Flat Head Syndrome
Conservative or Helmet Therapy?

Although there is no standardized classification, this patient’s would be considered a “moderate” case of bilateral deformational plagiocephaly/brachycephaly (DPB).
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Probiotics vs placebo against gastroenteritis

Of 973 preschool-aged children with acute gastroenteritis who visited 1 of 10 geographically diverse pediatric emergency departments (EDs), those who received a 5-day course of Lactobacillus rhamnosus GG, a commonly recommended and used probiotic, did not have better outcomes than those who received placebo, a prospective, randomized trial found.

Participants were children aged from 3 months to 4 years (median age, 1.4 years) who had experienced 3 or more episodes of watery stools each day, with or without vomiting, for fewer than 7 days. Participants were randomly assigned to receive L rhamnosus GG at a dose of $1 \times 10^{10}$ colony-forming units (CFUs) twice daily for 5 days or placebo. After the first dose of L rhamnosus GG or placebo was administered in the ED, caregivers provided subsequent doses and completed a daily diary in which they recorded symptoms for 5 days or until symptoms resolved. Investigators also conducted follow-up surveys 14 days and 1 month after enrollment.

Analysis of participants’ stool samples revealed that 45.6% were positive for viruses and 15.2% were positive for bacteria that are probable or possible pathogens. No pathogenic organisms were detected for 42.8% of participants. The proportion of participants who had received antibiotics or ondansetron was similar in the 2 groups.

Investigators used the Vesikari Scoring System scale to assess the severity of gastroenteritis during the 14-day follow-up period, with a score of 9 or higher indicating more severe disease. (Scores range from 0 to 20.) At the 14-day follow-up, the Vesikari score was 9 or higher in similar proportions of both groups: 11.8% of the L rhamnosus GG group and 12.6% of the placebo group. Treatment with L rhamnosus GG also failed to show benefit with regard to the duration or frequency of vomiting or diarrhea, the rate of household transmission, or the length of daycare or work absenteeism (Schnadower D, et al. N Engl J Med. 2018;379[21]:2002-2014).

THOUGHTS FROM

Dr. Burke

This is 1 of 2 large, simultaneously published, well-designed, placebo-controlled studies to evaluate the effectiveness of probiotics in treatment of acute gastroenteritis in young children. Neither study showed significant benefit for treatment of this condition. So, whereas various probiotic preparations have been shown to be useful in a variety of pediatric conditions (everything from treatment of colic to prevention of necrotizing enterocolitis in premature babies), acute gastroenteritis is not one of them, at least not for the strains tested here.

Michael G Burke, MD is Chairman, Department of Pediatrics, Saint Agnes Hospital, Baltimore, Maryland.
### Poverty raises risk of bacterial infection in febrile infants

Febrile infants from disadvantaged neighborhoods with high rates of childhood poverty are much more likely than their peers from more affluent neighborhoods to have a bacterial source for their fever, according to a retrospective study of infants aged 90 days or younger with a temperature of 100°F or greater who visited an emergency department (ED) of an urban children’s hospital.

Investigators identified the sociodemographic characteristics of participants and their families, including median household income, the existence of poverty and deprivation, crowded housing, and “social capital” (level of residents’ belief that neighbors are willing to help others and can be trusted along with a feeling of “belonging”). Of a total of 232 infants, who had a median age of 54 days, 31 (13.4%) had a bacterial infection and 117 (50.4%) were categorized as at high risk. *Escherichia coli* and group B *Streptococcus* accounted for most bacterial infections (55%).

Analysis showed that the risk of bacterial infection was greater than 3 times higher in children from neighborhoods with high rates of childhood poverty than it was in those from neighborhoods with low levels. In addition, infants from areas with higher measures of social capital tended to have a lower risk of bacterial infection, suggesting that living in such neighborhoods may be protective (Yaeger JP, et al. *J Pediatr*. 2018;203;336-344).

#### THOUGHTS FROM DR. BURKE

The researchers speculate the neighborhood-specific risks of bacterial disease might be due to differences in household crowding, smoke exposure, food insecurity/nutrition, and availability of diapers for frequent changes. If the findings of this small study can be replicated on a larger scale, we may see inclusion of measures of poverty and lack of connectedness included in the next generation of guidelines for evaluation of febrile infants.

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### Not sleeping through the night by age 12 months? Not to worry!

Many 6- and 12-month-old infants do not yet sleep through the night, but Canadian researchers found no significant associations between this situation and infants’ mental and psychomotor development or their mothers’ mood.

Using a definition of either 6 or 8 hours of uninterrupted sleep as “sleeping through the night,” investigators surveyed more than 300 women when their infants were aged 6 and 12 months about their children’s sleeping habits during the previous 2 weeks. At 6 months, using the 6-hour criterion, 37.6% of mothers reported that their child did not sleep through the night as did 57% under the 8-hour criterion. At age 12 months, the proportion of children reported not to sleep through the night under the 6- and 8-hour criteria had dropped to 27.9% and 43.4%, respectively.

Investigators used standard tests to evaluate the infant participants’ development at ages 6, 12, and 36 months and their mothers’ mood during the third trimester of pregnancy, and at 6, 12, and 36 months postnatally. Correlating these test results with the collected sleep data, investigators found that whether or not infants slept through the night—using either criterion—did not have any significant effect on their mental or psychomotor development or their mothers’ mood (Pennestri MH, et al. *Pediatrics*. 2018;142[6]:e20174330).

#### THOUGHTS FROM DR. BURKE

Parents of babies who do not sleep for a long stretch at night may find it reassuring that they are not alone, and that, in fact, a minority of 6-month-olds sleep for 8 hours at a time. Babies who didn’t sleep through the night were more likely to continue breastfeeding and, surprising to me, their mothers were no more likely to have depressed moods than mothers of infants who slept longer. Maybe we need to deemphasize this sleep milestone.
Child with a history of multiple fractures

ANKUR K SHAH, MD, PHD; EMILY C KING, MD, MS; LYNDA E POLGREEN, MD, MS; CATHERINE S MAO, MD; JENNIFER K YEE, MD

The patient, an 8-year-old male who recently immigrated to the United States from El Salvador, initially presented to the emergency department (ED) for a cough. The next day, he went to the general pediatrics clinic for follow-up and was noted to have a significant history of recurrent fractures.

The father reported his son had had 7 fractures of the upper extremities beginning at age 3 years (on later detailed inquiry, 10 fractures were reported: 2 fractures of the left arm and 8 fractures of the right arm), with the latest fracture occurring approximately 3 months ago to the right humerus. The fractures were sustained with minimal force. The family reported that their child was diagnosed with osteogenesis imperfecta in their home country. The ED had discharged the patient with the same diagnosis.

Physical examination

On physical exam, the patient was alert, cooperative, and in no apparent distress, with unremarkable vital signs. His height was 127.7 cm (40.5th percentile for age and sex) and weight was 23 kg (18.2th percentile for age and sex). There was a sizeable calculus and bowing deformity of the right forearm, as well as leg length discrepancy (right longer than left). The patient also was noted to have hyperpigmented macular skin lesions.

Consultations and additional studies

The patient was referred by the general pediatrics clinic to Pediatric Endocrinology. Further history revealed that he also had primary dentition issues, including losing his primary teeth early at the age of 4 years. Findings on physical exam included that the sclerae were white and not blue; the hyperpigmented macules were located on the left posterior thorax and left side of the neck and spared the midline; and scant pubic hair was present.

Initial laboratory test results had included normal values for serum calc-

**FIGURE 1** An X-ray of the right arm showing a comminuted fracture of the distal humerus, as well as a healing pathologic fracture of the humeral midshaft. Multiple well-defined, cystic-appearing, lucent lesions with a ground-glass appearance are apparent within the humerus, ulna, and radius, consistent with polyostotic fibrous dysplasia.
um (9.6 mg/dL), magnesium (2.1 mg/dL), phosphorus (4.5 mg/dL), and 25-hydroxy vitamin D (32.3 ng/mL). A serum immunoglobulin (Ig) E was within normal range. Parathyroid hormone intact (PTHi) was slightly elevated to 61 pg/mL (normal range, 9-59 pg/mL), and osteocalcin was elevated to 217 ng/mL (normal range, 47-142 ng/mL). Based on the clinical findings, further laboratory tests were ordered: insulin-like growth factor 1 (IGF-1) was 118 ng/mL (normal, 52-391 ng/mL); insulin-like growth factor binding protein 3 (IGF-BP3) was 3.6 mg/L (normal, 1.2-6.4 mg/L); total testosterone was 17 ng/dL (normal, <13 ng/dL); thyroid stimulating hormone (TSH) was <0.01 μIU/mL (normal, 0.35-4.94 μIU/mL); total thyroxine (T4) was 12.87 μg/dL (normal, 4.87-11.72 μg/dL); and free T4 was 2.27 ng/dL (normal, 0.7-1.48 ng/dL).

Bilateral radiographs of the forearm and humerus revealed numerous lucent lesions and areas of sclerosis with a bowing defect of the right humerus. A skeletal survey revealed a healing pathologic midshaft fracture in the right humerus. In addition, numerous right and left humeral, ulnar, and radial well-circumscribed, centrally lucent lesions with some areas of sclerosis were visualized. There was large distortion and mottled sclerosis of the left iliac wing. These radiograph findings were consistent with polyostotic fibrous dysplasia.

**Discussion**

The differential diagnosis for conditions leading to increased risk of fragility fractures in children is extensive, thus a thorough history is essential in narrowing the potential etiologies (Table).\(^1,^2\) Clinicians should always consider nonaccidental trauma as a potential cause for multiple healing fractures, especially when there is a discrepancy between the history provided by the caregivers and physical exam findings. In the present case, the history did not raise suspicion for nonaccidental trauma, and the multiple historical and physical findings strongly suggested a genetic etiology.

The patient was initially presumed to have osteogenesis imperfecta (OI), which is the most common cause of primary osteoporosis, leading to bone fragility and fractures due to defects in the quality or quantity of collagen type I.\(^3\) Multiple different subtypes of OI have been identified, with a range of severity and clinical presentations. The OI type I is the most common and mildest form of the disease, and is characterized by blue-tinted sclerae, normal to slightly below-normal stature, and no dental involvement. The OI type II patients usually do not survive beyond the newborn period, whereas OI type III is characterized by severe

| TABLE
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<tr>
<th>DIFFERENTIAL DIAGNOSIS OF MULTIPLE SKELETAL FRACTURES IN CHILDREN</th>
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<td><strong>Renal disease</strong></td>
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<td><strong>Medication related</strong></td>
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From Harrington J, et al; Boyce AM, et al.\(^2\)

\(\text{FIGURE 2}\) The left humerus, proximal ulna, and radius also demonstrate multiple well-defined, cystic-appearing, lucent lesions with a ground-glass appearance, indicating polyostotic fibrous dysplasia.
perplastic calluses at fracture sites. McCune-Albright syndrome (MAS) is also a rare disorder that can be easily mistaken for OI based on a history of multiple fractures. The prevalence is between 1/100,000 and 1/1,000,000. The classic triad of MAS consists of fibrous dysplasia, precocious puberty, and café au lait spots, However, multiple hyperfunctioning endocrinopathies are also seen in MAS, including hyperthyroidism, hypercortisolism, excess growth hormone production, renal phosphate wasting with possible rickets, and Cushing syndrome.5,6 Because the patient had polyostotic fibrous dysplasia, café au lait spots, and hyperthyroidism, a diagnosis of MAS was made.

An activation of the Gs protein encoded by the GNAS gene is the underlying genetic defect that leads to MAS.5 Melanocyte stimulating hormone (MSH), luteinizing hormone (LH), TSH, growth-hormone-releasing hormone (GHRH), and adrenocorticotropic hormone (ACTH) all use G-protein pathways for signaling. Thus, a constitutional activation of the G-protein pathways in MAS leads to increased cyclic adenosine monophosphate (cAMP) and increased production of melanin, estradiol, testosterone, thyroid hormone, growth hormone, and cortisol.

Because MAS is not vertically transmitted, patients are considered to be somatic mosaics; thus, the diagnosis is based on clinical findings, with no definitive genetic testing available.

Patient outcome
The patient was started on methimazole for hyperthyroidism. Bisphosphonate therapy was considered but not pursued initially, given studies are inconclusive regarding its effect on the progression of fibrous dysplasia, and given he was not experiencing significant bone pain when first seen in the clinic.

The patient has continued to be closely monitored for development of other potential endocrinopathies, which he has not developed, and he appears to be progressing through puberty6 in a normal timeline.

Lessons for the clinician
The differential diagnosis for a patient with a history of multiple fractures is expansive, and clinicians may see a patient with MAS and easily mistake it for a diagnosis of osteogenesis imperfecta. Diligent history taking, a thorough physical exam, focused laboratory studies, and careful review of imaging were key to unraveling this diagnosis.

In order to minimize the progression of fibrous dysplasia in MAS patients, correction of thyroid dysfunction, as well as proper supplementation of calcium and vitamin D, may be required. The potential benefits of bisphosphonate treatment have been shown to yield positive results in some MAS patients.7,8 However, no universal recommendation for bisphosphonate use is currently available.

For references, go to ContemporaryPediatrics.com/puzzler-0219
New therapeutic measure to combat Influenza

Growing resistance to current drugs for influenza has spurred development of a new class of antivirals that target virus replication.

NADINE PEART AKINDELE, MD

Traditional anti-influenza drugs have been comprised of 2 groups: neuraminidase inhibitors and M2 ion channel inhibitors (aka, adamantanes). Now the US Food and Drug Administration (FDA) has approved (October 24, 2018) the use of a new drug for influenza with a novel mechanism of action. Known as baloxavir marboxil (Xofluza; Genentech USA Inc., San Francisco, California), this new drug targets the cap-dependent endonuclease of influenza viruses and is being introduced because of concerns for resistance to current available drugs.1

Previous medications that target the influenza virus proteins included adamantanes, namely amantadine and rimantadine, and neuraminidase inhibitors, which include oseltamivir and zanamivir. Adamantanes, whose mechanism of action targets the M2 ion channel, prevent replication of influenza A viruses only. Neuraminidase inhibitors, effective against both influenza A and B viruses, prevent release of the progeny influenza virus from infected host cells.2 Recommendations no longer support the use of adamantanes as there has already been largely recognized resistance against these drugs and they only have activity against influenza A.1,3,4

Neuraminidase inhibitors have been used widely in patients for active influenza virus infection and for chemoprophylaxis. The Centers for Disease Control and Prevention (CDC) currently recommends use of oseltamivir, in particular, for treatment of influenza in pa-

This increase in resistance [to current antiviral drugs] has led to the study of other proteins within the influenza virus that can be targets of antiviral agents.

...patients of all ages and for chemoprophylaxis for children and adults aged 3 months and older.5 Zanamivir is only available in an inhaled dosage form and is used for treatment of children and adults, aged 7 years and older. Unfortunately, emergence of antiviral resistance to this group of drugs has led to growing concerns with continued use of this drug class.5

Early clinical trials with oseltamivir revealed emergence of resistance up to 4% in...
adults who received treatment during seasonal influenza. Spread of these resistant strains showed potential of enhanced viral replication fitness that was not seen before 2007, whereas the neuraminidase inhibitor-resistant strains had previously compromised replication fitness. The World Health Organization (WHO) declared an influenza pandemic on June 11, 2009, and during that time tested more than 27,000 H1N1 viruses for neuraminidase resistance and found that 447 were oseltamivir resistant. The prevalence of this resistance has continued to grow.

This increase in resistance has led to the study of other proteins within the influenza virus that can be targets of antiviral agents. The influenza virus RNA-dependent RNA polymerase complex is composed of 3 protein subunits: polymerase basic protein 1 (PB1), polymerase basic protein 2 (PB2), and polymerase acidic protein (PA). The acid polymerase protein in influenza virus functions to cleave the mRNA caps and initiate mRNA transcription. In 2016, Jones and colleagues published on RO-7, an endonuclease inhibitor found to inhibit influenza virus replication in vitro in several strains of influenza A (H1N1, H3N2) and influenza B (H5N1, H7N9, H9N2).

**What’s different about baloxavir?**

Baloxavir is a selective inhibitor of cap-dependent endonucleases. It first received global approval on February 23, 2018, in Japan for influenza A and B infections in otherwise healthy adults and children. It has in vivo and in vitro activity against oseltamivir-resistant strains with demonstrated synergism when combined with neuraminidase inhibitors. The pro-drug S-033188 undergoes hydrolysis to active form S-033447, which has a peak concentration within 4 hours as well as a large volume of distribution. It is metabolized by UGT 1A3 (major) and CYP3A (minor) with biliary excretion. Its half-life is up to 80 hours, compared with oseltamivir, the active form of which has a half-life of at most 10 hours.

The CAPSTONE trial was a randomized, double-blind, placebo- and active-controlled phase III trial with 1436 (1064 were included in intention-to-treat infected population) adolescents and adults aged 12 to 64 years with uncomplicated influenza A or B and symptoms for fewer than 48 hours. Patients in the phase III trial were from the United States and Japan, and were enrolled from December 2016 to March 2017. The trial found that those treated with baloxavir had a shorter time to alleviation of symptoms compared with placebo (53.7 hours vs 80.2 hours, respectively; \( P < 0.0001 \)). The trial also found that the time to cessation of viral shedding was decreased when compared with oseltamivir and a placebo (baloxavir group, 24 hours, vs placebo group, 96 hours, \( P < 0.001 \); and vs oseltamivir group, 72 hours, \( P < 0.0001 \)). Time to resolution of fever also was shorter with baloxavir than the placebo group (24.5 hours vs 42 hours, respectively; \( P < 0.001 \)).

In the study, influenza A (H3N2) accounted for 84.8% to 88.1% of infections in the 3 groups, and 77.2% of the patients were enrolled from Japan. When looking at adverse events reported in more than 1% of patients and believed to be related to the trial regimen, the most frequent adverse
The event was diarrhea occurring in 1.8% of patients in the baloxavir group.3 There were no adverse events that led to discontinuation of the trial that were believed to be related to the trial medication. The only 2 serious adverse events reported in the baloxavir group were inguinal hernia and aseptic meningitis.3,7

**Recommendations**

Currently, the FDA is recommending use of this medication in patients aged 12 years and older with symptoms for no more than 48 hours. The FDA recommends administration without dairy products, calcium-fortified beverages, polyvalent cation containing laxatives, or antacids. Baloxavir is currently available as 20-mg and 40-mg oral tablets as a single-dose regimen; 40 mg for those weighing 40 kg to less than 80 kg, and 80 mg for those weighing greater than 80 kg.8 One advantage of single dosing would be increased likelihood of patient adherence to medication regimen completion, especially in the outpatient setting. Similar to its predecessor oseltamivir, baloxavir is currently only recommended in uncomplicated infections as the trials so far have only tested the medication in this population. Further studies will be needed to understand better how to apply the use of baloxavir in the inpatient setting and with more complicated clinical presentations.3,8

Although it is not currently advised, and the studies are limited, there is a potential for synergism between oseltamivir with baloxavir.8 The agents work with completely different mechanisms and so far there are in vitro as well as murine studies that support their use together in humans.11 One small study with 18 healthy adults in Japan did explore this and concluded that there was evidence of synergism between the 2 agents in humans. The authors supported the use of both agents with no dose adjustment as deemed necessary by healthcare providers.12 This could be considered in more complicated or severe cases of influenza infection. However, the study was small and there is very little data that continue to support this, and no official recommendations have been provided as yet.

Further studies are underway to explore other drugs targeting the polymerase complex. However, even with these new drugs being explored, mutations leading to decreased viral susceptibility to antivirals can occur. Currently, there is a known mutation to baloxavir, although the known mutation leads to a virus with decreased ability to replicate.3 Still, while new drugs continue to be investigated, primary prevention with vaccination is currently the best way to prevent serious influenza infection as well as influenza epidemics and pandemics. Patients and providers alike should be encouraged to obtain their influenza vaccine at the early start of each season.13

**NOTE FROM DR LEE** Baloxavir is a welcomed new antiviral agent used for treating influenza. Its novel mechanism of action, single-dose regimen, and relatively mild adverse effect profile provide significant advantages. However, complete pediatric clinical pharmacology data and antiviral durability of this agent remain to be seen.

—Carlton K.K. Lee, PHARMD, MPH, FASHP, FPPAG

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**CONTEMPORARY PEDIATRICS CLINICAL VIDEO EXCLUSIVE**

For Contemporary Pediatrics, Dr Bobby Lazzara discusses the first global trial of a CAR T-cell therapy for children with refractory acute lymphoblastic leukemia that achieved promising survival rates—even remission—in some patients.

ContemporaryPediatrics.com/CAR-T-cell-trial-video
A pediatric epidemic
Deformational plagiocephaly/brachycephaly and congenital muscular torticollis

Pediatric healthcare providers are on the front lines to provide early identification and treatment of plagiocephaly/brachycephaly and torticollis for those infants spending more time supine/reclined and less time prone. Here’s why early intervention is so important.

REGINA FENTON, CRNP; SUSAN A GAETANI, PT, DPT

A pediatric epidemic is sweeping the country. The incidence of infant deformational plagiocephaly and brachycephaly (DPB) and congenital muscular torticollis (CMT) has been on an upward spiral since 1992 when the American Academy of Pediatrics (AAP) instituted the “Back to Sleep” campaign.1 Infants are spending more time supine and in reclined positions day and night and less time prone than in the past.2 We postulate that the widespread increase in DPB and CMT is multifactorial, including frequent use of and/or sleeping in reclined positioners and chairs such as bouncy seats, reclined rockers, swings, and car seats, and dramatically decreased tummy time.

Clinics and pediatrician offices have become inundated with patients exhibiting DPB and CMT, leading to a substantial escalation in costs to the healthcare system. Other repercussions from these diagnoses are an increased need for physical therapy (PT) services and use of helmet therapy (HTT), which place additional stress on a family’s time and financial resources. Most community- and government-funded programs (Birth-to-3, early intervention) are strained to accommodate expanding demand for these services.

The aim of this article is to heighten awareness of this epidemic. Pediatric healthcare providers are on the front lines to intervene early in its evolution, allowing them to identify, prevent, and/or treat DPB and CMT with conservative measures. Hopefully, these measures will reverse the process and decrease or eliminate associated exorbitant healthcare costs.

DPB and CMT
Deformational plagiocephaly/brachycephaly occurs from prolonged pressure on the baby’s skull in utero or soon after birth, causing an asymmetric (plagiocephaly) and/or wide (brachycephalic) head shape. The skull is soft and malleable until ossification
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begins at age 5 to 6 months. When a baby develops a preferred position, the skull will flatten in that area. If the misshapen area is unilateral, the ear, forehead, and cheek will shift anteriorly and impact cosmesis. If the misshapen area is bilateral, the back of the head will widen and may look tall or turricephalic. Incidence of DPB ranges from 18% to 19.7%.3 Congenital muscular torticollis occurs when the sternocleidomastoid (SCM) muscle becomes shortened or restricted unilaterally. The head then turns to the opposite side and/or tilts downward to the same side, resulting in a preferred head position. It becomes difficult for the infant to independently alter head position, and prolonged pressure on the same area occurs when the infant is in a reclined position or sleeping. Also, CMT may develop prenatally due to restricted intrauterine positioning, during delivery, or because of DPB or other external forces. This strains the SCM and surrounding neck musculature causing cervical muscle imbalance and positional preference. The 2 diagnoses usually occur together, creating a synergistic effect.4 Additionally, DPB is strongly associated with CMT—as high as 70% to 95%.3

In the United States, CMT is the third-most common orthopedic diagnosis in infants. Like DPB, its incidence has increased, with a reported range of 0.4% to 1.9% in earlier studies.1,3,7 A rate as high as 16% was reported by 2008.10 Also, CMT has been associated with comorbidities including DPB, facial asymmetries, mandibular asymmetry (MA), developmental hip dysplasia, and gross motor skill asymmetries. Children diagnosed with CMT are treated with skilled PT services to address weakness, range-of-motion limitations, postural deficits, and altered gross motor skill acquisition. A course of PT successfully resolves 90% to 99% of CMT. Surgical intervention (eg, SCM release) is rarely necessary.1,11 Congenital muscular torticollis has an association with MA that can lead to long-term facial asymmetry.1,12 Unilateral ramal height growth restriction, causing jaw asymmetry, results from CMT due to abnormal muscle forces. Mandibular asymmetry can be identified by approximating the mandible to the maxilla. The mandible will cant upward on the side of the head tilt. Physical therapy for the torticollis will address the MA, which is important because MA can affect feeding, especially the ability to achieve latch and adequate suction for breastfeeding.13 Addressing MA early means a greater potential for improvement and resolution. Craniofacial asymmetries, including MA, can become more severe with age when treatment of CMT is delayed or if CMT remains untreated.14

EARLY IDENTIFICATION OF DPB/CMT

- Incorporate evaluation of head shape at 1- and 2-month well-child checks.
- Assess range of motion of neck.
- Educate tummy time: importance of initiating tummy time in newborn period to goal of 81 min/d by age 4 mo.
- Refer to physical therapy if head shape and/or neck concerns.

Abbreviations: DPB, deformational plagiocephaly/brachycephaly; CMT, congenital muscular torticollis. Author created.
Identifying the problem
Most parents notice the flattening or misshaping of their infant’s head shape between age 1 and 2 months. Parents and primary care physicians (PCPs) do not always recognize CMT because presentation may be subtle. Parents tell us they mention their concern about abnormal head shape and/or positional preference to their PCP but are told it will spontaneously improve once the infant is rolling over and sitting upright. They are discouraged when this does not happen. Although many PCPs believe what they are telling concerned parents about spontaneous improvement, this is typically not the case unless interventions are initiated much earlier in infancy.

In the United States in 2017, 3.8 million babies were born. As noted earlier, incidence of DPB ranges from 18% to 19.7%—about 720,000 infants per year born with DPB. About 100 US pediatric plastic surgery/cleft-craniofacial centers each see nearly 100 patients with these diagnoses per month. This does not account for other providers including neurosurgeons or pediatricians. Only about 100,000 of 720,000 infants per year are currently being identified and treated, leaving 86% (620,000) unidentified and untreated. Given long-term, often irreversible, sequelae, this is a serious problem.

Our center’s experience
At our institution, the University of Pittsburgh Medical Center (UPMC) Children’s Hospital of Pittsburgh, Pennsylvania, the cleft-craniofacial center is embedded in the pediatric plastic surgery department. With more than 100 new patients referred to us monthly, most of whom having both DPB and CMT, we developed a multidisciplinary clinic in 2010. Our comprehensive team evaluation and treatment approach includes a nurse practitioner and a physical therapist. With this approach, we are able to institute PT and aggressive repositioning (AR) management at the initial appointment, beginning these conservative measures as soon as possible. Combining these services saves time and money for parents and/or guard-

[FIGURE 1 Normocephalic head shape.]
[FIGURE 2 Unilateral plagiocephaly.]
[FIGURE 3 Brachycephalic head shape.]
Patients receive a wealth of information during a medical appointment, of which about 80% is not retained once they leave the office. To reinforce our recommendations and instruction, we have developed printed patient-education materials to increase understanding and compliance. Handouts include information sheets on DPB and AR techniques as well as brochures about tummy time and torticollis that describe home exercises for CMT.

We also provide community outreach to our regional PCPs and pediatric therapists. Our purpose is to increase awareness of these diagnoses and emphasize the small but critical time frame available to institute conservative measures to treat DPB.

Diagnosis and evaluation
Diagnosis of DPB is determined by physical exam. The cranial exam is performed by having the parent/guardian hold the infant in his/her lap while the nurse practitioner examines the baby from the vertex view (Figure 1). This exam ascertains whether the DPB is unilateral or bilateral. Unilateral DPB most frequently manifests in a parallelogram shape of the head (Figure 2). The flattened side of the head displaces the ear forward anteriorly, causing forehead bossing and fullness of the cheek on the affected side. The orbital opening may be larger on the affected side. Bilateral DPB results in significant brachycephaly (Figure 3). Facial features are not as affected in brachycephalic patients unless both brachycephaly and asymmetry are demonstrated.

When assessing the cranial vault, a hand caliper is used to measure the cranial index (CI), also referred to as the cephalic ratio, defined as the width divided by the length. The oblique diagonal difference (ODD) is a measurement of the asymmetry of the cranial vault. The CI and ODD provide objective guidelines with which to determine DPB severity (Figure 4). Criteria for cranial vault measurements have not been standardized, but an ODD equal to or greater than 12 mm (and/or confidence index [CI] ≥1.0) has been used to denote DPB as severe. These measurements guide treatment decision-making; eg, mild DPB is treated conservatively with AR and PT.

If the baby is aged 4.5 to 5 months or older and has moderate or severe cranial vault measurements, the parent/guardian is offered HT as a choice. The infant must show adequate head and neck control. We verify this developmental achievement by performing a pull-to-sit test to ensure a strong chin tuck is present and there is no head lag (Figure 5). If head lag exists, we recommend increasing tummy time to achieve improved head and neck control and a return visit once adequate head and neck control is achieved. Helmets weigh about 8 ounces, which is a significant weight to place on an infant’s head. Infant safety must be ensured with HT as poor head and neck con-
trol combined with the weight of a helmet could potentially compromise respiratory status.

**Differential diagnosis**

When evaluating these patients, differential diagnoses including craniosynostosis, macrocephaly, hemifacial microsomia, and hydrocephalus must be considered. The occipital frontal circumference is obtained to evaluate for macrocephaly. If there are concerns about head size, we refer to neurosurgery for further evaluation. Cranial sutures are evaluated via palpation for any indication of suture ridging, which can be suggestive of craniosynostosis (fusion or premature closure of skull sutures). If cranial suture ridging is identified and findings are consistent with craniosynostosis, a 3-dimensional computed tomography (3D CT) scan is indicated and HT deferred until it is completed.

Skull x-rays are rarely indicated or helpful. If the 3D CT scan shows craniosynostosis, the patient is referred to a craniofacial surgeon. If the scan does not indicate craniosynostosis, HT can be considered. Some asymmetric facial features observed in children with mild hemifacial microsomia may also be seen in children with DPB and CMT. Children with hemifacial microsomia, however, typically do not present with DPB and/or CMT.

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**Flattening of the skull on the back or side of an infant’s head—also known as positional plagiocephaly and/or brachycephaly (PPB)—is a common problem seen in pediatric practice.** Although flattened skulls in infancy, often considered a benign issue, can be corrected, a new study investigates the long-term cognitive outcomes of more severe malformations.

In a new study published in *Pediatrics*, researchers evaluated the long-term cognitive and academic impact of PPB. In a separate study, published in the *European Journal of Pediatrics*, 37.8% of infants had some degree of plagiocephaly by age 8 to 12 weeks, and another 15% presented with brachycephaly. Plagiocephaly is defined as a flattened head on one side resulting in asymmetry, possibly accompanied by misaligned ears. In brachycephaly, the back of the head becomes flattened, resulting in a widened head and occasional bulging of the forehead. These conditions can be caused by positioning in the womb or after birth, with a spike in cases noted after the American Academy of Pediatrics issued its recommendation that infants sleep flat on their backs to prevent sudden infant death syndrome (SIDS).

**Not so benign?**

Whereas these common conditions have long been thought to be a benign cosmetic issue, the research team that developed the new *Pediatrics* study notes that associations have been made between PPB and neurodevelopmental deficits. In a new study published in *Pediatrics*, researchers evaluated the long-term cognitive and academic impact of PPB. In a separate study, published in the *European Journal of Pediatrics*, 37.8% of infants had some degree of plagiocephaly by age 8 to 12 weeks, and another 15% presented with brachycephaly. Plagiocephaly is defined as a flattened head on one side resulting in asymmetry, possibly accompanied by misaligned ears. In brachycephaly, the back of the head becomes flattened, resulting in a widened head and occasional bulging of the forehead. These conditions can be caused by positioning in the womb or after birth, with a spike in cases noted after the American Academy of Pediatrics issued its recommendation that infants sleep flat on their backs to prevent sudden infant death syndrome (SIDS).

To test these associations further, a research team evaluated 336 children with a mean age of 9 years who had had PPB in infancy. Researchers found that children with moderate to severe PPB were more likely to have required some form of developmental intervention than their peers, with 66% of the children who had PPB in infancy requiring intervention compared with 21% of their peers. Twenty-eight percent of the children in the PPB cohort had had mild PPB as infants and 72% had moderate to severe PPB. As for treatment during infancy, 34% had worn orthotic helmets to treat their PPB, and 45% had torticollis—a twisting of the neck muscles caused by positioning of the head.

Although mean cognitive and academic scores for the PPB cohort were generally within average range, the research team **continued on page 16**
Role of the physical therapist

The physical therapist evaluates the patient’s neck, spine, hips, feet, and provides gross motor skill screening. If the infant has CMT, parents and/or guardians are educated about it, taught exercises to begin immediately, and counseled on initiating PT services via outpatient or early intervention (Birth-to-3). In our state, parents/guardians often opt for early intervention because the state-funded programs do not require insurance and provide the convenience of a physical therapist coming to the home, daycare, or sitter’s home. Such services can take up to a month to initiate, so exercises must start right away. Frequency of PT is weekly or every other week, becoming less frequent as the infant improves. Standard of care for CMT is to continue with PT until the child is walking independently to ensure gross motor milestones are achieved and performed symmetrically.\textsuperscript{11}

Up to 99% of CMT resolves with PT and less than 0% to 1% requires surgical intervention.\textsuperscript{11} Often CMT manifests with soft tissue restriction of the neck and shoulders, including fibromatosis colli within the SCM in 10% to 50% of cases.\textsuperscript{1} Families are taught massage for the soft tissue restrictions, which can take months to resolve. Also, a 10% to 14.9% correlation of CMT with developmental hip dysplasia has been documented.\textsuperscript{1,16,17} The physical therapist undertakes a clinical hip evaluation, and if there are any concerns, the patient is referred to a pediatric healthcare provider or to orthopedics.

Critical importance of tummy time

Initiating awake prone time immediately is crucial in the newborn period. Although parents are well educated about the Back to Sleep campaign to prevent sudden infant death syndrome, they rarely receive sufficient information on the benefits and techniques of tummy time. Our brochure on tummy time reviews techniques for families to use to achieve the goal of 81 minutes by age 4 months.\textsuperscript{2}

Tummy time strengthens the infant’s neck and core and relieves pressure from the head. It is inexpensive, easy to do, and does not require additional products or have associated costs. It would be most beneficial if tummy time were reviewed by the pediatrician or healthcare personnel within the practice during the first newborn appointments. The slogan “Back to sleep, tummy to play”
establishes a simple but important message.

**Impact of aggressive repositioning**

If patients are referred early, between age 0 and 4 months, we initiate the conservative measures of AR and PT. Such techniques are effective then because the skull is soft and malleable until age 5 to 6 months. We strongly support the AAP recommendations of sleeping on a flat, firm surface. Many families have their babies sleeping in reclined chairs, which we believe exacerbates DPB and CMT. In an effort to minimize pressure on the misshaped side of the head, we teach families to use AR. We use a receiving blanket rolled up like a log and tucked behind the affected side of the head, shoulder, waist, and hip when the baby is resting, especially in reclined chairs (eg, bouncy, Fisher Price Rock ‘n Play, or swing chairs). The goal is to minimize repositioning and increase upright seating when developmentally appropriate.

Upright chairs for emerging sitters (eg, Bumbo, Fisher Price Sit-Me-Up, Summer Infant, BebePod) are recommended at age 3 to 4 months. These chairs provide necessary back support but allow pressure to be removed from the head. They should be introduced in short intervals, increased as the baby adjusts, and placed on the floor, never on a table or counter due to concern over fall risk. Parents are encouraged to use front carriers in their daily activities to remove pressure from the baby’s head.

Feeding techniques for both bottle-feeding and breastfeeding are provided to support the head and neck, reducing pressure on the affected side of the skull. It is important to reduce laying the baby’s affected side of the head on an arm or items like a pillow. Visual stimulation encourages the baby to look to the opposite side from the DPB.

We use AAP guidelines and state trooper guidelines for car-seat positioning.18 These guidelines require the infant be safely buckled into the car seat and the blanket roll tucked behind the affected side of the head, shoulder, and hip outside of straps and buckles. The family is taught to take the infant out of the reclined car seat upon reaching their destination to prevent further pressure on the affected side of the head. This can be done by holding the baby, using a front carrier, or, when developmentally appropriate, the stroller. We offer a prescription for AR if the baby is enrolled in daycare.

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**Cranial remolding helmet therapy**

Patients return for further evaluation between age 4.5 and 5 months. If conservative techniques have been effective in improving or halting progression of DPB and its severity does not meet criteria for HT, we recommend continuing AR and PT. If between 4.5 and 5 months infants still show significant DPB and meet criteria, we offer HT and many parents agree to it. Again, HT has proved most effective when the skull is still malleable, brain growth is robust, and when initiated prior to the ossification process.19 We inform families that DPB is a functional cosmetic issue because patients need to fit into safety helmets properly when they begin to ride bikes or play helmeted sports. Risk of concussion should not be increased by an ill-fitting helmet due to an abnormal head shape.

Although highly effective, HT can be time consuming and stigmatizing. Often, mothers tell us they feel they have done something to cause this problem. Many cultures are not open to HT. The potential adverse effects of HT include skin issues; ie, rashes, pressure areas, wounds, contact dermatitis, and exacerbation of eczema, seborrhea, or cradle cap. Infants also can become overheated when wearing helmets. Loss of work due to follow-up appointments for adjustments can impact the family. Finally, HT can be very expensive and insurance coverage may be lacking.

Of note, the AAP clinical report from 2011 found no evidence that molding helmets work any better.

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**TUMMY TIME EFFECTIVE POSITIONS**

- Baby lays with face to parent chest.
- Baby lays over parent lap.
- Chest down, hold over arm.
- Baby lays on floor with roll under chest.

**AGGRESSIVE REPOSITIONING**

- Tip baby to nonaffected side when reclined.
- Upright: Bumbo, Fisher Price Sit-Me-Up, Summer Infant, BebePod
- Front carrier
- Feeding: breast and bottle
- Car seat
- Sleeping

*Author created.*
It concludes that a body of nonrandomized evidence has shown “more significant and faster improvement of cranial shape in infants with positional plagiocephaly treated with a helmet in comparison with conservative therapy, especially if the deformity is severe, provided that helmet therapy is applied during the appropriate period of infancy.”

We propose, however, that AR and PT initiated early enough have the potential to be as effective as HT in addressing DPB. Patients are rarely referred to us in this early critical timeframe, but when they are, the conservative measures of AR and PT halt or reverse DPB, resulting in substantial improvement and even negating the need for HT. Although it has not been our experience, concerns exist about the overprescribing of HT, but that issue is beyond the scope of this article’s focus.

The epidemic of DPB and CMT has caused a significant financial burden on the healthcare system, especially when HT is used. As the majority of infants are referred too late to institute conservative measures, HT becomes the only option, one that we estimate costs $3.6 million at our center for approximately 900 patients per year.

The United States has over 100 craniofacial centers, and certainly specific costs attributed to this problem vary among them. Nevertheless, referencing our costs for HT as well as plastic surgery consults and PT evaluations and sessions, and multiplying it by 100 centers across the country, the rough gross estimate for costs nationwide quickly reaches more than $1 billion. As well, this estimate does not include costs for patients treated by neurosurgery centers or other providers, missed work, or transportation.

Prevention

Few medical issues occur with this prevalence in otherwise healthy infants, and little attention has been paid to prevention or early treatment in light of the increased numbers of infants with this diagnosis since 1992. Research supporting effective prevention strategies is scant. We recently completed a pilot study approved by the Institutional Review Board that demonstrated support of early referral resulting in less-frequent HT. A Finnish study also has shown that initiating preventive education in the maternity ward from the time infants are born provides significant reduction in the number of infants who develop deformational plagiocephaly or require HT.1

Conclusion

Pediatric healthcare providers are in the best position to identify and manage DPB and CMT. Evaluation of the infant’s head shape and range of motion of the neck should be incorporated into the 1- and 2-month well-child appointments. If any concerns are noted, AR and referral to PT should be initiated immediately.

Lack of intervention or suggesting it will resolve once the baby is rolling and sitting is usually a fallacy. Conservative measures are most effective when the skull is still malleable prior to onset of ossification. If no improvement is observed by the 4-month well-child appointment, referral to a specialist is recommended. Early identification and treatment are critical. They can dramatically improve the patient’s course and provide the momentum to begin to minimize, and hopefully reverse, this epidemic.
Ocular emergencies
What pediatricians and frontline physicians need to know

When a child presents with an eye injury, frontline clinicians should implement this 5-minute eye exam to quickly recognize what treatment is warranted and when to refer to an ophthalmologist.

MARY BETH NIERENGARTEN, MA

Five minutes. That’s how long it takes to do a basic eye exam to determine how urgent an ocular problem is and the appropriate approach for treatment. It is an exam that every pediatrician, pediatric emergency medicine physician, and other frontline clinicians need to know when presented with a child with an ocular problem, particularly those who present to the emergency department (ED).

“The first person to see the child in case of an eye emergency can be of enormous value in preventing and treating the eye injury and subsequent visual loss,” says Donny Suh, MD, FAAP, chief of Pediatric Ophthalmology and Adult Strabismus, Children’s Hospital and University of Nebraska Medical Center, Omaha, Nebraska.

As a pediatric ophthalmologist, Suh typically is not the first person to see an eye injury in a child and relies on the diagnostic and clinical skills of pediatricians and other frontline clinicians to know when an eye injury warrants referral to an ophthalmologist.

To help pediatricians and other frontline clinicians better understand when such a referral is needed, and how timely that referral needs to be, Suh provided some basic information about how to diagnose and triage a child who presents to the ED with an eye injury.

At the 2018 American Academy of Pediatrics (AAP) National Conference and Exhibition in Orlando, Florida, Suh presented such information during a session titled “Pediatric ocular emergencies you can’t afford to miss.” He was joined by Binita R. Shah, MD, FAAP, Distinguished Teaching Professor of Emergency Medicine and Pediatrics, State University of New York (SUNY) Downstate Medical Center, Brooklyn, New York, who spoke from the perspective of pediatric emergency medicine physician. Together they presented a number of case studies in an interactive presentation in which audience members were invited to participate to test and improve their knowledge of how to diagnose a given eye problem and, importantly, how to triage the patient based on the urgency of the injury.

“Within 5 minutes, you can do 5 essential eye examinations that will enable you to figure out if the patient has an emergency problem, an urgent problem, or a routine problem.”

–Binita R. Shah, MD, FAAP
“The presentation provides a practical step-by-step guide to evaluate and manage the pediatric ocular injuries resulting from trauma, infections, and tumors,” says Suh.

5 questions in 5 minutes

Suh began the presentation by talking about the importance of the simple 5-minute eye test that consists of 5 eye exams that every clinician needs to know (Table 1).

According to Shah, these eye exams are well known to physicians and are a part of their medical training. For children who arrive in the ED with an eye injury, using this 5-minute test is critical to appropriately triage the child based on the urgency of the condition. “This is very important,” says Shah. “Within 5 minutes, you can do 5 essential eye examinations that will enable you to figure out if the patient has an emergency problem, an urgent problem, or a routine problem.”

Table 2 lists conditions considered as emergency, urgent, and routine. For both a child who has an injury that is considered an emergency (immediate) or one that is considered urgent (can wait to be evaluated/treated within 24 to 48 hours), a pediatric ophthalmologist should be included to either confirm the diagnosis and/or manage treatment.

The rest of the presentation was devoted to presenting case studies to illustrate how a pediatrician, pediatric emergency physician, or other frontline clinician would approach a child presenting with given symptoms by first using the 5-minute exam and then deciding on the appropriate triage.

Case studies

A number of case studies were presented to illustrate the diagnostic and triage approach to each. Shah opened each case study by describing the pre-

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>5 ESSENTIAL EYE EXAMS IN 5 MINUTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>DETAILS</td>
<td>TRIAGE</td>
</tr>
<tr>
<td><strong>1</strong> Visual acuity</td>
<td>□ Patch the eye for accurate vision testing. □ Do a physical exam.</td>
</tr>
<tr>
<td><strong>2</strong> Pupil</td>
<td>□ Signs of intraocular damage: eye swelling with no view of the pupil. □ Suspected corneal abnormality: fluorescein stain with topical anesthetic or saline, moistened fluorescein strip, or fluorescein (orange color); fluoresces yellow-green when exposed to blue light.</td>
</tr>
<tr>
<td><strong>3</strong> External exam</td>
<td>□ Pull eyelid with history of trauma, foreign body, or lid laceration.</td>
</tr>
<tr>
<td><strong>4</strong> Motility</td>
<td>□ Double vision: warning sign indicating a possible blowout fracture.</td>
</tr>
<tr>
<td><strong>5</strong> Fundus exam</td>
<td>□ Attempt to look at the fundus if possible. Look for signs of optic nerve swelling.</td>
</tr>
</tbody>
</table>

From Shah B, et al.¹

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>OCULAR INJURIES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EMERGENCY: NEED IMMEDIATE ATTENTION</strong></td>
<td><strong>URGENT: NEED ATTENTION WITHIN 24-48 H</strong></td>
</tr>
<tr>
<td>Chemical injuries</td>
<td>Hyphema</td>
</tr>
<tr>
<td>Ruptured globe</td>
<td>Foreign body</td>
</tr>
<tr>
<td>Retrobulbar hemorrhage with high eye pressure</td>
<td>Eyelid lacerations</td>
</tr>
</tbody>
</table>

From Shah B, et al.¹
### TABLE 3
**CASE STUDIES**

<table>
<thead>
<tr>
<th>PRESENTING SYMPTOMS</th>
<th>DIAGNOSIS</th>
<th>TAKE-HOME MESSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT 1</strong> Formerly healthy infant presents with periorbital skin rash.</td>
<td>Ocular herpes simplex viral infection (HSV)</td>
<td>May present with recurrent ocular infections.</td>
</tr>
<tr>
<td><strong>PATIENT 2</strong> Adolescent with history of dry eyes presents with intense eye pain, excessive tearing, and foreign body sensation in the eye.</td>
<td>Corneal abrasion</td>
<td>Never dispense topical anesthetic for continued use.</td>
</tr>
<tr>
<td><strong>PATIENT 3</strong> An 11-month-old infant presents with anemia and weight loss.</td>
<td>Neuroblastoma</td>
<td>Most common metastatic tumor of the orbit (about 20% of patients with neuroblastoma).</td>
</tr>
<tr>
<td><strong>PATIENT 4</strong> Adolescent male hit in the eye with a ball in the gym; now complains of eye pain and somnolence.</td>
<td>Hyphema</td>
<td>Without history of trauma, exclude underlying disease such as coagulopathy or sickle cell disease.</td>
</tr>
<tr>
<td><strong>PATIENT 5</strong> A 6-year-old boy with history of rhinorrhea, cough for 12 d, and temperature of 104°F; not able to open his eye.</td>
<td>Orbital cellulitis</td>
<td>Recognize cardinal signs of orbital cellulitis (proptosis with globe displacement, impaired ocular motility, loss of visual acuity, ophthalmoplegia).</td>
</tr>
<tr>
<td><strong>PATIENT 6</strong> Child accidentally splashes the eye with an unknown solution.</td>
<td>Chemical injury</td>
<td>Initial treatment is irrigation, checking the PH, followed by more irrigation.</td>
</tr>
<tr>
<td><strong>PATIENT 7</strong> Adolescent male presents with blurry vision and eye pain after a forceful blow to the eye.</td>
<td>Ruptured globe</td>
<td>Stop further manipulation of the eye!</td>
</tr>
<tr>
<td><strong>PATIENT 8</strong> A 2-year-old previously healthy child incidentally noted to have white reflex of the eye (leukocoria).</td>
<td>Retinoblastoma</td>
<td>Presence of bilateral red reflexes suggests absence of cataracts or other intraocular pathology.</td>
</tr>
<tr>
<td><strong>PATIENT 9</strong> Infant admitted for bronchiolitis with chest radiograph showing incidental finding of bilateral rib fractures.</td>
<td>Abusive head trauma (shaken baby/impact syndrome) • Retinal hemorrhages • Acute subdural hematoma • Metaphyseal chip fractures • No external signs of trauma</td>
<td>Typically, numerous retinal hemorrhages, extensive, and involving multiple layers of the retina.</td>
</tr>
</tbody>
</table>

Abbreviation: FB, foreign body; IV, intravenous. 
From Shah B, et al.1
senting symptoms of a child, giving the audience time to weigh in (online using an app downloaded onto their smartphones, iPads, and other devices) on the diagnosis and/or initial treatment, and then discussing the correct answer.

“As the focus of our presentation was on ocular emergencies (related to either acute injuries, infections, or tumors), every case study included the need for an ophthalmologist,” says Shah, adding that each case study required referral to an ophthalmologist either for confirmation of the diagnosis or referral for treatment.

Table 3 lists 9 case studies along with presenting symptoms, diagnosis, and main take-home points.

Summary
It is important for pediatricians, pediatric emergency room physicians, and other frontline clinicians to implement a 5-minute eye exam when presented with a child with an eye injury to quickly recognize whether the injury warrants emergency attention, urgent attention, or is routine.

Referral to a pediatric ophthalmologist is warranted for most emergency and urgent cases. The case studies in this presentation illustrate injuries that would involve referral to an ophthalmologist. Table 4 provides a list of changes to your practice that both Suh and Shah recommend.

For more information on specific eye injuries, see “Eye terms and conditions” on the American Association for Pediatric Ophthalmology and Strabismus website: www.aapos.org/.

Readers also can explore additional information in the Resources section of this article.

TABLE 4
CHANGES TO MAKE IN PRACTICE

- Master the 5 essential steps of basic eye examination.
- Recognize the cardinal signs of orbital cellulitis as orbital infections are vision and/or life threatening.
- Know the indications for computed tomography scan and specialist consultations for “swollen eye.”
- Know how to recognize orbital tumors presenting with proptosis and periorbital discoloration. These tumors can mimic orbital infections. Misdiagnosis and delays in recognition of either condition can lead to serious consequences.
- Immediately irrigate the eye of a patient with suspected chemical exposure to the eye. Don’t wait for a specialist to see the patient first.
- Do not use or prescribe topical steroids for pink eye or in a patient with any signs of viral infection.
- An eye exam is needed for any patient who presents with suspected head trauma from abuse, even without any observable findings. Patients with abusive head trauma may only have ocular findings with retinal hemorrhage.

From Shah B, et al.1

ADDITIONAL RESOURCES

The clear message to pediatricians from a recent prospective study looking at new onset uveitis risk in juvenile idiopathic arthritis (JIA) is to encourage patients and families to get the recommended eye exams, even when patients don't have ocular or joint symptoms.1

Juvenile idiopathic arthritis is the most common pediatric rheumatic disease and uveitis is one of its most frequent and potentially devastating extra-articular manifestations with complications that can compromise eyesight, according to the article's senior author Karen N. Watanabe Duffy, MD, FRCPC, a rheumatologist in the Division of Rheumatology, Department of Pediatrics, at the Children's Hospital of Eastern Ontario (CHEO), Ottawa, Ontario, Canada.

"JIA-uveitis is most often asymptomatic, and those who are at highest risk for uveitis are younger children who are diagnosed with JIA before the age of 7 years and those with a positive antinuclear antibody (ANA). Children with JIA should have screening eye examinations for at least 5 years after JIA diagnosis," Watanabe Duffy writes, who is also an associate professor of Pediatrics at the University of Ottawa, writes in an e-mail to Contemporary Pediatrics.

**JIA and uveitis**
The prevalence of JIA is about 1 to 4 for every 1000 children, and when JIA-associated uveitis does occur in these patients, more than half will develop vision-threatening complications.2 Early detection and vigilant screening are essential to reduce ocular complications, including blindness, Watanabe Duffy writes.

**Key points from the study**
Watanabe Duffy and colleagues studied data from the Research in Arthritis in Canadian Children Emphasizing Outcomes (ReACCh-Out) inception cohort, including 1183 patients enrolled within 6 months of their JIA diagnosis. The researchers report 87 of those patients, who were followed for up to 5 years, developed new-onset uveitis post-enrollment.

The researchers found the incidence of new-onset uveitis was 2.8% each year in the first 5 years after diagnosis. Whereas the annual incidence fell slightly from the first through fifth year post-JIA diagnosis, incidence was still 2.1% in the fifth year.

"This article is the first to demonstrate the yearly incidence of uveitis, highlighting the importance of vigilance in screening."—AnneMarie C. Brescia, MD, FAAP, FACR

Notably, JIA subtype and female sex were not independent predictors for JIA-related uveitis. Rather, being aged younger than 7 years at JIA diagnosis and having positive ANA were independent predictors, according to the paper published in Arthritis Care and Research.1 "This article is the first to demonstrate the yearly incidence of uveitis, highlighting the importance of vigilance in screening. [It's] important to note, although we concentrate on the younger patient, the oldest patient was 18.4 years at uveitis diagnosis. So, although less likely, uveitis can still appear in older children," according to AnneMarie C. Brescia, MD, FAAP, FACR, chief of Pediatric Rheumatology at Nemours/Alfred I duPont Hospital for Children, Wilmington, Delaware. Brescia is not an author on the paper.

**What pediatricians need to know**
Although pediatric rheumatologists make it a point to encourage JIA pa-
tients to get recommended ophthalmology screenings, it’s often not enough to get families and patients to comply, according to Sheila T. Angeles-Han, MD, MSC, associate professor of Pediatrics, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio.

Families might not understand the urgency of going for regular screenings when their children don’t have symptoms and aren’t suffering. The demand on families can be substantial, says Han, whose research focus is in uveitis associated with JIA, but she is not an author of the paper featured here.

“Children who are at highest risk for uveitis need regular ophthalmology screening every 3 months for several years. [Because] they often have no symptoms, the best way to screen is through a slit-lamp examination. The frequent visits can be a burden for families, but that’s the only way to detect eye inflammation unless the child has developed eye complications. By then, the damage from uveitis has occurred. You want to detect the uveitis before you get complications,” Han says. “[Because] these children are regularly seen by their pediatricians with whom they have a close relationship, I think it’s important that pediatricians emphasize the importance of screening, as well.”

For how often those visits should occur according to risk, pediatricians can refer to “Ophthalmologic examinations in children with juvenile rheumatoid arthritis” published in 2006 in Pediatrics. They can also refer to the “Consensus-based recommendations for the management of uveitis associated with juvenile idiopathic arthritis: the SHARE initiative,” in an open access paper published August 2018 in the Annals of the Rheumatic Diseases.

“Ongoing monitoring by the pediatrician is crucial to ensure that patients undergo eye examinations on a recommended and ongoing basis according to contemporary and audited screening protocols,” Watanabe Duffy writes.4 Han says pediatricians should note that JIA patients need the screenings even when their arthritis is inactive or well controlled.

“Some patients think that because their arthritis is well controlled, they don’t need to continue with their eye screenings with ophthalmology, but the arthritis and uveitis activity don’t parallel each other. You can have arthritis that’s in remission or inactive and still develop the uveitis,” Han says.

Pediatricians should also note that ophthalmologists might treat JIA-associated uveitis with systemic immunosuppressive medicines when topical medicines are insufficient or result in adverse effects, such as glaucoma or cataracts, according to Brescia.

“Kids with JIA who are not on immunosuppressive medications can get all the vaccines. Kids with JIA on systemic immunosuppressive medicines should not get the live virus vaccines,” Brescia writes in an e-mail to Contemporary Pediatrics.

**Uveitis risk and JIA treatment**

Medications used to treat arthritis, including methotrexate and some of the tumor necrosis factor (TNF) inhibitors, are also used to treat uveitis, according to Han. Research is showing that being on these medications for JIA may change whether a child will develop uveitis, she says.

However, children with JIA who are in the process of tapering and stopping systemic immunosuppressive therapy after a period of remission are at risk for developing new-onset uveitis, according to Duffy.

“It is recommended that those who discontinue such treatment should have screening eye examinations every 3 months for 1 year,” Watanabe Duffy writes.4 The researchers note that a limitation of the study was that it was only for 5 years.

“It would be important to determine what the risk is after that 5-year period,” Han says.

Ms Hilton is a medical writer who has covered health and medicine for 25 years. She resides in Boca Raton, Florida. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

For references, go to ContemporaryPediatrics.com/JIA-eye-screening

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**PLUS** See “Ocular emergencies: What pediatricians and frontline physicians need to know,” page 19.
Dental caries (cavities) continues to be the most chronic disease of childhood. Although dental caries is multifactorial in its etiology, fluoride is an important chemotherapeutic intervention to strengthen teeth and prevent disease progression. The safety of fluoride has been demonstrated in numerous research studies and community water fluoridation heralded as one of the top 10 public health achievements of the 20th century by the Centers for Disease Control and Prevention (CDC).

How fluoride prevents dental caries
Fluoride works to prevent dental caries through both topical and systemic mechanisms via 3 processes: inhibiting tooth demineralization, enhancing remineralization, and inhibiting bacterial metabolism. Newer studies also suggest that fluoride interferes with bacterial adherence to the teeth. The topical effect provides the majority of the benefit. Through systemic mechanisms, the lesser effect, fluoride is incorporated into the tooth structure during tooth development to harden the enamel and make
it more resistant to demineralization. What type of fluoride is recommended

Topical fluoride in the form of toothpaste (at-home use) and varnish (in-office use) should be recommended for all children starting at tooth eruption.²,⁵ The American Academy of Pediatrics (AAP) and United States Preventive Services Task Force (USPSTF) also recommends dietary fluoride supplements for all children who do not have an adequate supply of fluoride in their primary drinking water. The AAP additionally recommends fluoride mouth rinse use for children aged 6 years and older who are at high risk for dental caries.²,⁶

**TOPICAL FLUORIDE**

**Toothpaste:** Fluoridated toothpaste is recommended upon initial tooth emergence during infancy and throughout life.²,⁴ Do not recommend fluoride-free “training toothpaste.”

1. From tooth emergence until age 3 years, a grain of rice-sized (or “dab”) amount of fluoride toothpaste should be used to brush the teeth both morning and night (Figure 1).

2. For children aged older than 3 years, or when a child can effectively spit, a pea-sized amount of fluoride toothpaste should be applied morning and night (Figure 2).

Children should be encouraged to spit after brushing. Post-brushing rinsing with water should be limited to provide optimal fluoride exposure to the teeth from the toothpaste.³,⁹ Fluoride toothpaste, like all other medications, should be kept out of reach of small children.

**Mouth rinses:** Over-the-counter fluoride rinses may be beneficial for use for children, particularly those who have high caries risk or live in fluoride-deficient areas. Mouth rinses should be reserved for high-risk children aged older than 6 years who can rinse and spit.²,¹⁰ Alcohol-containing mouth rinses should be avoided in pediatric populations.⁷ Fluoride mouth rinses, supplements, or gels can be used after brushing with fluoride toothpaste.

**Varnish:** Fluoride varnish is a highly concentrated form of topical fluoride that is applied to teeth in a professionally supervised setting. Research shows fluoride varnish is highly effective in caries reduction with a decrease in caries incidence between 18% to 24% in 1 study and as high as 59% in another.¹¹,¹² The USPSTF “recommends that primary care clinicians apply fluoride varnish to the primary teeth of all infants and children starting at the age of primary tooth eruption” through age 5 years.⁶ The recommended fluoride varnish dose is 0.25 mL unidose 5% NaF (2.26% F), and frequency is every 3 to 6 months, based on the child’s caries risk considerations.²,¹³ Fluoride varnish application is easy and fast. A thin layer should be placed on relatively dry teeth achieved by wiping the teeth with gauze.

The steps in fluoride application are:¹³

1. Assemble a light source, gauze, and varnish.
2. Use gauze to blot the teeth dry. Varnish does not adhere well to teeth if they are wet.
3. Prepare for application by stirring the varnish and apply varnish to dried teeth, starting on the back teeth. Apply a thin layer to all tooth surfaces with the supplied brush.
4. Apply varnish to the front teeth last. Saliva contamination after application is expected and varnish sets...
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Provide caregiver instructions about varnish application after care (Table 1).

Instructional videos of proper fluoride varnish application technique can be viewed online in the National Smiles for Life Curriculum Module 6: www.smilesforlifeoralhealth.com.

Fluoride varnish application is a safe and effective procedure now reimbursed by Medicaid in all 50 states and by private insurers in many states. In some states, not only physicians and advanced practitioners but also nurses and medical assistants can apply the varnish. In many states, trained individuals are available to instruct pediatric office personnel on fluoride varnish application. The AAP has a designated Chapter Oral Health Advocate in most states who can educate individuals and offices on fluoride varnish application or provide support as questions arise about oral health integration into practice.

Developing a clinical workflow to include fluoride varnish application can improve the oral health of children within a practice. A recent Qualis Health White Paper offers specific strategies for integration of oral health into practice workflow.

Other forms of topical fluoride: Dental providers may recommend other forms of topical fluoride, including highly concentrated fluoride gels. However, these are generally not recommended for young children aged younger than 6 years. In addition, silver diamine fluoride is a modality now being used in dentistry to help arrest caries in primary teeth.

Community water fluoridation: Lastly, fluoridated community water aids in prevention of dental caries by up to 27% and reduces dental expenditures per capita by providing both topical and systemic routes of fluoride. Fluoridated tap water use should be encouraged instead of bottled water use, which may not contain fluoride and may be more acidic than previously anticipated, thus promoting demineralization of tooth structure. Parents who live in areas with fluoridated water should be asked if their child drinks fluoridated water. Parents often use bottled water and therefore their children may not be receiving the benefits of fluoridated water. Pediatric medical and dental providers should continue to strongly advocate for community water fluoridation as it benefits not only children, but the entire population.

**SYSTEMIC FLUORIDE**

The AAP recommends systemic (dietary) fluoride supplementation in children aged 6 months to 16 years who live in areas where the primary water supply is fluoride deficient. It is important to ask about sources of fluoride in a child’s diet, such as fluoride in well water, and the fluoridation status of the local communities. Fluoride levels for well water should be determined before prescription of fluoride dietary supplements, as wells in some locations may exceed the recommended fluoride levels. For town water, the state Department of Health or the CDC’s My Water’s Fluoride website are good resources to determine fluoridated amounts in the water supply throughout individual states.

Systemic fluoride is usually prescribed by a medical or dental provider and comes in 2 forms, a liquid or a tablet. The liquid, most often used for young children aged younger than 3 years or whose primary molars are either not present or emerging, can be mixed with a small amount of water or applied into the mouth directly onto the teeth. In older children, the tablet is used and is available in 3 dosages: 0.25 mg fluoride, 0.5 mg fluoride, and 1 mg fluoride (Table 2). The tablet should be chewed or allowed to dissolve in the mouth for optimal exposure of the teeth to fluoride. Both the liquid and supplement should not

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**Primary care providers should be aware of the appropriate fluoride modalities to advise for children at each age.**
be given within 1 hour of milk products as calcium binds fluoride and inhibits its absorption.\textsuperscript{25}

**Challenges**

Inconsistencies remain in dietary fluoride prescribing guidelines among national organizations. The AAP and USPSTF recommend use of fluoride supplements for all children living in fluoride-deficient areas, whereas the American Academy of Pediatric Dentistry (AAPD) and the American Dental Association (ADA) recommend dietary fluoride supplementation only for children determined to be at high caries risk who drink fluoride-deficient water. Discrepancies in messaging between the medical and dental communities present a clinical challenge for primary care providers and underscores the value of a collaborative relationship between primary care and the local pediatric dental provider. Some primary care providers choose to let dental providers develop the plan of fluoride use once a child has established a dental home.

The fear of fluorosis has fueled some concerns about fluoride use. Fluorosis occurs when developing teeth are exposed to high quantities of fluoride. Fluorosis presents as white streaks or mottling on the tooth surface (Figure 4), with the milder presentations typically not noticeable except by a trained dental professional.\textsuperscript{26} The risk of fluorosis increases when fluoride is not used appropriately, such as eating large amounts of fluoride toothpaste during unsupervised brushing, or prescribing fluoride to a child who already is drinking fluoridated water. Recommend that caregivers always supervise young children during tooth brushing and keep toothpaste in a safe location out of reach of young children, just like other medications in the home.

Many other fears, such as fluoride causing cancer or a low IQ, do not have a basis in scientific evidence. A good AAP website to refer to patients to help address these myths is likemyteeth.org/. It is important to understand concerns regarding fluoride and seize the opportunity to use motivational interviewing beginning with open-ended questions that promote dialogue, such as: “What have you heard about fluoride?” or “Help me understand your concerns about fluoride use.”

There may be times when you have given the family all the facts and they may continue to refuse fluoride. In these situations, it is best to make certain the patient has early and consistent dental care to continue the discussion. Consistent messaging from the primary care provider and dental specialists may help allay fears and encourage families to use fluoride.

Three strategies to consider are:

1. **Reassure**—Use language such as: “Fluoride is safe to use in appropriate amounts.”

2. **Refer**—Provide information from credible websites such as likemyteeth.org/. Recommend early establishment of a dental home to help deliver consistent messages about fluoride use.

3. **Renegotiate**—Consider alternate fluoride usage routes if needed. Typical caregiver concerns about fluoride safety relate to ingestion of the product. As topical fluoride is the most beneficial, encourage compromise with use of limited fluoride in toothpaste, varnish, or mouth-rinse form.

### TABLE 2

**Fluoride Recommendations in the Primary Care Office**

<table>
<thead>
<tr>
<th>AGE</th>
<th>TOOTH ERUPTION TO &lt;3 Y</th>
<th>3 Y TO &lt;6 Y</th>
<th>6 Y +</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluoride toothpaste</strong></td>
<td>Grain of rice or “dab”</td>
<td>Pea-sized</td>
<td>Pea-sized or as recommended by the dentist</td>
</tr>
<tr>
<td><strong>Fluoride mouth rinse</strong></td>
<td>Yes, if at high caries risk and can spit</td>
<td>Yes, if at high caries risk and can spit</td>
<td>Yes, if at high caries risk and can spit</td>
</tr>
<tr>
<td><strong>Fluoride varnish</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td><strong>Dietary fluoride supplement (if primary drinking water is fluoride deficient)</strong></td>
<td>0.25 mg/d fluoride (starting at age 6 mo)</td>
<td>0.5 mg/d fluoride</td>
<td>1 mg/d fluoride (Use until age 16 y.)</td>
</tr>
<tr>
<td><strong>Dietary fluoride supplement (if primary drinking water is partially fluoridated (0.3-0.6 ppm))</strong></td>
<td>None</td>
<td>Yes, 0.25 mg/d fluoride</td>
<td>Yes, 0.5 mg/d fluoride (Use until age 16 y.)</td>
</tr>
</tbody>
</table>

*Typically performed in the dental home but covered in the primary care setting by Medicaid in some states through and after the age of 6 y.

From: Clark MB, et al; US Preventive Services Task Force.\textsuperscript{6}
Motivational interviewing is an exemplar for integration of oral health in primary care to address caregiver worries and encourage ongoing discussion (see “Sample conversation on fluoride use,” above).

**Take-home message for pediatricians**

To summarize, fluoride continues to be essential in caries prevention. Both topical and systemic fluoride play a role in maintaining good teeth and preventing oral disease, but the topical effects are foremost. Primary care providers should be aware of the appropriate fluoride modalities to advise for children at each age and whether that recommendation is universal or based on caries risk.

A well-informed pediatric provider can address concerns raised by fluoride-hesitant families through motivational interviewing and personalized communication. Early referral to establish a dental home may help provide clarity about fluoride use and improve dental health. Consistent messaging from the medical and dental communities about oral health and fluoride use will promote optimal dental and overall health.

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**SAMPLE CONVERSATION ON FLUORIDE USE**

**PCP:** To strengthen your child’s teeth and prevent cavities, I recommend daily use of fluoridated toothpaste morning and night and fluoride varnish in the office today. Because your child’s drinking water does not have fluoride, I also recommend use of a fluoride supplement at night.

**C:** I have heard really bad things about fluoride.

**PCP:** Heard? Tell me what you have heard and/or read about fluoride toothpastes, varnish, and/or supplements.

**C:** My friend told us not to use fluoride as it ruins the teeth and can cause cancer.

**PCP:** Do you have any additional concerns other than what you have heard from your friend?

**C:** Not really.

**PCP:** Professional websites, such as the CDC, AAP, and ADA provide scientific evidence to help you make informed decisions. Have you looked at any website that gives information about the various forms of fluoride? Would it be OK for us to discuss my reasons for wanting to give your child fluoride?

**C:** (Nods.)

**PCP:** Fluoride is a mineral that is naturally found in water but is not at high enough amounts in the community water to protect your child’s teeth. Appropriate use of fluoride can help prevent cavities and problems that arise after cavities, such as the need for dental procedures and infections. Fluoride is added to a toothpaste and water just as iodine is added to salt or vitamin D is added to milk. It is a dietary supplement that when given in appropriate amounts is safe for use. As far as the effects on cancer, this is also unproven. Many scientific studies have shown no link of fluoride use to cancer. I can give you a list of links about this and I encourage you to read them to make informed decisions.

**C:** What about the problems it causes with bad teeth?

**PCP:** Any medication can cause harm when not used appropriately. In appropriate doses, fluoride is protective and can prevent cavities. Based on this information we have discussed, what are your thoughts and feelings about including fluoride toothpaste, varnish, or the pill into your child’s routine oral health care?

**C:** Well, maybe, I can use the toothpaste, but I still don’t want her to eat the fluoride pill.

**PCP:** That’s a good start. Today, I see a few white spots on your child’s teeth that are the earliest signs of tooth decay. I recommend fluoride varnish application to the teeth. This is like the fluoride you have applied to your teeth at your dental visits. This is only applied at a dental or medical visit by a trained professional and gives an additional amount of protection for the next few months to help stop the progression of early cavities and aids in preventing new cavities. Knowing this information about your child’s teeth, can we proceed with application of fluoride varnish in the office today?

Abbreviations: ADA, American Dental Association; AAP, American Academy of Pediatrics; C, caregiver; CDC, Centers for Disease Control and Prevention; PCP, primary care provider.

For references, go to ContemporaryPediatrics.com/pediatric-oral-health-part-2-fluoride
New tool improves asthma prediction, prevention

Predicting the likelihood that a child will develop asthma has long been a challenge, but a new tool could offer more than previous assessments.

RACHAEL ZIMLICH, RN, BSN
Researchers have developed a new app that may help clinicians predict which children are at mild to moderate risk of developing asthma, compared with previous assessments that were only able to identify higher-risk patients.

The assessment, called the Pediatric Risk Asthma Score (PARS), was developed by researchers at the University of Cincinnati and Cincinnati Children’s Hospital Medical Center (CCHMC), Cincinnati, Ohio, and published in the Journal of Asthma and Clinical Immunology.1 Co-author of the report Gurjit K. Khurana Hershey, MD, PhD, Kindervelt Endowed Chair in Asthma Research, professor of Pediatrics, director of the Asthma Research division, co-director of the Office of Pediatric Clinical Fellowship, and attending physician at the CCHMC and director of the medical scientist training program at the University of Cincinnati College of Medicine, says the assessment will be most valuable for use with young children who have experienced wheezing by ages 1 and 2 years.

“Parents often ask, ‘does this mean my child will have asthma?’ or ‘what is my child’s risk of asthma?’” she says. “Now we can answer that more accurately.”

Asthma affects 25.7 million Americans including 7 million children, and costs $5 billion globally each year in drug costs alone, according to the report. Prevention of the disease has long been difficult, partly because clinicians have largely been unable to predict an individual’s risk of developing asthma. The National Institutes of Health has identified zeroing in on better predicting asthma risk as a goal, and several attempts have been made to reach this goal. The Asthma Predictive Index (API), developed in 2004, has been generally accepted as the most valid tool developed so far, according to the report. Although this tool is useful in identifying children who will not have asthma, researchers who developed the PARS tool say the API “leaves much room for improvement in terms of identifying children who will have asthma.”

Assessment beyond the API
The research team that developed the PARS reported working to create a tool that would take into consideration more stringent, personal criteria than the API, including sensitization to allergens and food allergies.

To create the PARS tool, the research team used the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) birth cohort and developed a personalized, predictive algorithm that integrates both clinical and demographic factors. The tool was tested against the API, and findings were replicated using the Isle of Wight birth cohort in addition to the CCAAPS cohort, according to the report.

Of the 762 participants in the CCAAPS cohort, researchers note that 589 were objectively assessed for asthma by age 7 years and that prevalence was 16%. Some of the factors included in the predictive analysis of the tool include incidence of parental asthma, early wheezing by the child, wheezing outside a

ASTHMA AFFECTS 25.7 MILLION AMERICANS INCLUDING 7 MILLION CHILDREN, AND COSTS $5 BILLION GLOBALLY EACH YEAR IN DRUG COSTS ALONE.1

“The PARS is superior to the API in predicting asthma, especially in children with mild to moderate risk. The API misses 40% of children with mild to moderate risk who go on to develop asthma.”

–Gurjit K. Khurana Hershey, MD, PhD
clinical brief

cold, eczema, age, gender, race, and skin-prick test results. According to the data, the children who had asthma at age 7 years were more likely to have a parent with asthma; eczema before age 3 years; a wheeze apart from the occurrence of a cold; early or frequent generalized wheezing; diagnosis of or probable presence of allergic rhinitis before age 3 years; have 2 or more positive skin-prick test responses to allergens or foods; or be African American.

When the PARS was compared with the API, the research team noted that the PARS tool was more effective at predicting asthma incidence in children with lower risk scores.

**A superior predictor for asthma**

“The PARS is superior to the API in predicting asthma, especially in children with mild to moderate risk. The API misses 40% of children with mild to moderate risk who go on to develop asthma,” Khurana Hershey says. “This is highly relevant, as these children may be the most amenable to prevention strategies. Future studies may incorporate genetics and other biomarkers into the risk assessment. If we can predict who will develop disease, we might be able to prevent the disease or intervene earlier to help alleviate worsening of the disease or reduce exacerbations.”

The PARS tool offers a continuous risk score with increased sensitivity over previous predictive models, according to the study, with the success of PARS primarily attributed to being able to predict asthma in children with mild to moderate risk—a population the API typically missed.

“The PARS is superior to API with an 11% increase in sensitivity. This increase is due to improved prediction in children with mild to moderate asthma risk. Specifically, the API identifies children at the highest risk for asthma,” the report concludes, with research noting the importance of increased recognition of children in less severe risk categories. “Children with mild to moderate risk have fewer risk factors and might be the most likely to respond favorably to prevention strategies. This is critical because the API and modified API (mAPI) are used to populate asthma prevention trials.”

One of these trials, according to the study, was the Prevention of Early Asthma in Kids (PEAK) trial, which investigated whether asthma prevalence in children aged younger than 3 years could be mitigated with certain therapies. By using a tool like PARS, this study could have included not just children in the high-risk category, but children at mild to moderate risk of developing asthma, the report notes—a population change that could have impacted the results of the study.

“It is critical to correctly identify children across the spectrum of asthma risk because the efficacy of preventions and interventions might be greater in those with mild to moderate risk,” the research team notes. “Past prevention studies have failed. This may be due in part to the fact that the children that were included in the studies were chosen based on the API. Their risk may have been too high or their disease already too advanced for prevention to be successful,” Khurana Hershey adds. “Future prevention studies using the PARS to select children for prevention interventions will be very useful and have the potential for tremendous impact.”

The PARS tool is already being used by clinicians, says lead author Jocelyn M. Biagini Myers, PhD, associate professor, Department of Pediatrics, Division of Asthma Research, University of Cincinnati and CCHMC, with 3449 users in 75 countries around the world. The tool can be downloaded in the Google Play and Apple App stores, and has been built into the Epic electronic medical record system at CCHMC. She says work will continue to improve the tool, such as performing additional studies to include other racial and ethnic groups in which asthma rates might be higher. She adds that the tool is designed

"[The PARS tool] should be of immediate benefit to providing more accurate prognosis to families of wheezing infants and is likely to be quite useful in identifying infants at risk for asthma who could benefit from interventions aimed at prevention.” —James E. Gern, MD
Reticulated rash CONTINUED FROM PAGE 36

Henoch-Schonlein purpura is an immunoglobulin (Ig) A-mediated small vessel vasculitis resulting in a purplish, petechial, or purpuric rash on the dependent part of the body, namely the legs and buttocks. The face, arms, and torso also may be affected. It is most commonly seen in young children, generally between ages 2 to 8 years, and is often triggered by infections. Arthralgia, hematuria, abdominal pain, and scrotal edema may indicate involvement of other organ systems.

Cutis marmorata telangiectatica congenita (CMTC) is a congenital venous anomaly characterized by persistent reticulated blanching erythema and subtle atrophy. Occasionally, ulcerations along the lines of atrophy may develop. It also can be associated with other anomalies such as limb asymmetry, port-wine stain, macrocephaly, and skeletal abnormalities such as clubfoot, hip dysplasia, and syndactyly. The vascular pattern is usually segmental and most likely represents a genetic mosaic condition.

Discussion
Erythema ab igne (which translates from Latin as “redness from fire”), also known as hot water bottle rash, toasted skin syndrome, ephelis ignea-lis, erythema caloric, or fire stains, is a skin condition characterized by localized areas of reticulated erythema and hyperpigmentation caused by chronic exposure to heat (infra-red radiation) at a level lower than is required to cause a burn. Rarely, EAI may take on a bullous form. The most common reported causes are hot water bottles and electric heating pads, but any heat source can potentially cause EAI, including laptops, space heaters, and heated seats.

Initially, EAI starts out as a mild erythema over the exposed areas. With repeated exposure, a reticular, mottled, hyperpigmented, brown, blue, or purple rash develops. Erythema ab igne is typically a benign and self-limiting rash that resolves with discontinuation of the heat exposure. However, chronic exposure to heat can lead to more permanent color changes, dysplasia, and, in rare cases, carcinoma.

Erythema ab igne is generally seen in individuals using heating devices to relieve local pain or cold. However, cases in which there was inadvertent exposure to heat, such as prolonged use of laptops placed over the thighs, and in professionals including jewelers or bakers who work with flames, also have been reported. On further inquiry, the patient revealed that he would spend the morning sitting in front of an electric base heater after he had showered to combat the New England winter.

Epidemiology/Pathophysiology
Erythema ab igne is uncommon, especially in countries such as the United States, where central heating is available. The use of open fires for warmth in underdeveloped countries is a known cause. It was also more common in populations whose work brought them into close contact with open flames or coal stoves. In developed countries, the condition is more likely to be seen in individuals who use local heating solutions such as electric heating pads or hot water bottles for pain relief. It occurs primarily in adults, with women being affected more than men. It is commonly seen on the lower back, legs, and abdomen, but can affect any body surface. There is an emerging trend of EAI in children using laptops on their thighs for extended periods of time.

The pathogenesis of EAI remains poorly understood. It is widely accepted that repeated heat exposure induces injury to the superficial blood vessels with hemosiderin deposition in the skin resulting in the characteristic reticular pattern. Microscopically, vacuolar degeneration at the dermo-epidermal junction, with necrotic keratinocytes and melanin deposition, are characteristic of EAI. Squamous cell carcinoma and Merkel cell carcinomas may rarely develop. This is much more common in adults and was a common phenomenon in the southern United States when fireplaces were the primary source of heating during the short winter season.

Management
There is no definitive therapy for EAI. Elimination of exposure to heat may
reverse the erythema and hyperpigmentation, especially if early in the disease process. More advanced cases require topical steroids or tretinoin to reduce the discoloration. Also, 5-fluorouracil has been shown to help clear atypical cells. Mesoglycan with topical flavonoids has shown promise in reducing the discoloration. Treatment with lasers is another option to reduce the pigmented changes. More important is the long-term monitoring and follow-up for the development of cutaneous malignancies.

**Patient outcome**

The patient was advised to avoid sitting by the heater for prolonged periods of time. His lesions resolved over a period of several weeks without other intervention.

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**Asthma** CONTINUED FROM PAGE 32

Wheezing vs asthma

James E. Gern, MD, a professor of Pediatrics with a focus on asthma at the University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, is one of the clinicians already using the PARS in practice, and says it is a step toward finding better ways to predict which children are at greatest risk of developing asthma.

“It remains difficult to predict which wheezing infants will go on to develop asthma,” Gern says. “Improved prediction would be useful for several reasons. First of all, it would help pediatricians and asthma specialists to provide more accurate information about prognosis to parents of wheezing infants. Second, there are a number of new approaches to asthma prevention that are under development. Clinical trials to test the efficacy of new preventive strategies will depend on being able to gauge the risk for asthma before it has actually developed.”

Gern says both the API and PARS were designed to use easily available information to estimate asthma risk, but whereas the outcomes from API are binary—revealing only high or low risk—the PARS provides a more continuous estimate of risk for children in more moderate categories.

“The PARS can provide improved estimates of asthma risk,” Gern concludes. “This should be of immediate benefit to providing more accurate prognosis to families of wheezing infants and is likely to be quite useful in identifying infants at risk for asthma who could benefit from interventions aimed at prevention.”

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**REFERENCE**


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The patient was a well-developed, well-nourished child. Examination of the affected area showed a non-blanching, nontender, dark brown-to-purple reticular discoloration over both shins, ankles, and dorsa of feet. The remainder of the physical examination was normal.

**Differential diagnosis**
The differential diagnosis for reticulated rash includes livedo reticularis, Henoch-Schonlein purpura (HSP), cutis marmorata telangiectatica congenita (CMTC), and erythema ab igne (EAI).

Livedo reticular is a skin condition characterized by a mottled reticular pattern with purplish discoloration caused by impaired blood flow to the skin. It may be physiologic and reversible (cutis marmorata in infants exposed to cold) or pathologic and persistent secondary to vasculitis, systemic lupus erythematosus, drugs/toxin, cryoglobulinemia, antiphospholipid syndrome, and other connective tissue disorders. Many of these individuals with livedo reticularis also will have features that are suggestive of the underlying cause.

**FOR MORE ON THIS CASE, TURN TO PAGE 33.**
Do-it-yourself pediatrics

I practice in northern Virginia, where we have access to all pediatric specialists, making it easy to refer out for many problems. Although tempting, this is not how I was trained, and not how I like to practice. Here are some common conditions/findings that are often, but unnecessarily, referred. In all the examples below, assume the child is otherwise well.

1. Most heart murmurs in children are innocent, and there is no hurry about referring a hemodynamically insignificant one anyway. If it sounds functional (e.g., a vibratory systolic ejection murmur that fades on sitting up), and you are comfortable you are not missing something major such as cyanotic heart condition or co-arctation, you can follow it in your office for a few visits to see if it goes away.

2. The occasional premature ventricular contraction in a baby is worth an electrocardiogram (EKG) to confirm but can be seen by you at checkups thereafter to see if it resolves on its own.

3. You can handle a first afebrile seizure in a child who is otherwise well. Standard of care is not to get an electroencephalogram or start medicine anyway.

4. I do not refer a toothless child until they are aged 15 months.

5. A classic first faint (e.g., teenaged girl on a hot day, with a prodrome) does not necessarily need evaluation beyond the history and physical, and if you do, an EKG is sufficient.

6. Benign-appearing, nontender, nonmatted, nonfixed lymph nodes, in typical locations, can be seen in the office in a few weeks to monitor their progress. (This does not apply to supraclavicular nodes.)

7. Mild tics are usually transient, and do not need a workup, nor do they usually interfere enough with activities to warrant treatment.

8. Congenital laryngomalacia, in the thriving child with good oxygenation, can forego an ears/nose/throat evaluation unless it does not improve on its own.

9. It is reasonable to have an endocrinologist see a patient with hypothyroidism the first time, but once on replacement therapy you should be able to handle the medicine and lab work yourself.

For more articles from Dr. Farber’s treasure chest of pediatric “pearls” go to ContemporaryPediatrics.com and search “Farber.”
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