How I found my calling as a volunteer

Joining a global telehealth program can profoundly change a child’s life—and yours!

HUGH BIGG, DO, FAAP

Like most physicians, I have always felt like I was born to help people. I was drawn to medicine by that inherent drive plus an acquired fascination with pathophysiology and how phenotypes are affected by corrupted metabolic and physiologic processes. I am blessed to have found a career that combines my determination to help people with my interest in understanding aberrant physiologic processes and how to treat them. I am even more fortunate to have had a job as a pediatrician at a community hospital in rural Missouri waiting for me upon graduation from residency.

I love my daily pediatrics practice and the team I work with. The unique long-term relationships I have formed with families, some beginning in the delivery room, have been more rewarding than I ever could have imagined. What I miss most about not being at an academic center, however, is the camaraderie of morning report, the collaboration inherent within a multidisciplinary team, and the deep communal dives into diagnosing and treating less-common conditions. Whereas relationship development and community outreach have been very rewarding, complex cases have been hard to find and the resources to care for them locally scarce.

It is an outstanding opportunity for me because it provides an intellectual challenge that may be missing from daily practice.

—Hugo Bigg, DO, FAAP

Embracing volunteerism

Combining my need to help solve medically complex cases with my commitment to ensuring rural pediatric patients receive quality and timely care, I have found great satisfaction in volunteering for Connecting Kids With Care (www.connectingkidswithcare.com), a volunteer telehealth program that pairs US physicians with preadoptive children on the other side of the world.

Connecting Kids With Care, a nonprofit outreach of Jackson Healthcare (Atlanta Georgia), has a network of relationships with orphanages around the globe. When US parents are considering adopting a medically fragile child from one of these orphanages, the staff refers the child’s medical files to a volunteer physician like me. Working with an online file that generally includes 8 to 15 pages of information, including photos, scans, sometimes videos, and a primary diagnosis, I review the child’s status and consider secondary diagnoses, prognosis, and treatment options.

It is an outstanding opportunity for me and for many physicians because it provides an additional intellectual challenge that may be missing from our daily practice. It allows me to profoundly—and positively—change a child’s life for the better. It fits into my life at a time when it’s convenient for me, taking as little as half an hour but sometimes as long as several hours of my discretionary time. Best of all, it doesn’t matter if I’m in Missouri or visiting family in New York. The opportunity to help is the same thanks to technology.

By reviewing each child’s file, I practice my skills in pattern recognition, solving puzzling cases, and enjoying the camaraderie of colleagues with whom I may never meet in person.

Editors’ Note: The views and opinions expressed in this article are those of the author and do not necessarily reflect the views and opinions of the US Army Medical Command, nor of Contemporary Pediatrics.
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OCTOBER 2018

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and interpreting complex medical records for parents considering adoption. I’ve helped with cases of complicated congenital heart conditions, exstrophy of the bladder, glaucoma and cataracts, rare infectious diseases, and much more.

Although the information I receive is sometimes incomplete or unclear, I see it as my role to make sense of the data and communicate it in an organized fashion for a family or future primary care provider. If the child has glaucoma, to what stage has it progressed? Will the child require surgery? How many specialists may the child require? Is medication necessary? What level of independence may be expected? Will he or she need a family’s care for the rest of his/her life?

Families that adopt a medically fragile child internationally are amazing people with an enormous capacity to love, but they deserve a frank evaluation of the challenges that lay before them. I don’t want parents to enter an adoption without the emotional and social resources they need, or without understanding the level of care their child may require. I hope that my analysis gives the child’s physician a global view of the child’s health, with suggestions for specialist involvement.

I enjoy pediatrics because children are innocent. Their medical problems are no fault of their own. Helping children locally through my practice and internationally through volunteering with Connecting Kids With Care is a way for me to continue to accomplish what I went into pediatrics to do—advocate for children and their families.

Dr. Bigg is a general pediatrician and major in the US Army, General Leonard Wood Army Community Hospital, Fort Leonard Wood, Missouri. He has no affiliations or financial interests to disclose.

ABOUT CONNECTING KIDS WITH CARE

Connecting Kids With Care is a not-for-profit initiative of Jackson Healthcare, a healthcare staffing firm located in Atlanta, Georgia. It works to expand worldwide access to quality healthcare, with a focus on orphans and vulnerable children.

The program connects medical professionals who donate their time from their homes or work settings to provide adoption medical assessment, urgent and episodic care, chronic disease care plans, chart reviews with physician collaboration, feeding and therapy plans, and clinical decision-making for these children and their caregivers. The children access better immediate care; prospective adoptive parents are able to anticipate and plan lifetime care; and local doctors benefit from specialist collaboration.

Since launching in July 2016, Connecting Kids With Care has served more than 1000 children from more than 100 humanitarian organizations in 17 countries, matching them with 100-plus caregivers from 17 different medical specialties.

Services are 100% free for both medical volunteers and patients. The Connecting Kids With Care platform utilizes existing technologies so there is no need for any volunteer to purchase additional equipment. The pairing of personal relationships with technology (live remote video, shared chart reviews, multimedia storage, and collaboration tools) allows medical experts to donate their skills with optimal efficiency and opens up new opportunities for children and medical providers alike.

Connecting Kids With Care has opportunities for physicians in a wide variety of specialties, as well as for family practitioners, nurse practitioners, physical therapists, and other pediatric healthcare providers.

Signing up does not obligate one in any way but will offer opportunities to volunteer one’s specialty to help a child or children around the world.

For more information, or to volunteer, visit ConnectingKidsWithCare.org
Kawasaki disease (KD) is associated with a gene expression pattern in the blood that differentiates it from the other infectious and inflammatory conditions with which KD is often clinically confused, a new study found. This suggests that a blood test based on measurements of the components of this 13-transcript gene expression signature could be developed to enable physicians to diagnose KD earlier and more accurately than they now can.

The study, which was conducted in pediatric centers in 4 different countries including the United States, had 2 groups of children. The training and test discovery group was comprised of 404 youngsters with infectious and inflammatory conditions, including KD, inflammatory diseases, and bacterial or viral infections, along with healthy controls. The independent validation group had 102 patients with KD, 72 of whom were in the first 7 days of illness (none had been ill for longer than 10 days), and 130 febrile controls. None of the participants had begun treatment with intravenous immunoglobulin.

At recruitment, investigators collected blood samples from all participants, which they evaluated for whole-blood gene expression. This analysis revealed that KD expressed 1600 genes differently than did other diseases and healthy controls. To identify a small signature group suitable for development as a diagnostic test, researchers pinpointed a 13-transcript signature in which some of the genes showed increased expression in KD compared with other infectious and inflammatory conditions and others decreased expression. In the discovery group, this signature distinguished KD from other infectious and inflammatory conditions with a sensitivity of 81.7% and specificity of 92.1%. In the validation group, the signature distinguished KD from febrile controls with a sensitivity of 85.9% and specificity of 89.1%.

Performance of the 13-transcript signature did differ depending on whether the child had clinically defined definite, highly probable, or possible KD, however, with diagnostic accuracy increasing with the certainty of clinical diagnosis. Also, performance was slightly reduced in patients who were diagnosed later than day 7 (Wright VJ, et al. JAMA Pediatr. August 6, 2018. Epub ahead of print.).

THOUGHTS FROM DR. BURKE

I can’t even count how many times I have explained to parents that we were considering KD but that the diagnosis was uncertain and there is no single blood test to make the answer clear. These researchers may be on the path to change that. Their work could lead to a practical, fast, accurate tool to help in diagnosis, especially for children with incomplete findings or an atypical course for KD.

Michael G Burke, MD is Chairman, Department of Pediatrics, Saint Agnes Hospital, Baltimore, Maryland.
Parents who have experienced adverse childhood experiences (ACEs), such as abuse, neglect, or household dysfunction, are more likely than parents without these experiences to have children with behavioral health problems, according to an analysis of data from several large, nationally representative surveys of US households that addressed ACEs and children’s behavioral problems and diagnoses.

Of the more than 2500 children for whom researchers had data, one-fifth had a parent who reported experiencing 4 or more ACEs during their own childhood. Compared with their peers whose parents reported having no ACEs during their childhood, these children had worse scores on standardized tests of child behavior problems and of positive behaviors (such as self-control, persistence, self-esteem, social competence, and compliance) as well as increased odds of attention-deficit/hyperactivity disorder and emotional disturbance. Mothers’ ACE counts had a far stronger influence on these child behavioral outcomes than did fathers’ (Schickedanz A, et al. Pediatrics. 2018;142[2]:e20180023).

I am not sure how results of this survey were affected by recruiting participants from an online support group of parents who use BSI. Are these parents who went online for help with particularly bad baby bedtimes or have they successfully tried these techniques and joined the group to share their endorsements? Either way, I suspect these results resonate and that you or some parents in your practice have had similar success with behavioral management at bedtime. You can use the evidence to promote this approach with dubious parents.
Includes mebendazole formulations, dosages and treatment duration

95% CURE RATE

- 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

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).

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 Convolutions: Convolusions 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:
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 intestinal infections caused by *Ancylostoma duodenale* (hookworm), *Ascaris lumbricoides* (roundworm), *Enterobius vermicularis* (pinworm), *Necator americanus* (hookworm), and *Trichuris trichiura* (whipworm).

**DOSE 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>Condition</th>
<th>Dose</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinworm (enterobiasis)</td>
<td>1 tablet, once</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
</tr>
<tr>
<td>Whipworm (trichuriasis)</td>
<td>1 tablet, once</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
</tr>
<tr>
<td>Roundworm (ascariasis)</td>
<td>1 tablet, once</td>
<td>1 tablet morning and evening for 3 consecutive days</td>
</tr>
<tr>
<td>Hookworm</td>
<td>1 tablet, once</td>
<td>1 tablet morning and evening for 3 consecutive days</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.

**Mebendazole 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>Condition</th>
<th>Adverse Reaction(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Agranulocytosis, Neutropenia</td>
</tr>
<tr>
<td>Immune System Disorders</td>
<td>Hypersensitivity including anaphylactic reactions</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Convulsions, Dizziness</td>
</tr>
<tr>
<td>Hepatobiliary Disorders</td>
<td>Hepatitis, Abnormal liver tests</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>TEN, SJS, Exanthema, Angioedema, Urticaria, Alopecia</td>
</tr>
</tbody>
</table>

*Includes mebendazole formulations, dosages and treatment duration other than EMVERM® 100 mg tablet

**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.

**Data**

**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 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 tablets 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.

**OVERDOSE**

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.

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**CLINICAL STUDIES**

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

<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>95%</td>
<td>68%</td>
<td>98%</td>
<td>96%</td>
</tr>
<tr>
<td><strong>Egg reduction</strong></td>
<td>—</td>
<td>93%</td>
<td>99%</td>
<td>99%</td>
</tr>
</tbody>
</table>
Teenager suffers diarrhea, emesis, and weight loss

ALEXANDRA J MIHALEK, MD; KATHERINE W CANTY, MD; MIRIAM CHAN, MD; MELINDA BRASKETT, MD; VRINDA BHARDWAJ, MD, FAAP; KIRA A MOLAS-TORREBLANCA, DO

A 16-year-old male with a history of nephrotic syndrome and gastritis presents to the emergency department (ED) with worsening emesis, diarrhea, weight loss, and abdominal pain of 3-weeks’ duration.

**History**
In the preceding 2 weeks, the patient had been evaluated on 3 separate occasions in the ED and was even admitted briefly for management of his abdominal pain, nausea, and dehydration. Laboratory studies obtained at these visits included a normal comprehensive metabolic panel and lipase level, as well as a complete blood count with a leukocytosis of 14.21 (reference range [RR], 5.0-13.0), absence of anemia or thrombocytopenia, and a differential with 10.2% eosinophils (RR, 0.0-3.0%).

An abdominal radiograph showed bowel wall edema involving the cecum, and an abdominal ultrasound demonstrated a large amount of free fluid in the abdomen, but a normal appendix. At first, clinicians suspected acute viral gastroenteritis, as laboratory and imaging studies were nonspecific aside from the peripheral eosinophilia.

This is now the patient’s fourth ED visit and his diarrhea is occurring more than 10 times daily, is associated with nocturnal stooling, and is significantly impacting his quality of life. His symptoms are also associated with a 10-pound weight loss over the prior 2 weeks, fatigue, and generalized weakness. However, he denies fever, rash, joint pain, oral ulcers, or blood per rectum. Ancillary history is remarkable for birth in the Philippines. However, he denies any recent travel or other exposures.

**Physical exam, lab studies, and imaging**
The patient’s physical examination is significant for mild, diffuse abdominal tenderness and absence of rebound or guarding. On further review, his weight has decreased from the 60th percentile to less than the 1st percentile over 2 years. His complete blood count shows a leukocytosis of 18.61 with an eosinophilia of 46% (absolute eosinophil count of 8640). His erythrocyte sedimentation rate and C-reactive protein are normal. Computed tomography (CT) scan of the abdomen is performed and shows diffuse small bowel and colonic wall thickening, most severe in the ascending colon and cecum (Figure 1). He is subsequently admitted to the inpatient pediatric ward for further workup and management.

▲ **FIGURE 1** An abdominal CT scan obtained during the patient’s previous admission demonstrated diffuse small bowel and colonic wall thickening, most severe in the ascending colon and cecum.
Differential diagnosis
This is a case of a 16-year-old male with a history of nephrotic syndrome and gastritis who presents with 3 weeks of generalized abdominal pain, diarrhea, and significant weight loss, with marked peripheral eosinophilia and diffuse bowel wall thickening on CT. There is an extensive differential for adolescents with abdominal pain and severe diarrhea (Table 1), however, the most striking feature of this case was his eosinophilia.

Peripheral eosinophilia is defined as an eosinophil count of 450 to 500 eosinophils/μL or greater.1 The possible etiology of peripheral eosinophilia is broad (Table 2) and major categories include infectious, allergic/immunologic, hematologic/oncologic, gastrointestinal (GI), and other syndromes such as allergic bronchopulmonary aspergillosis (ABPA) and sarcoidosis.

**INFECTION CAUSES**
Parasitic infections, in particular, are associated with this level of eosinophilia. The index of suspicion was high for a parasitic infection given the patient’s eosinophilia and travel to the Philippines. *Strongyloides stercoralis* infection was the primary concern because of this parasite’s ability to replicate in the host for years undetected, inducing varying degrees of eosinophilia. In addition, if a patient with subclinical strongyloidiasis is given systemic steroids, there is a potential to develop hyperinfection syndrome, a life-threatening condition associated with accelerated lifecycle of the parasite and high larvae burden.2,3

However, the patient’s serology was negative for *S stercoralis*. In addition, stool studies were negative for *Clostridium difficile*, a bacterial molecular panel, rotavirus, norovirus, adenovirus, a parasite molecular panel, and stains for ova and parasites. Serum studies for common viruses as well as human immunodeficiency virus (HIV), *Coccidioides, Taenia solium, Toxocara*, cisticercosis, and a tuberculin skin test were also negative.

**ALLERGIC CAUSES**
Medications are a leading cause of peripheral eosinophilia, and associated symptoms can range from subclinical to profound, as in the case in DRESS (drug reaction with eosinophilia and systemic symptoms) syndrome.1 Common culprits include antibiotics, especially penicillin and sulfonamides, anticonvulsants and nonsteroidal anti-inflammatory drugs.1,4

This patient did not have any recent medication exposures. Laboratory testing also was obtained to evaluate for allergic disorders and included a total immunoglobulin (Ig) E level, which was 309 (RR, ≤114), as well as IgE specific to wheat, cod, salmon, shrimp, egg white, peanut, walnut, almond, soy, milk, and sesame, which were undetectable.

**HEMATOLOGIC AND ONCOLOGIC CAUSES**
Peripheral eosinophilia can be seen in eosinophilic leukemia, Hodgkin disease, cutaneous T-cell lymphoma, and mastocytosis, as well as acute lymphoblastic leukemia and a variety of solid tumors.1 In addition, hypereosinophilic syndrome (HES) is a myeloproliferative disorder characterized by prolonged serum eosinophilia (≥1500 eosinophils/μL for 6 months) and end-organ dysfunction in absence of another cause.1,5

An oncologic process was consid-

---

**TABLE 1**
DIFFERENTIAL DIAGNOSIS FOR ABDOMINAL PAIN AND DIARRHEA IN ADOLESCENTS

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Viral (adenovirus, enterovirus, rotavirus, norovirus)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacterial (<em>Clostridium difficile, Escherichia coli, shigella, salmonella, Campylobacter, Yersinia</em>)</td>
</tr>
<tr>
<td></td>
<td>Parasitic infections</td>
</tr>
<tr>
<td>Allergic/Immunologic</td>
<td>Celiac disease</td>
</tr>
<tr>
<td></td>
<td>Immunodeficiency syndromes</td>
</tr>
<tr>
<td></td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td></td>
<td>Eosinophilic gastrointestinal disorders</td>
</tr>
<tr>
<td></td>
<td>Motility disorders</td>
</tr>
<tr>
<td></td>
<td>Brush border enzyme deficiency (ie, lactose)</td>
</tr>
<tr>
<td></td>
<td>Small intestinal bacterial overgrowth (SIBO)</td>
</tr>
<tr>
<td>Endocrinologic</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Other</td>
<td>Medications (including antibiotics)</td>
</tr>
<tr>
<td></td>
<td>Irritable bowel syndrome</td>
</tr>
</tbody>
</table>

Author created.
ered in this patient’s case given his marked weight loss and failure to thrive, in concert with his systemic symptoms. A peripheral blood smear was obtained and showed no leukemic cells, and flow cytometry of the patient’s serum also was negative. Additionally, given the likelihood that the patient would ultimately require treatment with systemic steroids, he underwent a bone marrow biopsy, which was negative.

GASTROINTESTINAL CAUSES

Eosinophils are present in multiple parts of the GI tract, and increased numbers can be seen in common diseases such as inflammatory bowel disease (IBD), celiac disease, and gastroesophageal reflux disease (GERD). In addition to these conditions, there are eosinophilic gastrointestinal disorders (EGIDs), which are a family of disorders of eosinophil inflammation of the GI tract that are not attributable to other causes of eosinophilia.1,6

This patient’s presentation was most consistent with a GI disease. Fecal calprotectin and IBD serology were unremarkable, as was an autoimmune hepatitis panel. An esophagogastroduodenoscopy (EGD) and colonoscopy were performed to obtain tissue samples for diagnosis. On endoscopy, normal-appearing mucosa was noted with the exception of erythema in the stomach and terminal ileum. However, biopsy specimens showed significant tissue eosinophilia in the upper and lower GI tract: esophagus (20/hpf), stomach (20/hpf), duodenum (90/hpf), terminal ileum (50/hpf), transverse colon and rectum (30/hpf), with eosinophil degranulation in the lamina propria, crypts, and muscularis mucosa, consistent with a diagnosis of EGID (Figure 2). He also underwent a small bowel capsule endoscopy, which showed scattered small bowel ulcerations and mucosal erythema.

Discussion

Eosinophilic gastrointestinal disorders are a group of rare disorders that cause selective GI eosinophil-induced inflammation, and include eosinophilic esophagitis (EoE), eosinophilic gastroenteritis, and eosinophilic colitis. Much about the pathophysiology and prognosis of EGID is still unknown, but it is thought to involve both genetic predisposition and environmental factors. There are no pathognomonic symptoms or tests for EGID, and patients have peripheral eosinophilia in only half of cases.6,8 Apart from food impaction in EoE, symptoms are nonspecific, and include irritability, weight loss, abdominal pain, vomiting, diarrhea, malabsorption, dysmotility, and ascites.6,9

Diagnosis requires tissue biopsies demonstrating an abnormal number or location of eosinophils. However, GI eosinophilia is not specific to EGID and can be seen in a variety of other disorders.6,10 Eosinophils also can be a normal part of the lamina propria of GI mucosa, which further complicates diagnosis. However, they should not be present in the esophagus, Peyer’s patches, or intraepithelial tissues, and free extracellular granule components should not be seen under normal conditions.6,9,11 Given the difficulty in diagnosing EGID, patients with this disorder are symptomatic for a mean of 4 years prior to diagnosis, as was seen in this patient who had begun to cross percentile lines more than 2 years prior to his admission.6

Treatment for EGID involves nutritional and medical therapies, such as elimination diets that restrict most like-
Professionally Recommended
Problem-Solving Products

ECZEMA CARE
DIAPER RASH
FUNGAL INFECTIONS

For samples, visit:
www.summers-direct.com/samples
ly or known food allergens and elemental diets that consist of an amino-acid formula.8,9,11 Topical enteral steroids are the primary medical therapy and systemic steroids are used for severe or refractory cases, such as this one.

**Patient outcome**

During this patient’s workup, he required peripheral parenteral nutrition (PPN) for severe protein-calorie malnutrition and food intolerance. Once the diagnosis of EGID was made, he was started on a strict elemental diet with resolution of his abdominal pain over a period of days. However, he continued to have profuse diarrhea. He was started on enteric-coated budesonide (topical enteral steroids) and systemic steroids, leading to resolution of his diarrhea and dramatic improvement in his peripheral eosinophilia.

The patient was discharged home on exclusive elemental nutrition therapy and topical enteral steroids. Three months after discharge, while on a strict elemental diet and enteric-coated budesonide therapy, the patient underwent a repeat upper endoscopy and colonoscopy that demonstrated marked histologic improvement with normal gastric, duodenal, and colonic mucosa, with the exception of focal distal eosinophilic esophageal involvement (30/hpf).

Unfortunately, 4 months after discharge, he was readmitted briefly for recurrence of symptoms in the setting of dietary noncompliance. After this recurrence, he was further treated with systemic and topical enteral steroids. He subsequently did well on an elemental diet and was able to reintroduce low-allergen foods.

**Summary**

The association between nephrotic syndrome and EGID is also not well described, and to the authors’ knowledge this is the sixth reported case of coexistent nephrotic syndrome and eosinophilic gastroenteritis.12-16 Interestingly, this patient’s recurrent steroid use for nephrotic flares may have masked an earlier presentation of his EGID, as this was the longest time period he had gone without a nephrotic flare, and thus without steroids, since his early childhood.

Given the diagnostic difficulties surrounding EGID, it is important to have a high index of suspicion for this diagnosis in patients presenting with eosinophilia and primary GI symptoms. Moreover, this case highlights the effectiveness of elemental diets in both confirming diagnosis and symptom control, and demonstrates challenges that patients, and particularly adolescents, might face in adherence to nutritional therapy.

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**For references, go to ContemporaryPediatrics.com/puzzler-1018**

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Kawasaki disease
AHA statement and recommendations

Pediatricians must suspect Kawasaki disease (KD) in children with prolonged unexplained fever. Here is the latest scientific statement on KD from the American Heart Association that is of practical importance for all clinicians.

ANK H ROWLEY, MD, FAAP

Kawasaki disease (KD) is an acute systemic vasculitis that occurs predominantly in children aged younger than 5 years. Exact information about the incidence of KD is lacking, but in developed countries it remains the most common cause of acquired heart disease in children.

The incidence of KD varies by race/ethnicity, being highest in Asian children, intermediate in black and Hispanic children, and lowest among white children.1 The disease is estimated to occur in 1 in 1000 US children by age 5 years.2 In a large pediatric practice caring for 1000 to 2000 non-Asian children in this age group, 1 to 2 cases would likely be diagnosed over a 5-year period. The attack rate is much higher in Asian children: 1 in 70 Japanese children develop KD by age 5 years.3 Therefore, in parts of the United States with high Asian populations, the index of suspicion for KD should be much higher, and many more cases will be observed.

The etiology of KD remains unknown and there is still no specific test for its diagnosis. Left untreated, KD is associated with the development of potentially fatal coronary artery aneurysms in at least 25% of cases.4 Because early treatment initiation improves the prognosis, it is critical that pediatricians maintain a proper index of suspicion for KD in children with prolonged unexplained fever.

In 2004, the American Academy of Pediatrics and the American Heart Association (AHA) issued a clinical report on KD diagnosis, treatment, and long-term management as guidance for clinicians rendering pediatric care.5 In 2017, the AHA published a new scientific statement reviewing recent evidence and containing updated recommendations for practitioners.4 This article highlights information from the 2017 AHA statement and other recent information that is of practical importance for pediatricians.

**Diagnosis**
The criteria for diagnosing KD were not changed in the new AHA statement.

Classic KD is diagnosed when a child has fever for at least 5 days along with at least 4 of the following 5 principal clinical features (Figure 1):
- Bilateral conjunctival injection.
- Changes of the oral cavity and lips.
- Polymorphous rash.
- Cervical lymphadenopathy.
- Erythema of the extremities.
It is important to keep in mind that any of the principal clinical features could have resolved by the time that the patient presents in the office, and so it is important to take a thorough history.

The new AHA statement includes a revised algorithmic flowchart to assist the diagnosis of incomplete KD during the effective window of therapy in children who lack full clinical features of classic KD (Figure 2).4 The primary change in the new statement is the recommendation to consider the diagnosis of KD in any infant aged younger than 1 year with unexplained fever for 7 days or longer, even in the absence of other clinical findings. According to the revised algorithm, these children, and children with fever for 5 days or longer

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**FIGURE 1 CLINICAL FEATURES OF CLASSIC KAWASAKI DISEASE**

A) **Rash:** maculopapular, diffuse erythroderma, or erythema multiforme-like. B) **Conjunctivitis:** bulbar conjunctival injection without exudate; bilateral. C) **Oral changes:** erythema and cracking of lips (cheilitis); strawberry tongue; erythema of oral and pharyngeal mucosa. D and E) **Palmar and plantar erythema:** usually accompanied by swelling; resolves with subsequent periungual desquamation in the subacute phase. F) **Cervical adenopathy:** usually unilateral, node ≥1.5 cm in diameter. G) **Coronary artery aneurysms:** magnetic resonance image of the left ventricular outflow tract showing a giant right coronary artery (RCA) aneurysm with nonocclusive thrombus (yellow arrow) and a giant left main coronary artery (LMCA) aneurysm: Ao indicates aorta; AoV, aortic valve; LV, left ventricle; and RV, right ventricle. H) **Peripheral artery aneurysms:** magnetic resonance image showing aneurysms in the axillary and subclavian arteries and the iliac and femoral arteries (yellow arrows).

Author’s note: Not all features may present simultaneously.

Reprinted with permission: Circulation.2017;135:e927-e999. Copyright 2017 American Heart Association (AHA). Inc. (All requests to use this information must come through the AHA. https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000484)

Patient photographs used with permission from the Kawasaki Disease Foundation, Inc.
and who have 2 or 3 of the principal clinical features, should have laboratory testing for C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). If the result of either test is abnormal, further laboratory evaluations and echocardiography are indicated to further assess for KD.

Pediatricians often may encounter children with fever for 5 days accompanied by rash and red eyes in their practice. Although the vast majority of these children do not have KD, pediatricians should still consider the possibility of KD whenever a patient has prolonged unexplained fever accompanied by any of the principal clinical features of KD. In such patients, initial laboratory assessment such as a complete blood count (CBC) with differential, ESR, and CRP may be useful in determining whether further consideration of a KD diagnosis is warranted.

Regarding the echocardiogram, the new statement is more specific than its predecessor about use of sedation. It recommends repeating the study under sedation as soon as possible within 48 hours after diagnosis and initial treatment if a first echocardiogram was done without sedation and was of poor quality.

The new statement also emphasizes that the echocardiogram report provides a quantitative assessment of luminal dimensions that are normalized as z scores adjusted for body surface area and not merely a qualitative description of vessel appearance. Studies of coronary artery dimensions in febrile children with non-KD illnesses confirm that coronary artery z scores greater than 2.5 are very specific for the diagnosis of KD.

### Treatment recommendations

#### PRIMARY THERAPY

Research continues to support the need for early diagnosis and treatment of KD, with initiation of intravenous immunoglobulin (IVIG) well before the tenth day of illness. Table 1 summarizes recommendations from the AHA statement pertaining to primary therapy.

There has been long-standing interest in the potential efficacy of using a corticosteroid as an adjunct to IVIG based on recognition that KD results in coronary arterial inflammation. A first randomized trial exploring this approach was conducted in the United States and found no benefit from adding a single high dose of methylprednisolone to IVIG for primary therapy of KD. More recently, the Randomized Controlled Trial to Access Immunoglobulin Plus Steroid Efficacy for Kawasaki Disease (RAISE) study, a Japanese multicenter trial enrolling patients at high risk of KD,
developing coronary artery abnormalities, demonstrated a significantly lower incidence of coronary artery abnormalities at 1 month after KD onset in the group that received a more prolonged (2- to 3-week) course of adjunctive prednisolone.9

Whereas illness severity scores (eg, the Kobayashi score) can accurately identify high-risk patients in Japanese populations, they have low sensitivity and cannot be reliably implemented in non-Japanese children.10,11 However, certain children with KD, such as infants aged younger than 6 months and those aged 8 years and older, are known to be at particularly high risk of developing coronary artery abnormalities following KD.12 The new AHA statement recommends that single-dose methylprednisolone should not be administered with IVIG as routine primary therapy for patients with KD. It states that the addition of a longer course of corticosteroids (eg, tapering over 2 to 3 weeks) to IVIG and aspirin may be considered for treatment of high-risk patients with acute KD, when such high risk can be identified in patients before initiation of treatment. In the RAISE study, prednisolone was initiated at 2 mg/kg/day and tapered over 2 to 3 weeks depending on fever response, decrease in CRP levels, and clinical course.8

The optimal dose of aspirin for acute KD remains controversial. The new AHA statement continues to recommend administering moderate- (30-50 mg/kg/d) to high-dose (80-100 mg/kg/d) aspirin until the patient is afebrile. Some recent research, however, suggests that low-dose aspirin is not inferior to high-dose aspirin for the treatment of acute KD.12,13

A multicenter retrospective study including approximately 1200 children with acute KD seen between 2004 and 2015 and treated with IVIG within 10 days of fever onset found no difference in the risk of coronary artery abnormalities comparing cohorts receiving low-dose (3-5 mg/kg/d) or high-dose (80 mg/kg/d) aspirin.13 A retrospective study including 249 patients treated at 2 centers in Canada found children receiving low-dose aspirin (3-5 mg/kg/d) were 3 times more likely to receive IVIG retreatment compared with children receiving high-dose acetylsalicylic acid (ASA; 80-100 mg/kg/d).14 Both the mean duration of hospital stay and incidence of coronary artery aneurysms, however, were similar in the 2 groups. Further study is needed to provide clarity on this issue.

**RESCUE THERAPY**

Further study is also needed to develop evidence-based recommendations on rescue therapy for IVIG-resistant patients, defined as those having persistent or recrudescent fever at least 36 h after the end of the first IVIG infusion. Additional therapy in the IVIG-resistant patient (“rescue therapy” for children with persistent or recrudescent fever at least 36 h after the end of the first IVIG infusion).

<p>| TABLE 1 | RECOMMENDATIONS FOR INITIAL TREATMENT OF PATIENTS WITH COMPLETE/INCOMPLETE KAWASAKI DISEASE |</p>
<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE AND ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IVIG</strong></td>
<td>2 g/kg IV within 10 d of illness onset, but as soon as possible after diagnosis. (May be given to children presenting after the 10th day of illness if they have persistent fever or coronary artery abnormalities together with ongoing systemic inflammation, as manifested by elevation of ESR or CRP.)</td>
</tr>
<tr>
<td><strong>Aspirin</strong></td>
<td>Moderate- (30-50 mg/kg/d) to high-dose (80-100 mg/kg/d) is reasonable until the patient is afebrile. (There is no evidence that it reduces coronary artery aneurysms.)</td>
</tr>
<tr>
<td><strong>Longer (tapering) course of corticosteroids</strong></td>
<td>May be considered in addition to IVIG and aspirin in high-risk patients; eg, prednisolone IV 2 mg/kg/d for 5 d with an oral taper for 2-3 wk.</td>
</tr>
</tbody>
</table>

Additional therapy in the IVIG-resistant patient (“rescue therapy” for children with persistent or recrudescent fever at least 36 h after the end of the first IVIG infusion).

Abbreviation: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IV, intravenous; IVIG, intravenous immunoglobulin.

From McCrindle BW, et al.4

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~80% OF PATIENTS WITH KAWASAKI DISEASE ARE AGED <5 YEARS

—Kawasaki Disease Foundation, 2018
0 lbs., 14 oz., and made for EVERY INCH

RECOMMEND AQUAPHOR FOR BABY’S SKINCARE NEEDS

Beiersdorf
Data on file. Beiersdorf Inc. ©2017
TABLE 2
TREATMENT OPTIONS FOR IVIG-RESISTANT KD PATIENTS

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most frequently administered</td>
<td></td>
</tr>
<tr>
<td>IVIG: second infusion</td>
<td>2 g/kg IV</td>
</tr>
<tr>
<td>IVIG + prednisolone</td>
<td>IVIG 2 g/kg IV + prednisolone 2 mg/kg/d IV divided every 8 h until afebrile, then prednisone PO until CRP normalized, and taper over 2-3 wk</td>
</tr>
<tr>
<td>Infliximab</td>
<td>5 mg/kg IV over 2 h</td>
</tr>
<tr>
<td>Alternative treatments</td>
<td></td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>IV: 3 mg/kg/d divided every 12 h PO: 4-8 mg/kg/d divided every 12 h Adjust dose to achieve trough 50-150 mg/mL; 2-h peak level, 300-600 ng/mL</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>2 mg/kg/d IV</td>
</tr>
<tr>
<td>Plasma exchange</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Abbreviations: CRP, C-reactive protein; IV, intravenous; IVIG, intravenous immunoglobulin; KD, Kawasaki disease; PO, oral.
Adapted from McCrindle BW, et al. 4

KAWASAKI DISEASE: A PARENTS’ GUIDE VIDEO
This helpful 12-minute video educates parents and caregivers of children who have been diagnosed with Kawasaki disease, providing information about the disease and its symptoms, treatment, and follow-up care.
https://www.youtube.com/watch?v=5knlkzIu2-4

Download a PDF of answers to frequently asked questions about Kawasaki disease, available in 18 languages, at:
https://medschool.ucsd.edu/som/pediatrics/researchcenters/kawasaki-disease/parents/Pages/Information.aspx

Because the clinical symptoms of KD are self-limited, it is difficult to determine whether patients who apparently responded to rescue therapies represent true clinical responses. The small number of IVIG nonresponders and the high cost of performing prospective clinical studies have been obstacles to conducting controlled trials of rescue therapies. A phase 3 multicenter study comparing infliximab to a second dose of IVIG in IVIG-resistant patients is now under way (NCT03065244). The identification of optimal intervention for children resistant to IVIG would likely be facilitated by elucidation of the etiology and pathogenesis of KD.

Long-term management
Newer information from histopathologic studies of coronary arteries obtained from KD patients provides a better understanding of specific events in damaged arteries and the potential for children with significant acute damage to develop serious complications over time. 15 The researchers in this study described a 3-step model of KD arteriopathy culminating with luminal myo-
fibroblastic proliferation that can lead to progressive arterial stenosis, thrombus formation, and myocardial infarction. This process reinforces the importance of ongoing periodic cardiology surveillance for all KD children with an aneurysm and highlights the potential pitfall of incorrectly interpreting normalization of the luminal dimension on an echocardiogram as being equivalent to return to a normally functioning artery.

The new scientific statement also includes a section on transition to adult care. As with other pediatric heart diseases, it is important to provide the patient who develops coronary artery aneurysms with a well-developed plan for transitioning to adult cardiology care.

The future
Research investigating genetic associations for KD susceptibility and treatment response are corroborating previous results and generating some interesting new findings. These studies have identified single nucleotide polymorphisms of several genes involved in immune response, including ITPKC, CASP3, FCGR2A, HLA, BLK, CD40, and, most recently, ORAI. It is likely that additional susceptibility genes will be identified in future studies.

In addition, evidence associating risk of aneurysm formation with variants in genes involved in the transforming growth factor-β pathway has provided a rationale for investigating the potential for statin treatment to decrease coronary artery inflammation and mitigate arterial damage. So far, understanding of genetic associations with KD has no impact for patient care.

Identification of the etiologic agent(s) remains the Holy Grail for achieving future advances in KD diagnosis, treatment, and prevention. New data continue to support the theory that KD is caused by a novel virus without substantial homology to known viruses. Developments in molecular technologies should facilitate attainment of this elusive goal that holds the key to reducing the burdens of KD.

For references, go to ContemporaryPediatrics.com/Kawasaki-disease-2017-AHA-guidelines

RIDDLE ME THIS!

If your memory of Gregor Mendel and his garden of pea plants has mutated. If it’s been a while since you confidently knew your genotypes from your phenotypes, and perhaps your knowledge of dominance has become, well, recessive. No worries!

With this issue, Contemporary Pediatrics is introducing a new online feature that will test your smarts on a clinical topic we’re showcasing that month.

Peer-to-peer challenge
Each month, we’ll riddle you with 5 online questions. You’ll test your knowledge on some aspects of the topic against your peers in real time—question-by-question—and see how you fare. So, for personal bragging rights (and to learn if it’s a topic about which you’d benefit from additional reading) go online now to see how you score. Each month, you’ll also find a treasure trove of additional resources for your own personal deep dive.

This month’s Riddle Me This! is on genetics. Rinke et al (2016) found that only 49% of pediatricians agree that they feel competent in providing healthcare to patients related to genetics. Which cohort are you in?

Red flags for genetic disorders

At a minimum, the pediatrician should be familiar with genetic disease on the newborn screen, but it’s also important to recognize the child with multiple medical issues who may need referral to a genetic or metabolic specialist.

PAT F BASS III, MD, MS, MPH; DARREL WAGGONER, MD

Genetic and metabolic disorders are relatively uncommon in the day-to-day practice of a pediatrician. However, there are a number of disorders every pediatrician should be able to recognize and for which he or she may need to make appropriate referral and provide care.

Consider the following 4 cases and think about what is the most likely diagnosis and what a pediatrician would do in the office. A brief discussion of each of the cases follows.

**CASE 1**

You receive a note from your nurse that the newborn screen for a 5-day-old neonate that you recently discharged from the hospital was positive for phenylketonuria (PKU). What are your essential next steps?

**DIAGNOSIS: PKU**

Phenylketonuria (PKU) is asymptomatic in the newborn period, and nearly 100% of cases are diagnosed in the newborn period by screening. Without identification and treatment, irreversible mental retardation, hyperactivity, autistic-like features, and seizures will occur. Phenylketonuria can result in severe hyperphenylalaninemia.

**PATHOPHYSIOLOGY**

Phenylalanine levels are elevated in PKU as a result of deficient liver phenylalanine hydroxylase (PAH) preventing ingested phenylalanine from being metabolized to tyrosine. Any infant with elevated phenylalanine should also have levels of tetrahydrobiopterin (BH4), itself an essential cofactor for PAH. Defects in BH4 metabolism may have progressive neurologic deterioration in infancy.
MANAGEMENT
Treatment of PKU is best done through an interdisciplinary team consisting of nutritionists, psychologists, social workers, metabolic specialists, and pediatricians. Lifelong restriction of phenylalanine is the mainstay of treatment and requires medical foods with phenylalanine-free protein substitutes.2,3

The goal of treatment is normalization of phenylalanine levels as this prevents the neurologic defects associated with PKU.

Sapropterin (Kuvan) is a pharmacologic treatment that can decrease phenylalanine levels in patients who are sensitive to BH4.1

OUTCOMES
Cognitive outcomes correlate with control of phenylalanine concentration in the blood, especially in early childhood. Even with strict adherence, some suboptimal cognitive outcomes may still occur.3

Attention deficit and information processing are noticed in adults with current elevated levels of phenylalanine as well as in those with elevated phenylalanine in the past. There is also a higher incidence of mental health issues such as anxiety, depression, phobia, and panic attacks among patients who discontinue therapy in the second decade of life.3

CASE 2
A 2-year-old toddler presents with progressive joint stiffness, progressive short stature, coarse facies, and macrocephaly. The family history is significant for the mother’s brother who died at age 12 years from complications of heart failure and loss of cognition (neuroregression). What is your diagnosis?

DIAGNOSIS: Hunter syndrome/
Mucopolysaccharidosis type II
Mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome, is an X-linked disorder with an early progressive component and a slowly progressive form of disease.4

SUGGESTIVE FINDINGS
The initial case in a family is a male aged between 18 months and 4 years with the following features predominating: short stature, hepatosplenomegaly, joint contractures, and coarse facies.4 Although nonspecific, frequent ear and sinus infections as well as an umbilical hernia are noted. Skeletal survey may show dysostosis multiplex.4

PATHOPHYSIOLOGY AND DIAGNOSIS
Mucopolysaccharidosis type II is an X-linked recessive disorder resulting from a deficiency of the lysosomal enzyme iduronate 2-sulphatase (I2S). This leads to a pathologic, progressive increase in lysosomal storage of glycosaminoglycans (GAGs) in nearly all cell types, tissues, and organs. There is significant variability in age of onset and rate of progression.4

Definitive diagnosis cannot be made on clinical findings alone and requires either absent or reduced I2S enzyme activity or the Identification of a hemizygous IDS pathogenic variant via molecular genetic testing.4

OUTCOMES
Central nervous system (CNS) involvement is the most significant feature of early progressive disease and progressive cognitive deterioration is the norm. Combined with airway

NEXT STEPS
The pediatrician who receives a positive screening result for a patient should:

- Contact the family and inform them of the positive result.
- Contact a metabolic specialist to discuss confirmatory diagnostic testing, evaluation, and treatment.
- See the patient in clinic for an evaluation and initiate confirmatory/diagnostic tests in consultation with the metabolic specialist.
- Report results to the newborn screening program.
- The National Institutes of Health (NIH) Consensus Development Conference Statement on PKU recommends phenylalanine testing weekly in the first year and then bimonthly until age 12 years.3

MANAGEMENT
Age-appropriate testing to establish the extent of disease may include:4
- Echocardiogram.
- Pulmonary function testing.
- Sleep study.
- Hearing test.
- Eye examination.
- Developmental assessment.
- Magnetic resonance imaging (MRI) of the brain.
- Nerve conduction study.

When specific organ systems are involved, the patient requires specific treatments such as cardiac valve replacement or repair; mechanical ventilation or tracheostomy; tonsillectomy; or shunting for hydrocephalus.

OUTCOMES
Central nervous system (CNS) involvement is the most significant feature of early progressive disease and progressive cognitive deterioration is the norm. Combined with airway
and cardiac problems, death usually occurs before age 20 years.\(^4\)

In the slowly progressive form of the disease, CNS is less affected, but GAG accumulation is similar to the early progressive. Survival into early adulthood with normal intelligence is common.\(^4\)

### CASE 3

A 4-month-old girl presents for evaluation for hypotonia, generalized muscle weakness, feeding difficulties, failure to thrive, and respiratory distress. Family history is negative, and physical exam of parents is normal. What is your diagnosis?

### DIAGNOSIS: Pompe disease/ Glycogen storage disease II

Pompe disease, also known as glycogen storage disease type II (GSD II) is an autosomal recessive disorder with a variable presentation depending on age of presentation.\(^5\)

### SUGGESTIVE FINDINGS

Both infantile-onset and late-onset Pompe disease should be suspected with a combination of clinical findings and test abnormalities.\(^5\)

#### Infantile-onset Pompe disease (IOPD) is suggested with a combination of:\(^5\)
- Poor feeding and failure to thrive.
- Motor delay and muscle weakness.
- Respiratory infections.
- Cardiomyopathy or other cardiac problems.

Additional symptoms may include hepatomegaly, enlarged tongue, absent deep tendon reflexes, enlarged tonsils, and normal cognition. Glycogen deposition may lead to conduction defects manifesting as a shortened PR interval on electrocardiogram (ECG).\(^5\)

### Presence of the following symptoms is associated with poor cognitive outcome:\(^4\)
- Sleep disturbance.
- Increased activity.
- Behavior difficulties.
- Seizure-like behavior.
- Perseverative chewing behavior.
- Inability to achieve bowel and bladder training.

### PATHOPHYSIOLOGY AND DIAGNOSIS

Late-onset Pompe disease (LOPD) is characterized by proximal muscle weakness and respiratory problems without cardiac involvement. Lower-limb weakness often requires use of a wheelchair. Adults often describe difficulty in participating in sports as a child and seek medical attention later in life with fatigue, difficulty going from sitting to standing, or walking up stairs.\(^5\)

Newborn screening may be abnormal but is not diagnostic of Pompe disease. Creatinine kinase is elevated but is nonspecific.\(^5\)

Idursulfase (Elaprase) is a recombinant form of human I2S. Enzyme replacement therapy with recombinant forms of human I2S have been shown to improve functional outcomes. However, it does not alter CNS disease as it does not cross the blood-brain barrier.\(^4\)

### MANAGEMENT

Enzyme replacement therapy is initiated as soon as possible with an IOPD diagnosis or as soon as a symptomatic Pompe disease is diagnosed.\(^5\)

### Testing examines the extent of disease progression and includes:\(^5\)
- Chest radiography.
- Electrocardiography.
- Echocardiography.
- Age-appropriate pulmonary function.
- Nutritional assessments.
- Hearing screening.
- Motor functioning.

### OUTCOMES

If IOPD is not treated, cardiomegaly and hypertrophic cardiomyopathy may occur in the first 2 weeks of life. This will progress to left ventricular outflow obstruction, and death occurs in the first 2 years of life because of cardiopulmonary insufficiency.\(^5\) Early IOPD treatment with enzyme replacement therapy is associated with both improved cardiac and respiratory outcomes as well as improved motor skills.\(^5\)

In LOPD, enzyme replacement therapy improves motor functions, respiratory function, and quality of life.\(^5\)
**DIAGNOSIS: Glycogen storage disorder type I**

Glycogen storage disease type I (GSDI), also known as von Gierke disease, is an autosomal recessive disorder characterized by accumulation of glycogen and fat in the liver and kidney. Although there are 2 subtypes, they are clinically indistinguishable.6

**SUGGESTIVE FINDINGS**

Glycogen storage disease type I should be suspected with a combination of clinical, test, and histopathologic abnormalities. These include:6

- Hypoglycemia.
- Seizures attributed to hypoglycemia.
- Hepatomegaly.
- Growth failure.
- Elevated blood lactate.
- Hyperuricemia.
- Elevated cholesterol and triglycerides.
- Distention of the liver cells by glycogen and fat.
- Periodic acid-Schiff (PAS) stain positive.
- Absence of fibrosis and cirrhosis.

Untreated infants usually present with the symptoms listed above by ages 3 to 4 months. They are often noted to have doll-like facies with fat cheeks, thin extremities, and a protuberant abdomen. Epistaxis may occur because of impaired platelet function.6

**PATHOPHYSIOLOGY AND DIAGNOSIS**

Most cases of GSDI result from a deficiency in the glucose 6-phosphate hydroxylase activity. Because this enzyme is primarily expressed in the liver and kidney, most problems relate to these organ systems.6

**MANAGEMENT**

Management targets medical nutritional therapy with a goal of maintenance of normal blood glucose levels and prevention of hypoglycemia. Allopurinol is often needed to prevent gout if diet does not normalize uric acid level. Lipid-lowering medication is often needed for the management of hyperlipidemia and citrate therapy is needed to prevent renal calculi. Angiotensin-converting enzyme inhibitors are indicated for microalbuminuria and kidney transplant is indicated for end-stage renal disease.6

Testing examines the extent of disease progression and includes:6

- Measurement of glucose, lactic acid, uric acid, 25-hydroxyvitamin D, liver function tests, and lipids.
- Nutritional assessment.
- Liver and kidney imaging.
- Platelet function tests.
- Bone density.
- Screening for pulmonary hypertension.

**OUTCOMES**

Most patients with GSDI will live into adulthood. Long-term complications of untreated GSDI include:6

- Short stature.
- Osteoporosis.
- Delayed puberty.
- Gout.
- Renal disease.
- Pulmonary hypertension.
- Hepatic adenomas with potential for malignant transformation.
- Polycystic ovaries.
- Pancreatitis.
- Changes in brain function.
- Irregular sense in women.

**Summary**

At a minimum, it is important for the pediatrician to be familiar with the disease on their state newborn screen as well other genetic diseases they may see in their office. Additionally, it is important to recognize that the child with multiple medical issues may have a syndromic condition and need referral to a genetic or metabolic specialist.

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**CASE 4**

A 4-month-old infant presents with a hypoglycemic seizure noted by the parents in the morning when they go to wake him. He is noted to have hepatomegaly and splenomegaly. The mother reports his pediatrician has been worried about the baby’s height being short, and she has been worried about her child’s protuberant abdomen. What is your diagnosis?
Part 2
Managing enuresis in primary care

The continuation of this informative article addresses treatments for nocturnal enuresis, constipation, UTIs, and extraordinary daytime urinary frequency in children.

NAN E TOBIAS, MSN, APRN

Treatment of nocturnal enuresis
It is paramount for primary care physicians (PCPs) to emphasize to the family that bedwetting is not the child’s fault, particularly when the parent conveys a feeling of blame or anger toward the child. It should be emphasized that punishments and shaming do not help. When the child is developmentally ready to work on the bedwetting, it is time to pursue intervention. Most often, this occurs when the child’s social interactions are reduced because of the bedwetting, usually in the form of sleepovers.

Families differ in their goals for treatment, so this needs to be clarified at the outset. Some families want to reduce their workload, whereas others want the assurance that nothing is physically wrong with their child, or a family vacation or school trip may occur in the near future for which they want to prepare. The pediatric PCP may then explain that a carefully constructed program can be developed that may involve several methods of treatment, used in sequence or combination.² It cannot be overemphasized that a long-term treatment plan needs to have the child’s involvement. In other words, the child needs to have the maturity and motivation to participate. It is also imperative that the family handle the bedwetting and its treatment in a positive fashion. Should negativity be demonstrated by family members, they should be counseled about the poor influence this attitude will have toward treatment and be encouraged to change their thinking.

Treatment of constipation
If constipation is diagnosed, a bowel cleanout is undertaken. Many PCPs initiate a bowel program with the family by starting with maintenance doses of laxatives. Quite frequently, the bowel program does not achieve its goals when begun in this manner. Parents

Ms Tobias is a pediatric nurse practitioner, Department of Pediatric Urology, Mercy Health Children’s Hospital, Toledo, Ohio. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.
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- Coronavirus
- Human Metapneumovirus
- Human Rhinovirus/Enterovirus
- Influenza A
- Influenza A/H1
- Influenza A/H1-2009
- Influenza A/H3
- Influenza B
- Parainfluenza Virus
- Respiratory Syncytial Virus

**Bacteria**
- Bordetella pertussis
- Chlamydophila pneumoniae
- Mycoplasma pneumoniae

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**Syndromic Testing:** The right test, the first time.
# TABLE 6

## DOSES OF COMMONLY USED ORAL AND RECTAL LAXATIVES/ENEMAS

### ORAL LAXATIVES

<table>
<thead>
<tr>
<th>Osmotic Laxatives</th>
<th>Maintenance: 0.2-0.8 g/kg/d.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miralax (polyethylene glycol [PEG] 3350)</strong></td>
<td><strong>Fecal disimpaction:</strong> 1-1.5 g/kg/d OR 7 capfuls (119 g) in 32 oz fluid—either dose given 3-6 consecutive days (must be taken in quickly over 2-3 h)</td>
</tr>
<tr>
<td>Lactulose</td>
<td>1-2 g/kg, once or twice a day; maximum dose, 40 g/d.</td>
</tr>
<tr>
<td>Milk of magnesia (magnesium hydroxide), 400 mg/5 mL</td>
<td>6-23 mo: 40 mg/kg/d or divided bid; maximum dose, 600 mg/d</td>
</tr>
<tr>
<td>Not for use with renal insufficiency or renal failure.</td>
<td>2-5 y: 400 to 1200 mg/d or divided bid-tid; maximum dose, 1200 mg/d</td>
</tr>
<tr>
<td>Magnesium citrate</td>
<td>2-5 y: 60-150 mL in single dose</td>
</tr>
<tr>
<td>Not for use with renal insufficiency or renal failure.</td>
<td>6-11 y: 180-300 mL in single dose</td>
</tr>
<tr>
<td></td>
<td>12 y and over: 300 mL in single dose</td>
</tr>
<tr>
<td></td>
<td>Fecal disimpaction may be given for 3 consecutive days; best taken if chilled and mixed in equal amount of fruit juice.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lubricant Laxative</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mineral oil</strong></td>
<td>1-18 y: 1-3 mL/kg/d, once or divided, maximum of 90 mL/d.</td>
</tr>
</tbody>
</table>

### Stimulant Laxatives

<table>
<thead>
<tr>
<th>Stimulant Laxative</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Senna (Ex-lax)</strong></td>
<td>2-6 y: 4.4-8.8 mg/d or twice daily; maximum dose, 17.2 mg</td>
</tr>
<tr>
<td>Syrup 8.8 mg/5 mL</td>
<td>6-12 y: 8.6-13.2 mg/d or twice daily; maximum dose, 34.2 mg</td>
</tr>
<tr>
<td>Chocolate flavored tablets:</td>
<td>12 y and older: 30 mg/d or twice daily; maximum dose, 60 mg</td>
</tr>
<tr>
<td>8.6 mg/tablet</td>
<td>Adjust doses individually for disimpaction and maintenance.</td>
</tr>
<tr>
<td>15 mg/tablet</td>
<td></td>
</tr>
<tr>
<td>Short-term use only.</td>
<td></td>
</tr>
</tbody>
</table>

### Rectal Suppositories/Enemas

<table>
<thead>
<tr>
<th>Osmotic Enema</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fleet Enema Extra rectal (sodium phosphate)</strong></td>
<td>2-4 y: 1/2 contents of 2.25-oz pediatric enema</td>
</tr>
<tr>
<td>Not for daily use or in renal insufficiency or renal failure.</td>
<td>5-11 y: 1 2.25-oz pediatric enema</td>
</tr>
<tr>
<td><strong>Normal saline enema (may add 1/2 -1 packet castile soap)</strong></td>
<td>Infant to 23 mo: 120-240 mL</td>
</tr>
<tr>
<td>2-4 y: 240-360 mL</td>
<td>5-10 y: 360-480 mL</td>
</tr>
<tr>
<td></td>
<td>11-16 y: 480-720 mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stimulant Enema</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fleet mineral oil enema</strong></td>
<td>2-11 y: 1/2 of 4.5-oz bottle</td>
</tr>
<tr>
<td>12 y and older: 1 4.5-oz bottle</td>
<td></td>
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</tbody>
</table>

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report that with initiation of the laxative, the child was either stooling constantly, having bowel accidents, or that no change existed at all in bowel habits. Instead, the preferred method is to begin with a bowel cleanout. Only after the bowel is cleaned out appropriately will the maintenance laxative doses be effective (Table 6).32

If a large stool load or balls of stool in the recto-sigmoid are identified on abdominal X-ray (AXR), it is often a good idea to initiate the cleanout with enemas. When hard stool is present in the rectum, painful abdominal cramping with oral laxatives given by mouth can occur. Enemas can be in the form of a small volume Fleet enema, a glycerin or bisacodyl suppository, or a soap suds enema. It is important to explain to parents when purchasing a Fleet enema that different types are available. The PCP should specify the specific type he/she recommends (Table 6). When making recommendations, it is imperative to recognize any presence of renal disease.

Once the bowel cleanout phase has been accomplished, maintenance doses of laxatives are continued. The length of bowel therapy has not been agreed upon by pediatric gastroenterologists as a group. Certainly rectal distention and an abnormally large stool burden can develop over several months-to-years’ time prior to constipation being identified. Even after successful initiation of therapy, it is common for children to have relapses of constipation and require further cleanouts over time. One study showed that children diagnosed with functional constipation continued to have chronic constipation 3 to 12 years after initial diagnosis and treatment.30 In this author’s setting, clinicians recommend that maintenance laxative therapy continue for at least a year prior to weaning the doses.31 Whereas stimulant laxatives are not recommended for chronic use, osmotic and lubricant laxatives and bulking agents may be used long term.29

Other recommended treatments for constipation are adequate fluid and fiber intake. Fluid recommendations can be given based upon the Holliday-Segar maintenance fluid requirements (Table 7).32 Fiber intake recommendations are based upon the formula: age in years plus 5 grams equals the number of grams of fiber recommended per day until the adult recommended amount of 25 grams to 35 grams/day.33 Current evidence does not support the use of fiber supplements.21 However, in children and adolescents who do not eat the recommended daily amount, fiber supplements such as fiber gummies, Benefiber, or fiber bars seem appropriate. Evidence does not support the use of probiotics in the treatment of childhood functional constipation. Anecdotal reports often do corroborate the successful use of probiotics and yogurt with active cultures (Bifidobacterium and Lactobacillus).

An important word of advice when discussing toileting habits with families is that children’s feet should be flat on the floor when using the toilet. Toilets in general are made for adults. If the child’s feet cannot be positioned flat on the floor comfortably when sitting on the toilet, a step stool or other device should be used. A child sitting on the toilet with dangling legs will be unable to push to have a bowel movement and may not be able to sufficiently evacuate.

It has been shown that at least 50% of children with bladder and bowel dysfunction will improve with successful constipation treatment and behavioral management.34 For those with nocturnal enuresis, the pattern of fluid intake is important so that the majority of fluids are consumed early in the day rather than late afternoon and evening. Many children are not in the habit of drinking the majority of fluids early in the day as school activities do not encourage this behavior. Teachers may be hesitant to allow children to use the bathroom when needed, so that children learn not to drink during school hours. This encourages the majority of fluids to be consumed late in the day, thus producing a good deal of urine during sleeping hours.

In contrast, the general recommendation is for fluid intake to be completed 2 to 3 hours prior to bedtime. The child should void at bedtime, so the night starts with an empty bladder. Using the maintenance fluid formula and giving the family written recommendations for a schedule of timing of fluid intake is helpful. It is also beneficial to write notes for water bottle and bathroom privileges to give to teachers.

**Other treatments for nocturnal enuresis**

When treatment of bowel issues and behavior modification techniques do not result in resolution of bladder issues, other therapies are suggested.
One therapy is the wetness alarm. Wetness alarms have been shown to give high cure rates for nocturnal enuresis. The alarm consists of a sensor worn on the underwear that causes an alarm to sound or vibrate when wetness is sensed. The wearer is then instructed to immediately get out of bed and go to the bathroom. At the initiation of alarm use, the child will often awaken to a totally wet bed. As more time passes with the use of the alarm, the child may awaken in the middle of urination and then eventually prior to its initiation. The conditioning occurs when the child awakens to the sensation of a full bladder and associates that sensation with the alarm.

It has been shown to take approximately 12 to 16 weeks of nightly use for the wetness alarm to be effective. Often the parent needs to get up with the child, particularly during the initial use of the alarm. The child may not respond to the alarm without parental assistance. The child needs to be awakened so that he/she realizes what is occurring for the conditioning to occur. As can be seen from this description, the use of a wetness alarm requires a motivated child and family member(s). It is generally not recommended for children aged younger than 8 years. Enuresis alarms can be obtained from online sites such as bedwettingstore.com and PottyMD.com. Insurance typically does not cover their cost.

One medication that has been used for children and adolescents for a “quick fix” for bedwetting is desmopressin (DDAVP). It is given for short periods, such as vacations, sleepovers, camping trips, or school trips. It works by increasing water permeability in the renal collecting tubules, which results in increased water reabsorption that causes decreased urine production. Its duration of action is estimated at 6 to 14 hours. Recommended dosing is to start at 0.2 mg and work up to a maximum of 0.6 mg nightly. It is recommended for use in nocturnal enuresis from age 6 years through adolescence. It is also recommended to keep fluid intake to a minimum in the hour prior to administration until at least 8 hours later. Desmopressin also may be used for long-term treatment of nocturnal enuresis, but is not considered a first-line therapy.

Other medications that are used for nocturnal enuresis are anticholinergics and the tricyclic antidepressant imipramine. Neither are used as first-line treatment. Some anticholinergics that are used are oxybutynin, tolterodine, and hyoscymine. These medications suppress detrusor overactivity that can be present in monosymptomatic nocturnal enuresis. Imipramine has anticholinergic effects as well as a stimulant effect that is thought to lighten the level of sleep, making arousal from sleep easier. It is used in much smaller doses when treating nocturnal enuresis, as compared with depression. It may be prescribed nightly for 2 to 4 months, then weaned gradually by administering every 2, then every 3 days over the next 3 to 4 months to reduce risk of relapse. If imipramine is prescribed, special care must be taken for its storage at home as it is highly lethal when taken in overdose. There is no known specific antidote for its toxicity and death is usually the result of cardiac arrhythmia and cardiovascular collapse.

**Urinary tract infections**

It is necessary for a urinary tract infection (UTI) to be culture proven to determine appropriate treatment and subsequent diagnostic evaluation (Figure 3). The diagnosis of urinary tract infection cannot be made on symp-
A properly collected urine specimen for a macroscopic and microscopic urinalysis is the first step. It has become common practice for some primary care offices to obtain a midstream urine specimen from toilet-trained children and perform only a reagent test strip (dipstick) in the office in an attempt to diagnose a UTI. As discussed previously, this practice reveals many false-positive and false-negative results when checking for nitrites and leukocyte esterase. The urine must be sent to a lab for urine culture. Growth of any single organism from a midstream urine that is at least 50,000 colony-forming units per high-power field (CFU/HPF) is indicative of a UTI. Bacterial counts of at least 10,000 CFU/HPF obtained by a catheter or any growth obtained by suprapubic tap are indicative of a UTI.35

A urine culture obtained by bagged specimen is not reliable unless it reveals negative results. Any growth of any bacteria in a bagged specimen renders the results unusable.36 Therefore, a bagged urine specimen should not be performed in a febrile, symptomatic child. The only reliable result of a bagged specimen is a negative one.

Children who exhibit daytime symptoms and incontinence and/or UTIs will benefit from a recommendation for adequate fluid intake, a recommended fluid intake schedule, and a recommended voiding schedule in which voiding occurs at a minimum of 5 times daily. Vibrating watches that are attractive to children can be obtained at a reasonable cost through the sites PottyMD.com or bedwettingstore.com. The watches’ alarms can be set to coincide with appropriate times during the school day for the child to take bathroom breaks. Reducing or eliminating acidic fruits and their juices (orange, grapefruit, tomato, lemon, lime) and caffeine and chocolate also may help, although much of this evidence is anecdotal.

When to image
If the clinician discovers findings of significant irritative voiding symptoms, interrupted urinary flow, urinary hesitancy or straining to void, daytime wetting, or UTI, urologic imaging can be undertaken. The PCP may initiate a workup with a renal and bladder ultrasound (US), which may diagnose structural abnormalities and determine bladder emptying. A voiding cystourethrogram (VCUG) also may be in order. Although the 2011 American Academy of Pediatrics (AAP) guidelines for diagnostic evaluation of the urinary tract after a first febrile UTI do not recommend a VCUG if the renal US is normal, many pediatric urologists are in disagreement with this recommendation. Many physicians believe that serious flaws existed in the interpretation of the data that was used to make this recommendation. Thus, many pediatric specialists recommend obtaining a VCUG after a first febrile UTI, particularly in a child aged younger than 4 years when the developing kidney is most prone to scarring. The data on this important topic continue to accumulate.

When to refer
A referral to a pediatric urologist or nephrologist can be made depending upon local referral practices. When this referral is made, the diagnostic images must be available, not just the written report. Children who present with monosymptomatic nocturnal enuresis or nonmonosymptomatic nocturnal enuresis who do not improve with standard therapies also should be referred. So should children with UTIs despite treated constipation. Physical findings of occult spinal dysraphism (lower lumbar spine abnormalities) may be referred to a pediatric neurosurgeon. For children who have evidence of nocturnal enuresis and enlarged tonsils and signs of sleep apnea, a referral to a pediatric ears/nose/throat (ENT) or sleep specialist can be made. Sleep apnea can be associated with an increased production of urine overnight. When constipation is refractory with continued attempts at cleanout and treatment, referral to a pediatric gastroenterologist is recommended.

### TABLE 8

<table>
<thead>
<tr>
<th>CONDITIONS TO BE CONSIDERED WITH PRESENTATION OF EXTRAORDINARY DAYTIME FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Bladder overactivity</td>
</tr>
<tr>
<td>Diabetes mellitus or diabetes insipidus</td>
</tr>
<tr>
<td>Medications (some antihistamines, psychotropic drugs)</td>
</tr>
<tr>
<td>Urinary tract obstruction</td>
</tr>
</tbody>
</table>

From Bergmann M, et al.37
Extraordinary daytime urinary frequency

Another urinary disorder that deserves explanation is extraordinary urinary frequency, or pollakiuria. This disorder can begin with an abrupt or more gradual onset of urinary frequency of extreme proportion. Some children, generally in the age range of 3 to 7 years, will urinate small amounts as often as every 5 to 10 minutes. Many will exhibit such a strong urge that they cannot leave the toilet. When parents finally get them off the toilet, many return almost immediately or begin to cry due to discomfort. Children may spend nearly their entire day on the toilet. Some may even drink less fluids in an attempt to help their problem. It is important to take a good history and perform a physical exam. The children do not generally have daytime incontinence in association with the frequency. To rule out organic disease, potential conditions that deserve consideration are listed in Table 8.

Should any of the factors be present that are listed in Table 9, appropriate diagnostic testing should be undertaken. To many PCPs, this may seem like such a benign problem that parents are advised to ignore it, or clinicians may advise that the children are merely vying for their parents’ attention. Parents also may be told that the children just like to visit bathrooms in various places. To the family, this problem is not benign. The child may be unable to leave the house for even a few minutes, which severely limits the family’s ability to accomplish day-to-day activities and can interfere with schooling. The symptoms can last for days to weeks prior to being referred to a specialist. Parents bring their children to the pediatric urology specialist’s office in total frustration, often at their wits’ end. In the past, specialists advised that extreme urinary frequency began as the result of psychosocial problems or emotional stress. Whereas such issues can be involved, it is a good idea to sort out other potential accompanying issues, in particular UTI and constipation.

Should a UTI and/or constipation be present, they should be treated appropriately. Families may be counseled about other potential causes of urinary frequency including those listed in Table 8. Potential stressors and worries should be identified, being cognizant of questioning the children as well as the parents. Children may reveal stressors of which the parents may not be aware. If so identified, they can be discussed and referrals made if appropriate. Other recommendations to treat urinary frequency are a liberal intake of fluids, in particular, water. Very concentrated urine may irritate the bladder further. Should the above treatments fail, referral to a pediatric specialist is in order.

Summary

The pediatric PCP can become comfortable with the evaluation and early treatment of enuresis, constipation, and UTIs. The treatment of constipation may ameliorate or resolve many wetting problems and should be attempted prior to referral. Daytime incontinence also may benefit from the use of timed voiding and adequate fluid intake. Nocturnal enuresis may show improvement as well using these techniques in addition to fluid restrictions late in the day and voiding at bedtime.

It is helpful to understand the psychologic effects of nocturnal enuresis on children and the limitations of their voluntary control of the problem. Using quantified criteria, particularly in the diagnosis of UTIs, will assist the PCP to correctly manage UTIs and recommend subsequent testing. In the long run, children and families will benefit from the pediatric PCP providing care of the child with urologic issues and making referrals for lack of response to treatment earlier rather than later.
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Vaccine refusal or delay played a major role in the 2013 measles outbreak—New York City’s largest since 1992—that cost the New York City Health Department nearly $400,000, according to a new report.

Published in *JAMA Pediatrics*, the report highlights the New York City Health Department’s response and the public health toll of the outbreak.1 Danielle De Souza, a spokesperson for the New York City Health Department, says the department learned that it is important to keep vaccine-preventable diseases on the list of differential diagnoses for patients with fevers or rashes—particularly when they have had recent international travel or when there is an active outbreak.

“The outbreak was fueled by the introduction of measles virus into a small number of families who had previously declined vaccination. They accounted for the majority—71%—of identified cases,” De Souza says.

**Tracking the outbreak**

The report assessed the response of health officials during the outbreak and included a cost analysis. Overall, there were 58 cases of measles in the outbreak and 3351 exposed contacts. Nearly 80% of the age-eligible cases were unvaccinated because of refusal or intentional delay, according to the data.

“Measles vaccine refusals or delays can lead to large outbreaks following measles importations, with costly and resource-intensive response and containment,” the report notes.

Characterized by a generalized rash with fever, measles is highly contagious and is transmitted through airborne and respiratory droplets. Nearly all—90%—of individuals exposed to the virus become sick, with infection beginning 4 days before a rash ever appears, extending the period during which infected individuals remain active and spread the virus. It’s for these reasons that a single case of measles can quickly and easily result in large outbreaks, according to the researchers. Postexposure prophylaxis can provide some help in an outbreak, the report notes, but the window for use is narrow.

Although measles was declared eliminated in the United States in 2000, its virus remains active around the world, and public health officials have long stood by the recommendations for sustaining the 2-dose measles/mumps/rubella (MMR) vaccine nationally.

Some pockets of the population have refused or delayed these vaccines, however, and researchers after the New York City outbreak tied the incident to an unvaccinated 13-year-old who had recently traveled abroad and brought the virus back. The patient had visited a doctor upon return from the trip, but the clinician didn’t report the suspected case until lab results confirmed measles—8 days after the initial patient visit.

The outbreak was characterized largely by the community in which patient cases were centered. All 58 infected individuals were Orthodox Jewish and resided in 2 Brooklyn neighborhoods, and the report concluded that the tight-knit nature of that community likely prevented further spread of the outbreak, although family-based infections also were a big part of the outbreak. Forty-one of the 58 individuals infected with measles were members of 8 extended families, and 52% of cases were believed to have come from a relative. Other transmission sources included building of residence, friend or playmate, healthcare setting, and community gathering.

In addition to the 78% of children aged 1 year and older who were not given the measles vaccine because of parental refusal or delay, the study also found that just 48% of those who were infected during the outbreak visited a healthcare provider who suspected measles and reported the case to the health department after the initial assessment.

As far as the healthcare response to the outbreak, the report found that in 7% of cases, patients visited a healthcare professional, but measles was not suspected. In 5 cases, rashes were present when the patients visited a doctor, but the cases were not report-
State of the anti-vax union

The number of kindergartners starting school without vaccination against preventable diseases is increasing in states that allow nonmedical exemptions to recommended immunizations.

RACHAEL ZIMLICH, RN
States that allow nonmedical vaccine exemptions are seeing an increase in the number of children entering their school years undervaccinated, leaving pockets of the country at risk for outbreaks of vaccine-preventable diseases, according to a new report.

Whereas immunization surveys reveal little change in national and state immunization rates over the last several years, the new report, published in *PLoS Medicine*, reveals increasing risk in specific areas where vaccine waivers have been most prevalent.

"Although immunization rates may not have changed recently, we now have a serious problem with widespread, nonmedical vaccine exemptions in several US counties, especially in Western states in the Pacific Northwest, and Texas and the Southwest," says Peter Hotez, MD, PhD, FASTMH, FAAP, dean of the National School of Tropical Medicine at the Baylor College of Medicine, Houston, Texas, and one of the study's authors. "Many of these counties are now at risk for breakthrough measles and other childhood illnesses."

Exemptions reduce herd immunity

Nonmedical exemptions are increasing in at least a dozen states, reaching "critical mass" in terms of herd immunity reductions to the point that breakthrough epidemics are possible, Hotez says.

According to the 2015 National Immunization Survey, 72.2% of children aged 19 to 35 months were fully vaccinated according to recommendations by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (CDC ACIP). Whereas national immunization data show that vaccination rates have not changed in recent years, the new report reveals a correlation between rates of nonmedical exemptions and vaccination rates, specifically for the measles, mumps, and rubella (MMR) vaccine.

“We need to do a better job providing pediatricians on the front lines with tools and resources to help them with vaccine-hesitant parents.”

—Peter Hotez, MD, PhD, FASTMH, FAAP

Nonmedical exemptions have plateaued over the last 3 years, the CDC survey points out, but that was after an acceleration in most states between 2009 and 2014. The new study found that in two-thirds of the states allowing exemptions, there has been a rise in the number of kindergartners starting school without being fully vaccinated. The study also notes that nonmedical vaccine exemptions
Teenagers plus heavy screen time equals ADHD?

Research now links self-reported attention-deficit/hyperactivity disorder symptoms in some adolescents to heavy digital media use.

RACHAEL ZIMLICH, RN

Digital media can connect adolescents to new people and experiences, but there is another side to the coin, and researchers warn that digital media use has the potential to increase symptoms of attention-deficit/hyperactivity disorder (ADHD).

The report, published in JAMA, studied teenagers aged 15 and 16 years at a baseline without symptoms of ADHD and found a "significant association" between high-frequency digital media use—"several times per day"—and the presence of ADHD symptoms after a 2-year follow-up.

"With more and more teens being connected to their digital devices around-the-clock, it is concerning that this well-designed longitudinal study found that teens who use 1 or more media devices many times daily were more likely to report difficulties with sustained attention over time," says Andrew Adesman, MD, chief of Developmental and Behavioral Pediatrics at Steven and Alexandra Cohen Children’s Medical Center of New York, New Hyde Park, New York. Adesman was not involved in the study but offered insight on the report’s findings to Contemporary Pediatrics.

Adesman adds that because the investigators relied on the teenagers for self-report of digital media use and of ADHD symptoms, it is possible that some response bias may have influenced these findings.

"Likewise, it is possible that some of the observed differences in digital media activities were due to—not a consequence of—differences in attention span," Adesman says. "The findings from this study cannot be ignored. On the one hand, parents and clinicians should be aware that very frequent digital media activity may—with time—have an adverse effect on attention span; on the other hand, this effect is not very large and further studies are needed for us to verify that this is indeed the case."

What researchers found

The longitudinal study investigated a group of students across 10 Los Angeles, California, high schools, reviewing their digital media use and display of ADHD symptoms at 6-, 12-, 18-, and 24 months. Students were asked to self-report on 14 different digital media activities, providing information on daily and weekly frequency of use.

The research team found that of the more than 2500 students without ADHD symptoms at baseline at the start of the study, nearly 81% reported high-frequency use of digital media after 24 months, and 5.9% of these teenagers experienced self-reported ADHD symptoms during the study period. Some of the most common high-frequency digital media use reported in the study was checking social media sites, with 54.1% of teenagers reporting this as a high-frequency activity.

Previous studies have addressed the use of traditional media exposure in relation to ADHD symptoms, but new digital media use is a different kind of exposure because of its speed, level of stimulation, and potential for high-frequency exposure, according to the report. The lure of digital media in mid-adolescence is high, the report notes, because teenagers are trying to develop their social identity and build relationships.

"Parents and clinicians should be aware that very frequent digital media activity may—in time—have an adverse effect on attention span."

—ANDREW ADESMAN, MD

"Modern media platforms provide unprecedented opportunities for social connection. Teens can converse with dozens of peers simultaneously via group text messages. Social media permits instantaneous communication with thousands. Video chatting enables immediate face-to-face interactions," the research team writes, adding a bit of caution. "Mid-
adolescence is also a period of high neural plasticity during which brain circuitry underlying attention and behavioral control mature rapidly and may be vulnerable to exposures that disrupt neurodevelopment."

Whereas digital media use may not be causative to ADHD symptoms, the study notes, ADHD is associated with “sensation seeking,” and digital media may satisfy a drive for stimulation in some individuals.

“Although alternative explanations remain possible, modern digital media use could play a role in the development of ADHD symptoms. The primary symptoms of ADHD are inattention—distractibility, trouble with organization—and hyperactivity-impulsivity—difficulty waiting, interrupting others, restlessness,” the report notes. “Modern media devices immediately notify users when new text messages, social media postings, or videogame play invitations arrive. Exposure to such notifications may draw attention away from focal tasks. Frequent distractions could disrupt normative development of sustained attention and organization skills.”

The speed at which digital media delivers stimulation also may make users more accustomed to rapid feedback, says the report, making it difficult for teenagers to develop impulse control and patience.

The report stops short of stating that digital media use can cause ADHD symptoms, but infers that data supports additional research in this area.

Adesman agrees with the need for further research and says that despite the association identified in the study between ADHD symptoms and frequent digital media use, the study did not prove a causative effect of digital media.

“This study did not solicit independent assessments of the teens’ attention span and it did not try to evaluate if there was any associated impairment of function—2 requirements for a diagnosis of ADHD,” he notes.

Ms Zimlich is a freelance writer in Cleveland, Ohio. She has no affiliations or financial interests to disclose.

**REFERENCE**

Coping basics: Medical decision-making is the key

Pediatricians need to document visits correctly to ensure continuity of care and to bill appropriately. Are you confident your office notes will pass muster with those inevitable insurance company audits?

ANDREW J SCHUMAN, MD

The current coding system is more than 20 years old and was developed at a time when physicians did not use electronic health records (EHRs). As a consequence of EHR use, notes have become bloated, take too much time to complete, and are a significant contributor to physician burnout. I reviewed a variety of ways to expedite completion of office notes in the article “Expediting medical documentation” in the January 2016 issue of Contemporary Pediatrics. The purpose of this month’s article is to simplify the process of assigning codes for your most common visit types.

Whereas only a handful of studies look at how well physicians code for office visits, all conclude that physicians undercode their established patient office visits. The most recent study examined the notes from 351 senior resident family physicians in 2 programs in Tennessee. Expert coders found that 33% of visits were undercoded based on the documentation; 50% were undercoded based on the medical decision-making (MDM); and 80% of the visits were undercoded based on the number of presenting problems.

Fortunately, the Centers for Medicare and Medicaid Services (CMS) is considering revising the coding guidelines. It is anticipated that CMS will relax requirements for the physical exam and history components of medical notes. This is expected to considerably reduce the documentation burden on providers.

A different approach

Providers have been “trained” to code by taking courses, reading articles, and having the office coders review your notes. We know that well-visit notes are straightforward and generally not susceptible to insurance scrutiny. The difficult part of coding is deciding whether an ill visit for an established patient should be coded as a 99213 (level 3) or a 99214 (level 4) visit. Physicians need to code correctly for services provided, neither downcoding for fear of an audit or upcoding to generate productivity or increase revenue.

I find that the best way to expedite coding is to decide during the visit whether it is a level-3 or a level-4 visit based on the MDM involved and then document accordingly.

Your MDM depends upon just 3 factors:

- The number of problems addressed/number of treatment options considered.
- The data reviewed.
- The risk involved.

This is a “bottom-up” or “backward” approach. By determining if you have a level-3 or level-4 visit, you can save considerable time by taking the history and performing the physical exam appropriate for the visit type.

Documenting a moderately complex visit

The elements of any note include: 1) the history; 2) the physical exam; and 3) the MDM.

To document the history sufficient for a 99214 visit (Table 1), your history should include the chief complaint (CC); the history of present illness (HPI); the past, family, and/or social history (PFSH); and the review of...
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Will my malpractice be paid for?
When will my travel itinerary be confirmed?
When will the job I want become available?
Will everything be taken care of?

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The HPI should include at least 4 of the following descriptive elements of the presenting problem (let’s say ear pain): location (eg, left ear); duration (eg, 3 days); quality (eg, burning or stinging); timing (eg, intermittent or constant); severity (eg, 7/10 on pain scale); context (eg, associated with urinary tract infection [URI] symptoms) including any modifying factors (eg, improved with ibuprofen); or any associated signs or symptoms (eg, fever, vomiting). This can easily be accomplished with a few short sentences per problem. For example: “Patient presents with dull ache in left ear x 3 days. Patient reports pain is 7/10 in severity, constant, improves with ibuprofen, and is associated with vomiting and temperature to 102°F.”

A level 99214 visit history also requires 1 element for PFSH that is pertinent to the presenting problem. A statement of drug allergies, list of medications, or exposure to ill persons is usually sufficient to satisfy this requirement. Lastly, 2 or more pertinent elements of ROS should be documented to satisfy the history component of the 99214 visit. That’s it! These 99214 histories are easy to document and in the context of continuity of care, less is often more.

Documenting the physical exam component of the 99214 visit is similarly easily accomplished, and according to the 1997 guidelines requires examination of just 12 exam elements, including the patient’s vital signs. Table 1 also provides helpful guidance regarding elements required for coding new and established patients for level-3, level-4, and level-5 visits.

Table 1
CODING ELEMENTS NEEDED FOR COMMON VISIT TYPES

<table>
<thead>
<tr>
<th>ELEMENT</th>
<th>99203 NEW PATIENT</th>
<th>99213 ESTABLISHED PATIENT</th>
<th>99204 NEW PATIENT</th>
<th>99214 ESTABLISHED PATIENT</th>
<th>99205 NEW PATIENT</th>
<th>98215 ESTABLISHED PATIENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPI</td>
<td>4 elements</td>
<td>1 element</td>
<td>4 elements</td>
<td>4 elements</td>
<td>4 elements</td>
<td>4 elements</td>
</tr>
<tr>
<td>ROS</td>
<td>2</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>PFSH</td>
<td>1</td>
<td>None</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>PE (1995 guidelines)</td>
<td>12 elements</td>
<td>6 elements</td>
<td>18 elements</td>
<td>12 elements</td>
<td>18 elements</td>
<td>18 elements</td>
</tr>
<tr>
<td>MDM (complexity)</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Time</td>
<td>30 min</td>
<td>15 min</td>
<td>45 min</td>
<td>25 min</td>
<td>60 min</td>
<td>40 min</td>
</tr>
</tbody>
</table>

Abbreviations: HPI, history of present illness; PE, physical exam; PFSH, past, family, and social history; ROS, review of systems; MDM, medical decision-making.

Author created.

Table 2
MEDICAL DECISION-MAKING (MDM)

<table>
<thead>
<tr>
<th>MDM</th>
<th>PROBLEM POINTS</th>
<th>DATA POINTS</th>
<th>RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212 Straightforward</td>
<td>1</td>
<td>1</td>
<td>Minimal</td>
</tr>
<tr>
<td>99213 Low</td>
<td>2</td>
<td>2</td>
<td>Low</td>
</tr>
<tr>
<td>99214 Moderate</td>
<td>3</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>99215 High</td>
<td>4</td>
<td>4</td>
<td>High</td>
</tr>
</tbody>
</table>

From US Department of Health and Human Services.6

The MDM quantifies the complexity of establishing a diagnosis and/or selecting a management option by measuring:

- The nature of the presenting problem (the number of possible diagnoses and/or the number of management options that must be considered).
- The data reviewed (the amount of medical records, diagnostic tests, and/or other information that must be obtained, reviewed, and analyzed).
- The risk of significant complications, morbidity and/or mortality associated with the patient’s presenting problem(s); the diagnostic
This is a medical decision-making (MDM) coding sheet. Circle highest level of risk, add up problem and data points, and determine the level of service.

<table>
<thead>
<tr>
<th>LEVEL OF RISK</th>
<th>PRESENTING PROBLEMS</th>
<th>DIAGNOSTIC PROCEDURES</th>
<th>MANAGEMENT OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal</td>
<td>• 1 self-limited or minor problem (eg, cold, insect bite, tinea corporis)</td>
<td>• Laboratory tests requiring venipuncture</td>
<td>• Rest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chest x-rays</td>
<td>• Gargles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EKG/EEG</td>
<td>• Elastic bandages</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Superficial dressings</td>
</tr>
<tr>
<td>Low</td>
<td>• 2 or more self-limited or minor problems</td>
<td>• Physiologic tests not under stress (eg, PFTs)</td>
<td>• Over-the-counter drugs</td>
</tr>
<tr>
<td></td>
<td>• 1 stable, chronic illness (eg, well-controlled hypertension, non–insulin-resistant diabetes, cataract, BPH)</td>
<td>• Noncardiovascular imaging studies with contrast (eg, barium enema)</td>
<td>• Minor surgery with no identified risk factors</td>
</tr>
<tr>
<td></td>
<td>• Acute uncomplicated injury or illness (eg, cystitis, allergic rhinitis, simple sprain)</td>
<td>• Superficial needle biopsy</td>
<td>• Physical therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Clinical lab tests requiring arterial puncture</td>
<td>• Occupational therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Skin biopsies</td>
<td>• IV fluids without additives</td>
</tr>
<tr>
<td>Moderate</td>
<td>• One or more chronic illnesses with mild exacerbation, progression, or adverse effects of treatment</td>
<td>• Physiologic tests under stress (eg, cardiac stress test, fetal contraction stress test)</td>
<td>• Minor surgery with identified risk factors</td>
</tr>
<tr>
<td></td>
<td>• 2 or more stable chronic illnesses</td>
<td>• Diagnostic endoscopies with no identified risk factors</td>
<td>• Elective major surgery (open, percutaneous, or endoscopic) with no identified risk factors</td>
</tr>
<tr>
<td></td>
<td>• Undiagnosed new problem with uncertain prognosis (eg, breast lump)</td>
<td>• Deep needle or incisional biopsy</td>
<td>• Prescription drug management</td>
</tr>
<tr>
<td></td>
<td>• Acute illness with systemic symptoms (eg, pyelonephritis, pleuritis, colitis)</td>
<td>• Cardiovascular imaging studies with contrast and with no identified risk factors (eg, arteriogram, cardiac catheterization)</td>
<td>• Therapeutic nuclear medicine</td>
</tr>
<tr>
<td></td>
<td>• Acute complicated injury (eg, head injury with brief loss of consciousness)</td>
<td>• Obtain fluid from body cavity (eg, LP, thoracentesis, culdocentesis)</td>
<td>• IV fluids with additives</td>
</tr>
<tr>
<td>High</td>
<td>• One or more chronic illnesses with severe exacerbation, progression, or adverse effects of treatment</td>
<td>• Cardiovascular imaging, with contrast, with identified risk factors</td>
<td>• Closed treatment of fracture or dislocation without manipulation</td>
</tr>
<tr>
<td></td>
<td>• Acute or chronic illness or injuries that pose a threat to life or bodily function (eg, multiple trauma, acute MI, PE, severe respiratory distress, peritonitis)</td>
<td>• Cardiac EP tests</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• An abrupt change in neurologic status (eg, seizure, TIA, weakness, sensory loss)</td>
<td>• Diagnostic endoscopies with identified risk factors</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Discography</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Problem points</th>
<th>Data reviewed points</th>
<th>Final analysis: Circle level of history, physical exam, and medical decision-making to determine level of service</th>
</tr>
</thead>
<tbody>
<tr>
<td>Points</td>
<td>Points</td>
<td>Element</td>
</tr>
<tr>
<td>Self-limited or minor (max 2)</td>
<td>1</td>
<td>99213</td>
</tr>
<tr>
<td>Established problem, stable or improving</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Established problem, worsening</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>New problem, no workup planned (max 2)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>New problem, additional workup planned</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ABG, arterial blood gas; BPH, benign prostatic hyperplasia; ECG, electrocardiogram; EKG, electroencephalogram; EP, electrophysiological; HPI, history of present illness; IV, intravenous; KOH, potassium hydroxide; LP, lumbar puncture; MI, myocardial infarction; PE, pulmonary embolism; PFSH, past, family, social history; PFT, pulmonary function test; ROS, review of systems; TIA, transient ischemic attack. From US Department of Health and Human Services. 

FIGURE 1 EXAMPLE OF MDM CODING SHEET FOR A 99214 VISIT
practice improvement

procedure(s); and/or the possible management options.

The MDM requirement of documenting an office visit is confusing and even frustrating at first look. Remember that the 99214 visit requires moderate MDM, which in turn requires adequate “passing scores” relating to 2 of the 3 components above—risk, amount of data reviewed, and the nature of the presenting problem. To decide on a level of MDM, you need to keep a coding sheet like the one on page 41 (Figure 1) handy. To bill for moderate MDM, your documentation must achieve at least 2 of the 3 following criteria on the coding sheet: 1) 3 problem points or higher; 2) 3 data points or higher; and 3) moderate risk in the risk table. As stated above, in my experience, the best approach to an established patient visit is to determine the level of risk at the time of the patient visit by assigning the highest applicable level of risk in the risk table.

You can see from the risk table that in pediatric practice, those patients who qualify as moderate risk most often present with:
- One or more chronic illnesses with mild exacerbation, progression, or adverse effects of treatment (asthma exacerbation, attention-deficit/hyperactivity disorder [ADHD] not responding to medication).
- Two or more stable chronic illnesses (asthma, enuresis).
- Undiagnosed new problem with uncertain prognosis (eg, blood in the stool).
- Acute illness with systemic symptoms (eg, pyelonephritis, pneumonia, colitis).
- Acute complicated injury (eg, head injury without loss of consciousness).
- Conditions that require prescription drug management.

If a patient falls into the moderate-risk category, then the provider determines the number of problems addressed at the visit as well as the data reviewed and assigns a point value to this information using the coding sheet. Remember that 3 or more problem points or 3 or more data points are needed to qualify a visit as a level 99214 as long as the problem or problems fall into the moderate risk level. If you determine that the visit should be assigned moderate MDM, make sure you document the necessary elements for the history and/or the physical exam to qualify your visit as a 99214 visit. Figure 2 is an example of documentation for a 99214 visit.

Coding by time

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You save $88.00!

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Our Price: $2,361.00
You save $234.00!

MI 24 touchTymp Tympanometer Screener
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Our Price: $3,162.00
You save $313.00!

Pediatric Vision Screeners
plusoptik S12R Mobile Vision Screener without Wireless Connection
Our Price: $5,495.00

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Vaccine refusals

CONTINUED FROM PAGE 34

Visit counseling the patient or parent or coordinating services, you can circumnavigate many of the coding requirements by adding a statement at the end of your note documenting the time spent and detailing what was discussed. For a 99213 visit, this time threshold component is 8 of 15 minutes, while for a 99214 visit it is 13 of 25 minutes.

Other coding nuances

Keep in mind that insurance companies prefer that every ill visit is level 3 and will flag and often challenge level-4 visits and scrutinize your documentation. You can reduce the possibility of an audit by listing all appropriate diagnosis codes associated with your visit, and, whenever possible, code by time if the visit warrants. If there is any area of your note that merits verbosity, it is in the assessment and plan. Indicate the problems addressed, workup planned, and recommendations made for each diagnosis made at the visit. By doing so, you will reduce the likelihood of claim denial and generate the appropriate compensation for your services.

Dr Schuman, section editor for Practice Improvement and Peds v2.0, and Editorial Advisory Board member of Contemporary Pediatrics, is clinical assistant professor of Pediatrics, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire. He is CEO of Medgizmos.com, a medical technology review site for primary care physicians.

For references, go to ContemporaryPediatrics.com/coding-with-MDM

Ms Zimlich is a freelance writer in Cleveland, Ohio. She has no affiliations or financial interests to disclose.

REFERENCE


Vaccine refusals

ed to the health department. Thirty-six percent of the patients didn’t seek medical help for their rash and were identified only through contact tracing of secondary-case patients, according to the report.

Additionally, patients in many cases were not placed into airborne isolation precautions, resulting in additional exposures at 11 separate healthcare facilities.

“It is essential to notify the local health department immediately to ensure outbreak control measures are taken to prevent further spread and illness,” DeSouza says. “Suspect measles cases also need to be put in airborne isolation to prevent transmission in healthcare facilities. In a practice without an isolation room, a patient can be seen and brought into a room after all other patients have left.”

The direct cost of the outbreak to the health department was $394,448, and more than 10,000 personnel hours were spent responding to and controlling the outbreak, according to the report.

“Vaccine refusals and delays appeared to have propagated a large outbreak following importation of measles into the United States,” the report concluded. “Prompt recognition of measles along with rapid implementation of airborne isolation of individuals suspected of measles infection in healthcare facilities and timely reporting to public health agencies may avoid large numbers of exposures. The response and containment of measles outbreaks are resource intensive.”

Outbreak control efforts included MMR vaccination given within 3 days of exposure to 114 patients who were aged older than 6 months, and immunoglobulin within 6 days of exposure to infants who could not or did not receive the MMR prophylaxis, according to the report.

“This outbreak was fueled by the introduction of measles virus into a small number of families who had previously declined vaccination. The outbreak was prolonged, in part, owing to the spread of measles to infants too young to have been vaccinated and to the delay of vaccination among children,” researchers conclude.

Of the patients and contacts observed in the report, 66% had immunity based on 2 doses of the MMR vaccine or through natural immunity; 11% had had 1 dose of a measles-containing vaccine; 10% were susceptible; and 13% had no record or knowledge of their immunity status.

“I would hope this report demonstrates how important measles vaccination is and that there are serious consequences of not being vaccinated,” De Souza says. “Further, as stated above, clinicians should consider measles in the differential diagnosis of a patient with fever and a rash, especially if they have travelled internationally or there is a reported outbreak.”

Ms Zimlich is a freelance writer in Cleveland, Ohio. She has no affiliations or financial interests to disclose.

REFERENCE

increased in 12 of the 18 states that permit such exemptions—Arizona, Arkansas, Idaho, Maine, Minnesota, Missouri, North Dakota, Ohio, Oklahoma, Oregon, Texas, and Utah—since 2009. Idaho has the highest levels of undervaccinated kindergartners, with almost 27% of incoming kindergartners in 1 Idaho county opting out of vaccinations in the 2016-2017 school year, according to the report.

Although the highest exemption rates appear to be in rural counties with smaller populations (under 50,000), the report also highlights a number of metropolitan areas with high numbers of nonmedical exemptions, including Seattle and Spokane in Washington state; Portland, Oregon; Phoenix, Arizona; Salt Lake City and Provo in Utah; Houston, Fort Worth, Austin, and Plano in Texas; and Kansas City, Missouri. In contrast, states that have ended allowance of nonmedical exemptions have seen increases in vaccine coverage. States with nonmedical exemptions had lower MMR vaccination rates overall, while states that have banned these exemptions—including California, Mississippi, and West Virginia—had the highest uptick in MMR vaccinations and lower incidence of disease outbreaks, according to the report.

The study did not reveal the reasons why parents requested nonmedical exemptions, but Hotez says he hopes the findings will spur a follow-up study that delves into social and demographic factors leading to exemption requests. Hotez also hopes that the report will inspire stakeholders and federal agencies to investigate nonmedical exemptions and their impact.

“Bottom line, the antivaccine movement in the US has become well organized and well financed, while the pro-vaccine side lacks visibility in many states,” Hotez says. “We need to do a better job providing pediatricians on the front lines with tools and resources to help them with vaccine-hesitant parents.”

Ms Zimlich is a freelance writer in Cleveland, Ohio. She writes regularly for Contemporary Pediatrics and sister publications Managed Healthcare Executive and Medical Economics. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

REFERENCE

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Data on *M. marinum* susceptibility are limited. Biopsy is the preferred diagnostic modality. Unlike rapid-growing mycobacteria, *M. marinum* usually requires several weeks before sufficient culture growth occurs. In this patient, granulomas were seen upon microscopic review of the biopsy sample, and culture eventually grew *M. marinum*.

*Mycobacterium marinum* disease in humans is uncommon, with rates of up to 0.27 cases per 100,000 persons.

**Management**

For moderate cutaneous *M. marinum* disease in pediatric patients, the following antibiotics can be considered: rifampin, trimethoprim-sulfamethoxazole, clarithromycin, or doxycycline. Extensive lesions may require surgical debridement. Susceptibility testing is not routinely required.

In one case series from France, adults with cutaneous infections were treated with a median duration of 4 months of antibiotics. Patients with cutaneous infection in this series mostly received monotherapy with clarithromycin or a cycline. Deeper structure infections were often treated with combination antibiotic therapy with regimens including clarithromycin, rifampin, and/or ethambutol. Of the 63 patients studied, 30 with cutaneous and/or deeper structure infections underwent surgery for excision and/or debridement.

Another retrospective case series from Duke University noted that boating or fishing exposure seemed to be associated with invasive disease, whereas fish tank exposure was associated with cutaneous disease. In this series, median time to diagnosis for invasive infection was 4 months. This delay in diagnosis indicates that the indolent nature of invasive *M. marinum* infection requires a high index of suspicion in those with aquatic exposure.

Of note, patients with a nontuberculous mycobacterium infection can have positive subsequent tuberculin test results because of shared antigens between *M. tuberculosis*-derived proteins and proteins from other nontuberculous species. Interferon-gamma release assays also may give positive results attributed to antigen cross-reactivity.

**Patient outcome**

The patient was treated with a 3-month course of trimethoprim-sulfamethoxazole, based on culture susceptibility testing. His lesions healed fully within 1 to 2 years.

__Dr Livaditis__ is a general pediatrician in Boston, Massachusetts. __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-1018](http://ContemporaryPediatrics.com/dermcase-1018)

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- Infant’s pustular eruption is not scabies

- Boy with red bumps all in a row
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THE CASE

A previously healthy 8-year-old boy presents to the dermatology clinic with a progressively worsening elbow rash over the course of the last week. The rash does not itch. He spent the previous weekend sailing on the Chesapeake Bay. His pediatrician prescribed a course of cephalexin as well as a trial of topical antiviral ointment, neither of which improved the rash. The patient denies any other new exposures.

A previously healthy 8-year-old boy presents with a progressively worsening elbow rash over the course of the last week. The rash does not itch. He spent the previous weekend sailing on the Chesapeake Bay. His pediatrician prescribed a course of cephalexin as well as a trial of topical antiviral ointment, neither of which improved the rash. The patient denies any other new exposures.

MYCOBACTERIUM MARINUM INFECTION

Discussion

*Mycobacterium marinum* is a slow-growing, nontuberculous photochromogen found in a variety of bodies of water.\(^1\) Also known as “swimming pool granuloma” or “fish tank granuloma,” cutaneous *M marinum* infections are most often reported among fish fanciers and those who participate in waterborne activities.\(^2\)

*Mycobacterium marinum* disease in humans is uncommon, with rates of up to 0.27 cases per 100,000 persons noted in the literature.\(^2\) Although cutaneous *M marinum* on the limbs is the most common form of the infection, invasive disease (tenosynovitis, arthritis, osteomyelitis) also can occur. The incubation period is usually within 4 weeks following trauma to the skin but can be up to 9 months.

Lesions resulting from cutaneous *M marinum* infection can present as nodules, ulcers, abscesses, and/or pustules (Figure).\(^1\)

For more on this case, turn to page 47.
Advice for new parents and their babies

By the time most of us become parents, we have been pediatricians for a while and do not find parenting all that scary. To get the right dose of empathy, think back to when we first started handling babies—in medical school. Here are some things I tell new parents.

1. **Some practices are clear cut, such as having babies sleep on their backs.** In many instances, however, such as swaddling or not, how often to bathe, and so on, there are many ways to raise a baby properly. (I don’t even know that burping is essential, let alone the “right” way to do it.) Most of the time, if something feels right to do, go for it.

2. **Newborns spend two-thirds of their time sleeping,** and the remaining third is divided between feeding, watchful wakefulness, and, yes, crying (2 to 3 hours per day)!

3. **All babies spit up,** have gas, give little body jerks when falling asleep, open 1 eye at a time, sneeze, and hiccup. These are normal.

4. **You can have visitors over, as long as they promise (and are trustworthy) that they are not ill and wash their hands very well.** However, if you prefer not to have visitors, tell them no and say it is doctor’s orders. I will back you up.

5. **The worst place to take a newborn is to work/church/crowded places.** People often go to work while ill, and they also feel, because they know you, that they should be allowed to hold the baby.

6. **I am a strong proponent of breastfeeding.** That having been said, if you cannot/will not breastfeed, formula and water supplies in this country are such that you should not feel guilty about this.

7. **For slightly older babies with colic,** I will give parents advice and help them to cope, but I tell them up front that nothing may work, and they may have to ride it out for a few months. They will remember the colic when older, but the baby will not.

8. **If you have a question,** you can go to a reliable source such as healthychildren.org or the app Pediatric SymptomMD. If you still do not have answers, call me. That’s why I’m here. (See “Top 10 apps for pediatrics,” Contemporary Pediatrics, February 1, 2017.)

9. **I have said this before in print,** but it is so important that I will say it again: I tell parents to talk and sing to their baby. If a parent comes home from work and the spouse is too tired to hear how the day went, tell your baby instead. They love to listen to language. Let the words wash over them.

10. **It is impossible to spoil a new baby.** If you create a bad habit, you can always break it when the child is older. If babies want to be held, hold them. If they want to be fed, feed them. They’re the boss.

**REFERENCE**

FLARES AREN'T GOING TO PREVENT THEMSELVES

BABY ECZEMA RELIEF BODY CREME helps prevent the incidence of flare over time with daily use¹

80% of children remained flare-free for six months¹
The September Asthma Epidemic: How To Prevent Fall Asthma Episodes
Myron Liebhaber MD | Andre Valcour, PhD, MBA, DABCC

Abstract
This review addresses three important factors that contribute to asthma exacerbations during the Fall season: Fall viral infections, Fall allergy exposures and failure to adhere to medically recommended use of preventative controller medications. We stress the importance of physician involvement in preventing exacerbations by identifying patients at risk, providing influenza vaccinations, doing targeted exposure reduction with quality allergy testing, and counseling the use of daily controller medications according to National Asthma Education and Prevention Program (NAEPP) guidelines (EPR-3).

Introduction
The risk of asthma exacerbations with frequent unscheduled visits to physician offices, urgent care and even hospitalizations increases during the back-to-school season. Allergic sensitization, exposure to allergic triggers and viral infections significantly increase the risk of asthma exacerbations and hospitalizations. Asthma does not go on summer vacation, but adherence to medications in the summer tends to decrease, placing children at increased risk for moderate to severe symptoms in the Fall (Figure 1).

Three primary factors that contribute to the risk of asthma symptom exacerbations in the Fall:
1. Contagious viruses such as human rhinoviral infections (HRV), enteroviruses and adenoviruses
2. Exposure to inhalant allergens such as to dust mites, cockroach, mold and pollen
3. Lack of adherence to prescribed pharmacotherapy (i.e., inhaled corticosteroids)

Increased exacerbation risk can be estimated by the use of a seasonal asthma exacerbation predictive index (saEPI). saEPI is calculated using numerous risk variables, including: age, allergic propensity (total IgE and allergen skin test positivity), percentage of blood eosinophils, exacerbation in the prior season, inhaled corticosteroids (ICS) as used in steps 2 to 4 in the EPR-3 guidelines, FEV1/forced vital capacity (FVC), and fractional exhaled nitric oxide (FeNO).

In the guideline-based treatment group, used in the development of the predictive index, the following were predictive of Fall exacerbations, with or without omalizumab treatment:
- Younger age
- High total IgE
- Higher blood eosinophil percentage
- Higher ICS usage, steps 2-4 as recommended by the guidelines

Pediatricians are in an ideal position to mitigate and prevent these exacerbations by identifying at-risk patients, ordering appropriate testing, and providing education and counseling to children and their families.
The following evaluations should be considered to help identify children with asthma who may be at an increased risk of symptom exacerbations:

1. Perform a history and physical exam. Look for a previous seasonal history of cough, congestion, wheezing, school absences and exercise intolerance.

2. Review past medical history of eczema, rhinitis and wheezing with infections or allergy exposures. Forty-three percent of children with eczema will develop asthma by school age.7

3. Consider pulmonary function testing for children 5 years of age or older; spirometry with FEV1 response to bronchodilator (the American Thoracic Society criterion for diagnosing asthma is 12% improvement after bronchodilator use).8 The use of FeNO to determine the presence of allergic airway TH2 inflammation and impulse oscillometry (IOS) to determine large vs. small airway obstruction should also be considered in children 2 years of age or older.

4. Administer the Asthma Control Test questionnaire for children as an ongoing assessment of asthma control.9

5. Order confirmatory allergen-specific IgE (sIgE) blood testing or skin prick testing to common aeroallergens. There is a high false-positive rate of allergy diagnosis based on patient opinion or history alone without allergy testing (in vitro diagnostic or skin test).10 There should be a correlation between allergy history and allergy test results in order to confirm the diagnosis. Evidence of sensitization to a particular allergen is not synonymous with clinically relevant disease.

Steps To Help Prevent Fall Symptom Episodes

The following have proven effective in modifying the synergistic risk of exposure to allergic triggers and viral infections. (Figure 2):

- Utilize convenient, patient-friendly sIgE testing to identify the patient’s allergic triggers,
- Provide flu shots
- Regularly monitor and ensure correct use of asthma medication(s)

Viral Exposure

Viruses commonly circulate in late Summer and early Fall near the start of school, and are detectable in approximately 80% of children who experience acute asthma exacerbations.7 The EPR-3 guidelines recommend that clinicians consider inactivated influenza vaccinations for patients with asthma. However, it is important to note the flu vaccine should not be given with the expectation it will reduce either the frequency or severity of asthma exacerbations during the influenza season due to the presence of other viruses. Once a child’s airway is sensitized by any of these viruses, subsequent wheezing may occur with other viral exposures. The guidelines state that flu vaccine is safe for children >6 months of age.5

Targeted Exposure Reduction to Allergic Symptom Triggers

Environmental control of allergic and non-allergic (i.e., tobacco smoke) triggers is a significant component of symptom management. As many as 90% of children have one or more allergic triggers11 and exposure to these triggers creates a source of chronic airway inflammation. Identification of a patient’s specific symptom triggers provides the information needed to manage exposure.

Guided by sIgE in vitro or skin prick test results, the goal is to decrease the targeted allergen exposure burden below an individual’s symptomatic threshold (Figure 3). For example, Morgan et al. showed reducing dust mite exposure in dust-mite sensitized children over a 2-year period significantly decreased the burden of asthma compared to no allergen avoidance. Outcomes included 3 weeks (21.3 days) per year with fewer symptoms, a month (34 days) each year with less wheezing, fewer missed school days, and unscheduled emergency department and office visits.12

Evidence supporting targeted exposure reduction is significant. Both the testing and implementation of targeted exposure reduction is Evidence Category A in the EPR-3 guidelines stating that “patients with persistent asthma should be evaluated for the role of allergens as possible contributing factors.”6 5
Indications for allergy testing include:
1. Patients of any age with a high asthma burden (i.e., presence of chronic lower respiratory symptoms)
2. Young children with recurrent wheeze
3. Anyone meeting the Rules of Two criteria while on daily controller or maintenance therapy:
   - >2 days per week of daytime asthma symptoms
   - >2 nights per month of nighttime asthma symptoms
   - >2 asthma exacerbations or attacks per year resulting in a burst of oral steroids or antibiotics
   - >2 rescue albuterol inhaler fills/refills per year not just to cover different sites like home/school/day care/office
4. Patients with a history suggestive of a specific IgE-mediated allergic disease diagnosis, which most commonly includes but is not limited to: respiratory diseases (e.g., asthma, allergic rhinitis), food allergy, skin diseases (e.g., eczema, urticaria), hymenoptera venom allergy, and drug allergy.  

Considerations for the Use of sIgE Testing
- Requires a single blood draw
- Is appropriate for children 3 months of age and older
- Is not affected by prescription or over-the-counter medications commonly used to treat asthma, including antihistamines of all types, sympathomimetic drugs and low doses of corticosteroids.  
- In patients experiencing chronic lower and/or upper respiratory symptoms, the order of a geographic-specific aeroallergen profile should be considered.
- The following regional respiratory profiles available from LabCorp have been created to efficiently assess sensitization to the most common triggers including pollens, mold, dust mites, furry animals and insect emanations (Table 1).

### Table 1. Regional Respiratory Allergen Profiles Available from LabCorp

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<td>602641</td>
<td>AZ mtns, CO, ID, mtns, MT, NM, UT mtns, WY</td>
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<tr>
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<td>603719</td>
<td>Southern AZ desert area, Southern CA desert area</td>
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<td>GA, North FL, SC</td>
<td>602643</td>
<td>Southern CA coastal area</td>
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<td>FL, South of Orlando</td>
<td>602644</td>
<td>Central CA</td>
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<td>IN, KY, OH, TN, WV</td>
<td>602638</td>
<td>NV, Southern ID</td>
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Lack of Adherence to Medications
Clinical experience has shown many children are taken off their asthma controller medications and do not comply with targeted exposure reduction during the summer months, as some families mistakenly assume “asthma takes a vacation during the summer.” While this may be partially true because there are fewer circulating respiratory viruses during the summer, it is clear that even in the absence of symptoms there is on-going allergic inflammation as evidenced by abnormal pulmonary function testing and elevated FeNO during asymptomatic periods. Use of therapy to control asthma may be at its lowest just before school starts, and parents may be waiting for the first Fall exacerbation to resume compliance. Unfortunately, this may often lead to an acute exacerbation from the synergistic effect of an acute viral infection and may result in an emergency room visit and/or hospital admission.

Allergen-specific IgE Testing in the Clinical Setting
Allergen sIgE tests can be used in an initial assessment of patients with a clinical history consistent with sensitization to food and/or inhalant allergens. Specific IgE tests should not be used as a first-line in the evaluation of patients suspected of having allergy to hymenoptera venom allergy (stinging insects) or specific drugs. The presence of sIgE indicates sensitization to the allergen(s) tested but is not necessarily synonymous with clinically relevant disease. Sensitization is a prerequisite for an IgE-mediated, allergic reaction and increases the likelihood of clinical allergy. Absence of sIgE diminishes the likelihood of an allergy to the allergen(s) tested. Contemporary sIgE testing can be easily accessed and is effective in diagnosing allergy with test performance comparable to skin prick testing. The clinical efficiency of sIgE testing is equivalent to standard skin prick testing (88.8 and 89.2, respectively) The major advantage of sIgE testing is in its ability to quantify allergen-specific IgE antibody levels and the lack of interference from allergen-specific IgG antibodies. The physician plays a critical role in the interpretation of sIgE test results within the context of the patient’s history and exposure to the relevant allergens. The results of sIgE testing are reported quantitatively in kU/L, with the probability of symptoms increasing as sIgE levels increase. The physician should rank the highest levels of sIgE and focus on reducing exposure to those antigens. Counseling and education can be used to reduce exposure to allergens to which the patient is sensitized. It has been shown that targeted exposure reduction is more effective when combined with allergy testing than with empiric management.
A Case Report

An 11-year old female patient was referred to the allergy clinic in the Spring of 2018 for recurrent episodes of cough, congestion and wheezing that had occurred during the Fall of 2017. There was no family history of allergies or asthma. On physical exam, she had coarse bronchial breath sounds with partial clearing after cough. The patient’s environmental exposure history indicated mold around her window seals with a moldy tree stump and mulch outside her bedroom window. The patient was diagnosed with suboptimal control of mild persistent asthma with recent exposure to mold, confirmed by elevated sIgE antibodies to Alternaria spores and recent viral infections.

Treatment Recommendations

Peak flow-guided asthma management as follows:

• Fluticasone 44, two puffs twice daily (for peak flows greater than 250 L/min)
• Albuterol sulfate quick reliever every 4 hours for acute relief (for peak flows 150-250 L/min) prednisone 20 mg for 5 days (if needed for peak flows less than 150L/min)
• Mold mitigation measures.

Follow-up later in the Summer of 2018

Asymptomatic with peak flows in the normal range.

Mold control completed with removal of the moldy tree stump underneath her bedroom window and installation of a HEPA air purifier in her bedroom.

Continued current medication regimen of fluticasone (intranasal corticosteroid) throughout the Fall.

Follow-Up Test Results

• Total IgE = 164 kU/L
• Respiratory aeroallergen test results reported elevated sIgE antibodies to Alternaria mold at 30.8 kU/L. The sIgE test results to the other aeroallergens were negative.
• Forced vital capacity (FVC) = 2.39L at 73% predicted
• Forced expiratory volume (FEV1) = 2.24L at 81% predicted (mild obstruction)
• Asthma Control Test score = 27, asthma under good control
• Chest x-ray = normal

Summary

Our review cites three important factors involved in asthma exacerbations during the Fall season: viral infections, allergic airway sensitization, and lack of adherence to controller therapy. The role of the pediatrician in preventing these asthma symptom exacerbations includes moderating the viral challenge through appropriate vaccinations, sIgE testing to facilitate targeted exposure reduction of specific allergens, and summertime surveillance with education to ensure on-going adherence to asthma medication regimens.

References

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