Migraine
4-tier treatment approach

PLUS
Red flags in considering neuroimaging

Anaphylaxis essentials for infants

6 ways to counter burnout

Oral health in primary care

PUZZLER
Teen with fever, headache, rash, and arthralgias
YOUR VOICE
5  Juuling: What kids don’t know will hurt them

DISPATCHES
7  How to bring oral health to primary care
12  Journal Club

PUZZLER
17  Fever, headache, arthralgias, and rash

CLINICAL FEATURE
22  Pediatric migraine: Diagnostic criteria and treatment

CLINICAL FEATURE
31  Burnout
Pediatrician, heal thyself

PEER-REVIEWED FEATURE
38  Anaphylaxis essentials for infants

DERMCASE
42  Teenager with sudden diffuse dermatitis

PRACTICAL PEDIATRICS
43  More about allergies and other oddities

41  Advertising Index

Our Mission
Office- and hospital-based pediatricians and nurse practitioners use Contemporary Pediatrics’ timely, trusted, and practical information to enhance their day-to-day care of children. We advance pediatric providers’ professional development through in-depth, peer-reviewed clinical and practice management articles, case studies, and news and trends coverage.

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JUULING: What kids don’t know will hurt them

Healthcare providers must communicate to their adolescent and young adult patients the dangers of electronic nicotine delivery systems.

LINDA M GIBSON-YOUNG, PHD, ARNP, FNP-BC, CNE, AE-C, CRNP, FAANP; MARY MARTINASEK, PHD, CPH, MCHES, RRT

Nearly 4.7 million adolescents and young adults in the United States smoke traditional cigarettes. These statistics represent an all-time low in a population in which tobacco use primarily begins. Nine of 10 young persons have tried a cigarette by the time they turn 18 years of age.

From 2011 to 2016, there has been a decline in traditional cigarette smoking, particularly among middle school and high school students. The continued concern is the progression of youth smoking into adult smoking attributed to the addicting characteristics of nicotine.

Two novel nicotine-laden products called JUUL (pronounced “jewel”) and PHIX (pronounced “fix”) are on the market, and smoking these has become an epidemic in schools and colleges across the country. The JUUL (JUUL Labs Incorporated; San Francisco, California) and PHIX (PhixVapor, Brea, California) are not unlike the electronic cigarettes, or electronic nicotine delivery systems (ENDS), that adults are using in an attempt to quit smoking traditional cigarettes.

However, JUUL and PHIX provide flavored products that lure young people.

These devices are similar in function to the ENDS that adolescents have been trialing, although there is not degradation to a zero-nicotine product. Another difference is that JUUL and PHIX do not have the appearance of a cigarette or typical vaping device, and they can be wrapped to customize them with designs.

In fact, these products appear to replicate the appearance of an extended flash drive or stick and are popular among adolescents and young adults who like to customize.

These devices have a slender style, create an energy boost or calming experience, and provide flavorings. Additionally, they are sleek and compact, making them easy to conceal. Both devices are charged using a cord that attaches to a USB port. They require no maintenance to refill the liquid nicotine because they feature convenient disposable “pods” that connect directly to the nondisposable section of the device. All JUUL and PHIX pods contain liquid nicotine that is vaporized and inhaled.

Health concerns

The practice of juuling is raising significant health concerns given previous research on electronic vaping devices and the high amount of nicotine delivery within 1 JUUL pod and more in the PHIX devices.

The Truth Initiative research indicates that 25% of adolescents and young adults refer to the practice as juuling, and 37% are unsure if the device contained nicotine. Previous research on ENDS products indicate that most products have varying amounts of nicotine compared with what is advertised, with most having more of the addictive component.

The US Surgeon General has concluded that e-cigarette aerosol is not harmless and can contain harmful and potentially harmful chemicals, including nicotine, which is damaging to the developing brain. Research is continual and ongoing on ENDS products. Although nicotine is not consistent across devices, it is clear that vaping or ripping is a risky behavior based solely on having...
HEALTH RISKS OF SMOKING AND OTHER TOBACCO USE

Every day more than 3200 children aged 18 years or younger smoke their first cigarette. Nearly 9 of 10 smokers start before age 18 years. Young people who smoke are in danger of:

- Addiction to nicotine
- Reduced lung function
- Reduced lung growth
- Early cardiovascular damage
- Adverse effects on brain development

Centers for Disease Control and Prevention.

nicotine. Each JUUL pod contains 0.7mL with 5% nicotine by weight, approximately equivalent to 1 pack of cigarettes or 200 puffs.10 PHIX pods contain 1.7mL of nicotine, equivalent to the amount of nicotine in 2 packs of cigarettes.11 Research on ENDS products has revealed cancer-causing agents, respiratory irritants, heavy metals, and volatile organic compounds. Studies have found these agents in both the vaper’s (person who vapes) urine and saliva, as well as in the surrounding air.12-16

Action steps
The increasing prevalence and known harm to young persons through the use of ENDS products have prompted action. The American Academy of Pediatrics (AAP), who previously championed the Child Nicotine Poison Prevention Act of 2015 because of child illness and deaths from the overingestion of liquid nicotine, has provided a fact sheet for healthcare providers and parents that underscores the greatest concern related to JUULs—addiction and the potential risk of becoming a traditional cigarette smoker.17

The US Food and Drug Administration (FDA) has taken enforcement steps against the underage selling of the products to young persons and has indicated it will be developing a comprehensive plan to curb adolescent and young adult uptake.18

The American Association for Cancer Research and the American Society of Clinical Oncology have a policy statement supporting regulation, discouraging youth-oriented marketing and sales, and prohibiting the promotion of flavors that appeal to the young.19

The JUUL company has revamped its website to focus on adult users20 and is making statements in an effort to curb the acquisition of its products by young persons through age verification, marketing to adults only, and collaborating with law enforcement and school systems.21 This is similar to what the tobacco companies’ websites do to curb tobacco smoking among teenagers, which has been found to do more harm than good.22 These websites require a click on a tab to enter the website, stating one verifies one’s age of least 21 years. On the PHIX website, there is no evident indication that the product is to help quit smoking.

What you can do
Almost half a million people die each year in the United States because of tobacco use through cigarettes, making it this nation’s greatest cause of preventable death, far deadlier than obesity, alcohol, or motor-vehicle accidents. Risky behaviors are defined as potential actions leading to harm, loss, or danger in relation to health or happiness, and the literature often points out that risky behaviors start in the early teenaged years.23-25 Risky behaviors in these young populations are especially concerning because nicotine exposure in undeveloped brains can lead to reduction in focus, attention, and impulse control, as well as potential cognition or mood disorders.24

Research on the health risks of ENDS products, and particularly novel products, is in progress, but it takes time for the findings to become published. When

4.7 million middle school and high school students were tobacco users in 2015.

1 in 20 high school seniors was a daily smoker in 2016.

- US Department of Health and Human Services.

examining adolescents and college students, it is imperative that healthcare providers communicate to these young persons that harmful components are being delivered.
A pig-tailed girl of 6 years, I readied myself for school each morning near a motion-activated talking tooth. When I passed by, this googly-eyed molar shouted, “Hey! Don’t forget to brush your teeth!” Adjacent to my animatronic reminder, a tooth-shaped hourglass ticked away the seconds while I brushed with an electric toothbrush and flossed with a water pick.

My father, a small-town dentist, announced that he was “off to stamp out tooth decay,” and dropped his office keys into the pocket of his zippered smock. Oral health was central to our daily routines. My childhood smile was cavity free.

A challenge for pediatricians

Yet for most children—and most pediatricians—oral health is often buried in a long list of priorities. In my general pediatric clinic now, a terrified 2-year-old sits crying in her mother’s lap, the scars of prior cardiac surgeries on her chest. Dental caries dot her smile. “Dentist?” her mother repeats to me. She is too busy with the child’s many appointments, and her child is too frightened. How do I improve this child’s oral health during a short health-maintenance visit? I have minutes to spare, and mom’s motivation to change appears to be low.

We know well that dental caries is among the most common chronic diseases of childhood—far more prevalent than asthma. We know that dental caries can impair development, school performance, quality of life, and overall health. Caries lesions (eg, cavities) lead to financial burdens, inconvenience and missed work for parents, and suffering for our young patients.

We also know that as primary care providers, we are expected to provide oral healthcare to children, in accordance with the recommendations of reliable resources including the American Academy of Pediatrics (AAP), the American Academy of Pediatric Dentistry (AAPD), the American Dental Association (ADA), the US Preventive Services Task Force (USPSTF), and the Bright Futures Periodicity Schedule. However, the addition of this oral health responsibility is challenging: How are we to serve as pediatrician and play dentist, too?

How we faced the oral health challenge

Our clinic recently worked with the Michigan Caries Prevention Program (MCPP; see “More about the MCPP,” page 39) to incorporate and sustain solutions that would make this challenge less daunting.

Through the MCPP, we received support as a pilot site to achieve 4 shared goals:

- Identify children at risk for caries.
- Apply fluoride varnish at well-child exams.
- Educate about oral health.
- Encourage patients to establish care with a primary dentist (find a dental home).

It worked! At the end of the pilot, we had good provider buy-in; were able to streamline documentation and billing; could complete
varnish, anticipatory guidance, and confidence in how to screen for oral health risk factors. Similar trainings for pediatric providers are accessible online. The Smiles for Life national oral health curriculum (SmilesforLifeoralhealth.org) is free, endorsed by the AAP and ADA for primary care training in oral health, and available with instructions for moderating the training.8

3 **Make oral health easy for providers.** We found several strategies that are critical for efficiency and sustainability of provider efforts. First, we chose a target population of children presenting for well-child visits aged between 6 months and 3 years. For these children, we added oral health screening to our intake paperwork using a 1-page form with embedded educational messages (Figure 1). To create a visual reminder and to save time during the visit, we placed the necessary varnish supplies in a small packet in the exam room within arm’s reach of the provider (Figure 2). To assist our providers in referring patients to a dental home, we created an easily accessible electronic list of local dentists accepting pediatric patients with all insurance plans. Finally, to improve the efficiency of postvisit documentation and billing, we added language about the visit’s oral health screening and intervention to our electronic health record (EHR) note templates (Figure 3) and built the appropriate billing codes into our EHR order sets. (To support implementation of these steps, the AAP offers resources for ordering dental supplies,9 an oral health coding fact sheet,10 and a more in-depth oral health risk assessment tool.11)

---

**6 steps to success**

Here’s how you can make this happen in your own pediatric practice:

1 **Find a co-champion of oral health.** A single pediatric or family dentist in your area can help answer your questions about dentistry as they arise, provide a referral site, and be present at an initial training in assessment and varnish application. For us, key dental school faculty and local private dentists have proven to be invaluable allies.

2 **Train your providers.** A 1-hour MCPP training imparted our providers with comfort in the procedural aspects of fluoride varnish application in under 90 seconds; and were screening for oral health risk at sustained rates of 100%.

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*FIGURE 1* An Oral Health Screening Intake Form includes a risk assessment tool for providers, and preventive habit messages for marking and redistribution to the parent. Used with permission from Margherita Fontana, DDS, PHD.
4 Make oral health easy for patients. We apply the fluoride varnish during routine well-child visits to ensure appropriate 3-month to 6-month intervals between varnish applications. When the family leaves the visit, they have several oral health reminders to take with them. The intake oral health screening tool is returned to them after we have circled specific preprinted “preventive habit” messages based on assessed risk factors (Figure 1). A list of local dentists accepting patients and accepting various types of insurance coverage is added to checkout paperwork if indicated. We make verbal recommendations to obtain the needed oral health products and, if needed, we dispense age-appropriate toothbrushes and fluoride toothpaste to eliminate inconvenience, and expense.

5 Make your efforts stick. We monitored our rates of screening and varnish application over time, and for the first few months we held weekly focus groups to review barriers and troubleshoot solutions. We incorporated tasks such as ordering and organizing supplies into the job descriptions of certain staff members. We set procedures in place to provide oral health training to new staff and providers as they were hired. We have created a clinic culture that is supportive of oral health, and we believe that so long as someone continues to carry the torch of oral health champion, we will sustain it indefinitely.

6 Enjoy your results. It required a moderate level of “institutional inertia” to set this oral health initiative in motion, but once rolling, there were few questions or concerns from returning families. Gradually, we felt a shift. Families spontaneously offered updates on their child’s oral health. Consent to varnish became extremely brief. Lengthy discussions in defense of healthy preventive habits became rare. Families expressed gratitude for our oral health efforts.

CONTINUED ON PAGE 39
Is there a better way to estimate probability of UTI in febrile infants?

Perhaps. Investigators compared the accuracy of an American Academy of Pediatrics (AAP) practice guideline algorithm for diagnosing urinary tract infection (UTI) in children aged 2 to 23 months with a new tool (UTICalc; University of Pittsburgh, Pennsylvania) that first estimates UTI probability based on clinical variables and then, if laboratory testing is performed, updates the estimate based on the results.

Investigators developed the tool by analyzing electronic medical records (EMRs) of 2070 febrile children aged 2 to 23 months who were brought to an emergency department (ED) with a temperature of 100.4°F or higher. When the UTICalc then was applied to a hypothetical group of 1000 febrile children, it reduced testing by 8.1% and decreased the number of missed UTIs from 3 to none.

The researchers tested 5 different models of the UTICalc for predicting risk of UTI, 1 of which had only clinical variables: aged younger than 12 months; temperature of 102.2°F or greater; nonblack race; female or uncircumcised male; and no other fever source. The other 4 models also incorporated a range of laboratory tests, such as leukocyte esterase and nitrite values; results of a Gram-stained urine smear; or urine white blood cell count.

The solely clinical model predicted the probability of UTI less accurately than the models that included laboratory tests. Models with a Gram-stained smear performed better than those without this test. Compared with empirically treating all children with a leukocyte esterase test result of 1+ or higher, the UTICalc model that included variables from the clinical model plus leukocyte esterase and nitrite values would have reduced the number of treatment delays by 10.6%.

Using the UTICalc to decide if urine sampling is warranted, the clinician first inputs data on the 5 clinical variables, and the UTICalc assigns a “low” or “high” risk. Then, if testing is performed, the clinician enters the results into UTICalc, which automatically selects the model corresponding to the test(s) and estimates the probability of UTI, again assigning a risk category (Shaikh N, et al. JAMA Pediatr. April 16, 2018. Epub ahead of print).

When the UTICalc was applied to a hypothetical group of 1000 febrile children, it reduced testing by 8.1% and decreased the number of missed UTIs from 3 to none.
Includes mebendazole formulations, dosages and treatment duration

- **EMVERM** contains mebendazole, the active ingredient that has been prescribed by physicians for MORE THAN 40 YEARS.

- Recommended by the AAP Red Book as one of the **DRUGS OF CHOICE** for highly contagious pinworm infections.

- The CDC recommends **TREATING THE ENTIRE HOUSEHOLD**, since family members are frequently infected.

- **ONE 100 mg CHEWABLE TABLET**, for **ONE DAY**, is the same dosage schedule for children and adults.

INDICATION

EMVERM® is indicated for the treatment of patients two years of age and older with gastrointestinal infections caused by Ancylostoma duodenale (hookworm), Ascaris lumbricoides (roundworm), Enterobius vermicularis (pinworm), Necator americanus (hookworm), and Trichuris trichiura (whipworm).

IMPORTANT SAFETY INFORMATION

**Contraindication:** EMVERM is contraindicated in persons with a known hypersensitivity to the drug or its excipients (mebendazole, microcrystalline cellulose, corn starch, anhydrous lactose, sodium starch glycolate, magnesium stearate, stearic acid, sodium lauryl sulfate, sodium saccharin, and FD&C Yellow #6).

**Warnings and Precautions:**
- **Risk of Convulsions:** Convulsions in infants below the age of 1 year have been reported.
- **Hematologic Effects:** Neutropenia and agranulocytosis have been reported in patients receiving mebendazole at higher doses and for prolonged duration. Monitor blood counts in these patients.
- **Metronidazole and Serious Skin Reactions:** Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) have been reported with the concomitant use of mebendazole and metronidazole. Avoid concomitant use of mebendazole and metronidazole.

**Adverse Reactions Reported in Mebendazole-treated Subjects from 39 Clinical Trials**: anorexia, abdominal pain, diarrhea, flatulence, nausea, vomiting, rash.

**Adverse Reactions Identified During Postmarketing Experience with Mebendazole**: agranulocytosis, neutropenia, hypersensitivity including anaphylactic reactions, convulsions, dizziness, hepatitis, abnormal liver tests, glomerulonephritis, Stevens-Johnson syndrome/toxic epidermal necrolysis, exanthema, angioedema, urticaria, alopecia.

Includes mebendazole formulations, dosages and treatment duration other than EMVERM 100 mg chewable tablet.

**Drug Interactions:** Concomitant use of EMVERM and metronidazole should be avoided.

**Pregnancy:** The available published literature on mebendazole use in pregnant women has not reported a clear association between mebendazole and a potential risk of major birth defects or miscarriages. There are risks to the mother and fetus associated with untreated helminthic infection during pregnancy.

**REFERENCES**


Unintended soil transmitted helminth infections in pregnancy are associated with adverse outcomes including maternal iron deficiency anemia, low birth weight, neonatal and maternal death.

**Lactation:** Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. There are no reports of effects on the breastfed infant, and the limited reports on the effects on milk production are inconsistent. The limited clinical data during lactation precludes a clear determination of the risk of EMVERM to a breastfed infant; therefore, developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for EMVERM and any potential adverse effects on the breastfed infant from EMVERM or from the underlying maternal condition.

**Pediatric Use:** The safety and effectiveness of EMVERM 100 mg chewable tablet has not been established in pediatric patients less than two years of age. Convulsions have been reported with mebendazole use in children less than one year of age.

**Geriatric Use:** Clinical studies of mebendazole did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects.

**Overdosage:** In patients treated at dosages substantially higher than recommended or for prolonged periods of time, the following adverse reactions have been reported: alopecia, reversible transaminase elevations, hepatitis, agranulocytosis, neutropenia, and glomerulonephritis.

**Symptoms and signs of overdose:** In the event of accidental overdose, gastrointestinal signs/symptoms may occur.

**Treatment of overdose:** There is no specific antidote.

**Patient Counseling:** Healthcare professionals should advise the patient to read the FDA-approved patient labeling (Patient Information). Advise patients that:
- Taking EMVERM and metronidazole together may cause serious skin reactions and should be avoided.
- EMVERM can be taken with or without food.
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. To report SUSPECTED ADVERSE REACTIONS contact Impax Laboratories, Inc. at 1-877-994-6729.

Please see Full Prescribing Information at www.EMVERMHCP.com and Brief Summary on following pages.

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EMVERM® (mebendazole) 100 mg Chewable Tablets

BRIEF SUMMARY: Complete information about EMVERM® can be found in the Full Prescribing Information.

INDICATIONS AND USAGE
EMVERM® is indicated for the treatment of patients two years of age and older with gastrointestinal infections caused by Ancylostoma duodenale (hookworm), Ascaris lumbricoides (roundworm), Enterobius vermicularis (pinworm), Necator americanus (hookworm), and Trichuris trichiura (whipworm).

DOSEAGE AND ADMINISTRATION
The recommended dosage for EMVERM® is described in Table 1 below. The same dosage schedule applies to adults and pediatric patients two years of age and older. The tablet may be chewed, swallowed, or crushed and mixed with food.

Table 1: Dosage of EMVERM in Adult and Pediatric Patients (two years of age and older)

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Pinworm (enterobiasis)</th>
<th>Whipworm (trichuriasis)</th>
<th>Roundworm (ascariasis)</th>
<th>Hookworm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 tablet, once</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
<td></td>
</tr>
</tbody>
</table>

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

CONTRAINDICATIONS
EMVERM® is contraindicated in persons with a known hypersensitivity to the drug or its excipients (mebendazole, microcrystalline cellulose, corn starch, anhydrous lactose, sodium starch glycolate, magnesium stearate, stearic acid, sodium lauryl sulfate, sodium saccharin, and FD&C Yellow #6).

WARNINGS AND PRECAUTIONS
Risk of Convulsions
Although EMVERM® is approved for use in children two years of age and older, convulsions have been reported in infants below the age of 1 year during post-marketing experience with mebendazole, including EMVERM®.

Hematologic Effects
Agranulocytosis and neutropenia have been reported with mebendazole use at higher doses and for more prolonged durations than is recommended for the treatment of soil-transmitted helminth infections. Monitor blood counts if EMVERM® is used at higher doses or for prolonged duration.

Metronidazole Drug Interaction and Serious Skin Reactions
Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) have been reported with the concomitant use of mebendazole and metronidazole. Avoid concomitant use of mebendazole, including EMVERM® and metronidazole.

ADVERSE REACTIONS
Clinical Studies
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of mebendazole was evaluated in 6276 subjects who participated in 39 clinical trials for treatment of single or mixed parasitic infections of the gastrointestinal tract. In these trials, the formulations, dosages and duration of mebendazole treatment varied. Adverse reactions reported in mebendazole-treated subjects from the 39 clinical trials are shown in Table 2.

Table 2: Adverse Reactions Reported in Mebendazole-treated Subjects from 39 Clinical Trials*

<table>
<thead>
<tr>
<th>Adverse Reaction(s)</th>
<th>Gastrointestinal Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anorexia, Abdominal Pain, Diarrhea, Flatulence, Nausea, and Vomiting</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Skin and Subcutaneous Tissue Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rash</strong></td>
</tr>
<tr>
<td>*Includes mebendazole formulations, dosages and treatment duration other than EMVERM® 100 mg tablet</td>
</tr>
</tbody>
</table>

Postmarketing Experience
The following adverse reactions have been identified in adult and pediatric patients postmarketing with mebendazole formulations and dosages other than the EMVERM® 100 mg chewable tablet. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Table 3: Adverse Reactions Identified During Postmarketing Experience with Mebendazole*

<table>
<thead>
<tr>
<th>Adverse Reaction(s)</th>
<th>Blood and Lymphatic System Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agranulocytosis, Neutropenia</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immune System Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Convulsions, Dizziness, Hepatitis, Abnormal liver tests</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nervous System Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatobiliary Disorders</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal and Urinary Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glomerulonephritis</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Skin and Subcutaneous Tissue Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEN, SJS, Exanthema, Angioedema, Urticaria, Alopecia</strong></td>
</tr>
<tr>
<td>*Includes mebendazole formulations, dosages and treatment duration other than EMVERM® 100 mg chewable tablets</td>
</tr>
</tbody>
</table>

DRUG INTERACTIONS
Concomitant use of mebendazole, including EMVERM®, and metronidazole should be avoided.

USE IN SPECIFIC POPULATIONS
Pregnancy
Risk Summary
The available published literature on mebendazole use in pregnant women has not reported a clear association between mebendazole and a potential risk of major birth defects or miscarriages [see Data]. There are risks to the mother and fetus associated with untreated helminthic infection during pregnancy [see Clinical Considerations].

In animal reproduction studies, adverse developmental effects (i.e., skeletal malformations, soft tissue malformations, decreased pup weight, embryolethality) were observed when mebendazole was administered to pregnant rats during the period of organogenesis at single oral doses as low as 10 mg/kg (approximately 0.5-fold the total daily maximum recommended human dose [MRHD]). Maternal toxicity was present at the highest of these doses [see Data].

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Clinical Considerations
Disease-Associated Maternal and/or Embryo/Fetal Risks
Untreated soil transmitted helminth infections in pregnancy are associated with adverse outcomes including maternal iron deficiency anemia, low birth weight, neonatal and maternal death.

Human Data
Several published studies, including prospective pregnancy registries, case-control, retrospective cohort, and randomized controlled studies, have reported no association between mebendazole use and a potential risk of major birth defects or miscarriage. Overall, these studies did not identify a specific
pattern or frequency of major birth defects with mebendazole use. However, these studies cannot definitely establish the absence of any mebendazole-associated risk because of methodological limitations, including recall bias, confounding factors and, in some cases, small sample size or exclusion of first trimester mebendazole exposures.

**Animal Data**

Embryo-fetal developmental toxicity studies in rats revealed no adverse effects on dams or their progeny at doses up to 2.5 mg/kg/day on gestation days 6–15 (the period of organogenesis). Dosing at ≥10 mg/kg/day resulted in a lowered body weight gain and a decreased pregnancy rate. Maternal toxicity, including body weight loss in one animal and maternal death in 11 of 20 animals, was seen at 40 mg/kg/day. At 10 mg/kg/day, increased embryo-fetal resorption (100% were resorbed at 40 mg/kg/day), decreased pup weight and increased incidence of malformations (primarily skeletal) were observed. Mebendazole was also embryotoxic and teratogenic in pregnant rats at single oral doses during organogenesis as low as 10 mg/kg (approximately 0.5-fold the total daily MRHD, based on mg/m²).

In embryo-fetal developmental toxicity studies in mice dosed on gestation days 6–15, doses of 10 mg/kg/day and higher resulted in decreased body weight gain at 10 and 40 mg/kg/day and a higher mortality rate at 40 mg/kg/day. At doses of 10 mg/kg/day (approximately 0.2-fold the total daily MRHD, based on mg/m²) and higher, embryo-fetal resorption increased (100% at 40 mg/kg) and fetal malformations, including skeletal, cranial, and soft tissue anomalies, were present. Dosing of hamsters and rabbits did not result in embryotoxicity or teratogenicity at doses up to 40 mg/kg/day (1.6 to 3.9-fold the total daily MRHD, based on mg/m²).

In a peri- and post-natal toxicity study in rats, mebendazole did not adversely affect dams or their progeny at 20 mg/kg/day. At 40 mg/kg (1.9-fold the total daily MRHD, based on mg/m²), a reduction of the number of live pups was observed and there was no survival at weaning. No abnormalities were found on gross and radiographic examination of pups at birth.

**Lactation**

**Risk Summary**

Limited data from case reports demonstrate that a small amount of mebendazole is present in human milk following oral administration. There are no reports of effects on the breastfeeding infant, and the limited reports on the effects on milk production are inconsistent. The limited clinical data during lactation precludes a clear determination of the risk of EMVERM® to a breastfed infant; therefore, developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for EMVERM® and any potential adverse effects on the breastfed infant from EMVERM® or from the underlying maternal condition.

**Pediatric Use**

The safety and effectiveness of EMVERM® 100 mg chewable tablets has not been established in pediatric patients less than two years of age. Conclusions have been reported with mebendazole use in children less than one year of age.

**Geriatric Use**

Clinical studies of mebendazole did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects.

**OVERDOSAGE**

In patients treated at dosages substantially higher than recommended or for prolonged periods of time, the following adverse reactions have been reported: alopecia, reversible transaminase elevations, hepatitis, agranulocytosis, neutropenia, and glomerulonephritis.

**Symptoms and signs**

In the event of accidental overdose, gastrointestinal signs/symptoms may occur.

**Treatment**

There is no specific antidote.

---

**CLINICAL STUDIES**

Efficacy rates derived from various studies are shown in Table 4 below:

**Table 4: Mean Cure Rates and Egg Reductions from Clinical Studies**

<table>
<thead>
<tr>
<th></th>
<th>Pinworm (enterobiasis)</th>
<th>Whipworm (trichuriasis)</th>
<th>Roundworm (ascariasis)</th>
<th>Hookworm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cure rates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>95%</td>
<td>68%</td>
<td>98%</td>
<td>96%</td>
</tr>
<tr>
<td><strong>Egg reduction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>—</td>
<td>93%</td>
<td>99%</td>
<td>99%</td>
</tr>
</tbody>
</table>

**PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Advise patients that:

- Taking EMVERM® and metronidazole together may cause serious skin reactions and should be avoided.
- EMVERM® can be taken with or without food.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. To report SUSPECTED ADVERSE REACTIONS contact Impax Laboratories, Inc. at 1-877-994-6729.

Please see Full Prescribing Information including Patient Information at www.emvermhcp.com.

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07/2017 PP-XPI-MEB-US-0008
Antibiotics or antacids in infancy may increase a child’s later risk of allergy

Exposure to acid-suppressive medications or antibiotics in the first 6 months of life is associated with development of allergic disease, according to a retrospective study in more than 750,000 children from within 35 days of birth until aged at least 1 year. Data for each child were available for a median of 4.6 years.

During the first 6 months of life, 7.6% of the study group were prescribed a histamine-2 receptor antagonist (H₂RA), 1.7% a proton pump inhibitor (PPI), and 16.6% an antibiotic. The most commonly prescribed H₂RA was ranitidine (95.1% of all such prescriptions), followed by nizatidine and famotidine. Lansoprazole was the PPI used most often (75.5% of total PPI prescriptions), and for antibiotics, penicillins were the medications of choice (65.3%).

Children who received H₂RAs and PPIs were twice as likely as those who did not to develop food allergy (adjusted hazard ratios were 2.18 and 2.59, respectively). These children also had an elevated risk for medication allergy, anaphylaxis, allergic rhinitis, and asthma. Antibiotic prescriptions were associated with a doubling of risk for asthma, as well as increased risk for allergic rhinitis, anaphylaxis, and allergic conjunctivitis (Mitre E, et al. JAMA Pediatr. April 2, 2018. Epub ahead of print).

Poverty and lack of a car lead to failure to fill prescriptions

A retrospective study of data from a regional community pharmacy chain in the Midwest encompassing 98 zip codes found that almost 1 in 8 new prescriptions for individuals aged up to 18 years went unfilled after the pharmacy received the prescription. This form of nonadherence was significantly associated with living in an area with a high rate of poverty and not having access to a vehicle.

The 54 pharmacies included in the study received about 213,700 prescriptions during the 6-month study period, and 12.2% were unfilled (not picked up within 30 days). Older children, boys, and those with public insurance were slightly more likely to have unfilled prescriptions. Oral anti-infectives were least likely to go unfilled (4.2% of those prescribed), whereas multivitamins and nutritional supplements had the highest rate (29.3%) of going unfilled.

Those living in zip codes with the highest poverty rates were 60% more likely not to fill a prescription than those residing in areas with the lowest poverty rates. Investigators found a similar pattern with regard to vehicle access (Hensley C, et al. Pediatrics. 2018;141[4]:e20173402).
Fever, headache, arthralgias, and rash

HITESH VASHI, MD; ALINE TANIOS, MD

A 15-year-old Caucasian male with a past medical history of attention-deficit/hyperactivity disorder (ADHD) presents to the hospital emergency department (ED) with a 1-week history of fever, headache, arthralgias, vomiting, and rash.

History

The patient states that initial symptoms all began around the same time 1 week prior to hospital presentation when he developed severe back pain throughout his entire upper and lower midline spine, followed by generalized headache and nonbloody, nonbilious vomiting. Four days prior to presentation, he began to have bilateral wrist pain that migrated to his bilateral shoulders, knees, and ankles. The pain worsened with movement and palpation, and the only alleviating factor was taking ibuprofen, which gave mild and brief pain relief. The pain was constant and described as sharp. This was followed by a flat, dark-purple rash on bilateral arms, hands, and legs that spared his chest and abdomen.

The constellation of his symptoms as well as a new onset of limping and difficulty bearing weight led to the patient’s ED visit. He did not experience neck pain, nor redness or warmth of his joints. He did not have any confusion, weakness in any of his extremities, or visual changes. He denied any chest pain, shortness of breath, or abdominal pain.

The teenager lives at home with 7 dogs and 2 cats. He had been visiting his father in Iowa who owns 1 dog and a pet rat. He recalls feeding the rat 3 weeks ago, when he was bitten on his fourth left finger. He had minimal bleeding that resolved after a few minutes. There was neither pus nor other drainage from the lesion. A small purple blister formed and resolved without intervention after 3 days. He did not have any other symptoms for the 2 weeks following the rat bite, until the back pain began.

Physical exam

The patient’s vital signs were normal and stable for his age, with blood pressure of 116/64 mm/Hg; pulse, 68 beats per minute; and respiratory rate of 18 breaths per minute. He was afebrile at 98.2°F 1 hour after given ibuprofen. A review of his growth chart revealed normal and symmetric growth with no recent weight changes. He was well appearing and well hydrated. He was alert and oriented to person, place, and time, and had no focal neurologic deficits. Mucous membranes were moist, and his posterior oropharynx was benign. His neck was supple with no pain on range of motion and no lymphadenopathy. He had regular heart rate and rhythm, no murmurs, and good distal pulses. His lungs were clear.

The patient’s abdomen was soft, nondistended, and nontender to palpation. He had positive bowel sounds and no hepatosplenomegaly. He had 5/5 strength in all extremities. He had a 0.5-cm to 1-cm purple closed blister without drainage on his left fourth digit.
puzzler

it (Figure 1) with a nonblanching macular petechial rash on bilateral hands, forearms, anterior lower legs, and feet. No rash was present on his chest, abdomen, palms, or soles. There was no erythema nor edema surrounding the blister on his left hand.

**Laboratory tests**
Initial laboratory evaluation revealed a normal complete blood count with differential, electrolytes, renal function, transaminases, creatine kinase, lactic acid, and coagulation factors; elevated erythrocyte sedimentation rate, 89 mm/hr (normal range [NR], 0-15 mm/hr); C-reactive protein of 20.8 mg/dL (NR, <0.5 mg/dL); and procalcitonin of 0.89 ng/mL (NR, <0.15 ng/mL).

Wound culture was obtained via puncturing the blister to express fluid, and blood culture was obtained on sodium polyanethole sulfonate (SPS)-free blood culture medium. Serum *Streptobacillus moniliformis* polymerase chain reaction (PCR) and serum *Francisella* fluorescent antibodies also were collected.

**Differential diagnosis**
The differential diagnosis for a teenager with fever, headache, arthralgias, and rash in the setting of a known animal bite is wide. This includes rabies, Rocky Mountain Spotted Fever, *Anaplasma* species, and rat bite fever caused by *S. moniliformis* or *Spirillum minus* (Table 1).

Rabies includes initial symptoms such as fever, headache, and vomiting that make it difficult to distinguish among other illnesses. However, as rabies progresses and affects the brain and meninges, symptoms include agitation and confusion. Rabies is unique in that it causes muscle spasms in the throat when trying to swallow, which cause dysphagia, excess salivation, and hydrophobia. In animals, rabies is diagnosed with the presence of rabies virus antigen in brain tissue using the direct fluorescent antibody (DFA) test. In humans, diagnosis can be made by DFA test on skin biopsy from the neck; isolation of the virus from saliva; by detection of antibody in serum in unvaccinated people and cerebrospinal fluid (CSF) in all people; and by detection of viral nucleotide sequences in saliva or skin. Treatment for a patient once bitten by an animal suspected of being rabid includes rabbits immunization and human rabies immune globulin (HRIG), but after symptoms have developed, neither the vaccine nor immune globulin improves prognosis. Rocky Mount Spotted Fever is caused by the bacterium *Rickettsia rickettsii* and typically presents with fever, headache, myalgias, and a distinctive rash in the presence of a tick bite. The characteristic rash is a red petechial rash initially involving the wrists and ankles, and within hours spreading to the palms and soles and then inward to the trunk. Hyponatremia and thrombocytopenia typically accompany the illness. The gold standard for diagnosis is the indirect fluorescent antibody (IFA) serology test. Treatment is 7 to 10 days of oral doxycycline.

**Ehrlichiosis** is a tick-borne infection that usually consists of headache, myalgias, and fatigue. Rash may be present but is uncommon. Diagnosis is made by serologic testing, but the organism also can be isolated in blood or CSF culture as well as via PCR assay. Treatment is oral doxycycline for 5 to 10 days.

Tularemia is caused by the bacterium *Francisella tularensis* and causes fever, headache, fatigue, and a skin rash in the presence of a tick bite. The characteristic rash is a red petechial rash initially involving the wrists and ankles, and within hours spreading to the palms and soles and then inward to the trunk. Hyponatremia and thrombocytopenia typically accompany the illness. The gold standard for diagnosis is the indirect fluorescent antibody (IFA) serology test. Treatment is 7 to 10 days of oral doxycycline.

### Table 1

**Differential Diagnosis for Fever, Headache, Arthralgias, and Rash in the Setting of Rat Bite**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Specific Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabies via Lyssavirus</td>
<td>Vomiting, agitation, confusion, difficulty swallowing, excess salivation.</td>
</tr>
<tr>
<td>Rocky Mounted Spotted Fever via <em>Rickettsia rickettsii</em></td>
<td>Vomiting; rash starting on wrists and ankles spreading to palms of hands and soles of feet, then to arms/legs/torso.</td>
</tr>
<tr>
<td>Ehrlichiosis via <em>Ehrlichia</em> and <em>Anaplasma</em></td>
<td>Vomiting, fatigue.</td>
</tr>
<tr>
<td>Tularemia via <em>Francisella tularensis</em></td>
<td>Fatigue; skin ulcer at point of contact with animal or bite site; swollen lymph nodes near ulcer.</td>
</tr>
<tr>
<td>Rat bite fever via <em>Streptobacillus moniliformis</em></td>
<td>Primarily in United States; vomiting, skin rash with reddish-brown or purple plaques, ulceration at the bite site.</td>
</tr>
<tr>
<td>Rat bite fever via <em>Spirillum minus</em></td>
<td>Primarily in Asia; vomiting, skin rash with reddish-brown or purple plaques, ulceration at the bite site.</td>
</tr>
</tbody>
</table>
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ulcer at point of contact with the bite site along with swollen lymph nodes near the ulcer. Diagnosis is generally via serologic testing, but PCR assay or DFA assay also may be used. Treatment is 7 to 10 days of intravenous (IV) gentamicin.1

Rat bite fever is caused by S moniliformis or S minus. The main presenting symptoms of rat bite fever caused by S moniliformis include fever, chills, headache, migratory polyarthritis, rash, and absence of lymphadenopathy. In addition, S minus causes the same symptoms as S moniliformis but does include lymphadenopathy. The bacterium S moniliformis accounts for most cases of rat bite fever in the United States with S minus infections occurring primarily in Asia.2

Hospital course and diagnosis
Because of concern for possible rabies infection, the patient was given rabies vaccine and rabies immune globulin, then admitted. Infectious Disease was consulted, and the patient was started on IV penicillin G at 3,000,000 units every 4 hours for 4 days. Endocarditis can be a rare complication, so echocardiography was performed and was normal.

After starting antibiotic therapy, the patient remained afebrile for 4 days. Polyarthritis in his shoulders, knees, ankles, and back gradually improved over his hospital stay. The blood culture on SPS-free culture media obtained on admission resulted to grow S moniliformis. Thus, it was determined that the patient’s rat bite fever was caused by S moniliformis.

Discussion
The bacterium S moniliformis is a highly pleomorphic, filamentous, gram-negative, nonmotile, and non-acid-fast rod. More than 2 million

![FIGURE 2](image)

INFECTION TRANSMISSION ROUTES FOR STREPTOBACILLUS MONILIFORMIS

- Bites or scratches from rodents.
- Does NOT include person-to-person transmission.
- Handling of rodents without bite or scratch.
- Consuming food or drink contaminated with bacteria.

Adapted from Centers for Disease Control and Prevention.3

Animal bites occur each year in the United States with rats contributing to about 1% of these cases. Infection from S moniliformis can be transmitted by rats, mice, gerbils, squirrels, or weasels via bites or scratches, handling of these rodents, or consuming food contaminated by these bacteria. It cannot be spread from one person to another (Figure 2).2

The incubation period ranges from 3 days to more than 3 weeks. There is generally little-to-no inflammation and no lymphadenopathy around the bite site. A maculopapular, purpuric, or petechial rash develops in about 75% of the patients and is generally on the peripheral extremities within a few days of fever onset. More than 50% of patients eventually develop migratory polyarthritis. The mortality rate of untreated rat bite fever is approximately 10%.3,4

A fatal case of rat bite fever occurred to a healthy 10-year-old male who owned pet rats.5 He initially began to experience fevers to 102.6°F; vomiting, headache, and leg pain. He was seen by his primary care physician and discharged with a diagnosis of viral gastroenteritis. In the next 24 hours, he developed confusion and weakness and then collapsed at home. Paramedics found him unresponsive with dilated pupils, and 1 hour of resuscitation efforts were unsuccessful. During resuscitation, labs were obtained revealing that the patient had anemia, thrombocytopenia, and leukocytosis with bandemia. He also had evidence of disseminated intravascular coagulation, and lung, liver, and epiglottis tissue collected postmortem was positive for S moniliformis DNA by PCR.

Complications of rat bite fever include endocarditis; vasculitis; soft tissue and solid organ abscesses; osteomyelitis, and septic arthritis (Table 2). Endocarditis is the most common complication of rat bite fever with mortality at about 53%, although the majority of these deaths occur without appropriate antibiotic therapy.5,6 Endocarditis is suspected after rat bite fever has been confirmed in a patient with a new heart murmur.

In another case report, a 26-month-old male presented with 5 days of fever to 103°F improved with antipyretics, rash, malaise, and bilateral lower extremity arthralgias.7 He was initially diagnosed with a viral exanthema and subsequently discharged. Three days later, he developed bilateral edema of the feet and ankles that caused him to refuse to ambulate. He was found to have a grade II/VI systolic murmur. Expanded workup including preliminary blood and wound cultures were negative. The toddler’s fever and edema both improved on antipyretics after 3 days, and he was discharged. Two days later, his bacte-
rial wound culture grew *S moniliformis* and the family admitted he had been exposed to pet rats at home. He was readmitted and received 7 days of IV/intramuscular (IM) penicillin G. Repeat blood and wound cultures were negative and due to the presence of the heart murmur, an echocardiogram was obtained, which was normal. The child’s fevers and swelling improved and he was discharged.

If the patient had been found to have endocarditis, the treatment regimen typically would be 4 weeks of IV penicillin G plus 2 weeks of IV gentamicin. In those persons with penicillin sensitivity, vancomycin with gentamicin may be used. Rat bite fever has been seen to cause a spinal epidural abscess as well. A patient had been complaining of diffuse abdominal pain that was later discovered via ultrasound to be due to a bulging bladder. Neurological exam revealed paresthesias and hypesthesia distal to dermatome T-10 along with enhanced reflexes of his lower extremities. Magnetic resonance imaging (MRI) revealed an epidural space-occupying lesion compressing the spinal cord. The abscess was drained via laminectomy and the patient received IV penicillin G for 2 weeks, then oral penicillin V for 4 weeks after the abscess fluid was shown positive for *S moniliformis*.

In another case, a patient exhibited classic rat bite fever symptoms in addition to lower back tenderness. An MRI revealed vertebral osteomyelitis that required surgical debridement. Blood culture revealed *S moniliformis*. The patient received 6 weeks of ceftriaxone.

In yet another case, a patient diagnosed with rat bite fever began to have right hip pain on range of motion. Ultrasound showed right hip joint effusion, and right hip joint aspiration was collected, which proceeded to grow *S moniliformis*. A subsequent MRI revealed bone marrow edema in proximal femoral epiphysis with concern for osteomyelitis. The patient was treated with 4 weeks of IV penicillin G and then 4 weeks of oral amoxicillin.

### Diagnosis and treatment recommendations

The American Academy of Pediatrics (AAP) states that *S moniliformis* can be isolated from blood, synovial fluids, abscess aspiration, or the site of the bite lesion. Because SPS is inhibitory to *S moniliformis* growth, SPS-free media should be used when culturing. Culture should be held for up to 3 weeks if *S moniliformis* is suspected. The bacterium also can be detected using a nucleic acid amplification-based assay.

The Centers for Disease Control and Prevention (CDC) notes that in the absence of a positive culture, identification of pleomorphic gram-negative bacilli in appropriate specimens supports a preliminary diagnosis of *S moniliformis*.2

Treatment recommendations from the AAP include IV penicillin G for 7 to 10 days or IV penicillin G for 5 to 7 days followed by oral penicillin V for 7 days. There is limited evidence for use of ampicillin, cefuroxime, and cefotaxime. Doxycycline or streptomycin may be used if severe penicillin allergy exists. In cases complicated by endocarditis, antibiotic therapy requires dual therapy via high-dose penicillin G for 4 weeks in combination with streptomycin or gentamicin.1

Treatment for the 50% of patients with rat bite fever presenting with migratory polyarthralgias is achieved through symptomatic care and nonsteroidal anti-inflammatory drugs (NSAIDs) for pain control.12

### Patient outcome

The patient was transitioned to amoxicillin on day 5 of his hospitalization, and he was discharged on oral amoxicillin 500 mg 3 times a day for 5 days. Follow-up with the Infectious Disease clinic 1 week after discharge revealed completion of his antibiotic course and that his pain and oral intake continued to improve.

### Reference

For references, go to ContemporaryPediatrics.com/puzzler-0618

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### TABLE 2

**TYPICAL SIGNS, SYMPTOMS, AND COMPLICATIONS OF RAT BITE FEVER**

<table>
<thead>
<tr>
<th>SIGNS</th>
<th>SYMPTOMS</th>
<th>COMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Chills</td>
<td>Endocarditis</td>
</tr>
<tr>
<td>Reddish-brown or purple plaque rash</td>
<td>Headache</td>
<td>Vasculitis</td>
</tr>
<tr>
<td>Ulceration at bite site</td>
<td>Vomiting</td>
<td>Abscess</td>
</tr>
</tbody>
</table>

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**Dr. Vashi** is a third-year pediatric resident at Saint Louis University School of Medicine, St. Louis, Missouri.

**Dr. Tanios** is associate professor of General Pediatrics, Saint Louis University School of Medicine, and hospitalist, SSM Health Cardinal Glennon Children’s Hospital, St. Louis, Missouri.
A common complaint among children and adolescents, headaches including migraines remain the top reason for referrals to pediatric neurology.\(^1,2\) The worldwide prevalence of migraine in children and adolescents is 7.7%.\(^3\) Reported prevalence increases with age, from 3% (age 3 to 7 years) to 8% to 23% (age 11 to 15+ years).\(^4\) Approximately 10% of school-aged children suffer from migraine, with boys being more frequently affected before puberty, and girls more frequently thereafter.\(^5\) A comprehensive 2010 survey estimated that migraine has a global prevalence of 14.7%, making it the third-most-common disease in the world in men and women.\(^6\)

All these headaches carry costs beyond their physical toll. On average, children with migraine miss 8 school days yearly, versus 4 for children without migraines.\(^7\) Among adults globally, migraine ranks seventh among specific causes of disability, and among the top 10 causes of disability in 14 of 21 world regions.\(^6\) One analysis reveals that between 2008 and 2013, patients with migraine had significantly higher direct and indirect healthcare costs ($10,363 and $11,294, respectively) than did patients without migraines ($4,619 and $8,945, respectively).\(^8\)

Additionally, the migraine burden cannot be measured with dollars alone. Researchers have likened the impact of migraines on children’s quality of life to that of arthritis, diabetes, and cancer.\(^9,10\) Yet the seriousness of migraine remains underappreciated by parents, teachers, primary care providers,\(^11\) and often migraine sufferers themselves, most of whom are never diagnosed or treated.\(^5\) The psychosocial and economic burden of pediatric migraine, coupled with the relief offered by newer treatments including triptans, lends urgency to accurately identifying and promptly treating migraine.\(^2,12\)

Migraine classification
The considerable variability of migraine within and among patients stems from dysfunction of an ion channel in brainstem nuclei that normally modulates sensory input and regulates the meningeal blood vessels.\(^13\) Pathophysiologically, neural abnormalities drive dilation of cranial blood vessels, resulting in further nerve activation and pain.\(^14\)

**Physicians must understand current diagnostic criteria for pediatric migraine and its variants, and exercise their best clinical judgment regarding treatment.**

THOMAS KOCH, MD, FAAP, FAAN; CHRISTOPHER B OAKLEY, MD
MEDICAL WRITING SUPPORT PROVIDED BY JOHN JESITUS, MA

**Dr Koch** is professor of Pediatrics at the Medical University of South Carolina, Charleston.

**Dr Oakley** is assistant professor of Neurology, Johns Hopkins School of Medicine, Baltimore, Maryland. The authors report no financial interests relevant to any manufacturers of products or providers of services mentioned in this article. The article discusses off-label use (most medications used for pediatric migraine are off-label.) Mr Jesitus is a Denver, Colorado-based healthcare writer and editor. He 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.
The International Classification of Headache Disorders, 3rd edition (ICHD-3), classifies headaches into primary, secondary, and those caused by cranial neuropathies and other headaches (Table 1).15

**PRIMARY HEADACHES**

This category includes diagnostic criteria for migraine and its variants, along with tension-type headache (TTH) and other trigeminal autonomic cephalalgias (TACs).

Migraines can occur with or without aura; specifically, at least 2 attacks that include 1 or more reversible visual, sensory, or other symptoms that meet specific temporal criteria.

**TABLE 1**

**ICHD-3 CRITERIA FOR HEADACHE DISORDERS: MIGRAINE**

<table>
<thead>
<tr>
<th>TYPE OF MIGRAINE</th>
<th>DESCRIPTION</th>
<th>SYMPTOMS OR CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine with brainstem aura (formerly basilar migraine)</td>
<td>Migraine with aura symptoms clearly originating from the brainstem, with no motor or retinal symptoms</td>
<td>≥2 of these (reversible) symptoms: ■ Dysarthria ■ Vertigo ■ Tinnitus ■ Hypacusis ■ Diplopia ■ Ataxia not attributable to sensory deficit ■ Decreased consciousness</td>
</tr>
<tr>
<td>Chronic migraine</td>
<td>Prolonged migraine that lasts &gt;90 d, or very frequent migraine attacks that fulfill the symptoms/characteristics to the right: ■ Occurring on ≥15 d/mo for &gt;3 mo ■ ≥5 attacks fulfilling migraine or migraine with aura criteria</td>
<td>≥8 d monthly for &gt;3 mo fulfilling criteria for migraine or migraine with aura, or believed by patient to be migraine at onset and relieved by a triptan or ergot derivative</td>
</tr>
<tr>
<td>Status migrainosus</td>
<td>Debilitating migraine with or without aura lasting 72-90 h (migraine persisting &gt;90 d becomes chronic migraine)</td>
<td>Pain and/or associated symptoms cause disability. ■ Typical of previous attacks except for duration and severity</td>
</tr>
<tr>
<td>Familial hemiplegic migraine (FHM)</td>
<td>Migraine with aura, occurring in patients with ≥1 first- or second-degree relative with history of attacks fulfilling hemiplegic migraine criteria</td>
<td>■ Both of the following, fully reversible: ■ Motor weakness ■ Visual, sensory and/or speech/language disturbances</td>
</tr>
<tr>
<td>Cyclic vomiting syndrome (CVS)</td>
<td>Recurrent episodic attacks of intense nausea and vomiting, usually occurring with: ■ Predictable pattern ■ Normality between attacks ■ Self-limiting overall duration</td>
<td>Additional characteristics: ■ Nausea or vomiting ≥4 times/h ■ Attacks lasting ≥1 h, up to 10 d and ≥1 wk apart</td>
</tr>
<tr>
<td>Abdominal migraine</td>
<td>≥5 attacks of abdominal pain lasting 2-72 h when untreated or unsuccessfully treated</td>
<td>Pain has ≥2 of these characteristics: ■ Midline or periumbilical location, or poorly localized ■ Dull or sore quality ■ Moderate to severe intensity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th><strong>ICHD-3 CRITERIA FOR PEDIATRIC MIGRAINE</strong></th>
<th><strong>ICHD-3 CRITERIA FOR MIGRAINE WITH AURA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine—Episodic headache with ≥5 attacks lasting 2-72 h that cannot be better explained by another diagnosis or medication overuse, with ≥2 of these characteristics: ■ Bilateral location (vs unilateral predilection in adults. Although usually frontotemporal, rare occipital headache in children calls for diagnostic caution.) ■ Pulsating quality ■ Moderate to severe pain ■ Aggravation by routine physical activity</td>
<td>≥1 aura symptoms spread over ≥5 minutes ■ Each individual aura symptom lasts 5-60 min ■ ≥1 symptom is unilateral ■ ≥1 symptom is positive (scintillations, pins and needles) ■ Aura is accompanied or followed within 60 min by headache</td>
<td></td>
</tr>
<tr>
<td>Plus ≥1 of these symptoms:</td>
<td>■ Nausea or vomiting ■ Photophobia and phonophobia</td>
<td></td>
</tr>
</tbody>
</table>
**ICHD-3 CRITERIA FOR TENSION-TYPE HEADACHE (TTH)**

<table>
<thead>
<tr>
<th>TTH TYPE</th>
<th>FREQUENCY</th>
<th>DURATION</th>
<th>NAUSEA</th>
<th>PHONOPHOBIA/PHOTOPHOBIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent episodic</td>
<td>≤10 episodes occurring on ≤1 d monthly on average (&lt;12 d/y)</td>
<td>30 min-7 d</td>
<td>No</td>
<td>≤1 (but not both)</td>
</tr>
<tr>
<td>Frequent episodic</td>
<td>≤10 episodes occurring on 1-14 d/mo on average for &gt;3 mo</td>
<td>30 min-7 d</td>
<td>No</td>
<td>≤1 (but not both)</td>
</tr>
<tr>
<td>Chronic</td>
<td>≥15 d/mo for &gt;3 mo (≥180 d/y)</td>
<td>Hours to days or unremitting</td>
<td>Mild</td>
<td>≤1 (but not both)</td>
</tr>
</tbody>
</table>

**ICHD-3 CRITERIA FOR TRIGEMINAL AUTONOMIC CEPHALALGIA (TAC)**

<table>
<thead>
<tr>
<th>TAC TYPE</th>
<th>NO. OF ATTACKS</th>
<th>SEVERITY</th>
<th>FREQUENCY</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster</td>
<td>≥5</td>
<td>Very severe</td>
<td>Every 2/d-8/d</td>
<td>15-180 min (untreated)</td>
</tr>
<tr>
<td>Short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)</td>
<td>≥20</td>
<td>Moderate to severe</td>
<td>≥1/d</td>
<td>1-600 sec, as single or multiple stabs or in sawtooth pattern</td>
</tr>
<tr>
<td>Paroxysmal hemicrania</td>
<td>≥20</td>
<td>Severe</td>
<td>≥5/d</td>
<td>2-30 min*</td>
</tr>
<tr>
<td>Hemicrania continua</td>
<td>Persistent</td>
<td>Exacerbations of moderate intensity</td>
<td>N/A</td>
<td>≥3 mo*</td>
</tr>
</tbody>
</table>

---

*Photophobia/phonophobia
*Blurred vision
*Yawning
*Pallor.

Additional types of primary headaches include TTH and TAC.

All forms of TTH typically involve a mild-to-moderate bilateral headache, pressing or tightening in quality. Increased pericranial tenderness is the most significant abnormal finding in patients with any type of TTH. Pain does not worsen with routine physical activity and may or may not be associated with nausea, phonophobia or photophobia may occur.

Finally, TACs are unilateral headaches, usually accompanied by prominent cranial parasympathetic autonomic features (such as conjunctival injection and/or lacrimation, nasal congestion, and facial sweating), which are lateralized and ipsilateral to the headache.

**OTHER PRIMARY HEADACHES**

Additional forms of primary headaches include the following (see ICHD-3 for descriptions and details):

- Cough
- Exercise
- Sexual activity-associated
- Thunderclap
- Cold stimulus
- External-pressure
- Stabbing
- Nummular
- Hyptic
- New daily persistent headache (NDPH).

**SECONDARY HEADACHES**

Secondary headaches include new headaches and preexisting or significantly worsening preexisting headaches caused by primary disorders such as trauma and systemic diseases.

Other causes include:

- Trauma or injury to head and/or neck
- Cranial and/or cervical vascular disorder
- Nonvascular intracranial disorder
- Increased intracranial pressure
- Substance or its withdrawal
- Infection
- Disorder of homeostasis
- Psychiatric disorder
- Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial/cranial structure.

Cranial neuropathies, centrofacial pain, and other headaches include painful cranial-nerve lesions and other facial pains deriving from a complex catalog of causes such as trigeminal, glossopharyngeal, occipital, and other neuralgias; optic neuritis; ischemic oculomotor nerve palsy; and various facial neuropat-
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CONTINUED FROM PAGE 24

thies and syndromes.15

Evaluation
Evaluating pediatric migraine requires a systematic approach involving the following steps.16,17

1 Medical history—Usually, a thorough headache history provides enough clues for accurate diagnosis.18 Questions (Table 2) are structured to identify more concerning headache patterns early in the process.19

Keep in mind that there are red flags that should trigger consideration of neuroimaging for suspicion of intracranial pathology (see “Red flags for considering neuroimaging,” page 27).20

2 Physical examination—This portion of the evaluation should include the following measurements/investigations:

- Take vital signs (including blood pressure, temperature, signs of hypertension or infection).
- Measure head circumference, even in older children.
- Palpate head and neck for sinus, jaw, ocular or temporomandibular joint tenderness, thyromegaly, or nuchal rigidity.
- Identify trigger points or areas of maximum tenderness to help determine nature of the pain.
- Check skin for signs of neurocutaneous syndromes, particularly neurofibromatosis and tuberous sclerosis, which are highly associated with intracranial neoplasms.

3 Neurologic examination—More than 98% of children with brain tumors who present with headache have objective neurologic findings.21 Look for abnormalities in these areas during the basic neurologic exam:

- Optic discs
- Eye movements
- Pronator drift
- Gait (including tandem gait)
- Deep tendon reflexes.

Routine neuroimaging is not indicated in children with recurrent headaches and normal examination. However, physicians should consider neuroimaging if certain warning signs appear:

- Recent onset of severe headache
- Change in headache quality or frequency
- Abnormal neurologic examination
- Coexistence of seizures.

4 Ancillary testing as indicated—No evidence supports the use of routine laboratory studies, lumbar puncture, or electroencephalogram (EEG) in headache-affected children with normal physical and neurologic

<table>
<thead>
<tr>
<th>TABLE 2 MEDICAL HISTORY QUESTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUESTION</td>
</tr>
<tr>
<td>What is the pattern of your headaches, and at what time of day do they occur?</td>
</tr>
<tr>
<td>How and when did your headaches begin?</td>
</tr>
<tr>
<td>How often do they occur, and how long do they last?</td>
</tr>
<tr>
<td>Where is the pain located?</td>
</tr>
<tr>
<td>What is the quality of the pain?</td>
</tr>
<tr>
<td>What other symptoms accompany your headaches?</td>
</tr>
<tr>
<td>Does anyone in your family suffer from headaches?</td>
</tr>
<tr>
<td>What do you think might be causing your headaches?</td>
</tr>
</tbody>
</table>

Abbreviations: TAC, trigeminal autonomic cephalalgias; TTH, tension-type headache. Adapted from Rothner AD.19
findings. However, if findings in steps 1 to 3 warrant further exploration, consider appropriate modalities.

**Imaging as indicated**—Similarly, no evidence supports the use of routine neuroimaging in children with a history of recurring headaches who have a normal neurologic exam. Neuroimaging in children with headaches should be considered when findings in steps 1 to 3 warrant further investigation.17

More specifically, when the neurologic exam is abnormal, when other simultaneous neurologic concerns such as seizures are present, or when headache historical factors such as first, worst, or marked change in headache pattern are reported, neuroimaging should be considered. When considering neuroimaging, magnetic resonance imaging (MRI) would be the preferred imaging modality unless there is a concern for an acute or life-threatening etiology.
that warrants quick imaging such as computed tomography (CT).

**Treatment**

Treatment of pediatric migraines requires a multitiered approach (Table 3), which tailors an individualized treatment plan to each patient’s headache pattern and lifestyle and that can accommodate changes if needed.22 Headache frequency may spontaneously increase, for example, and patients may require higher or lower doses than for previous headaches, or, for more difficult headaches, combination therapy. Each child’s degree of headache burden should determine how aggressively one treats and manages his or her headaches, considering the following factors:

- Headache frequency, duration and intensity,
- Patient’s functional disability and pain tolerance;
- Patient’s comorbidities; and
- Patient’s quality of life.

Many patients with moderate-to-severe migraine respond well to oral treatment with analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) administered at the time of an attack (acute/abortive treatment; Table 4). Patients must be educated and able to use their medication as early during the headache as possible. This requires ready access to medications in school, home, and social situations:2,12,23 Patients also must avoid medication overuse, a known cause of headaches, by limiting analgesic and NSAID use to 2 to 3 days or less weekly. Keeping a headache diary can track drug use patterns.

Additional agents require caution. For example, aspirin-butalbital-cafeine is frequently prescribed for adult headaches, although, like other aspirin-containing products, it should be avoided in children aged younger than 16 years due to the risk of Reye syndrome.24 Always avoid opiates and other narcotics in children.

**Triptans**

Physicians typically reserve serotonin 5-HT1B/1D receptor agonists (triptans; Table 5)22,26-30 for moderate-to-severe headaches unresponsive to

---

**TABLE 4**

**NONSPECIFIC TREATMENTS FOR PEDIATRIC MIGRAINE**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>10 mg/kg every 6 h</td>
<td>The most widely studied analgesic for pediatric headaches.</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>10-15 mg/kg</td>
<td>Considered second-line, reserved for children with hypersensitivity or other contraindications to NSAIDs:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Upper gastrointestinal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Bleeding disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Renal impairment</td>
</tr>
<tr>
<td>Naproxen</td>
<td>10-20 mg/kg/d</td>
<td>Tends not to cause rebound headache.</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>0.5 mg/kg IV, 15 mg max</td>
<td>Works best in combination with prochlorperazone.</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs.

---

**TABLE 5**

**TRIPTANS APPROVED FOR PEDIATRIC MIGRAINE**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE</th>
<th>AGE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan/naproxen a (Treximet)</td>
<td>10/60 mg Daily max: 85/500 mg</td>
<td>12-17 y</td>
</tr>
<tr>
<td>Sumatriptan nasal spray b (Approved in Europe, Asia, and other countries; intranasal sumatriptan also has support from a strong RCT performed in the United States.)</td>
<td>5 or 20 mg</td>
<td>12-17 y</td>
</tr>
<tr>
<td>Rizatriptan d</td>
<td>Weight &lt;40 kg: 5 mg Weight &gt;40 kg: 10 mg</td>
<td>6-17 y</td>
</tr>
<tr>
<td>Almotriptan e</td>
<td>6.25 or 12.5 mg Daily max: 25 mg</td>
<td>12-17 y</td>
</tr>
<tr>
<td>Zolmitriptan nasal spray f</td>
<td>2.5 mg or 5 mg Daily max: 10 mg</td>
<td>12-17 y</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs.

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clinical feature

Over-the-counter analgesic therapy. Unlike ergot derivatives, triptans offer selective activity, along with well-established dosing regimens, safety, and tolerability. Sumatriptan, almotriptan, zolmitriptan, and rizatriptan have earned US Food and Drug Administration (FDA) approval for acute pediatric migraine.

All triptans activate the atypical 5-HT1B/1D receptor that has been implicated in the pathophysiology of migraine, and, to a lesser degree, other 5-HT receptors. They do this through 3 main mechanisms of action:

- Cranial vasoconstriction;
- Peripheral trigeminal inhibition; and
- Inhibition of transmission through second-order neurons of the trigeminal cervical complex.

In 2006, the FDA warned consumers that taking triptans with selective

FIGURE

AMPP MIGRAINE PREVENTION CRITERIA

Migraine Freq (d/mo)

<table>
<thead>
<tr>
<th>Function Normally</th>
<th>Some Impairment</th>
<th>Severe Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4–5</td>
<td>6–10</td>
<td>11+</td>
</tr>
</tbody>
</table>

Degree of Impairment

<table>
<thead>
<tr>
<th>Degree of Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Prevention</td>
</tr>
<tr>
<td>Consider Prevention</td>
</tr>
<tr>
<td>Offer Prevention</td>
</tr>
</tbody>
</table>

serotonin reuptake inhibitors (SSRIs) or selective serotonin/norepinephrine reuptake inhibitors (SNRIs) could raise users’ risk of life-threatening serotonin syndrome. However, careful review of the available evidence has shown that this is not the case.

Experts have suggested guidelines for triptan use in pediatric migraine (Table 6). Adverse effects of triptan generally last less than 30 minutes.

### Additional treatment options

With few medications approved for pediatric migraine, physicians frequently prescribe drugs used for migraine in adults (Table 7).

### Migraine prevention

Whereas no consensus exists for when and how to implement preventive therapy for migraine in children, various authors suggest considering prophylaxis in patients who experience at least 3 to 4 migraines monthly, and in those for whom acute treatments prove insufficient and/or poorly tolerated. Children who experience significant pain and/or disability also may warrant prophylaxis.

Authors of the American Migraine Prevalence and Prevention (AMPP) trial recommend considering and offering prophylaxis to patients aged 12 years and older (Figure). The only agent the FDA has approved for preventive use in children is topiramate. Insufficient and often conflicting evidence notwithstanding, additional drugs commonly used for this purpose in children include antidepressives, antihypertensives, antiepileptics, antihistamines, and nutraceuticals (Table 8).

### On the horizon: CGRP antagonists

A promising strategy for acute and preventive migraine treatment involves blocking calcitonin gene-related peptide (CGRP), a potent vasodilator whose concentration in the external jugular vein rises during migraine attacks and decreases in the serum after triptan administration and symptomatic relief. Developers of the following monoclonal antibodies targeting CGRP have filed for FDA review, with decisions expected in 2018:

- **Erenumab**
- **Fremanezumab**
- **Galcanezumab**

Additional treatments under study specifically for pediatric headaches including migraine are propofol, prochlorperazine, dexamethasone, diclofenac, fentanyl, and several behavioral and nutraceutical approaches. As the array of interventions for preventing and treating pediatric migraine grows, timely and appropriate application of such agents will continue to reduce its burden.
Burnout is a real medical problem for the physician workforce. Here’s advice how to recognize when one is at risk from workplace stressors and what can restore quality of life.

PAT R BASS III, MD, MS, MPH; GENA CASTRO RODRIGUEZ, PSYD, LMFT

Changes in healthcare systems, payment, and the practice of medicine have made significant impacts on the personal and professional lives as well as well-being of pediatricians. Although pediatricians commonly enter medicine with a strong desire to help their patients and provide comprehensive patient care, and anticipate a fulfilling and satisfying career, all is not well with the physician workforce.

Several well-publicized articles in the lay press reporting suicide deaths of resident trainees, one study indicating as many as 400 physicians per year commit suicide, and another revealing that 1 in 16 surgeons experiences suicidal ideation while not seeking help all point to problems in the physician workforce in understanding, preventing, and avoiding burnout while promoting personal and career satisfaction and well-being.

Although not commonly examined in the research arena, pediatrics is not exempt. This article will focus on the impacts of burnout among pediatricians and steps pediatricians can take to avoid burnout and promote physician well-being.

Symptoms of burnout

Let’s take a closer look at the symptoms of burnout. (See “What is burnout?” on page 32.)

**EMOTIONAL EXHAUSTION**

This can include feelings of being tapped out or the inability to recover after time off. Physical and emotional energy are both low and the pediatrician may find himself/herself saying things like “I’m not sure how much longer I can keep going like this.” The pediatrician has only so much energy and empathy for others.

Emotional exhaustion can affect the physician at home as well, leaving less emotional capacity for family, friends, and loved ones.

**DEPERSONALIZATION**

The pediatrician may notice increased cynicism, sarcasm, and complaints about his or her job. One can think of this as a dysfunctional coping mechanism. “Compassion fatigue” may leave the pediatrician with a lack of emotional energy and not emotionally available for patients. Depersonalization is a dissociative coping mechanism that makes one feel as if he or she is outside one’s body or that experiences are not real or dreamlike. It allows us to manage difficult situa-
WHAT IS BURNOUT?
Burnout can be thought of as the antithesis of wellness and a constellation of symptoms primarily due to workplace stressors over time in the following domains:

1. Emotional exhaustion
2. Depersonalization
3. Diminished sense of accomplishment
4. Reduced satisfaction with work and the work environment

There are a number of negative consequences associated with burnout related to job performance:
- Elevated levels of job dissatisfaction
- Increased job turnover
- Increased medical errors
- Negative attitudes toward patients
- Patient dissatisfaction
- Lack of energy and motivation

On a personal level, burnout is associated with:
- Failed relationships and relationship challenges
- Depression
- Anxiety
- Substance abuse
- Suicidal ideation


REDUCED SENSE OF ACCOMPLISHMENT
The pediatrician begins to have a lack of meaning in his or her practice and questions both the quality of one’s work and whether he or she is making a difference in patient’s lives. The internal motivation for the work is challenged, including feeling part of a bigger system, making a difference, or having an impact. The balance of internal and external motivators is necessary to provide balance when working in high-demand careers.

REDUCED SATISFACTION WITH WORK
A number of things decrease satisfaction with work, such as hassles related to managing the practice, the call schedule, the compensation model, or getting along with partners. All these things can lead to increased time away from other important things in life, such as family and outside interests and decreased work satisfaction. Unfortunately, pediatricians often ignore these issues and may increase the risk of burnout. The effects of burnout are cumulative and decreased satisfaction builds over time, having a greater impact the longer the problem persists.

Pediatrician burnout is a big problem
In general, burnout is greater in the physician workforce compared with the general population. General pediatrics experiences less burnout than most other specialties, with 35% (approximately 50% among all physicians) reporting burnout and nearly 60% (also approximately 50% among all physicians) of pediatricians feeling that their practices leave them with enough time for personal and family matters. Pediatric subspecialists report burnout and satisfaction levels of approximately 40%, respectively. Although burnout may impact pediatrics less than other specialties, the numbers still indicate a significant problem.

One recent study by Starmer and colleagues looked at early career pediatricians who are particularly at risk for burnout due to multiple transitions such as moving from residency into private practice as well as beginning families. Even though these pediatricians reported career and life satisfaction (83% and 71%, respectively), significant concern is raised from the reports of burnout (30%) and a satisfactory work/life balance (43%). Women also were more likely to report burnout and less likely to report career satisfaction—a significant problem given current demographic trends in the pediatric workforce.

Importantly, there were a number of modifiable factors that impacted the results. Good health, a supportive and collegial environment among physicians, and adequate patient care resources all were associated with improved outcomes related to burnout and work/life balance.

35% of general pediatricians experience burnout

Other factors also may contribute to increased burnout and less career satisfaction. Increased workloads were identified by Starmer and other studies as a risk for burnout. Starmer found that pediatricians reporting
chaotic schedules were 5 times more likely to report burnout. Other factors that may be associated with burnout are less control of schedule and decreased autonomy in practice. Work/home conflicts also are associated with increased burnout in general, and pediatricians reporting feeling sad or depressed also were more likely to experience burnout.

**How to reduce burnout in pediatricians**

Interventions to decrease burnout can be divided into organizational-directed and physician- or individual-directed interventions. Based on current research, there is more evidence to support organizational-directed compared with physician/individual-directed interventions for a relatively small improvement in measures of physician burnout. However, large organizational interventions are much less common and not always rigorously evaluated.

**ORGANIZATIONAL-DRIVEN INTERVENTIONS**

In one study, the Mayo Clinic provided 1 hour of protected time every other week for a facilitated small-group curriculum for 9 months. Control group subjects could schedule and use this hour of protected time in any manner they believed appropriate. Topics in the curriculum included: 1) meaning in work; 2) personal and professional balance; 3) medical mistakes; 4) community; 5) caring for patients; and other topics relevant to the work experiences of practicing physicians. Each session followed the same structure: check-in and welcome; preparing the environment (eg, journaling and reflective exercise); facilitated group discussion; learned skills and solutions; and checkout and summary.

Measurements in empowerment and engagement at work significantly increased by month 3 in the intervention arm of the study (5.3-point increase vs a 0.5-point decline; \( P = .04 \)) and were maintained at the 12-month conclusion (+5.5 points vs +1.3 points; \( P = .03 \)). Similarly, there was a significant decline in rates of depersonalization (15.8% vs 0.8%; \( P = .004 \)) at 3 months, and this difference was still present at the 1-year conclusion (9.6% vs 1.5% decrease; \( P = .02 \)). No statistically significant differences were seen in stress, symptoms of depression, overall quality of life, or job satisfaction.

In a study by Lucas and colleagues, shortening inpatient rotations from 4 weeks to 2 weeks was associated with a decrease in attending physician burnout, but also resulted in poorer resident evaluations of faculty. The study was powered primarily to see if shortening the rotations might improve 30-day readmission rates, which were unchanged. Findings such as these will force hospitals or practice managers to consider a number of different potential secondary outcomes when considering changes that ultimately do not impact patient care.

In a 2015 study, Linzer and associates implemented a complex intervention in 34 primary care clinics to see if improving work conditions could decrease burnout and improve quality of care. Burnout was documented in 37% of clinic physicians at baseline. Improvements could broadly be defined into 3 categories:

- Improved communication;
- Changes in workflow; and
- Targeted quality improvement (QI) projects.

More specifically, intervention clinics chose to individually implement programs at the clinic level that were drawn from the literature. After 12 to 18 months, burnout was reassessed. Some interventions included:

- Monthly provider meetings that focused on work/life or practice management issues.
- Off-loading nonessential tasks such as medical assistants (MAs) scribing.
- Removing rooming bottlenecks to increase physician/patient contact time.
- Creating clinicwide policies for MAs related to diabetic foot screenings and other appropriate tasks.
- Pairing MAs with particular physicians.
- Increasing appointment times by 5 minutes.
- Instituting a prescription refill line.
- Nurse coordinators leading support for patient issues and sharing calls.

Intervention clinicians showed more improvements in burnout (21.8% vs 7.1% less burned out; \( P = .01 \)); were more satisfied (23.1% vs 10.0% more satisfied; \( P = .04 \)); and were less likely to report an intention to leave the practice (odds ratio [OR], 4.2; \( P = .06 \)). It appears that a systemic intervention to apply workflow redesign and improve communication between clinic and physician staff might decrease burnout and potentially improve retention.

**INDIVIDUAL-DRIVEN INTERVENTIONS**

Although, as previously stated, the evidence currently seems to support organizational-driven interventions versus individual-driven interventions, there is likely little chance of harm and more potential for individual benefit. If burnout is a system problem, it is also less likely to be mitigated at the individual level. The following are some interventions that stressed-out individuals can use for personal benefit.
MINDFULNESS
Aguero and colleagues6 delivered a comprehensive mindfulness program consisting of 18-hour program followed by 8 weekly 2.5-hour sessions. Activities included mindfulness-based coping strategies, mindfulness practice, and yoga. There were didactic presentations, group discussions, direct practice, and exercises. For example, some of the didactic topics included dealing with pleasant and unpleasant events, conflict management, burnout prevention, setting boundaries, exploring self-care, caring for suffering patients, and end-of-life care. Participants were provided instruction and practice with mindfulness meditation. Participants also participated in narrative exercises where they wrote brief stories about personal experiences in medical practice focusing on the current educational topics.

The intervention group showed improvements in all outcome measurements (mood disturbance [difference between groups, -7.1; standardized effect-size (SES), 1.15]; mindfulness [difference between groups, 11; SES, 0.9]; burnout [difference between groups, -7; SES, 0.74]; and empathy scales [difference be-

HOW I PREVENT BURNOUT
PAT R BASS III, MD, MS, MPH

I do a number of things personally to try to decrease risk of burnout, and I was surprised by my research for this article indicating that organizational interventions were significantly better than individual interventions—perhaps because I have never felt any of the organizations I worked in have made systematic attempts to decrease or intervene related to burnout. Admittedly, early in my career I was unaware of burnout but took active steps to “improve my mental health” so as not to let medicine get the better of me as I had seen it do to others.

In my early career, all I needed to defend against burnout was exercise and what I now know as a “life calendar.” As a medical student, resident, and in my early career I was an avid athlete running triathlons and marathons. The aerobic benefits of long runs and cycling outings provided me with much of the mental health benefits I needed to address issues of burnout. The second and only other thing I did in residency and my early career was investing in the relationship with my wife. I had the wonderful advantage of having seen much of this in my own parents’ relationship and just had to model what I saw as successful.

Over the childless years of our new relationship and early marriage, my wife and I invested in each other. We cooked together, traveled to and lived in places we did not know, and were far away from family. We were poor and had only each other. We learned how to be better communicators together, developed a love for wine and travel, and saw very early on that we had to plan to make sure our life together did not get crowded out from everything else we were doing. We almost always had our next trip planned before the current one was complete. This provided me a great deal of solace. My relationship with my wife recharges and strengthens me every day.

I am always amazed at colleagues who do not plan. Between my wife and kids and my work, if I did not have a life calendar I would be a mess. I make an effort to be at as many of my kids’ events as I can, and I would miss many if my wife did not put them on a calendar for me. I have a boundary ritual that when I pull into the garage and turn off my car, I take in and release a big breath, saying that I am going to be present for my wife and kids. On most days it helps me separate from whatever happened at work.

As a family, we continue to travel and mostly have a year’s worth of adventures planned out at any given time. Although arthritis of the knee has limited my triathlons and marathons in my late 40s, I wake up early and walk about 5 miles every day before work. It’s not the same “aerobic high” I used to get, but the days that I walk before work are always better than those when I do not.

Over the last several years, I also have had an on/off relationship with both meditation and gratitude journaling. Although I have not incorporated them into my life with the same religiosity of my exercise regimen, I can say that I have less feelings of burnout when I do both regularly.

In closing, preventing burnout is all about active planning. Through hyperscheduling my calendar, I make sure that I am at as many family events as possible and always have some fun vacation or outing in the not-too-distant future. I similarly schedule exercise and alone time for my personal health and time with my wife so that we can recharge together.
tween groups, 5.2; SES, 0.71]) compared with the control group. The intervention group also reported feeling better and having more energy after the intervention.\(^{20}\)

A similarly designed intervention focusing more on specific mindfulness interventions improved emotional exhaustion, depersonalization, and personal accomplishment measures among physicians from multiple specialties, nurses, psychologists, and social workers practicing in both university and community settings.\(^{27}\)

**JOURNALING**

Although not well studied in burnout, there is an evidence base for journaling or expressive writing to provide benefit. Self-reflection allows the pediatrician to process events or a stressful day. Expressive writing has been associated with improved wound healing and immune function in adults, as well as decreased hospital visits.\(^{18,19}\) In adult breast cancer patients, expressive writing reduced visits for cancer-related morbidities and decreased physical symptoms.\(^{20}\)

Gratitude journaling has been studied for years and can provide many benefits that might decrease physician burnout. Gratitude journaling, which can be beneficial even if performed only on a weekly basis, may lead to benefits such as:  

- Improved immune function;
- Lower blood pressure and improved cardiovascular health;
- Improved sleep;
- More positive emotions, optimism, and happiness;
- Less feelings of isolation; and
- Becoming more outgoing and forgiving.

If thought of as a self-administered treatment, journaling can easily and inexpensively be self-administered by physicians. There is also some evidence that these treatments may be as effective as traditional therapy. The pediatrician might think of journaling as a preventive psychologic support that might be started before psychosocial dysfunction develops.\(^{22}\)

**IDENTIFYING BROKEN-RECORD MOMENTS**

Broken-record moments are opportunities for a physician to decrease stress and have more energy by optimizing his or her work environment. If the physician is writing similar notes or providing similar education (can be identified by asking oneself “Is this the third time I have done this activity this week?”), he or she can create templates for documentation and handouts or videos to provide patient education. Similarly, the pediatrician can set up automated processes to report results to patients and use citation software to make communication with other physicians more efficient.

**Prioritizing oneself**

If pediatricians do not prioritize themselves, their careers can crowd out their lives. There are a number of things the pediatrician can do to energize himself or herself to decrease burnout.\(^{23}\)

**Create a life calendar.** The pediatrician schedules patients, meetings, and other important professional events. Scheduling exercise, time for journaling, reading, or a date night will increase the chance these regenerative activities occur.\(^{25}\)

1. **Create a “boundary ritual.”** This is like an off switch that creates a boundary between work and home. It signifies the turning off of medical practice and is the equivalent of “No Doctoring Beyond This Point.” This will allow one to drop his/her day-to-day practice concerns and truly focus on family and other important matters in one’s life.\(^{24}\) Successful boundary rituals involve 3 components (see “How I prevent burnout,” page 34):

   - An intention to let go of work;
   - A release of breath; and
   - An action such as changing clothes.

2. **Date night.** Healthy relationships recharge and strengthen the pediatrician, and unhealthy relationships lead to many different problems. If the pediatrician does not have a significant other, he or she could spend time to get to know someone better or do something unexpected by oneself.\(^{23}\)

3. **Create a bucket list.** Bucket lists are things one wants to personally accomplish before “kicking the bucket.” These lists allow the pediatrician to work toward things that are personally meaningful to himself or herself and provide a sense of purpose and excitement that will boost energy and increase resiliency.\(^{21}\)

4. **In conclusion**

   Burnout is a real medical problem for the physician workforce. Prioritize your own activities to decrease burnout and advocate that your organization do the same.

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**For references, go to ContemporaryPediatrics.com/pediatrician-burnout**

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**READ MORE** Are you looking for more advice about de-stressing? See Preventing (and treating) physician burnout online at contemporarypediatrics.com/preventing-burnout

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Anaphylaxis

Essentials for infants

The American Academy of Pediatrics (AAP) has updated its Allergy and Anaphylaxis Emergency Action Plan for the treatment of infants at risk for an allergic emergency.

TODD A MAHR, MD, FAAP, FAAAI, FACAAI

Food allergy and anaphylaxis in infants and toddler-aged children are growing trends. Food allergy is the leading cause of anaphylaxis in infants and toddlers, and the most common food triggers causing anaphylaxis in infants are cow’s milk, egg, and peanut. Although far less is known about the prevalence and nature of anaphylaxis in the infant/toddler population compared with older children and adults, over the last several years food allergy and food-related anaphylaxis have continued to grow among the infant/toddler age group.

For instance, between 1997 and 2007, food allergy in children increased by 18% in the United States. From 2007 to 2012, another study found a 50% increase in episodes of food-induced anaphylaxis presenting to the emergency department (ED). A more recent study showed that the increase in ED visits for anaphylaxis in children aged 0 to 5 years between 2005 to 2014 was 129%. It is likely that a child’s first reaction will occur when aged younger than 1 year. Therefore, these children are more likely to be brought to the ED and hospitalized. This becomes an opportunity to recommend referral to allergy specialty providers and deliver education on anaphylaxis.

Obstacles to rapid treatment in this population have been identified as a lack of recognition of reaction severity, not having epinephrine available, and parent/caregiver fear of giving epinephrine. Progress toward identification, accurate diagnosis, and management of anaphylaxis in infants and toddlers will require that pediatric healthcare providers recognize important barriers to appropriate management.

Is it anaphylaxis?

Accurate diagnosis of anaphylaxis requires that healthcare providers understand the possible presentations of anaphylaxis in infants and toddlers. A unique aspect of anaphylaxis in this age group is that a reaction itself may be difficult to recognize (Table), and therefore diagnosis can be challenging. This is because some of the symptoms of...
anaphylaxis (eg, vomiting, throat itching/tightness, gastrointestinal changes, hives, or hypotension) can manifest in an infant/toddler as regurgitation, irritability and fussiness, drooling, inconsolable crying, apparent contact rash from food, and lethargy/sleepiness.

Unfortunately, the latter behaviors can be perceived as normal in healthy children even during an allergic reaction. Another unique aspect of anaphylaxis in infants and toddlers that influences the ability to recognize a reaction is that they are not able verbalize their symptoms in particular, symptoms such as feeling faint, throat tightness, or the feeling of impending doom. These symptoms, which can be described by older children and adults, are sometimes critical to understanding the severity of a life-threatening reaction and the need to act.

Although hives and vomiting are more commonly described during anaphylaxis in infants and toddlers, the precise symptomatology or criteria for diagnosis of anaphylaxis for these children is not well defined. Anaphylaxis also may be characterized by cough, wheeze, stridor, lethargy/drowsiness, or gastrointestinal symptoms. In some cases, persistent vomiting may be the only sign.

A 2011 study reported the symptoms that infants presented with in the ED. The initial presentation of anaphylaxis in infants is cutaneous in 98% (95% confidence interval [CI], 94% to 100%), involves the respiratory system in 59% (95% CI, 47% to 71%), and involves the gastrointestinal system in 56% (95% CI, 44% to 67%) of cases. In some cases, changes in skin color and behaviors such as drooling and scratching can be signs of an emerging allergic reaction. Cardiovascular symptoms were reported as infrequent.

<table>
<thead>
<tr>
<th>TABLE</th>
<th>DIFFICULTIES IN RECOGNIZING ANAPHYLAXIS IN INFANTS/TODDLERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>POTENTIAL ANAPHYLAXIS SIGNS/ SYMPTOMS IN INFANTS/TODDLERS</td>
<td>REASONS WHY SYMPTOMS ARE DIFFICULT TO INTERPRET</td>
</tr>
<tr>
<td>Behavioral changes (eg, crying, irritability, fright)</td>
<td>Can be normal behaviors.</td>
</tr>
<tr>
<td>Flushing/redness</td>
<td>Can occur with fever, hyperthermia, or persistent crying.</td>
</tr>
<tr>
<td>Hoarseness/dysphonia</td>
<td>Common after persistent crying.</td>
</tr>
<tr>
<td>Drooling/increased secretions</td>
<td>Common in infants.</td>
</tr>
<tr>
<td>Spitting up/regurgitation</td>
<td>Common after feeding.</td>
</tr>
<tr>
<td>Loose stools</td>
<td>Normal in breastfed infants.</td>
</tr>
<tr>
<td>Colicky abdominal pain</td>
<td>Common in infants; discomfort/gas from cow’s milk-based formulas.</td>
</tr>
<tr>
<td>Drowsiness/somnolence</td>
<td>Common after feeding.</td>
</tr>
</tbody>
</table>

Adapted from Simons FE.

In real-world settings, the ability to distinguish normal infant/toddler behaviors, or contextual incidents (eg, contact rash on the face from food or vomit), from the manifestations of anaphylaxis are important for accurate diagnosis and treatment. For example, a contact rash on a child’s face after vomiting in the crib is different from hives that appear on the face after ingesting a possible allergen. However, some parents may suspect an allergic reaction. If hives appear on a child’s back, arms, or legs following ingestion of a potential allergen, then an allergic reaction should be suspected (ie, contextual and temporal indicators).

The addition of wheezing, trouble breathing, retching/repeat vomiting, or cyanosis to cutaneous symptoms are clear indicators that an anaphylactic reaction is happening. All patients are different, so considerations of core symptoms in any order, their severity, and the level of concern demonstrated by the parent or caregiver at the time of the reaction can help inform anaphylaxis treatment decision making.

**How treatment in infants/toddlers is different**

Epinephrine is the mainstay of treatment for anaphylaxis regardless of age. If anaphylaxis is certain, epinephrine given by intramuscular injection to the mid-outer thigh at a dose of 0.01 mg/kg is currently recommended. In the absence of a more ideal therapeutic option, pediatric epinephrine autoinjectors (EAs) containing a 0.15 mg dose of epinephrine, and indicated for children weighing 3 lb to 66 lb, have been the only option. However, there is some evidence that suggests these EAs may not be ideal for these young children.

It has been demonstrated that the exposed needle length (0.5 inch) in available 0.15-mg pediatric EAs could unintentionally strike the bone in some children weighing less than 33 lb

**JUNE 2018 | CONTEMPORARYPEDIATRICS.COM 37**
(Figure 1). In one study, 29% of children weighing less than 33 lb (n=100) had a skin-to-bone depth (STBD) by ultrasound that was less than 0.5 inch, which would put these children at risk for an unintentional bone strike. In a subgroup of children weighing less than 22 lb in this study, 60% (n=25) were at risk for this type of injury.

In a more recent study, 43.1% of patients (16.5 lb to 33 lb; n=51) would be at risk of an accidental bone injection if using the available 0.15-mg pediatric EAs. This study determined that the appropriate needle length for children weighing 16.5 lb to 33 lb would be 0.28 inch to 0.31 inch. Furthermore, injuries (lacerations and embedded needles) have been reported in infant/toddler-aged children using pediatric 0.15-mg EAs (Figure 2). As a result, the prescribing information of pen-style EAs was updated in 2016 to ensure that a child’s leg is held firmly during an injection.

To address these unmet needs (ie, lower dose and shorter needle length), a new EA containing an epinephrine dose of 0.1 mg and with a 0.29-inch needle was recently approved by the US Food and Drug Administration (FDA) for children weighing 16.5 lb to 33 lb. This new EA (Auvi-Q; kaléo Incorporated; Richmond, Virginia) is the only FDA-approved device engineered for infants and toddlers weighing 16.5 lb to 33 lb.

**Summary**

Available therapeutic options used to treat infants with anaphylaxis may not be ideal, but have been prescribed because of the lack of a more appropriate, FDA-approved option.

In August 2017, Contemporary Pediatrics highlighted the release of the first-ever written Allergy and Anaphylaxis Emergency Plan published by the AAP. In response to the need for individualized treatment of infants, the AAP has updated this plan to include the 0.1-mg dose EA for children weighing 16.5 lb to 33 lb. The updated plan can be downloaded at: www.aap.org/en-us/Documents/AAP_Allergy_and_Anaphylaxis_Emergency_Plan.pdf.

Medical writing and editorial assistance was provided by Sean M. Gregory, PhD, Hybrid Healthcare Communications LLC, and funded by kaléo, which had no role in the development, review, or final approval of the manuscript.

For references, go to ContemporaryPediatrics.com/infant-anaphylaxis

**FIGURE 1**

**PATIENT SKIN-TO-BONE DEPTH AS IT RELATES TO EXPOSED EA NEEDLE LENGTH**

Illustration shows how exposed EA needle length can be greater than the STBD of the patient’s thigh, which can put children at risk for accidental bone injections. Image is not to scale.

Abbreviations: EA, epinephrine autoinjector; STBD, skin-to-bone depth.

Author created.

**FIGURE 2**

Images of lacerations caused by pediatric epinephrine autoinjectors.

Juuling CONTINUED FROM PAGE 6

through these products.

Here are 3 steps that healthcare providers can institute in their practice to inform patients and their families about the health risks associated with nicotine delivery devices:

1. Ask specific and detailed questions regarding social use of cigarettes, electronic cigarettes, vape or vaping, and JUULs or particular product names. Practitioners should stay current with the terminology for multiple device delivery of nicotine and current adolescent/young adult-focused products on the market.

2. Discuss the contents of ENDS with patients and express the concerns you have as a healthcare provider. Advise them and their families regarding the specific delivery systems and the harmful effects of their chemicals on the body.

3. Post resources in the office and in the examining rooms, such as those provided by the AAP, and consider your practice’s statement regarding the use of these products.

Dr. Gibson-Young is an associate professor with Auburn University School of Nursing, Auburn, Alabama.

Dr. Martinasek is an associate professor of Public Health and assistant dean, Health Sciences and Human Performance, College of Natural and Health Science, University of Tampa, Florida.

For references, go to ContemporaryPediatrics.com/juuling

Pediatric oral health CONTINUED FROM PAGE 11

MORE ABOUT THE MCPP

The Michigan Caries Prevention Program (MCPP) was a partnership between Altarum, Delta Dental of Michigan, the University of Michigan School of Dentistry, and the Michigan Department of Health and Human Services. The goal of the program under a 3-year award from the Center for Medicare and Medicaid Innovation was to reduce the burden of childhood dental disease for a million Michigan children by identifying children at risk, linking them to appropriate providers, promoting evidence-based preventive care, and managing and monitoring the program’s impact.

For more information about the Michigan Caries Prevention Program, go to Miteeth.org

Your inner animatronic tooth

Not every kid’s dad is a dentist. Not every kid lives with a robotic talking molar that greets him or her with oral health imperatives. Yet nearly every kid has a pediatrician who can take simple steps to guarantee healthy smiles—and that pediatrician can be you!

Dr. Dickson would like to acknowledge the support of the University of Michigan Dental School faculty and staff, and the Michigan Caries Prevention Program staff: Margherita Fontana, DDS, PhD, who invited the University of Michigan East Ann Arbor (EAA) Pediatric Clinic to join in her inspired work; John Girdwood, PhD, who was critically present at EAA along the way, as well as Imen Alem, Emily Yanca, and Rachel Putnam-Farley; the University of Michigan’s Department of Pediatrics-Division of General Pediatrics for its support of oral health; EAA pediatricians—Heather Burrows, Paramjeet Kochhar, Sara Laule, Adrienne Musci, and Guwendolyn Zirngibl—and the EAA clinic staff, with key contributors Sandra Ellis and Ashley Major; Robert Dickson, MD, who provided a deep well of generous support and academic consultation for this project’s long duration; and lastly, her father Nicholas Schmit, DDS, who has been stamping out tooth decay as a general dentist in Delphos, Ohio, for 40 gentle years.

For references, go to ContemporaryPediatrics.com/pediatric-oral-health
Diffuse dermatitis CONTINUED FROM PAGE 42

discontinuation of the inciting agent, and initiation of supportive care.3

Clinical manifestations of SJS/TEN
Patients present with variable prodromal symptoms for up to a week with fever, malaise, sore throat, pain on swallowing, and ocular involvement ranging from mild conjunctival erythema to hemorrhagic conjunctivitis.3,4 Mucosal membrane involvement is common and can include the mouth, eyes, and genitals. This is followed by discrete and confluent red-to-dusky papules, patches, and plaques on the head, neck, and extremities with variable dissemination and full thickness epidermal sloughing. Oral involvement is usually severe.

Morbilliform eruptions followed by urticaria account for most drug-induced skin reactions, and neither is associated with sloughing of mucous membranes.6 Morbilliform drug eruptions are characterized by erythematous macules and papules that start on the head, neck, and trunk with downward spread. Drug-induced urticaria is marked by transient, migratory, erythematous, edematous, pruritic papules and plaques. Other drug hypersensitivity reactions include fixed drug eruptions, characterized by sharply demarcated target lesions with red borders and dusky centers that may blister and recur in the same locations after repeat exposure to the offending drug. Additional considerations include erythema multiforme (EM), which is primarily associated with infections, but a minority may be drug related.2,6 It typically presents with edematous target lesions on the distal extremities including the palms and soles, with occasional lesions scattered at other sites. The exact rate of oral mucosa involvement in drug-induced EM is not well studied, but studies of recurrent EM mostly attributed to infections report roughly 70% of oral involvement with ulcerations.7

“Big burger sign”
So what is the “big burger sign”? When a child is brought to the ED for evaluation of a rapidly progressive skin eruption within 3 weeks to 3 months of initiating a new medication, clinicians can ask “Are you hungry?” followed by “Can you eat a big burger?” If the answers to both questions are yes, the clinician recognizes that the child is hungry and eager to eat, which should exclude serious oral mucous membrane involvement and thus SJS/TEN. Pediatric dermatologists who are often consulted via phone or hybrid teledermatology use this mantra to screen for SJS/TEN when evaluating a drug-associated eruption.

Conclusion
In SJS/TEN, oral mucous membrane involvement is usually severe and oral intake is virtually impossible. A positive big burger sign, which indicates a hungry child who is eager to eat, helps the ED practitioner to distinguish between SJS/TEN and other drug-induced skin reactions not associated with significant mucous membrane involvement.

Dr Doong is a first-year resident at Santa Clara Valley Medical Center, San Jose, California.

Dr Cohen, section editor for Dermcase, is professor of Pediatrics and Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland. The author and section editor have 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. Vignettes are based on real cases that have been modified to allow the author and editor to focus on key teaching points. Images also may be edited or substituted for teaching purposes.

For references, go to ContemporaryPediatrics.com/dermcase-0618
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Teenager with sudden diffuse dermatitis

JUDY C DOONG, MD; BERNARD A COHEN, MD

A 16-year-old boy developed a diffuse, rapidly progressive eruption on his trunk, face, and extremities 4 days after starting oral amoxicillin for presumed strep throat. He presents to the emergency department (ED) where Stevens-Johnson syndrome is considered. The ED physician notes no mucous membrane involvement.

**MORBILLIFORM DRUG ERUPTION**

**Discussion**

Morbilliform drug eruption on presentation often can be concerning for Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). Together, SJS/TEN represent severe immune-mediated dermatoses, most commonly triggered by drug hypersensitivity reactions. Early diagnosis, discontinuation of the offending agent, and initiation of inpatient supportive care is critical.

The clinician in an ED setting must quickly distinguish SJS/TEN from self-limited eruptions that can be monitored at home. The authors propose the “big burger sign” as a screening tool to help distinguish these reactions.

Drugs are the most common trigger of SJS/TEN, with antibiotics most frequently identified, followed by analgesics, nonsteroidal anti-inflammatory drugs, antigout medications, psycholeptics, and cough preparations. Sloughing of multiple mucous membranes occurs in both SJS and TEN, which varies based on total body surface area of epidermal detachment with less than 10% in SJS, greater than 30% in TEN, and intermediates of 10% to 30% termed SJS/TEN overlap syndrome. The estimated overall annual risk is 1.1 and 0.93 cases per million for SJS and TEN, respectively. Although these conditions are very rare, it is important to reduce morbidity and mortality with early recognition.

FOR MORE ON THIS CASE, TURN TO PAGE 40.
Parents often worry about switching their breastfed baby to cow’s milk-based formula because they worry about lactose. This is not a concern, as breast milk contains lactose.

Similarly, Lactaid milk will not work for children with a true milk allergy. Allergies are to the protein in milk, not the sugar.

Breastmilk jaundice is not a contraindication to breastfeeding, nor is supplementation with water or formula needed, unless there is dehydration/excessive weight loss.

Spicy foods do not need to be avoided in children with gastroesophageal reflux, unless these foods are clearly causing problems.

Many (not all) allergists advise against exercise after allergy shots for at least 2 hours. I am not aware of any literature in support of this practice once the waiting period in the office, in case of an anaphylactic response, has passed.

As with asthma, it is very unusual to get hay fever in the first 2 years of life, and it’s almost unheard of in the first year, especially without a strong family history of allergies. If you are making such a diagnosis in a child this age, double-think it.

A scrape on the lower back over the spine is often from sitting on the edge of the pool, and then lowering oneself in.

Many circumcised boys present with a whitish discharge from the penile sulcus. This discharge is dead skin, like ear wax, because there is a small opening in the skin with a “tunnel” beneath it, and the dead skin can accumulate there. Although it is tempting to push the material out, as if you were squeezing toothpaste out a tube, this is not necessary. Leave it alone, and it will eventually close on its own.

I started pediatrics shortly after we learned not to manually “correct” phimosis in young boys. However, the analogous situation, labial adhesions in girls, was still widely treated with estrogen creams. This works, but the adhesions often recur, and I have not used estrogen creams for girls for over a decade now (I was a slow learner).

I had another child, aged 5 years, who was cyanotic around the mouth. Examination showed purplish smooth discoloration, perioral but sparing the lips, again without dyspnea. History revealed that he had a hickey from applying a vacuum cleaner around his mouth.

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I had a teenager come to the office with the complaint that he was cyanotic, and indeed he was blue from the neck down. He was not dyspneic, and cyanosis does not present that way. Wiping his skin with an alcohol pad removed the blue dye that he had picked up from his new blanket, having slept nude and not showering for a few days.

REFERENCE


Jon Matthew Farber, MD is a pediatrician in Woodbridge, Virginia. He 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.

Want to read more from Dr. Farber’s treasure chest of pediatric “pearls”? Find the popular series at: ContemporaryPediatrics.com/practical-pediatrics
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