompliant with acne treatment regimens because they are more concerned with the appearance of PIH. It is important to stress to these patients that control of acne, using the prescribed therapeutic regimens, will decrease the amount of PIH in the future as it decreases new lesion formation. Meanwhile, the offer of treatment of PIH often helps promote adherence to acne therapy.

The data are sparse on specific treatments for acne in younger patients with skin of color, but it is reasonable to extrapolate from efficacy and safety studies that included patients between 12 and 17 years of age with similar skin colors.

### *Acne-Related Scarring*

Acne can also be associated with keloidal scars in skin of color, with acne lesions often transforming almost imperceptibly into keloids. In some cases, the only indication that acne is the underlying cause of keloids is the distribution of the lesions over the chest, back, upper arms, and jaw. In such cases, aggressive therapy with isotretinoin might be warranted, even in younger adolescents. New acne/keloid lesion formation will stop and the keloids can subsequently be treated.

## Perceptions, Customs, Habits, and Fads

Some patients and/or their parents hold the perception and belief that "natural" agents are superior to "drugs" in the treatment of a variety of diseases, including acne vulgaris. In fact, the only such product on which there are even meager data regarding benefit in acne is tea-tree oil, which may be of minor benefit in mild acne. Patients who resist topical pharmacotherapy are often even more resistant to the use of oral medications, which they perceive as dangerous.

Sometimes these individuals attempt to be well informed, but the source of their information is deficient—for example, Internet sites and blogs that are opinion-rich and fact-poor, resulting in the dissemination of incorrect notions and the perpetuation of myths. Parental fears arising from misinformation can interfere with the appropriate treatment of adolescents with moderate to severe acne. Countering the effects of erroneous notions and beliefs requires a great deal of patience, discussion, and education.

### *Tanning*

Artificial and natural sunlight may improve the appearance of acne temporarily. Tan skin provides some camouflage for the redness of acne lesions. In addition, as it is a crude form of light therapy, sun exposure may also result in an short-term improvement in lesions, and the observation that sunlight improves acne is not lost on patients. In colder climates, some patients prolong their suntans by using tanning beds. Unfortunately, the temporary improvement in appearance makes it difficult for clinicians to convince patients of the long-term skin damage associated with ultraviolet light exposure.

### *Culture, Doctors, and Medication Adherence*

In a recent meta-analysis of adherence of people of color and language diversities to medications in general, Manias and Williams[10] failed to identify any factors that would be helpful in improving adherence to medication regimens among these populations. Thus, it is up to the clinician's awareness and sensitivity to work with individual patients and their families.

Some patients distrust authority, in general; others have a particular bias against doctors whose cultural or racial backgrounds are dissimilar to their own. It is likely that dermatologists see this more than clinicians in other specialties because racial differences are readily apparent. It often behooves the clinician to address possible concerns in an open and direct manner at the initial visit.

At the other end of the spectrum are patients who embrace authority literally without question. In some cultures, asking questions of an authority figure, such as a physician, is considered to be an insult. When dealing with such patients, it is incumbent on the physician to draw out questions during a clinical encounter, or the patient may leave with inadequate information or understanding of his or her condition or the prescribed treatment regimen.

### *Folk Remedies*

Folk remedies for dermatologic and other conditions are commonly used, particularly by patients of Hispanic, Asian, and Caribbean descent. As many as 50% of inner-city patients use folk remedies on a regular basis, either as replacements for or adjuncts to prescribed medications. These practices are often not mentioned and may interfere with the intended treatment plan. The folk remedies may cause irritation and, thus, increase the risk for hyperpigmentation in patients of color, as well as decreasing the acceptance and use of topical medications that would otherwise be effective.

## Consequences of Ineffective/ Delayed Treatment

Numerous articles have been published regarding the negative psychological impact of acne vulgaris. Layton and colleagues[11] showed that emotional scarring often persists into adulthood, long after acne has resolved, even in the absence of physical scarring.

In addition to their medical benefits, interventions to improve appearance are important to patient comfort and quality of life. Dalgard et al[12] showed that the appearance of the skin is important in social interactions, as well as having a crucial impact on self-image and self-worth. In current American culture, with society's ongoing emphasis on beauty (if not outright physical perfection), teenagers and even preadolescent patients may interpret acne as life-altering if not life-ending.

It has been well documented that acne is associated with social dysfunction—including decreased dating, participation in sports, and social interactions with peers—as well as having an adverse effect on academic performance.[13]

There is evidence that psychological problems caused by acne decrease with treatment and that identifying early acne and treating it improve quality of life.[14] Several studies have shown that rapid improvement with treatment is particularly important in the pediatric population. Therapeutic strategies that result in rapid improvement have the greatest beneficial effect on the psychological well-being of patients with acne. For example, acne surgery and injections of existing lesions can be helpful adjuncts to initial pharmacologic treatment, because they have a more immediate effect on appearance.

Physical scarring is a tendency that is unique to the individual. Furthermore, the severity of the lesions does not necessarily correlate with the risk for scarring. Some patients with very small papules and comedones develop "icepick" scars, whereas some others with nodulocystic acne eventually clear with no visible sequelae. It is not possible to predict which patients or which lesions will develop acne scars; however, the more lesions occur, the greater the risk for scarring. Prompt, effective treatment is the best way to prevent scarring. The development of scarring in a patient with acne constitutes a cutaneous emergency and merits aggressive treatment to reduce the risk of further scarring.[14,15]

### *Recent Evidence on Mental Health and Suicide*

A recently published study by Halvorsen and colleagues[16] provides evidence supporting the observation that suicidal ideation and mental health problems are increased in teenagers with acne. Of almost 5,000 adolescents enrolled in that study, 14% self-identified as having substantial acne (described by study participants as "a lot" or "very much acne"). Suicidal ideation was reported more than twice as frequently by girls and more than three times as frequently in boys with substantial acne than by the patients who reported no or little acne. The study also demonstrated a strong association between substantial acne and an increase in mental health problems, such as poor social interactions, lack of thriving in school, and increased bullying.

This study supports a long history of experience with adolescents with acne and indicates that it would be appropriate for all clinicians to consider the psychological impact of the disease. At the very least, clinicians should have a heightened awareness about and establish an informal assessment of the psychosocial impact of acne on each patient. Patients with severe acne (or any patients with acne, regardless of severity) who have any indication of mental health problems may benefit from a more formal evaluation and possible counseling.

For many years, drugs like isotretinoin were implicated in increasing the risk of depression and suicidal ideations in patients with acne. The study by Halvorsen and colleagues[16,17] supports the view of many clinicians that such problems in patients with acne exist exclusive of any therapeutic intervention. As the authors of this study conclude: "Adverse events including suicidal ideation and depression that have been associated with therapies for acne may reflect the burden of substantial acne rather than the effects of medication." This evidence should be communicated to patients and their parents when oral therapy—including isotretinoin—is indicated as a treatment of choice.

## Conclusion

Acne is commonly associated with postinflammatory hyperpigmentation in patients of color, which often can be more bothersome to patients than are the acne lesions that caused the dyschromia. In skin of color, PIH can occur secondary to any acne lesion, even comedonal lesions with no clinical appearance of inflammation.

Early and effective therapy, tailored not only to the acne severity but also to the level of psychological distress, is extremely important.

In determining treatment regimens, clinicians must take into consideration the widely varying differences that exist among patients of different ages and of different ethnic and cultural backgrounds.

*continued on page 23*

# Approach to Pediatric Acne Treatment: An Update

Albert C. Yan, MD,* Hilary E. Baldwin, MD,† Lawrence F. Eichenfield, MD,‡
Sheila Fallon Friedlander, MD,§ and Anthony J. Mancini, MD¶

**By late adolescence, almost all individuals have experienced some degree of acne. A broad range of acne treatments has been shown to be safe and effective in adults. While still sparse, emerging data now also document similar safety and efficacy of these agents for children >12 years of age. For younger children with preadolescent acne, where data are more limited or unavailable, it seems reasonable to extrapolate from the findings of studies involving older children >12 years of age. This article reviews the latest evidence and current expert opinions on acne therapies in the pediatric age group.**
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Acne is a nearly universal phenomenon typically affecting American children between the ages of 12 and 17 years of age.[1] Given this high prevalence, it is not surprising then that the 2005 report on *The Burden of Skin Diseases* estimated that total direct costs associated with the treatment of acne vulgaris in the United States exceeded $2.2 billion, including the substantial costs of both over-the-counter and prescription products.[1]

*Chief, Pediatric Dermatology, Children's Hospital of Philadelphia, Associate Professor, Pediatrics and Dermatology Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
†Associate Professor and Vice Chair, Department of Dermatology, SUNY Downstate, Brooklyn, NY
‡Clinical Professor of Pediatrics and Medicine (Dermatology), Chief, Pediatric and Adolescent Dermatology, Children's Hospital San Diego, University of California, San Diego School of Medicine, San Diego, CA
§Clinical Professor of Pediatrics and Medicine, Dermatology, University of California, San Diego, Rady Childrens Hospital, San Diego, CA
¶Professor of Pediatrics and Dermatology, Northwestern University's Feinberg School of Medicine, Head, Division of Pediatric Dermatology, Children's Memorial Hospital, Chicago, IL
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Albert C. Yan, MD, has no relevant financial relationships with any commercial interests.
Hilary E. Baldwin, MD, has served as a consultant and speaker for Allergan, Galderma, Medicis, and Onset. She has also been a speaker for GlaxoSmithKline and Ortho Dermatologics.
Lawrence F. Eichenfield, MD, has served as an investigator for Galderma, GlaxoSmithKline, Johnson & Johnson, Neutrogena, and Stiefel. He has also been consultant and/or served on the advisory board for Coria and Galderma, GlaxoSmithKline, Intendis, Medicis, Ortho Dermatologics, Stiefel, and Valeant.
Sheila F. Friedlander, MD, has served on an advisory board for Galderma and Onset.
Anthony J. Mancini, MD, FAAP, has served as a consultant for Galderma, Medicis, and Stiefel. He has also been a speaker for Galderma.
Corresponding author: Albert C. Yan, MD, Chief, Pediatric Dermatology, Children's Hospital of Philadelphia, Associate Professor, Pediatrics and Dermatology Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA. E-mail: yana@email.chop.edu

Acne vulgaris is traditionally managed with a variety of topical and systemic medications (Table 1), as well as acne surgery techniques. Although the disease is commonly encountered by pediatric specialists, other primary care practitioners, and dermatologists, it is interesting to note that differences in prescribing practices have been described between different practitioners. In one analysis of nationally representative data regarding the prescribing patterns of pediatricians and dermatologists, Yentzer et al[2] found that dermatologists prescribe topical retinoids most, followed by topical clindamycin, oral minocycline, and topical benzoyl peroxide (BP) for the treatment of acne. Pediatricians rely on BP most, followed by topical clindamycin, topical tretinoin, and oral erythromycin (Table 2). There appears to be considerable overlap in terms of employment of retinoids, BP, topical clindamycin, as well as fixed combination topical products such as BP + clindamycin and BP + erythromycin. Both groups of practitioners utilize BP equally, with this agent representing about 11% of prescriptions for dermatologists and 17% for pediatricians.

However, there are some distinct differences in prescribing patterns. Although retinoids have demonstrated good efficacy for comedonal as well as mildly inflammatory acne and represent about 46% of prescribed acne products among dermatologists, retinoids represent only about 12% of pediatrician-prescribed agents.[2] Given that pediatricians likely manage a large cohort of patients with comedonal and mildly inflammatory acne, these data suggest that topical retinoids may be somewhat underutilized by pediatricians for acne management. The decreased rates of topical retinoid utilization among pediatricians have been attributed to a heightened sensitivity to potential adverse effects or less familiarity with topical retinoids.

In addition to the selection of appropriate therapeutic agents, the choice of vehicle is important because cosmetic tolerability favorably influences adherence (compliance) with treatment regimens. Ointments, creams, gels, and solutions have been among those most commonly employed; however, several new vehicle formulations as well as novel

delivery options have been introduced and should be considered among the therapeutic options to individualize treatment and, thereby, optimize treatment outcomes.

A number of new topical products for acne treatment have been developed and introduced recently. These include products formulated with foam and hydrogel vehicles, novel fixed combinations of components, and a recently introduced topical gel formulation of the sulfone antibiotic/anti-inflammatory dapsone.

Foam and hydrogel vehicles have the advantage of easy spreadability with little residue. These vehicle formulations may be especially suited to treatment of hair-bearing areas (such as in male patients) or applied more easily over larger body surface areas such as on the chest and back. Clindamycin is available in a hydroethanolic foam, and a new tretinoin 0.025% + clindamycin 1.2% fixed combination product is available in a hydrogel formulation. Other novel fixed combinations include those containing antibiotic + BP, antibiotic + retinoid, and BP + retinoid (Table 3). Although use of the component agents separately may be more economical, fixed-combination products guarantee the stability of the components within these formulations and improve adherence to therapy because fewer applications are needed during the day.

**Table 1. Acne Medications Currently Available**

**Topical Agents, by class**
- Retinoid agents
  - Adapalene
  - Tazarotene
  - Tretinoin
- Benzoyl peroxide formulations (numerous over-the-counter and prescription products)
- Antibiotics
  - Clindamycin
  - Erythromycin
  - Sodium sulfacetamide
  - Sulfur
- Combination products
  - Antibiotic-benzoyl peroxide fixed combinations
  - Antibiotic-retinoid fixed combinations
  - Benzoyl peroxide-retinoid fixed combinations
- Keratolytic agents (eg, salicylic acid)
- Anti-inflammatory agents (eg, dapsone)

**Systemic Agents, by class**
- Oral antibiotics
  - Tetracycline derivatives
    - Doxycycline
    - Minocycline
    - Tetracycline
  - Macrolide derivatives
    - Azithromycin
    - Erythromycin
  - Cephalosporins
    - Cephalexin
  - Penicillins
    - Amoxicillin
  - Trimethoprim-sulfamethoxazole
- Combination oral contraceptives
  - Drospirenone
  - Drospirenone/levomefolate
  - Ethinyl estradiol/norethindrone
  - Ethinyl estradiol/norgestimate
- Hormonal agents
  - Spironolactone
- Systemic retinoids
  - Isotretinoin

**Table 2. Most Frequently Prescribed Medications by Specialty**

| Pediatricians | Dermatologists |
|---|---|
| Benzoyl peroxide | Adapalene |
| Clindamycin | Tretinoin |
| Tretinoin | Clindamycin |
| Erythromycin | Minocycline |
| Clindamycin 1%/ benzoyl peroxide 5% topical gel | Benzoyl peroxide |
| Erythromycin 3%/ benzoyl peroxide 5% topical gel | Doxycycline |
| Adapalene | Erythromycin 3%/ benzoyl peroxide 5% topical gel |
| Doxycyline | Tetracycline |
| Tetracycline | Clindamycin 1%/ benzoyl peroxide 5% topical gel |
| Minocycline | Erythromycin |

**Source:** Adapted from Yentzer BA, Irby CE, Fleischer AB Jr, Feldman SR. *Pediatr Dermatol.* 25:635-639, 2008.

Systemic antibiotic therapy has been a mainstay of treatment for acne. These agents include primarily tetracycline derivatives in patients 8 years of age and older; the age restriction reflects concerns about dental enamel staining in individuals younger than 8 years of age. Data on prescribing patterns show that dermatologists tend to favor doxycycline and minocycline, whereas pediatricians frequently use tetracycline.[2] Tetracycline generally is less costly than the other derivatives, but the longer half-lives of doxycycline and minocycline permit once- or twice-daily dosing compared to the four-times-daily dosing typically required with tetracycline. Less frequent dosing of any medication is more likely to result in better treatment adherence. Moreover, data on antibiotic resistance patterns of *Propionibacterium acnes* indicate that the proportion of organisms resistant to doxycycline and minocycline are lower than with either erythromycin or tetracycline. Finally, photosensitivity and gastrointestinal side effects tend to be somewhat lower with doxycycline and minocycline compared to tetracycline.

Alternative agents have been used when traditional tetracycline derivative agents have proved insufficiently effective or in cases in which side effects preclude the use of antibiotics

**Table 3. Novel Therapeutic Options**

**Novel Agent**
- Dapsone

**Novel Combinations of Components**
- Antibiotic/benzoyl peroxide fixed combinations
- Antibiotic/retinoid fixed combinations
- Benzoyl peroxide/retinoid fixed combinations

in the tetracycline class. Although randomized clinical trial data are not available for these alternative agents, case series have documented the efficacy and apparent tolerability of amoxicillin,[3] cephalexin,[4] trimethoprim and trimethoprim-sulfamethoxazole,[5] and azithromycin[6] for patients with acne who were either unable to take or had previously failed therapy with more conventional therapeutic agents.

The published data on amoxicillin are scant and involve assessments from retrospective chart reviews.[3] One large case series by Fenner and colleagues[4] reviewed the responses of 93 acne patients who received 98 courses of cephalexin. These investigators reported that only 22% of patients showed no response or worsened with therapy, whereas the remaining patients were either somewhat improved (29%), much improved (45%), or cleared (4%). Trimethoprim and trimethoprim-sulfamethoxazole have seen considerable pediatric usage for treatment of a variety of both cutaneous and extracutaneous infections, but the use of these agents in acne generally has been regarded as a third-line option.[5,7]

More extensive data are available regarding the use of azithromycin for acne. A review of the available literature reveals three randomized controlled trials[8-10] and one nonrandomized controlled trial[11] that demonstrated noninferiority of azithromycin to doxycycline; azithromycin also was not inferior to minocycline in one open-label study.[12] In addition, four open, noncontrolled studies[13-16] and one retrospective chart review[17] indicated that azithromycin improved acne. However, there is heterogeneity in study design as well as dosage regimens of the azithromycin and the control drug. Most of these studies acknowledged the long half-life of azithromycin and typically gave the drug as often as three to four times a week or as seldom as three times per month.

Erythromycin, an older macrolide derivative, is used less often now because of the emergence and establishment of antibiotic resistance among *P. acnes* organisms. There is evidence for significant antibiotic resistance among *P. acnes*, and it is clear that erythromycin has been largely abandoned by both dermatologists (2.8%) and pediatricians (7.2%),[2] except perhaps for use in prepubertal children or pregnant females in whom alternative agents may be less appropriate. Clinicians have become increasingly aware of the impact of acne therapy on causing "ecological mischief."[18] Widespread use of antibiotics for acne has been presumed to be one possible driving force for the selection of antibiotic-resistant *P. acnes* species. Studies looking at *P. acnes* antibiotic resistance profiles have indicated increasing rates of antibiotic resistance over time.[19]

This provides a rationale for incorporation of BP into acne therapeutic regimens where possible, either as a separate agent or as part of a fixed combination, particularly when antibiotics are employed, as the use of BP has been associated with a reduction in development of antibiotic resistance among *P. acnes*. Likewise, use of subantimicrobial doses of antibiotics has shown some limited benefit for patients with comedonal and inflammatory lesions, while at the same time not demonstrating a significant impact on altering native resident microbial flora.[20]

## Preadolescent Acne

Data are limited on the use of acne medications in the preadolescent population (ie, patients ≥7 to 11 years of age). A number of case series highlight the heterogeneous group of medications used for children with infantile acne. Two clinical trials have evaluated the use of tretinoin for preadolescent acne. In one open-label study involving 40 patients between 8 and 12 years of age, tretinoin 0.04% in a microsphere gel vehicle demonstrated good efficacy and safety, with patients showing both tolerability and also moderate improvement on the Evaluator's Global Severity Score.[21] The U.S. Food and Drug Administration granted an age indication of 10 years or older for tretinoin 0.05% gel, based on the trial data submitted. Otherwise, most acne medications are indicated for use in individuals 12 years of age or older (Table 4).

Despite the limited data available for the use of these medications in infants and preadolescent patients, clinical judgment should be exercised to select appropriate therapies for children with acne. Topical BP, topical retinoids, and topical antibiotics have been used with some success in younger children with acne.[22] For those with more severe acne, systemic antibiotic therapy has included erythromycin and its derivatives, trimethoprim, and cephalexin; these have been used with success in cases in which tetracycline and its derivatives are less desirable, given their propensity for dental enamel staining. Tetracycline and doxycycline are generally recommended for children 8 years of age and older with severe acne; minocycline carries a recommendation for children 12 years of age and older with moderate-to-severe acne.

Combination oral contraceptives may be helpful for postmenarchal adolescents and adults. However, because of concerns about premature epiphyseal closure, their use in premenarchal patients generally is not advised except in consultation with an endocrinologist. Spironolactone and its analog, drospirenone, are sometimes used in the treatment of adults and some adolescents, but these agents do not currently play a significant role in preadolescent acne.

## Improving Adherence in Pediatric Patients

A recent literature search using the key terms *adherence*, *compliance,* or *concordance* yielded a list of more than 168,000 articles. Although this is a highly heterogeneous group of articles, some key themes are highlighted in these references.

***Simplify treatment regimens.*** Successful adherence is inversely related to the number of agents that must be taken or applied and the number of times each day that they must be taken or used. For patients who have difficulty with adequate compliance, fixed-combination products may improve adherence to the prescribed regimen. Interestingly, however, one multistep, multicomponent, over-the-counter acne product has generated a reported $830 million in sales worldwide,[23] attesting to the popularity of therapeutic rituals, particularly among adolescents.

**Table 4. FDA Approvals and Pediatric Age Indications for Medications Commonly Employed for Acne**

| Drug Category | Active Drug | Common Brand Names | Date of Earliest FDA Approval | Age Indication |
|---|---|---|---|---|
| Topical retinoid | Tretinoin | Retin-A 0.025%, 0.05%, 0.1%<br>Avita 0.025%<br>Atralin 0.05% | October 1971<br>January 1997<br>July 2007 | ≥12 years<br>≥12 years<br>≥10 years |
| | Adapalene | Differin 0.1%, 0.3% | May 1996 | ≥12 years |
| | Tazarotene | Tazorac 0.05%, 0.1% | June 1997 | ≥12 years |
| Topical antibiotic | Erythromycin | Akne-Mycin, Erygel, Emgel | January 1985 | Indicated for pediatric use; no specific age restrictions |
| | Clindamycin | Cleocin T<br>Evoclin | July 1980<br>October 2004 | ≥12 years<br>≥12 years |
| Topical antiinflammatory | Dapsone | Aczone | July 2005 | ≥12 years |
| Fixed combination product | | | | |
| BP+*Abx* | BP+erythromycin | Benzamycin | October 1984 | ≥12 years |
| | BP+clindamycin | Benzaclin<br>Duac<br>Acanya | December 2000<br>August 2002<br>October 2008 | ≥12 years<br>≥12 years<br>≥12 years |
| BP+*retinoid* | BP+tretinoin | Epiduo | December 2008 | ≥12 years |
| Retinoid+*Abx* | Tretinoin+ clindamycin | Ziana<br>Veltin | November 2006<br>July 2010 | ≥12 years<br>≥12 years |
| Oral antibiotic | Erythromycin | EES, Eryped, Ery-tab | April 1965 | Indicated for pediatric use; no specific age restrictions |
| | Tetracycline | Sumycin and others | September 1954 | ≥8 years |
| | Doxycycline | Vibramycin, Doryx and Adoxa | December 1967 | ≥8 years |
| | Minocycline | Dynacin, Minocin, and others<br>Solodyn | August 1982<br>May 2006 | ≥12 years<br>≥12 years |
| | Trimethoprim-sulfamethoxazole | Bactrim, Septra | July 1973 | 2 months |
| | Amoxicillin | Amoxil | November 1979 | Indicated for pediatric use; no specific age restrictions |
| | Cephalexin | Keflex | January 1971 | Indicated for pediatric use; no specific age restrictions |
| | Azithromycin | Zithromax | November 1991 | ≥6 months |
| Systemic retinoid | Isotretinoin | Accutane<br>Amnesteem<br>Sotret<br>Claravis | May 1982<br>November 2002<br>December 2002<br>April 2003 | ≥12 years<br>≥12 years<br>≥12 years<br>≥12 years |

Abx=antibiotics; BP=benzoyl peroxide. **Source:** Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm).

***Consider vehicle appropriateness.*** Adherence also depends on identifying patient preferences and matching vehicle selections to those preferences. For example, gels and foams are easier to spread on hairy areas such as the male chest. Other patients may prefer the tactile sensation of a cream over an ointment. Patients with oily skin may tolerate gels or solutions, whereas those with dry or combination skin may prefer lotions or creams.

***Adjust regimens for tolerability.*** Side effects may arise with use of topical acne medications, particularly at the start of a new treatment. It is possible to mitigate these side effects by matching the vehicle to the patient's skin type, as mentioned above. Some patients who may have more sensitive skin may have concerns about tolerating topical retinoid therapy; these individuals may benefit from gradual escalation of the retinoid, initially applying the medication every other night for 1 to 2 weeks before advancing to every-night therapy. Alternatively, some patients prefer using medication every night by using short-contact applications for 30 to 60 minutes during the first 1 to 2 weeks before advancing to overnight therapy. Starting with lower-potency retinoids and advancing to higher-potency retinoids at follow-up visits may also improve efficacy while minimizing irritancy.

***Provide written action plans, videos, text-messaging reminders.*** Written action plans, educational videos, and text-messaging reminders about using prescribed medications are among the various techniques advocated to reinforce treatment recommendations and improve adherence. "Cheerleading" by the clinician and staff who see signs of improvement can encourage patients to continue with their prescribed regimens.

***Manage expectations.*** It is important to anticipate side effects and educate patients in advance that most side effects do not require stopping a medication but can be managed successfully with minor adjustments in the regimen. Pediatric and especially adolescent patients also benefit from understanding the definition of a "reasonable time frame" for seeing signs of improvement. These patients often have unrealistic expectations of seeing improvement in hours to days (often reinforced by what they see in advertisements for over-the-counter products that promise overnight results), whereas the typical improvement is measured in weeks to months.

***Monitor for psychological comorbidities.*** The psychological impact of acne can be considerable. One study[24] affirmed that adolescent patients often have psychological and especially mood issues related to their acne in a severity-dependent fashion. The more severe the acne, the more severe and more prevalent were the mood disturbances that were noted. Clinicians who care for patients with acne should remain alert for the presence of depression or other emotional or social issues, and may provide encouragement for the patient and family to seek counseling or other therapy, as appropriate.

***Consider cost issues.*** Medication costs can have a substantial impact on whether a prescription is filled and on whether a patient who begins using a medication remains adherent with the recommended regimen in the long term. Cost considerations should be taken into account when selecting appropriate medications.

## Conclusion

A wide range of acne therapies are available for pediatric use. Although most of these are indicated for use in patients ≥ 12 years of age, judicious use of these medications in an off-label fashion for children with preadolescent acne is reasonable until more research is available regarding use of these agents in the preadolescent population.

Most children with mild acne will tolerate topical agents such as BP, topical retinoids, and topical antibiotics, either as single agents or in fixed combinations, especially if the dosing of these agents is escalated gradually, using some of the techniques discussed. Those with moderate-to-severe acne may require systemic therapy. Children 8 years of age and older should be able to tolerate tetracycline derivatives, including doxycycline and minocycline, which have more favorable antibiotic-resistance profiles and dosing schedules than does tetracycline. When possible, BP should be incorporated into topical regimens in an effort to reduce the potential for "ecological mischief" and the risk of altering native resident microbial flora. When effective, subantimicrobial doses of antibiotics are preferable to higher doses, although many patients with moderate-to-severe acne may require antimicrobial doses to control their disease.

Ultimately, optimal outcomes require not only selection of appropriate pharmacotherapy, but also an understanding about factors that may affect compliance with recommended therapeutic regimens.

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# Parents as Partners in Pediatric Acne Management

Cooperation and communication between parents or other caregivers and a child's clinicians are essential to providing the highest quality of medical treatment, regardless of the health issue at hand. The provision of written materials has long been recognized as a valuable means of enhancing the parents' knowledge about the child's condition, diagnostic tests, therapeutic procedures, and medications. Written materials also can be effective tools for reinforcing information and instructions provided directly to the patient and parents in clinical encounters.

The treatment of acne in preadolescent patients is sometimes a challenge for clinicians, for two main reasons. First, when a child between 7 and 11 years of age presents with facial acne lesions, parents usually require reassurance about the accuracy of the diagnosis and the fact that acne is normal in children in this age group. Acne generally is thought of as a "teenager's disease" and is usually associated with the onset of puberty. The appearance of lesions in a child who may not have any external signs of puberty may cause parents to worry that the child has some underlying disease, such as hormonal imbalance.

Second, once the parents are comfortable with the diagnosis, the issue of treatment options must be addressed. With few exceptions, standard acne therapy is approved by the U.S. Food and Drug Administration (FDA) for patients as young as 12 years of age. The recommendations for use of over-the-counter (OTC) topical products for mild acne (such as those containing benzoyl peroxide) are unlikely to cause parental concerns; however, a child with moderate-to-severe acne may require more aggressive therapy with prescription products that are FDA-indicated for pages 12 years of age and older. The authors have experienced resistance from some parents who hesitate to allow their children to be treated with "adult" medications. This is a particular issue when oral medication is an appropriate option—even including, in rare cases, isotretinoin.

The average age of onset of puberty has decreased over the past 50 years, and the presentation of preadolescent acne is no longer either unusual or a cause for concern. Many clinicians who treat children now are aware of this phenomenon, as well as its implications, whereas most parents are not.

The authors collaborated in developing a parent education handout that is designed to help bridge this information gap. It includes background information on acne, reinforces the message regarding the normalcy of preadolescent acne, discusses appropriate skin care, and addresses acne treatment options and their appropriate use.

Lawrence F. Eichenfield, MD
Anthony J. Mancini, MD
Albert C. Yan, MD
Sheila Fallon Friedlander, MD
Hilary E. Baldwin, MD

## The Acne Continuum: An Age-Based Approach to Therapy

*continued from page 11*

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# My Child Has Acne: Information and a Guide to Home Care for Parents

## Information About Acne

### *Isn't My Child Too Young to Have Acne?*

Acne most commonly affects teenagers, but it is not just a condition of adolescence. Acne is often seen in children as young as 7 years old. In many preadolescent children, acne is the first sign of puberty (sexual development). For example, in a girl, acne may be seen before the development of breasts, pubic and underarm hair, and first menstruation (period). In a boy, acne can occur before the testicles and penis enlarge, pubic and underarm hair appear, or the voice deepens.

Occasionally, acne can even develop in babies or very young children. When this occurs, it is particularly important that the condition be evaluated by a health care provider.

### *What Causes Acne?*

There are four contributors to acne—the body's natural oil (sebum), clogged pores, bacteria (with the scientific name *Propionibacterium acnes*, or *P. acnes*), and the body's reaction to the above (inflammation). Here's what happens:

1) Sebum is produced in glands in the deeper layers of the skin and reaches the surface through the skin's pores. An increase in certain hormones occurs around the time of puberty, and these hormones trigger the oil glands to produce increased amounts of sebum.
2) Pores with excess oil tend to become clogged more easily.
3) At the same time, *P. acnes*—one of the many types of bacteria that normally live on everyone's skin—thrives in the excess oil and creates a skin reaction (inflammation).
4) If a pore is clogged close to the surface, there is little inflammation. The result is the formation of whiteheads (closed comedones) or blackheads (open comedones) at the surface of the skin.
5) A plug that extends to or forms a little deeper in the pore, or one that enlarges or ruptures, causes more inflammation. The result is red bumps (papules) and pus-filled pimples (pustules).
6) If plugging happens in the deepest skin layer, the inflammation is more severe, resulting in the formation of nodules or cysts.

### *Does Acne Look Different in Preadolescents Than in Older Children?*

In most preadolescents, acne is a milder condition. Typically, children in this age group have whiteheads and blackheads (comedones) and sometimes red pimples (papules) in the T zone of the face—across the forehead, on and along the nose, and on the chin. They may also occur on the ears. Comedones are usually small bumps and usually are not reddened (inflamed).

However, some preadolescents do have more severe acne. This may be a sign that a child will have more serious acne later on.

### *Should My Child's Acne Be Treated by a Doctor?*

There are a number of conditions that can look like acne, so your child should be examined and diagnosed by a health care practitioner. If a child has mild acne (comedones that are not inflamed or too numerous) and if the condition is not bothersome to your child, good skin care may be all that is needed at this point.

However, your child's health care provider will advise you whether your child needs to use an over-the-counter (OTC) or prescription medication applied to the skin (topical medication), to use an oral medication (taken by mouth), or both. There are several factors to be considered when making the decision about whether a preadolescent child needs one or more prescription medications. Certain findings would make it more appropriate to start treatment. They include the following:

1) Acne is more than mild (there is inflammation, or there are many comedones, whether they are inflamed or not).
2) There is some sign that acne scars have developed. Scarring is most common when acne is severe, but it can happen even in children with mild acne.
3) The child is having emotional problems because of the acne or is experiencing negative comments from other children.

### *How Should the Face Be Washed?*

Everyone with acne should wash twice a day—once in the morning and once in the evening. It's also important to wash the face as soon as possible after playing sports or other activities that cause a lot of sweating (such as bike riding).

Acne does not come from "dirt," and scrubbing is not necessary to get the skin clean. Dryness and irritation make it harder for the patient to tolerate acne medications and should be avoided. Use a gentle touch when washing, and use a mild soap (such as those that are labeled "for sensitive skin"), unless the health care provider advises otherwise. Avoid using deodorant soaps as well.

Many preadolescents seem to have skin that tends to become irritated or dry, so it's important to be aware of this when using a nonprescription acne "wash." Some of these over-the-counter (OTC) products contain ingredients such as salicylic acid and benzoyl peroxide that can be very helpful in reducing skin bacteria and clearing surface oil from the skin, but they may also cause irritation and dryness.

### *Are Acne Treatments Safe for Preadolescents?*

Most acne treatments have not been formally tested in clinical trials in pediatric patients younger than 12 years old. However, these treatments have been fully tested in adolescents and young adults and have been found to be safe and effective. These same treatments also have been used safely and effectively for many years in preadolescents.

# Acne Treatments

Facials and other treatments to remove, squeeze, or "clean out" pimples are not recommended. Manipulating the skin in this way can make acne worse and can lead to scarring. It also makes it more likely that the skin will not be able to tolerate acne medications. For the same reason, children should be discouraged from picking at their pimples.

What do acne treatments do? Medications for acne stop the formation of *new* pimples by reducing or removing the oil, bacteria, and other things (like dead skin cells) that clog the pores. They can also decrease the inflammation or irritation response of the skin to bacteria. It can take from 4 to 8 weeks before it is clear whether the medication is effective for your child. These medications do not "cure" the condition—the acne improves because of the medication, and it therefore must be continued in order to prevent return of the acne lesions.

There are many types of acne treatments. Some are applied to the skin (topical medications) and some are taken by mouth (oral medications). In most cases of mild acne, the doctor will start with a topical medication. Mild acne is the most common type seen in preadolescent children. If acne is more severe, if it does not respond adequately to topical medication, or if it covers large body surface areas such as the back and chest, oral antibiotics are usually prescribed. In the most severe cases, isotretinoin may be used, but it is uncommon to need this last medication in preadolescents. It is always best to start with the agents least likely to cause side effects, such as topical medications, in mild disease.

Some patients have a good result with just one medication, but many will need to use a combination of treatments: two or more different topical agents or an oral plus a topical medication.

Other treatments used for acne include corticosteroid injections, which are used to help relieve pain and to decrease the size and encourage healing of large, inflamed acne nodules. Also, dermatologists sometimes perform "acne surgery," using a fine needle, a pointed blade, or an instrument known as a comedone extractor to mechanically clean out a clogged pore. One must always balance the risk for inducing a scar with the potential benefits of any procedure. Many health care providers will start out with topical or combination topical/oral treatment plans before using more invasive treatments. Some believe that prior treatment with topical retinoids can "loosen" whiteheads and blackheads and so make it easier to physically remove such bumps.

Heat-based devices as well as light and laser therapy are being studied to see whether there is any role for such treatments in mild to moderate acne. At this time, there is not enough evidence to make recommendations about their use.

| Topical Medications | Oral Medications |
|---|---|
| • **Benzoyl peroxide** helps to fight inflammation and bacteria and is believed to help prevent resistance of bacteria to topical antibiotics.<br>• **Retinoids** unplug the oil glands by helping peel the layers of skin and other things plugging the opening of the glands.<br>• **Antibiotics** (topical or oral) fight bacteria and help shrink the pimples. Antibiotics commonly used in acne include clindamycin, erythromycin, and combination agents (such as erythromycin/benzoyl peroxide).<br>• **Other topical agents** include salicylic acid, azelaic acid, dapsone, and sulfacetamide. | • **Antibiotics** include tetracycline-class medicines (tetracycline, minocycline, and doxycycline, which are all used only in children 8 years of age or older); erythromycin; trimethoprim-sulfamethoxazole; and occasionally cephalexin or azithromycin. These drugs may decrease bacteria and inflammation, and are most effective for moderate-to-severe acne.<br>• **Hormonal treatment** usually consists of combination oral contraceptives (birth control pills); spironolactone also is sometimes used.<br>• **Isotretinoin**, a derivative of vitamin A, is a powerful drug with several significant potential side effects. It is reserved for acne which is severe or when other medications have not worked well enough. |

## *General Information About Using Topical Acne Medications*

- Apply medication to clean, dry skin and spread it around the entire area of the face affected by acne. Avoid the corners of the eyes, nose, and lips, as the skin in these areas is more sensitive.
- Less is usually better. A thin layer of medication is less likely to cause dryness and irritation and will save money in the long run.
- Redness with a lot of itchiness may mean that the child is allergic to or highly irritated by the medication. Stop using it and call the health care provider.
- To prevent irritation and dryness when first using a medication, the health care provider may tell you to apply it every other day or every third day for the first few weeks. If the child's skin is still too irritated, the doctor may prescribe a milder medication or give you other instructions about using the medicine.
- The same medications often come in various forms: cream, ointment, lotion, gel, microsphere, or foam. Use the formulation that has been recommended and don't switch to other forms unless instructed. Some forms (such as gels) may be more drying and less tolerable for certain skin types.
- Antibiotics and retinoids can increase the skin's sensitivity to the sun. **Always use sunscreen!** Generally, SPF 30 is sufficient.
- If the skin looks or feels dry or tight, a light, nonoily moisturizer (labeled "noncomedogenic" or "nonacnegenic") can be used. Apply moisturizers after putting on the medication.
- Retinoids generally should be applied at bedtime as some can be inactivated by sunlight. If a retinoid product and a benzoyl peroxide product are prescribed separately, the benzoyl peroxide should be applied during the day.
- Sometimes individual medications are not as effective as a combination of two or more agents. The doctor may need to try several medications or combinations before finding the one that is best for your child.
- When starting prescription acne medications, use *only* those agents for at least 2 weeks. After that time, if desired, a nonprescription product OTC such as an acne wash or cleanser can be tried. If irritation develops, stop using the OTC product.
- Facial waxing or any other traumatizing procedures can lead to excessive irritation and should be avoided during retinoid therapy.
- Benzoyl peroxide bleaches fabrics and even hair. Don't get it on clothing, upholstery, linens, or carpeting.

## *Side Effects of Oral Acne Medications*

- Tetracycline, minocycline, and doxycycline are in the same class of drugs, and they have several possible side effects in common. If you notice any of the following, stop using the medication and notify the health care provider: headaches; blurred vision; dizziness; sun sensitivity; heartburn or stomach pain; irritation of the esophagus; darkening of scars, gums, or teeth (more common with minocycline); nail changes; yellowing of the skin (indicating possible liver disease); joint pains; or flu-like symptoms.
- In addition to the tetracycline drugs, many other oral medications can cause irritation and a sensation of burning (heartburn) or pain in the esophagus. To reduce the risk of these kinds of problems: (1) always take the pills with lots of water and (2) don't take a pill right before getting into bed—stay upright for at least 1 hour.

For further information about acne, including more information on this disease in adolescents and young adults, the following two Internet sites are recommended:

- American Academy of Dermatology: http://www.aad.org/skin-conditions/dermatology-a-to-z/acne
- National Institute of Arthritis and Musculoskeletal and Skin Diseases: http://www.niams.nih.gov/Health_Info/Acne

continued from page 6

## Conclusion

The epidemiology, demographics, and pathophysiology of acne in adolescents have been well described in the literature. Fewer studies have focused on acne and acneiform conditions in pediatric patients less than 12 years of age. True acne is rarely seen in patients less than about 6 or 7 years of age, but it is important to note—and to educate parents—that acne may be the first sign of onset of puberty in preadolescent children (ie, those from 7 through 11 years of age). Ongoing research continues to elucidate and expand on the etiologic factors involved in the development of acne.

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## The Effects of Culture, Skin Color, and Other Nonclinical Issues on Acne Treatment

continued from page 14

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# Pediatric Acne Management: Optimizing Outcomes: CME Post-test Evaluation Form

**CME Post-Test Answer Sheet and Evaluation Form • Original Release Date: September 2011 • Most Recent Review Date: September 2011 • Expiration Date: September 3, 2012 • Estimated Time to Complete Activity: 2.0 hours**

To get instant CME credits online, go to **http://uofl.me/acnemanag11.** (Type the above address into your address bar in Internet Explorer. If you are unfamiliar with what an address bar is or how to access yours, open Internet Explorer, then hold down the control key and press the "O" key on your keyboard. A dialogue box will open – this is where you will type the above address. After you have typed the address, click OK to go to the evaluation.)

Upon successful completion of the online test and evaluation form, you'll be directed to a webpage that will allow you to receive your certificate of credit via e-mail. Please add chse@louisville.edu to your email "safe" list.

Once you have completed the evaluation, it will give you a password. Please be sure to write it down; you will then be able to access your certificate. Please note, certificates will not be mailed, so be sure to print a copy for your records. If you have any questions or difficulties, please contact the University of Louisville School of Medicine Continuing Health Sciences Education office at (502) 852-5329.

**CME Questions Instructions: For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate.**

**1.** Up to 20% of newborns present with:
- **a.** *Malassezia* species colonization
- **b.** Cysts and nodular lesions
- **c.** Neonatal acne
- **d.** Truncal acne

**2.** Mid-childhood acne—that is, acne in children between 1 and 7 years of age—is:
- **a.** Common
- **b.** Normal
- **c.** Rare
- **d.** Usually self-limited and requires no special workup

**3.** Preadolescent acne is:
- **a.** Acne in a child between 7 and 11 years of age
- **b.** Acne in any patient less than 12 years of age
- **c.** Rare
- **d.** Usually due to underlying endocrinopathy

**4.** Puberty is considered to be precocious if it occurs:
- **a.** Before 6 years of age in African-American girls
- **b.** Before 9 years of age in white girls
- **c.** Before 10 years of age in boys
- **d.** In any child 8 years of age or less

**5.** Which of the acne agents below would not be considered to induce resistant *Propionibacterium acnes*:
- **a.** Topical clindamycin
- **b.** Oral antibiotics
- **c.** Topical benzoyl peroxide combination products
- **d.** Topical erythromycin

**6.** Which one of the following statements regarding postinflammatory hyperpigmentation is true?
- **a.** PIH is seen only in skin of color
- **b.** PIH is seen secondary to cystic lesions only
- **c.** PIH is seen secondary to cystic and pustular lesions only
- **d.** PIH is seen with lesions of all types

**7.** A recently published study by Halvorsen and colleagues regarding the risk for depression and suicidal ideation in patients with acne supports the view that such risks:
- **a.** Are inevitable
- **b.** Are more likely to result from the burden of acne than from any acne treatment
- **c.** Are rare
- **d.** Are strongly associated with systemic treatments such as isotretinoin

**8.** Acne in children between 7 and 11 years of age (preadolescent acne):
- **a.** May be the first sign of impending pubertal maturation
- **b.** Never occurs before pubic hair or areolar development in girls
- **c.** Typically presents with small, inflammatory lesions on the face
- **d.** Usually includes lesions on the back and trunk, especially in boys

**9.** All of the topical and systemic agents specifically indicated for acne were tested in clinical trials in individuals 12 years of age and older, except _____, which was studied in children as young as 8 years of age, and _____, which was studied in children as young as 10 years of age.
- **a.** Benzoyl peroxide; salicylic acid
- **b.** Dapsone; benzoyl peroxide/clindamycin combination
- **c.** Tretinoin 0.04% microsphere; tretinoin 0.05% gel
- **d.** Tretinoin; isotretinoin

**10.** Which one of the following statements is true regarding the choice of topical treatments for preadolescent patients with acne?
- **a.** Antibiotics will not induce bacterial resistance in preadolescents
- **b.** Clinical experience supports the use of the entire spectrum of topical acne therapies for all children who need treatment
- **c.** Off-label use of acne medications should be avoided
- **d.** Post-inflammatory hyperpigmentation mandates use of oral isotretinoin

**EVALUATION FORM: We would appreciate your answering the following questions in order to help us plan for other activities of this type. Please print.**

**Name:** _____ **Specialty:** _____

**Degree:** ☐ MD ☐ DO ☐ PharmD ☐ RPh ☐ NP ☐ RN ☐ BS ☐ PA ☐ Other _____

**Affiliation:** _____

**Address:** _____

**City:** _____ **State:** _____ **Zip:** _____

**Telephone:** _____ **Fax:** _____

**E-mail:** _____

**Signature:** _____ **(All information is confidential.)**

**CME Credit Verification**

**I verify that I have spent _____ hour(s)/_____ minutes of actual time working on this CME activity. No more than 2.0 CME credit(s) will be issued for this activity.**

**COURSE EVALUATION: GAPS**

**This supplement was created to address the professional practice gaps listed below. Please respond regarding how much you agree or disagree that the following gaps were addressed:**
- **Pediatric acne and new treatment strategies.**
- **Therapeutic options.**
- **Multiple treatment delivery systems best suited for a pediatric patient's history, skin condition, and age.**
- **The safety and efficacy of topical and oral acne medications in younger pediatric patients.**
- **Impact of acne vulgaris on patients' quality of life.**
- **Evaluating acne patients across the age spectrum.**

**Did the journal change your KNOWLEDGE in the professional practice gaps that are listed above?**

| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

**Please elaborate on your answer.**

_____

**Did the journal change your COMPETENCE in the professional practice gaps that are listed on the left?**

| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

**Please elaborate on your answer.**

_____

**Did the journal change your PERFORMANCE in the professional practice gaps that are listed on the left?**

| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

**Please elaborate on your answer.**

_____

**Please identify a change that you will implement into practice as a result of reviewing this journal (new protocols, different medications, etc.)** _____

**How certain are you that you will implement this change?**

| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |

**What topics do you want to hear more about and what issue(s) in your practice will they address?**

_____

**Were the patient recommendations based on acceptable practices in medicine? Yes No**
**If you answered no, on the question above, please explain which recommendation(s) were not based on acceptable practices in medicine.**

_____

**Do you think the journal was without commercial bias? Yes No**
**If you answered no, on the above question, please list the topic(s) that were biased.**

_____

**Please provide any additional comments you may have about this journal.**

_____