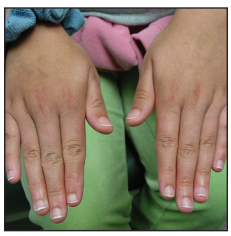
CMPMedica
United Business Media

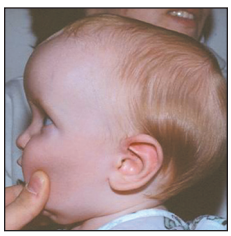
PEER-REVIEWED / A CLIGGOTT PUBLICATION

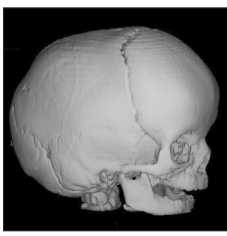
SEPTEMBER 2006
VOL.5 NO.9

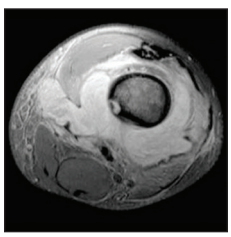
Consultant® FOR PEDIATRICIANS

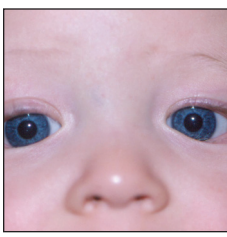
www.ConsultantLive.com











Musculoskeletal Infections: Combating the Major Pathogens

Unhappy Camper With Intense Tibial Pain

Pediatric Migraine: Clinical Pearls in Diagnosis and Therapy

Tetany in a 9-Year-Old Girl: Your Diagnosis?

ALSO:

Consultant Advisors

EDITORIAL BOARD

BOARD OF CONSULTANTS

Consultant
FOR PEDIATRICIANS
www.ConsultantLive.com

CMPMedica
Cliggott Publishing Group
330 Boston Post Road, Box 4027
Darien, CT 06820-4027
(203) 662-6400
www.cmphealth.com

Group Vice President and General Manager: JONATHAN L. BIGELOW

Group Editorial Director: SUSAN KWESKIN
Editor: JULIE BOWEN
Managing Editor: SUSAN B. BECK
Senior Editor: ELLEN K. KAPUSTKA, PhD
Associate Editor: LINDA GEISLER
Group Art Director: TOM JERMANTOWICZ
Associate Art Director: ANTHONY P. SCIARRILLO
Copy Editors: CHERYL A. BOGERT, Chief
LYNN FLINT
PERRYN REYELTS
MIRIAM V. SEVA
LINDSAY WADE
AMY ZEISZ
Editorial Assistant: BARBARA HADAD

Group Publisher: DAVID S. MARCH
Publisher: JILL BRESNICK
National Sales Manager: BRIAN BLITZ, PA-C
Director of Web Content Development: STEPHEN K. MURATA
Group Director of Research/Circulation/Reprints: BEATRIX ERIKSEN
Research: AMY ERDMAN, Associate Director
URSZULA MISIAK, Manager
AMY BARKER, Assistant
Marketing Promotion Manager: JENNIFER HUBAL
Advertising Coordinator: CINDY CARDOZO
Production Director: STEVE SANBORN
Production Manager: MARY A. HLAVAC
Senior Circulation Manager: WILHELMINA DINGLE (800) 280-0628

CMPMedica
CEO: HENRY ELKINGTON
Director of Business Development: KARIN HOGSANDER

Group President, USA: VICKI MASSERIA
Senior Vice President, USA: SALLY SHANKLAND
Vice President Finance, USA: DENISE BRADY
Senior Vice President Strategic Development, USA: KAREN KLAUSE
Director of Online Media, USA: MICHAEL GROVER

CEO Asia: MEI CHAN WONG
CEO Benelux: JEAN-PIERRE DEHASPE
CEO Eastern Europe: KERRI McCARTNEY
CEO France: GERARD KOUCHNER
CEO Germany: UWE RICHTER
General Manager, Iberia: JAVIER SANZ
CEO Australia/Pacific: CHRIS WILLS
Business Director, United Kingdom: PHIL CALLOW

CMPMedica brands include such leading healthcare publications as *The AIDS Reader, Applied Neurology, BioMechanics, Consultant, Consultant for Pediatricians, Diagnostic Imaging, Diagnostic Imaging Europe, Drug Benefit Trends, Infections in Medicine, Issues in Urology, The Journal of Musculoskeletal Medicine, The Journal of Respiratory Diseases, Oncology, Oncology News International, Psychiatric Times, The Journal of Critical Illness, Psychiatric Issues in Emergency Care Settings,* and *Abstracts in Hematology & Oncology.*

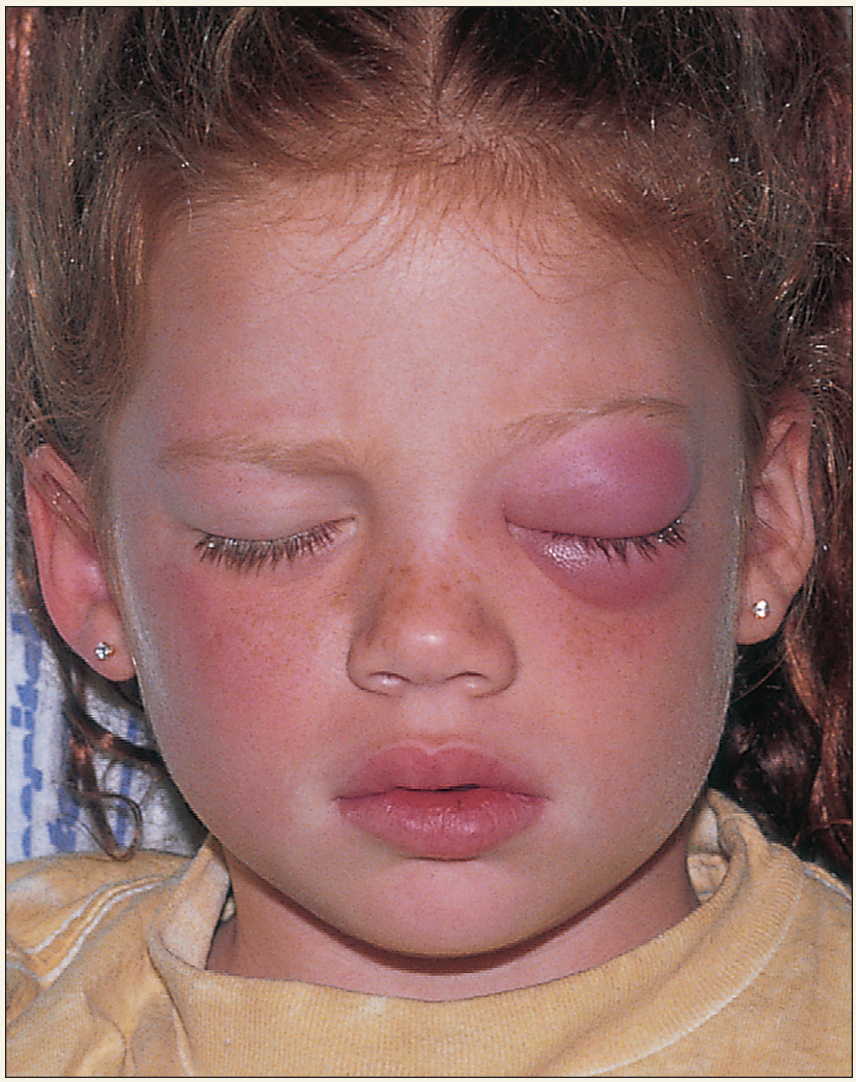
CMPMedica
United Business Media

e-Photo Quiz

Self-Test Your Diagnostic Acumen

Take the Monthly Online Challenge

NEW!



THE CASE: A 7-year-old girl is brought to your office by her parents, who state that she has had redness around her left eye for the past 2 to 3 days. During the last 24 hours, there has been a marked increase in redness and soft tissue swelling that has impeded the child's vision. There is no history of trauma or eye infection.

Which of the choices below describes the patient's condition?

- ❍ **A.** Preseptal cellulitis.
- ❍ **B.** Mucormycosis.
- ❍ **C.** Allergic reaction.
- ❍ **D.** Orbital cellulitis.

For the answer and discussion log-on to . . .

www.ConsultantLive.com/pedsquiz

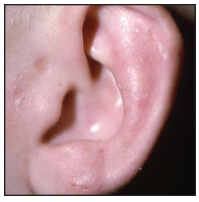
. . . or look for the answer in the October issue of Consultant For Pediatricians.

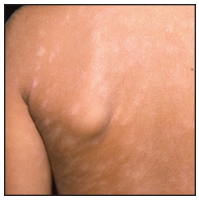
PEER-REVIEWED / A CLIGGOTT PUBLICATION

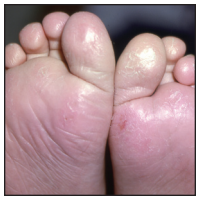
SEPTEMBER 2006
VOL.5 NO.9

Consultant® FOR PEDIATRICIANS

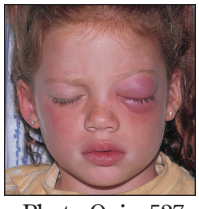
www.ConsultantLive.com







Dermclinic, 538



e-Photo Quiz, 527

FEATURES

CONTENTS CONTINUED ON PAGE 532

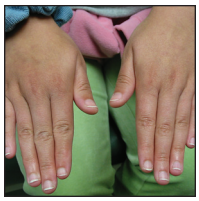
AMP The Association of Medical Publications, Inc.

AMERICAN BUSINESS MEDIA The Association of Business Media Companies

CONSULTANT FOR PEDIATRICIANS (ISSN 1545-8539) is published 12 times a year by the Cliggott Publishing Group, a division of CMPMedica. It is distributed to over 60,500 physicians, MD and DO, plus nurse practitioners and physician assistants. Subscription rates: $80 a year in the U.S.; $90 a year (U.S. funds only) for Canada and overseas countries (foreign delivery not guaranteed). Periodicals postage paid at Darien, CT 06820-4027 and additional mailing offices. Postmaster: If undelivered, send form 3579 to CONSULTANT FOR PEDIATRICIANS, 330 Boston Post Road, Box 4027, Darien, CT 06820-4027.

Contents

Continued



Genetic Disorders, 554

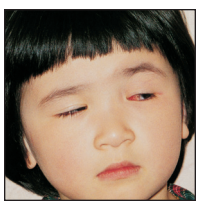
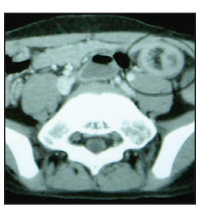


Photo Essay, 561



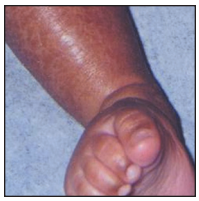
Case In Point, 570

FEATURES

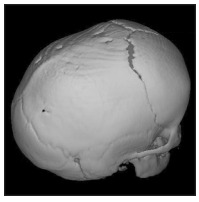
CONTENTS CONTINUED ON PAGE 534

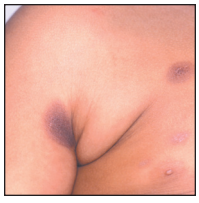
Contents

Continued



What's Your Diagnosis? 573





Photoclinic, 588

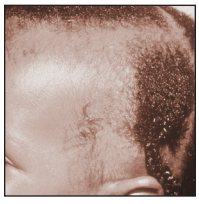


Photo Finish, 597

FEATURES

Consultations & Comments

Reader Reaction and Timely Answers From Experts

Stumped by a clinical problem?
Send us your query; we'll pose it to an expert and forward the reply to you.

Have a comment on an article?
Share your views on clinical or management issues that concern you.

By mail: Editor, CONSULTANT FOR PEDIATRICIANS
330 Boston Post Road, Box 4027, Darien, CT 06820-4027

By FAX: 203-662-6776

By e-mail: SKweskin@cmp.com

Refractory Diaper Dermatitis? Two Additional Strategies . . .

I enjoyed reading the article "Diaper Dermatitis" in your June issue.[1] To the many treatments discussed, I would offer 2 additional management points.

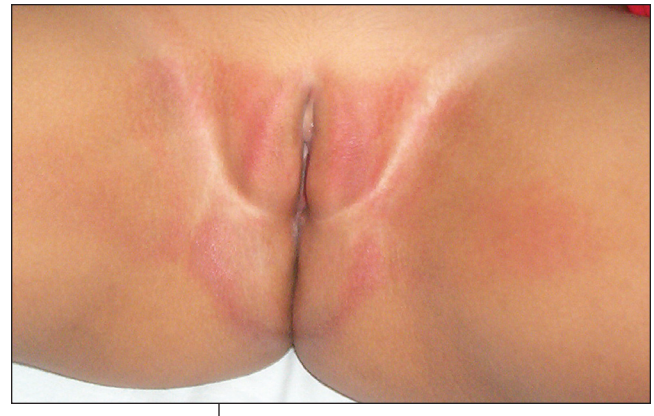
First, persistent and/or recurrent diaper rash is more common when children older than 12 months continue to drink from the bottle. Excess fluid intake leads to soppy diapers and often, sloppy stools. When the cup replaces the bottle, diapers and firmer stools ensue—and accompanying rashes disappear.

Second, even at the risk of waking their infant (regardless of his or her age), parents achieve much better diaper hygiene when diapers are checked—and, if need be, changed—once or twice during the night as well as frequently during the day.

In over 32 years of office practice, I've seen many otherwise refractory diaper rashes clear, with or without topical therapy, when only these 2 strategies are employed.

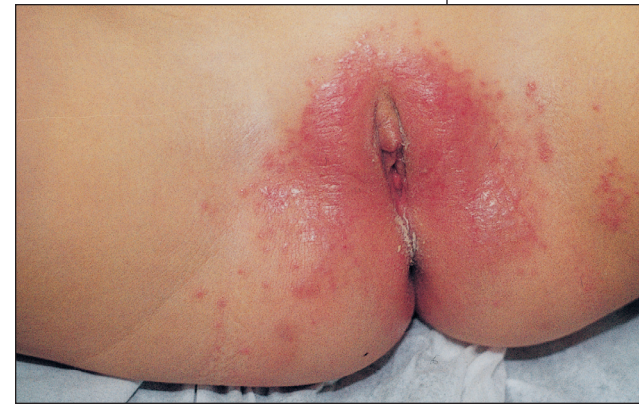
—— *Allan H. Robinson, MD*
Suburban Pediatric Associates
Cincinnati and Mason, Ohio

REFERENCE:
1. Nield LS, Kamat DM. Diaper dermatitis: from "A" to "Pee." *Consultant For Pediatricians.* 2006;5:373-380.



This 1-year-old girl has irritant contact dermatitis. Note the involvement of the skin prominences and sparing of the flexural creases.

(© DermAtlas; http://www.DermAtlas.org. Courtesy of Jayakar Thomas, MD, PhD.) ◀



This erythematous, sharply demarcated rash had been present for a week. A potassium hydroxide preparation of skin scrapings showed budding yeasts and hyphae. A culture was positive for *Candida albicans*.

(Courtesy of Alexander K. C. Leung, MD.) ▶

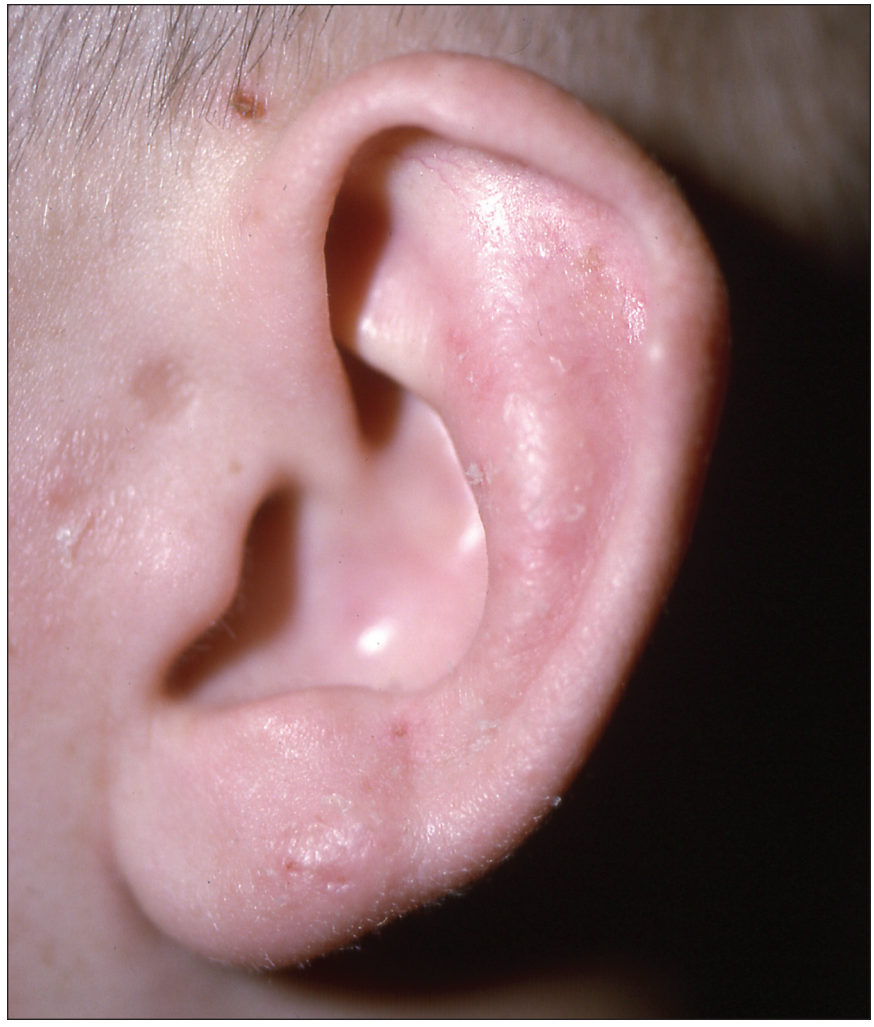
Erratum: The July 2006 issue, which featured an update on STDs, included a case on primary syphilis in a teenager (page 427). Therapy with intramuscular penicillin G (weekly for 3 weeks) or ceftriaxone (daily for 2 weeks) was recommended. However, the CDC's newly published guidelines on STD treatment recommend therapy with a single intramuscular dose of 2.4 million units of penicillin G.[1] If the patient is allergic to penicillin, the alternative is therapy with doxycycline (100 mg orally bid for 14 days) or tetracycline (500 mg qid for 14 days). Ceftriaxone is not a recommended treatment for syphilis.

REFERENCE:
1. Centers for Disease Control and Prevention. Sexually transmitted diseases. Treatment guidelines, 2006. *MMWR.* 2006;55(RR-11):1-100. Available at: www.cdc.gov/std/treatment/2006/rr5511.pdf. Accessed August 14, 2006.

Dermclinic

DAVID L. KAPLAN, MD
University of Missouri Kansas City, University of Kansas

A Photo Quiz to Hone Dermatologic Skills



Case 1:
For several weeks, an 18-year-old man has been bothered by itchy ears. He has seasonal allergies that are well controlled with oral antihistamines. He has not been exposed to contactants and has not used any nutritional supplements or new shampoos or conditioners. He works out at a gym 5 days a week.

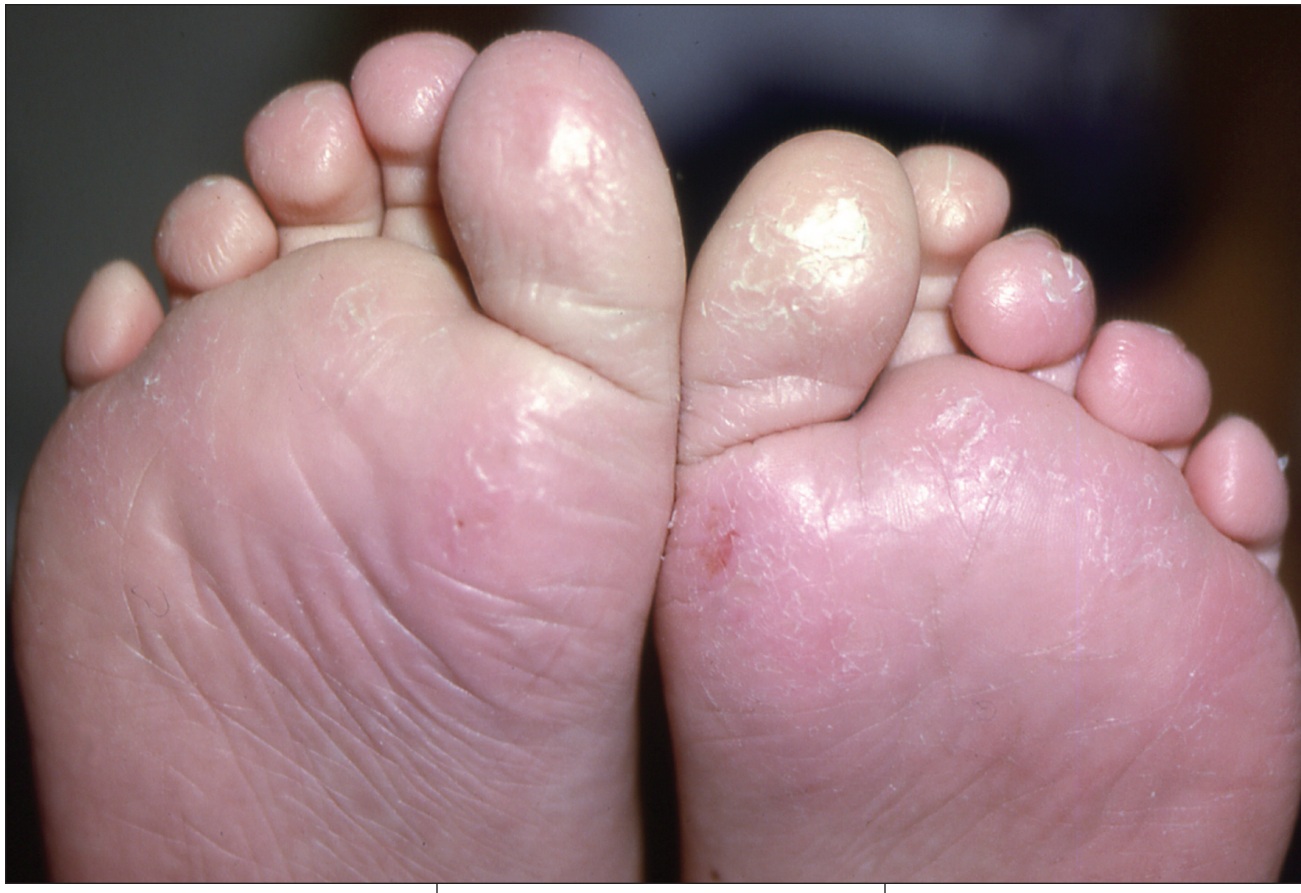
Which of the following do you suspect?

A. Relapsing polychondritis.
B. Atopic dermatitis.
C. Seborrheic dermatitis.
D. Psoriasis.
E. Contact dermatitis.

(Answer on page 542.)

Dr Kaplan is clinical assistant professor of dermatology at the University of Missouri Kansas City School of Medicine and at the University of Kansas School of Medicine. He practices adult and pediatric dermatology in Overland Park, Kan.

To page 540.



Case 2:
For several weeks, a 10-year-old boy's feet have been scaly and pruritic. He plays basketball and soccer and recently bought new shoes. A trial of over-the-counter miconazole was ineffective. The patient has a history of childhood eczema but outgrew it about 5 years ago.

What might explain the boy's symptoms?

A. Contact dermatitis to new shoes.

B. Juvenile plantar dermatitis.

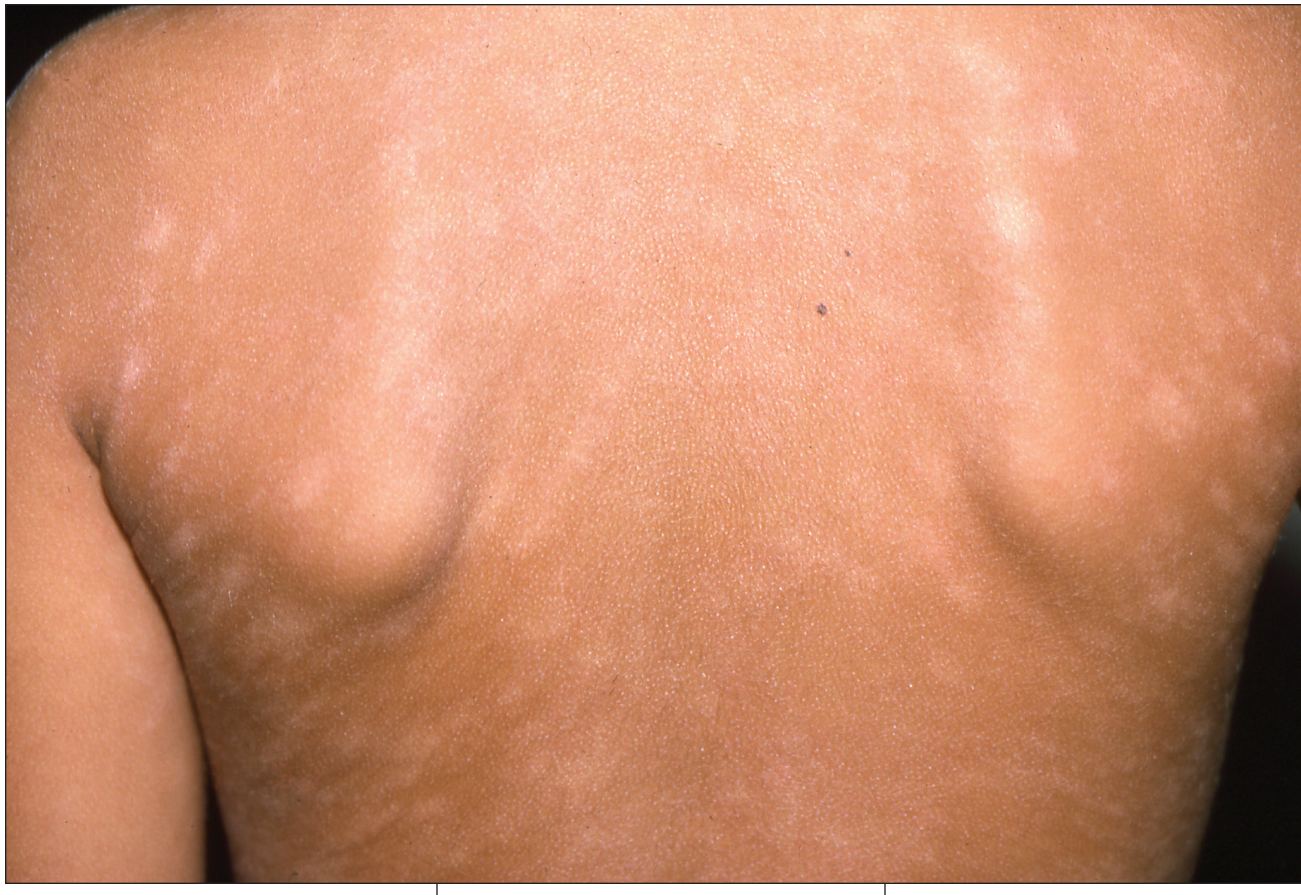
C. Tinea pedis.

D. Psoriasis.

E. Keratoderma.

(Answer on page 542.)

To page 541.



Case 3:
A 10-year-old boy has noticed asymptomatic discoloration on his back this summer. He has mild seasonal allergies that are controlled with over-the-counter medications. He plays soccer and has been swimming in a pool. He has had a dog and a cat for the past 2 years.

Which of the conditions in the differential is the likely diagnosis?

A. Vitiligo.

B. Pityriasis alba.

C. Tinea versicolor.

D. Tinea corporis.

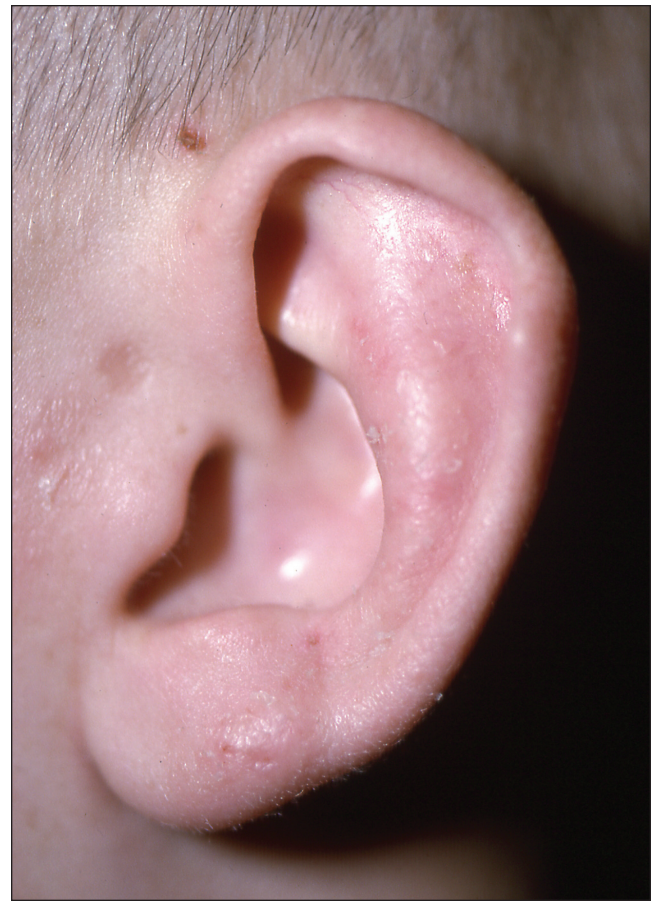
E. Pityriasis rosea.

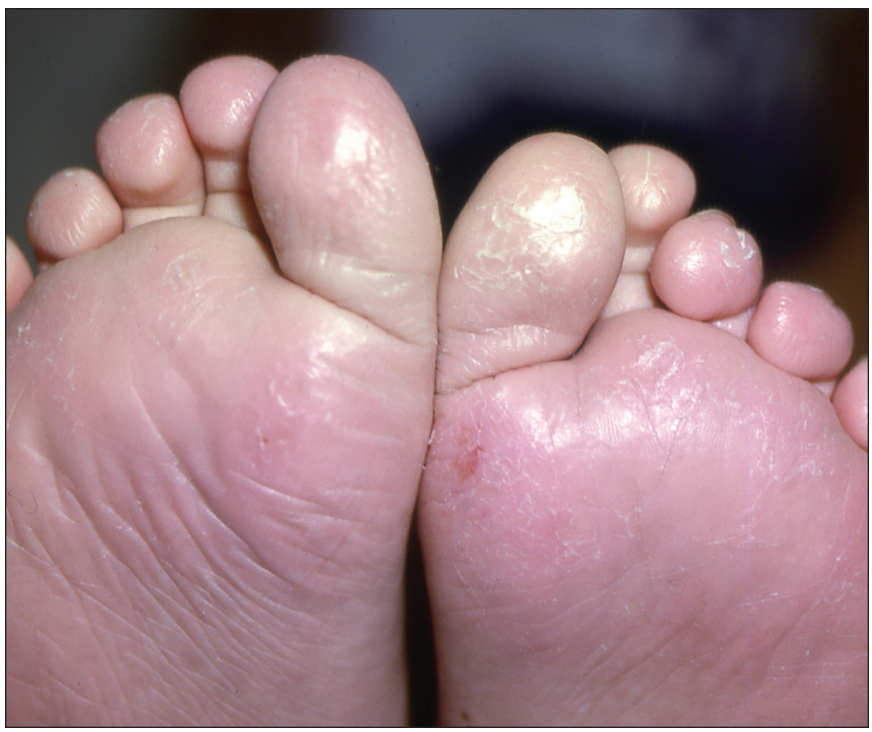
(Answer on page 544.)

Cases begin on page 538

Case 1: This patient had a flare of **atopic dermatitis, B.** A mid-potency topical corticosteroid helped relieve the symptoms. No obvious cause was identified.

Relapsing polychondritis is typically painful, not pruritic. Seborrheic dermatitis and psoriasis usually involve the external auditory canal and the area behind the ears. Contact dermatitis may be ruled out because there was no exposure history.

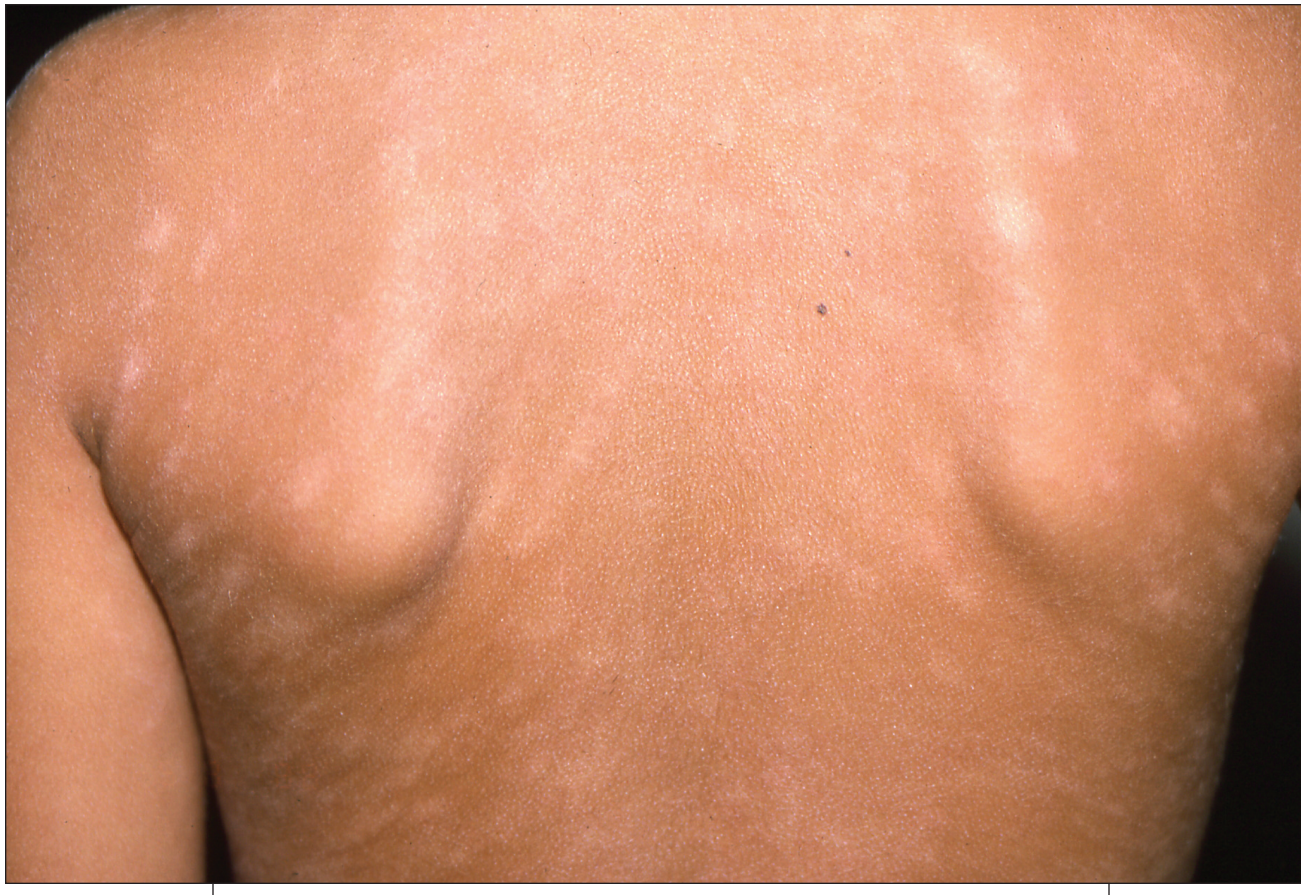




Case 2: The triad of sweaty feet, occlusive footwear, and a history of eczema suggests **juvenile plantar dermatitis, B.** Symptoms can be controlled if patients keep their feet dry by using foot powder and changing socks frequently. Topical corticosteroids or topical immunomodulators, such as tacrolimus and pimecrolimus, are also effective. Juvenile plantar dermatitis typically improves at puberty.

Contact dermatitis to shoes usually manifests on the dorsa of the feet. Tinea pedis is usually scalier and, unlike juvenile plantar dermatitis, involves the toe webs. Psoriasis is unlikely to involve just the soles and features more erythema and scale. Keratoderma is characterized by a thickened layer that produces a waxy appearance.

To page 544.



Case 3: This patient has **pityriasis alba, B,** a postinflammatory hypopigmentation associated with chronic eczema; it interferes with normal tanning. The patient was advised to change his bathing routine (no washcloth, lukewarm water, no antibacterial soaps, avoid washing rash) and to apply a moisturizer, sunscreen, and a low-potency topical corticosteroid. His skin color evened out during the next 4 to 6 weeks.

Vitiligo consists of permanent depigmentation, not reversible hypopigmentation. Tinea versicolor, tinea corporis, and pityriasis rosea all feature scaling, and the latter 2 are usually pruritic. ■

JEFF UNGER, MD
Loma Linda University School of Medicine

Pediatric Migraine:
Clinical Pearls in Diagnosis and Therapy

Dr Unger is professor of family medicine at Loma Linda University School of Medicine in Loma Linda, Calif. He is also director of the Chino Medical Group Diabetes and Headache Intervention Center in Chino, Calif.

ABSTRACT: Recurrent headaches are frightening for many parents, who may believe that their child's headache is caused by a secondary disorder such as a malignancy. Parental concerns may trigger workups that may be unpleasant for the patient and costly for the health care payer. Although underlying malignancy is uncommon, chronic and severe headache episodes in children are disabling and require intervention.

Key words: pediatric migraine, medication overuse headache, abdominal migraine, cyclic vomiting syndrome, benign paroxysmal vertigo

Steven, a 13-year-old boy, experienced his first headache at age 7 years. The frequency, intensity, and duration of his headaches have been increasing over the past 6 months. Steven now experiences 7 to 10 headaches each month that last up to 8 hours. The headaches are associated with mild nausea, light and sound sensitivity, dizziness, fatigue, occasional abdominal discomfort, and difficulty in concentrating. Last year, he had a vomiting episode because of a headache. The pain is usually more prominent in the forehead and does not favor either side of the head. The headaches usually begin in the morning before he leaves for school. As a result, Steven has missed nearly 25% of his school days this semester; his parents are considering home tutoring for "sick children who are unable to attend school."

Steven's mother has treated the headaches with various over-the-counter medications. The pain typically resolves slowly and often recurs the next day. Steven would like to study martial arts but was advised against participation because exercise exacerbates his headaches. Steven's mother suffers from "terrible sinus headaches" that worsen during menstruation. She is very concerned that her son may have a brain tumor or chronic infection.

On presentation, Steven complained of a mild headache and photophobia. His vital signs were stable. Results of the physical and neurologic examination were normal. He had no evidence of meningeal signs.

By age 15 years, 75% of children will have had a significant headache.[1] Ten percent of children aged 5 to 15 years and 28% of adolescents aged 15 to 19 years report experiencing migraine headaches.[2] Those who experience recurrent headaches are challenged with issues related to school attendance. Within a typical 2-week period in the United States, an estimated 975,000 children reported having a migraine; this resulted in 164,454 missed school days.[3] Recurrent headaches also affect a child's participation in social and sporting events, as Steven's case attests. The child's health status can also influence family dynamics.

Here I review the salient details of the history that offer diagnostic clues, discuss the latest diagnostic criteria for migraine in children

under 16 years old, describe pediatric migraine precursors, and offer therapeutic recommendations.

CLINICAL EVALUATION

Headache specialists agree that the vast majority of pediatric patients who seek consultation for recurring, disabling headache are migraineurs.[3] In a study by Ward and colleagues,[4] meningitis, shunt malfunction, and hydrocephalus were diagnosed in only 6% of all emergency department visits prompted by severe headache. All cases of secondary headache disorders in that study were associated with abnormal physical and neurologic findings.[4]

The diagnosis of pediatric headache disorders is best accomplished by taking a detailed history from the patient and the patient's parents. Key features in children with intracranial disease include altered mental status, abnormal eye movements, optic disc distortion, motor or sensory asymmetry, balance disturbances, and abnormal deep tendon reflexes. Those patients who have abnormalities on examination should undergo additional diagnostic testing.

Focus the history on the patient's headache patterns. Intermittent, disabling headaches in an otherwise healthy and fully functioning person are typical of a primary headache disorder such as migraine. An acute headache that gradually increases in severity over time warrants further investigation to identify possible intracranial disease.

MRI scanning is warranted for those patients who have a chronic-progressive headache pattern or any worrisome features (**Table 1**). An electroencephalogram is indicated only when the child's headaches are associated with alterations in consciousness or with abnormal involuntary movements.[5]

Lumbar puncture should be performed in patients in whom acute CNS infection is suspected or in those patients with signs of meningeal irritation or lateralizing signs on neurologic examination. Opening and closing pressures should be measured when pseudotumor cerebri, subarachnoid hemorrhage, or meningitis is suspected.

A useful tool for evaluating the impact of migraine on a child's quality of life is the Pediatric Quality of Life Inventory (Peds QL 4.0) generic core scales.[6] This age-specific, 23-question document is divided to address 4 age groups and offers questions for parents and children. Evaluated domains include physical, emotional, social, and school health.

DIAGNOSIS AND CLASSIFICATION

In 2004, the International Headache Society updated the criteria required for the diagnosis of both migraine with and without aura in children aged 15 years and younger (**Table 2**).[7] The primary difference between adult and pediatric migraines is headache duration, which tends to be shorter in the latter, although they are equally disabling. Like adult migraineurs, pediatric patients experience nausea, photophobia, phonophobia, and difficulty in concentrating. Headaches are exacerbated by exertion and often resolve after vomiting or with sleep. Ninety percent of pediatric migraineurs have at least 1 primary relative who is affected by migraine.[3] These children inherit neurologic sensitivity, which makes them easy targets for migraine triggers. Sensitive migraineurs also tend to experience motion sickness and dizziness.

In children, headache pain is likely to be diffuse rather than unilateral. Pain is localized to the frontotemporal regions. Occipital headaches in children, whether unilateral or bilateral, are rare. The child in whom they occur should be evaluated for a structural lesion.[3,8] Photophobia or phonophobia occurring in conjunction with nausea or vomiting in children younger than 12 years is most often migraine-related.[9] Very young children may become irritable, cry, or cling to a parent because they are sensitive to light and sound during migraine. Unlike adults who have resolution of aura followed by migraine, children may experience an aura and headache simultaneously.

Table 1 – Indications for neuroimaging in children with headache

First or "worst" headache
Thunderclap headache
Chronic-progressive headache pattern that worsens over time
Focal neurologic finding or any abnormalities on neurologic examination
Papilledema
Ataxia
Abnormal or asymmetric deep tendon reflexes
Presence of a ventriculoperitoneal shunt
Presence of a neurocutaneous syndrome (neurofibromatosis or tuberous sclerosis)
Age younger than 3 years
Pain localized to the occipital region
Nuchal rigidity or other signs of meningeal irritation

PEDIATRIC MIGRAINE PRECURSORS

Paroxysmal disorders are common in patients who will ultimately be predisposed to migraine. Childhood periodic syndromes—such as cyclic vomiting, abdominal migraine, and benign paroxysmal vertigo—are self-limited and generally do not require an extensive or expensive workup.

Table 2 – Classification of adolescent and pediatric migraine with and without aura

Without aura	With aura
A. At least 5 distinct attacks	A. Fulfills criteria for migraine without aura
B. Headache attack lasting 1 to 72 hours	B. At least 3 of the following:
C. Headache has at least 2 of the following:	1. One or more fully reversible aura symptoms indicating focal cortical and/or brain stem dysfunction
1. Bilateral location (frontal/temporal) or unilateral location	2. At least 1 aura developing gradually over more than 4 minutes, or 2 or more symptoms occurring in succession
2. Pulsating quality	3. No aura lasting more than 60 minutes
3. Moderate to severe intensity	4. Headache follows in less than 60 minutes
4. Aggravation by routine physical activity	
D. During headache, at least 1 of the following:	
1. Nausea and/or vomiting	
2. Photophobia and/or phonophobia	

From Headache Classification Subcommittee of the International Headache Society. *Cephalalgia.* 2004.[7]

Cyclic vomiting syndrome (CVS) in infants and children is characterized by repeated bouts of explosive vomiting, at times to the point that the child becomes dehydrated. The median age of onset is 5 years, but CVS has been observed in infants as young as 6 days. Attacks, which last 1 hour to 5 days, are separated by periods of well-being. Symptoms usually have a rapid onset at night or in the early morning and last 6 to 48 hours. Associated symptoms include abdominal pain (80%), nausea (72%), retching (76%), anorexia (74%), pallor (87%), lethargy (91%), photophobia (32%), phonophobia (28%), and headache (40%). Eighty-two percent of patients with CVS have a family history of migraine.[10]

The diagnosis of CVS warrants the exclusion of secondary causes of cyclic vomiting in young children, such as intussusception, intracranial hypertension, and inborn errors of metabolism. Prophylactic agents such as cyproheptadine and amitriptyline can be useful in reducing the frequency, severity, and intensity of these disabling attacks.[11] Children older than 3 years who have severe and persistent symptoms of CVS associated with recurrent dehydration may be treated with ondansetron 0.15 mg/kg IV q6h.

Abdominal migraine is an idiopathic recurrent disorder characterized by episodic midline abdominal pain. The attacks, which last 1 to 72 hours, are moderate to severe in intensity and are associated with nausea, vomiting, pallor, and anorexia. Between attacks, patients are pain- and symptom-free. The attacks interfere with daily routines and often become sources of concern when a comprehensive diagnostic workup fails to identify a cause. Although patients infrequently experience headache in association with their abdominal discomfort, migraine will most often develop later in life.[3]

Benign paroxysmal vertigo (BPV) affects younger children (median age, 18 months). During a typical attack, children exhibit acute unsteadiness on their feet, which requires them to grab on to a parent or to a nearby object to avoid falling. Loss of consciousness does not occur, but nystagmus is common. Vomiting may occur and may be vigorous; spells may last several minutes. After each attack, the patient will sleep and return to normal activities on waking.

BPV attacks tend to occur in clusters over several days and then may subside for weeks or months. BPV, like abdominal migraine, is a precursor to adult migraine.[12]

PATIENT EDUCATION

Treatment of children and adolescents with migraine should focus foremost on behavioral modification and education. Both the patient and the parents should understand the importance of differentiating primary (benign) from secondary (organic) headache disorders. The likelihood of finding a brain tumor in a child with migraine headache who is older than 6 months and whose neurologic function is normal is approximately 0.4%.[13] Headaches occur in fewer than 50% of all patients with brain tumors and emerge as the tumor causes an increase in intracranial pressure.[14] Concerned parents should be informed that usual symptoms of brain tumors include an altered level of consciousness, ataxia, nausea, vomiting, seizures, or acute onset of weakness in an extremity.

Lifestyle intervention. Successful management of headache disorders requires an integrative approach be-

Table 3 – Behavioral approaches to treating pediatric migraine

- Make certain that the patient goes to bed and wakes up at the same time each day, including weekends. Sleeping on weekends may cause "hangover" headaches. The patient, therefore, should wake up at the usual time, get out of bed, and have a juice drink or light snack. The patient may then go back to sleep and will most often not wake up with a headache.
- Do not skip or delay meals. Hunger is a migraine trigger.
- Participate in some form of physical activity for 30 to 45 minutes at least 5 days per week.
- Limit caffeine consumption to no more than 250 mg/d. (Excessive caffeine intake can either induce headaches or result in caffeine withdrawal headaches when caffeine is not consumed for 1 to 2 days. Caffeine withdrawal headaches may last up to 1 week.) Food elimination diets are not recommended for headache management.
- Do not smoke. Avoid exposure to passive smoke whenever possible. (Smoke and other strong odors can trigger migraine.)
- Avoid excessive use of over-the-counter analgesics for acute headache management. Medication overuse headaches can be managed simply by discontinuing use of the offending analgesics.

tween pharmacotherapy and behavioral intervention. Parents appreciate physicians who spend time discussing lifestyle changes that can reduce the frequency, intensity, and duration of their child's headaches. Most parents prefer behavioral interventions to pharmacotherapy. Integration of the suggestions in **Table 3** can prevent many pediatric migraines.

PHARMACOTHERAPY

Reserve preventive and acute medications for patients with frequent and disabling headaches. Acute intervention should begin within 30 minutes; pediatric migraines rapidly reach peak pain intensity within 4 hours and then usually resolve. Medications should be available and accessible both at school and at home. School health services need to be aware of a patient's diagnosis and of the need to rapidly administer the proper medication.

Acute medications. Acute migraine therapies can be classified as migraine-specific or migraine nonspecific (**Table 4**). Although both types of therapies are effective in pediatric patients, some patients fail to achieve a pain-free state within 2 hours of taking an over-the-counter analgesic. Nevertheless, therapeutic trials of simple analgesics are warranted as first-line acute migraine therapy in treatment-naive pediatric patients. Be on guard for medication overuse headache (MOH).

Analgesics and MOH. Ibuprofen in doses of 7.5 to 10 mg/kg is effective for acute migraine.[3] However, using simple analgesics more than twice weekly can lead to MOH.[15] Up to 30% of children with chronic daily headache have been shown to use analgesics daily.[16]

MOH can occur at any age, even in children as young as 2 years. A headache pattern may represent MOH if it typically occurs 15 days or more per month for more than 3 successive months in a patient who frequently uses a simple analgesic. MOH worsens as the patient accelerates analgesic use. Adolescents may complain that the headache awakens them from sleep and is present when they wake up. Immediately on sensing the return of the headache, the patient will take another analgesic or be given additional medication by a parent. Over time, the patient rarely experiences a pain-free interval. Intermittent severe, disabling migraines develop into mild to moderate daily headache.

When analgesics are abruptly discontinued, the headache pattern intensifies once again. However, successful discontinuation of analgesics results in an 80% reduction in headache frequency in most patients.[17] As in adults, MOH is associated with the use of simple analgesics; combination drugs that contain butalbital and caffeine; and triptans, opioids, and ergotamines.

Triptans. Several large multicenter double-blind, placebo-controlled trials have shown that triptans are safe and well tolerated in children aged 12 years and older.[8] Unfortunately, because of trial design flaws, placebo response rates are high in pediatric migraine studies, which limits our ability to determine the true effectiveness of oral triptans. Open-label trial evidence supports the effectiveness of oral zolmitriptan and subcutaneous sumatriptan in patients 12 to 17 years old.[18] Unlike oral sumatriptan, the nasal spray formulation has been found to be safe and effective in acute adolescent migraine.[19] Although not approved for use in patients younger than 18 years, triptans should be con-

sidered first-line therapy for acute treatment of disabling migraines that are unresponsive to simple analgesics.

A MANAGEMENT GAME PLAN

Always make certain that each patient and his or her family members are completely in agreement on the "game plan" for preventing migraines—as well as how acute medications should be administered. Adherence to the following suggestions improves the overall success of acute migraine management:

- Early intervention (within 30 minutes); this most often results in resolution of pain within 2 hours and less chance of headache recurrence.
- Avoid the frequent use of "backup" or rescue medications.
- Practice and adhere to the lifestyle intervention strategies to reduce neurologic sensitivity.

If you are concerned about possible adverse events associated with triptan use in young children, consider giving the initial dose in the office setting under observation—regardless of whether the patient is symptomatic. Patients who use nasal spray or injections should also practice how to properly use the drugs in the office setting before self-treating their first migraine.

The effectiveness, tolerability, and safety of acute migraine therapy can be evaluated with the help of a headache diary. Patients or their parents are asked to record the date and time of the attack, the trigger, the location of pain, symptoms, severity (on a 10-point severity scale), medication (name, formulation, and dose), time the medication was taken, and the quality of relief (none, moderate, complete) achieved after 2 and 4 hours. Encourage patients or parents to record any other notes about each headache episode that they feel are important to bring to your attention.

PREVENTIVE THERAPY

If frequent or disabling attacks persist despite adequate trials of acute treatments, consider preventive therapy. Choose a regimen based on co-

Table 4 – Pharmacologic therapies for pediatric migraine*

Nonspecific acute migraine medications	**Suggested dose**
Acetaminophen[23]	15 mg/kg up to 1000 mg
NSAIDs[23]	
Ibuprofen	10 mg/kg up to 800 mg
Naproxen sodium	10 mg/kg up to 400 mg
Migraine-specific acute medications*	**Dose strengths**
Sumatriptan (Imitrex)	Injection: 6 mg Nasal spray: 5 mg, 20 mg Tablet: 25 mg, 50 mg, 100 mg
Zolmitriptan (Zomig)	Tablet: 2.5 mg, 5 mg ODT: 2.5 mg, 5 mg
Rizatriptan (Maxalt)	Tablet: 5 mg, 10 mg ODT: 5 mg, 10 mg
Naratriptan (Amerge)	Tablet: 1.25 mg, 2.5 mg
Almotriptan (Axert)	Tablet: 6.25 mg, 12.5 mg
Frovatriptan (Frova)	Tablet: 2.5 mg
Eletriptan (Relpax)	Tablet: 20 mg, 40 mg

ODT, orally disintegrating tablet.

*All are currently approved by the FDA for adults 18 years and older. Triptans are safe and well tolerated in patients 12 years and older. However, with the exception of nasal spray sumatriptan and oral zolmitriptan, statistically significant efficacy rates greater than that of placebo have not been demonstrated. If the initial dose is given in the office setting, monitor the patient for at least 1 hour. Adverse effects include episodes of paresthesia, chest pressure, and sedation; triptan use may potentially prolong a migraine aura.

existing conditions and on drug tolerability profiles. Unfortunately, recommendations on preventive medications in children and adolescents are based on information on their use in adults. Data are scant on effectiveness or optimal duration of preventive therapy in pediatric patients.

In children younger than 9 years, cyproheptadine in dosages of 2 to 8 mg/d given at bedtime, or divided and given twice a day, are effective and well tolerated. In older children, adolescents, and adults, adverse effects (such as sedation and weight gain) limit its use. If sleep disturbance is a significant coexisting condition, then cyproheptadine is an appropriate choice. Other preventive agents that can help with sleep are the tricyclic antidepressants amitriptyline and imipramine taken at night in dosages of 10 to 50 mg/d. These agents are also appropriate choices when hyperactivity or enuresis is present. Common side effects are sedation, weight gain, and dry mouth. β-Blockers such as propranolol are often used in dosages of 20 to 80 mg/d that are divided for twice-a-day dosing, although many

Table 5 – Preventive therapies for pediatric migraine

Agent	Dosage	Notes
Antidepressants		
Amitriptyline[24]	Starting dosage 0.25 mg/kg/d increasing every 2 weeks to maximum of 1 mg/kg/d	•Most studies using amitriptyline in children have been open-label •Efficacy in 50% - 80% of children[20,24] •Adverse effects: somnolence, dry mouth, arrhythmia •Use with caution in children aged < 12 years
Anticonvulsants		
Divalproex sodium (Depakote)	10 - 30 mg/kg/d PO bid in divided doses	•Reduced headache frequency of 50% - 75% in children aged 7 - 17 years[21,25] •Adverse effects: weight gain, heartburn, hair loss •Not for use in children aged < 2 years for any reason
Topiramate (Topamax)	2 - 3 mg/kg/d (maximum dose 200 mg)	•Reduced headache frequency from 5.4 - 1.9 days per month in 162 children aged 6 - 15 years[21]; results trended toward significance (P = .065) •Adverse effects: weight loss, episodes of paresthesia, cognitive dysfunction •Indicated in epilepsy for children as young as 2 years
Antiserotonergic agents		
Cyproheptadine	•Age < 2 years: not recommended •2 - 6 years: 0.25 mg/kg/d PO tid (tablet or syrup) •Age ≥ 7 years: 2 mg PO bid or tid; then titrate to 3 - 4 mg PO bid or tid	•Used more in toddlers because weight gain and somnolence is primary adverse effect in older children •In children aged 3 - 12 years, drug was effective in up to 83% of patients in 1 retrospective study[26]
β-Blockers		
Propranolol	•1 mg/kg/d PO qd if slow-release dosage form or divided bid or tid if immediate-release dosage form; gradually increase to 4 mg/kg/d over 2 wk to < 16 mg/kg (higher dosages discouraged)	•May lower blood pressure or cause depressive adverse effects or exercise-induced asthma •71% of children aged 7 - 16 years had complete remission using 60 - 120 mg/d in 1 double-blind, crossover trial[27]; other trials, however, have failed to show any improvement in headache frequency in patients using propranolol[28]

teenagers do not tolerate the fatigue and exercise intolerance that may occur with this regimen.[20]

Antiepileptic medications are very effective in preventing migraine attacks. Divalproex sodium is an effective migraine preventive for adults and is often used to treat epilepsy in children and adolescents. However, the adverse-effect profile—weight gain, hair loss, tremor, and risk of birth defects—makes it less desirable as a migraine preventive in this population.[21]

Topiramate is currently being investigated as a migraine preventive agent in children and adolescents. Dosages for migraine prevention range from 50 to 200 mg/d in single or divided doses.[22]

The FDA has not approved any medication for the prevention of migraine in children. The National Headache Consortium Guidelines has suggested that preventive medications should attempt to reduce headache frequency to less than 2 attacks per month for 4 to 6 months. The doses of preventive medications should be titrated slowly to minimize adverse effects. Once sustained relief is achieved, consider weaning the patient from the preventive medications. Preferred preventive therapies for pediatric migraine are summarized in **Table 5**.

Several herbal remedies (feverfew, riboflavin, coenzyme Q10) have been suggested for use in adults with headaches. However, none of these alternative medicines has been adequately studied for the prevention of headaches in children. ■

REFERENCES:

1. Maytal J, Young M, Shechter A, Lipton RB. Pediatric migraine and the International Headache Society (IHS) criteria. *Neurology.* 1997;48:602-607.
2. Lewis DW, Ashwal S, Dahl G, et al. Quality Standards Subcommittee of the American Academy of Neurology; Practice Committee of the Child Neurology Society. Practice parameter: evaluation of children and adolescents with recurrent headaches: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology.* 2002;59:490-498.
3. Pearlman EM. Managing migraine in children and adolescents. *Prim Care.* 2004;31:407-415, viii.
4. Ward TN, Levin M, Phillips JM. Evaluation and management of headache in the emergency department. *Med Clin North Am.* 2001;85:971-985.
5. Kramer U, Nevo Y, Neufeld MY, Harel S. The value of EEG in children with chronic headaches. *Brain Dev.* 1994;16:304-308.
6. Varni JW, Seid M, Kurtin PS. Peds QL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care.* 2001;39:800-812.
7. Headache Classification Subcommittee of the International Headache Society. International classification of headache disorders: 2nd edition. *Cephalalgia.* 2004;24(suppl 1):9-160.
8. Lewis D, Ashwal S, Hershey A, et al; American Academy of Neurology Quality Standards Subcommittee; Practice Committee of the Child Neurology Society. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. *Neurology.* 2004;63:2215-2224.
9. Winner P, Martinez W, Mate L, Bello L. Classification of pediatric migraine: proposed revisions to the IHS criteria. *Headache.* 1995;35:407-410.
10. Li BU, Murray RD, Heitlinger LA, et al. Is cyclic vomiting syndrome related to migraine? *J Pediatr.* 1999;134:567-572.
11. Andersen JM, Sugerman KS, Lockhart JR, Weinberg WA. Effective prophylactic therapy for cyclic vomiting syndrome in children using amitriptyline and cyproheptadine. *Pediatrics.* 1997;100:977-981.
12. Lindskog U, Odkvist L, Noaksson L, Wallquist J. Benign paroxysmal vertigo in childhood: a long-term follow-up. *Headache.* 1999;39:33-37.
13. Medina LS, Kuntz KM, Pomeroy S. Children with headache suspected of having a brain tumor: a cost-effectiveness analysis of diagnostic strategies. *Pediatrics.* 2001;108:255-263.
14. Fisher PG, Carson BS. Childhood brain tumors. In: Johnson RT, Griffin JW. *Current Therapy in Neurologic Disease.* 5th ed. Mosby: New York; 1997:239-245.
15. Kossoff EH, Mankad DN. Medication-overuse headache in children: is initial preventive therapy necessary? *J Child Neurol.* 2006;21:45-48.
16. Koenig MA, Gladstin J, McCarter R, et al. Chronic daily headache in children and adolescents presenting to tertiary headache clinics. *Headache.* 2002;42:491-500.
17. Wiendels NJ, van der Geest MC, Neven AK, et al. Chronic daily headache in children and adolescents. *Headache.* 2005;45:678-683.
18. Linder SL, Dowson AJ. Zolmitriptan provides effective migraine relief in adolescents. *Int J Clin Pract.* 2000;54:466-469.
19. Winner P, Rothner AD, Saper J, et al. A randomized, double-blind, placebo-controlled study of sumatriptan nasal spray in the treatment of acute migraine in adolescents. *Pediatrics.* 2000;106:989-997.
20. Levinstein B. A comparative study of cyproheptadine, amitriptyline, and propranolol in the treatment of adolescent migraine. *Cephalalgia.* 1991;11:122-123.
21. Caruso JM, Brown WD, Exil G, Gascon GG. The efficacy of divalproex sodium in the prophylactic treatment of children with migraine. *Headache.* 2000;40:672-676.
22. Winner P, Pearlman EM, Linder SL, et al; Topiramate Pediatric Migraine Study Investigators. Topiramate for migraine prevention in children: a randomized, double-blind, placebo-controlled trial. *Headache.* 2005;45:1304-1312.
23. Lewis DW. Headaches in children and adolescents. *Am Fam Physician.* 2002;65:625-632.
24. Hershey AD, Powers SW, Bentti AL, Degrauw TJ. Effectiveness of amitriptyline in the prophylactic management of childhood headaches. *Headache.* 2000;40:539-549.
25. Serdaroglu G. Erhan E, Tekgul H, et al. Sodium valproate prophylaxis in childhood migraine. *Headache.* 2002;42:819-822.
26. Lewis DW, Diamond S, Scott D, Jones V. Prophylactic treatment of pediatric migraine. *Headache.* 2004;44:230-237.
27. Ludgivsson J. Propranolol used in the prophylaxis of migraine in children. *Acta Neurol Scand.* 1974;50:109-115.
28. Forsythe WI, Gillies D, Sills MA. Propranolol ('Inderal') in the treatment of childhood migraine. *Dev Med Child Neurol.* 1984;26:737-741.
29. Rothner AD. The evaluation of headaches in children and adolescents. *Semin Pediatr Neurol.* 1995;2:109-118.

EVIDENCE-BASED MEDICINE

■ Lewis D, Ashwal S, Hershey A, et al; American Academy of Neurology Quality Standards Subcommittee; Practice Committee of the Child Neurology Society. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. *Neurology.* 2004;63:2215-2224.

■ Winner P, Pearlman EM, Linder SL, et al; Topiramate Pediatric Migraine Study Investigators. Topiramate for migraine prevention in children: a randomized, double-blind, placebo-controlled trial. *Headache.* 2005;45:1304-1312.

Therapeutic Agents in This Article

Acetaminophen (Tylenol)
Almotriptan (Axert)
Amitriptyline (Elavil)
Butalbital (multiple trade names)
Cyproheptadine (Periactin)
Divalproex sodium (Depakote)
Eletriptan (Relpax)
Frovatriptan (Frova)
Ibuprofen (multiple trade names)
Imipramine (Tofranil)
Naproxen sodium (multiple trade names)
Naratriptan (Amerge)
Ondansetron (Aloxi)
Propranolol (Inderal)
Rizatriptan (Maxalt)
Sumatriptan (Imitrex)
Topiramate (Topamax)
Zolmitriptan (Zomig)

Genetic Disorders

What Is This Disorder—And What Is The Prognosis?

GERMAINE L. DEFENDI, MD, MS
Olive View–UCLA Medical Center

Tetany in a 9-Year-Old Girl

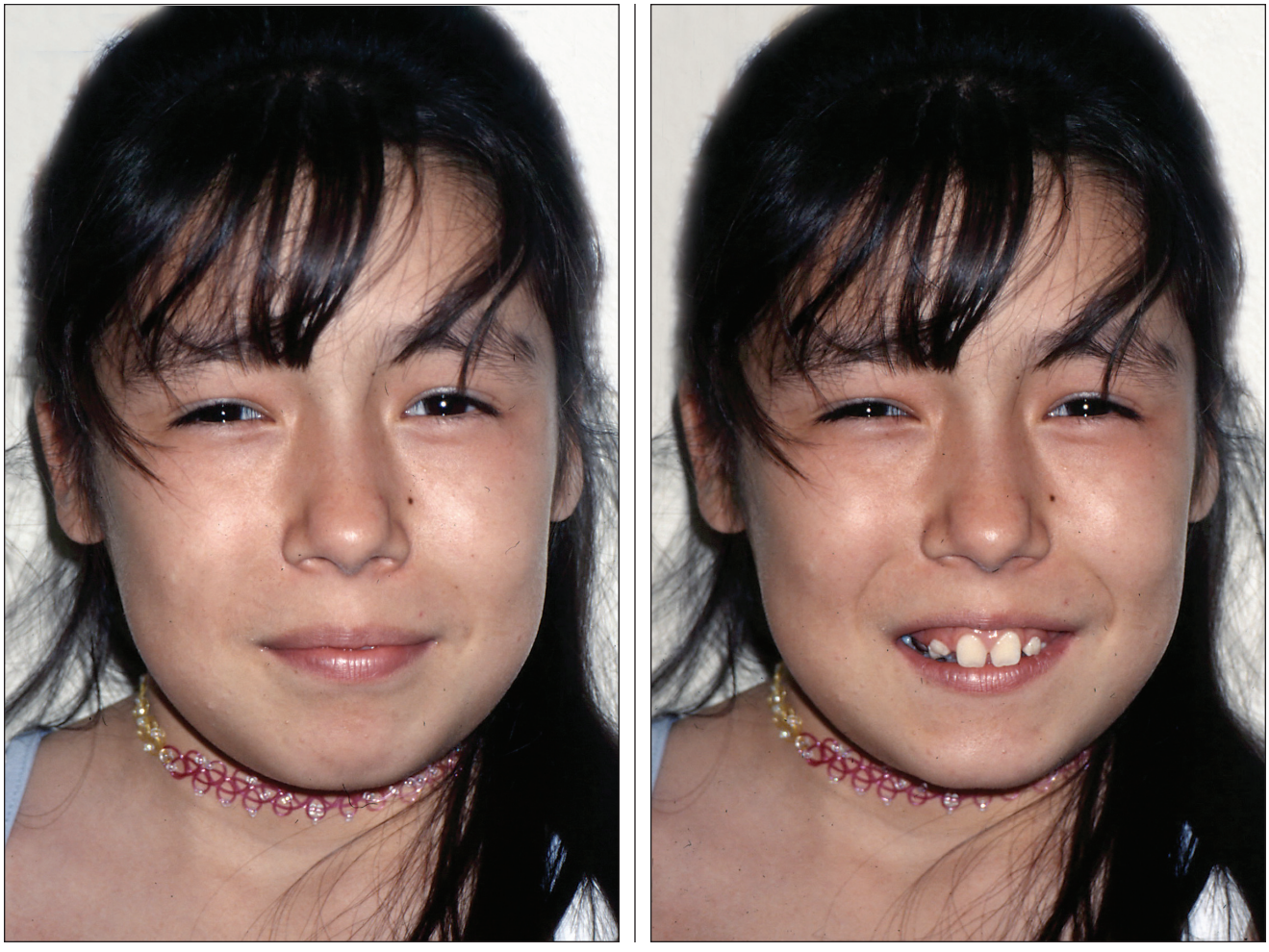


Figure 1 – The patient had a long face with narrow palpebral fissures, tubular nose, recessed mandible, and high arched palate.

A 9-year-old girl presented with a 3-hour history of unremitting severe cramping in her hands and legs. A similar episode occurred a month earlier, but it resolved with massage. She was taking no medications. The patient had a heart murmur; 3 years earlier, she had undergone cardiac surgery to repair a large atrial septal defect. She had been well since then.

Examination revealed an alert, oriented girl in pain from persistent cramping and flexion of her hands, wrists, and legs. Her speech was hypernasal. Her oral temperature was 37.1°C (98.8°F); heart rate, 91 beats per minute; respiratory rate, 28 breaths per minute; oxygen saturation, 99% on room air; and blood pressure, 109/54 mm Hg. She experienced carpal spasm after inflation of the blood pressure cuff on her left arm (Trousseau sign).

The patient had no history of recurrent illnesses or recurrent infections (such as otitis media). She had been able to tolerate vaccinations without adverse reactions. There was no history of psychiatric illness. She weighed 25.4 kg (25th percentile) and was 124 cm tall (3rd percentile). There were no developmental delays. However, the patient had a history of learning disabilities and reported difficulty with her school studies. At age 9 years, she was a second-grade student.

The patient had a long face with narrow palpebral fissures, tubular nose, recessed mandible, and high

Dr Defendi is associate clinical professor in the department of pediatrics at Olive View–UCLA Medical Center in Sylmar, Calif.

arched palate (**Figure 1**). A positive Chvostek sign (facial muscle spasm induced by tapping over the facial nerve about 2 cm anterior to the earlobe and below the zygomatic arch) was present. Her fingers were long and tapered (**Figure 2**).

Cardiac examination revealed a 2/6 systolic ejection murmur. A well-healed scar was present on the right side of her chest.

Neurologic examination revealed increased tone in her forearms and hands with flexion of her wrists and fingers. She was unable to straighten her fingers and had a weak handgrip. Decreased strength was also noted in her lower extremities and she had pain when walking on her heels and tiptoes. Her deep tendon reflexes were +3 in both upper and lower extremities. Sensation and function in cranial nerves II through XII were intact.

Laboratory data included white blood cell count, 4200/µL (normal, 4000 to 11,000/µL); lymphocyte count, 39.8% (normal, 22% to 69%); sodium, 147 mEq/L; potassium, 3.8 mEq/L; chloride, 106 mEq/L; bicarbonate, 23 mEq/L; urea nitrogen, 12 mg/dL; creatinine, 0.6 mg/dL; glucose, 93 mg/dL; total calcium, 6.6 mg/dL (normal, 8 to 10.5 mg/dL); phosphorus, 6 mg/dL (normal, 3.2 to 6.3 mg/dL); magnesium, 1.5 mEq/L (normal, 1.3 to 2.0 mEq/L); albumin, 4.7 g/dL per 100 mL (normal, 3.2 to 5.0 g/dL per 100 mL); and parathyroid hormone, 7 pg/mL (normal, 10 to 65 pg/mL). The ECG showed a QT corrected (QTc) interval of 0.42 (normal, less than 0.44) and normal rhythm.

CD3, CD4, and CD8 counts were not checked because the patient's white blood cell and lymphocyte counts were within normal limits and she had no history of recurrent illnesses or infections.

TO WHAT DIAGNOSIS DO THESE FINDINGS POINT?

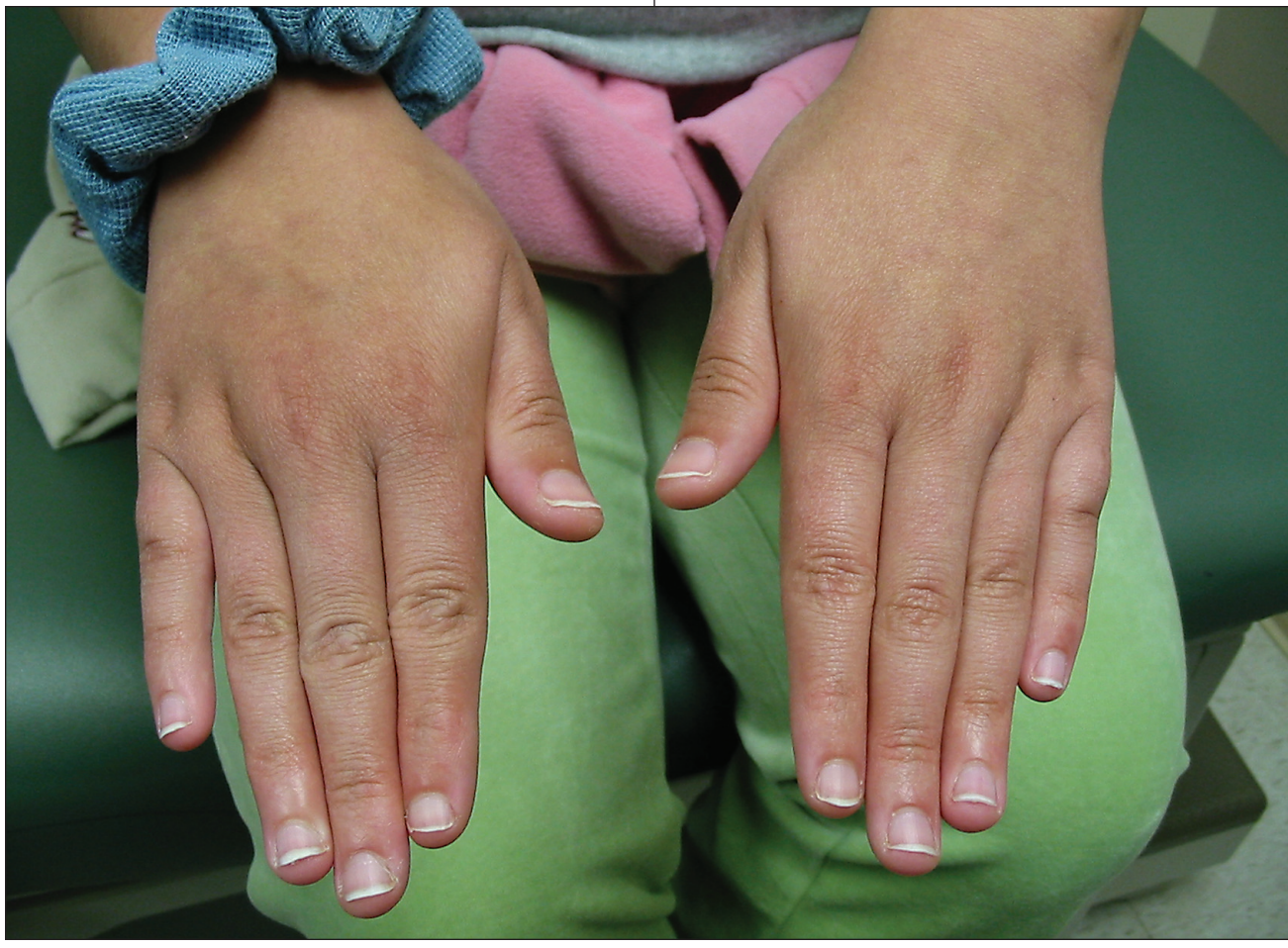


Figure 2 – The patient's fingers were long and tapered; she was unable to straighten them and had a weak handgrip.

ANSWER: VELOCARDIOFACIAL SYNDROME

In hypocalcemia, the salient clinical symptoms are neuromuscular. Our patient presented in tetany, with positive Chvostek and Trousseau signs (peripheral neurologic findings seen in hypocalcemia).[1,2] She was given an intravenous infusion of 10% calcium gluconate and was placed on continuous cardiac monitoring. Her neuromuscular symptoms resolved once her total serum calcium improved (to 7.6 mg/dL).

Other symptoms associated with acute hypocalcemia are[1,2]:

- Bronchospasm.
- Laryngeal stridor.
- Dysphagia.
- Vomiting.
- Muscle weakness and/or muscle spasms.
- Distal extremity numbness and tingling.
- Irritability and confusion.
- Seizures.
- Prolongation of the QTc interval.

Normal laboratory values for magnesium, phosphorus, albumin, and renal function helped exclude key metabolic disorders that cause hypocalcemia.[1,2] A genetic cause of hypocalcemia was suspected because of the patient's history of congenital heart disease, her craniofacial features, and the absence of a clear metabolic cause.

Chromosome analysis and a fluorescence in situ hybridization (FISH) study of a probe on chromosome 22 were done. The karyotyping was conducted as part of a standard genetic workup for patients in whom a chromosomal abnormality is suspected to check for translocations or more apparent deletions (macrodeletions) in the chromosomes. Chromosome analysis showed a normal female karyotype (46,XX).

FISH analysis was also ordered to rule out a microdeletion syndrome, because only one third of interstitial chromosomal deletions are detected by standard cytogenetic analyses.[3,4] FISH uses a DNA cosmid probe tagged with a fluorescent label for a specific region within the genome. In this patient, FISH analysis showed a small deletion in the long arm (q) of chromosome 22 at band site 11.2. This deleted area represents an interstitial deletion of chromosome 22q of bands 11.21 to 11.23—a chromosomal deletion consistent with DiGeorge syndrome and velocardiofacial syndrome (VCFS).[4]

VELOCARDIOFACIAL SYNDROME

The spectrum of clinical presentations seen in patients with DiGeorge syndrome and VCFS represents phenotypic variability of a single genetic defect. In 1993, Wilson and colleagues[5] proposed a collective acronym for genetic syndromes with the common etiology of monosomy 22q11. The acronym is CATCH 22: **C**ardiac defects, **A**bnormal facies, **T**-cell deficit from thymic hypoplasia, **C**left palate, and **H**ypocalcemia from parathyroid hypoplasia.[4-6] Both DiGeorge syndrome and VCFS fall within this spectrum. As such, the variability of clinical presentation seen in these patients is extensive: DiGeorge syndrome resides at the severe end of the spectrum (T-cell immunodeficiency, thymic and parathyroid hypoplasia, and outflow tract cardiac defects) and VCFS at the mild end.[7] In DiGeorge syndrome, hypocalcemia and immune defects from T-cell deficiency are typically recognized in the newborn period; in VCFS, these findings are less common. VCFS is generally diagnosed at an older age in patients with craniofacial and palatal abnormalities.[3,6]

Also known as Shprintzen syndrome, VCFS was characterized in 1978 by Dr Robert Shprintzen and colleagues.[8] The syndrome involved cleft palate, cardiac anomalies, typical facies, and learning disabilities.[6,8] Today, the worldwide prevalence of VCFS is estimated to be 1 in 4000.[4] The defining phenotype of VCFS is divided into 3 clinical areas:

- *Velo-:* palatal deformities, such as cleft of the secondary palate and/or velopharyngeal incompetence.
- *Cardio-:* congenital cardiac defects, present in 85% of patients. Ventricular septal defect (62%), right aortic arch (52%), and tetralogy of Fallot (21%) are the most common.
- *Facial-:* craniofacial findings, such as microcephaly (40% to 50%), narrow palpebral fissures, a prominent bulbous nose and nasal root from hypoplastic alae nasi, a long narrow face with a small mouth, and a recessed mandible with a small chin (micrognathia).[3,6]

To page 557.

Other features include[6]:
- Postnatal growth retardation leading to short stature (in 33% of those affected).
- Hypernasal speech.
- Conductive hearing loss related to cleft palate and auricular anomalies.
- Hyperextensible hands and tapering fingers (in 63%).

In newborns, hypotonia may be present (in 70% to 80%) along with transient neonatal hypocalcemia (20%). In about 40% of older patients, delayed speech development, learning disabilities, and mild intellectual impairment are seen.[3] Psychiatric illness—especially schizophrenia and bipolar spectrum disorders—is present in about 25% of patients. This high rate of psychosis suggests a genetic link between 22q and these psychiatric disorders.[6]

VCFS occurs in patients as a new mutational event about 85% of the time. In the remaining cases, monosomy 22q is inherited with an autosomal dominant Mendelian inheritance pattern. In these cases, there is a 50% chance that the deletion will be passed from one generation to the next. Parental chromosomal studies and FISH analyses are recommended for those couples with an affected child who are planning to have more children.[6] These studies clarify potential recurrence risks for these families.

TREATMENT

Therapy to prevent recurrence of acute hypocalcemia is lifelong. This patient started a daily regimen of calcium carbonate, calcitriol, and aluminum hydroxide to maintain balanced serum levels of calcium and phosphorus. The family was given nutritional guidelines to help their child maintain a low phosphate diet. Outpatient follow-up was scheduled to monitor calcium and phosphorus serum levels and for renal ultrasonography to evaluate for nephrocalcinosis from the daily exogenous calcium load. ■

REFERENCES:
1. Cronan KM, Norman ME. Renal and electrolyte emergencies. In: Fleisher GR, Ludwig S, eds. *Textbook of Pediatric Emergency Medicine.* 3rd ed. Baltimore: Lippincott Williams & Wilkins; 1993:670-717.
2. Beach CB. Hypocalcemia. Available at: www.emedicine.com/EMERG/topic271.htm. Accessed June 29, 2006.
3. Jones KL. Shprintzen syndrome. In: *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia: WB Saunders; 1997:266-267.
4. DiGeorge syndrome. Available at: www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=188400. Accessed August 2, 2006.
5. Wilson DI, Burn J, Scambler P, Goodship J. DiGeorge syndrome: part of CATCH 22. *J Med Genet.* 1993;30:852-856.
6. Velocardiofacial syndrome. Available at: www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=192430. Accessed June 29, 2006.
7. Leana-Cox J, Pangkanon S, Eanet KR. Familial DiGeorge/velocardiofacial syndrome with deletions of chromosome area 22q11.2: report of five families with a review of the literature. *Am J Med Genet.* 1996;65:309-316.
8. Shprintzen RJ, Goldberg RB, Lewin ML, et al. A new syndrome involving cleft palate, cardiac anomalies, typical facies, and learning disabilities: velo-cardio-facial syndrome. *Cleft Palate J.* 1978;15:56-62.
9. Siegel NJ, Carpenter T, Gaudio KM. The pathophysiology of body fluids. In: Oski FA, DeAngelis CD, Feigin RD, Warshaw JB, eds. *Principles and Practice of Pediatrics.* 2nd ed. Philadelphia: JB Lippincott; 1994:58-77.
10. Halpern J, Wang NE. Hypoparathyroidism. Available at: www.emedicine.com/EMERG/topic276.htm. Accessed June 29, 2006.

Hypocalcemia: Lessons for the Clinician

Hypocalcemia is almost always a response to an underlying disorder—genetic or metabolic. This case illustrates a genetic cause of hypocalcemia; however, there are a variety of metabolic abnormalities that cause hypocalcemia:
- Hypoalbuminemia, the most common, may be the result of nephrosis, malnutrition, burns, chronic illness, or sepsis. Forty percent of serum calcium is protein-bound to albumin. Hypoalbuminemia decreases calcium's binding capacity and causes hypocalcemia.[1,2,9]
- Hypomagnesemia can occur secondary to pancreatitis; therapy with an aminoglycoside, amphotericin, or loop diuretics; alcoholism; and malnutrition. Hypomagnesemia induces hypocalcemia by causing end-organ resistance to parathyroid hormone and inhibiting the hypocalcemic feedback loop.[1,2,9]
- Hyperphosphatemia occurs in patients with renal disease, malignancy, or medication misuse, and in those receiving hyperalimentation. Phosphate keenly binds to calcium, causing acute hypocalcemia.[1,2,9]
- Hypoparathyroidism—part of the CATCH 22 diagnostic criteria—occurs in both DiGeorge syndrome and VCFS. Parathyroid hormone works with vitamin D to regulate total body calcium as a response to hypocalcemia. This hormonal response stimulates osseous and renal absorption of calcium and activates vitamin D conversion to facilitate calcium absorption from the GI tract. Parathyroid hormone deficiency can be idiopathic or the result of a variety of causes: genetic (as in this case), iatrogenic (from drugs), radiation or surgical removal of parathyroid glands, infiltrative diseases (such as Wilson disease), and metastatic cancer.[1,10]

As illustrated in this case, it is important to keep a wide differential in mind when managing a patient with hypocalcemic tetany. By understanding the causes of acute hypocalcemia, appropriate short- and long-term medical management can be achieved.

Case In Point

An Intriguing Diagnosis

Infant With Aldosterone Deficiency

NEDIM ÇAKAN, MD, PRASAD LAKSHMINARASIMHIAH, MD,
CHANDRA EDWIN, MD, and DEEPAK M. KAMAT MD, PhD
Wayne State University

A 45-day-old boy was referred for evaluation of persistent hyponatremia and hyperkalemia. On the 9th day of the boy's life, his serum potassium level was elevated (8 mEq/L) and on the 12th day, his serum sodium level was low (131 mEq/L). Supplementation with sodium chloride was initiated.

The patient was born at 30 weeks gestation to a 39-year-old woman. Delivery was by cesarean section because of the fetus's breech presentation and because of premature membrane rupture, which had occurred 6 weeks earlier. The mother was given dexamethasone during labor and the baby received intratracheal surfactant during neonatal resuscitation.

At birth, the baby weighed 1470 g (50th percentile); his head circumference was 28.5 cm (50th percentile); and length was 41 cm (50th percentile). Apgar scores were 5 and 7 at 1 and 5 minutes, respectively. Respiratory distress subsequently developed, and the patient was intubated in the delivery room and transferred to the neonatal ICU. Hyaline membrane disease was diagnosed, and the patient was placed on ventilatory support until day 6 of life.

He received total parenteral nutrition (TPN) exclusively until day 6. He was then fed breast milk with human milk fortifier (HMF); this was supplemented with TPN on day 7. By day 10, the child was fed breast milk with HMF exclusively. Sodium supplementation was started at 1 mEq/feed on day 12; this was gradually increased to 4 mEq/4h on day 40.

The patient had no history of seizure-like activity, irritability, drowsiness, excessive or decreased urination, altered feeding patterns, diuretic use, head trauma, or abdominal distention. There was no family history of similar illness or of ambiguous genitalia.

On examination, the patient was alert, responsive, and comfortable. Both his weight and length had dropped to 10th percentile, however. His temperature was 36.1°C (97°F); heart rate, 154 beats per minute; respiratory rate, 52 breaths per minute; oxygen saturation, 98% on room air; and blood pressure, 70/36 mm Hg. Results of a systemic examination were normal. The genitourinary examination showed normal male genitalia with bilateral descended testicles.

Laboratory evaluation at the referring hospital showed that in addition to low serum sodium and a high serum potassium level, the patient's serum 11-deoxycortisol level was 120 ng/mL. Results of a newborn metabolic screen were negative for congenital adrenal hyperplasia. Plasma renin activity (PRA) was 113.18 ng/mL/h (normal, 2.0 to 3.7 ng/mL/h). Serum aldosterone was 29.7 ng/dL; this was thought to be low given the low serum sodium levels and high PRA. 17-OH progesterone was 136 ng/dL (normal, 53 to 186 ng/dL for this age). Renal sonograms were normal.

On the day of presentation at our hospital (day 45 of life), the patient's serum sodium was 135 mEq/L; serum potassium, 6.5 mEq/L; blood urea nitrogen, 10 mg/dL; creatinine, 0.4 mg/dL; urinary sodium, 87 mEq/L; and urinary potassium, 48.6 mEq/L. Serum aldosterone level was 34 ng/dL (normal, 1 to 31 ng/dL); serum cortisol, 6.2 µg/dL (normal, 4 to 29 µg/dL); PRA, 299.3 ng/mL/h (normal, 2 to 3.7 ng/mL/h); 11-deoxycortisol, 67 ng/dL (normal, less than 30 ng/dL); deoxycorticosterone, 31 ng/dL (normal, 7 to 57 ng/dL); 17-OH progesterone, 134 ng/dL (normal, 40 to 200 ng/dL); 18-OH corticosterone, 950 ng/dL (normal, 5 to 220 ng/dL); and corticosterone, 535 ng/dL (normal, 80 to 1500 ng/dL). Head and renal sonograms were normal.

Breast milk analysis showed sodium and potassium levels of less than 75 and 13.6 mEq/L, respectively. An adrenocorticotropic hormone (ACTH) stimulation test showed the pre-ACTH aldosterone level to be 34 ng/dL; the post-ACTH aldosterone level was 37 ng/dL (not a significant increase).

*The diagnosis of **aldosterone deficiency**, or **corticosterone methyl oxidase (CMO) type II deficiency**, was made. This diagnosis was based on the increased 18-OH corticosterone level, the inappropriately low aldosterone level relative to the degree of hyponatremia and high PRA, and the increased ratio of 18-OH corticosterone to aldosterone.*

Sodium chloride supplementation was given at 2 mEq/L with every feeding along with a low-iron infant formula (Similac PM 60/40). The patient had a partial response; fludrocortisone, 0.1 mg/d, was therefore

The authors are affiliated with the department of pediatrics at Children's Hospital of Michigan and Wayne State University in Detroit. Drs Çakan and Edwin are staff endocrinologists at Children's Hospital and assistant professors of pediatrics. Dr Lakshminarasimhiah is a resident in the department of pediatrics. Dr Kamat is professor of pediatrics, vice chair of education, and director of the Institute of Medical Education at the Carman and Ann Adams department of pediatrics at Children's Hospital.

Table – Differences between corticosterone methyl oxidase (CMO) deficiency types I and II

Steroid	CMO I	CMO II
Aldosterone	↓↓	↓
Cortisol	Normal	Normal
Desoxycorticosterone	↑↑	↑↑
Corticosterone	Normal, ↑	Normal, ↑
18-OH corticosterone	↓	↑↑
Corticosterone/18-OH corticosterone	↑	↓
18-OH corticosterone:aldosterone	< 10	> 40

added to the regimen. He responded well to this combination and his sodium level remained stable at 138 to 140 mEq/L.

At follow-up visits, the baby showed good catch-up growth.

ALDOSTERONE DEFICIENCY

The first 3 steps of aldosterone biosynthesis from cholesterol to progesterone are identical to those of cortisol biosynthesis. However, aldosterone synthase (*CYP11B2*) is only expressed in the zona granulosa of adrenal glands.[1,2] The most common cause of aldosterone deficiency is congenital adrenal hyperplasia (CAH) from 21-hydroxylase (*CYP21*) deficiency. In CAH, cortisol deficiency is associated with increased levels of sex steroids that can present as ambiguous genitalia in female infants.[1-4]

Aldosterone deficiency is an autosomal recessive disorder characterized by a defect in the terminal step of aldosterone. Affected persons appear to be homozygous for 2 different mutations—Arg 181 Trp and Val 1385 Ala. Family members who are homozygous for only 1 of these mutations remain unaffected. This effect is associated with biochemical evidence of chronic salt depletion.[3-6]

Two forms of aldosterone synthase deficiency are described—CMO deficiency types I and II. Clinical features of patients with either syndrome are identical; the only differences are found in the intermediate steroid profiles (**Table**).[7,8]

The clinical presentation of aldosterone synthase deficiency and the severity of presentation vary with age. Newborns (within the first several weeks of life) exhibit a salt-wasting syndrome, which can present as failure to gain weight followed by signs of dehydration.[4] Affected adults are usually asymptomatic but may experience problems during periods of stress or acute illness (such as gastroenteritis) or in very hot climates where they may not tolerate salt losses.[1,2,5,7]

If aldosterone deficiency is not corrected, the result may be hypotension from hypovolemia, shock, and sometimes death associated with hyponatremia, hyperkalemia, and hyperreninemia. Patients usually present with serum levels of sodium of 120 to 130 mEq/L and potassium of 6.0 to 8.5 mEq/L. Their PRA is markedly elevated and aldosterone levels are inappropriately low.

Diagnostic laboratory findings are hyponatremia, hyperkalemia, hyperreninemia, with hypoaldosteronemia. Other very important laboratory findings are normal cortisol and sex steroid levels that are appropriate for the infant's age. Patients with aldosterone synthase deficiency who present after infancy usually have anorexia, mild dehydration, and abnormal growth. Electrolyte abnormalities may be present, but most of the children older than 4 years have normal serum electrolyte levels at the time of diagnosis.[3,7,8]

TREATMENT

Treatment of affected infants includes oral sodium supplementation (sodium chloride 1 to 2 g/d) and fludrocortisone (0.1 to 0.3 mg/d). Establishing normal fluid and electrolyte balance will result in rapid catch-up growth. Mineralocorticoid therapy (fludrocortisone) and sodium supplementation should be continued and the child should be monitored regularly throughout childhood. Older patients can be treated with fludrocortisone alone.[1-5] ■

REFERENCES:
1. White PC. Abnormalities of aldosterone synthesis and action in children. *Curr Opin Pediatr.* 1997;9:424-430.
2. Root AW, Shulman DI. Clinical adrenal disorders. In: Pescovitz OH, Eugster EA, eds. *Pediatric Endocrinology, Mechanisms, Manifestations, and Management.* Philadelphia: Lippincott Williams & Wilkins; 2004:592-593.
3. White PC. Aldosterone synthase deficiency and related disorders. *Mol Cell Endocrinol.* 2004;217:81-87.
4. Picco P, Garibaldi L, Cotellessa M, et al. Corticosterone methyl oxidase type II deficiency: a cause of failure to thrive and recurrent dehydration in early infancy. *Eur J Pediatr.* 1992;151:170-173.
5. Lee PD, Patterson BD, Hintz RL, Rosenfeld RG. Biochemical diagnosis and management of corticosterone methyl oxidase type II deficiency. *J Clin Endocrinol Metab.* 1986;62:225-229.
6. Veldhuis JD, Melby JC. Isolated aldosterone deficiency in man: acquired and inborn errors in the biosynthesis or action of aldosterone. *Endocr Rev.* 1981;2:495-517.
7. Ulick S. Diagnosis and nomenclature of the disorders of the terminal portion of the aldosterone biosynthetic pathway. *J Clin Endocrinol Metab.* 1976;43:92-96.
8. Ulick S, Wang JZ, Morton DH. The biochemical phenotypes of two inborn errors in the biosynthesis of aldosterone. *J Clin Endocrinol Metab.* 1992;74:1415-1420.

A Collage of Infectious Diseases in Children

ALEXANDER K. C. LEUNG, MD
C. PION KAO, MD
University of Calgary and Alberta Children's Hospital

Perichondritis

A 10-year-old girl presented with a 7-day history of severe pain in the left ear. During the past 2 days, the left auricle had become erythematous and markedly tender. The child was treated with cloxacillin, and symptoms subsided in a week.

Perichondritis presents with erythema, edema, and extreme tenderness over the affected area. Because of the lack of cartilage, the ear lobe is not affected—unlike in cellulitis of the auricle, which generally involves the earlobe. Because the skin of the external ear is attached to the perichondrium, the severity of the pain may be disproportionate to the degree of inflammation. ■

Dr Leung is clinical associate professor of pediatrics at the University of Calgary and pediatric consultant at the Alberta Children's Hospital in Calgary, Alberta. Dr Kao is pediatric consultant at the same hospital.

Photo Essay

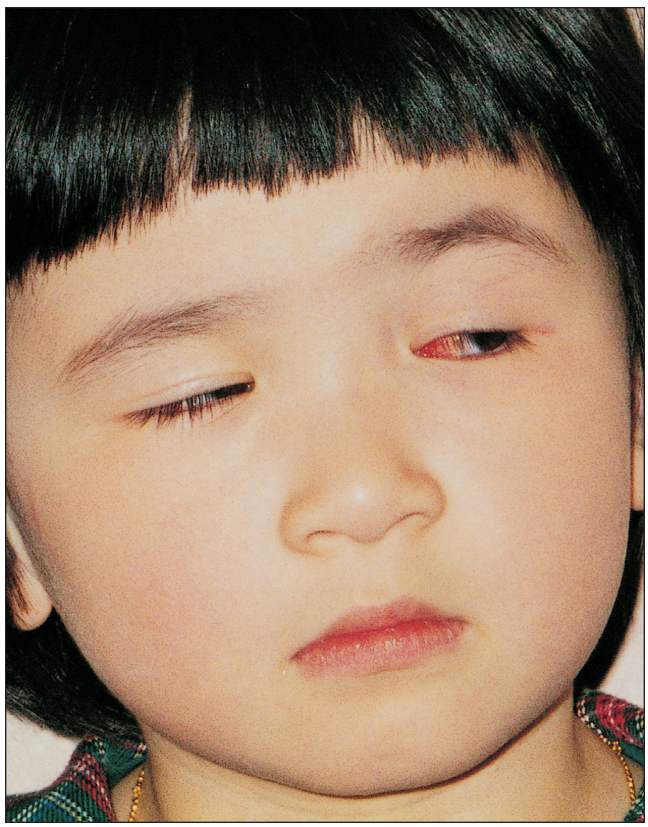
A Collage of
Infectious Diseases in Children

Periorbital Cellulitis

A 7-year-old girl presented with a 2-day history of pain and swelling in the right periorbital area. Her temperature was 38°C (100.4°F). The periorbital area and the adjacent area of the face were erythematous and tender. Her vision and eye movements were normal.

The child had periorbital cellulitis. This condition can be caused by trauma, an infected wound, or sinusitis. The usual causes are *Haemophilus influenzae,* pneumococci, streptococci, and staphylococci. Proptosis, decreased vision, and decreased eye mobility indicate orbital extension.

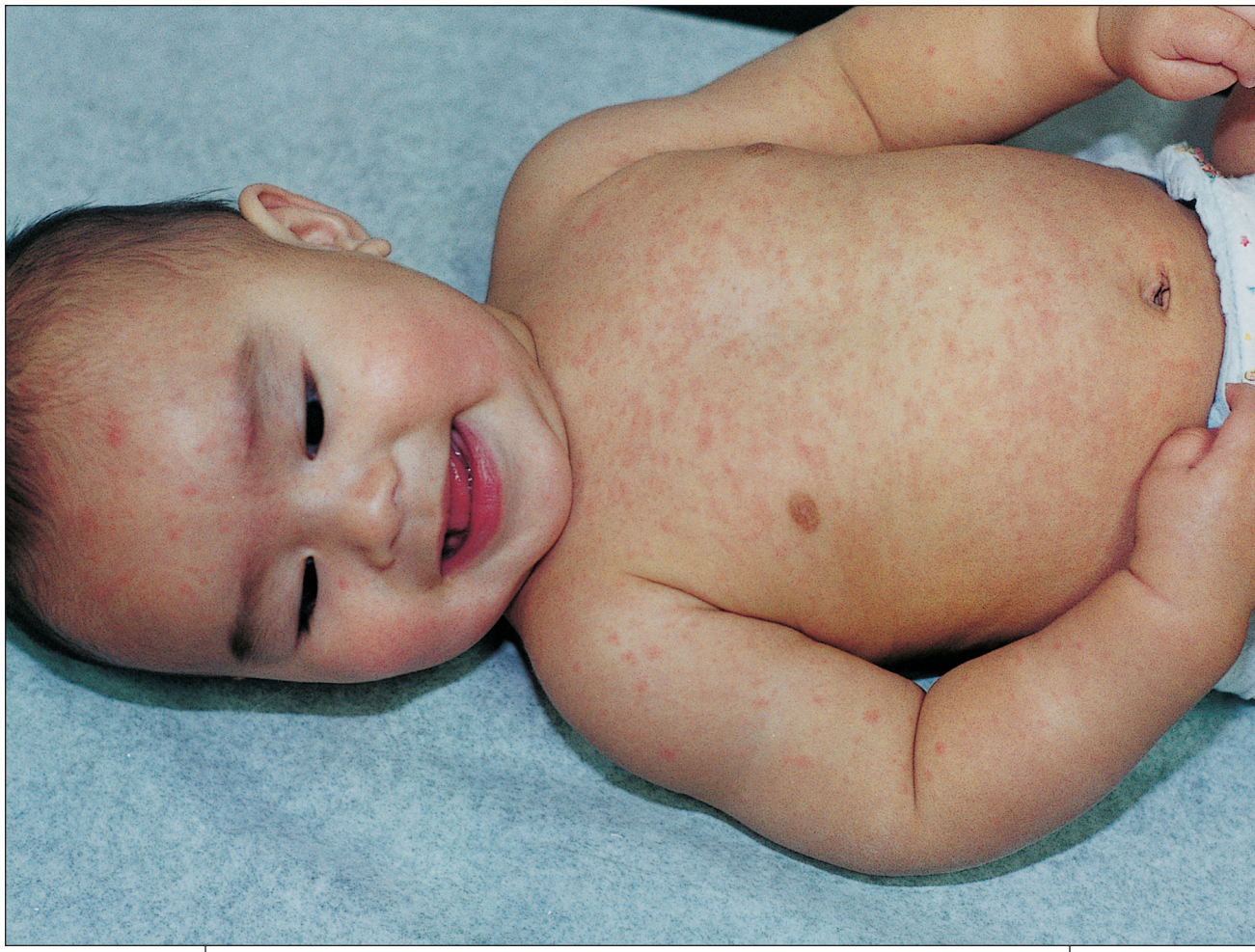
Prompt antimicrobial therapy is mandatory. Oral antibiotics are acceptable if the eyelid swelling is modest and there is no evidence of toxicity. If the child appears toxic, parenteral antibiotics and hospitalization are recommended. First-line agents include amoxicillin/potassium clavulanate, cephalexin, clarithromycin, and erythromycin/sulfisoxazole. Alternatively, a parenteral antibiotic such as cefuroxime or ceftriaxone may be given. ■



Bacterial Conjunctivitis

For 2 days, a 4-year-old girl had complained of discomfort and a yellow discharge from the left eye. The left conjunctiva was hyperemic, but there was no preauricular lymphadenopathy. A swab from the left eye grew *Haemophilus influenzae.* The child was treated with topical chloramphenicol 0.5% eyedrops and had an uneventful recovery.

Bacterial conjunctivitis in children is characterized by conjunctival hyperemia, mucopurulent discharge, and various degrees of ocular discomfort. Unlike viral conjunctivitis, the bacterial form is characterized by an absence of preauricular lymphadenopathy (except in the case of gonococcal conjunctivitis). The onset is usually acute; involvement may be unilateral or bilateral. *H influenzae* is the most commonly isolated organism. Others include pneumococci, staphylococci, streptococci, and *Moraxella catarrhalis.* ■

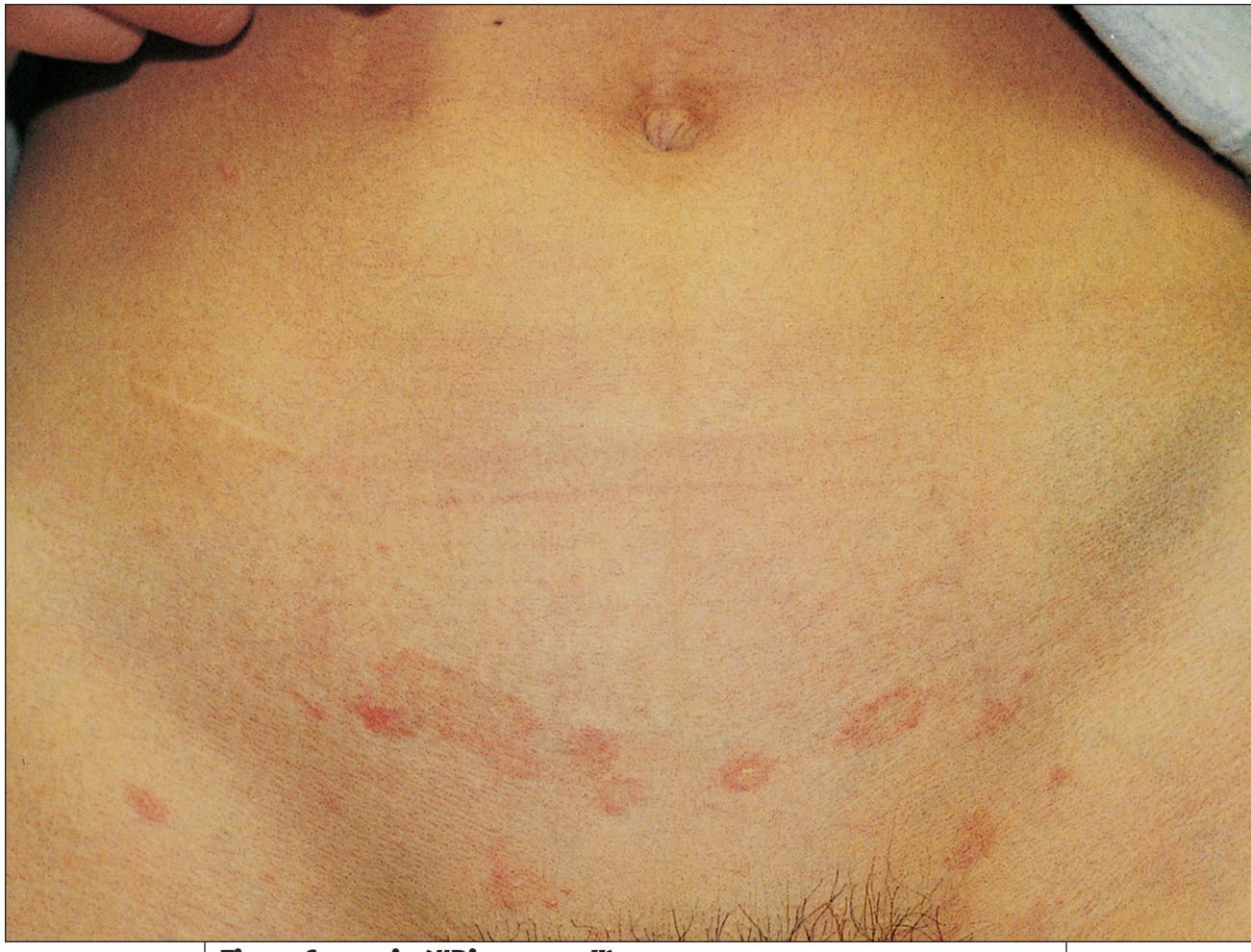


Roseola Infantum (Exanthem Subitum)

A 10-month-old infant presented with a 3-day history of fever (39°C to 40°C [102.2°F to 104°F]). The physical examination results were essentially normal, apart from the fever. On the following day, the fever subsided and an erythematous rash erupted.

Roseola infantum is caused by human herpesvirus 6. Most cases occur during the first year of life. The illness is characterized by high fever (39°C to 42°C [102.2°F to 105.8°F]) that lasts 3 to 4 days followed by the sudden appearance of rash at defervescence (hence the term "exanthem subitum," or sudden rash). The rash usually subsides in 2 to 4 days. Roseola infantum may be complicated by febrile seizures.

There is no specific treatment. An antipyretic may be used to reduce fever and discomfort. ■



Tinea Corporis ("Ringworm")

This 14-year-old boy presented with an erythematous, itchy suprapubic rash of 2 weeks' duration. Microscopic examination of a potassium hydroxide wet mount preparation of skin scrapings showed yeast hyphae. The boy was treated with topical terbinafine and the lesions resolved.

Tinea corporis is a superficial fungal infection of the nonhairy (glabrous) skin, excluding the groin, palms, and soles. The major causes include *Trichophyton tonsurans, Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis,* and *Epidermophyton floccosum.* The most characteristic lesion is an annular, scaly plaque that has a papular border and some degree of central clearing (hence the name "ringworm"). Pruritus is common. Lesions may vary in size from a few millimeters to several centimeters and may be solitary or multiple. The condition can be acquired by direct contact with infected persons or by autoinoculation. ■

SEVERINO R. BAUTISTA, MD
PURUSHOTTAM GHOLVE, MD
Children's Hospital of Philadelphia
JOHN P. DORMANS, MD
University of Pennsylvania

Pediatric Musculoskeletal Infections: Combating the Major Pathogens

Drs Bautista and Gholve are research fellows and Dr Dormans is chief of orthopedic surgery at the Children's Hospital of Philadelphia. Dr Dormans also is professor of orthopedic surgery at the University of Pennsylvania School of Medicine in Philadelphia.

ABSTRACT: Septic arthritis and several other types of musculoskeletal infections in children are caused by group A *Streptococcus.* Methicillin-resistant *Staphylococcus aureus* is emerging as a cause of skin infections in the sports community. *Neisseria meningitidis* in purpura fulminans usually is not associated with direct infection of musculoskeletal structures. *Streptococcus pneumoniae* has been reported as a causative organism for osteomyelitis and septic arthritis. The diagnosis of *Neisseria gonorrhoeae* infection is confirmed by culture that needs to be done under warm conditions with low carbon dioxide levels. Tuberculosis infections have been on the rise in the United States. Lyme disease, caused by the spirochete *Borrelia burgdorferi,* often presents as an episodic musculoskeletal synovitis affecting 1 or more joints.

Key words: pediatric musculoskeletal infections, septic arthritis, osteomyelitis, pyomyositis, methicillin-resistant *Staphylococcus aureus* infection, *Neisseria gonorrhoeae* infection, tuberculosis, Lyme disease

Musculoskeletal infections in children include osteomyelitis, septic arthritis, and pyomyositis. Most of these infections are bacterial. *Staphylococcus aureus* is the most common organism in children in all age categories. Others include group A *Streptococcus, Neisseria meningitidis* in purpura fulminans, *Streptococcus pneumoniae, Neisseria gonorrhoeae, Mycobacterium tuberculosis,* and *Borrelia burgdorferi.*

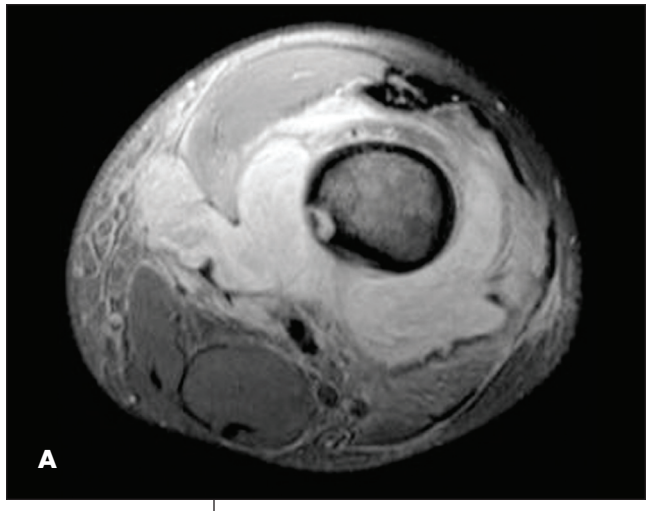
In this, the second of 2 articles, we review management approaches to musculoskeletal infections in children. In part 1, which appeared in the August 2006 issue of this journal, we reviewed the principles of patient evaluation, classification of osteomyelitis and corresponding approaches to management, special forms of osteomyelitis, and diagnosis and management of septic arthritis.

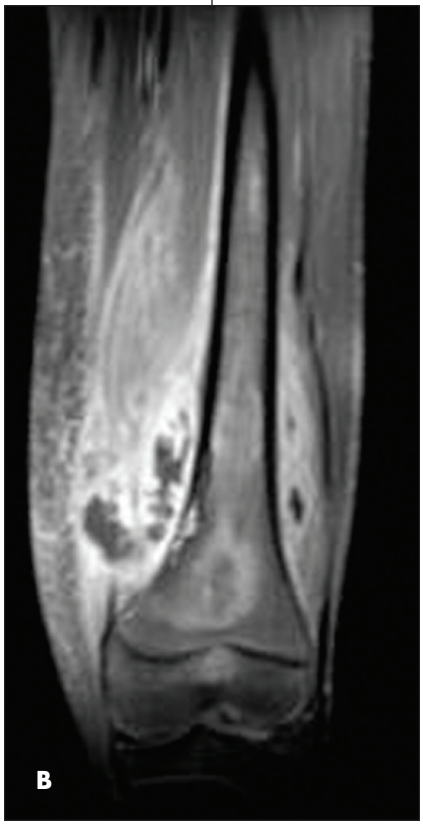
Here the focus is on the significant organisms to watch out for in pediatric musculoskeletal infections.

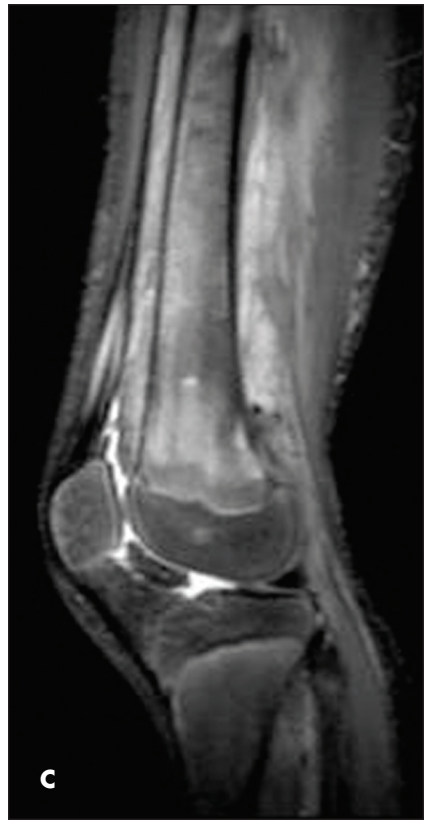
GROUP A *STREPTOCOCCUS*

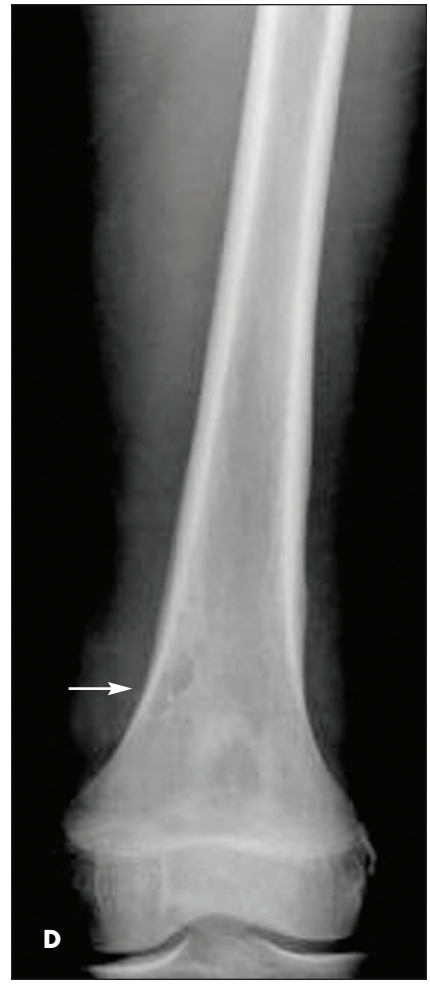
This organism is responsible for several types of musculoskeletal infections in children, especially septic arthritis. Of note, the most common complication of chickenpox is group A *Streptococcus* superinfection of the varicella lesions. It has been the usual infecting organism in reported cases of septic arthritis. In one study, *Streptococcus pyogenes* was reported to cause septic arthritis in chickenpox, especially in cases without bacterial superinfection of the skin.[1]

The most serious complication involves a toxic shock–like syndrome characterized by severe local tissue destruction and life-threatening systemic manifestations.[2] When group A *Streptococcus* infection is associated with fulminant findings, aggressive resuscitation is necessary, along with timely surgical decompression of the foci of infection after a vigilant search









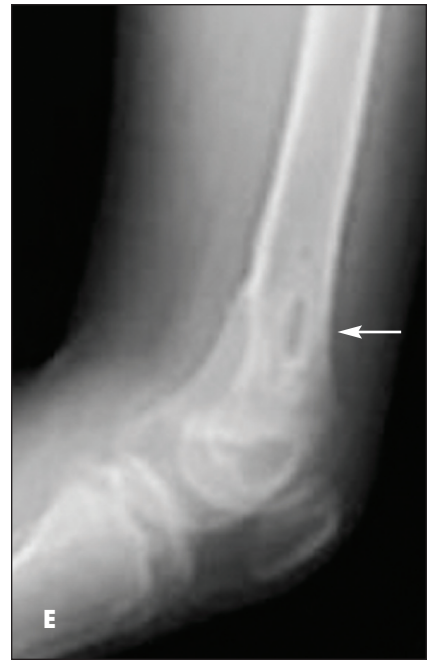


Figure – A 14-year-old boy presented with a painful left thigh and knee and a soft tissue mass on the left anteromedial distal femur. MRI (A, B, and C) revealed multiple fluid collections within the soft tissues surrounding the distal femur. There was abnormal enhancement and signal intensity within the distal femur, predominantly within the metaphysis, consistent with osteomyelitis. Radiographs (D and E) showed lucency with sclerosis and irregularity in the distal femur. There was also periosteal thickening and reaction. Blood cultures taken during biopsy grew methicillin-resistant *Staphylococcus aureus*.

The purulent material (arrows) was drained and the patient underwent multiple procedures involving debridement of soft tissues around the distal femur. Vancomycin-impregnated calcium sulfate pellets were applied in the distal femur during decompression, and the patient received oral antibiotics.

for such sites. *S pyogenes* also may cause osteomyelitis or septic arthritis by hematogenous inoculation.[3]

METHICILLIN-RESISTANT *S AUREUS* (MRSA)

Musculoskeletal infection with MRSA is common in septic arthritis and osteomyelitis. It may be acquired in the nosocomial setting, primarily in premature infants in neonatal ICUs. During the past 6 years, however, MRSA has emerged as a major pathogen in the community in many areas of the United States and around the world.[4,5] Now it is emerging as a cause of skin infections in the sports community.

Transmission of *S aureus*—both antimicrobial-susceptible and resistant strains—usually occurs through close contact with a person who has a draining lesion or who is an asymptomatic carrier of *S aureus*. Factors that may contribute to transmission in athletes include abrasions and other skin trauma, which could facilitate entry of pathogens. Even with less direct contact, protective clothing may be hot and chafe skin, resulting in abrasions and lacerations. The use of shared equipment or other personal items that are not cleaned or laundered between users could be a vehicle for *S aureus* transmission. Previous outbreaks of staphylococcal skin infection have been reported in wrestlers and rugby and football players.

When community-acquired MRSA is suspected (**Figure**), the first-line options include clindamycin, the addition of an aminoglycoside and, rarely, vancomycin.[6] Vancomycin is the first-line agent for MRSA infection secondary to nosocomial infection. Clindamycin may be given as the first-line drug for community-acquired MRSA, particularly in patients who are allergic to or intolerant of β-lactam antibiotics. Although a number of the newer antibiotics (eg, linezolid and quinupristin/dalfopristin) have been shown to be effective against MRSA, these agents should be used only with the advice of an infection specialist.

In most patients, the clinical response determines the total duration of therapy. The number of febrile days and hospital days has increased in children with musculoskeletal infection caused by MRSA.[7]

PRACTICE POINTS

- ❑ *Streptococcus* superinfection of varicella lesions is the most common complication of chickenpox.
- ❑ Factors that may contribute to transmission of methicillin-resistant *Staphylococcus aureus* infection in athletes include abrasions and other skin trauma.
- ❑ *Neisseria meningitidis* is significant as a causal organism in purpura fulminans that produces devastating musculoskeletal consequences.

NEISSERIA MENINGITIDIS IN PURPURA FULMINANS

Although *N meningitidis* usually is not associated with direct infection of musculoskeletal structures, it is significant as a causal organism in purpura fulminans that produces devastating musculoskeletal consequences. This is characterized by the acute onset of progressive dermal vascular thrombosis, disseminated intravascular coagulation, and shock.[8]

Treatment involves initial resuscitation with appropriate antibiotics. A third-generation cephalosporin, such as ceftriaxone, usually is effective.

STREPTOCOCCUS PNEUMONIAE

This organism is more commonly associated with bacteremia, pneumonia, or meningitis, but it has been reported as a causative organism for osteomyelitis and septic arthritis in infants and children. The femur and humerus are the bones most often affected, and the hip and knee are the joints most commonly involved. Immaturity of the child and concomitant immune deficiencies have been reported to increase the risks of *S pneumoniae* infection.[9]

NEISSERIA GONORRHOEAE

Septic arthritis caused by *N gonorrhoeae* is monarticular or pauciarticular. Gonococcal bacteremia is more likely to be associated with polyarthralgias and skin lesions. When gonococcal infection is suspected, cultures should be obtained from joint fluid; the cervix of postpubertal girls; urethral or prostatic discharge of boys; and the vagina, pharynx, and rectum of children in whom sexual abuse is suspected. The diagnosis of *N gonorrhoeae* infection is confirmed by culture that needs to be done under warm conditions with low carbon dioxide levels on Thayer-Martin agar.

Management of gonococcal arthritis initially involves intravenous administration of a third-generation cephalosporin. Then, because of the prevalence of resistant strains, local aspiration and irrigation of the joint are also indicated.

MYCOBACTERIUM TUBERCULOSIS

Tuberculosis infections have been on the rise in the United States, mainly because of an influx of immigrants from high-prevalence countries and marginalized populations.[10] Signs and symptoms of osteomyelitis, dactylitis, or septic arthritis may take

months to years to manifest. More than half of all cases of tubercular osteomyelitis involve the spine, followed in incidence by infections around the hip and knee. Spinal involvement usually occurs in the anterior third of the vertebral body. Paravertebral abscess is almost pathognomonic.

Diagnosis requires a high index of suspicion, skin tests for tuberculosis using purified protein derivative, and identification of the organism in culture material. Often, the white blood cell count is normal but the erythrocyte sedimentation rate is elevated.

Current treatment recommendations involve quadruple-drug therapy (isoniazid, rifampin, pyrazinamide, and streptomycin) for 2 months followed by isoniazid and rifampin for another 10 months. Surgical decompression is rarely needed. Indications for spinal surgery include neurologic involvement, spinal instability, and failure of medical treatment.[11]

BORRELIA BURGDORFERI

Lyme disease is caused by this spirochete; its common vector is the deer tick. Lyme disease often presents as an episodic musculoskeletal synovitis affecting 1 or more joints. It may progress to septic arthritis of the joint.

The serologic tests conducted for diagnosis are the enzyme-linked immunosorbent assay and the immunoblot (Western blot) analysis. These tests should be considered only in patients in whom there is a reasonable clinical suspicion of infection. Initial treatment consists of 10 to 30 days of oral antibiotics (amoxicillin or doxycycline). In cases of neurologic or cardiac manifestations or recurrence after oral therapy, intravenous ceftriaxone may be needed for 14 to 28 days.

A post–Lyme disease syndrome has been described as involving recurrent arthralgias, myalgias, headache, neck pain, and fatigue. Treatment with antibiotics is controversial, and spontaneous resolution within 6 months is common.[12] ■

REFERENCES:
1. Bradley TM, Dormans JP. *Streptococcus pyogenes* septic arthritis of the elbow complicating the chickenpox. *Pediatr Emerg Care.* 1997;13:380-381.
2. Jackson MA, Burry VF, Olson LC. Multisystem group A β-hemolytic streptococcal disease in children. *Rev Infect Dis.* 1991;13:783-788.
3. Perlman MH, Patzakis MJ, Kumar PJ, Holtom P. The incidence of joint involvement with adjacent osteomyelitis in pediatric patients. *J Pediatr Orthop.* 2000;20:40-43.
4. Chambers HF. The changing epidemiology of *Staphylococcus aureus? Emerg Infect Dis.* 2001;7:178-182.
5. Gwynne-Jones DP, Stott NS. Community-acquired methicillin-resistant *Staphylococcus aureus:* a cause of musculoskeletal sepsis in children. *J Pediatr Orthop.* 1999;19:413-416.
6. Steer AC, Carapetis JR. Acute hematogenous osteomyelitis in children: recognition and management. *Paediatr Drugs.* 2004;6:333-346.
7. Martinez-Aguilar G, Avalos-Mishaan A, Hulten K, et al. Community-acquired, methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* musculoskeletal infections in children. *Pediatr Infect Dis J.* 2004;23:701-706.
8. White B, Livingstone W, Murphy C, et al. An open-label study of the role of adjuvant hemostatic support with protein C replacement therapy in purpura fulminans–associated meningococcemia. *Blood.* 2000;96:3719-3724.
9. Bradley JS, Kaplan SL, Tan TQ, et al. Pediatric pneumococcal bone and joint infections. The Pediatric Multicenter Pneumococcal Surveillance Study Group (PMPSSG). *Pediatrics.* 1998;102:1376-1382.
10. Furin J, Johnson J. Recent advances in the diagnosis and management of tuberculosis. *Curr Opin Pulm Med.* 2005;11:189-194.
11. Vohra R, Kang HS, Dogra S, et al. Tuberculous osteomyelitis. *J Bone Joint Surg.* 1997;79B:562-566.
12. Weinstein A, Britchkov M. Lyme arthritis and post–Lyme disease syndrome. *Curr Opin Rheumatol.* 2002;14:383-387.

Therapeutic Agents Mentioned in This Article

Amoxicillin (multiple trade names)
Ceftriaxone (Rocephin)
Clindamycin (multiple trade names)
Doxycycline (multiple trade names)
Isoniazid (INH)
Linezolid (Zyvox)
Pyrazinamide (PZA)
Quinupristin/dalfopristin (Synercid)
Rifampin (Rifadin, Rimactane)
Streptomycin (multiple trade names)
Vancomycin (Vancocin)

An Unusual Case of Ileal-Ileo Intussusception

PAUL TROMBLEY, MD
Española, NM

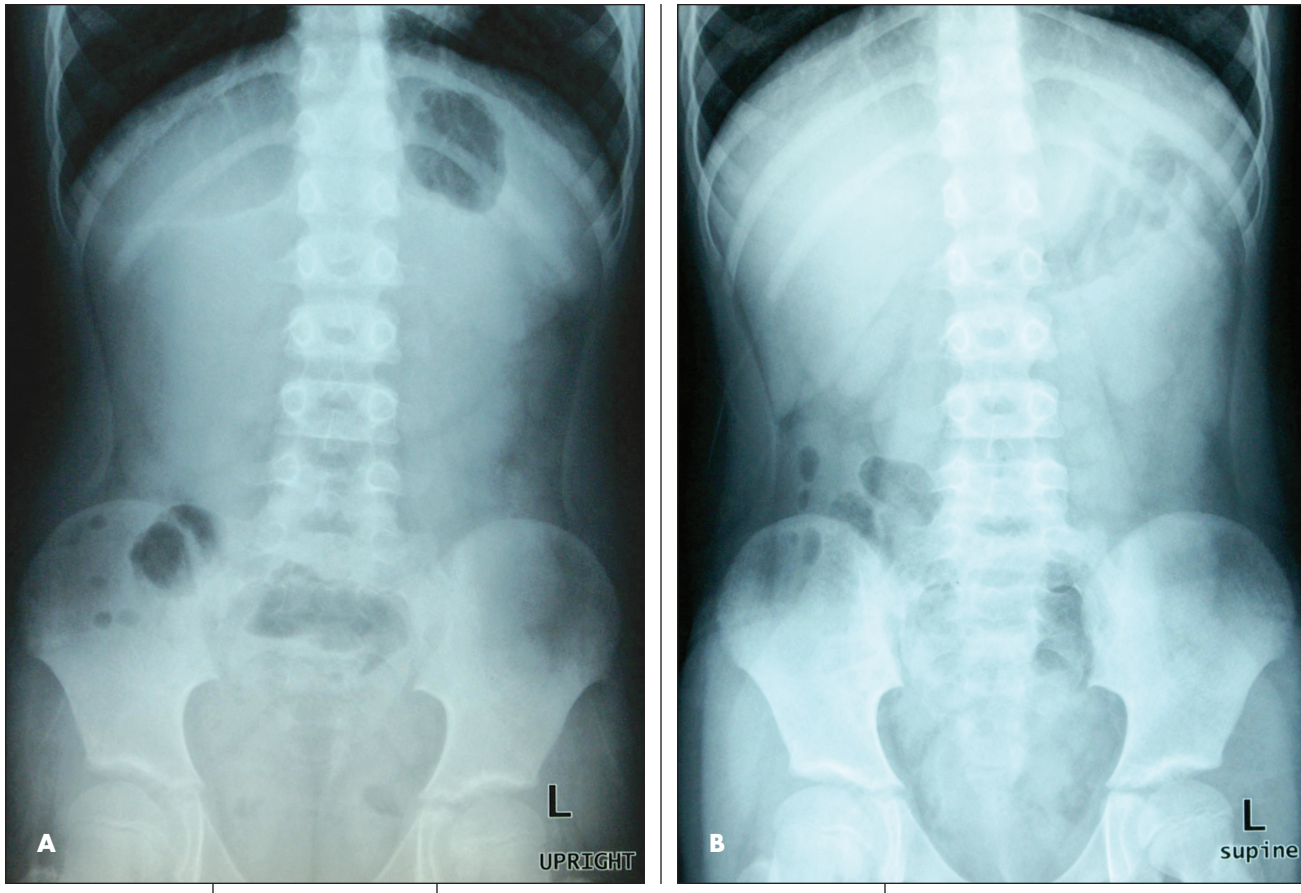


Figure 1 – An upright abdominal film showed no sign of obstruction or pathology (A). Findings were nonspecific on the supine film (B).

An 8-year-old Hispanic child with no significant medical history presented to our pediatric clinic after 2 episodes of vomiting, diarrhea, and abdominal pain. Symptoms had begun earlier the same morning; the child and his parents described the vomitus as "yellowish" and diarrhea "watery." There was no associated fever.

The abdominal pain was "sharp," intermittent, and confined to the left lower quadrant and periumbilical area. It did not radiate and lasted only for a few minutes. Nothing seemed to exacerbate the pain, nor was it relieved with vomiting or diarrhea.

Dr Trombley is a general pediatrician at the Multi-Specialty Clinic of Presbyterian Española Hospital in Española, NM.

The patient's last meal the previous night was a taco. No other family member had eaten the same thing.

The patient denied sore throat, dysphagia, urinary symptoms, and rash. There was no recent travel history. His parents had given him a single dose of Pepto-Bismol before they brought him in for evaluation.

On physical examination, the child was afebrile and his vital signs were stable—except for tachycardia, with a pulse of 137 beats per minute. The child was well-developed and well-nourished. He was in obvious distress—lying on the examination table, clutching his abdomen—but appeared to be nontoxic.

There were no remarkable physical findings other than marked pain

to palpation of the left lower quadrant with guarding. There was equivocal rebound tenderness to the same area. The patient had no significant periumbilical tenderness and no tenderness in other quadrants. He had hyperactive bowel sounds in all 4 quadrants without succussion splash. There were no palpable masses.

The patient had negative psoas and obturator signs and no obvious Murphy sign. Pain was not relieved by sitting forward and upright. He did have some equivocal bilateral costovertebral angle tenderness. There were no purpuric lesions or rashes.

*After the history and physical examination, urinalysis was done and an acute abdominal series was obtained. Urinalysis results were negative, including for ketones. Chest films were normal. Results of the abdominal series were negative; there were no air fluid levels, no free fluid, and no signs of obstruction (**Figure 1**).*

Shortly after the patient returned to the office from the radiology department, a fluid challenge was attempted. Initially he did well, but then he writhed with abdominal pain and vomited a yellowish—almost greenish—vomitus. After this witnessed emesis, the patient was sent directly back to the hospital for laboratory work and a CT scan of the abdomen/pelvis with contrast.

The white blood cell count was elevated (19,500/µL); there was a left shift with 92% segmented neutrophils and 2% band forms. Results of a complete metabolic profile were within normal limits. There was no metabolic gap. Amylase levels were normal at 47 U/L. The C-reactive protein value was also normal at 0.0 mg/dL, as was lipase at 17 U/dL.

*The abdominal CT scan showed the problem: the patient had a significant length of ileal-ileo intussusception (**Figure 2**).*

After the patient returned to the office from the radiology department, an intravenous line was placed and a fluid bolus of normal saline given. This was followed by infusion of dextrose 5% with half normal saline at a 100% maintenance rate. An emergent surgical consult was obtained in the pediatric office. A local surgeon felt that the child would be best served at a tertiary care facility for pediatric surgical services. Subsequently, the child was emergently transferred by air to such a facility for emergent reduction of his ileal-ileo intussusception.

The pediatric radiologists who reviewed his CT scan agreed with the diagnosis of ileal-ileo intussusception. However, during laparotomy, sur-

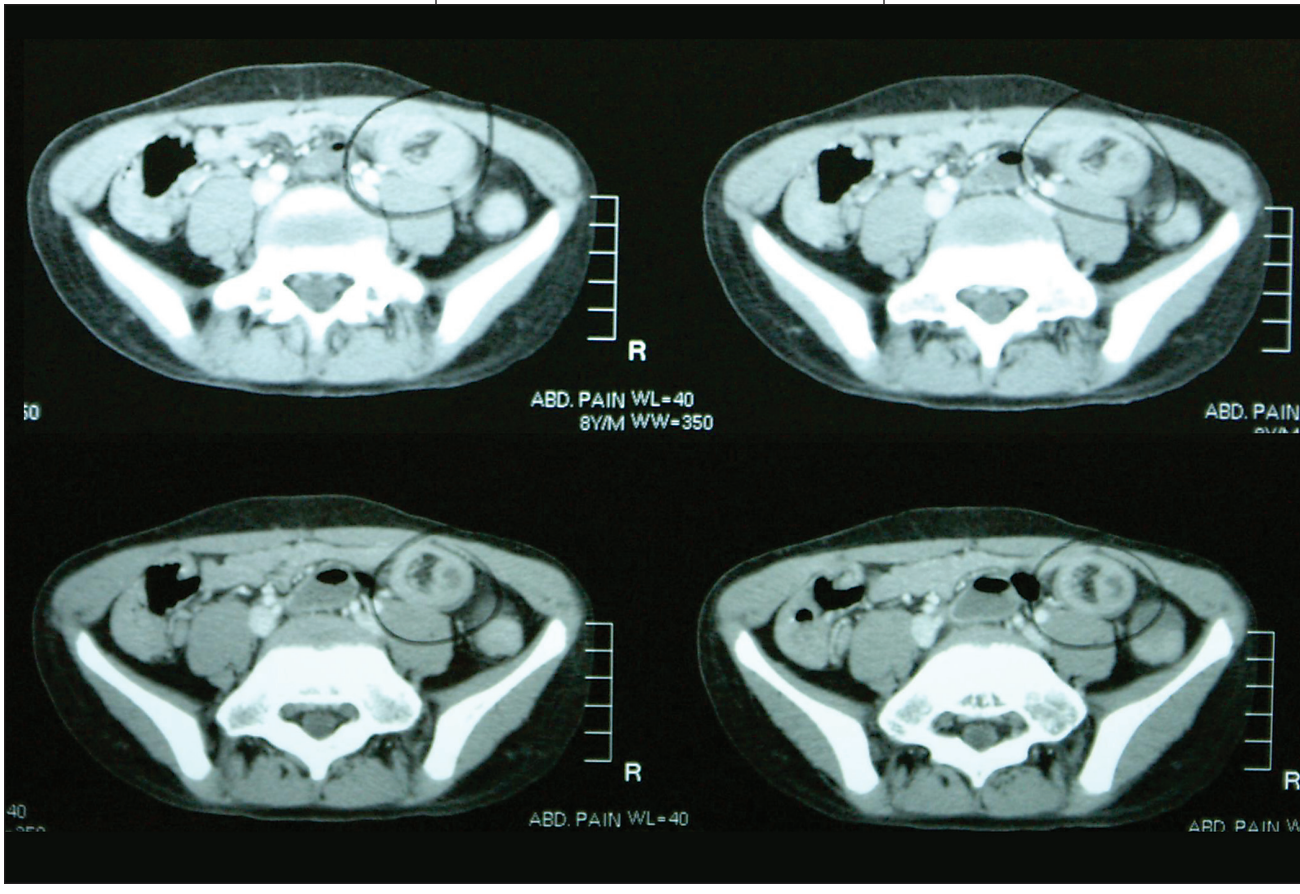


Figure 2 – CT findings demonstrate small-bowel intussusception; the telescoped portion is evident (circle).

geons could not find the intussusceptum. They believed that it may have spontaneously resolved with the barium from the CT scan sometime during transport. Lucky for this child, they also identified no lead point. He was subsequently discharged after 4 days of postoperative care.

INTUSSUSCEPTION

Intussusception is the invagination of a portion of the bowel into itself, which is pulled along further into itself during peristalsis. As the intussusceptum invaginates further, lymphatic flow occurs, followed by venous obstruction. As the intussusceptum obstructs the lumen of the intestine, distention occurs and further peristaltic waves cause colicky, episodic abdominal pain. As the edema from lymphatic and venous obstruction increases, arterial flow is eventually also obstructed, resulting in ischemic bowel and subsequent shedding of mucus into the bowel lumen. Further, venous engorgement promotes leakage of blood through the capillary membranes into the lumen. Together, this forms the classic "currant jelly" stools noted in intussusception. However, though relatively diagnostic, this finding occurs only in a small percentage of cases and is a fairly late sign of already occurring bowel ischemia.

Intussusception is the most common cause of intestinal obstruction in children 3 months to 3 years old. It occurs most frequently between 3 and 18 months: approximately 65% of cases develop before 12 months.[1,2] Although 10% of patients may have had a history of diarrhea—and many have signs and symptoms of an upper respiratory tract infection—no clear cause of intussusception is typically identified. In older children, anatomic abnormality often acts as a lead point. Abnormalities include polyps, Meckel diverticulum, nodular or ectopic pancreas, intestinal lymphoma, cysts, localized edema or hemorrhages (such as with abdominal trauma), Henoch-Schönlein purpura, hemophilia, and leukemia. Postoperative intussusception and intussusception in children with cystic fibrosis are also fairly common.[1]

The "classic" picture is that of a well infant who suddenly appears to have significant abdominal pain and vomiting. After colicky pain, normal stool is typically passed and the infant may appear well again. Vomitus is nonbilious at first but may become bilious as the obstruction progresses, and abdominal distention can be seen. The classic triad of vomiting, colicky abdominal pain, and bloody stool is not universal and may occur in as few as 10% of cases. As the obstruction progresses, the child may appear profoundly lethargic and quite ill.[1,2]

If the intussusceptum extends to the anus, it can sometimes be palpated on rectal examination. About 95% of cases are ileocolic; consequently, a sausage-shaped mass can also typically be palpated in the area of the hepatic flexure. In 3% of cases, the intussusception can prolapse through the rectum. A typical intussusception involves the invagination of the terminal ileum into the cecum and colon, which pulls the ileocecal region distally. As a result, the right lower quadrant may feel empty to palpation: this is known as the Dance sign.[1]

The diagnosis is typically made from the clinical history. Physical findings, including a sausage-shaped mass, bloody stool, or guaiac-positive rectal examination with colicky abdominal pain and vomiting should also raise clinical suspicion of this process. Plain films of the abdomen may reveal obstruction, a soft tissue density outlined by an air-filled colon (a so-called crescent sign on plain films), or no abnormality.[2]

Sonograms may also identify an intussusception if patients are too ill for diagnostic and possibly therapeutic enema. The gold standard for diagnosis is the contrast enema, which may also reduce the intussusception during the procedure. A failed reduction with contrast enema demands immediate surgical reduction. Reduction with air or radiocontrast enema is successful in up to 80% of cases; however, nearly 25% of patients require surgical resection of nonviable intestine on diagnosis.

The recurrence rate after either enema or surgical reduction is approximately 5%.[1] A small-bowel intussusception typically is diagnosed with an upper GI series with a small-bowel follow-through series. Surgical reduction is usually required.[2]

A delay in diagnosis and therapy can lead to infarction of the affected bowel, peritonitis, perforation, and (if untreated) death within 2 to 5 days.[1] ■

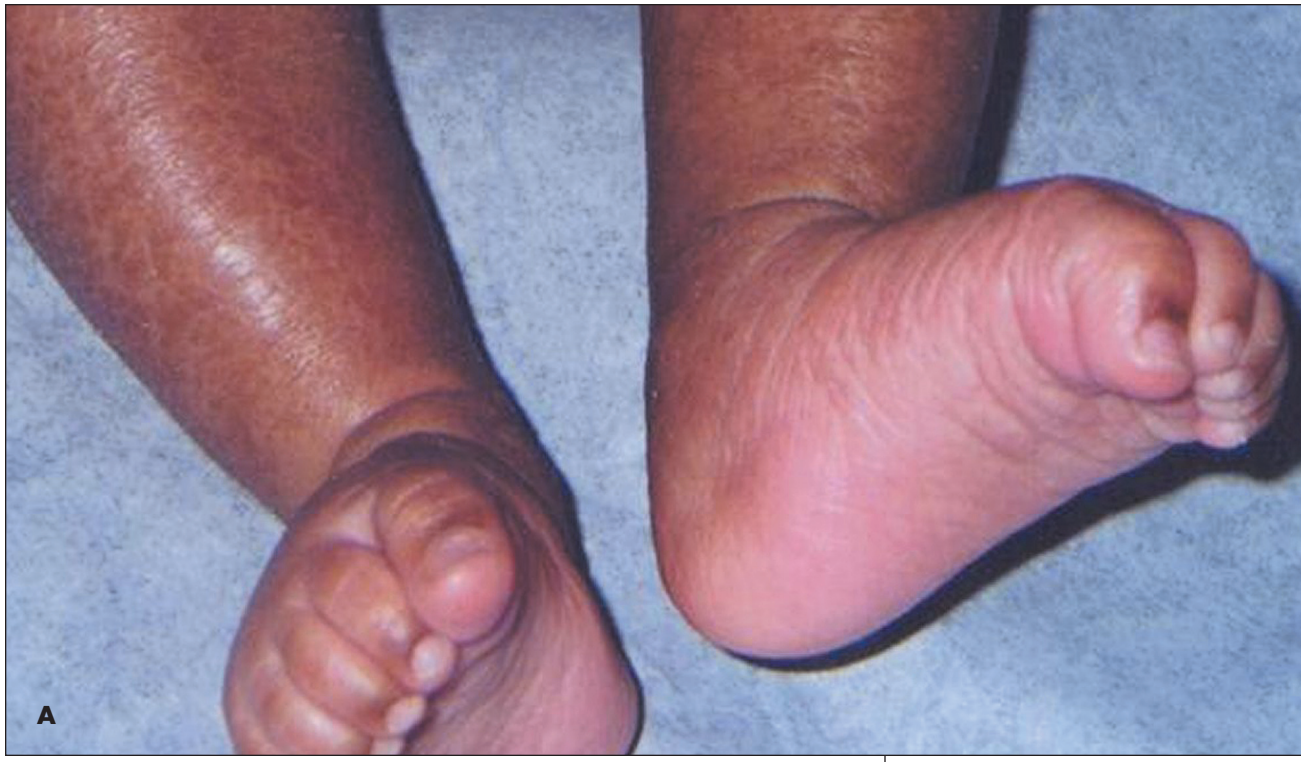
REFERENCES:
1. Brandt ML. Intussusception. In: McMillan JA, Oski FA, eds. *Oski's Pediatrics: Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999:1652-1654.
2. Zitelli BJ, Davis HW, eds. *Atlas of Pediatric Physical Diagnosis.* 3rd ed. St Louis: CV Mosby; 1997:497-498.

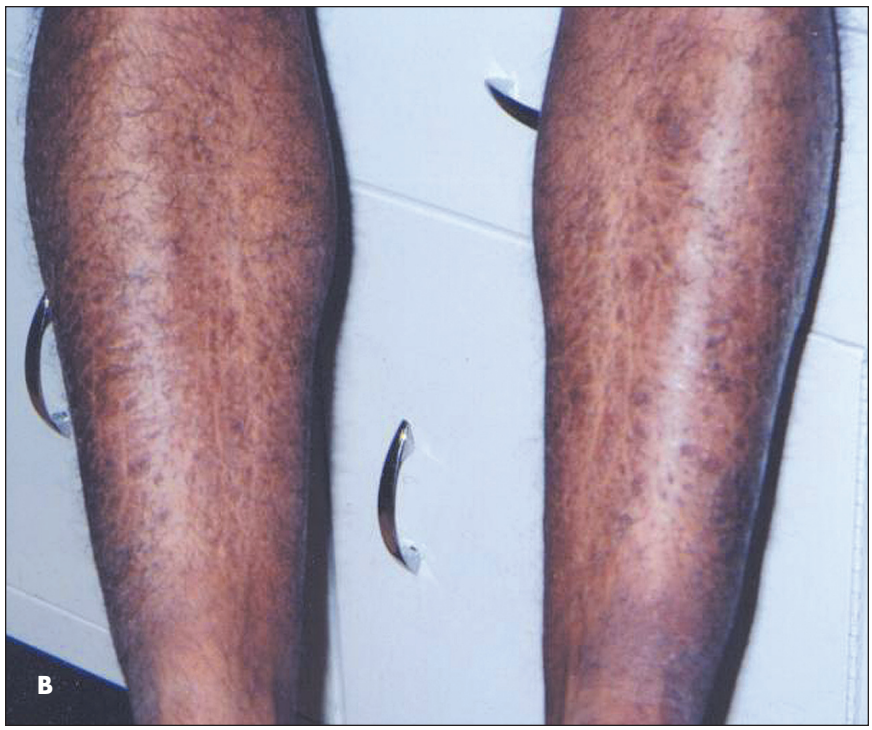
Consultant

WHAT'S YOUR DIAGNOSIS?®

By ALEXANDER K. C. LEUNG, MD—Series Editor,
and WM. LANE M. ROBSON, MD

Dr Leung is clinical associate professor of pediatrics at the University of Calgary, and pediatric consultant at the Alberta Children's Hospital. Dr Robson is the Medical Director of The Childrens' Clinic in Calgary, Alberta.





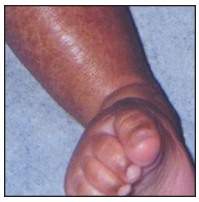
HISTORY

Seven-month-old boy with hyperpigmented lesions on his legs (**A**). Lesions first noted at 4 months of age. His 32-year-old father (**B**) and 58-year-old grandfather had similar lesions on their legs.

PHYSICAL EXAMINATION

Brown, polygonal scales present on both shins. No other notable findings. Palms and soles normal. Both testicles in scrotum. No corneal opacity or atopic dermatitis.

WHAT'S YOUR DIAGNOSIS?

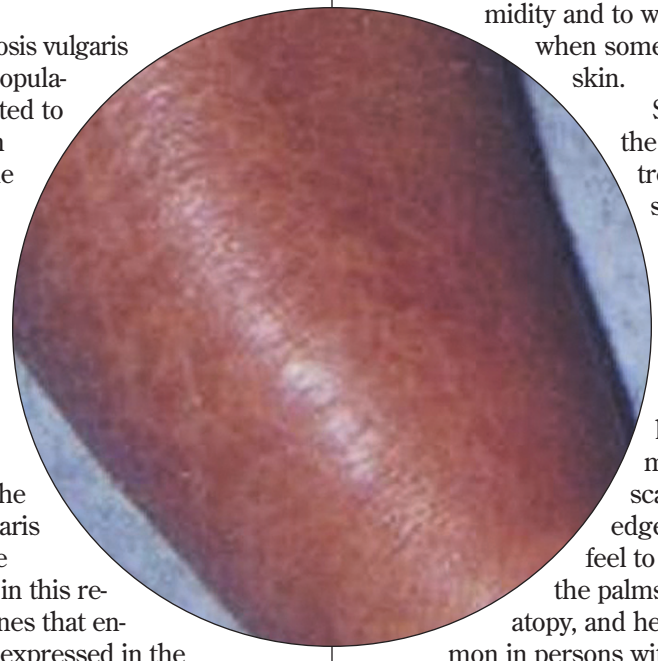


ANSWER:
ICHTHYOSIS VULGARIS

The term ichthyosis is derived from the Greek word *ichthys,* which means fish, and was chosen because the lesions have the appearance of fish scales. Ichthyosis is a disorder of cornification characterized by the development of dry, rectangular or polygonal scales. Ichthyosis is caused by altered profilaggrin expression, which leads to scaling and desquamation. Over 95% of those with the problem have ichthyosis vulgaris—the mildest form.[1] Synonyms for ichthyosis vulgaris include ichthyosis simplex and autosomal dominant ichthyosis.

EPIDEMIOLOGY

The prevalence of ichthyosis vulgaris varies by race; in the white population the prevalence is estimated to be about 0.3% to 0.4%,[2] and in the East Asian population, the prevalence is approximately 2.3%.[3] Both sexes are affected equally.



GENETICS

Ichthyosis vulgaris is transmitted as an autosomal dominant trait with variable phenotypic expression between and within families.[1] The gene locus of ichthyosis vulgaris might reside on chromosome 1q22.[2] The profilaggrin gene in this region is part of a cluster of genes that encodes for structural proteins expressed in the terminally differentiating epidermis.

PATHOGENESIS

Profilaggrin is synthesized in the granular layer of the epidermis. Profilaggrin is stored in keratohyaline granules in a highly phosphorylated form[4] and undergoes various post-translational modifications to become filaggrin, a filament-aggregating protein.[1] Filaggrin is proteolyzed and metabolized into free amino acids that might play a critical role as water-binding compounds in the upper stratum corneum. Profilaggrin, filaggrin, and keratohyaline granules are decreased or absent in the epidermis of persons with ichthyosis.[4,5] The primary genetic defect might be a factor that reduces profilaggrin and filaggrin synthesis.[6]

CLINICAL MANIFESTATIONS

The lesions are not usually present at birth but appear in most patients during the first year of life and in the vast majority by age 5 years. The scaling is symmetric and usually intensifies until puberty and subsequently decreases with age. The color of the fine, fish-like scales varies from white to dirty gray to brown.[1] In general, darker scales are seen in dark-skinned persons.[1] The lesions can vary from barely visible roughness and dryness to strong, horny plates. The lesions tend to improve during the summer and with increasing humidity and to worsen during the winter,[7] when some patients report "lizard-like" skin.

Scaling is most prominent on the extensor aspects of the extremities, particularly the shins. The back is involved more often than the abdomen. The diaper and flexural areas, such as the axillae and antecubital and popliteal fossae are spared, perhaps because of the higher temperature and humidity in these areas. The scales often curl up at the edges, which imparts a rough feel to the skin. Hyperlinearity of the palms and soles, keratosis pilaris, atopy, and heat intolerance are more common in persons with ichthyosis vulgaris.[8,9] Secondary infections can develop in fissures of the hands and feet.

HISTOPATHOLOGY

An attenuated or reduced granular layer, a decreased rete-papillae pattern, and a reduced number of sebaceous glands are characteristic histologic findings.[1,7] Ultrastructural studies reveal reduced or absent keratohyaline granules.[1,7] These granules have a crumbly or spongy appearance, which reflect defective keratohyaline synthesis.[1]

DIFFERENTIAL DIAGNOSIS

Ichthyosis vulgaris should be distinguished from X-linked recessive ichthyosis, lamellar ichthyosis, non-

bullous congenital ichthyosiform erythroderma, and bullous congenital ichthyosiform erythroderma (epidermolytic hyperkeratosis).

In X-linked recessive ichthyosis, the scales tend to be larger and darker. Sites of predilection include the extremities, preauricular area, neck, and trunk.[10] The palms, soles, and face are characteristically spared. Affected persons might have undescended testes and corneal opacities. Female carriers may present with a fine, silver-light scaling on the legs.[11] In contrast to ichthyosis vulgaris, the lesions in X-linked recessive ichthyosis do not significantly diminish with age.

Lamellar ichthyosis—an autosomal recessive disorder—usually presents at birth with a parchment-like collodion membrane (hence the term collodion baby), which desquamates over the next 10 to 14 days.[12] Over time, large, dark brown, plate-like scales develop; these are centrally adherent with raised edges, and resemble a suit of armor. Tautness of the facial skin might result in eversion of the eyelids (ectropion) and lips (eclabium). Unlike ichthyosis vulgaris, flexural areas are involved in lamellar ichthyosis and the palms and soles are almost always affected.

Nonbullous congenital ichthyosiform erythroderma, an autosomal recessive disorder, also presents at birth with a collodion membrane. After shedding of the membrane, pronounced erythroderma and fine white scales distinguish this condition from other forms of ichthyosis.

Bullous congenital ichthyosiform erythroderma, an autosomal dominant disorder, usually presents at birth with erosions, large areas of denuded skin, and erythroderma. Over time, blistering and erythroderma diminish and hyperkeratosis develops. Thick brown scales cover most of the skin surface, especially in the flexural areas. ■

Management

Hydration of the skin and prevention of evaporation are important. Bathing once or twice daily in warm water for approximately 5 to 10 minutes helps to hydrate the skin. Afterward, the body should be gently patted dry to minimize trauma to the affected areas. A moisturizing cream or ointment should be immediately applied to minimize evaporation and to keep the skin soft and flexible. Frequent application of a moisturizing agent throughout the day helps to maintain a high level of hydration of the stratum corneum. Preparations that contain urea and alpha-hydroxy acids, such as lactic acid or pyruvic acid, are particularly effective hydration agents.[8]

REFERENCES:

1. Okulicz JF, Schwartz RA. Hereditary and acquired ichthyosis vulgaris. *Int J Dermatol.* 2003;42:95-98.
2. Zhong W, Cui B, Zhang Y, et al. Linkage analysis suggests a locus of ichthyosis vulgaris on 1q22. *J Hum Genet.* 2003;48:390-392.
3. Lei G, Zhang Y, Hu Y. Investigation on the prevalence of ichthyosis in Sichuan Province. *Chin J Dermatol.* 1992;25:105-106.
4. Fleckman P, Brumbaugh S. Absence of the granular layer and keratohyalin define a morphologically distinct subset of individuals with ichthyosis vulgaris. *Exp Dermatol.* 2002;11:327-336.
5. Sybert VP, Dale BA, Holbrook KA. Ichthyosis vulgaris: identification of a defect in synthesis of filaggrin correlated with an absence of keratohyaline granules. *J Invest Dermatol.* 1985;84:191-194.
6. Nirunsuksiri W, Zhang SH, Fleckman P. Reduced stability and bi-alleic, coequal expression of profilaggrin mRNA in keratocytes cultured from subjects with ichthyosis vulgaris. *J Invest Dermatol.* 1998;100:854-861.
7. Richard G, Moss C, Traupe H, et al. Ichthyosis and disorders of cornification. In: Schachner LA, Hansen RC, Happle R, et al, eds. *Pediatric Dermatology.* Philadelphia: Mosby; 2003:385-445.
8. Leung AK, Kao CP. Keratosis pilaris. *Consultant For Pediatricians.* 2004;3:188-191.
9. Richard G, Ringpfeil F. Ichthyosis, erythrokeratomas and related disorders. In: Bolognia J, Jorizzo JL, Rapini RP, eds. *Dermatology.* Philadelphia: Mosby; 2003:775-808.
10. Okano M, Kitano Y, Yoshikawa K, et al. X-linked ichthyosis and ichthyosis vulgaris: comparison of their clinical features based on biochemical analysis. *Br J Dermatol.* 1988;119:777-783.
11. Voss M. Clinical picture of X chromosome recessive ichthyosis. *Dermatol Monatsschr.* 1985;171:25-37.
12. Leung AK. Collodion baby. *Consultant For Pediatricians.* 2004;3:233.

Case In Point

An Intriguing Diagnosis

Spontaneous Pneumothorax in a Teenage Boy

CURT STANKOVIC, MD
PRASHANT MAHAJAN, MD, MPH, MBA
Wayne State University

A 17-year-old Asian male with no significant medical history presented to the emergency department (ED) with acute shortness of breath and associated left-sided chest pain. Symptoms began while the patient was at rest: the pain was sharp and worsened with inspiration. He denied a history of fever, trauma, cough, or any other constitutional complaints.

*In the ED, the patient's temperature was 37.8°C (100°F); heart rate was 100 beats per minute; respiratory rate, 28 breaths per minute; and blood pressure, 124/96 mm Hg. Oxygen saturation was 100% on room air. He had no nasal flaring but used accessory respiratory muscles. The trachea was in midline. Breath sounds were markedly diminished on the left side, with good air entry on the right. No crepitus, wheezing, stridor, or crackles were appreciated. Cardiac examination revealed a normal S_1 and S_2, without any murmurs, rubs, or gallops. Mediastinal shift could not be detected clinically. Chest films showed a left-sided tension pneumothorax (**Figure 1**).*

*A chest tube was placed, and symptoms resolved (**Figure 2**). The patient underwent surgery to resect an apical pleural bleb.*

SPONTANEOUS PNEUMOTHORAX

A spontaneous pneumothorax (SP) is a collection of air or gas be-

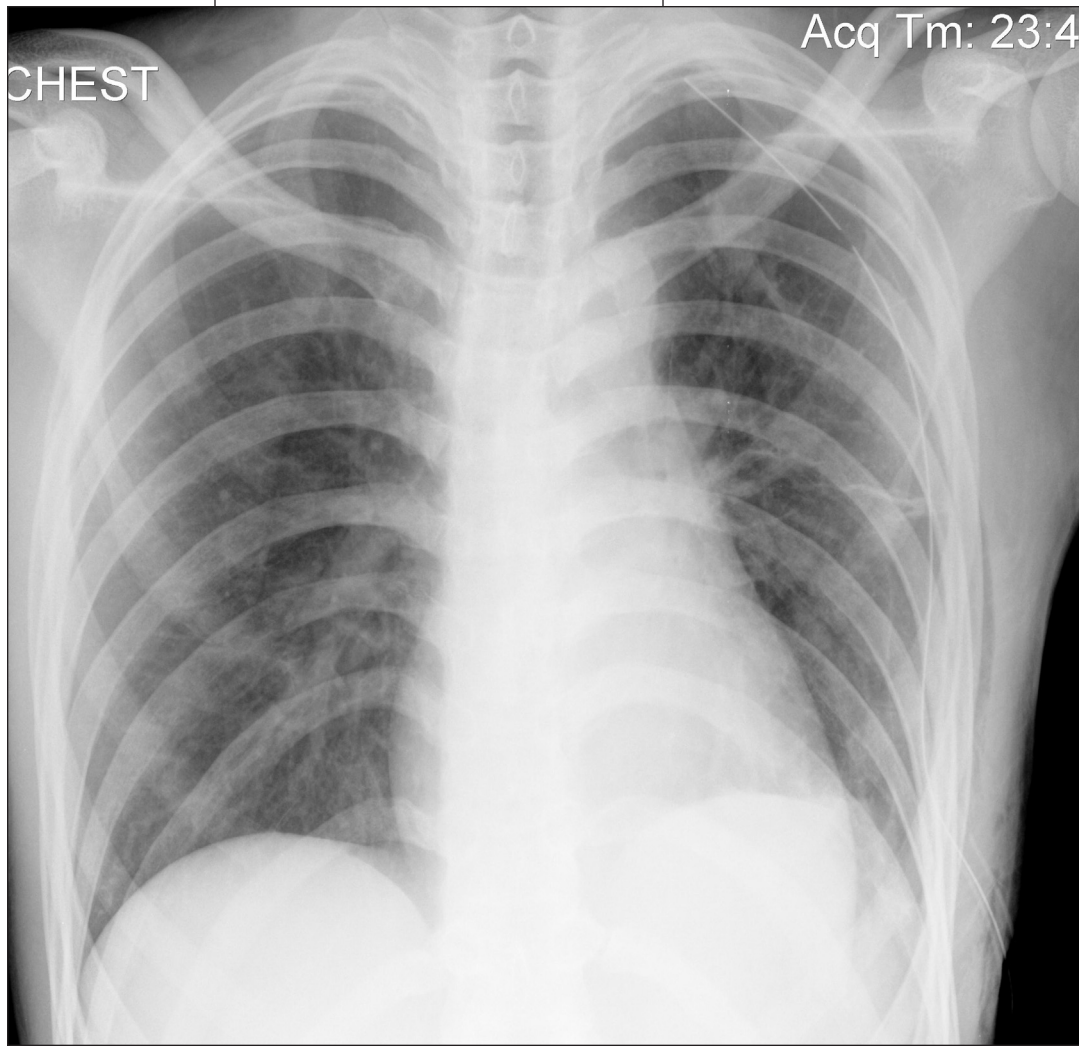


Figure 1 – This chest film shows a left-sided pneumothorax. Mediastinal structures have shifted to the right.

Dr Stankovic is a pediatric emergency medicine fellow at the Carman and Ann Adams Department of Pediatrics, Children's Hospital of Michigan in Detroit. Dr Mahajan is associate professor of pediatrics and emergency medicine at Wayne State University; he is also research director in pediatric emergency medicine at the Carman and Ann Adams Department of Pediatrics at Children's Hospital.

tween the visceral and parietal pleura that causes the lung to collapse in the absence of a traumatic injury to the chest or lung. Primary spontaneous pneumothorax (PSP) occurs in persons with no previously known lung disease. Typically, the cause of this type of pneumothorax is the rupture of a subpleural bleb or cyst in the lung.

A secondary spontaneous pneumothorax (SSP) occurs in persons with known lung disease—most often chronic obstructive pulmonary disease in adults. In pediatric patients, cystic fibrosis, pneumonia, and asthma are the most common causes of SSP. Other conditions less commonly associated with SSP are tuberculosis, cystic adenomatoid malformation, Marfan syndrome, and certain types of interstitial lung disease.

SSP is generally more severe than PSP—and is often life threatening. Mortality associated with SSP is about 15%.[1]

Smoking greatly increases the risk of SP.[2] Men who smoke a pack a day or less have a 20-fold increased risk of SP; in women, the risk rises by 10-fold. In men who smoke more than a pack per day, the risk of SP increases more than 80-fold; in women, the risk increases more than 40-fold.

SP also can be an inherited disorder, although this is not common. One literature review described 61 cases of familial SP in 22 families.[3]

SYMPTOMS

The major symptom is sudden-onset chest pain with breathlessness. This pain may be dull, sharp, or stabbing; it typically begins suddenly while the patient is at rest. Pain can be associated with dyspnea, tachypnea, and hypoxia; typically, it is exacerbated by breathing deeply or by coughing.

Patients with SSP may also experience dyspnea disproportional to the size of the pneumothorax as well as tachycardia, hypotension, and cyanosis.

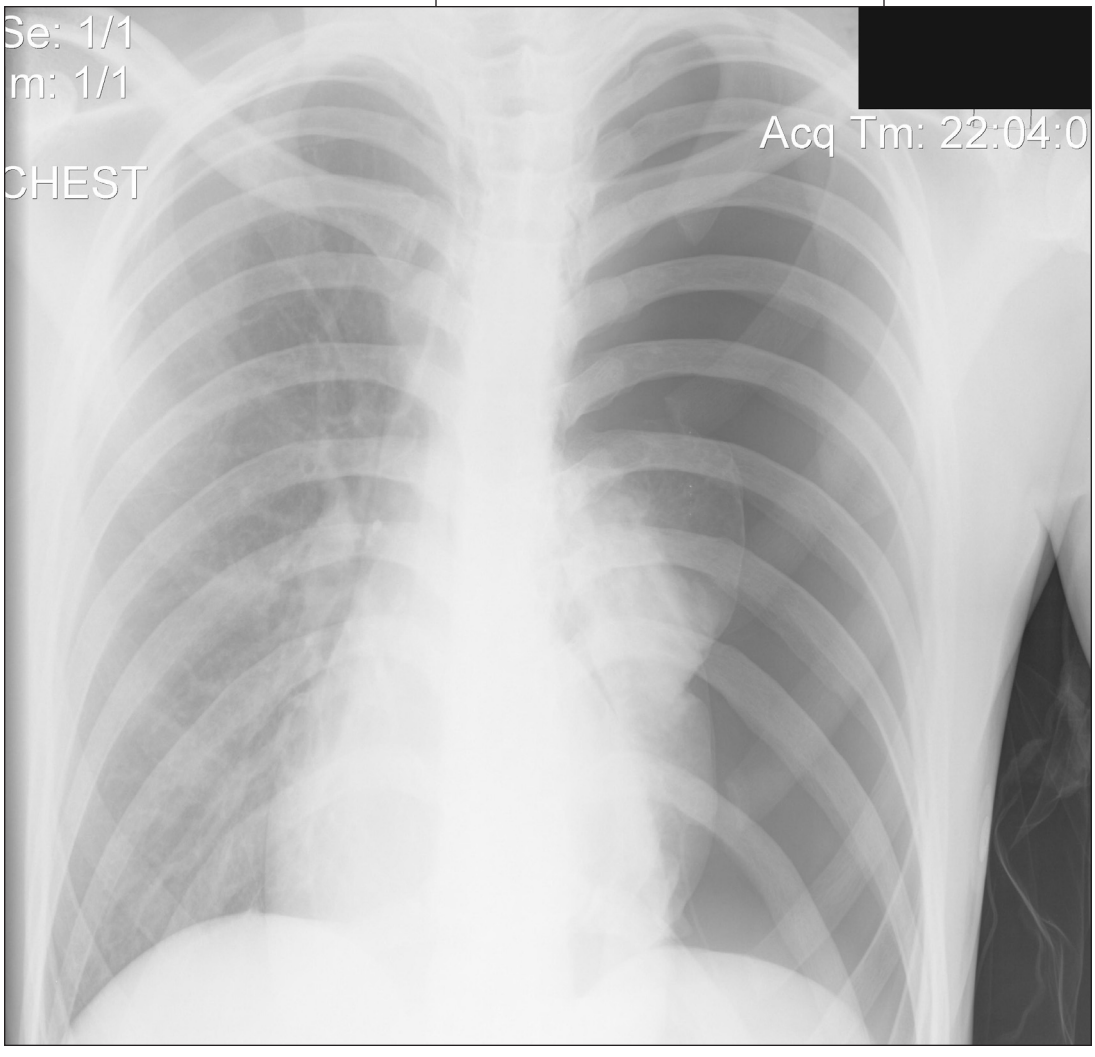


Figure 2 – Chest tube placement relieved the pneumothorax. There is marked improvement in left lung volume. The chest tube is correctly positioned.

DIAGNOSIS AND MANAGEMENT

The diagnosis usually can be made after a detailed history and physical examination. Chest radiographs can confirm the diagnosis and determine the size of the pneumothorax. A recent randomized controlled trial found no advantage for inspiratory/expiratory films.[4]

The objectives of management are to eliminate the intrapleural air collection, to facilitate pleural healing, and to prevent recurrence. The treatment of SP is multifactorial and depends on its size, course, and classification. A small pneumothorax may resolve spontaneously. Needle decompression or chest tube placement may be needed to facilitate reexpansion when air accumulation is relatively large. Strongly consider therapeutic interventions for patients with recurrent pneumothorax.

While the treatment options for PSP and SSP are the same, the conditions are managed differently. In asymptomatic patients with PSP who have less than 15% air accumulation, simple observation and administration of 100% oxygen have been successfully used as a treatment option.[1] Oxygen increases the resorption rate of the pneumothorax 3-fold to 4-fold; the greatest increases occur in patients with larger pneumothoraces. The application of oxygen creates a gas pressure gradient between the pleural space and the tissue capillaries that surround the pleural space. This enhances the absorption of nitrogen and other gases within this space.[5]

If the pneumothorax is smaller than 15% and if the patient is symptomatic but hemodynamically stable, needle aspiration is considered the treatment of choice. Advantages include its relative simplicity and lack of invasiveness.[6]

SSP, on the other hand, can be life-threatening. Most patients are treated with a chest tube. Tube thoracostomy has been advocated for patients with PSP in whom simple aspiration fails—and for most patients with SSP.[1,6] Other more invasive management options include pleural sclerosis (pleurodesis) and video-assisted thoracic surgery (VATS).

RECURRENCE

Recurrence rates can be high, espeically if SP is untreated. Recurrence rates as high as 30% at 6 months and 50% at 2 years have been reported.[1] More specifically, recurrence rates have been reported at 28% for PSP and 53% for SSP.[1] There is a 15% rate of recurrence on the contralateral side in patients with PSP. Recurrence is more likely in patients who are tall and thin and who smoke; however, there is no relationship with the number or size of apical blebs on CT. Once a recurrence has occurred, the risk for repeated pneumothoraces exceeds 50%.[7]

Chest tube insertion helps relieve the pneumothorax and improve symptoms. However, it does not reduce the risk of recurrence as significantly as VATS or pleurodesis. One randomized trial compared simple needle aspiration with tube thoracostomy in the management of first-time PSP.[8] Recurrence rates were measured at 1 week (11% vs 12%), at 3 months (15% vs 8%), at 1 year (22% vs 42%), and at 2 years (31% vs 25%). There were no statistically significant differences between the 2 treatment modalities.

LONG-TERM CARE

Patients who have had SP need to stop smoking and to avoid high altitudes, scuba diving, or flying in an unpressurized aircraft in attempt to limit the risk of a recurrent pneumothorax.

TAKE-HOME MESSAGE

Cardiac causes of pediatric chest pain are uncommon. If the pain is associated with shortness of breath, especially in a thin adolescent who smokes, consider spontaneous pneumothorax (SP). When SP is diagnosed, it is important to differentiate between a primary and secondary cause because management differs. ■

REFERENCES:
1. Light RW. Pneumothorax. In: Murray JF, Nadel JA, eds. *Textbook of Respiratory Medicine.* Philadelphia: WB Saunders; 1994:2193-2210.
2. Melton LJ 3rd, Hepper NG, Offord KP. Incidence of spontaneous pneumothorax in Olmsted County, Minnesota: 1950-1974. *Am Rev Respir Dis.* 1979;20: 1379-1382.
3. Wilson WG, Aylsworth AS. Familial spontaneous pneumothorax. *Pediatrics.* 1979,64:172-175.
4. Seow A, Kazerooni EA, Pernicano PG, Neary M. Comparison of upright inspiratory and expiratory chest radiographs for detecting pneumothoraces. *AJR.* 1996;166:313-316.
5. Chada TS, Cohn MA. Noninvasive treatment of pneumothorax with oxygen inhalation. *Respiration.* 1983;44:147-152.
6. Light RW. Spontaneous Pneumothorax. In: *Pleural Diseases.* 3rd ed. Baltimore: Williams & Wilkins; 1995;24.
7. Mason RJ. Pneumothorax, chylothorax, hemothorax, and fibrothorax. In: *Murray and Nadel's Textbook of Respiratory Medicine.* 3rd ed. Philadelphia: Elsevier; 2005:1964.
8. Ayed AK, Chandrasekaran C, Sukumar M. Aspiration versus tube drainage in primary spontaneous pneumothorax: a randomized study. *Eur Respir J.* 2006;27:477-482.

Musculoskeletal Clinics

What Next For This Patient?

16-Year-Old Camper With Tibial Pain

EDWARD J. SHAHADY, MD
University of Miami

WILLIS PAULL, PhD
Florida Atlantic University

ANJAN PATEL
Florida State University College of Medicine

PATIENT PROFILE:

A 16-year-old boy complains of right lower leg pain that began 2 weeks earlier, after his first week at a summer basketball conditioning camp. Before he left for the camp, he was jogging off and on, averaging a few miles a week. At camp he began running 7 miles a day and doing sprints 3 times a week.

The leg pain initially began at the end of a run and quickly disappeared. It now is present as soon as he starts his run, and after 15 to 20 minutes it is so intense that he cannot continue. The pain persists for 1 to 2 hours after a run. It is located on the posteromedial aspect of the right tibia, covering an area that starts about 1 inch above the medial malleolus and extends upward about 4 inches (**Figure 1**). He does not note any numbness or dragging of his right foot. He is in good health and has never had a similar problem.

Physical examination reveals no gross difference in appearance between the 2 lower extremities. The patient pronates when he walks. Both plantar flexion against resistance and standing on tiptoes reproduce the pain in his right leg. The result of a tuning fork test is negative, and he exhibits no pinpoint tenderness. He has no neurologic or vascular deficit. His shoes are 2 years old and were used by his brother for a full season. They provide minimal support medially, and the soles are significantly worn.

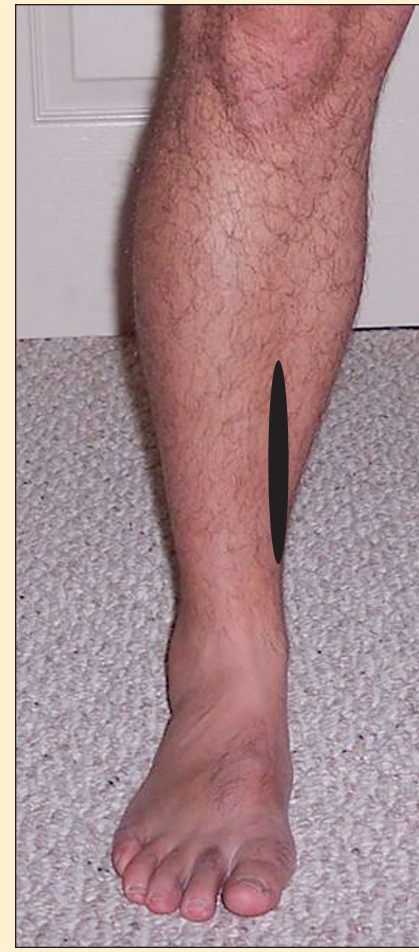


Figure 1 – The pain of medial tibial stress syndrome is located over the posteromedial tibia beginning just above the medial malleolus and extending superiorly for 3 to 5 inches.

WHICH DIAGNOSIS IS MOST LIKELY?

A. Tibial stress fracture.

B. Compartment syndrome.

C. Posterior tibial tendonitis.

D. Medial tibial stress syndrome (MTSS).

Dr Shahady is clinical professor of family medicine at the University of Miami in Florida, an associate faculty member in the Tallahassee Memorial Hospital Family Practice Residency Program, and medical director of the Diabetes Master Clinician Program of the Florida Academy of Family Physicians Foundation in Jacksonville. Dr Paull is professor of biomedical science at Florida Atlantic University in Boca Raton. Anjan Patel is a third-year medical student at Florida State University College of Medicine in Tallahassee.

16-Year-Old Camper With Tibial Pain

THE CONSULTANT'S CHOICE

Given the patient's age, the lack of acute trauma, the gradual onset of symptoms, and the recent initiation of intense physical activity, this is most likely an overuse injury. All 4 choices represent overuse injuries that can occur in runners.

The location of the pain and the lack of symptoms of neurologic or vascular compromise (such as numbness or footdrop) make compartment syndrome (B) less likely. Compartment syndrome associated with running is usually located in the anterior or lateral portion of the leg (**Figure 2**).

Posterior tibial tendinitis or tendinopathy (C) follows the path of the posterior tibial tendon, posterior to the medial malleolus. The pain associated with this injury is usually located behind the medial malleolus (**Figure 3**) and is typically accompanied by swelling. The lack of swelling and of pain in the location of the medial malleolus makes this diagnosis unlikely.

The location of the pain over the area of the posterior medial tibia is characteristic of both stress fractures (A) and MTSS (**D**). Although stress fractures are usually located in the medial posterior region of the tibia, the area of pain is typically much smaller than that seen in this patient.

The tuning fork test can help rule out a stress fracture. With the fork vibrating, place the blunt end superior to the area of pain. Feeling increased pain in the area previously described as painful is considered a positive result. However, this test is of more diagnostic

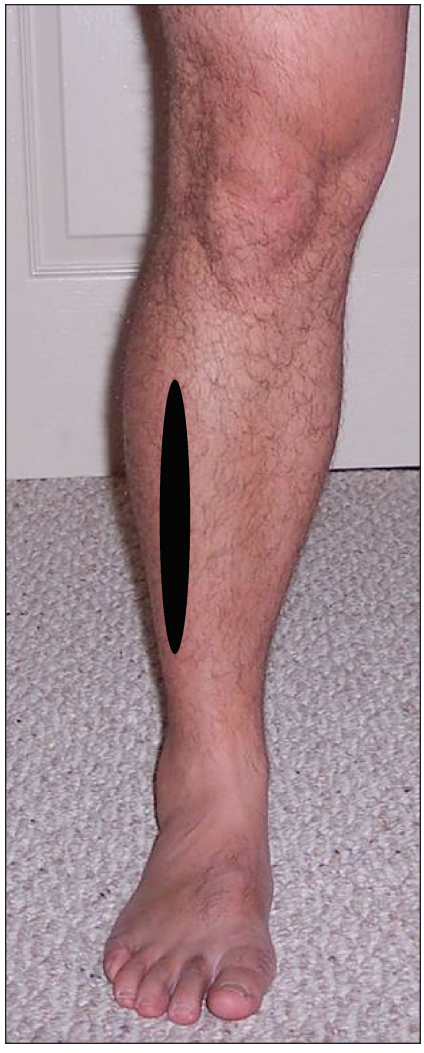


Figure 2 – The pain of compartment syndrome associated with running is usually located in the anterior or lateral portion of the leg.

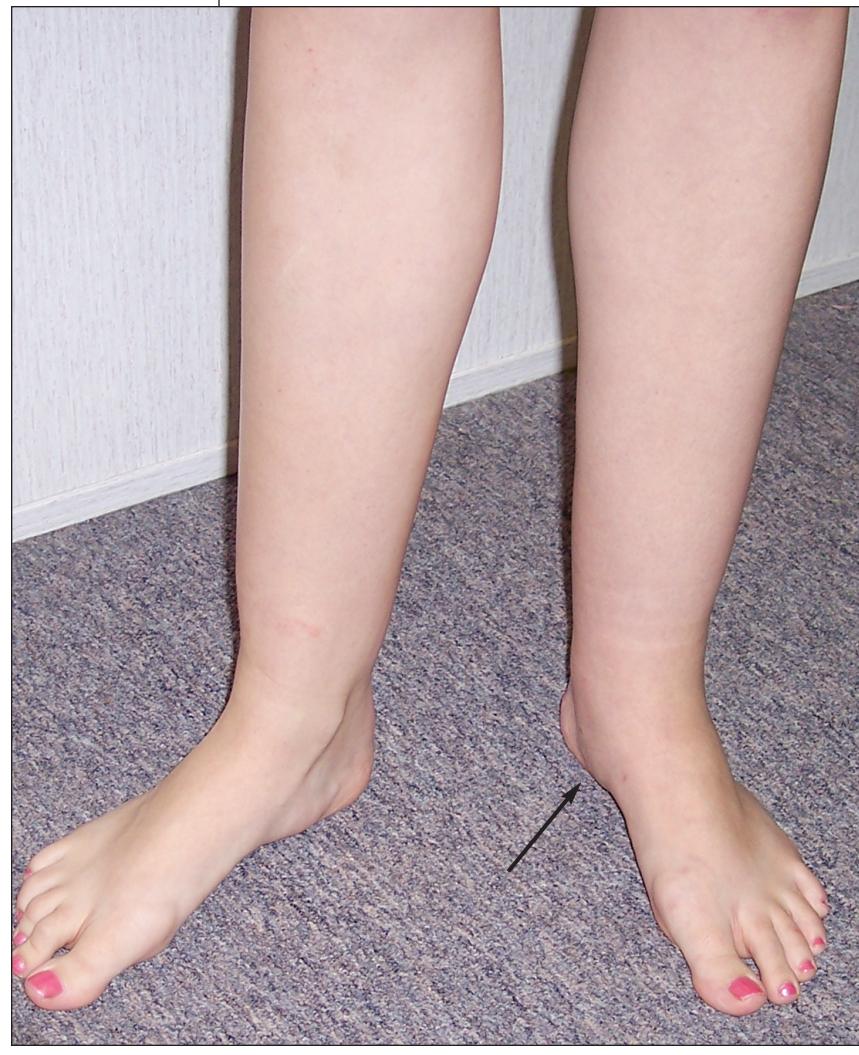


Figure 3 – The pain of posterior tibial tendinitis is usually located behind the medial malleolus (arrow). It is usually accompanied by swelling of the medial malleolus, as can be seen in this patient, who has posterior tibial tendinitis in her left leg.

value when the result is negative (ie, when there is no increase in perceived pain). The negative result on a tuning fork test and the lack of pinpoint tenderness both make a stress fracture unlikely here.

Pronation—which this patient exhibits—predisposes the posterior musculature of the lower leg to pull excessively on the tibia. This pull or stretch causes a periosteal reaction on the tibia at its posterior medial border. Because this boy's shoes provide minimal medial support, they aggravate the medial tibial stress. These clues, in conjunction with the location of the pain, point to **MTSS** (also called "shin splint syndrome").

WHICH STUDY WOULD YOU ORDER NOW?

A. Plain radiograph.

B. MRI scan.

C. Measurement of compartment pressures.

D. No further testing.

THE CONSULTANT'S CHOICE

Compartment pressures (C) are not indicated because compartment syndrome seems unlikely. An MRI scan (B) is overkill at this point: it is not indicated and thus would add considerable unnecessary expense. Many clinicians would order a plain radiograph as a precaution, to check for stress fracture; however, this, too, is an additional expense. If the patient does not respond to treatment, a radiograph would then be indicated. At this time, however, no further testing is recommended.

Pathophysiology of MTSS. This overuse syndrome is caused by a mismatch between overload and recovery. Repetitive overload on tissues that are not able to adapt to new or increased demands leads to tissue breakdown. Specifically, MTSS results from traction of the posterior tibial, flexor digitorum longus, and soleus muscles on the periosteum of the tibia (**Figure 4**). The traction produces an overload stress, which leads to an inflammatory response in the tibial periosteum (periostitis).

Clinical findings. The pain of MTSS is located over the posteromedial tibia beginning just above the medial malleolus and extending superiorly for 3 to 5 inches (see **Figure 1**). It is activity-related, and chronic neurologic symptoms, such as numbness and footdrop, are usually absent. Diffuse pain and tenderness along the posteromedial border of the tibia that are aggravated by

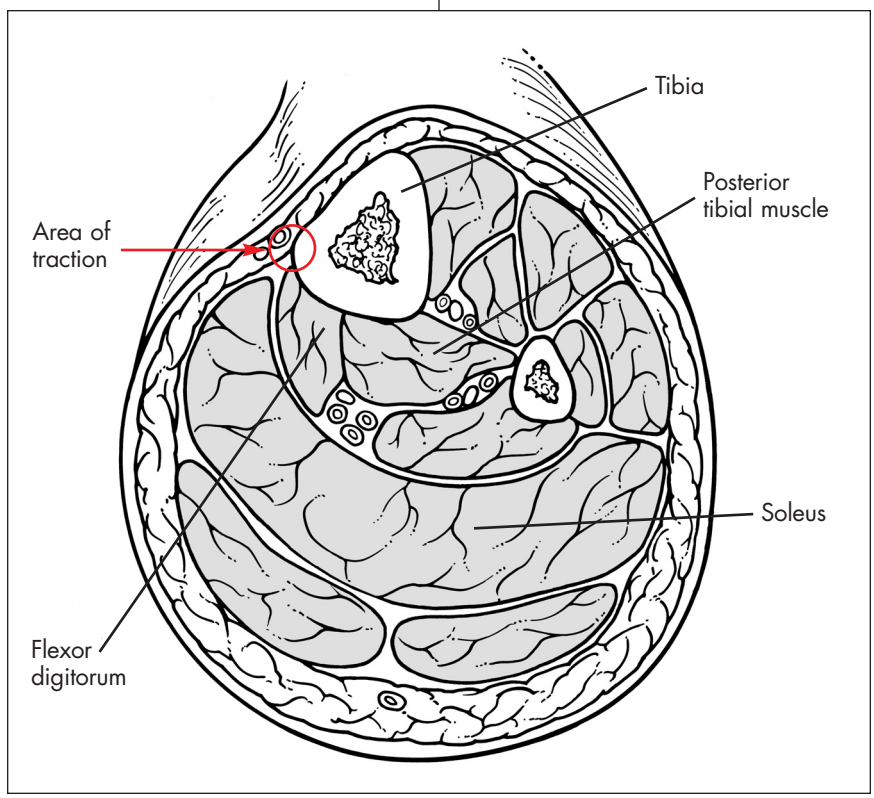
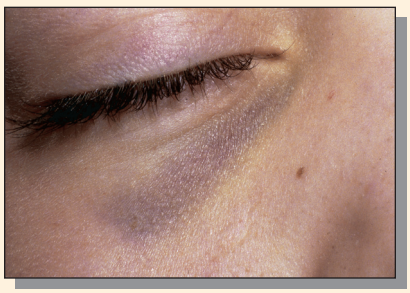
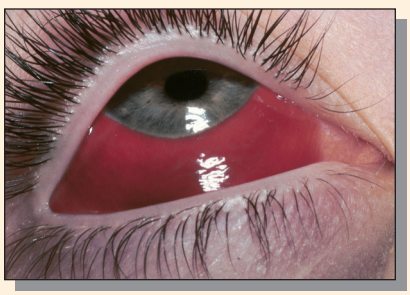


Illustration by Charles H. Boyter

Figure 4 – Traction of the posterior tibial, flexor digitorum, and soleus muscles on the periosteum of the tibia is the cause of medial tibial stress syndrome. The location of this traction is indicated by the arrow.

Do You Have a Lesson to Teach Your Colleagues?





- If you have good clinical photographs with a teaching message, we invite you to share them with your colleagues in *Consultant For Pediatricians*.
- We offer a $50 honorarium for each published image. Pictures are selected on the basis of visual interest and educational value.
- **Please send your cases to:**
  Photoclinic Editor
  Consultant For Pediatricians
  330 Boston Post Road
  Box 4027
  Darien, CT 06820-4027
  or
  By e-mail:
  LGeisler@cmp.com

16-Year-Old Camper With Tibial Pain

plantar flexion are characteristic findings. Pronation of one or both feet may be present.

Contributing factors. Multiple factors can contribute to or increase the risk of overload. A prior injury or lack of conditioning may lead to muscle imbalance, inflexibility, weakness, and instability. Other factors that can contribute to the development of MTSS include poor exercise technique, improper equipment, and changes in the duration or frequency of activity (training errors). Some persons seem to be more vulnerable to MTSS than others. This boy was not well conditioned when he began camp, his equipment (footwear) was faulty, and he pronated. His anatomy predisposed him to overload his posterior leg musculature, and his lack of conditioning contributed muscle weakness and lack of flexibility.

WHICH TREATMENT WOULD YOU RECOMMEND?

A. A course of NSAIDs.

B. An orthosis to correct the patient's pronation.

C. Calf strengthening exercises.

D. Cross training on a stationary bicycle.

E. All of the above.

THE CONSULTANT'S CHOICE

Treatment of MTSS is conservative. Running needs to be stopped for a short period, but alternative activities, such as swimming or use of a stationary bicycle, can be substituted. Additional treatment options include NSAIDs to reduce inflammation, orthoses to correct pronation, and exercises to strengthen the calf muscles.

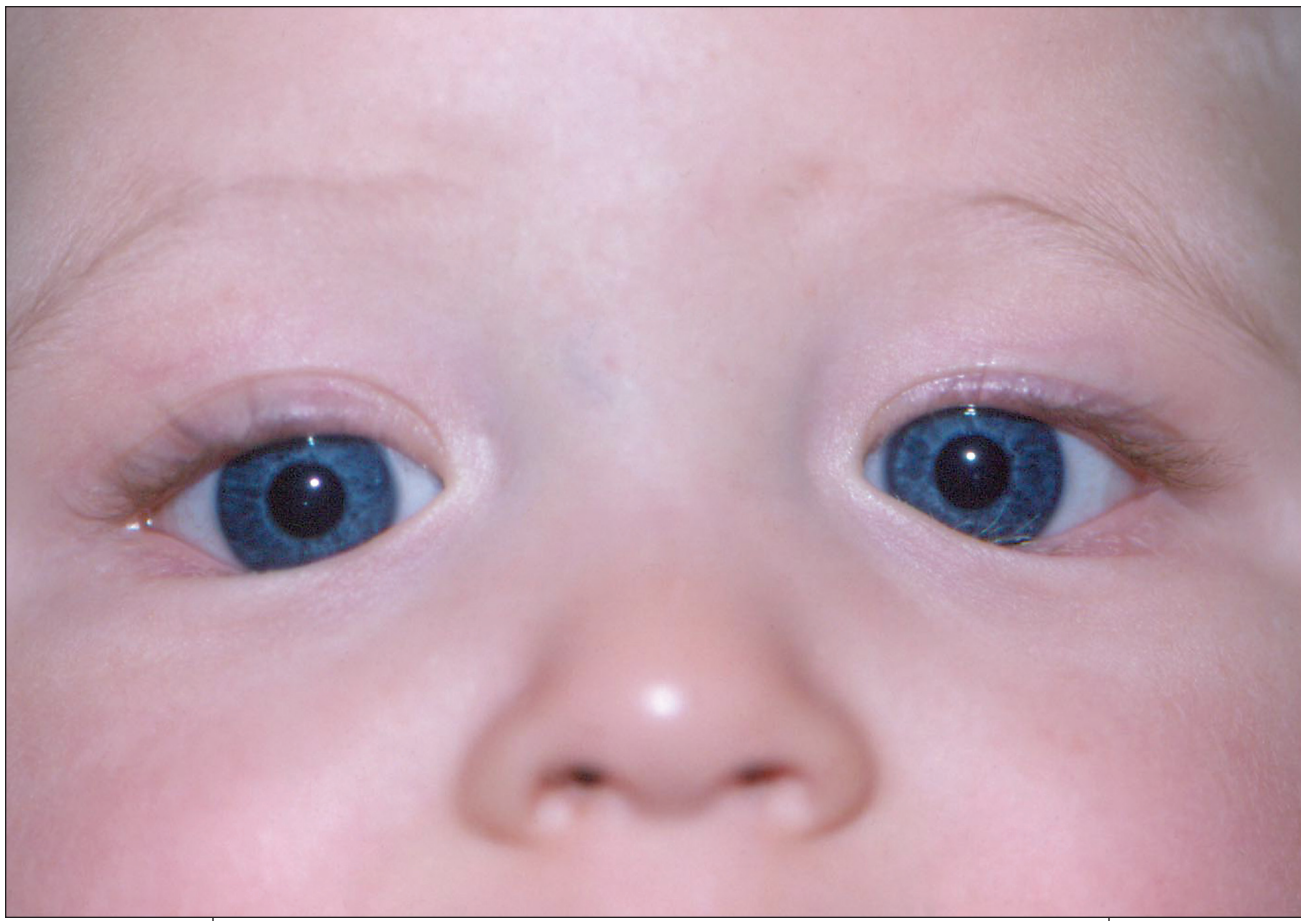
Outcome of this case. This patient's treament included all of these options. He began a 10-day course of ibuprofen, 600 mg tid. An orthosis was prescribed to correct his pronation. (He also obtained new shoes that had strong medial support.) He refrained from competitive basketball for 2 weeks and from weight-bearing exercise for 1 week. He used a stationary bicycle for 1 week; then he began to alternate walking/jogging with riding the stationary bike. The camp's trainer oversaw a program of gradually increasing activity. He did very well, and within 4 weeks had returned to full play. ■

Photoclinic

Foresee Your Next Patient

DEEPAK M. KAMAT, MD, PhD—Series Editor

Dr Kamat is professor of pediatrics at Wayne State University in Detroit. He is also director of the Institute of Medical Education and vice chair of education at Children's Hospital of Michigan, both in Detroit.



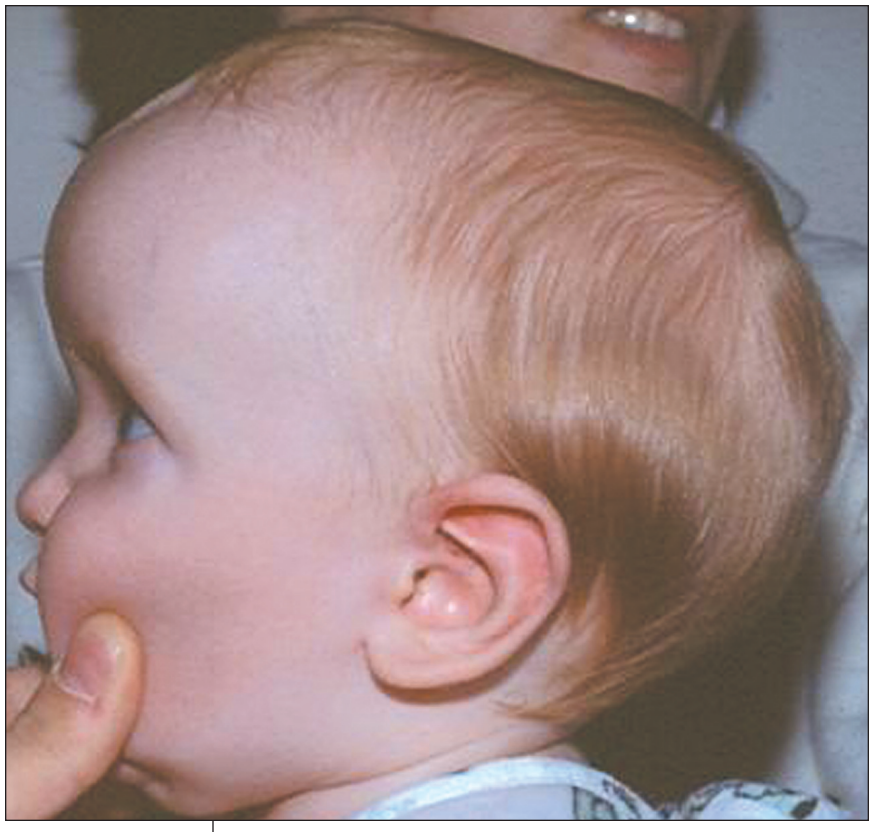
Bilateral Epiblepharon

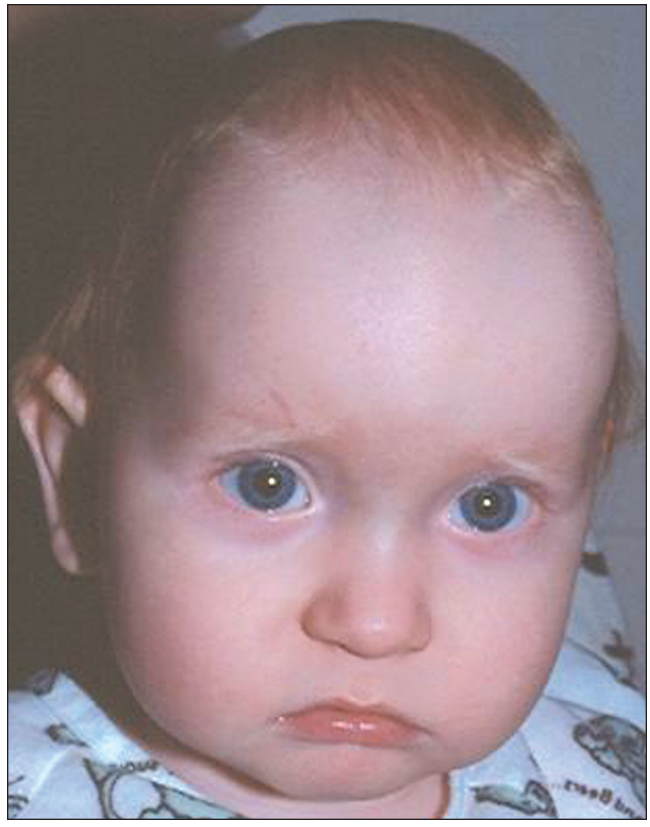
An 11-month-old infant was referred by his pediatrician for possible surgical correction of a bilateral entropion. The mother stated that her son's lashes appear to turn in on occasion; however, he never rubbed his eyes, the eyes were not red, and no discharge or drainage was noted.

Leonid Skorin, Jr, DO, of Albert Lea, Minn, diagnosed bilateral epiblepharon. This congenital condition appears as an extra horizontal fold of skin across the lower eyelid, which forces the lashes against the cornea. It is often seen in Asian persons and may be familial. Epiblepharon frequently resolves on its own, with the differential growth of the facial bones. Surgical correction with tarsal fixation of Hotz is required only when the patient has keratitis and compromised corneal integrity. An elliptical excision of the orbicularis muscle is performed, and the skin edges are reapproximated at the level of the inferior border of the tarsal plate. The procedure helps create a new skin crease and relieves a secondary entropion.

For patients without symptoms, a watch and wait approach is appropriate. After a thorough discussion of the condition with the mother, she decided to simply monitor the infant for any eye irritation. The infant has remained asymptomatic. ■

To page 589.





Scaphocephaly

This 9-month-old infant was brought for evaluation of anteroposterior elongation of the cranium. The infant was born at term via uncomplicated vaginal delivery. His mother had noticed that his head was more elongated and narrower than his sibling's. He had achieved appropriate motor and social milestones for his age. Neither parent had a family history of abnormal head shape. The rest of the examination findings were unremarkable.

Christian Sonnefeld, MD, and Atiya Khan, MD, of Morgantown, WVa, diagnosed scaphocephaly (boat-shaped head). A noncontrast CT scan of the head with 3-D reconstruction (see next page) revealed early sutural synostosis of the posterior portion of the sagittal suture as the cause of the dolichocephalic configuration of the cranium.

Premature closure of 1 or more of the cranial sutures—craniosynostosis—can be associated with various anomalies and genetic disorders.[1] Apert, Chotzen, Pfeiffer, Carpenter, and Crouzon syndromes all have extracranial manifestations, such as syndactyly, polydactyly, dysmorphic facies, midfacial hypoplasia, beaklike nose, and proptosis. This patient had none of these extracranial findings.

The type of craniosynostosis depends on the suture or sutures involved. The most common type is sagittal synostosis, also known as scaphocephaly (or dolichocephaly), which accounts for about 60% of all cases of craniosynostosis.[2] It is characterized by an elongated anteroposterior diameter of the skull and a ▶

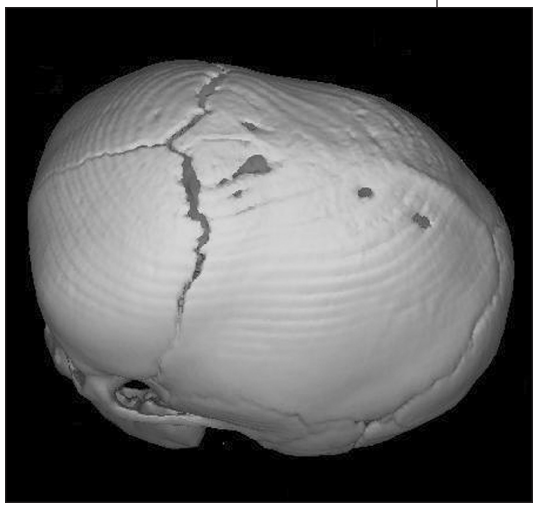
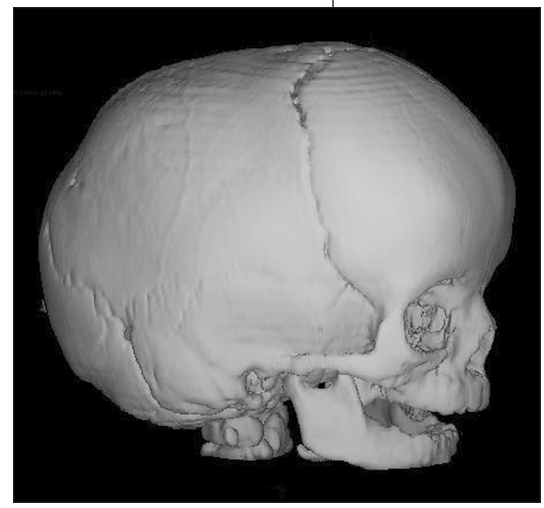
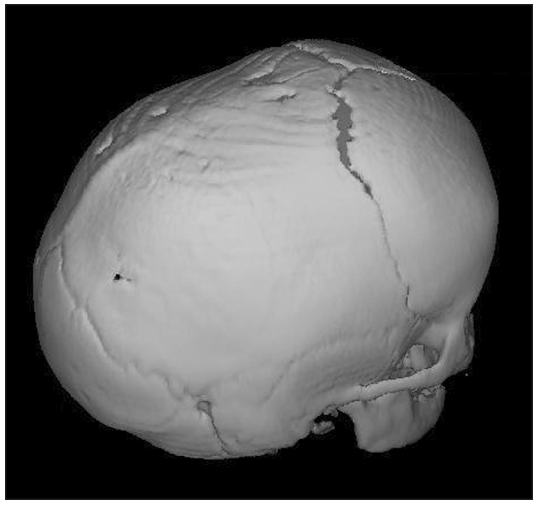
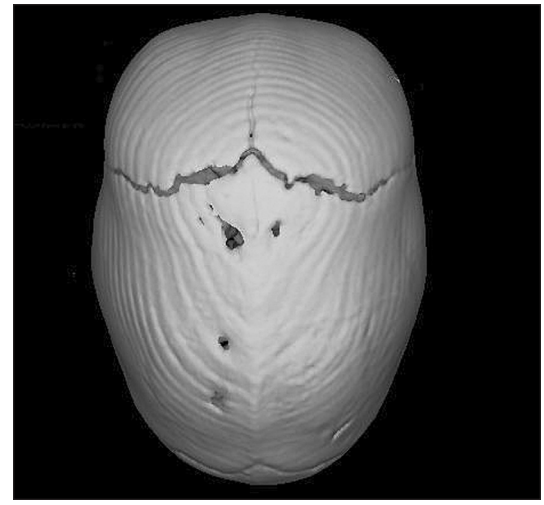
(Scaphocephaly, continued)

decreased transverse diameter. Palpable ridging over the sagittal suture may be noted at birth. The cranial index approaches 60 (normal cranial index is about 80). However, recent data suggest that measurements of internal skull planes, surface landmarks, and skull base planes may produce more reliable indices than the traditional cranial index.[3]

Boys are more commonly affected than girls, and 2% to 8% of cases are familial.[2] Isolated sagittal synostosis is rarely associated with deformity of the skull base or facial bones. Neurologic findings are usually normal. In premature infants, scaphocephaly develops because of positional molding of the poorly mineralized skull.

Craniosynostosis is managed surgically to allow normal brain growth and to prevent increased intracranial pressure and compromise of visual and auditory function. In infants with scaphocephaly, the shape of the skull may become normal with maturity. For those with mild scaphocephaly, such as this patient, reassurance and clinical follow-up may be all that is needed. Molding helmets may be tried. For infants with severe scaphocephaly, surgery may be indicated for cosmesis. Early surgery is optimal and can provide an excellent cosmetic result.[4] In sagittal craniosynostosis, surgery within 3 to 6 months permits restoration of near-normal skull contour.[5] ■

REFERENCES:
1. Fenichel GM. *Clinical Pediatric Neurology: A Signs and Symptoms Approach.* 4th ed. Philadelphia: WB Saunders Co; 2001:368.
2. Swaiman KF. *Pediatric Neurology: Principles and Practice.* 2nd ed. St Louis: Mosby; 1994:455-460.
3. Ruiz-Correa S, Sze RW, Starr JR, et al. New scaphocephaly severity indices of sagittal craniosynostosis: a comparative study with cranial index quantifications. *Cleft Palate Craniofac J.* 2006; 43:211-221.
4. Olds MV, Storrs B, Walker ML. Surgical treatment of sagittal synostosis. *Neurosurgery.* 1986; 18:345-347.
5. Persing JA, Jane JA. Treatment of syndromic and nonsyndromic bilateral coronal synostosis in infancy and childhood. *Neurosurg Clin N Am.* 1991;2: 655-663.

To page 593.

Postinflammatory Hyperpigmentation

Two children—one with a history of infection, the other with a history of an allergic reaction—were noted to have postinflammatory hyperpigmentation.

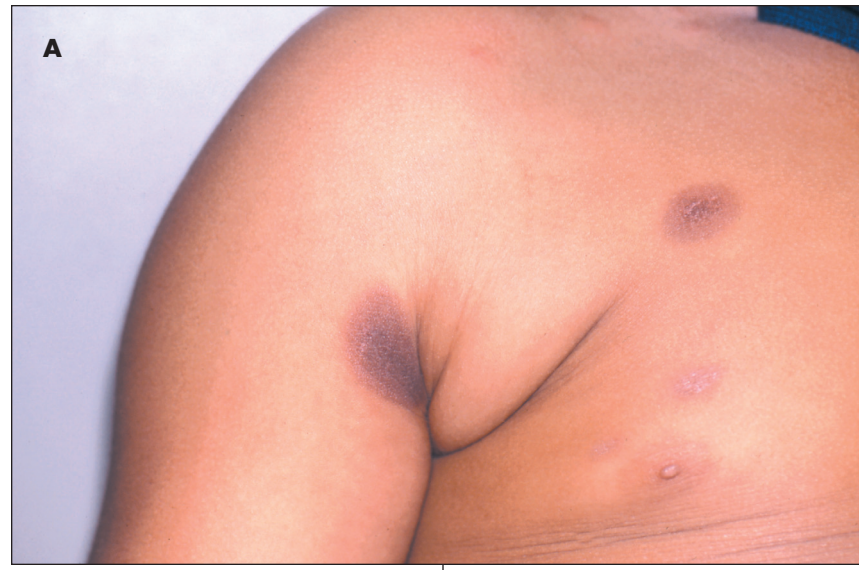
Photo A shows a 6-year-old girl with 2 hyperpigmented areas, 1 on the right anterior chest and 1 on the upper arm. The previous month, she had impetigo and was treated with oral cephalexin and topical mupirocin ointment. **Photo B** shows a 14-year-old boy with areas of light tan hyperpigmentation on the neck. At 3 years of age, he had poison ivy dermatitis that resulted in thick black scabs, which eventually peeled away from the edges over several weeks. The resultant hyperpigmentation has remained unchanged for the past 11 years.

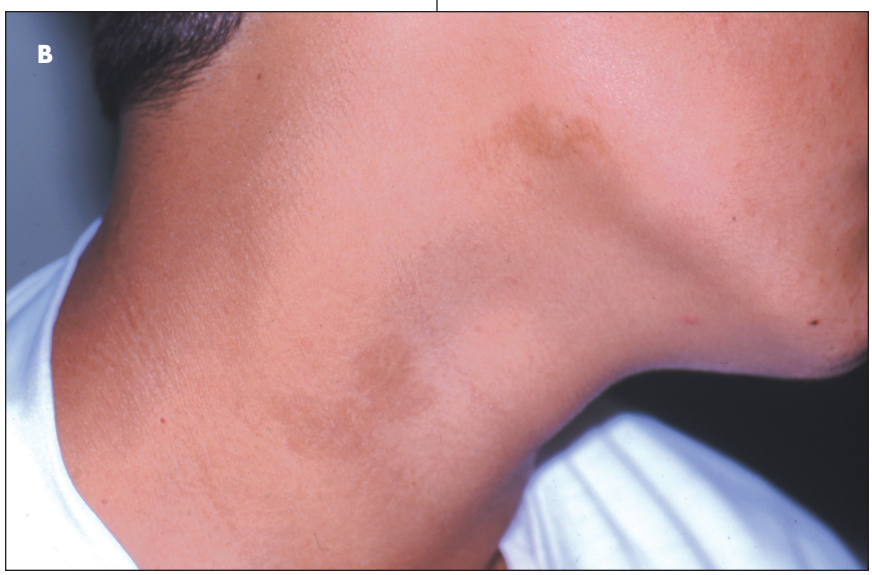
Robert P. Blereau, MD, of Morgan City, La, writes that inflammation from allergic or infectious causes can result in hypopigmentation or hyperpigmentation of the involved area. Melanin hyperpigmentation or melanoderma may be classified as follows[1]:

- Chloasma
- Incontinentia pigmenti
- Secondary to skin diseases (eg, tinea versicolor, fixed drug eruption)
- Secondary to external agents (eg, UV light, photosensitizing chemicals)
- Secondary to internal disorders (eg, Addison disease, hyperthyroidism, acanthosis nigricans)
- Secondary to drugs, such as sex hormones

Hypopigmenting agents are the mainstay of treatment, although the results vary and some agents may even worsen the lesions. Hydroquinone is the best topical bleaching agent. A combination cream that contains hydroquinone, tretinoin, and fluocinolone acetonide (Tri-Luma cream) has proved to be more effective than other single agents; in 2 studies, efficacy was 13% and 38% in the resolution of melasma lesions after 8 weeks.[2] Topical tretinoin and azelaic acid may also be used as monotherapy. Chemical peels using trichloroacetic acid and alpha hydroxy acids are somewhat effective; however, these treatments have been known to cause postinflammatory hyperpigmentation or hypopigmentation. Laser therapy has shown mixed results.

Use of sunscreens that block UVA and UVB light can prevent further pigmentation. Cosmetics may be used to camouflage the pigmented lesions. ■





REFERENCES:
1. Hall JC. *Sauer's Manual of Skin Diseases.* 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2000:244.
2. Habif TP. *Clinical Dermatology: A Color Guide to Diagnosis and Treatment.* 4th ed. St Louis: Mosby; 2004:692.

Corneal Abrasion

On waking up from a nap, a 5-month-old infant was noted to have a watery right eye. The mother thought an eyelash was the problem and flushed the eye with water. Soon afterward, the eye watered again and began to close. There was no history of injury, foreign body, upper respiratory tract symptoms, or fever.

The infant was alert, active, and in no distress. Vital signs were stable, and general physical examination findings were normal. Her right eye was partly closed. No foreign body was seen when the eyelid was everted. The pupil was round and reactive; the conjunctiva was mildly hyperemic. There were no scratches on the face.

After instilling proparacaine and fluorescein dye in the eye, Manu Madhok, MD, and Devi Meyyappan, MBBS, of Children's Hospitals of Minnesota in Minneapolis used a Wood lamp to examine the cornea. The uptake of fluorescein dye by damaged corneal epithelial cells revealed an abrasion.

Corneal abrasion is usually caused by a foreign body or direct injury from a fingernail, stick, or piece of paper.[1] Examination under a slit lamp or Wood lamp after staining with fluorescein dye reveals the denuded epithelium and confirms the diagnosis.

Topical antibiotic therapy for corneal abrasions is prescribed to prevent bacterial infection and a corneal ulcer. The use of a patch to treat a simple corneal abrasion does not improve healing rates and the patient is temporarily deprived of binocular vision. Therefore, patches are not routinely recommended in this setting.[2]

Follow-up with the infant's primary physician is usually adequate. When an abrasion is visible even without fluorescein staining or an ulcer is noted, antibiotic drops, patching, and close follow-up by an ophthalmologist are indicated.

Consider a corneal abrasion in infants with normal physical findings who cry inconsolably.[3]

The infant's long fingernails were thought to be the cause of her corneal abrasion. The mother was asked to trim the baby's nails, instill ofloxacin ophthalmic drops for 5 days, and prevent bright light from shining into the infant's eye. She was also instructed to bring the infant to the primary physician for follow-up in 1 week. ■

REFERENCES:
1. Wirbelauer C. Management of the red eye for the primary care physician. *Am J Med.* 2006;119:302-306.
2. Turner A, Rabiu M. Patching for corneal abrasion. *Cochrane Database Syst Rev.* 2006. Apr 19;(2):CD004764.
3. Harkness MJ. Corneal abrasion in infancy as a cause of inconsolable crying. *Pediatr Emerg Care.* 1989;5:242-244.

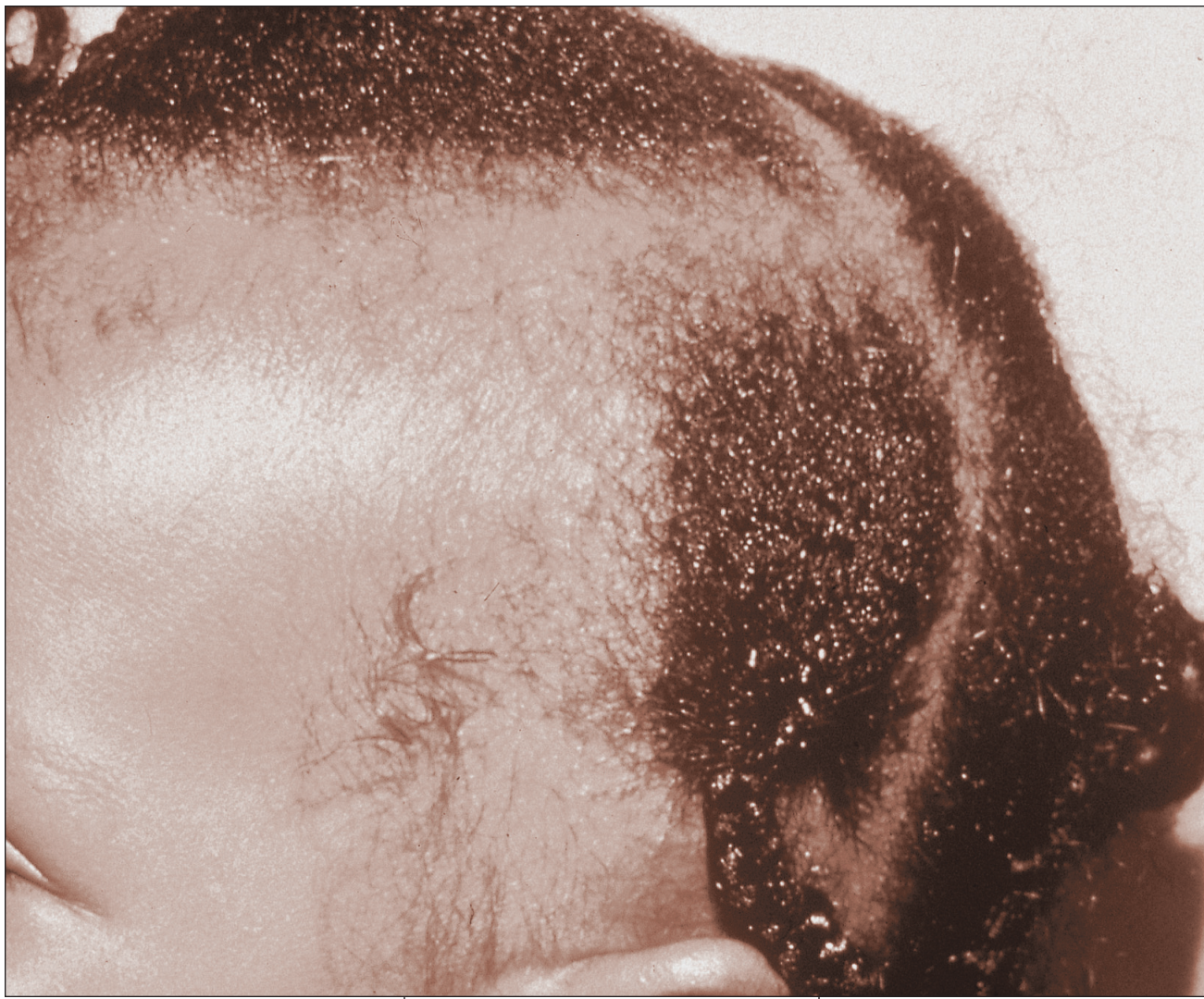
Submit your medical images for publication in Photoclinic. Images should be clear and well exposed. Please include a precise description of each image and its significance, with relevant history, findings, and outcome. If a patient is recognizable, indicate whether you have signed permission to use his or her photograph. Images are chosen on the basis of visual interest and educational value, and a $50 honorarium is awarded for each image accepted. **By mail send to:** Photoclinic Editor, CONSULTANT FOR PEDIATRICIANS, 330 Boston Post Road, Box 4027, Darien, CT 06820-4027. **By e-mail:** LGeisler@cmp.com.

Photo Finish

Acute Dx: What Cause of Sudden Illness?

DAVID EFFRON, MD—Series Editor

Dr Effron is assistant professor of surgery at Case Western Reserve University, attending physician in the department of emergency medicine at the MetroHealth Medical Center, and consultant emergency physician at the Cleveland Clinic Foundation, all in Cleveland.



THE CASE: The parents of a 4-year-old girl are concerned because she has experienced hair loss for several weeks. The child is otherwise healthy and active, has no known disorders, and takes no medications.

What do you suspect?

- Tinea capitis
- Trichotillomania
- Traction alopecia
- Discoid lupus erythematosus

(Answer and discussion on the next page.)

Photo Finish

Continued

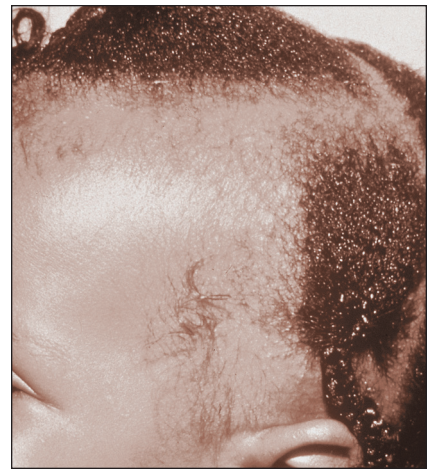
DISCUSSION: This child has **traction alopecia,** an entity first described in 1907 in girls and women in Greenland who styled their hair in a ponytail. It is found primarily in African American women and girls and is also seen in Japan. In India, the condition is observed in Sikh men who pull their scalp hair into a bun and tightly roll their beard hair.

Hairstyling practices such as braiding, cornrows, and the use of weaves and rollers may also cause traction alopecia. Sustained tension on the scalp results in breakage of the outermost hairs. Hair loss is often symmetric; it frequently occurs along the frontotemporal hairline. The initial loss is reversible; however, prolonged traction may result in permanent hair loss.

In the first stages of traction alopecia, pruritus and perifollicular erythema are often present. They may be accompanied by secondary hyperkeratosis that resembles seborrheic dermatitis. Over time, scales and pustules may develop. Eventually, follicular atrophy results in the replacement of normal long, coarse hair by thinner, finer short hair.

Traction alopecia may be marginal or nonmarginal. Marginal alopecia (alopecia linearis frontalis) is a pattern of hair loss associated with the use of rollers, tight curlers, or straighteners in childhood. It occurs in the temporal region of the scalp and extends in a triangle from the preauricular area. Chignon alopecia is a form of nonmarginal alopecia that is characterized by hair loss in the occipital region where a bun is located. This condition is typically seen in middle-aged women who have pulled their hair into a bun for many years.

Early diagnosis is important to help prevent irreversible hair loss. Once the offending practices have been discontinued, it may take several months before regrowth occurs.



Antibiotics may be required for secondary inflammation and infection. No medical treatment is available once hair loss has become irreversible; hair transplantation procedures may be considered.

Trichotillomania, a traumatic alopecia, is a psychiatric disorder characterized by compulsive hair pulling that results in patchy hair loss. Hair loss may cover from several centimeters to large portions of the scalp. In addition to the scalp, the eyebrows, eyelashes, and pubic area may be affected. Treatment is directed toward the underlying disorder. Most adult and teenage patients are women; in younger patients, boys are affected slightly more often than girls. In children, nail biting may be seen concurrently with trichotillomania.

Tinea capitis is the most common dermatophytosis of childhood (it accounts for up to 90% of dermatophytoses in children younger than 10 years) and is characterized by partial alopecia and scaly patches. This superficial fungal infection affects the skin of the scalp, eyelashes, and eyebrows. The affected areas have hairs broken 1 to 3 mm above the skin. Patches of hair loss occur singly or in groups and are usually round or oval. *Microsporum* and *Trichophyton* are the usual culprits. The diagnosis is confirmed by Wood lamp examination, potassium hydroxide wet-mount preparations, or fungal cultures.

Discoid lupus erythematosus is a chronic dermatosis that primarily affects women aged 40 to 60 years. The lesions consist of erythematous papules or plaques with slight to moderate scaling and are characterized by central hypopigmentation with peripheral areas of hyperpigmentation. The lesions are most commonly seen on the head and neck but may extend to the oral cavity, arms, palms, and soles. Atrophy and scarring alopecia of the scalp are typical findings. ■

FOR MORE INFORMATION:

■ Hantash BM, Schwartz RA. Traction alopecia in children. *Cutis.* 2003;71:18-20.

■ Muller SA. Trichotillomania and related disorders. In: Orfanos CE, Happle R, eds. *Hair and Hair Diseases.* Berlin: Springer-Verlag; 1990.

■ Springer K, Brown M, Stulberg DL. Common hair loss disorders. *Am Fam Physician.* 2003;68:93-102.